Alkynyl- and Dialkynyl-quinoxalines. Synthesis of Condensed Quinoxalines

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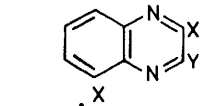
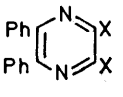
Condensation of 2-chloro- and 2,3-dichloro-quinoxalines with alk-1-ynes in the presence of bis(triphenylphosphine)palladium(II) dichloride and copper(I) iodide gives mono- and di-alkynylquinoxalines. Addition of amines to these products gives stable enamines; hydration gives 2′-oxoalkyl compounds which exist predominantly in the intramolecularly hydrogen-bonded enol form. Condensation of the alkynylquinoxalines with diethyl sodiomalonate, and related compounds, yields pyrido[1,2-*a*]quinoxalin-4-one derivatives. 2-Alkynyl-3-chloroquinoxalines are intermediates for convenient syntheses of pyrrolo[2,3-*b*]quinoxalines.

SONOGASHIRA and his collaborators [1] have reported a new synthesis of arylacetylenes by condensation of aryl *iodides* with alk-1-ynes in the presence of diethylamine,



	X	Y
(1) a	C:CPh	C:CPh
b	Cl	C:CPh
c	C:CCH$_2$OH	C:CPh
d	NEt$_2$	C:CPh
e	NEt$_2$	NEt$_2$
f	NHEt	C:CPh
g	NHEt	C:C[CH$_2$]$_2$OH
h	NHMe	C:CPh
i	NHMe	NHMe
j		



(2) a; X = Br
b; X = C:CPh

bis(triphenylphosphine)palladium(II) dichloride, and copper(I) iodide. 2-*Bromo*-pyridine similarly gave 2-phenylethynylpyridine on condensation with phenylacetylene, using the same catalysts in triethylamine–dimethyl sulphoxide, gave 2,3-bisphenylethynylquinoxaline (1a) as a crystalline product in 71% yield. Use of a smaller proportion of phenylacetylene furnished 2-chloro-3-phenylethynylquinoxaline (1b) in 80% yield. 2-Chloro- and 2-chloro-3-methyl-quinoxaline reacted similarly and prop-2-yn-1-ol, but-3-yn-1-ol, and pent-4-yn-1-ol were also used successfully in these condensations (Table 1). An unsymmetrical diyne (1c) was also obtained by reaction of 2-chloro-3-phenylethynylquinoxaline (1b) with prop-2-yn-1-ol. The analogous 2,3-dibromo-5,6-diphenylpyrazine (2a) was similarly converted into 2,3-diphenyl-5,6-bisphenylethynylpyrazine (2b).

When the condensation of 2,3-dichloroquinoxaline with phenylacetylene was carried out in the presence of diethylamine, displacement of halide ion by amine also occurred to give 2-diethylamino-3-phenylethynylquinoxaline (1d) (66%) but under these conditions prop-2-yn-1-ol gave only 2,3-bis(diethylamino)quinoxaline (1e). Similarly with ethylamine as base, phenylacetylene yielded 2-ethylamino-3-phenylethynylquinoxaline (1f) whereas prop-2-yn-1-ol gave 2,3-bis(ethylamino)quinoxaline. But-3-yn-1-ol was converted into 2-ethylamino-3-(4-hydroxybut-1-ynyl)quinoxaline (1g) (95%) when a mixture of ethylamine and triethylamine was used. Methylamine (with phenylacetylene) yielded a mixture

TABLE 1

Preparation of alkynylquinoxalines

Halide (1) X	Halide (1) Y	Amount (mmol)	Alkyne (RC:CH) R	(mmol)	Base	Product (1) X	Product (1) Y	Yield (%)	Found (%) C	H	N	Formula	Required (%) C	H	N	M.p. (°C)
Cl	Cl	10	Ph	20	Et$_3$N	C:CPh	C:CPh	71	86.9	4.2	8.8	$C_{24}H_{14}N_2$	87.3	4.3	8.5	128—130 *a*
Cl	Cl	20	Ph	20	Et$_3$N	Cl	C:CPh	80	72.8	3.5	10.4	$C_{16}H_9ClN_2$	72.6	3.4	10.6	90—91 *b*
Cl	Cl	5	HO·CH$_2$	15	Et$_3$N	Cl	C:CCH$_2$OH	63	60.6	3.3	12.7	$C_{11}H_7ClN_2O$	60.4	3.2	12.8	153—154 *c*
Cl	Cl	20	HO[CH$_2$]$_2$	28	Et$_3$N	Cl	C:C[CH$_2$]$_2$OH	76	61.9	3.9	12.0	$C_{12}H_9ClN_2O$	62.1	4.0	12.1	118—119 *a*
Cl	Cl	5	HO[CH$_2$]$_2$	15	Et$_3$N	C:C[CH$_2$]$_2$OH	C:C[CH$_2$]$_2$OH	66	71.9	5.3	10.6	$C_{16}H_{14}N_2O_2$	72.2	5.3	10.5	151—152 *c*
Cl	Cl	5	HO[CH$_2$]$_3$	7.5	Et$_3$N	Cl	C:C[CH$_2$]$_3$OH	72	63.3	4.5	11.9	$C_{13}H_{11}ClN_2O$	63.4	4.5	11.4	80—81 *a*
Cl	Cl	5	HO[CH$_2$]$_3$	20	Et$_3$N	C:C[CH$_2$]$_3$OH	C:C[CH$_2$]$_3$OH	56	73.7	6.3	9.5	$C_{18}H_{18}N_2O$	73.5	6.2	9.5	104—105 *a*
Cl	C:CPh	2.5	HO·CH$_2$	5	Et$_3$N	C:C·CH$_2$OH	C:CPh	67	80.4	4.1	9.7	$C_{19}H_{12}N_2O$	80.3	4.3	9.9	176—177 *b*
Cl	H	10	Ph	15	Et$_3$N	C:CPh	H	54	83.2	4.5	12.2	$C_{16}H_{10}N_2$	83.5	4.4	12.2	68—69 *b*
Cl	Me	10	Ph	12.5	Et$_3$N	C:CPh	Me	51	83.3	5.1	11.5	$C_{17}H_{12}N_2$	83.6	5.0	11.5	105—106 *b*
Cl	Me	5	HO[CH$_2$]$_2$	7.5	Et$_3$N	C:C[CH$_2$]$_2$OH	Me	78	73.6	5.9	13.1	$C_{13}H_{12}N_2O$	73.6	5.7	13.2	112—113 *c*
Cl	Cl	10	Ph	20	Et$_2$NH	NEt$_2$	C:CPh	66	79.9	6.5	13.6	$C_{20}H_{18}N_2$	79.7	6.4	13.9	87—89 *b*
Cl	Cl	10	Ph	20	EtNH$_2$ *d*	NHEt	C:CPh	57	79.4	5.5	15.6	$C_{18}H_{15}N_3$	79.1	5.5	15.4	81—82 *b*
Cl	Cl	5	HO[CH$_2$]$_2$	7.5	Et$_3$N + EtNH$_2$ *d*	NHEt	C:C[CH$_2$]$_2$OH	95	69.5	6.3	17.3	$C_{14}H_{15}N_3O$	69.7	6.3	17.4	101—102 *b*
Cl	Cl	6	Ph	9	MeNH$_2$ *e*	NHMe	C:CPh	54	78.7	5.1	16.0	$C_{17}H_{13}N_3$	787.	5.1	162	140—141 *f*

