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4-Quinazolinones have been cyclised to [1,2,4]triazoloquinazolinones and to imidazoquinazolinones. The direction of cyclisation has been proved by the unambiguous synthesis of their ethylation products.

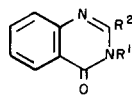
J. Heterocyclic Chem., **23**, 833 (1986).

The initial aim of the work was to synthesise 4-ethyl-1-phenyl[1,2,4]triazolo[4,3-*a*]quinazolin-5-one and analogous compounds for potential bronchospasmolytic activity. The cyclisation of 2-substituted-4-quinazolinones with various reagents led to a number of isomeric tricyclic compounds the structural elucidation of which proved interesting.

2-Hydrazino-4-quinazolinone (**1a**) can react with carboxylic acids or their derivatives to give either angular [1,2,4]triazolo[4,3-*a*]quinazolin-5-ones or linear [1,2,4]triazolo[3,4-*b*]quinazolin-5-ones. Heating **1a** in 90% formic acid [1] yielded mainly the angular compound **2a** as shown by ethylation to **2b**, identical to the compound obtained by reacting 3-ethyl-2-hydrazino-4-quinazolinone (**1b**) with triethyl orthoformate.

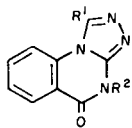
An attempt to prepare 1-phenyl[1,2,4]triazolo[4,3-*a*]quinazolin-5-one by reacting **1a** with benzoyl chloride in dimethylformamide and then refluxing the supposed benzhydrazide suspension yielded a product with no additional aryl protons in its pmr spectrum. Also, there appeared to be only one lowfield multiplet in contrast to the two found in the spectrum of **2a** (Table 1). It was therefore concluded that **1a** had been formylated by the Vilsmeier-Haach type reagent and that linear cyclisation had then taken place to produce compound **3a**. Ethylation of **3a** gave compound **3b** and not its isomer **5a** which was obtained by treatment of 1-ethyl-2-hydrazino-4-quinazolinone (**4**) with trimethyl orthoformate.

Reaction of **1a** with a hot mixture of acetic anhydride and hydrochloride acid [1] gave approximately equal amounts of angular compound **2c** and its linear isomer **3c**.



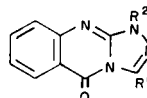
1

- a, R¹ = H, R² = NHNH₂
b, R¹ = Et, R² = NHNH₂
c, R¹ = NH₂, R² = NH₂
d, R¹ = NH₂, R² = NHNH₂
e, R¹ = NH₂, R² = NHEt
f, R¹ = H, R² = NH(CH₂)₃OH
g, R¹ = NH₂, R² = NH(CH₂)₃OH
h, R¹ = Et, R² = NHCH₂CH(OH)Ph
i, R¹ = H, R² = NHCH₂CH(OMe)₂



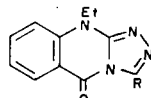
2

- a, R¹ = H, R² = H
b, R¹ = H, R² = Et
c, R¹ = Me, R² = H
d, R¹ = Me, R² = Et
e, R¹ = p-ClC₆H₄, R² = H
f, R¹ = p-ClC₆H₄, R² = Et
g, R¹ = H, R² = (CH₂)_nCl



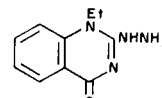
3

- a, R¹ = H, R² = H
b, R¹ = H, R² = Et
c, R¹ = Me, R² = H
d, R¹ = Me, R² = Et
e, R¹ = H, R² = (CH₂)_nCl

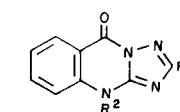


4

- a, R = H
b, R = Me



5



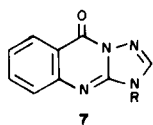
6

- a, R¹ = H, R² = H
b, R¹ = H, R² = Et
c, R¹ = Me, R² = H
d, R¹ = Me, R² = Et
e, R¹ = H, R² = (CH₂)_nCl

The corresponding ethyl derivatives **2d** and **3d** were prepared and compared with isomer **5b** obtained from reaction of **4** with triethyl orthoacetate.

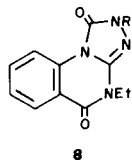
During a large-scale preparation of **3a**, prolonged refluxing of the dimethylformamide solution gave a product which was neither that required nor the angular isomer **2a**. It was also found that **3a** could be converted into this new product by treatment with hot aqueous sodium hydroxide. On the basis of its pmr spectrum it was concluded that the product was the isomeric [1,2,4]triazolo[5,1-*b*]quinazolin-9-one (**6a**) formed by a Dimroth-type rearrangement well known in polyazaindolizines [2,3]. The up-field shift of the triazole proton is as expected from that observed in triazolopyrimidinones [4] where the carbonyl group no longer exerts its deshielding effect. Compound **6a** has been proposed [5] as the product of a reaction between potassium *o*-iodobenzoate and 3-amino-1,2,4-triazole but the reported melting-point is much lower than that of **6a** or its isomers **2a** and **3a**. Compound **6a** is obtained, however, from alkaline treatment of 1,5-diamino-1*H*-[1,2,4]triazolo[1,5-*c*]quinazolinium cation and by cyclisation of 2,3-diamino-4-quinazolinone with triethyl orthoformate [6].

Two products were obtained on ethylation of **6a** the major being identical to that produced by treatment of **5a** with hot aqueous ethanolic sodium hydroxide and therefore of structure **6b**. The minor product was assumed to be isomer **7a** by analogy with **7b** discussed later. In the



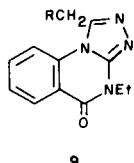
7

- a, R = Et
 b, R = (CH₂)_nCl
 c, R = (CH₂)₃OH
 d, R = NHCOCH₂Cl
 e, R = NHCOCH₂N(CH₂)₆NCO₂Et



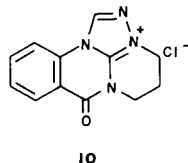
8

- a, R = H
 b, R = (CH₂)_nCl

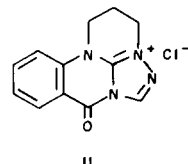


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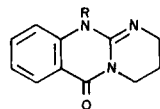
- a, R = Cl
 b, R = N(CH₂)₆



10

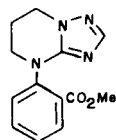


11



12

- a, R = CN
 b, R = H



13

methyl series Dimroth-type rearrangement of **3c** gave **6c**, ethylation of which yielded only derivative **6d** identical to the product from rearrangement of isomer **5b**.

Reaction of **1a** with *p*-chlorobenzaldehyde to form a hydrazone and then treatment with hot ethanolic ferric chloride resulted in an oxidative cyclisation to angular compound **2e** as shown by ethylation to **2f**, identical to that prepared from **1b** by reaction with *p*-chlorobenzoyl chloride. Compound **1b** also reacted with carbonyldiimidazole to give the dione **8** and with chloroacetyl chloride to give compound **9a** which with piperidine then yielded derivative **9b** [7].

Compounds **2a**, **3a**, **6a** and **8a** were chloroalkylated to derivatives **2g**, **3e**, **6e**, **7b** and **8b** (Table 2) for reaction with amines to give compounds for screening in pharmacological tests predicting antihistamine and bronchospasmolytic activity. The chloropropyl derivatives underwent an interesting reaction on melting or heating in dimethylformamide. Thus compound **2g** (*n* = 3) cyclised to quaternary salt **10** and compound **3e** (*n* = 3) to salt **11**. Warming **10** in methanolic triethylamine ruptured the triazole ring with loss of hydrogen chloride to yield *N*-cyano compound **12a** while refluxing the solution resulted in formation of the known pyrimidoquinazolinone **12b** [8]. Treatment of a methanolic solution of salt **11** with morpholine yielded ester **13** due to fracture of the pyrimidone ring. Compounds **6e** and **7b** were the major and minor products respectively from chloroalkylation of **6a** and when *n* = 3 both cyclised on heating to the same salt, thought to be **14**. The minor product led to the most interesting pharmacological compounds [9,10] and therefore a more efficient synthesis was required which would also serve as proof of structure.

2-Hydrazino-4-quinazolinone (**1a**) was synthesised by reacting 2-chloro or 2-mercapto-4-quinazolinone with hydrazine hydrate under mild conditions. More vigorous treatment, namely refluxing in neat reagent, caused a Dimroth-type rearrangement of **1a** to 2,3-diamino-4-quinazolinone (**1c**) which could not be isolated since the 2-amino group was easily displaced by hydrazine to give 3-amino-2-hydrazino-4-quinazolinone (**1d**) [11]. The same product was obtained from 3-ethyl-2-hydrazino-4-quinazolinone (**1b**) by displacement of ethylamine from intermediate **1e**. Similar reactions have been reviewed [12]. Compound **1a**, however, reacted with refluxing propanolamine without rearrangement to give quinazolinone **1f**. It was therefore surmised that key intermediate **1g** would be obtained by reaction of **1d** with propanolamine and this was indeed found to be so.

