New route to 4-alkoxyquinazoline-2-carbonitriles

Thierry Besson† [a] and Charles W. Rees [b]

[a] *Laboratoire de Génie Protéique et Cellulaire, Groupe de Chimie Organique, Pôle Sciences et Technologies, Université de La Rochelle, Avenue Marillac, F-17042 La Rochelle cedex 1, France*

[b] *Department of Chemistry, Imperial College of Science, Technology and Medicine, London SW7 2AY, UK*

A new, direct synthesis is described for the relatively rare but synthetically very versatile quinazoline-2-carbonitriles from anthranilonitriles and 4,5-dichloro-1,2,3-dithiazolium chloride 1. Treatment of iminodithiazole 6, from 4,5-dimethoxyanthranilonitrile and the salt 1, with alcohols and a base gives 4-alkoxyquinazoline-2-carbonitriles 8 in good yield. Treatment of the parent iminodithiazole 2 (R = H; X = CN) with alcohols and sodium hydride gives the analogous quinazolines 12 in lower yield, though these yields are much improved and the reaction times reduced under microwave irradiation. Alternatively the imine 6 can be converted into the more reactive cyanothioformamide 7 which on brief heating in alcohols gives the same quinazolines 8 in high yield.

We have shown that anthranilic acid and its 5-chloro and 4,5-dimethoxy derivatives condense readily with 4,5-dichloro-1,2,3-dithiazolium chloride **1** in dichloromethane at room temperature to give, after addition of pyridine, the iminodithiazoles **2**,[1] as previously described for aromatic amines generally.[2-4] However, on treatment with triphenylphosphine (2 equiv.) the imines **2** derived from these anthranilic acids did not give the *N*-arylcyanothioformamides **3** as did those from other anilines, but rather 2-cyano-3,1-benzothiazin-4-ones **4** quantitatively. When heated in boiling toluene the same imines **2** gave benzoxazin-4-ones **5** in virtually quantitative yields.[1] This latter transformation requires the loss of both sulfur atoms from **2** and we assumed that singlet diatomic sulfur (S_2) may be formed.

There is still a demand for a convenient precursor which would generate S_2 under mild conditions.[5] During attempts to maximise the generation of S_2, we found that the behaviour of the iminodithiazole **6** obtained from 2-amino-4,5-dimethoxybenzonitrile (4,5-dimethoxyanthranilonitrile) was different from all the other *N*-arylimines **2** investigated. With triphenylphosphine (2 equiv.) in moist dichloromethane at room temperature imine **6** gave the cyanothioformamide **7** which separated from the reaction mixture, but was not very stable. Attempted recrystallisation of this product from ethanol was accompanied by the characteristic odour of hydrogen sulfide and afforded a blue (UV) fluorescent product purified by chromatography and characterised as 4-ethoxy-6,7-dimethoxyquinazoline-2-carbonitrile **8** (R = Et).

† E-mail:tbesson@bio.univ-lr.fr

Table 1 Synthesis of quinazolines **8** from cyanothioformamide **7**

R	Reaction conditions	Yield (%)
Me	Methanol, reflux, 4 h	76
Et	Ethanol, reflux, 4 h	76
Pr^i	Propan-2-ol, reflux, 2 h	87
Bu	Butanol, reflux, 45 min	97
SEt (for OR)	Ethanethiol,[a] 30 °C, 12 h	24

[a] No reaction was detected on treatment of **7** with EtSH (1 or 10 equiv.) in the aprotic solvent toluene at reflux.

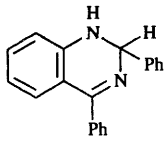
Analogous quinazolines were easily obtained by heating the cyanothioformamide **7** in other alcohols [methanol, propan-2-ol, butanol and a thiol (ethanethiol)] (Table 1).

This transformation presumably involves addition of the alcohol or thiol to the cyano group, with accompanying cyclisation and aromatisation (*cf.* Scheme 1).

