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Analogues of deoxyvasicinone (**1**) in which the pyrrolo ring is substituted, enlarged, or attached to the a face of the quinazolone system were prepared and several reactions of these analogues with electrophilic reagents have been investigated.

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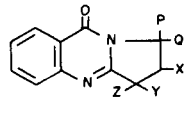
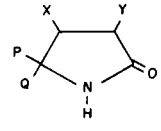
For several years we have been interested in the reaction of **1** with electrophiles [1-3]. We have now extended this study to analogues of **1** in which the pyrrolo ring carries a substituent, is enlarged, or is fused to the face of the quinazolone ring. This paper describes the synthesis of these analogues and their reactions with various electrophiles.

Substituents on the Pyrrolo Ring.

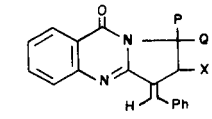
Analogues of **1** in which the pyrrolo ring carries a substituent were readily obtained by the condensation of anthranilic acid and the appropriate substituted 2-pyrrolidinone or its imidate. Only 5-methyl-2-pyrrolidinone **2** was commercially available and the other alkylated pyrrolidinones required for this study (**3**, **4** and **5**) were obtained by a method devised by us. The nitroesters **6**, **7** and **8** prepared by condensation of the appropriate nitroalkane and α,β-unsaturated ester [4a] were reductively cyclised with iron powder and aqueous acetic acid to give the substituted 2-pyrrolidinones **3**, **4** and **5** respectively. Thermal cyclisation of diethyl glutamate gave 5-carbethoxy-2-pyrrolidinone **9** [5]. Pyrrolidinones **4** and **9** were converted into their imidates **10** and **11** by reaction with triethyloxonium tetrafluoroborate followed by aqueous potassium carbonate.



1 P = Q = X = Y = Z = H
12 P = Me, Q = X = Y = Z = H
13 P = Q = Me, X = Y = Z = H
14 X = Me, P = Q = Y = Z = H
15 X = Me, P = Q = X = Z = H
16 P = CO_2Et, Q = X = Y = Z = H
21 P = Me, Q = X = H, Y = Z = CO_2Et
22 P = Q = Me, X = H, Y = Z = CO_2Et



2 P = Me, Q = X = Y = H
3 P = Q = Me, X = Y = H
4 X = Me, P = Q = Y = H
5 Y = Me, P = Q = X = H
9 P = CO_2Et, Q = X = Y = H



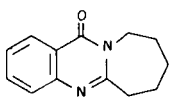
17 P = Me, Q = X = H
18 P = Q = Me, X = H
19 X = Me, P = Q = H
20 P = CO_2Et, Q = X = H

6 $(CH_3)_2-C(NO_2)-CH_2-CH_2-CO_2Me$
7 $O_2N-CH_2-CH(CH_3)-CH_2-CO_2Me$
8 $O_2N-CH_2-CH_2-CH(CH_3)-CO_2Me$

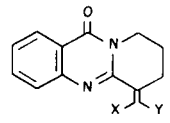
When the pyrrolidinones **2**, **3** and **5** were heated with anthranilic acid in phosphorus oxychloride solution [6] the methyl substituted deoxyvasicinones **12**, **13** and **14** were obtained, whilst condensation of the imidates **10** and **11** with anthranilic acid in hot toluene [7] gave compounds **15** and **16**. When the methyl derivatives **12-14** and the carbethoxy derivative **16** were heated with benzaldehyde phenylmethylene (benzylidene) compounds **17-20** were obtained. However, no condensation occurred when **15** was treated similarly due to the presence of a methyl group at C-3. With the exception of **15** all these analogues had similar reactivities compared to **1**. For example when the 1-methyl compound **12** was heated with an excess of ethyl chloroformate [2] the diester **21** was obtained whilst lithiation of **13** followed by reaction of the intermediate with excess ethyl chloroformate [1] gave the diester **22**.

Pyrido and Azepino Analogues.