Cyclisation of **1g** with triethyl orthoformate gave hydroxypropyl compound **7c** which with thionyl chloride in refluxing chloroform was converted into **7b**, identical to the minor product obtained on chloropropylation of

Table 1

PMR Spectra of Triazoloquinazolinones in DMSO-d₆

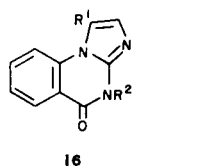
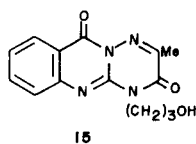
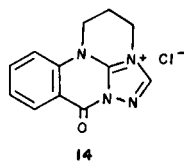
	R ₁	Aromatic protons	R ₂
2a	0.72	1.92 dd (2H), 2.18 t, 2.55 t	—
2b	0.67	1.93 dd (2H), 2.19 t, 2.54 t	5.82 q, 8.70 t
2c	Insoluble	—	—
2d	7.20	1.82 dd, 1.95-2.66 m (3H)	5.85 q, 8.73 t
3a	0.93	1.83 dd, 2.18 t, 1.54 dd, 2.71 t	—
3b	0.97	1.93 dd, 2.15-3.00 m (3H)	5.84 q, 8.53 t
3c	7.35	2.39 dd, 2.56-3.37 m (3H)	—
3d	7.29	1.95 dd, 2.12-3.00 m (3H)	5.92 q, 8.65 t
5a [a]	0.87	1.75 dd, 2.08 t, 2.27 dd, 2.65 t	5.50 q, 8.64 t
5b	7.28	1.80 dd, 1.90-2.85 m (3H)	5.58 q, 8.68 t
6a	1.77	1.80 dd, 2.16 t, 2.30-2.80 m (2H)	—
6b [a]	1.74	1.67 dd, 2.06 t, 2.22 dd, 2.55 t	5.45 q, 8.63 t
6c	7.65	1.78 dd, 2.16 t, 2.33-2.78 m (2H)	—
6d	7.63	1.69 dd, 1.85-2.75 m (3H)	5.51 q, 8.68 t
7a [a]	1.10	1.78 dd, 2.20 t, 2.38 dd, 2.60 t	5.88 q, 8.53 t

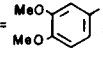
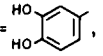
Aromatic triplets are further split. *Ortho* coupling constant 8 Hz. *Meta* coupling constant 2 Hz. *Ethyl* coupling constant 7 Hz. [a] Run on a Bruker WP2005Y at 200 MHz.

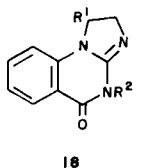
Table 2

Compound	n	Yield	Mp	Formula	C	% Found H	(Calcd.) N	Cl
2g	2	58	204-205	C ₁₁ H ₉ ClN ₄ O	52.9 (53.1)	3.6 (3.65)	22.1 (22.5)	14.3 (14.3)
2g	3	50	122-124	C ₁₂ H ₁₁ ClN ₄ O	54.6 (54.9)	4.2 (4.2)	21.3 (21.3)	13.2 (13.5)
2g	4	72	153-154	C ₁₃ H ₁₃ ClN ₄ O	56.2 (56.4)	4.8 (4.7)	20.4 (20.25)	12.8 (12.8)
3e	2	53	140 dec	C ₁₁ H ₉ ClN ₄ O	53.0 (53.1)	3.7 (3.65)	22.4 (22.5)	13.9 (14.3)
3e	3	68	116-117 dec	C ₁₂ H ₁₁ ClN ₄ O	54.8 (54.9)	4.3 (4.2)	21.2 (21.3)	13.4 (13.5)
3e	4	45	108-109	C ₁₃ H ₁₃ ClN ₄ O	56.1 (56.4)	4.7 (4.7)	20.3 (20.25)	12.4 (12.8)
6e	3	48	270 dec	C ₁₂ H ₁₁ ClN ₄ O	54.7 (54.9)	4.2 (4.2)	21.4 (21.3)	13.5 (13.5)
6e	4	42	128-129	C ₁₃ H ₁₃ ClN ₄ O	56.2 (56.4)	4.8 (4.7)	20.3 (20.25)	
6e	5	21	130-132	C ₁₄ H ₁₅ ClN ₄ O	57.8 (57.8)	5.2 (5.2)	19.0 (19.3)	12.0 (12.2)
7b	3	19	290-292 dec	C ₁₂ H ₁₁ ClN ₄ O	54.7 (54.9)	4.3 (4.2)	21.3 (21.3)	13.5 (13.5)
7b	4	18	162-165	C ₁₃ H ₁₃ ClN ₄ O	56.3 (56.4)	4.8 (4.7)	20.2 (20.25)	
7b	5	17	153-154	C ₁₄ H ₁₅ ClN ₄ O	57.8 (57.8)	5.1 (5.2)	19.2 (19.3)	12.3 (12.2)
8b	2	100	134-139	C ₁₃ H ₁₃ ClN ₄ O ₂	53.25 (53.3)	4.5 (4.5)	19.1 (19.1)	12.1 (11.8)
8b	3	98	102-103	C ₁₄ H ₁₅ ClN ₄ O ₂	54.5 (54.8)	4.85 (4.9)	18.3 (18.3)	11.75 (11.6)
8b	4	94	86-89	C ₁₅ H ₁₇ ClN ₄ O ₂	55.9 (56.2)	5.3 (5.3)	17.6 (17.5)	11.1 (11.1)

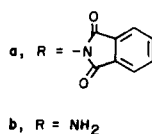
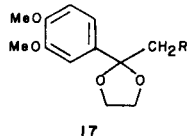
parent molecule **6a**. Derivatives of 3-amino[1,2,4]triazolo[5,1-*b*]quinazolin-9-one can be obtained from **1d**. Thus reaction with chloroacetyl chloride and cyclisation of the unisolated intermediate with triethyl orthoformate gave the chloroacetamide **7d**. Reaction with ethyl piperazine-1-carboxylate then gave ester **7e**. Diaminoquinazolinones such as **1g** are useful intermediates in the synthesis of other heterocyclic systems. For example, reaction with ethyl pyruvate in hot acetic acid gave a high yield of the [1,2,4]triazolo[6,1-*b*]quinazolinone **15**.



- a, R¹ = H, R² = Et
 b, R¹ = Me, R² = Et
 c, R¹ = , R² = Et
 d, R¹ = , R² = Et
 e, R¹ = H, R² = H



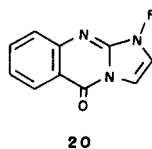
- a, R¹ = Ph, R² = Et
 b, R¹ = OMe, R² = H






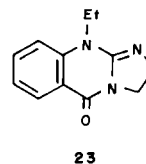
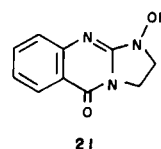
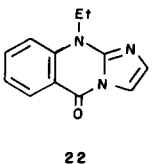
- a, R = Cl
 b, R = NEt₂

Imidazo[1,2-*a*]quinazolin-5-ones can be unambiguously synthesised by reacting 2-chloro-3-ethyl-4-quinazolinone with suitably functionalised amines. Thus aminoacetaldehyde dimethyl acetal gave compound **16a** and propargylamine gave compound **16b**. Aminomethyldioxolane **17b**, readily synthesised from the appropriate bromoacetophenone *via* phthalimide derivative **17a**, produced compound **16c** which was subsequently demethylated to **16d** in hot hydrobromic acid. 2-Phenylethanolamine gave aminoquinazolinone **1h** which cyclised to dihydro compound **18a** in hot thionyl chloride.

Functionalised 2-amino-4-quinazolinones unsubstituted in the 3-position can cyclise to either linear or angular imidazoquinazolinones [13]. Reaction of 2-chloro-4-quinazolinone with aminoacetaldehyde dimethyl acetal gave the amino derivative **1i**. Treatment of **1i** with hot hydrobromic acid gave imidazo[1,2-*a*]quinazolin-5-one (**16e**) as the major product but in hot acetic acid, a mixture of **16e**



- a, R = H
 b, R = Et
 c, R = (CH₂)₄Cl
 d, R = (CH₂)₄N  NCO₂Et
 e, R = (CH₂)₄N  N 



and dihydro compound **18b** was obtained, the latter being converted to the former in hot hydrobromic acid. Ethylation of compound **16e** afforded derivative **16a** thus establishing the direction of cyclisation. Reaction of **16e** with hot phosphorus oxychloride gave chloro derivative **19a** which with diethylamine yielded compound **19b**. This product was also obtained in low yield by reacting 2-chloro-*N,N*-diethyl-4-quinazolinamine with aminoacetaldehyde dimethyl acetal and then cyclising the intermediate in polyphosphoric acid.

Treatment of compound **1i** with hot concentrated sulphuric acid on the other hand yielded predominantly imidazo[1,2,*b*]quinazolin-5-one (**20a**), previously obtained [14] by dehydration of the *N*-hydroxy compound **21**. Ethylation of compound **20a** in the presence of strong base gave a major product **20b** and a minor product **22** the structure of the latter being proved by dehydrogenating the known dihydro compound **23** [15]. The major product from chlorobutylation of compound **20a**, assigned structure **20c** by comparison of its ultraviolet spectrum with that of **20b**, was reacted with secondary amines to give derivatives **20d** and **20e**.

EXPERIMENTAL

Melting points were determined either with a Townson and Mercer capillary melting point apparatus or with a Reichert Kofler hot-stage. The ir spectra were determined for potassium bromide discs with a Pye-Unicam SP1000 spectrophotometer. The nmr spectra were determined with a Perkin-Elmer R12A spectrometer at 60 MHz, with tetramethylsilane as internal standard; all OH and NH peaks were removed by the addition of deuterium oxide. The uv spectra were determined with a Perkin-Elmer 402 spectrophotometer in methanol solution.