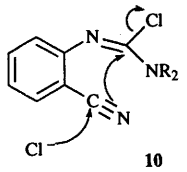
Scheme 1

A few analogous cyclisation processes involving derivatives of anthranilonitrile have been reported. Thus 2-acetamidobenzonitrile and boiling methanolic sodium methoxide gave

4-methoxy-2-methylquinazoline;[6] phenylmagnesium bromide added to the cyano group of the benzylidene derivative of anthranilonitrile in THF to give the cyclised product **9** which was oxidised to 2,4-diphenylquinazoline;[7] and anthranilonitrile reacted with phosgeniminium salts to give 2-dialkylamino-4-chloroquinazolines *via* **10**.[8] As far as we are aware, the last



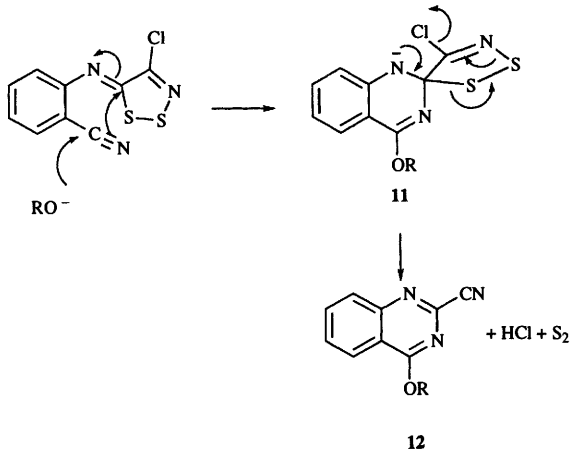
9



10

reaction and ours (Scheme 1) are the only cyclisations that result in functional groups on the quinazoline 2-position.

Although the *N*-arylimino-1,2,3-dithiazole **6** was considerably more stable than the derived cyanothioformamide **7**, it seemed possible that this too might react with alcohols to give the same quinazolines **8**, and this proved to be so. Long heating of **6** in the alcohols at reflux (5 days) did give the corresponding quinazolines **8** in low to modest yields (Table 2). The yields were increased when the alcohol was first treated with one equivalent of a base (NaH or KF), sodium hydride generally being the better (Table 2). Thus a reasonable mechanism (*cf.* Scheme 2)



Scheme 2

would appear to be addition of the alkoxide ion to the cyano group and cyclisation to give the spiro intermediate, **11**, or its *N*-protonated form, which could rapidly fragment to give the aromatic quinazoline-2-carbonitrile, together with disulfur and hydrogen chloride.

Somewhat surprisingly, under the conditions described above, only low yields of the quinazolines **12** were obtained from *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)anthranilonitrile (**2**, X = CN; R = H) which was made from anthranilonitrile and the dithiazolium chloride **1**. However the yield of these products was much improved, in a shorter reaction time, by microwave irradiation of the reaction mixture. Although the yield of compound **12** (R = Me) was still relatively low (41%), microwave activation provided the only way to obtain this quinazoline in the one step procedure. The rate of formation of the 4-ethoxy compound **8** (R = Et) was similarly increased by microwave irradiation (Table 2). These results are in accord with many recent reports of faster and cleaner synthetic reactions on microwave irradiation, compared to conventional heating.[9]

Quinazoline-2-carbonitriles are surprisingly rare, though the cyano group is reactive and can be converted into corresponding amides, esters, amidines and ketones by standard methods, and can be displaced by nucleophiles such as methoxide and ethoxide ions.[10] 4-Alkoxyquinazoline-2-carbonitriles have been made by a Reissert type reaction by treatment of the 4-alkoxyquinazoline 1-oxide with potassium cyanide and benzoyl chloride.[11] However the new method reported here, which is the first where the cyano group is produced during the cyclisation process, compares very favourably with the Reissert reaction in availability of the starting materials and ease of variation of the 4-substituent. Presumably our method should extend to the addition of nucleophiles other than alkoxide to the cyano group of the starting material, and this aspect is now under investigation.

Experimental

Mps were determined using a Kofler hot-stage apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer Paragon 1000PC instrument. UV spectra were recorded on a Lambda 16 Perkin-Elmer UV–VIS spectrometer. NMR spectra were recorded on Bruker AM300WB (^{1}H NMR) and Avance DPX250 (^{1}H and ^{13}C NMR) spectrometers (ICOA, Orléans, France). Coupling constants *J* are given in Hz. Mass spectra refer to the isotopomer with the most abundant isotopes (^{35}Cl and ^{32}S). Focused microwave irradiations were carried out with a Synthewave S402 Prolabo microwave reactor (monomode system) which has a quartz reactor, variable speed rotation, visual control, irradiation monitored by PC computer, infrared measurement and continuous feedback temperature control (by PC). Column chromatography was on silica gel (C60). Light petroleum refers to the fraction bp 40–60 °C.