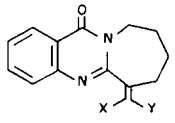
Both the pyrido and azepino analogues **24** and **26** have been reported [8-9] but we prepared them by heating anthranilic acid with a slight excess of the appropriate imidates **23** and **25** in hot toluene. When the pyrido analogue **24** was heated with benzaldehyde the phenylmethylene



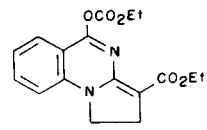
26



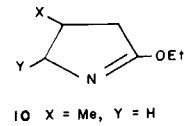
27 X = H, Y = Ph
35 X = HO, Y = OEt



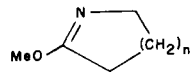
28 X = H, Y = Ph
29 X = Ph, Y = H
30 X = Ph, Y = OCOPh
31 X = OCOPh, X = Ph



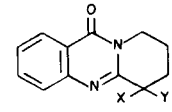
43



10 X = Me, Y = H
11 X = H, Y = CO_2Et



23 n = 2
25 n = 3

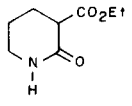


24 X = Y = H
32 X = Y = CO_2Et
33 X = H, Y = CO_2Et

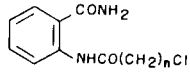
compound **27** resulted whilst the azepino compound **26** gave both the *E* and *Z* isomers **28** and **29** under the same reaction conditions. The major isomer is assumed to have the *E* configuration for steric reasons. Both compounds **24** and **26** are less reactive towards electrophiles compared to **1** and differences in the types of products obtained were observed.

For example when **24** was heated with benzoyl chloride [2] a complex mixture was obtained from which no pure products were isolated. Under similar conditions the azepino analogues **26** produced two major and two minor products. The major products were separated by hplc [10] and shown by analysis and spectroscopy to be the isomeric enol benzoates **30** and **31**. The major isomer was assumed, for steric reasons, to be the *E* isomer. The minor products from this reaction were not investigated further.

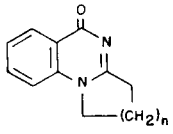
When the monoester **33** [11], prepared by the reaction of anthranilic acid and 3-carbethoxy-2-piperidone **34** in the presence of phosphorus oxychloride, was heated with ethyl chloroformate the diester **32** resulted. Spectroscopic evidence suggests that the monoester does not exist as **33** but probably as **35**. Previous authors [11] have attributed the absorption as 1680 cm^{-1} in the ir spectrum to the ester



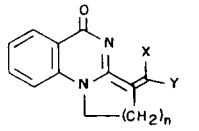
34



36 n = 3
37 n = 4



38 n = 1
37 n = 2



40 n = 1, X = H, Y = Ph
41 n = 2, X = H, Y = Ph
42 n = 2, X = Ph, Y = H

carbonyl, however we believe in the absence of any other carbonyl bands that this is due to the quinazolone carbonyl group which is found typically between 1660-1680 cm^{-1} in these [2,1-*b*] systems. Although it is difficult to state with any certainty whether a H-O stretch is present in the ir spectrum the pmr spectrum contains a low field exchangeable broad singlet at δ 12.40 integrating for approximately one proton.

We have previously noted [2-3] that many carbonyl derivatives of **1** prefer to adopt an enol form probably due to the formation of an intramolecular hydrogen bond between the HO proton and the sp^2 nitrogen atom. Reaction of the pyrido analogue **24** with ethyl chloroformate also gave the diester **32** but treatment of the azepino compound **26** with ethyl chloroformate failed to yield any products other than the hydrochloride of **26**.

[1,2-*a*] Fused Quinazolones.

Gatta [12] and Möhrle [13] have previously described the preparation of the [1,2-*a*] analogues **38** and **39**. For this study a modification of the former method was used [12]. Condensation of anthranilamide with the appropriate ω haloalkanoyl chloride in the presence of sodium acetate gave the diamides **36** and **37** in high yield. Cyclisation of the diamide **36** with methanolic sodium methoxide gave a mixture of deoxyvasicinone **1** and the tricycle **38** whilst compound **37** gave **24** and **39**. When compound **38** was reacted with benzaldehyde the phenylmethylene derivative **40** was obtained whilst **39** yielded two phenylmethylene compounds **41** and **42** when treated similarly. The major isomer was again assumed to be the *E* isomer. When **38** was heated with benzoyl chloride extensive decomposition occurred and no pure products were isolated from the reaction mixture. Reaction of **38** with ethyl chloroformate gave a bright yellow crystalline compound which was assigned structure **43**. The ir spectrum contained two ester absorptions at 1780 and 1695 cm^{-1} and a strong band at 1680 cm^{-1} which we have attributed to a C=C. No band was found in the region 1640-1630 cm^{-1} where the carbonyl group of [1,2-*a*] fused quinazolones is usually found.

The pmr spectrum also indicates that the hydrogen atom on C-6 no longer experiences an anisotropic effect due to a carbonyl group at C-5.

EXPERIMENTAL

For general methods see [1-3]. All pmr spectra were measured in deuteriochloroform unless otherwise stated.

