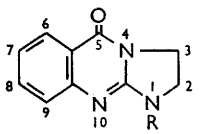
711. *Cyclic Amidines. Part XII.*[1] *Imidazo*[2,1-b]*quinazolines and Oxazolo*[2,3-b]*quinazolines.*

By R. J. Grout and M. W. Partridge.

Basic ethers of 2-chloro-4-hydroxyquinazoline have been shown to undergo a thermal rearrangement, followed by cyclisation to imidazo[2,1-*b*]-quinazolines (I). The latter were also obtained by a direct synthesis, which with modification led to oxazolo[2,3-*b*]quinazolines (II). No useful chemotherapeutic activity was observed in these compounds.

Experiments on rearrangements of basic ethers of quinazolines led to the production of a derivative of 5-oxoimidazo[2,1-*b*]quinazoline (I). The work now described relates to compounds of this type and to analogous oxazolo[2,3-*b*]quinazoline derivatives (II).

2,4-Dichloroquinazoline and sodium 2-diethylaminoethoxide at 10° afforded a chloro-ether, easily hydrolysable to 2,4-dihydroxyquinazoline, and which, in view of the difference in reactivity of the halogens in 2,4-dichloroquinazoline,[2] was assigned the structure (III; R = NEt_2). On distillation, this ether (III; R = NEt_2) lost the elements of ethyl chloride to give 1-ethyl-1,2,3,5-tetrahydro-5-oxoimidazo[2,1-*b*]quinazoline (I; R = Et)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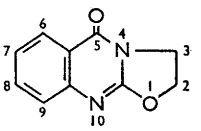
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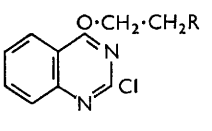
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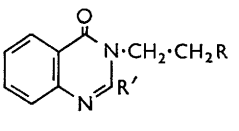

(IV)

which was unambiguously synthesised from 2-chloro-3-2′-chloroethyl-3,4-dihydro-4-oxoquinazoline [1] (IV; R = R′ = Cl) and ethylamine and, as expected, was stable to concentrated hydrochloric acid and to permanganate in acetone. It was spectroscopically very similar to both 2-amino-3-ethyl-3,4-dihydro-4-oxo- (IV; R = H, R′ = NH_2) and 2-ethylamino-4-hydroxy-quinazoline.[3]

The 1-methylimidazoquinazoline (I; R = Me) was analogously produced when the quinazoline ether (III; R = NMe_2) was heated at 140°; 1,2,3,4-tetrahydro-3-methyl-2,4-dioxoquinazoline was an additional product of this reaction. This result, together with our observations on the rearrangements of basic ethers of quinazolines,[1] implied that 3-aminoalkylquinazolines (IV; R = NEt_2 or NMe_2, R′ = Cl), formed by an intramolecular rearrangement of the ethers (III; R = NEt_2 or NMe_2), were intermediates in the cyclisation.

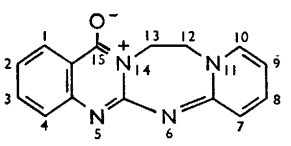
A direct synthesis of this type of intermediate was not achieved. The corresponding 2-hydroxyquinazoline (IV; R = NEt_2, R′ = OH) was produced by alkylation of 2,4-dihydroxyquinazoline with 2-diethylaminoethyl chloride, by treatment with hot nitrous acid of the product (IV; R = NEt_2, R′ = NH_2) of a similar alkylation of 2-amino-4-hydroxyquinazoline, and unambiguously from methyl *o*-ethoxycarbonylaminobenzoate and 2-diethylaminoethylamine. However this 3-substituted 2-hydroxyquinazoline (IV; R = NEt_2, R′ = OH) could not be caused to react with a phosphorus chloride. We are not aware of a previous example of this type of reaction.