N-(4-Chloro-5*H*-1,2,3-dithiazol-5-ylidene)anthranilonitrile 2 (X = CN; R = H)

Following procedures previously described,[1-4] treatment of anthranilonitrile (1.118 g, 1 mmol) with dithiazolium salt **1** (0.208 g, 1 mmol) then addition of pyridine (0.18 ml, 2 mmol) followed by column chromatography (light petroleum–diethyl ether, 6:4) gave the *title compound* (0.196 g, 78%) as orange needles, mp 128 °C (from light petroleum–dichloromethane) (Found: C, 42.6; H, 1.3; N, 16.5. $C_9H_4ClN_3S_2$ requires C, 42.6; H, 1.6; N, 16.55%); ν_{max}(KBr)/cm^{-1} 2232 (CN), 1589, 1568, 1478, 1423, 1266; δ_H(300 MHz, $CDCl_3$) 7.29–7.35 (2H, m), 7.66–7.78 (2H, m); *m/z* 253 (M^+, 53%), 192 (M^+ − CN − Cl, 59), 160 (M^+ − CN − Cl − S, 25), 128 (M^+ − CN − Cl − S_2, 8).

N-(4-Chloro-5*H*-1,2,3-dithiazol-5-ylidene)-4,5-dimethoxyanthranilonitrile 6. Prepared following the earlier procedure:[1] δ_C(250 MHz, $CDCl_3$) 56.84 (2C), 94.44, 101.26, 114.97, 117.18, 147.54, 148.49, 148.75, 154.25, 161.32.

N-(Cyanothioformyl)-4,5-dimethoxyanthranilonitrile 7. Prepared following the earlier procedure:[1] *m/z* 247 (M^+, 4%), 220 (M^+ − CN − H, 100), 205 (M^+ − CN − H − CH_3, 49), 177 (M^+ − CSCN, 20), 162 (M^+ − CSCN − CH_3, 7), 147 (M^+ − CSCN − 2 CH, 5).

4-Substituted quinazoline-2-carbonitriles: general procedures

(a) From imines 2. *Conventional heating*: a stirred mixture of *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)anthranilonitrile **2** or **6** (1 mmol) and sodium hydride (NaH, 1 mmol) in the appropriate alcohol (5 ml) was heated at reflux for 40 h. The hot solution obtained was filtered, the solvent evaporated from the filtrate and the residue purified by column chromatography. *Microwave experiments*: The reaction mixture was placed in a microwave oven (Synthewave S402) in an open vessel. The irradiation was programmed for 2 h with an initial delay of 10–15 seconds before attaining reflux. The product was purified as described above (see Table 2).

(b) From cyanothioformamides 3. As previously described,[1] compound **2** was stirred with triphenylphosphine (2 equiv.) at room temperature in moist dichloromethane for 2 h. The orange solution obtained was filtered and the precipitate washed with

Table 2 Preparation of quinazolines **8** and **12** from imines **6** and **2** (R = H, X = CN) respectively

Product	R	Reaction conditions	Yield (%)
		No irradiation	
8	Me	Methanol, reflux, 5 days[a]	0
8	Me	Methanol, NaH (1.1 equiv.), reflux, 40 h[b]	77
8	Me	Methanol, KF 10%, reflux, 40 h	40
8	Et	Ethanol, reflux, 5 days[c]	37
8	Et	Ethanol, NaH (1.1 equiv.), reflux, 40 h	77
8	Et	Ethanol, KF 10%, reflux, 40 h	74
8	Bu	Butanol, reflux, 5 days	60
8	Bu	Butanol, NaH (1.1 equiv.), reflux, 40 h[d]	82
8	Bu	Butanol, KF 10%, reflux, 40 h	72
8	Pr^i	Propan-2-ol, NaH (1.1 equiv.), reflux, 40 h	63
12	Et	i, PPh_3, CH_2Cl_2, room temp., ii, ethanol, reflux, 12 h	30
12	Et	Ethanol, NaH (1.1 equiv.), reflux, 40 h	29
12	Et	Ethanol, KF 10%, reflux, 40 h	12
		Microwave irradiation	
8	Et	Ethanol, NaH (1.1 equiv.), reflux, 2 h[e,f]	80
12	Me	Methanol, NaH (1.1 equiv.), reflux, 2 h	41
12	Et	Ethanol, NaH (1.1 equiv.), reflux, 2 h	80

[a] Also no reaction after 5 days of heating in the presence of a catalytic amount of $HgCl_2$. [b] Similar results were obtained with commercially available or previously prepared sodium methoxide. Commercial potassium *tert*-butoxide gave a complex reaction. [c] When 1.1 equiv. of dry KF was added, the yield was 30% and the reaction was more complex. [d] No reaction was detected with 10 equiv. of butanol in toluene at reflux. [e] Incomplete reaction after 1 h (yield 50%). [f] Incomplete reaction without NaH after 5 h of irradiation.

dichloromethane to afford product **3** of good enough quality to be used for the next step without further purification. An emulsion of this compound in the alcohol was heated at reflux and after evaporation of solvent the product was purified by column chromatography with light petroleum–dichloromethane as the eluent (for reaction times and yields see Table 2).