a From benzene–light petroleum (b.p. 60—80 °C). *b* From light petroleum (b.p. 80—100 °C). *c* From benzene. *d* Ethylamine (70% in water). *e* Methylamine (33%) in water). *f* Also isolated: 2,3-bis(methylamino)quinoxaline (13%), m.p. 175—176 °C, from benzene–light petroleum (b.p. 60—80 °C) (Found: C 63.9; H, 6.5; N, 29.6%; M^+, 188.1. $C_{10}H_{12}N_4$ requires C, 63.8; H, 6.4; N, 29.8%; *M*, 188.2).

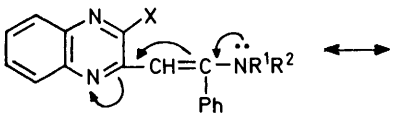
acetylene [1] and the process is of considerable potential value in heterocyclic syntheses.[2] In the present work its application to *chloro*-quinoxalines was examined.

Condensation of 2,3-dichloroquinoxaline with excess of

of mono- (1h) (54%) and di-amines (1i) (14%) whereas dimethylamine gave only the diamino-derivative.

A series of mono- (3; X = H or Me) and di-enamines (4) were prepared (see Table 2) as crystalline products by addition of amines to these acetylenic compounds. The enamines were very stable and unreactive, presumably owing to the electron-attracting effect of the diazine ring producing resonance between (3) and (3a). These enamines are formulated with the amino-group at C-2 of the side-chain, as would be expected from polarisation of an acetylene group conjugated with the diazine ring. The assignment was confirmed by the ^{1}H n.m.r. spectrum of the enamine (5a; R^1 = Me) which showed a singlet at δ 5.19 (1 H; 1′-CH) and two triplets at δ 2.65 and 3.92 (2 H; 3′- and 4′-CH_2). This evidence excludes the alternative structure (5b) in which the 2′-methine and 3′-methylene groups would be coupled.

Treatment of 2-phenylethynylquinoxaline with a large excess of aqueous dimethylamine yielded 2-(2-hydroxy-2-phenylvinyl)quinoxaline (6a) (74%). The i.r. spectrum of this product showed a very weak carbonyl peak at 1 690 cm^{-1} corresponding to the oxo-form, 2-phenacylquinoxaline (6b). A broad hydroxy-band ($\nu_{max.}$ 2 920 cm^{-1}) indicated that the intramolecularly hydrogen-bonded enol-form (6a) predominates.[3] This is consistent with the ^{1}H n.m.r. spectrum which includes peaks at δ 4.74 (1 H, s, OH) and 6.27 (1 H, s, 1′-H).



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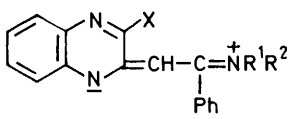
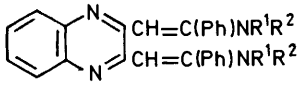


(3a)



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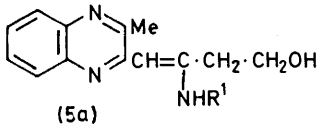
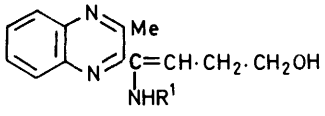
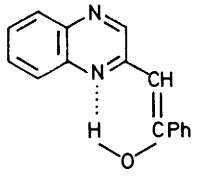


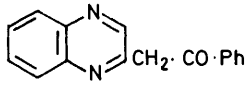
(5a)



(5b)



(6a)



(6b)

TABLE 2

Preparation of enamines (3), (4), and (5).