Methyl 4-Methyl-4-nitropentanoate (**6**).

Methyl acrylate was condensed with 2-nitropropane in the presence of Triton B as described by Moffett [4a] to yield pure **6** as a colourless oil (71%), bp 68°/0.7 mm Hg (reported [4a] bp 79°/1 mm Hg).

Methyl 3-Methyl-4-nitrobutanoate (**7**).

Nitromethane and methyl crotonate were condensed as previously described [4a] to yield **7** as a colourless oil (50%), bp 84°/2 mm Hg (reported [14] bp 77-79°/1 mm Hg).

Methyl 2-Methyl-4-nitrobutanoate (**8**).

Nitromethane and methyl methacrylate were treated as described [4a] to yield **8** in low yield (16%), bp 64-66°/0.8 mm Hg (reported [14] bp 76-77°/2 mm Hg).

All nitroesters **6-8** had spectroscopic properties in accord with their structures.

5,5-Dimethyl-2-pyrrolidinone (**3**).

A solution of methyl 4-methyl-4-nitropentanoate **6** (1 mole) in glacial acetic acid (2.5 *l*)/water (300 ml) was stirred at 100° and reduced iron powder (500 g) added portionwise over 2 hours. (Additional water (300 ml) was added after 1 hour). The mixture was cooled, diluted with acetone, filtered and the solids washed well with acetone. The filtrate and washings were combined, concentrated *in vacuo* and the residue was distilled twice under high vacuum to yield pure **3** as a colourless oil (37%), bp 89°/0.4 mm Hg (reported [46] bp 126.5-128°/12 mm Hg), which rapidly crystallised on cooling.

4-Methyl-2-pyrrolidinone (**4**).

Reduction of methyl 3-methyl-4-nitrobutanoate (**7**) with iron powder as described above gave pure **4** (57%) as a colourless oil which crystallised on cooling, bp 98°/1.5 mm Hg (reported [15] bp 118°/8 mm Hg).

3-Methyl-2-pyrrolidinone (**5**).

Reductive cyclisation of methyl 2-methyl-4-nitrobutanoate **8** as described above gave pure **5** (47%) as a colourless oil which crystallised slowly on standing, bp 76°/0.4 mm Hg (reported [15] bp 96-97°/4 mm Hg).

All pyrrolidinones **3-5** had pmr and ir spectra in accord with their structures.

1-Aza-2-ethoxy-4-methyl-1-cyclopentene (**10**).

A solution of **4** (9.9 g, 0.1 mole) in dichloromethane (100 ml) was treated at room temperature was a dichloromethane solution of freshly prepared triethyloxonium tetrafluoroborate (0.11 moles) and the mixture stirred at room temperature for 24 hours. The solution was shaken with 50% potassium carbonate and the dried organic phase concentrated *in vacuo*. Vacuum distillation gave pure **10** as a colourless liquid (81%), bp 80-82°/30 mm Hg; ir (film, sodium chloride): 1645, 1635 cm^{-1}; pmr: δ 4.30 (2H, q), 4.12-2.92 (5H, complex), 1.72-1.12 (6H, complex).

1-Aza-5-carbethoxy-2-ethoxy-1-cyclopenene (**11**).

Treatment of 5-carbethoxy-2-pyrrolidinone (**9**) as described under **10** gave pure **11** as a colourless oil (65%), bp 78°/0.5 mm Hg; ir (film, sodium chloride): 1740, 1635, 1380, 1340, 1270 cm^{-1}; pmr: δ 4.60-3.88 (4H, complex), 3.62-3.32 (1H, complex), 2.72-2.00 (4H, complex), 1.28 and 1.24 (6H, 2t).

Analogues of Deoxyvasicinone **1**.

Method A.

A mixture of anthranilic acid (1 mole equivalent), the pyrrolidinone or other cyclic amide (1.5 mole equivalents) and phosphorus oxychloride (2.5 ml/g of anthranilic acid) was heated at 100° for 1 hour. The cooled mixture was poured onto ice, basified with concentrated aqueous ammonia and then extracted (× 3) with dichloromethane. After decolourisation and concentration the residue was purified by either recrystallisation or vacuum distillation.

Method B.

A solution of anthranilic acid (1 mole equivalent), and the imidate (1.1 mole equivalents) were heated in toluene (20 ml/g anthranilic acid) at reflux for 1-2 hours. The solvents were removed *in vacuo* and the residue partitioned between saturated sodium bicarbonate and dichloromethane (× 2). The dried, decoulorised organic extracts were concentrated *in vacuo* and the residue purified by recrystallisation or vacuum distillation.