4,6,7-Trimethoxyquinazoline-2-carbonitrile 8 (R = Me)
Treatment of *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-4,5-dimethoxyanthranilonitrile **6** (0.313 g, 1 mmol) with sodium hydride (NaH, 0.024 g, 1 mmol) in methanol (10 ml) followed by column chromatography (light petroleum–dichloromethane, 1:9) gave the *title compound* (0.190 g, 77%) as colourless needles, mp 238 °C (from methanol) (Found: M^+, 245.0800. $C_{12}H_{11}N_3O_3$ requires *M*, 245.0800); ν_{max}(KBr)/cm^{-1} 3011, 2987, 2942, 2238 (CN), 1611, 1578, 1559, 1513, 1482, 1432, 1420, 1377, 1315, 1267, 1252, 1224, 1214, 1183, 1168, 1106, 1022; λ_{max}(EtOH)/nm (log ε) 327 (4.63), 313 (4.70); δ_H(300 MHz, $CDCl_3$) 4.04 (6 H, s, 6-, 7-OMe), 4.20 (3 H, s, 4-OMe), 7.31 (1 H, s), 7.39 (1 H, s); δ_C(250 MHz, $CDCl_3$) 14.79, 56.91 (2 C), 64.54, 101.64, 107.53, 112.21, 117.07, 148.45, 152.12, 156.56, 165.87; *m/z* 245 (100%), 230 (27), 216 (31), 202 (11), 188 (4), 174 (6), 163 (4), 145 (6), 131 (4).

4-Ethoxy-6,7-dimethoxyquinazoline-2-carbonitrile 8 (R = Et)
Microwave irradiation. Treatment of *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-4,5-dimethoxyanthranilonitrile **6** (0.313 g, 1 mmol) with sodium hydride (NaH, 0.024 g, 1 mmol) in ethanol (10 ml) followed by column chromatography (dichloromethane) gave the *title compound* (0.208 g, 80%) as pale yellow needles, mp 228 °C (from ethanol) (Found: M^+, 259.0949. $C_{13}H_{13}N_3O_3$ requires *M*, 259.0956); ν_{max}(KBr)/cm^{-1} 3024, 2996, 2940, 2236 (CN), 1608, 1577, 1570, 1560, 1507, 1483, 1474, 1458, 1430, 1400, 1380, 1307, 1268, 1250, 1225, 1213, 1169, 1151, 1107, 1022; λ_{max}(EtOH)/nm (log ε) 327 (4.37), 313 (4.46); δ_H(300 MHz, $CDCl_3$) 1.54 (3 H, m, CH_3CH_2O), 4.03 (3 H, s, OMe), 4.06 (3 H, s, OMe), 4.64 (2 H, q, *J* 7.36, CH_3CH_2O), 7.31 (1 H, s), 7.38 (1 H, s); δ_C(250 MHz, $CDCl_3$) 14.81, 56.91, 56.97, 64.56, 101.63, 107.52, 112.21, 117.08, 138.64, 148.43, 152.10, 156.54, 165.86; *m/z* 259 (M^+, 87%), 244 (84), 231 (100), 216 (42), 202 (8), 188 (26), 173 (6), 163 (11), 145 (23), 131 (3).

4-Isopropoxy-6,7-dimethoxyquinazoline-2-carbonitrile 8 (R = Pr^i)
Treatment of *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-4,5-dimethoxyanthranilonitrile **6** (0.313 g, 1 mmol) with sodium hydride (NaH, 0.024 g, 1 mmol) in propan-2-ol (10 ml) followed by column chromatography (dichloromethane) gave the *title compound* (0.172 g, 63%) as colourless needles, mp 206 °C (from propan-2-ol); ν_{max}(KBr)/cm^{-1} 3022, 2985, 2237 (CN), 1611, 1579, 1514, 1472, 1424, 1387, 1372, 1334, 1304, 1272, 1247, 1224, 1209, 1169, 1144, 1113, 1023; δ_H(300 MHz, $CDCl_3$) 1.49 (6 H, 2 × d, *J* 6, 2 × CH_3), 4.03 (3 H, s, OMe), 4.06 (3 H, s, OMe), 5.61 [1 H, m, $CH(CH_3)_2$], 7.29 (1 H, s), 7.35 (1 H, s); *m/z* 273 (M^+, 87%), 231 (100), 216 (21), 204 (5), 188 (8), 173 (2), 160 (2), 145 (9).