3-Ethyl-2-hydrazino-4-quinazolinone (**1b**).

A mixture of 3-ethyl-2-mercapto-4-quinazolinone [16] (5 g), hydrazine hydrate (10 ml) and ethanol (50 ml) was refluxed overnight and allowed to cool to deposit **1b** as pale yellow crystals (from ethanol), mp 160-163°; ν max 3260 and 1640 cm^{-1} ; τ (DMSO- d_6): 2.17 (1H, dd, J 8 Hz and 2 Hz, 5-H), 2.30-3.15 (3H, m, ArH), 6.10 (2 H, q, J 7 Hz, CH₂), 8.88 (3 H, t, J 7 Hz, CH₃).

Anal. Calcd. for C₁₀H₁₂N₄O: C, 58.8; H, 5.9; N, 27.4. Found: C, 58.6; H, 5.9; N, 27.4.

3-Amino-2-hydrazino-4-quinazolinone (**1d**).

2-Hydrazino-4-quinazolinone (**1a**) [17] or 3-ethyl-2-hydrazino-4-quinazolinone (**1b**) was refluxed overnight in hydrazine hydrate (5 volumes), cooled and diluted with water to crystallise **1d** (80-90%) as a colourless solid, mp 219-120° (lit [11] 219-220°).

2-(3-Hydroxypropylamino)-4-quinazolinone (**1f**).

A solution of 2-chloro-4-quinazolinone [18] (10 g) and 3-aminopropanol (10 g) in ethanol (100 ml) was refluxed for 4 hours, cooled and filtered to give **1f** (10.1 g, 91%) as colourless crystals (from dimethylformamide-ethyl acetate), mp 212-214°; ν max 1700 and 1615 cm^{-1} . The same compound was obtained by stirring a suspension of **1a** overnight in refluxing 3-aminopropanol and diluting with water to precipitate the product.

Anal. Calcd. for C₁₁H₁₃N₃O₂·1/4 H₂O: C, 59.1; H, 6.1; N, 18.8. Found: C, 59.2; H, 5.9; N, 18.9.

3-Amino-2-(3-hydroxypropylamino)-4-quinazolinone (**1g**).

A suspension of **1d** (3 g) in 3-aminopropanol (20 ml) was stirred over-

night under reflux. The resultant solution was diluted with water to crystallise **1g** (2.7 g, 73%) as a colourless solid (from methanol), mp 160-162°; ν max 3390, 3310, 3210, 1680, 1640 and 1595 cm^{-1} ; τ (DMSO- d_6): 1.82-2.07 (1 H, m, 5-H), 2.07-3.00 (4 H, m, ArH and NH), 4.47 (2 H, s, NH₂), 5.30 (1 H, broad s, OH), 6.20-6.80 (4 H, m, 1-CH₂ and 3-CH₂), 7.94-8.50 (2 H, m, 2-CH₂).

Anal. Calcd. for C₁₁H₁₄N₄O₂: C, 56.4; H, 6.0; N, 23.9. Found: C, 56.2; H, 6.0; N, 23.9.

3-Ethyl-2-(2-hydroxyphenethylamino)-4-quinazolinone (**1h**).

A mixture of 2-chloro-3-ethyl-4-quinazolinone (2.1 g) prepared by known methods [19] and used crude, 2-amino-1-phenylethanol (1.4 g) and triethylamine (4 ml) was refluxed overnight in ethanol (70 ml). The solvent was removed under reduced pressure, the residue shaken with a mixture of dichloromethane and water and the organic layer evaporated to leave a thick oil which deposited crystals (1.8 g) on trituration with ether. Treatment of a solution of the base in ether with dry ether hydrogen chloride precipitate the hydrochloride of **1h** as crystals (from ethanol-ether), mp 152-154°; ν max 3130, 2980, 2930, 1720, 1670, and 1620 cm^{-1} ; τ (DMSO- d_6): 1.92-2.91 (9 H, m, ArH), 4.75-6.50 (5 H, m, 2 x CH₂ and CH), 8.83 (3 H, t, J 7 Hz, CH₃).

2-(2,2-Dimethoxyethylamino)-4-quinazolinone (**1i**).

A mixture of 2-chloro-4-quinazolinone [18] (7.2 g) and 2,2-dimethoxyethylamine (9 g) was refluxed for 3 hours in ethanol (100 ml). The hot solution was filtered and evaporated to dryness and the residue triturated with water to give **1i** (7.3 g, 73%) as yellow crystals (from ethanol), mp 174-180°; ν max 3360, 2950, 2830 and 1645 cm^{-1} ; τ (deuteriochloroform + perdeuteriomethanol): 2.02 (1 H, dd, J 2 Hz and 8 Hz, 5-H), 2.28-3.09 (3H, m, ArH), 5.50 (1 H, t, J 5 Hz, CH), 6.45 (2 H, d, J 5 Hz, CH₂), 6.60 (6 H, s, 2 x CH₃).

Anal. Calcd. for C₁₂H₁₅N₃O₃: C, 57.8; H, 6.1; N, 16.9. Found: C, 57.9; H, 5.9; N, 16.7.

[1,2,4]Triazolo[4,3-*a*]quinazolin-5-one (**2a**).

As in ref [1], 2-hydrazino-4-quinazolinone (**1a**) (15 g) was heated in fomic acid (90%, 100 ml) on a steam-bath for 4 hours, cooled and poured into water to precipitate **2a** (10 g, 63%) as a crystalline solid (from dimethylformamide-ethyl acetate), mp 295-300° (lit [17] 295-300°); ν max 1695, 1683, 1628 and 1616 cm^{-1} .

Anal. Calcd. for C₉H₈N₄O: C, 58.1; H, 3.25; N, 30.1. Found: C, 57.9; H, 3.4; N, 30.1.

Neutralisation of the mother liquors with potassium carbonate precipitated compound **3a** (1.5 g).

4-Ethyl[1,2,4]triazolo[4,3-*a*]quinazolin-5-one (**2b**).

A mixture of **1b** (1.0 g) and *p*-toluenesulphonic acid (10 mg) was refluxed in triethyl orthoformate (15 ml) for 5 minutes, cooled and diluted with ether to crystallise compound **2b** (0.9 g, 90%), mp 248-250° (from ethanol); ν max 1685, 1620 and 1607 cm^{-1} .

Anal. Calcd. for C₁₁H₁₀N₄O: C, 61.7; H, 4.7; N, 26.15. Found: C, 61.6; H, 4.6; N, 25.8.

The same compound was obtained by ethylating **2a**. A suspension of **2a** in dimethylformamide (10 volumes) was stirred with sodium hydride (80%, 1.1 moles) at room temperature until effervescence had ceased. A slight excess of iodoethane was then added and stirring continued until the reaction was complete (tlc). The mixture was diluted with chloroform (3 volumes), washed three times with water and the organic layer evaporated under reduced pressure to give product **2b**.

1-Methyl[1,2,4]triazolo[4,3-*a*]quinazolin-5-one (**2c**).

The hydrochloric acid mother liquors from the preparation of the [3,4-*b*]isomer **3c** were neutralised with potassium carbonate to precipitate **2c** (2.2 g, 40%) as a colourless solid (from dimethylformamide), mp 350°; ν max 1695, 1635 and 1608 cm^{-1} .

Anal. Calcd. for C₁₀H₈N₄O: C, 60.0; H, 4.0; N, 28.0. Found: C, 59.8; H, 4.1; N, 27.9.

4-Ethyl-1-methyl[1,2,4]triazolo[4,3-*a*]quinazolin-5-one (**2d**).

A mixture of **1b** (3 g) and *p*-toluenesulphonic acid (10 mg) was refluxed in acetic anhydride (30 ml) for 2 hours, poured into water and neutralised with potassium carbonate to crystallise **2d** (2.9 g, 85%), mp 224°; ν max 1700, 1621 and 1609 cm^{-1} .

Anal. Calcd. for $\text{C}_{12}\text{H}_{12}\text{N}_4\text{O}$: C, 63.15; H, 5.3; N, 24.55. Found: C, 62.9; H, 5.3; N, 24.4.

The same compound was obtained by ethylating **2c**. Sodium hydride (80%, 0.2 g) was reacted with ethanol (20 ml). Compound **2c** (1.0 g) and iodoethane (1.0 g) were added and the mixture refluxed overnight. Evaporation to dryness under reduced pressure and addition of water enabled filtration of **2d** (0.5 g, 44%).

1-(4-Chlorophenyl)[1,2,4]triazolo[4,3-*a*]quinazolin-5-one (**2e**).

A solution of 4-chlorobenzaldehyde (0.9 g) and **1a** (0.9 g) in dimethylformamide (25 ml) was heated on a steam-bath for 2 hours, filtered and diluted with ether to give 2-(4-chlorobenzylideno)-4-quinazolinone (0.8 g, 52%), mp 269-270° (from ethanol).

Anal. Calcd. for $\text{C}_{15}\text{H}_{11}\text{ClN}_4\text{O}$: C, 60.3; H, 3.7; Cl, 11.9; N, 18.8. Found: C, 60.25; H, 3.8; Cl, 12.0; N, 18.9.