2,3-Dihydro-1-methylpyrrolo[2,1-*b*]quinazolin-9(1*H*)-one (**12**).

Anthranilic acid and 5-methyl-2-pyrrolidinone (**2**) were reacted as described in method A to yield **12** as a white solid (55%), mp 70-71° (ether/light petroleum); ir (potassium bromide): 1670 cm^{-1}; pmr: δ 8.00 (1H, complex d), 7.72-6.98 (3H, complex), 4.62 (1H, complex), 3.32-2.72 (2H, complex), 2.60-1.60 (2H, complex), 1.29 (3H, d, J = 6 Hz); ms: m/e 200 (100%) M^+.

Anal. Calcd. for $C_{12}H_{12}N_2O$: C, 72.0; H, 6.0; N, 14.0. Found: C, 71.6; H, 6.1; N, 13.9.

2,3-Dihydro-1,1-dimethylpyrrolo[2,1-*b*]quinazolin-9(1*H*)-one (**13**).

Anthranilic acid and 5,5-dimethyl-2-pyrrolidinone (**3**) were condensed as described in method A to yield **13** (67%), mp 105-106° (ether); ir (potassium bromide): 1670 cm^{-1}; pmr: δ 8.06 (1H, complex d), 7.64-7.00 (3H, complex), 3.00 (2H, t), 2.02 (2H, t), 1.68 (6H, s); ms: m/e 214 (100%) M^+.

Anal. Calcd. for $C_{13}H_{14}N_2O$: C, 72.8; H, 6.6; N, 13.1. Found: C, 72.4; H, 6.8; N, 12.7.

2,3-Dihydro-2-methylpyrrolo[2,1-*b*]quinazolin-9(1*H*)-one (**14**).

Anthranilic acid and **10** were condensed in toluene as described in method B to yield **14** as a white solid (42%), mp 105-106° (ether); ir (potassium bromide): 1670 cm^{-1}; pmr: δ 8.10 (1H, complex d), 7.78-7.05 (3H, complex), 4.48 (1H, dd), 3.64 (1H, dd), 3.42-2.98 (3H, complex), 1.24 (3H, d, J = 7 Hz); ms: m/e 200 (66%) M^+, 185 (100%) $(M\text{-}CH_3)^+$.

Anal. Calcd. for $C_{12}H_{12}N_2O$: C, 72.0; H, 6.0; N, 14.0. Found: C, 71.9; H, 6.0; N, 13.8.

2,3-Dihydro-3-methylpyrrolo[2,1-*b*]quinazolin-9(1*H*)-one (**15**).

Anthranilic acid and 3-methyl-2-pyrrolidinone (**5**) were condensed as described in method A to yield **15** (26%) as a white crystalline solid, mp 135-135.5° (ether); ir (potassium bromide): 1665 cm^{-1}; pmr: δ 8.08 (1H, complex d), 7.80-7.00 (3H, complex), 4.24-1.58 (5H, complex), 1.24 (3H, d, J = 7 Hz); ms: m/e 200 (82%) M^+.

Anal. Calcd. for $C_{12}H_{12}N_2O$: C, 72.0; H, 6.0; N, 14.0. Found: C, 71.7; H, 6.0; N, 13.9.

1-Carbethoxy-2,3-dihydropyrrolo[2,1-*b*]quinazolin-9(1*H*)-one (**16**).

Anthranilic acid and **11** were reacted as described in method B to yield **16** as a colourless needles (44%), mp 118.5-120° (ether); ir (potassium bromide): 1740, 1690 cm^{-1}; pmr: δ 8.08 (1H, complex d), 7.80-7.00 (3H, complex), 5.20-4.80 (1H, dd), 4.16 (1H, complex d), 7.80-7.00 (3H, complex), 5.20-4.80 (1H, dd), 4.16 (2H, q, J = 7 Hz), 3.68-2.00 (4H, complex), 1.24 (3H, t, J = 7 Hz).

Anal. Calcd. for $C_{14}H_{14}N_2O_3$: C, 65.1; H, 5.4; N, 10.85. Found: C, 65.0; H, 5.4; N, 10.65.

11*H*-6,7,8,9-Tetrahydropyrido[2,1-*b*]quinazolin-11-one (**24**).

Anthranilic acid and 1-aza-2-methoxycyclohexene (**23**) were reacted as described in method B to yield **24** as a white solid (29%), mp 99-100° (ether), reported mp 99-100° [8]; ir (potassium bromide): 1660 cm^{-1}; pmr: δ 8.22 (1H, complex d), 7.80-7.10 (3H, complex), 4.06 (2H, t), 2.96 (2H, complex), 2.40-1.80 (4H, complex); ms: m/e 200 (100%) M^+.