4-Butoxy-6,7-dimethoxyquinazoline-2-carbonitrile 8 (R = Bu)
Treatment of *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)-4,5-dimethoxyanthranilonitrile **6** (0.313 g, 1 mmol) with sodium hydride (NaH, 0.024 g, 1 mmol) in butanol (10 ml) followed by column chromatography (dichloromethane) gave the *title compound* (0.235 g, 82%) as colourless needles, mp 174 °C (from butanol) (Found: M^+, 287.1270. $C_{15}H_{17}N_3O_3$ requires *M*, 287.1269); ν_{max}(KBr)/cm^{-1} 3009, 2961, 2874, 2238 (CN), 1609, 1578, 1505, 1481, 1430, 1401, 1362, 1352, 1307, 1268, 1250, 1222, 1208, 1169, 1149, 1111, 1059, 1020; λ_{max}(EtOH)/nm (log ε) 327 (4.65), 313 (4.74); δ_H(300 MHz, $CDCl_3$) 1.03 (3 H, t, *J* 7.36, $CH_3CH_2CH_2CH_2O$), 1.54 (2 H, sextet, *J* 7.35, CH_3CH_2-CH_2CH_2O), 1.89 (2 H, m, $CH_3CH_2CH_2CH_2O$), 4.04 (3 H, s, OMe), 4.06 (3 H, s, OMe), 4.51 (2 H, t, *J* 7.38, $CH_3CH_2CH_2$-CH_2O), 7.30 (1 H, s), 7.37 (1 H, s); δ_C(250 MHz, $CDCl_3$) 14.28, 19.67, 31.14, 56.87, 56.96, 68.44, 101.57, 107.55, 112.24, 117.07, 138.68, 148.45, 152.13, 156.56, 166.01; *m/z* 287 (M^+, 14%), 258 (2), 244 (6), 231 (100), 216 (17), 204 (6), 188 (6), 173 (2), 161 (2), 145 (6).

4-Ethylthio-6,7-dimethoxyquinazoline-2-carbonitrile 8 (SEt for OR)
From cyanothioformamide **7**. Heating of a mixture of cyanothioformamide **7** (0.247 g, 1 mmol) and ethanethiol (5 ml) at 30 °C for 12 h followed by column chromatography (light petroleum–dichloromethane, 85:15) gave the *title compound* (0.066 g, 24%) as yellow needles, mp 194 °C (from light petroleum–dichloromethane); ν_{max}(KBr)/cm^{-1} 2977, 2929, 2874, 2853, 2241 (CN), 1610, 1560, 1501, 1459, 1415, 1355, 1307, 1268, 1244, 1210, 1160, 1016; δ_H(300 MHz, $CDCl_3$) 1.41 (3 H, t, *J* 7.00, CH_3CH_2S), 3.47 (2 H, q, *J* 7.00, CH_3CH_2S), 4.04 (3 H, s, OMe), 4.06 (3 H, s, OMe), 7.21 (1 H, s), 7.29 (1 H, s); *m/z* 275 (M^+, 100%), 260 (41), 247 (71), 242 (86), 229 (21), 215

(24), 200 (10), 188 (14), 162 (30), 149 (15), 145 (6), 134 (5), 132 (5).

4-Methoxyquinazoline-2-carbonitrile 12 (R = Me)

Microwave irradiation. Treatment of *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)*anthra*nilonitrile **2** (X = CN; R = H) (0.1 g, 0.4 mmol) with sodium hydride (NaH, 0.011 g, 0.44 mmol) in methanol (5 ml), at reflux for 2 h, followed by column chromatography (hexanes–ethyl acetate, 1:1) gave the title compound (0.03 g, 41%) as colourless needles, mp 130 °C (lit.,[11] mp 131–133 °C); ν_{max}(KBr)/cm^{-1} 3056, 2954, 2929, 2230 (CN), 1723, 1657, 1594, 1573, 1484, 1447, 1301, 1266, 1235, 1179, 1162, 1103, 1073; δ_H(300 MHz, $CDCl_3$) 4.10 (3 H, s, OCH_3), 7.11 (1 H, d, *J* 8.00), 7.32 (1 H, dt, *J* 0.90, 7.60), 7.58–7.77 (2 H, m).