The above compound (0.4 g) was added to a solution of anhydrous ferric chloride (1.2 g) and triethyl orthoacetate (1.2 ml) in ethanol (12 ml) which had been heated under reflux for 1 hour and the mixture refluxed for 3 hours. The solution was filtered and concentrated under reduced pressure; water was added and precipitated material filtered off, washed and dried. The solid was treated with a refluxing mixture of chloroform-methanol-acetone (1:1:1, 75 ml) for 20 minutes, the mixture filtered and the filtrate evaporated to dryness to give **2e** (0.18 g, 45%), crystals (from methanol), mp 300°; ν max 1695, 1638 and 1610 cm^{-1} .

Anal. Calcd. for $\text{C}_{15}\text{H}_9\text{ClN}_4\text{O} \cdot 1/4 \text{H}_2\text{O}$: C, 58.9; H, 3.3; Cl, 11.6; N, 18.3. Found: C, 59.3; H, 3.2; Cl, 11.9; N, 18.5.

1-(4-Chlorophenyl)-4-ethyl[1,2,4]triazolo[4,3-*a*]quinazolin-5-one (**2f**).

A stirred solution of **1b** (2 g) in glacial acetic acid (20 ml) was treated with benzoyl chloride (2.8 g). After 20 minutes trifluoroacetic acid (0.5 ml) was added and the mixture stirred under reflux until a clear solution was obtained and no amide could be detected (tlc). The solution was poured into water and extracted with chloroform. The extract was washed (aqueous sodium bicarbonate), dried and evaporated to dryness to give **2f** (2.2 g 78%) as colourless crystals (from ethyl acetate), mp 213-215°; ν max 1680, 1620 and 1600 cm^{-1} ; τ (DMSO- d_6): 1.37-1.67 (1H, m, 6-H), 2.20-2.90 (7 H, m, ArH), 5.52 (2 H, q, J 7 Hz, CH_2), 8.52 (3 H, t, J 7 Hz, CH_3).

Anal. Calcd. for $\text{C}_{17}\text{H}_{13}\text{ClN}_4\text{O}$: C, 62.9; H, 4.0; Cl, 10.9; N, 17.25. Found: C, 62.9; H, 4.2; Cl, 10.9; N, 17.3.

4-(ω -Chloroalkyl)[1,2,4]triazolo[4,3-*a*]quinazolin-5-ones (**2g**).

These compounds were obtained by alkylating compound **2a** as in the preparation of **2b** but using ω -chloroalkyl bromides instead of iodoethane and are listed in Table 2.

[1,2,4]Triazolo[3,4-*b*]quinazolin-5-one (**3a**).

2-Hydrazino-4-quinazolinone (**1a**) (10 g) was added to a stirred solution of benzoyl chloride (20 g) in dimethylformamide (40 ml). The mixture was refluxed until a clear solution was obtained and then poured into water to precipitate **3a** (8 g, 75%) as a colourless solid (from dimethylformamide-ethyl acetate), mp 282-284° dec; ν max 1737 and 1655 cm^{-1} .

Anal. Calcd. for $\text{C}_9\text{H}_6\text{N}_4\text{O}$: C, 58.1; H, 3.25; N, 30.1. Found: C, 57.9; H, 3.3; N, 29.7.

1-Ethyl[1,2,4]triazolo[3,4-*b*]quinazolin-5-one (**3b**).

A mixture of **3a** (1 g), potassium carbonate (1 g) and iodoethane (1.2 g) in butanone (20 ml) was stirred and heated under reflux for 24 hours. After filtering the solution was evaporated to dryness under reduced pressure. The residue was dissolved in chloroform, washed with water and the solvent evaporated to give **3b** (0.8 g, 70%) as colourless crystals (from ethanol), mp 261-262°; ν max 1695, 1625 and 1609 cm^{-1} .

Anal. Calcd. for $\text{C}_{11}\text{H}_{10}\text{N}_4\text{O}$: C, 61.7; H, 4.7; N, 26.3. Found: C, 61.6; H, 4.8; N, 26.3.

3-Methyl[1,2,4]triazolo[3,4-*b*]quinazolin-5-one (**3c**).

As in ref [1], compound **1a** (5 g) was heated in a mixture of acetic anhydride (20 ml) and concentrated hydrochloric acid (1 ml) on a steam-bath for 4 hours. The solution was poured into water to precipitate a solid (5.5 g) which was dissolved in warm hydrochloric acid (5.5*N*, 20 ml). The solution was diluted with water to precipitate **3c** (2 g, 35%) as a colourless solid (from dimethylformamide), mp 308° (change) and 342-344°; ν max 1720 and 1660 (broad) cm^{-1} .

Anal. Calcd. for $\text{C}_{10}\text{H}_8\text{N}_4\text{O}$: C, 60.0; H, 4.0; N, 28.0. Found: C, 59.8; H, 4.0; N, 28.0.

1-Ethyl-3-methyl[1,2,4]triazolo[3,4-*b*]quinazolin-5-one (**3d**).

Sodium hydride (80%, 0.15 g) was added to a stirred suspension of **3c** (1 g) in dimethylformamide (10 ml). When effervescence had ceased iodoethane (1 g) was added and the solution left at room temperature for 1 hour. Addition of water then precipitated **3d** (0.6, 53%) as a colourless solid [from petroleum ether (bp 60-80°)], mp 99-100°; ν max 1700, 1630 and 1610 cm^{-1} .

Anal. Calcd. for $\text{C}_{12}\text{H}_{12}\text{N}_4\text{O}$: C, 63.15; H, 5.3; N, 24.55. Found: C, 63.1; H, 5.4; N, 24.6.

1-(ω -Chloroalkyl)[1,2,4]triazolo[3,4-*b*]quinazolin-5-ones (**3e**).

These compounds were obtained by alkylating compound **3a** as in the preparation of **3b** but using ω -chloroalkyl bromides instead of iodoethane and are listed in Table 2.

1-Ethyl-2-hydrazino-4-quinazolinone (**4**).

(*cf.* ref [20]) *N*-Ethylisatoic anhydride [21] (7 g) was added in portions to molten thiourea (7 g) at 200° and the mixture heated at that temperature for 5 hours. Cooling and digesting with hot ethanol enabled filtration of 1-ethyl-1,3-dihydro-2-thioxo-4-quinazolinone (4.1 g, 54%) as a brown crystalline solid, mp 233-234° (as lit [22]). A solution of the thioxo compound (4 g) and hydrazine hydrate (4 ml) in ethanol (40 ml) was refluxed overnight, cooled, filtered and evaporated to dryness. Addition of water to the residue enabled filtration of **4** (2.2 g, 54%) as a pale yellow solid (from ethanol), mp 190° dec; ν max 1691, 1652 and 1606 cm^{-1} .

Anal. Calcd. for $\text{C}_{10}\text{H}_{12}\text{N}_4\text{O}$: C, 58.8; H, 5.9; N, 27.4. Found: C, 58.9; H, 5.9; N, 27.0.

10-Ethyl[1,2,4]triazolo[3,4-*b*]quinazolin-5-one (**5a**).

A mixture of **4** (0.5 g) and *p*-toluenesulphonic acid (5 mg) was heated in refluxing trimethyl orthoformate for 1 hour. The solution was evaporated to dryness under reduced pressure and ethyl acetate added to the residue to enable filtration of **5a** (0.35 g, 67%) as yellow crystals (from ethyl acetate), mp 182-184°; ν max 1718, 1609, 1592 and 1561 cm^{-1} .

Anal. Calcd. for $\text{C}_{11}\text{H}_{10}\text{N}_4\text{O}$: C, 61.7; H, 4.7; N, 26.15. Found: C, 61.5; H, 4.7; N, 25.9.

10-Ethyl-3-methyl[1,2,4]triazolo[3,4-*b*]quinazolin-5-one (**5b**).

Use of triethyl orthoacetate instead of trimethyl orthoformate in the preparation of **5a** gave **5b** (89%) as yellow crystals (from ethanol), mp 210-212°; ν max 1711, 1608 and 1593 cm^{-1} .

Anal. Calcd. for $\text{C}_{12}\text{H}_{12}\text{N}_4\text{O}$: C, 63.15; H, 5.3; N, 24.55. Found: C, 63.2; H, 5.4; N, 24.5.

[1,2,4]Triazolo[5,1-*b*]quinazolin-9-one (**6a**).

Compound **3a** (5 g) was heated in a refluxing mixture of aqueous sodium hydroxide (10%), (10 ml) and ethanol (20 ml) for 2 hours. The ethanol was removed under reduced pressure, the solution diluted with water (10 ml) and then acidified (acetic acid) to crystallise **6a** (4 g, 80%) as a colourless solid (from ethanol), mp 305-310° (lit [6] 325-326°); ν max 1730, 1663 and 1614 cm^{-1} .

Anal. Calcd. for $\text{C}_9\text{H}_6\text{N}_4\text{O}$: C, 58.1; H, 3.25; N, 30.1. Found: C, 58.0; H, 3.5; N, 29.8.

4-Ethyl[1,2,4]triazolo[5,1-*b*]quinazolin-9-one (**6b**).

a) A solution of **5a** (0.4 g) in aqueous sodium hydroxide (15%, 1 ml) and ethanol (5 ml) was refluxed for 2 hours and then evaporated to dryness. The residue was dissolved in water and neutralised (concentrated hydrochloric acid) to precipitate **6b** (0.35 g, 88%) as pale yellow crystals (from ethanol), mp 235-236°; ν max 1711, 1609 and 1563 cm^{-1} .