Quinoxaline (1) X	Y	Amine	Conditions	Enamine X	R^1	R^2	Found (%) C	H	N	Formula	Required (%) C	H	N	M.p. (°C)
H	C:CPh	Morpholine	Reflux/6 h	(3) H	$[CH_2]_2O[CH_2]_2$		75.6	6.2	13.3	$C_{20}H_{19}N_3O$	75.7	6.0	13.2	120—121 [a]
H	C:CPh	Piperidine	Reflux/6 h	(3) H	$[CH_2]_5$		80.0	7.1	13.4	$C_{21}H_{21}N_3$	80.0	6.7	13.3	133—135 [a]
H	C:CPh	$HN([CH_2]_2)_2NMe$	Reflux/4 h	(3) H	$[CH_2]_2NMe[CH_2]_2$		76.0	7.1	16.9	$C_{21}H_{22}N_4$	76.3	6.8	17.0	104—105 [b]
Me	C:CPh	Morpholine	Reflux/6 h	(3) Me	$[CH_2]_2O[CH_2]_2$		76.1	6.5	13.1	$C_{21}H_{21}N_3O$	76.1	6.4	12.7	156—157 [a]
Me	C:CPh	Piperidine	Reflux/7 h	(3) Me	$[CH_2]_5$		80.3	6.9	12.9	$C_{22}H_{23}N_3$	80.2	7.0	12.8	126—127 [a]
Me	C:CPh	$HN([CH_2]_2)_2NMe$	Reflux/10 h	(3) Me	$[CH_2]NMe[CH_2]_2$		76.4	7.1	16.0	$C_{22}H_{24}N_4$	76.7	7.0	16.3	130—132 [a]
C:CPh	C:CPh	$EtNH_2$ [e]	20 °C/11 days	(4)	H	Et	79.6	6.6	12.8	$C_{28}H_{28}N_4$	79.9	6.7	13.3	186—188 [d]
C:CPh	C:CPh	$MeNH_2$ [e]	20 °C/2.5 days	(4)	H	Me	79.5	6.0	14.4	$C_{26}H_{24}N_4$	79.6	6.2	14.3	186—187 [a]
C:CPh	C:CPh	$PhCH_2NH_2$	20 °C/10 days	(4)	H	CH_2Ph	83.9	5.8	10.2	$C_{38}H_{32}N_4$	83.8	5.9	10.3	194—195 [d]
C:CPh	C:CPh	Morpholine	Reflux/6 h	(4)	$[CH_2]_2O[CH_2]_2$		75.9	6.6	11.1	$C_{32}H_{32}N_4O_2$	76.2	6.3	11.1	213—215 [d]
C:CPh	C:CPh	Piperidine	Reflux/6 h	(4)	$[CH_2]_5$		81.4	7.4	11.0	$C_{34}H_{36}N_4$	81.6	7.3	11.2	153—155 [a]
C:CPh	C:CPh	$HN([CH_2]_2)_2NMe$	Reflux/6 h	(4)	$[CH_2]_2NMe[CH_2]_2$		76.8	7.3	15.5	$C_{34}H_{36}N_6$	76.9	7.2	15.8	155—157 [a]
NEt_2	C:CPh	Morpholine	Reflux/6 h	(3) NEt_2	$[CH_2]_2O[CH_2]_2$		74.3	7.0	14.6	$C_{24}H_{28}N_4O$	74.2	7.3	14.4	124—125 [a]
Me	C:CPh	$EtNH_2$ [c]	20 °C/28 h	(5a)	Et		69.9	7.2	16.2	$C_{15}H_{19}N_3O$	70.0	7.4	16.3	149—150 [b]
NHEt	C:CPh	$EtNH_2$	20 °C/48 h	(3) NHEt	H	Et	75.6	7.2	17.6	$C_{20}H_{22}N_4$	75.4	7.0	17.6	156—158 [a]

[a] Recryst. from light petroleum (b.p. 60—80 °C). [b] Recryst. from light petroleum (b.p. 60—80 °C)-benzene. [c] 70% in H_2O [d] Recryst. from ethanol. [e] 33% in H_2O. All these products were obtained as yellow crystals in almost quantitative yields; all showed $\nu_{max.}$ 1 580—1 595 cm^{-1}.

2-(2-Hydroxy-2-phenylvinyl)-3-methylquinoxaline was obtained similarly but the di-enol, 2,3-bis-(2-hydroxy-2-phenylvinyl)quinoxaline could only be isolated in very small yield. Attempts to obtain these enols by other acid- or base-catalysed hydration reactions were unsuccessful.

Several alternative reactions were encountered when

TABLE 3

1,2-Disubstituted-pyrrolo[2,3-*b*]quinoxalines(8) prepared by method A

Compound (8; R^3 = H) R^1	R^2	Yield (%)	Found (%) C	H	N	Formula	Required (%) C	H	N	M.p. (°C)
p-EtO·C_6H_4	Ph	86	78.9	5.3	11.7	$C_{24}H_{19}N_3O$	78.9	5.2	11.5	215—216 [a]
Ph	Ph	83	82.2	4.8	13.2	$C_{22}H_{15}N_3$	82.2	4.7	13.1	230—232 [b,c]
Me	CH_2OH	78	67.4	5.3	19.6	$C_{12}H_{11}N_3O$	67.6	5.2	19.7	180—181 [d]
Et	CH_2OH	97	68.8	5.4	18.6	$C_{13}H_{13}N_3O$	68.7	5.8	18.5	143—145 [a]
$[CH_2]_2OH$	CH_2OH	90	64.1	5.5	17.3	$C_{13}H_{13}N_3O_2$	64.2	5.4	17.3	174—175 [a]
p-EtO·C_6H_4	CH_2OH	76	71.6	5.4	12.9	$C_{19}H_{17}N_3O_2$	71.5	5.4	13.2	218—219 [d]
Me	$[CH_2]_2OH$	80	68.4	5.7	18.5	$C_{13}H_{13}N_3O$	68.7	5.8	18.5	173—174 [a]
Et	$[CH_2]_2OH$	73	69.3	6.2	17.6	$C_{14}H_{15}N_3O$	69.7	6.3	17.4	142—143 [d]
$[CH_2]_2OH$	$[CH_2]_2OH$	94	65.3	6.1	16.1	$C_{14}H_{15}N_3O_2$	65.4	5.9	16.3	195—196 [a]
Ph	$[CH_2]_2OH$	63	74.6	5.2	14.5	$C_{18}H_{15}N_3O$	74.7	5.2	14.5	173—174 [a]
p-EtO·C_6H_4	$[CH_2]_2OH$	72	71.9	5.7	12.6	$C_{20}H_{19}N_3O_2$	72.0	5.7	12.6	177—178 [a]
CH_2Ph	$[CH_2]_2OH$	90	74.0	5.7	13.9	$C_{19}H_{17}N_3O$	75.2	5.7	13.9	144—145 [b]
Me	$[CH_2]_3OH$	88	69.5	6.3	17.3	$C_{14}H_{15}N_3O$	69.7	6.3	17.4	151—152 [a]
Et	$[CH_2]_3OH$	95	70.8	6.8	16.9	$C_{15}H_{17}N_3O$	70.6	6.7	16.5	166—167 [d]
$[CH_2]_2OH$	$[CH_2]_3OH$	95	66.4	6.2	15.4	$C_{15}H_{17}N_3O_2$	66.4	6.3	15.5	189—190 [a]
p-EtO·C_6H_4	$[CH_2]_3OH$	97	72.2	6.0	12.0	$C_{21}H_{21}N_3O_2$	72.6	6.1	12.1	194—195 [a]