The imidazoquinazolines (I; R = H, OH, Bu^n, $[CH_2]_2$·OH, C_6H_{11}, CH_2Ph, Ph, *p*-C_6H_4Me, *p*-MeO·C_6H_4, *p*-HO·C_6H_4, *p*-Me_2N·C_6H_4, *p*-Et_2N·C_6H_4, β-$C_{10}H_7$) were synthesised from the appropriate amine and 2-chloro-3-2′-chloroethyl-3,4-dihydro-4-oxoquinazoline (IV; R = R′ = Cl). 2-Aminopyridine afforded two products; the spectroscopic

[1] Part XI, preceding paper.
[2] Lange and Sheibley, *J. Amer. Chem. Soc.*, 1931, **53**, 3867; 1933, **55**, 1188; Curd, Landquist, and Rose, *J.*, 1947, 775.
[3] Grout and Partridge, *J.*, 1960, 3540.

similarity between the colourless product and its phenyl analogue favoured the structure (I; R = 2-pyridyl). Either of the possible tetracyclic compounds having a seven-membered ring was consistent with the composition of the yellow product; its high-intensity absorption band at 365—400 mμ appears to be referable to an extended chromophore as in (V), and not to a displaced and intensified $n \longrightarrow \pi$-band of a simpler quinazoline.

Interaction of 2-aminoethylammonium toluene-*p*-sulphonate and methyl *o*-ethoxycarbonylaminobenzoate appeared to offer an alternative route to the imidazoquinazoline (I; R = H). However, its isomer (VI) was formed in low yield.



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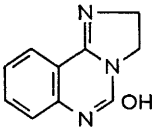

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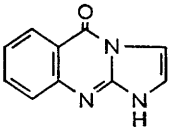
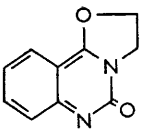


(VII)

1,2,3,5-Tetrahydro-5-oxoimidazo[2,1-*b*]quinazoline (I; R = H) was not dehydrogenated by palladised charcoal, and the hydrobromide of a bromo-derivative could not be fully dehydrobrominated. Ethyl hydantoate, benzenesulphonyl chloride, and methyl anthranilate, possibly by interaction of intermediately formed ethoxycarbonylmethylcyanamide [3] with the methyl anthranilate, afforded an acidic substance $C_{10}H_7N_3O_2$ which may have been a 2- or 3-hydroxy-derivative of (VII), but it could not be converted into a chloro-derivative for reduction to the imidazoquinazoline (VII). However, the cyclic secondary hydroxylamine (I; R = OH) with benzenesulphonyl chloride in pyridine did yield the dehydrogenated imidazoquinazoline (VII) (a similar dehydration has recently been described [4]). The presumption of elimination of benzenesulphonic acid from an intermediate ester (I; R = Ph·SO_2·O) makes the process consistent with other decompositions involving elimination of an arenesulphonic acid.[5] This imidazoquinazoline (VII) was amphoteric and furnished two isomeric *N*-methyl derivatives.

The oxazolo[2,3-*b*]quinazoline (II) was produced by cyclization of 3-2′-chloroethyl-3,4-dihydro-2-hydroxy-4-oxoquinazoline (IV; R = Cl, R′ = OH) with alkali, or by alkylation of 2,4-dihydroxyquinazoline with ethylene dibromide. The possibility of the formation of the angular isomers (VIII), or the corresponding oxazolo[3,2-*a*]quinazoline, was not excluded by these syntheses. However, the assigned linear structure was confirmed by alkaline hydrolysis to 3,4-dihydro-2-hydroxy-3-2′-hydroxyethyl-4-oxoquinazoline [1] (IV; R = R′ = OH) and by direct synthesis from 2-chloro-4-hydroxyquinazoline and ethylene oxide. 2- and 3-Methyl derivatives of compound (II) were analogously formed by the cyclisation of appropriate 3-2′-chloroalkyl-2-hydroxyquinazolines.

A number of projected syntheses of the oxazoloquinazoline (II) were unsuccessful. 2-Chloro-4-hydroxyquinazoline failed to react with ethylene chlorohydrin. Cyclisation



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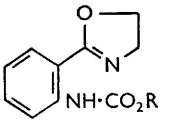

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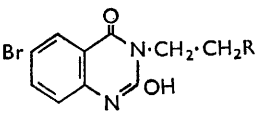

(X)

of the cyclic imidoate (IV; R = Cl, R′ = OEt) by elimination of ethyl chloride could not be effected. Attempted syntheses of the angular isomer (VIII) by thermal cyclisation of the substituted oxazolines (IX; R = Et or Ph) furnished no recognisable product.

[4] Bonnett, Brown, Clark, Sutherland, and Todd, *J.*, 1959, 2094.
[5] Cooper and Partridge, *J.*, 1954, 3429; Partridge and Turner, *J.*, 1958, 2086.