Anal. Calcd. for $C_{12}H_{12}N_2O$: C, 72.0; H, 6.0; N, 14.0. Found: C, 72.0; H, 6.1; N, 14.0.

7,8,9,10-Tetrahydroazepino[2,1-*b*]quinazolin-12(6*H*)-one (**26**).

Anthranilic acid and 1-aza-2-methoxycycloheptene (**25**) were heated in toluene as described in method B to yield **26** as small white crystals (70%), mp 98°, reported mp 95-97° [9]; ir (potassium bromide): 1660 cm^{-1}; pmr: δ 8.19 (1H, complex d), 8.00-7.10 (3H, complex), 4.30 (2H, broad s), 3.07 (2H, broad s), 2.26-1.26 (6H, broad complex); ms: m/e 214 (100%) M^+.

Anal. Calcd. for $C_{13}H_{14}N_2O$: C, 72.8; H, 6.6; N, 13.1. Found: C, 72.75; H, 6.8; N, 13.0.

11*H*-6-Carbethoxy-6,7,8,9-tetrahydropyrido[2,1-*b*]quinazolin-11-one (**33**).

Anthranilic acid and 3-carbethoxy-2-piperidone (**34**) were reacted as described in method A to yield **33** as pale yellow needles (12%), mp 131° (ether/ethyl acetate), reported mp 110-112° [11]; ir (potassium bromide): 1680 cm^{-1}; pmr: δ 12.40 (~1H, broad s, exchangeable), 8.20-6.70 (4H, complex), 4.50-3.60 (4H, complex), 2.70-1.66 (4H, complex), 1.31 (3H, t, J = 7 Hz); ms: m/e 272 (100%) M^+.

Anal. Calcd. for $C_{15}H_{16}N_2O_3$: C, 66.2; H, 5.9; N, 10.3. Found: C, 66.4; H, 5.9; N, 10.3.

N-(2-Benzamido)-4-chlorobutanamide (**36**) and *N*-(2-Benzamido)-5-chloropentanamide (**37**).

Acylation of anthranilamide with 4-chlorobutanoyl chloride as described by Gatta [12] gave **36** (81%), mp 114-115°, reported mp 120° [12]. Similar treatment of anthranilamide with 5-chloropentanoyl chloride gave **37** as colourless needles (82%), mp 117-118°.

36. *Anal.* Calcd. for $C_{11}H_{13}ClN_2O_2$: C, 54.94; H, 5.45; Cl, 14.90; N, 11.67. Found: C, 55.11; H, 5.43; Cl, 14.73; N, 11.73.

37. *Anal.* Calcd. for $C_{12}H_{15}ClN_2O_2$: C, 56.69; H, 5.90; Cl, 13.98; N, 11.00. Found: C, 56.91; H, 5.90; Cl, 14.01; N, 10.88.

2,3-Dihydropyrrolo[1,2-*a*]quinazolin-5(1*H*)-one (**38**).

Solid **36** was added to cold methanolic sodium methoxide solution (10 ml of 0.4*M* solution/g **36**) and the mixture heated under reflux for 4 hours. The cooled mixture was filtered, solvents removed *in vacuo* and the residue extracted (× 3) with warm chloroform. The chloroform extracts were concentrated *in vacuo* and the resulting solids extracted with ether in a Soxhlet extractor for 4 hours to remove the [2,1-*b*] isomer **1**. The residual solids were dissolved in hot ethanol and decolourised. On cooling pure **38** (12%) mp 216-218° (ethanol), reported mp 222° [12], was obtained; ir (potassium bromide): 1635 cm^{-1}; pmr: δ 8.19 (H, complex d), 7.73-7.08 (3H, complex), 4.21 (2H, t), 3.12 (2H, t), 2.55-2.12 (2H, complex); ms: m/e 186 (100%) M^+.

Anal. Calcd. for $C_{11}H_{10}N_2O$: C, 71.0; H, 5.4; N, 15.1. Found: C, 70.6; H, 5.4; N, 15.1.

6*H*-1,2,3,4-Tetrahydropyrido[1,2-*a*]quinazolin-6-one (**39**).