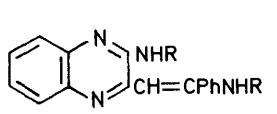
[a] From ethyl acetate. [b] From ethanol. [c] *cf.* Russian Pat. 539,884/1976; C. Iijima and E. Hayashi, *Yakugaku Zasshi*, 1977, **97**, 712. [d] From benzene.

2-chloro-3-phenylethynylquinoxaline (1b) was treated with amines. Thus piperidine, *N*-methylpiperazine, morpholine, and 2-hydroxyethylamine gave the corresponding diamines (1j), *etc.* This unexpected nucleophilic displacement of the phenylethynyl ion is attributed to the electron-withdrawing effect of the chlorine substituent, enhancing resonance effects in the diazine ring.

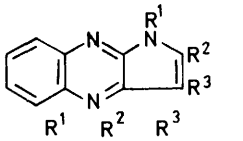
Such displacement of phenylethynyl ion was not observed when H, Me, or C:C·Ph groups were present in place of the 2-chloro-substituent. The less stable aliphatic acetylide ion was apparently not displaced from 2-chloro-3-hydroxyalkynylquinoxalines.

2-Chloro-3-phenylethynylquinoxaline (1b) reacted with dimethylamine to form 2-dimethylamino-3-phenylethynylquinoxaline while ethylamine and 2-hydroxyethylamine behaved similarly but with further addition of amine to the alkyne giving the enamines (7a) and (7b) respectively.

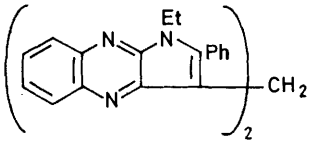
Action of primary aliphatic or aromatic amines on 2-chloro-3-alkynylquinoxalines generally gave the 1,2-disubstituted pyrrolo[2,3-*b*]quinoxalines (8) in good yields (Table 3) and this constitutes a convenient two-step synthesis of these compounds from 2,3-dichloroquinoxaline. 2-Ethylamino-3-phenylethynylquinoxaline (1f) was also readily cyclised to the pyrroloquinoxaline (8a) by various acidic or basic catalysts. Mercury(II) acetate in acetic acid effected this reaction and also cyclised 2-diethylamino-3-phenylethynylquinoxaline (1d) with loss of one ethyl group. In only one case did action of an amine (ethylamine) on 2,3-dichloroquinoxaline and alkyne in the presence of bis(triphenylphosphine)palladium(II) dichloride and copper(I) iodide lead to the pyrrolo-compound (8a) directly.



(7a) R = Et
(7b) R = $[CH_2]_2OH$



	R^1	R^2	R^3
(8a)	Et	Ph	H
(8b)	Et	Ph	CH_2OAc
(8c)	Et	Ph	CHO



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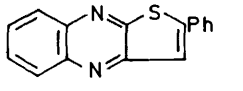


(10)

1-Ethyl-2-phenylpyrrolo[2,3-*b*]quinoxaline (8a) condensed with formaldehyde in the presence of acetic acid and dimethylamine to give 3-acetoxymethyl-1-ethyl-2-

TABLE 4

Pyrido[1,2-*a*]quinoxalines (11) and dipyrido[1,2-*a* : 2′,1′-*c*]quinoxalines (12)