Anal. Calcd. for $\text{C}_{11}\text{H}_{10}\text{N}_4\text{O}$: C, 61.7; H, 4.7; N, 26.15. Found: C, 61.6; H, 4.8; N, 25.9.

b) A suspension of **6a** (5.4 g) in dimethylformamide (50 ml) was reacted with sodium hydride (80%, 1 g), iodoethane (5.4 g) added and the resultant solution stood at room temperature for 2 hours. Addition of water precipitated a mixture (3.6 g) of 3-ethyl (**7a**) and 4-ethyl (**6b**) isomers (3:17) which were separated by chromatography on silica (200:1) in ethyl acetate-methylene chloride (3:7). Compound **6b** was eluted first.

2-Methyl[1,2,4]triazolo[5,1-*b*]quinazolin-9-one (**6c**).

A solution of **3c** (1 g) and potassium carbonate (2 g) in water (20 ml) was heated on a steam-bath for 6 hours and then neutralised (acetic acid) to precipitate **6c** (1 g, 100%) as colourless crystals (from dimethylformamide) mp 345° dec; ν max 1715 and 1650 broad cm^{-1} .

Anal. Calcd. for $\text{C}_{10}\text{H}_8\text{N}_4\text{O}$: C, 60.0; H, 4.0; N, 28.0. Found: C, 59.8; H, 4.1; N, 27.9.

4-Ethyl-2-methyl[1,2,4]triazolo[5,1-*b*]quinazolin-9-one (**6d**).

This compound was prepared from **5b** as for **6b** in 75% yield as colourless crystals (from ethanol), mp 225-226°; ν max 1710 and 1608 cm^{-1} .

Anal. Calcd. for $\text{C}_{12}\text{H}_{12}\text{N}_4\text{O}$: C, 63.15; H, 5.3; N, 24.55. Found: C, 63.1; H, 5.4; N, 24.5.

 ω -Chloroalkyl[1,2,4]triazolo[5,1-*b*]quinazolin-9-ones **6e** and **7b**.

A mixture of **6a** (15 g), ω -chloroalkyl bromide (15 g) and potassium carbonate (15 g) was stirred in refluxing butanone (300 ml) for 24 hours. The hot solution was filtered, solvent removed under reduced pressure and the residue dissolved in acetone to crystallise the 3-isomers (**7b**) listed in Table 2.

The acetone mother liquors were concentrated under reduced pressure to crystallise the 4-isomers (**6e**) listed in Table 2.

If the products would not crystallise then the isomers were separated by chromatography on alumina. The 4-isomers were eluted with chloroform-petroleum ether (bp 60-80°) (1:1) and the 3-isomers were eluted with chloroform.

3-Ethyl[1,2,4]triazolo[5,1-*b*]quinazolin-9-one (**7a**).

Further elution of the mixture described in preparation b) of **6b** with ethyl acetate-methylene chloride (3:7) yielded a sample of **7a** as colourless crystals, mp 300°; ν max 1688, 1621 and 1607 cm^{-1} .

Anal. Calcd. for $\text{C}_{11}\text{H}_{10}\text{N}_4\text{O}$: C, 61.7; H, 4.7; N, 26.15. Found: C, 61.45; H, 4.8; N, 26.0.

3-(3-Hydroxypropyl)[1,2,4]triazolo[5,1-*b*]quinazolin-9-one (**7c**).

A mixture of **1g** (1 g), triethyl orthoformate (1 g) and *p*-toluenesulphonic acid (10 mg) was heated in refluxing dimethylformamide (3 ml) for 1.5 hours. The solution was cooled and diluted with ethyl acetate to crystallise **7c** (0.8 g, 77%) as a colourless solid, mp 192-194°; ν max 3260, 1705, 1628 and 1605 cm^{-1} ; τ (DMSO- d_6): 1.01 (1 H, s, 2-H), 1.54-1.84 (1 H, m, 8-H), 1.84-2.79 (3 H, m, ArH), 5.29 (1 H, t, J 5 Hz, OH), 5.79 (2 H, t, J 7 Hz, propyl 1- CH_2), 6.30-6.80 (2 H, m, propyl 3- CH_2) 7.70-8.23 (2 H, m, propyl 2- CH_2).

Anal. Calcd. for $\text{C}_{12}\text{H}_{12}\text{N}_4\text{O}_2$: C, 59.0; H, 4.95; N, 22.9. Found: C, 59.0; H, 5.0; N, 22.8.

Refluxing a solution of **7c** (3 g) and thionyl chloride (3 ml) in chloroform (125 ml) overnight, washing with aqueous potassium carbonate and evaporating to dryness gave the 3-(3-chloropropyl) derivative **7b** ($n = 3$) (2.2 g, 68%) listed in Table 2.

N-(3,9-Dihydro-9-oxo[1,2,4]triazolo[5,1-*b*]quinazolin-3-yl)chloroacetamide (**7d**).

A suspension of **1d** (5.7 g) in dimethylformamide (25 ml) was stirred in an ice-bath while chloroacetyl chloride (4 g) was added dropwise. After 0.5 hour at room temperature, triethyl orthoformate (10 ml) was added and the mixture heated on a steam-bath for 4 hours. The solution was poured into water and cooled in ice to crystallise **7d** (3.6 g, 43%) as a colourless solid (from chloroform-methanol), mp 227-230° dec; ν max 1720, 1708, 1653 and 1620 cm^{-1} ; τ (DMSO- d_6): 0.90 (1 H, s, 2-H), 1.60-1.85 (1 H, m, 8-H), 1.90-2.75 (3 H, m, ArH), 5.50 (2 H, s, CH_2).

Anal. Calcd. for $\text{C}_{11}\text{H}_8\text{ClN}_5\text{O}_2 \cdot 1/2\text{H}_2\text{O}$: C, 46.1; H, 3.2; Cl, 12.4; N, 24.4. Found: C, 45.8; H, 3.2; Cl, 12.5; N, 24.3.

Ethyl 4-[(3,9-Dihydro-9-oxo[1,2,4]triazolo[5,1-*b*]quinazolin-3-amino)carbonylmethyl]piperazine-1-carboxylate (**7e**).

A solution of **7d** (1.4 g) and ethyl piperazine-1-carboxylate (1.4 g) in dimethylformamide (10 ml) was heated on a steam-bath for 2 hours. The solution was then diluted with chloroform and shaken with water to crystallise **7e** (1.2 g, 60%). The product was dissolved in warm methanol, treated with concentrated hydrochloric acid (1.2 ml) and the solution diluted with ethyl acetate to crystallise the hydrochloride of **7e** (1.0 g) as colourless crystals, mp 222-224° dec; ν max 1710 inf, 1695, 1642 and 1609 cm^{-1} .

Anal. Calcd. for $\text{C}_{18}\text{H}_{21}\text{N}_7\text{O}_4 \cdot \text{HCl} \cdot 1/2\text{H}_2\text{O}$: C, 48.6; H, 5.2; Cl, 8.0; N, 22.1. Found: C, 48.6; H, 5.2; Cl, 8.0; N, 22.1.

4-Ethyl-3,5-dihydro[1,2,4]triazolo[4,3-*a*]quinazolin-1,5-dione (**8a**).

A mixture of **1b** (71 g) and 1,1-carbonyldiimidazole (65 g) was refluxed for 1.5 hours in dry toluene. The solvent was evaporated and the residue shaken with a mixture of chloroform and water. Insoluble material (45.9 g) was filtered off and combined with a second crop, obtained on evaporation of the chloroform to give **8a** (54.8 g, 68%) as a crystalline solid (from dimethylformamide-ethanol) mp 254-256°; ν max 3180, 1745, 1690, 1630, 1605 and 1585 cm^{-1} ; τ (DMSO- d_6): 1.45 (1 H, dd, J 2 Hz and 8 Hz, 6-H), 1.80-2.75 (3 H, m, ArH), 6.04 (2 H, q, J 7 Hz, CH_2), 8.76 (3 H, t, J 7 Hz, CH_3).

Anal. Calcd. for $\text{C}_{11}\text{H}_{10}\text{N}_4\text{O}_2$: C, 57.4; H, 4.4; N, 24.3. Found: C, 57.3; H, 4.3; N, 24.3.

2-(ω -Chloroalkyl)-4-ethyl-3,5-dihydro[1,2,4]triazolo[4,3-*a*]quinazolin-1,5-diones (**8b**).

These compounds were obtained by alkylating **8a** with ω -chloroalkyl bromides as in the preparation of **2g** and are listed in Table 2.

1-(Chloromethyl)-4-ethyl[1,2,4]triazolo[4,3-*a*]quinazolin-5-one (**9a**).

A solution of **1b** (2 g) in dimethylformamide (20 ml) was treated with chloroacetyl chloride (1.25 g), heated on a steam-bath for 2 hours and then poured into water to precipitate **9a** (2.25 g, 87%) as colourless crystals (from ethyl acetate), mp 198°; ν max 1698, 1618 and 1605 cm^{-1} ; τ (DMSO- d_6): 1.70-1.93 (1 H, m, 6-H), 1.94-2.60 (3 H, m, ArH), 4.61 (2 H, s, ClCH_2), 5.79 (2 H, q, J 7 Hz, CH_2), 8.69 (3 H, t, J 7 Hz, CH_3).