Diamide **37** was cyclised exactly as described for **38**. The pure tricycle **39** was obtained as colourless needles (31%), mp 222-227° (ethanol), reported mp 218-219° [13]; ir (potassium bromide): 1630 cm^{-1}; pmr: δ 8.11 (1H, complex d), 7.90-7.40 (3H, complex), 4.08 (2H, t), 2.87 (2H, t), 1.89 (4H, complex); ms: m/e 200 (100%) M^+.

Anal. Calcd. for $C_{12}H_{12}N_2O$: C, 72.0; H, 6.0; N, 14.0. Found; C, 71.9; H, 6.0; N, 14.0.

Condensation Reactions between Benzaldehyde and Fused Quinazolones.

A mixture of the quinazolone (0.5 g) and benzaldehyde (5 ml) was heated at 150-160° for 10-30 minutes. If no phenylmethylene (benzylidene) derivative appeared on cooling the reaction mixture was diluted with ether and scratched. The products were recrystallised or fractionally recrystallised until material of chromatographic homogenuity was obtained.

2,3-Dihydro-1-methyl-3-(phenylmethylene)pyrrolo[2,1-*b*]quinazoline-9(1*H*)-one (**17**).

Condensation between benzaldehyde and **12** gave **17** as fine needles (54%), mp 168.5-169.5° (ethanol); ir (potassium bromide): 1665 cm^{-1}; ms: m/e 288 (40%) M^+, 287 (100%) $(M-1)^+$.

Anal. Calcd. for $C_{20}H_{18}N_2O$: C, 79.5; H, 6.0; N, 9.3. Found; C, 78.9; H, 6.25; N, 9.4.

2,3-Dihydro-1,1-dimethyl-3-(phenylmethylene)pyrrolo[2,1-*b*]quinazoline-9(1*H*)-one (**18**).

Condensation between benzaldehyde and **13** gave **18** as pale yellow prisms (66%), mp 172.5-173° (ethanol); ir (potassium bromide): 1665 cm^{-1}; ms: m/e 302 (58%) M^+, 301 (100%) $(M-1)^+$.

Anal. Calcd. for $C_{20}H_{18}N_2O$: C, 79.5; H, 6.0; N, 9.3. Found; C, 78.9; H, 6.25; N, 9.4.

2,3-Dihydro-2-methyl-3-(phenylmethylene)pyrrolo[2,1-*b*]quinazoline-9(1*H*)-one (**19**).

Condensation between benzaldehyde and **14** gave **19** as colourless needles (50%), mp 154.5-155° (ethanol); ir (potassium bromide): 1670 cm^{-1}; ms: m/e 288 (36%) M^+, 287 (100%) $(M-1)^+$.

Anal. Calcd. for $C_{19}H_{16}N_2O$: C, 79.5; H, 5.55 N, 9.7. Found; C, 79.15; H, 5.65; N, 9.6.

1-Carbethoxy-2,3-dihydro-3-(phenylmethylene)pyrrolo[2,1-*b*]quinazolin-9(1*H*)-one (**20**).

Condensation between benzaldehyde and **16** gave **20** as needles (76%), mp 204-205° (ethanol); ir (potassium bromide): 1735, 1680 cm^{-1}; ms: m/e 346 (35%) M^+, 273 $(M-CO_2Et)$ (100%).

Anal. Calcd. for $C_{21}H_{18}N_2O_3$: C, 72.8; H, 5.2; N, 8.1. Found; C, 72.7; H, 5.3; N, 8.0.

11*H*-6,7,8,9-Tetrahydro-6-(phenylmethylene)pyrido[2,1-*b*]quinazolin-11-one (**27**).

Condensation between benzaldehyde and **24** gave **27** as fine needles (39%), mp 141° (ethanol); ir (potassium bromide): 1665 cm^{-1}.

Anal. Calcd. for $C_{19}H_{16}N_2O$: C, 79.2; H, 5.55; N, 9.7. Found; C, 79.0; H, 5.6; N, 9.7.

E-7,8,9,10-Tetrahydro-7-(phenylmethylene)azepino[2,1-*b*]quinazolin-12(6*H*)-one (**28**) and *Z*-7,8,9,10-Tetrahydro-7-(phenylmethylene)azepino-[2,1-*b*]quinazolin-12(6*H*)-one (**29**).

Condensation between **26** and benzaldehyde gave a two component solid. The major isomer was easily obtained by recrystallisation as colourless needles (54%). This is assumed for steric reasons to be **28**. The compound has mp 158-159.5° (ethanol); ir (potassium bromide): 1675 cm^{-1}; pmr: δ 8.30 (1H, complex d), 8.10-7.10 (9H, complex), 4.30 (2H, broad s), 2.75 (2H, broad s), 1.90 (4H, broad complex).