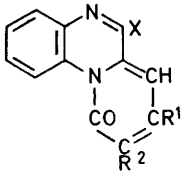
Quinoxaline (1) X	Y	Reactant	Product	X	R^1	R^2	Yield (%)	Found (%) C	H	N	Formula	Required (%) C	H	N	M.p. (°C)
Me	C:CPh	$CH_2(CO_2Et)_2$	(11)	Me	Ph	CO_2Et	41	73.3	5.2	7.8	$C_{22}H_{18}N_2O_4$	73.7	5.1	7.8	145—147 [a]
NHMe	C:CPh	$CH_2(CO_2Et)_2$	(11)	NHMe	Ph	CO_2Et	55	70.8	5.3	11.2	$C_{22}H_{19}N_3O_3$	70.8	5.1	11.3	159—160 [b]
NHEt	C:CPh	$CH_2(CO_2Et)_2$	(11)	NHEt	Ph	CO_2Et	82	71.5	5.6	10.7	$C_{23}H_{21}N_3O_3$	71.3	5.5	10.9	193—194 [a]
H	C:CPh	$AcCH_2CO_2Et$	(11)	H	Ph	H	51	79.4	4.6	10.4	$C_{18}H_{12}N_2O$	79.4	4.4	10.3	197—198 [c]
Me	C:CPh	$AcCH_2CO_2Et$	(11)	Me	Ph	H	41	79.8	5.2	9.8	$C_{19}H_{14}N_2O$	79.7	5.0	9.8	194—196 [a]
NHMe	C:CPh	$AcCH_2CO_2Et$	(11)	NHMe	Ph	H	23	75.6	4.7	14.0	$C_{19}H_{15}N_3O$	75.7	5.0	14.0	243—245 [b]
H	C:CPh	$NCCH_2CO_2Et$	(11)	H	Ph	CN	40	76.4	3.6	14.0	$C_{19}H_{11}N_3O$	76.7	3.7	14.1	210—212 [c]
Me	C:CPh	$NCCH_2CO_2Et$	(11)	Me	Ph	CN	36	77.3	4.4	13.7	$C_{20}H_{13}N_3O$	77.2	4.2	13.5	194—195 [c]
C:CPh	C:CPh	$CH_2(CO_2Et)_2$	(12)		Ph	CO_2Et	45	73.3	4.8	5.2	$C_{34}H_{26}N_2O_6$	73.1	4.7	5.0	263—265 [a]
C:CPh	C:CPh	$AcCH_2CO_2Et$	(12)		Ph	H	22	81.1	4.3	6.6	$C_{28}H_{18}N_2O_2$	81.1	4.4	6.8	314—316 [d]

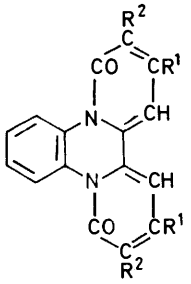
[a] From acetone. [b] From acetone–light petroleum (b.p. 60—80 °C). [c] From benzene–light petroleum (b.p. 80—100 °C). [d] From benzene–acetone.

phenylpyrrolo[2,3-*b*]quinoxaline (8b). Similar reaction using diethylamine, however, gave mainly bis-(1-ethyl-2-phenylpyrrolo[2,3-*b*]quinoxalin-3-yl)methane (9) with a little of the acetate (8b). Formylation of the 1-ethylpyrrolo-compound (8a) by the Vilsmeier–Haack method with phosphoryl chloride–dimethylformamide [4] yielded the aldehyde (8c).

Treatment of 2-chloro-3-phenylethynylquinoxaline with ethanolic sodium sulphide gave 2-phenylthieno-[2,3-*b*]quinoxaline (10).

Addition of carbanions to 2-alkynylquinoxalines provided a route to a series of pyrido[1,2-a]quinoxalines (11) (see Table 4). Thus diethyl sodiomalonate and 2-phenyl-





	X	R^1	R^2
(11a)	H	Ph	CO_2Et
(11b)	H	Ph	H

(12)

ethynylquinoxaline gave 9-ethoxycarbonyl-8-phenylpyrido[1,2-*a*]quinoxalin-10-one (11a) (30%). Addition of ethyl sodio-acetoacetate involved simultaneous ethanolysis of the acetyl group to give 8-phenylpyrido[1,2-*a*]-quinoxalin-10-one (11b) (41%). Analogous reactions with 2,3-diphenylethynylquinoxaline yielded the corresponding dipyrido[1,2-*a*:2′,1′-*c*]quinoxaline-1,8-diones (12) (Table 4).

EXPERIMENTAL

Evaporations were carried out below 35 °C using a rotary evaporator. I.r. spectra were recorded using a Perkin-Elmer 257 spectrometer and ^{1}H n.m.r. spectra with a Perkin-Elmer R32 (90 MHz) instrument.

Condensation of Chloroquinoxalines with Alkynes. General Procedure (cf. *Reference* 1).—Copper(I) iodide (10 mg) and bis(triphenylphosphine)palladium(II) dichloride (50 mg) were added to the chloroquinoxaline (1.0 g, 5 mmol) in dimethyl sulphoxide (15 ml) and amine (40 ml) in a slow stream of nitrogen. The mixture was stirred and, after 10 min, the alkyne (7.5 mmol) was added. Stirring was continued for 6 h and then the mixture was evaporated, treated with water, and extracted with benzene. The dried solution was concentrated to small volume, passed through a short column of silica gel to remove catalysts, and then evaporated to give the crude product for crystallisation (Table 1).

When 2,3-dichloroquinoxaline (10 mmol) was treated with prop-2-yn-1-ol (7.5 mmol) in diethylamine only 2,3-*bis*-(*diethylamino*)*quinoxaline* (1e) (71%) was obtained, m.p. 76—77 °C (from aqueous ethanol) (Found: C, 70.4; H, 8.7; N, 20.8. $C_{16}H_{24}N_4$ requires C, 70.5; H, 8.9; N, 20.6%). Ethylamine similarly gave 2,3-bis(ethylamino)-quinoxaline (76%), m.p. 157—158 °C (from aqueous ethanol) (lit.,[5] 157—159 °C). Similarly 2,3-dichloroquinoxaline with phenylacetylene in dimethylamine gave 2,3-*bis*(*dimethylamino*)*quinoxaline* (79%), m.p. 62—63 °C (from aqueous ethanol) (Found: C, 66.5; H, 7.3; N, 25.8%; M^+, 216.0. $C_{12}H_{16}N_4$ requires C, 66.6; H, 7.5; N, 25.9%; *M*, 216.2). Condensations with oct-1-yne, non-1-yn-3-ol, dec-9-yn-4-ol, ethyl prop-2-ynoate, and allyl alcohol were unsuccessful under these conditions.