1-(Piperidinomethyl)-4-ethyl[1,2,4]triazolo[4,3-*a*]quinazolin-5-one (**9b**).

Compound **9a** (1 g) was warmed with piperidine in dimethylformamide (5 ml) and the solution diluted with ethanol to crystallise **9b** (1 g, 84%). The hydrochloride was prepared by dissolving **9b** in warm methanol, treating with the same weight of concentrated hydrochloric acid and then diluting with ethyl acetate to crystallise; mp 180-185°; ν max 1730, 1668 and 1618 cm^{-1} .

Anal. Calcd. for $\text{C}_{17}\text{H}_{21}\text{N}_5\text{O} \cdot 2\text{HCl} \cdot \text{H}_2\text{O}$: C, 50.8; H, 6.3; Cl, 17.4; N, 17.6. Found: C, 51.0; H, 6.1; Cl, 17.5; N, 17.4.

4,5,6,8-Tetrahydro-8-oxoquinazolino[3,2,1-*hi*][1,3,8]triazaindolizinium Chloride (**10**).

A solution of **2g** ($n = 3$) (1 g) in dimethylformamide (3 ml) was refluxed for 1 hour and cooled to crystallise **10** (0.9 g, 90%) as a colourless solid (from methanol), mp 260° dec; m/e 226 (M^+); ν max 1715, 1682 and 1622 cm^{-1} ; τ (DMSO- d_6): -0.34 (1 H, s, 1-H) 1.30-2.40 (4 H, m, ArH), 5.63 and 5.88 (2 x 2 H, 2 x t, J 6 Hz, 4- CH_2 and 6- CH_2), 5- CH_2 obscured by the DMSO peak.

1,2,3,8-Tetrahydro-8-oxoquinazolino[1,2,3-*hi*][1,3,8]triazaindolizinium Chloride (**11**).

A solution of **3e** ($n = 3$) (1 g) in dimethylformamide (3 ml) was refluxed for 1 hour to crystallise **11** (0.9 g, 90%), mp 260° dec; ν max 1742, 1685 and 1610 cm^{-1} ; τ (DMSO- d_6 + deuterium oxide): 0.26 (1 H, s, 6-H), 1.50-2.57 (4 H, m, ArH), 5.48 (4 H, t, J 6 Hz, 1- and 3- CH_2), 2- CH_2 obscured by the DMSO peak.

3,4,6,11-Tetrahydro-6-oxo-2*H*-pyrimido[2,1-*b*]quinazoline-1-carbonitrile (**12a**).

A solution of **10** (0.5 g) and triethylamine (0.5 ml) in methanol (5 ml) was heated on a steam-bath for 10 minutes and then evaporated to dryness. The residue was dissolved in chloroform, filtered and the filtrate evaporated to dryness. Trituration of the residue with ether crystallised **12a** (0.4 g, 93%) (from methanol); ν max 2238, 1697, 1665 and 1615 cm^{-1} ; τ (DMSO- d_6): 2.00-2.12 (4 H, m, ArH), 6.21 (2 H, t, J 6 Hz, 4- CH_2), 2- CH_2 obscured by HOD peak, 7.60-8.36 (2 H, m, 3- CH_2).

Anal. Calcd. for $\text{C}_{12}\text{H}_{10}\text{N}_4\text{O}$: C, 63.7; H, 4.5; N, 24.8. Found: C, 63.7; H, 4.5; N, 24.8.

2,3,4,6-Tetrahydro-1*H*-pyrimido[2,1-*b*]quinazolin-6-one (**12b**).

Prolonged refluxing during the preparation of **12a** produced **12b** as a crystalline solid, mp 237-238° (from aqueous dimethylsulphoxide) (lit [8], 227-229°); ν max 1685, 1630 and 1622 cm^{-1} ; τ (DMSO- d_6): 2.10-3.22 (4 H, m, ArH), 6.11 (2 H, t, J 6 Hz, 4- CH_2), 6.74 (2 H, t, J 6 Hz, 2- CH_2), 7.85-8.30 (2 H, m, 3- CH_2).

Anal. Calcd. for $\text{C}_{11}\text{H}_{11}\text{N}_3\text{O}$: C, 65.7; H, 5.5; N, 20.8. Found: C, 65.4; H, 5.6; N, 20.75.

Methyl 2-(4,5,6,7-Tetrahydro[1,2,4]triazolo[1,5-*a*]pyrimidin-4-yl)benzoate (**13**).

A solution of **11** (0.4 g) and morpholine (0.25 ml) in methanol (10 ml) was evaporated to dryness under reduced pressure. The residue was titrated with ether to crystallise **13** (0.3 g, 75%) as a colourless solid (from ether), mp 125°; ν max 1733 cm^{-1} ; τ (DMSO- d_6): 2.15-2.92 (5 H, m, ArH and 2-H), 5.96 and 6.31 (2 x 2 H, 2 x t, J 6 Hz, 5- CH_2 and 7- CH_2), 6.50 (3 H, s, CH_3), 7.60-8.00 (2 H, m, 6- CH_2).

Anal. Calcd. for $\text{C}_{13}\text{H}_{14}\text{N}_4\text{O}_2$: C, 60.5; H, 5.5; N, 21.7. Found: C, 60.5; H, 5.5; N, 21.85.

1,2,3,8-Tetrahydro-8-oxoquinazolino[1,2,3-*hi*][1,2,8]triazaindolizinium Chloride (**14**).

A solution of either **6e** ($n = 3$) or **7b** ($n = 3$) in dimethylformamide was stirred under reflux for 1 hour to crystallise **14** (75%) as a colourless solid (from methanol), mp 295° dec; τ (deuterium oxide): 0.94 (1 H, s, 5-H), 1.42 (1 H, dd, J 2 Hz and 8 Hz, 10-H), 1.58-2.36 (3 H, m, ArH), 5.30-5.70 (m, 1- CH_2 , 3- CH_2 and HOD), 7.60 (2 H, m, 2- CH_2).

3,4-Dihydro-4-(3-hydroxypropyl)-2-methyl[1,2,4]triazino[6,1-*b*]quinazolin-3,10-dione (**15**).

A mixture of **1g** (4.7 g) and ethyl pyruvate (2.5 g) was heated in acetic acid (12 ml) on a steam-bath for 2 hours and then diluted with water to give **15** (4.2 g, 73%) as colourless crystals (from methanol), mp 220°; ν max 3470, 1720, 1695 and 1588 cm^{-1} ; τ (DMSO- d_6 + deuterium oxide): 2.04 (1 H, dd, J 2 Hz and 8 Hz, 9-H), 2.16-2.87 (3 H, m, ArH), 5.83 (2 H, t, J 7 Hz, propyl 1- CH_2), 6.51 (2 H, t, J 7 Hz, propyl 3- CH_2), 7.68 (3 H, s, CH_3), 7.86-8.40 (2 H, m, propyl 2- CH_2).

Anal. Calcd. for $\text{C}_{14}\text{H}_{14}\text{N}_4\text{O}_3$: C, 58.7; H, 4.9; N, 19.6. Found: C, 58.5; H, 5.0; N, 19.4.

4-Ethylimidazo[1,2-*a*]quinazolin-5-one (**16a**).

A mixture of 2-chloro-3-ethyl-4-quinazolinone (2.1 g) and 2,2-dimethoxyethylamine (2.1 g) was refluxed in dimethylformamide (10 ml) for 15 minutes. Aqueous sodium chloride (saturated) was added to precipitate **16a** (1.2 g, 57%) as needles (from ethyl acetate), mp 176-178°; ν max 3140, 3120, 2980, 1680 and 1620 cm^{-1} ; τ (deuteriochloroform): 1.61 (1 H, dd, J 2 Hz and 8 Hz, 6-H), 2.05-2.85 (5 H, m, ArH), 5.60 (2 H, q, J 7 Hz, CH_2), 8.59 (3 H, t, J 7 Hz, CH_3); λ max 203, 204, 206, 217, 224 and

235 nm (ϵ 20290, 21739, 23188, 36231, 37681 and 10145).

Anal. Calcd. for $\text{C}_{12}\text{H}_{11}\text{N}_3\text{O}$: C, 67.6; H, 5.2; N, 19.7. Found: C, 67.4; H, 5.3; N, 19.6.

4-Ethyl-1-methylimidazo[1,2-*a*]quinazolin-5-one (**16b**).

A mixture of 2-chloro-3-ethyl-4-quinazolinone (10 g) and 2-propynylamine (3 g) in dimethylformamide (10 ml) was heated at 80° for 1.5 hours, diluted with water and extracted with ethyl acetate. Evaporation of the solvent gave a dark oil which deposited a solid on trituration with ether. The solid was heated at 80-100° in concentrated sulphuric acid for 1 hour and the cooled solution poured onto ice. Extraction with ethyl acetate gave **16b** (4.8 g, 44%) as needles (from ethyl acetate-petroleum ether), mp 171-174°; ν max 2960, 1665 and 1615 cm^{-1} ; τ (deuteriochloroform): 1.57 (1 H, dd, J 2 Hz and 8 Hz, 6-H), 1.98-2.74 (3 H, m, ArH), 3.04 (1 H, m, 2-H), 5.59 (2 H, q, J 7 Hz, CH_2), 7.28 (3 H, d, J 1 Hz, 1- CH_3), 8.60 (3 H, t, J 7 Hz, CH_3); λ max 215, 221, 234, 272 and 315 nm (ϵ 36963, 40787, 13171, 3526 and 3229).