Anal. Calcd. for $C_{20}H_{18}N_2O$: C, 79.5; H, 6.0; N, 9.3. Found; C, 79.1; H, 6.3; N, 9.2.

The minor isomer from the reaction was obtained by repeated fractional recrystallisation (8%) and was assumed to be the *Z* isomer **29**. The compound has mp 140-141° (ether); ir (potassium bromide): 1670 cm^{-1}; pmr: δ 8.23 (1H, complex d), 7.90-6.50 (9H, complex), 4.36 (2H, broad s), 2.57 (2H, broad s), 1.85 (4H, broad complex).

Anal. Calcd. for $C_{20}H_{18}N_2O$: C, 79.5; H, 6.0; N, 9.3. Found: C, 79.3; H, 6.1; N, 9.2.

2,3-Dihydro-3-(phenylmethylene)pyrrolo[1,2-*a*]quinazolin-5(1*H*)-one (**40**).

Condensation between benzaldehyde and **38** gave **40** as long colourless needles (79%), mp 280-282° (ethanol); ir (potassium bromide): 1630 cm^{-1}.

Anal. Calcd. for $C_{18}H_{14}N_2O$: C, 78.8; H, 5.1; N, 10.2. Found; C, 78.8;

H, 5.1; N, 10.2.

E-6*H*-1,2,3,4-Tetrahydro-4-(phenylmethylene)pyrido[1,2-*a*]quinazolin-6-one (**41**) and *Z*-6*H*-1,2,3,4-Tetrahydro-4-(phenylmethylene)pyrido[1,2-*a*]-quinazolin-6-one (**42**).

Condensation between **39** and benzaldehyde gave a two component solid. Recrystallisation from ethyl acetate gave the major product **41** (56%) which was assigned the *E* configuration for steric reasons. It had mp 238-241° (ethyl acetate); ir (potassium bromide): 1630 cm^{-1}; pmr (hexadeuteriodimethylsulphoxide): δ 8.15 (2H, complex), 7.95-7.15 (8H, complex), 4.20 (2H, t), 2.89 (2H, complex), 2.05 (2H, complex).

Anal. Calcd. for $C_{19}H_{16}N_2O$: C, 79.2; H, 5.6; N, 9.7. Found: C, 78.9; H, 5.6; N, 9.7.

Concentration of the mother liquors gave a two component solid which was repeatedly fractionally recrystallised to yield **42** (11%), mp 240-243° (ether); ir (potassium bromide): 1635 cm^{-1}; pmr (hexadeuteriodimethylsulphoxide): δ 8.10 (2H, complex), 8.00-7.20 (8H, complex), 4.21 (2H, t), 2.96 (2H, complex), 2.10 (2H, complex).

Anal. Calcd. for $C_{19}H_{16}N_2O$: C, 79.2; H, 5.6; N, 9.2. Found: C, 79.15; H, 5.6; N, 9.7.

Reactions of Fused Quinazolones with Ethyl Chloroformate.

Method A.

The quinazolone was treated with excess ethyl chloroformate, as described in reference [2], for 24-40 hours at 140-150°. The reaction mixtures were diluted with ethyl acetate, filtered and the ethyl acetate extracts concentrated *in vacuo* to yield the dicarbethoxy derivatives.

Method B.

The quinazolone was lithiated using LDA, as described in reference [1], and then treated with excess ethyl chloroformate. After removal of the solvents the crude product was recrystallised from the appropriate solvent.

3,3-Dicarbethoxy-2,3-dihydro-1-methylpyrrolo[2,1-*b*]quinazolin-9(1*H*)-one (**21**).

Condensation between **12** and ethyl chloroformate as described in method A gave colourless prisms of pure **21** (41%) mp 112.5-113° (ether); ir (potassium bromide): 1740, 1730, 1680 cm^{-1}; pmr: δ 8.18 (1H, complex d), 7.82-7.16 (3H, complex), 4.92-4.60 (1H, complex), 4.58-4.06 (4H, q, J = 7 Hz), 3.16 (1H, dd), 2.56 (1H, dd), 1.52 (3H, d, J = 6 Hz), 1.36 (6H, t, J = 7 Hz).

Anal. Calcd. for $C_{18}H_{20}N_2O_5$: C, 62.8; H, 5.8; N, 8.1. Found: C, 63.0; H, 5.8; N, 8.2.

3,3-Dicarbethoxy-2,3-dihydro-1,1-dimethylpyrrolo[2,1-*b*]quinazolin-9(1*H*)-one (**22**).