2,3-*Bisphenylethynyl*-5,6-*diphenylpyrazine* (2b).—Condensation of 2,3-dibromo-5,6-diphenylpyrazine (2a) (1.25 mmol) with phenylacetylene (3.75 mmol) by the general procedure gave the *product* (2b) (74%), m.p. 173—175 °C [from benzene–light petroleum (b.p. 60—80 °C)] (Found: C, 88.8; H, 4.6; N, 6.4. $C_{32}H_{20}N_2$ requires C, 88.9; H, 4.7; N, 6.5%), $\nu_{max.}$ 2 205 cm^{-1} (C≡C).

2-[4-*Hydroxy*-2-*methylaminobut*-1-*enyl*]-3-*methylquinoxaline* (5a; R = Me).—2-(4-Hydroxybut-1-ynyl)-3-methylquinoxaline (70 mg) was added to methylamine (10 ml; 33%) in ethanol with stirring. After 24 h, the solution was evaporated and the residue crystallised from benzene–light petroleum (b.p. 60—80 °C) to give the *enamine* as yellow needles, m.p. 135—136 °C, in almost quantitative yield (Found: C, 68.8; H, 7.1; N, 17.4. $C_{14}H_{17}N_3O$ requires C, 69.1; H, 7.0; N, 17.3%), $\nu_{max.}$ 3 240 (OH) and 1 580 cm^{-1} (C=C), δ 2.45 (1 H, s, OH, exchanges with D_2O), 2.58 (3 H, s, Me), 2.68 (2 H, t, *J* 7 Hz, CH_2CH_2-OH), 3.06 (3 H, d, *J* 5 Hz, NH*Me*, collapsed to a singlet with D_2O), 3.92 (2 H, t, *J* 7 Hz, CH_2CH_2OH), 5.19 (1 H, s, CH), 7.33—7.98 (4 H, m, ArH), and 10.88 (1 H, br, s, NH, exchanges with D_2O). The other enamines are described in Table 2.

2-(2-*Hydroxy*-2-*phenylvinyl*)*quinoxaline* (2-*Phenacylquinoxaline*) (6a).—A mixture of 2-phenylethynylquinoxaline (0.2 g) and dimethylamine (25 ml; 60% in water) was stirred at room temperature for 24 h. Evaporation and crystallisation from light petroleum (b.p. 80—100 °C) yielded the *enol* (0.16 g, 74%), m.p. 145—146 °C (Found: C, 77.5; H, 5.0; N, 11.1%; M^+, 248.00. $C_{16}H_{12}N_2O$ requires C, 77.4; H, 4.9; N, 11.3%; *M*, 248.27); $\nu_{max.}$ (CCl_4) 2 920br (OH) and 1 690w cm^{-1} (C=O); δ 4.74 (1 H, s, OH) 6.27 (1 H, s, 1′-CH), 7.28—8.20 (9 H, m, ArH), and 8.46 (1 H, s, 3-CH).

Similarly prepared were 2-(2-hydroxy-2-phenylvinyl)-3-methylquinoxaline (48%), m.p. 119—120 °C (lit.,[6] 125.6—126.5 °C) (Found: C, 77.7; H, 5.4; N, 10.8. Calc. for $C_{17}H_{14}N_2O$: C, 77.8; H, 5.4; N, 10.7%); $\nu_{max.}$ (CCl_4) 2 920br (OH) and 1 690w cm^{-1} (C=O); δ 2.62 (3 H, s, CH_3), 4.74 (1 H, s, OH), 6.27 (1 H, s, CH), and 7.28—8.18 (9 H, m, ArH); and 2,3-bis-(2-hydroxy-2-phenylvinyl)quinoxaline (8%), m.p. 202—204 °C (lit.,[6] 204.5—205.2 °C) (Found: C, 79.8; H, 5.3; N, 8.0%; M^+, 366.16. Calc. for $C_{24}H_{18}N_2O_2$: C, 78.7; H, 5.0; N, 7.7%; *M*, 366.40).

Conversion of 2-*Chloro*-3-*phenethymylquinoxaline* (1b) *into* 2,3-*Dipiperidinoquinoxaline* (1i). The chloro-compound (200 mg) and piperidine (10 ml) were heated under reflux (bath, 110 °C) for 5 h. The cooled mixture was poured into sodium carbonate solution; isolation with ethyl acetate gave 2,3-dipiperidinoquinoxaline (1j) (189 mg), m.p. 140—141 °C (lit.,[7] 148 °C) (Found: C, 72.8; H, 8.2; N, 18.8. Calc. for $C_{18}H_{24}N_2$: C, 72.9; H, 8.2; N, 18.9%), δ 1.48—1.93 (12 H, m, 2 × $[CH_2]_3$), 3.26—3.66 (8 H, m 2 × CH_2NCH_2), and 7.26—7.80 (4 H, m, ArH). Similarly *N*-methylpiperazine gave 2,3-*bis*-(4-*methyl*-1-*piperazinyl*)*quinoxaline* (94%), m.p. 176—177 °C [from light petroleum (b.p. 60—80 °C)] (Found: 66.6; H, 8.2; N, 25.7%, M^+, 326.42. $C_{18}H_{26}N_6$ requires C,

66.2; H, 8.0; N, 25.8%; *M*, 326.44); morpholine gave 2,3-dimorpholinoquinoxaline (95%), m.p. 209—210 °C, [from benzene-light petroleum (b.p. 60—80 °C)] (lit.,[7] 225 °C) The same product, m.p. 210 °C, was obtained quantitatively from 2,3-dichloroquinoxaline and morpholine by the same procedure.