4-Ethoxyquinazoline-2-carbonitrile 12 (R = Et)

Microwave irradiation. Treatment of *N*-(4-chloro-5*H*-1,2,3-dithiazol-5-ylidene)anthranilonitrile **2** (X = CN; R = H) (0.253 g, 1 mmol) with sodium hydride (NaH, 0.024 g, 1 mmol) in ethanol (10 ml), at reflux for 2 h, followed by column chromatography (light petroleum–dichloromethane, 9:1) gave the title compound (0.160 g, 80%) as colourless needles, mp 140 °C (lit.,[11] mp 143 °C) (from light petroleum–dichloromethane, 9:1) (Found: M^+, 199.0740. $C_{11}H_9N_3O$ requires *M*, 199.0745); ν_{max}(KBr)/cm^{-1} 2994, 2925, 2853, 2245 (CN), 1610, 1570, 1550, 1499, 1429, 1387, 1345, 1218, 1169, 1141, 1120, 1012; δ_H(300 MHz, $CDCl_3$) 1.54 (3 H, t, *J* 7.10, CH_3), 4.70 (2 H, q, *J* 7.10, CH_2CH_3), 7.71 (1 H, t, *J* 7.60), 7.93 (1 H, t, *J* 7.60), 8.01 (1 H, t, *J* 8.23), 8.23 (1 H, t, *J* 8.23); δ_C(250 MHz, $CDCl_3$) 14.63, 64.98, 116.77, 117.51, 124.24, 128.74, 130.02, 135.16, 140.32, 150.96, 167.74; *m/z* 199 (M^+, 30%), 184 (15), 171 (100), 155 (40), 143 (28), 116 (12), 103 (36), 90 (27).

Acknowledgements

We thank the *Comité de Charente-Maritime de la Ligue Nationale Contre le Cancer* and MDL Information Systems (UK) Ltd for financial support, the Wolfson Foundation for establishing the Wolfson Centre for Organic Chemistry in Medical Science at Imperial College, Professor G. Guillaumet (ICOA, Université d'Orléans, France), Professor M.-D. Legoy and M. Therisod (LGPC, Université de La Rochelle, France) for generous support, and Jérome Guillard for technical assistance.

References

1 T. Besson, K. Emayan and C. W. Rees, *J. Chem. Soc., Chem. Commun.*, 1995, 1419; *J. Chem. Soc., Perkin Trans. 1*, 1995, 2097.
2 R. Appel, H. Janssen, M. Siray and F. Knoch, *Chem. Ber.*, 1985, **118**, 1632.
3 R. F. English, PhD Thesis, University of London, 1989; C. W. Rees, *J. Heterocycl. Chem.*, 1992, **29**, 639.
4 T. Besson and C. W. Rees, *J. Chem. Soc., Perkin Trans. 1*, 1995, 1659.
5 K. Steliou, *Acc. Chem. Res.*, 1991, **24**, 341; C. R. Williams and D. N. Harpp, *Sulfur Rep.*, 1990, **10**, 103.
6 K. W. Breukink, L. H. Krol, P. E. Verkade and B. M. Wepster, *Recl. Trav. Chim. Pays-Bas*, 1957, **76**, 401.
7 L. Strekowski, M. T. Cegla, D. B. Harden, J. L. Mokrosz and M. J. Mokrosz, *Tetrahedron Lett.*, 1988, **29**, 4265.
8 B. Kokel, G. Menichi and M. Hubert-Habart, *Tetrahedron Lett.*, 1984, **25**, 1557.
9 S. Caddick, *Tetrahedron*, 1995, **51**, 10 403; K. Bougrin, M. Soufiaoui, A. Loupy and P. Jacquault, *New J. Chem.*, 1995, **19**, 213, and refences cited therein.
10 W. L. F. Armarego, *Quinazolines*, Wiley-Interscience, New York, 1967, ch. 10.
11 T. Higashino, *Yakugaku Zasshi*, 1959, **79**, 699 (*Chem. Abstr.*, 1959, **53**, 21 997).

Paper 6/01364A
Received 7*th May* 1996
Accepted 5*th August* 1996