Anal. Calcd. for $\text{C}_{13}\text{H}_{13}\text{N}_3\text{O}$: C, 68.7; H, 5.8; N, 18.5. Found: C, 68.6; H, 5.8; N, 18.5.

1-(3,4-Dimethoxyphenyl)-4-ethylimidazo[1,2-*a*]quinazolin-5-one (**16c**).

A mixture of 2-chloro-3-ethyl-4-quinazolinone (2.4 g) and **17a** (2.1 g) was heated in refluxing dimethylformamide for 45 minutes, cooled, diluted with ethyl acetate and washed with water. The organic layer was evaporated to dryness and the residue trituted with ether to give **16c** (3.3 g, 95%) as buff crystals (from ethanol), mp 166-168°; ν max 2960 and 1670 cm^{-1} ; τ (deuteriochloroform): 1.45-1.70 (1 H, m, 6-H), 2.45-3.05 (7 H, m, ArH), 5.53 (2 H, q, J 7 Hz, CH_2), 6.02 and 6.15 (2 x 3 H, 2 x s, 2 x OCH_3), 8.54 (3 H, t, J 7 Hz, CH_3).

Anal. Calcd. for $\text{C}_{20}\text{H}_{19}\text{N}_3\text{O}_3$: C, 68.75; H, 5.5; N, 12.0. Found: C, 68.5; H, 5.5; N, 11.9.

1-(3,4-Dihydroxyphenyl)-4-ethylimidazo[1,2-*a*]quinazolin-5-one (**16d**).

Compound **16c** (0.6 g) was heated for 2 hours in refluxing hydrobromic acid (48%, 10 ml). The solution was evaporated to dryness, water added to the residue and the mixture cooled overnight at 5° to crystalline **16d** (0.27 g, 47%), mp 262-264° (from ethanol); ν max 3330 and 1650 cm^{-1} .

Anal. Calcd. for $\text{C}_{18}\text{H}_{15}\text{N}_3\text{O}_3$: C, 67.3; H, 4.7; N, 13.1. Found: C, 67.3; H, 4.8; N, 13.0.

Imidazo[1,2-*a*]quinazolin-5-one (**16e**).

Compound **1i** (38 g) was heated for 5 hours in refluxing hydrobromic acid (48%, 190 ml). The solution was cooled, poured into water and neutralised with sodium bicarbonate to precipitate **16e** (24 g, 87%) as needles (from dimethylformamide), mp 280-284°; ν max 3140, 3120, 2710 broad, 1690 and 1620 cm^{-1} ; τ (DMSO- d_6): 1.82 (1 H, dd, J 2 Hz and 8 Hz, 6-H), 1.90-2.70 (4 H, m, ArH), 2.90 (1 H, d, J 2 Hz, 1-H or 2-H); λ max 214, 216, 222, 263 and 312 nm (ϵ 40749, 41116, 35976, 5140 and 5140).

Anal. Calcd. for $\text{C}_{10}\text{H}_7\text{N}_3\text{O}$: C, 64.9; H, 3.8; N, 22.7. Found: C, 64.9; H, 3.85; N, 22.7.

2-(3,4-Dimethoxyphenyl)-2-(phthalimidomethyl)-1,3-dioxolane (**17a**).

A mixture of 2-bromo-3',4'-dimethoxyacetophenone [23] (27 g), ethylene glycol (13.5 ml) and *p*-toluenesulphonic acid (250 mg) was heated in refluxing benzene (200 ml) under a Dean Stark condenser until no more water distilled. The solution was washed and evaporated to dryness. The residue was dissolved in hexamethylphosphoramide (200 ml), potassium phthalimide (30 g) added and the mixture heated with stirring at 180° for 6 hours. The solution was cooled, diluted with ethyl acetate (500 ml) and washed with water. The organic phase was dried (magnesium sulfate and charcoal) and evaporated to crystallise **17a** (15 g, 39%), mp 153° (from methanol); ν max 1775, 1720 broad and 1606 cm^{-1} ; τ (DMSO- d_6): 2.16 (4 H, s, ArH), 3.06 (3 H, s, ArH), 6.10-6.35 (4 H, m, 4- CH_2 and 5- CH_2), 6.28 and 6.33 (2 x 3H, 2 x s, 2 x OCH_3), 6.70 (2 H, s, CH_2).

Anal. Calcd. for $\text{C}_{20}\text{H}_{19}\text{NO}_6$: C, 65.0; H, 5.2; N, 3.8. Found: C, 65.2; H, 5.2; N, 3.8.

2-(Aminomethyl)-2-(3,4-dimethoxyphenyl)-1,2-dioxolane (**17b**).

A mixture of **17a** (4 g) and hydrazine hydrate (2 ml) was heated in refluxing ethanol (60 ml) for 1 hour. The solution was cooled, filtered and evaporated to dryness and the residue shaken with a mixture of chloroform and water. The organic layer was evaporated to dryness and the residue dissolved in ether (charcoal), filtered and solvent removed under reduced pressure. The residue was triturated with petroleum ether to crystallise **17b** (2.0 g, 77%), mp 65° [from petroleum ether (bp 60-80°)]; ν max 3350, 3270, 3200, 1623 and 1604 cm^{-1} ; τ (DMSO- d_6): 3.05 (3 H, s, ArH), 5.80-6.30 (4 H, m, 4-CH₂ and 5-CH₂), 6.24 (6 H, s, 2 x OCH₃), 7.24 (2 H, s, NCH₂).

Anal. Calcd. for C₁₂H₁₇N₃O₄: C, 60.2; H, 7.2; N, 5.85 Found: C, 60.3; H, 7.1; N, 5.75.

4-Ethyl-1,2-dihydro-1-phenylimidazo[1,2-*a*]quinazolin-5-one (**18a**).

Compound **1h** (0.9 g) was heated in refluxing thionyl chloride (9 ml) for 1 hour. The excess thionyl chloride was removed under reduced pressure and the residue treated with ice and aqueous sodium hydroxide (6*N*) to deposit a solid which was extracted with dichloromethane. Evaporation of the solvent gave a yellow oil which crystallised under ether. The product was purified by forming the hydrochloride in ethereal hydrogen chloride and then precipitating the base from an aqueous solution to give **18a** (0.5 g, 59%) as a colourless solid, mp 147-152°; ν max 2980, 2940, 2870, 1690 and 1610 cm^{-1} ; τ (deuteriochloroform): 1.96 (1 H, dd, J 2 Hz and 8 Hz, 6-H), 2.30-3.25 (7 H, m, ArH), 3.55 (1 H, m, 9-H), 4.65 (1 H, dd, J 6 Hz and 11 Hz, 1-H), 5.53 (1 H, dd, J 11 Hz and 13 Hz, 2-H), 5.85 (2 H, q, 7 Hz, CH₂), 6.25 (1 H, dd, J 6 Hz and 13 Hz, 2-H), 8.65 (3 H, t, J 7 Hz, CH₃).

Anal. Calcd. for C₁₈H₁₇N₃O: C, 74.2; H, 5.9; N, 14.4 Found: C, 73.9; H, 6.0; N, 14.1.

1,2-Dihydro-1-methoxy imidazo[1,2-*a*]quinazolin-5-one (**18b**).

Compound **1i** (3 g) was heated for 15 hours in refluxing acetic acid (30 ml). The solution was cooled and neutralised with aqueous sodium bicarbonate to precipitate **16e** (0.9 g, 40%). The mother liquors were extracted with ethyl acetate to give **18b** (0.4 g, 27%) as a colourless solid (from ethanol), mp 185-188°; ν max 3400-2460, 1715, 1700, 1675 and 1620 cm^{-1} ; τ (DMSO- d_6): 1.88-3.13 (4 H, m, ArH), 4.15 (1 H, dd, J 2 Hz and 8 Hz, 1-H), 6.29 (1 H, dd, J 6 Hz and 11 Hz, 2-H), *ca* 6.6 (1 H, m, masked by OCH₃, 2-H), 6.57 (3 H, s, OCH₃).

Anal. Calcd. for C₁₁H₁₁N₃O₂: C, 60.8; H, 5.1; N, 19.3. Found: C, 60.65; H, 5.0; N, 19.2.

5-Chloroimidazo[1,2-*a*]quinazolin-5-one (**19a**).

A suspension of **16e** (5 g) in phosphorus oxychloride (250 ml) was stirred and heated at 90° for 16 hours and then the excess phosphorus oxychloride removed under reduced pressure. The residue was treated with ice and neutralised with aqueous sodium bicarbonate while keeping the temperature below 20°. The mixture was shaken with ethyl acetate to deposit a solid which was filtered off and combined with a second crop obtained on evaporation of the organic layer to give **19a** (5.2 g, 94%), colourless crystals (from ethyl acetate), mp *ca* 210° dec; ν max 3130 and 1615 cm^{-1} ; τ (deuteriochloroform + DMSO- d_6): 1.70 (1 H, dd, J 2 Hz and 8 Hz, 6-H), 1.80-2.66 (5 H, m, ArH).