A solution of 2-chloro-3-phenylethynylquinoxaline (1b) (200 mg) and 2-hydroxyethylamine (0.5 ml) in benzene–ethanol (20 ml; 1 : 1 v/v) was boiled under reflux for 15 h. Isolation as before gave 2,3-bis-(2-hydroxyethylamino)-quinoxaline (74%), m.p. 175—177° [from acetone–light petroleum (b.p. 60—80 °C)] (lit.,[8] 181°).

2-Dimethylamino-3-phenylethynylquinoxaline.— 2-Chloro-3-phenylethynylquinoxaline (1b) (200 mg) and dimethylamine (20 ml; 60% in water) were heated under reflux for 4 h and the solution evaporated. The residue was dissolved in 2M-hydrochloric acid (15 ml), basified with 8M-sodium hydroxide solution (20 ml), and the product was isolated with chloroform. The *base* (120 mg; 58%) had m.p. 97—98 °C [from light petroleum (b.p. 60—80 °C)] (Found: C, 79.2; H, 5.3; N, 15.5. $C_{18}H_{15}N_3$ requires C, 79.1; H, 5.5; N, 15.4%); $\nu_{max.}$ 2 210 cm^{-1} (C≡C); δ 3.23 (6 H, s, NMe_2) and 7.24—7.98 (9 H, m, ArH).

2-(2-Hydroxyethylamino)-3-(2-hydroxyethylamino-2-phenylvinyl)quinoxaline(7b).— 2-Chloro-3-phenylethynylquinoxaline (1b) (200 mg) and 2-aminoethanol (10 ml) were stirred at room temperature until the solid dissolved (45 min). The solution was left at room temperature for 7 h and then poured into 2M-sodium carbonate solution. Isolation with ethyl acetate gave the *diamine* (7b) (320 mg; 91%), m.p. 164—165 °C (from ethyl acetate) (Found: C, 68.0; H, 6.5; N, 15.4. $C_{20}H_{22}N_4O_2$ requires C, 68.5; H, 6.3; N, 15.9%); $\nu_{max.}$ 3 360 (NH) and 1 600 cm^{-1} (C=C); δ 2.85 (3 H, br, s, 2 OH and NH, exchange with D_2O), 3.35 (2 H, t, *J* 7 Hz, C=C–NH–CH_2), 3.70 (6 H, t, *J* 7 Hz, 3 × CH_2), 5.25 (1 H, s, CH), 6.20 (1 H, br s, ArNH, exchanges with D_2O), and 7.10—7.72 (9 H, m, ArH).

1-Alkyl-2-substituted-pyrrolo[2,3-b]*quinoxalines* (8; R^3 = H) (*see Table* 3).—*Method A. From 2-chloro-3-alkynylquinoxalines and amines.* Methylamine (10 ml; 33% in ethanol) was stirred with 2-chloro-3-phenylethynylquinoxaline (1b) (200 mg) for 48 h. Addition of 1M-sodium carbonate solution and isolation with ethyl acetate gave *1-methyl-2-phenylpyrrolo*[2,3-b]*quinoxaline* (8; R^1 = Me, R^2 = Ph, R^3 = H) (0.15 g, 77%) as yellow crystals, m.p. 144—145.5 °C (Found: C, 78.2; H, 5.3; N, 16.1%; M^+, 259.04. $C_{17}H_{13}N_3$ requires C, 78.7; H, 5.1; N, 16.2%; *M*, 259.30), δ 3.92 (3 H, s, Me), 6.80 (1 H, s, 3-CH), and 7.43—8.26 (9 H, m, ArH). Aromatic amines (3 mol) and chloro-compound (1 mol) were refluxed in benzene–ethanol (1 : 1) until reaction was complete (t.l.c.) ($PhNH_2$, 0.5 h; *p*-EtO·$C_6H_4NH_2$, 16—22 h).

Method B. From 2-alkylamino-3-alkynylquinoxalines. 2-Ethylamino-3-phenylethynylquinoxaline (1f) (2 g) and mercury(II) acetate (0.5 g) in acetic acid (100 ml) were heated under reflux for 4 h. Evaporation, addition of water (150 ml), and isolation with ethyl acetate gave *1-ethyl-2-phenylpyrrolo*[2,3-b]*quinoxaline* (8a) (1.51 g; 83%) as yellow needles, m.p. 120—121 °C (from ethanol) (Found: C, 79.0; H, 5.5; N, 15.3%; M^+, 273.04. $C_{18}H_{15}N_3$ requires C, 79.1; H, 5.5; N, 15.4%; *M*, 273.32), δ 1.32 (3 H, t, *J* 7 Hz, CH_2CH_3), 4.48 (2 H, q, *J* 7 Hz, CH_2CH_3), 6.78 (1 H, s, 3-CH), and 7.44—8.26 (9 H, m, ArH). Cyclisation of the amino-alkynes was also effected using dimethylamine (60% in water, room temp., 72 h), or potassium hydroxide (0.5M in water–methanol, 1 : 2 v/v, refluxed for 3 h), or concentrated hydrochloric acid–acetic acid (1 : 8 v/v, refluxed 3 h).

2-Diethylamino-3-phenylethynylquinoxaline (1d) (250 mg), acetic acid (12.5 ml), sulphuric acid (0.1 ml), and mercury(II) acetate (63 mg) were heated under reflux for 4 h. Isolation as before gave the 1-ethyl compound (8a) (53%), identical with the previous sample. Action of dimethylamine (60% in water) for 14 d gave the same product.

Method C. From 2,3-dichloroquinoxaline. The dichloro-compound (10 mmol) was condensed with phenylacetylene (20 mmol) according to the general procedure with ethylamine (60 ml, 70% in water) and dimethyl sulphoxide (15 ml). Chromatography in benzene on silica gel yielded 1-ethyl-2-phenylpyrrolo[2,3-*b*]quinoxaline (8a) (56%), identical with the previous sample.