Reaction between **13** and ethyl chloroformate as described in method B gave **22** as heavy prisms (58%), mp 91° (ether/light petroleum); ir (potassium bromide): 1730, 1720, 1680 cm^{-1}; pmr: δ 8.13 (1H, complex d), 7.78-7.07 (3H, complex), 4.30 (4H, q, J = 7 Hz), 2.80 (2H, s), 1.72 (6H, s), 1.30 (6H, t, J = 7 Hz).

Anal. Calcd. for $C_{19}H_{22}N_2O_5$: C, 63.7; H, 6.1; N, 7.8. Found: C, 63.7; H, 6.2; N, 7.7.

11*H*-6,6-Dicarbethoxy-6,7,8,9-tetrahydropyrido[2,1-*b*]quinazolin-11-one (**32**).

Compound **24** was treated with ethyl chloroformate as described in method A to yield large colourless prisms of **32** (7%), mp 103-104° (ether/light petroleum); ir (potassium bromide): 1735, 1725, 1670 cm^{-1}; pmr: δ 8.12 (1H, complex d), 7.80-7.10 (2H, complex), 4.50-3.90 (6H, complex), 2.61 (2H, complex q), 2.04 (2H, complex), 1.28 (6H, t, J = 7 Hz).

Anal. Calcd. for $C_{18}H_{20}N_2O_5$: C, 62.8; H, 5.8; N, 8.1. Found: C, 62.85; H, 5.8; N, 7.85.

Treatment of **38** with Ethyl Chloroformate.

The [1,2-*a*] analogue **38** was heated for 40 hours with excess ethyl chloroformate as described in method A. From the reaction extracts an intensely yellow solid was obtained which was recrystallised from xylene/light petroleum to afford deep yellow needles of **43** (19%), mp 138-139°; ir (potassium bromide): 1780, 1695 cm^{-1}; pmr: δ 8.00-6.50 (4H, complex), 4.80-3.60 (6H, complex), 2.95 (2H, complex), 1.35 (6H, 2t); ^{13}C nmr: 13.8 (q), 14.6 (q), 26.1 (t), 45.7 (t), 59.3 (t), 65.1 (t), 85.3 (s), 111.9 (d), 113.2 (s), 121.2 (d), 136.0 (d), 141.3 (s), 144.8 (s), 149.9 (s), 159.0 (s), 164.6 (s).

Anal. Calcd. for $C_{17}H_{18}N_2O_6$: C, 61.8; H, 5.45; N, 8.5. Found: C, 62.3; H, 5.5; N, 8.5.

REFERENCES AND NOTES

[1] Part **3**. A. D. Dunn and K. I. Kinnear, *J. Heterocyclic Chem.*, **22**, 311 (1985).

[2] A. D. Dunn, E. L. M. Guy and K. I. Kinnear, *J. Heterocyclic Chem.*, **20**, 779 (1983).

[3] A. D. Dunn and K. I. Kinnear, *J. Heterocyclic Chem.*, **21**, 603 (1984).

[4a] R. B. Moffett, "Organic Syntheses", Coll Vol IV, p 652. [b] R. B. Moffett, *ibid.*, p 357.

[5] F. F. Blicke and C. J. Lu, *J. Am. Chem. Soc.*, **77**, 29 (1955).

[6] T. Onaka, *Tetrahedron Letters*, 4387 (1971).

[7] Kh. M. Shakhidoyatov, A. Irisbaev, L. M. Yun, E. Oripov and Ch. Sh. Kadyrov, *Khim. Geterotsikl. Soedin.*, 1564 (1976).

[8] E. Späth and N. Platzer, *Chem. Ber.*, **68**, 2221 (1935).

[9] S. Petersen and E. Tietze, *Ann. Chem.*, **623**, 166 (1959).

[10] We thank the late Dr. J. S. Nicholson for providing this service.

[11] T. Kametani, C. V. Loc, T. Higa, M. Koizumi, M. Ihara and F. Fukumoto, *J. Am. Chem. Soc.*, **99**, 2306 (1977).

[12] R. Landi Vittory and F. Gatta, *Gaz. Chim. Ital.*, **99**, 59 (1969).

[13] H. Möhrle and C. M. Siedel, *Chem. Ber.*, **106**, 1595 (1973).

[14] S. Kambe and H. Yasude, *Bull. Soc. Chem. Japan*, **39**, 2549 (1966).

[15] J. Cologne and J-M. Pouchol, *Bull. Soc. Chim. France*, 598 (1962).