Anal. Calcd. for C₇H₆ClN₃: C, 59.0; H, 3.0; Cl, 17.4; N, 20.6. Found: C, 58.8; H, 3.0; Cl, 17.3; N, 20.6.

N,N-Diethylimidazo[1,2-*a*]quinazolin-5-amine (**19b**).

a) A mixture of **19a** (0.5 g) and diethylamine (0.5 g) was heated in dimethylformamide (5 ml) at 80-100° until no starting material remained (tlc). The mixture was cooled, poured onto aqueous sodium chloride (saturated) and extracted with ethyl acetate to give on removal of solvent **19b** (0.33 g, 59%) as pale green crystals (from ethyl acetate), mp 115-118°; ν max 3100, 2970, 1615 and 1600 cm^{-1} ; τ (deuteriochloroform): 2.00 (1 H, dd, J 2 Hz and 8 Hz, 6-H), 2.15-2.80 (5 H, m, ArH), 6.43 (4 H, q, J 7 Hz, 2 x CH₂), 8.73 (6 H, t, J 7 Hz, 2 x CH₃).

Anal. Calcd. for C₁₄H₁₆N₄: C, 70.0; H, 6.7; N, 23.3. Found: C, 69.8; H, 6.8; N, 23.25.

b) A solution of 2-chloro-*N,N*-diethyl-4-quinazolinamine [24] (15 g) and 2,2-dimethoxyethylamine (16 g) in ethanol (150 ml) was refluxed overnight. The solvent was evaporated under reduced pressure and the residue dissolved in ethyl acetate. The solution was washed with water and solvent removed to give an orange oil (21 g). The oil was added in portions to stirred polyphosphoric acid (25 ml) during which the temperature rose to 100°. The resulting black mixture was heated at 50° for 15 minutes and then poured into water. Neutralisation with sodium bicarbonate and extraction with chloroform gave a black oil (3.9 g) which was dissolved in methanolic hydrogen chloride. Addition of ether precipitated a colourless salt (1.1 g) (from methanol-ether). Liberation of the free base gave **19b**.

Imidazo[2,1-*b*]quinazolin-5-one (**20a**).

Compound **1i** (38 g) was stirred overnight in concentrated sulphuric acid (190 ml) at room temperature. The solution was poured on to ice and the pH adjusted to 9 with sodium carbonate to precipitate **20a** (26.6 g, 97%) as colourless crystals (from methanol) mp 281-284° (lit [14] 302° dec); ν max 3160, 3120, 2720 broad, 1710 and 1650 cm^{-1} ; τ (DMSO- d_6): 1.83 (1 H, dd, J 2 Hz and 8 Hz, 6-H), 2.06-2.90 (3 H, m, ArH); λ max 212, 237, 257, 286, 297 and 352 nm (ϵ 15463, 35602, 14385, 5035, 4675 and 5035).

Anal. Calcd. for C₁₀H₇N₃O: C, 64.9; H, 3.8; N, 22.7. Found: C, 64.8; H, 3.9; N, 22.6.

Ethylation of Imidazo[2,1-*b*]quinazolin-5-one (**20a**).

Sodium hydride (50%, 0.8 g) was added to a stirred solution of **20a** (2.95 g) in dimethylformamide (45 ml) under nitrogen at room temperature. To the resulting orange solution was added bromethane (1.4 ml) and a further amount (0.7 ml) 24 hours later. Twenty-four hours after the second addition the solution was poured into aqueous sodium chloride (saturated) and the mixture extracted with ethyl acetate. Evaporation of the solvent gave a yellow oil (3.3 g, 97%) which was subjected to high pressure liquid chromatography on silica.

The major component was eluted with ethyl acetate-hexane (1:5) to give 1-ethylimidazo[2,1-*b*]quinazolin-5-one (**20b**) (1.6 g) as colourless crystals (from carbon tetrachloride), mp 112-116°; ν max 3160, 3120, 3080, 1680 and 1610 cm^{-1} ; τ (deuteriochloroform): 1.68 (1 H, dd, J 2 Hz and 8 Hz, 6-H), 2.20-2.60 and 2.60-2.95 (4 H, m, ArH), 3.10 (1 H, d, J 3 Hz, ArH), 5.87 (2 H, q, J 7 Hz, CH₂), 8.55 (3 H, t, J 7 Hz, CH₃); λ max 211, 238, 258, 291, 298 and 353 nm (ϵ 17538, 30516, 17538, 9470, 10172 and 6314).

Anal. Calcd. for C₁₂H₁₁N₃O: C, 67.6; H, 5.2; N, 19.7 Found: C, 67.4; H, 5.2; N, 19.7.

The minor component was eluted with ethyl acetate-dichloromethane (1:50) to give 10-ethylimidazo[2,1-*b*]quinazolin-5-one (**22b**) (0.13 g) as colourless crystals [from dichloromethane-petroleum ether (bp 40-60°)], mp 132-134°; ν max 3140, 2920, 1690 and 1620 cm^{-1} ; τ (deuteriochloroform): 1.57 (1 H, dd, J 2 Hz and 8 Hz, 6-H), 2.05-2.90 (5 H, m, ArH), 5.44 (2 H, q, J 7 Hz, CH₂), 8.54 (3 H, t, J 7 Hz, CH₃); λ max 210, 239, 263, 284 and 354 nm (ϵ 16905, 43153, 12902, 4894 and 4894).

Anal. Calcd. for C₁₂H₁₁N₃O: C, 67.6; H, 5.2; N, 19.7. Found: C, 67.5; H, 5.2; N, 19.7.

Compound **22b** was also prepared by refluxing a mixture of 10-ethyl-2,3-dihydroimidazo[2,1-*b*]quinazolin-5-one (**23**) [15] (1.7 g) and manganese dioxide (3.5 g) in xylene (30 ml) for 8 hours, adding more manganese dioxide (2.0 g) and refluxing for a further 12 hours. After cooling the mixture was filtered, solid material washed well with di-chloromethane and the combined solutions evaporated to give the product.

1-(4-Chlorobutyl)imidazo[2,1-*b*]quinazolin-5-one (**20c**).

Compound **20a** was alkylated with 1-bromo-4-chlorobutane as in the preparation of **20b** and the major product isolated by chromatography on silica using ethyl acetate-petroleum ether (bp 60-80°) to give **20c** (58%) as colourless crystals (by sublimation), mp 130-131°; ν max 3140, 3130, 3090, 2940, 1680, 1665, 1620 and 1600 cm^{-1} ; τ (deuteriochloroform): 1.67 (1 H, dd, J 2 Hz and 8 Hz, 6-H), 2.25-2.94 (4 H, m, ArH), 3.10

(1 H, d, J 3 Hz, ArH), 5.92 (2 H, t, J 7 Hz, NCH₂), 6.42 (2 H, t, J 7 Hz, ClCH₂), 7.62-8.52 (4 H, m, CH₂CH₂); λ max 219, 238, 259, 290, 297 and 354 nm (ε 15103, 37640, 17073, 9456, 10244 and 6698).

Anal. Calcd. for C₁₄H₁₄ClN₅O: C, 61.0; H, 5.1; Cl, 12.9; N, 15.2. Found: C, 61.0; H, 5.1; Cl, 12.9; N, 15.2.

Ethyl 4-[4-(5-Oxo-1,5-dihydroimidazo[2,1-*b*]quinazolin-1-yl)butyl]piperazine-1-carboxylate (**20d**).

Compound **20c** was reacted with ethyl piperazine-1-carboxylate (2.2 moles) in dimethylformamide on a steam-bath. The solution was diluted with chloroform, washed with aqueous potassium carbonate and solvent removed under reduced pressure to give a solid which in ethereal hydrogen chloride yield the hydrochloride of **20d** (54%) as colourless crystals (from ethanol), mp 204-211°; ν max 3090, 3050, 2440 broad, 1715 and 1670 cm⁻¹.

Anal. Calcd. for C₁₂H₂₇N₅O₃·2HCl: C, 53.6; H, 6.2; Cl, 15.1; N, 14.9. Found: C, 53.6; H, 6.3; Cl, 15.0; N, 14.9.

1-[4-(4-*m*-Chlorophenyl-1-piperazinyl)butyl]imidazo[2,1-*b*]quinazolin-5-one (**20e**).

This compound was prepared as for **20d** using 1-*m*-chlorophenylpiperazine to give the hydrochloride (62%) as colourless crystals (from ethanol), mp 191-201°; ν max 2950, 2430 broad, 1690, 1620 and 1610 cm⁻¹.

Anal. Calcd. for C₂₄H₂₆ClN₅·HCl: C, 61.0; H, 5.8; Cl, 15.0; N, 14.8. Found: C, 60.9; H, 5.8; Cl, 15.0; N, 14.8.

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Note Added in Proof.

The synthesis of compounds **5a** and **5b** from 1-ethyl-2-hydrazino-4-quinazolinone (**4**) has recently been published; *Pharmazie*, **39**, 868 (1984) using an improved preparation of 1-ethyl-1,3-dihydro-2-thioxo-4-quinazolinone. Unfortunately we have not been able to repeat this work in order to investigate the discrepancies in melting points of the compounds. We have however further examined their pmr spectra and have noted a strong Nuclear Overhauser Enhancement between the ethyl CH₂ and the adjacent aromatic proton in compounds **4**, **5a** and **6b**. There is also a weaker interaction between the ethyl CH₂ and 2-H in compound **7a**.