Condensation of 1-Ethyl-2-phenylpyrrolo[2,3-b]*quinoxaline* (8a) *with Formaldehyde.*—(*a*) The pyrrolo-compound (200 mg), formaldehyde (1.5 ml; 40% in water), dimethylamine (1 ml; 60% in water), and acetic acid (90 ml) were heated under reflux for 8 h. Evaporation, addition of water, and isolation with ethyl acetate gave *3-acetoxymethyl-1-ethyl-2-phenylpyrrolo*[2,3-b]*quinoxaline* (8b) (hemihydrate) (178 mg; 78%), yellow needles, m.p. 115—117 °C [from light petroleum (b.p. 60—80 °C)] (Found: C, 71.5; H, 5.3; N, 11.7. $C_{21}H_{19}N_3O_2$·0.5H_2O requires C, 71.2; H, 5.6; N, 11.9%); $\nu_{max.}$ 1 723 cm^{-1} (C=O); δ 1.30 (3 H, t, *J* 7 Hz, CH_2-CH_3), 2.04 (3 H, s, CH_2–O–COCH_3), 4.35 (2 H, q, *J* 7 Hz, CH_2CH_3), 5.33 (2 H, s, CH_2–O–$COCH_3$), and 7.43—8.38 (9 H, m, ArH).

(*b*) The pyrrolo-compound (270 mg), formaldehyde (1.5 ml; 40% in water), diethylamine (1 ml), and acetic acid (25 ml) were heated under reflux for 9 h. Isolation as in (*a*) and chromatography in ethyl acetate–light petroleum (b.p. 80—100 °C)–acetic acid (7 : 7 : 1 v/v/v) on silica yielded *bis-(1-ethyl-2-phenylpyrrolo*[2,3-b]*quinoxalin-3-yl)methane* (9) (168 mg, 30%) as yellow needles, m.p. 158—159 °C [from light petroleum (b.p. 60—80°)] (Found: C, 79.5; 5.6; N, 15.4. $C_{37}H_{30}N_6$ requires C, 79.5; H, 5.4; N, 15.0%), δ 1.17 (6 H, t, *J* 7 Hz, CH_2CH_3), 4.19 (4 H, q, *J* 7 Hz, CH_2CH_3), 4.58 (2 H, s, CH_2Ar_2), 7.18—8.19 (18 H, m, ArH). Further elution yielded the above acetoxy-compound (8b) (15%).

1-Ethyl-3-formyl-2-phenylpyrrolo[2,3-b]*quinoxaline* (8c) (cf. *ref.* 4).—Phosphoryl chloride (0.5 ml) was added dropwise to dimethylformamide (2.0 ml) with shaking at 10—20 °C. A solution of 2-chloro-3-phenylethynylquinoxaline (0.3 g) in benzene–dimethylformamide (15 ml; 2 : 1 v/v) was added with shaking at 20—30 °C. The mixture was kept at 30—35 °C for 1 h, then poured onto ice; sodium hydroxide (2.5 g) in water (30 ml) was added gradually until the mixture was at *ca.* pH 5 and the remainder was then added in one portion. The solution was boiled for 1 min and cooled; isolation with benzene yielded a gum which crystallised on trituration with ethanol. Recrystallisation from ethanol gave the *formyl compound* (8c), m.p. 158—160 °C (Found: C, 75.5; H, 5.3; N, 14.0. $C_{19}H_{15}N_3O$ requires C, 75.7; H, 5.0; N, 13.9%), $\nu_{max.}$ 1 627 cm^{-1} (C=O); δ 1.60 (3 H, t, *J* 7 Hz, CH_2CH_3), 4.49 (2 H, q, *J* 7 Hz, CH_2CH_3), 7.2—8.5 (9 H, m, ArH), and 8.51 (1 H, s, CHO).

2-Phenylthieno[2,3-b]*quinoxaline* (10).—2-Chloro-3-phenylethynylquinoxaline (1b) (264 mg) was added to a stirred suspension of sodium sulphide dihydrate (125 mg) in ethanol (50 ml) and the mixture was stirred at room temperature for 72 h. Evaporation to small volume, addition of water, and isolation with ethyl acetate gave the *thieno-compound* (10) (34%), m.p. 178—179 °C (from ethanol)

(Found: C, 73.1; H, 3.8; N, 11.0. $C_{16}H_{10}N_2S$ requires C, 73.2; H, 3.8; N, 10.7%); δ 6.80 (1 H, s, 3-H) and 7.36—8.35 (9 H, m, ArH).

9-*Ethoxycarbonyl*-8-*phenylpyrido*[1,2-a]*quinoxalin*-10-*one* (11a).—2-Phenylethynylquinoxaline (0.23 g; 1 mmol) and diethyl malonate (0.24 g; 1.5 mmol) were added to a cooled solution of sodium ethoxide [from sodium (0.034 g) and ethanol (10 ml)]. The solution was slowly heated to 100 °C (oil-bath), kept under reflux for 1 h, cooled, and poured into water. Isolation with benzene yielded the *product* (11a) (0.16 g; 30%) as yellow needles, m.p. 146—148 °C [from benzene–light petroleum (b.p. 60—80 °C)] (Found: C, 73.0; H, 4.7; N, 8.2. $C_{21}H_{16}N_2O_3$ requires C, 73.2; H, 4.7; N, 8.1%); $\nu_{max.}$ 1 720 (CO_2Et) and 1 655 cm^{-1} (pyridone C=O); δ 1.10 (3 H, t, *J* 7 Hz, CH_2CH_3), 4.24 (2 H, q, *J* 7 Hz, CH_2CH_3), 6.82 (1 H, s, 1-H), 7.28—8.05 (9 H, m, ArH), and 8.60 (1 H, s, 10-H). Other pyrido- and dipyridoquinoxalines (Table 4) were prepared similarly.

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