Bromination of the oxazoloquinazoline (II) resulted in fission of the oxazolidine ring, yielding the dibromoquinazoline (X; R = Br), the orientation of which was deduced by comparison of the product of its alkaline hydrolysis (X; R = OH) with a specimen unequivocally synthesised from methyl 5-bromoanthranilate. The dibromoquinazoline (X; R = Br) with dimethylaniline afforded the tertiary base (X; R = NMePh).

A number of the foregoing compounds were examined for schistosomicidal, molluscicidal, and viricidal activity; none was observed.

Experimental

1-*Ethyl*-1,2,3,5-*tetrahydro*-5-*oxoimidazo*[2,1-b]*quinazoline* (I; R = Et).—(i) 2-Diethylaminoethanol (50 ml.) containing sodium (0·58 g.) was treated at 5—10° during 25 min. with 2,4-dichloroquinazoline (5 g.), stirred at 5—10° for 30 min., kept at room temperature for 1 hr., and filtered. The oil resulting from the removal of 2-diethylaminoethanol *in vacuo* was collected in ether, washed with water, dried (K_2CO_3), and recovered as 2-chloro-4-2′-diethylaminoethoxyquinazoline (III; R = NEt_2) (5·6 g.) which was characterised as its *picrate*, m. p. 152° (Found: C, 47·2; H, 4·3; N, 16·5. $C_{20}H_{21}ClN_6O_8$ requires C, 47·2; H, 4·2; N, 16·5%), as its *hydrochloride*, m. p. 190° (from ethanol) (Found: C, 53·6; H, 6·1. $C_{14}H_{19}Cl_2N_3O$ requires C, 53·2; H, 6·1%), and by its hydrolysis with concentrated hydrochloric acid to 2,4-dihydroxyquinazoline, m. p. and mixed m. p. 350°.

On distillation at 211°/1·3 mm., this oil gave the *imidazoquinazoline* (I; R = Et) (3 g., 56%), which crystallised from benzene–light petroleum as prisms, m. p. 105—106°, $\lambda_{max.}$ 232, 273, and 331 mμ (ε 35,200, 17,600, and 3200) [Found: C, 67·4; H, 5·9; N, 19·9%; *M* (Rast), 214. $C_{12}H_{13}N_3O$ requires C, 67·0; H, 6·1; N, 19·5%; *M*, 215]. Its *picrate* crystallised from ethanol as prisms, m. p. 257·5—258° (decomp.) (Found: C, 48·6; H, 3·6; N, 18·8. $C_{18}H_{16}N_6O_8$ requires C, 48·7; H, 3·6; N, 18·9%). With bromine in chloroform it furnished a *bromo-derivative hydrobromide* which separated from ethanol as prisms, m. p. 297—298° (decomp.) (Found: C, 38·4; H, 3·8; N, 10·7. $C_{12}H_{13}Br_2N_3O$ requires C, 38·4; H, 3·5; N, 11·2%).

(ii) 2-Chloro-3-2′-chloroethyl-3,4-dihydro-4-oxoquinazoline (IV; R = R′ = Cl) (2·4 g.) was kept in ethanol (30 ml.) with ethylamine (4·1 g.) for 6 days. Removal of the solvent yielded an oil which when crystallised from aqueous ammonia and from benzene–light petroleum afforded the imidazoquinazoline (I; R = Et), m. p. and mixed m. p. 104—105° [picrate, m. p. and mixed m. p. 257—258° (decomp.)].

1,2,3,5-*Tetrahydro*-1-*methyl*-5-*oxoimidazo*[2,1-b]*quinazoline* (I; R = Me).—2,4-Dichloroquinazoline (10 g.) and 2-dimethylaminoethanol (4·5 g.), boiled in acetone (90 ml.) for 90 min., deposited 2-*chloro*-4-2′-*dimethylaminoethoxyquinazoline hydrochloride* (III; R = NMe_2,HCl) (11·1 g.) which crystallised from methanol–ether as plates, m. p. 186—186·5° (Found: C, 50·1; H, 5·1. $C_{12}H_{15}Cl_2N_3O$ requires C, 50·0; H, 5·3%); the derived *picrate* had m. p. 171—172° (decomp.) (Found: C, 45·3; H, 3·6. $C_{18}H_{17}ClN_6O_8$ requires C, 45·0; H, 3·6%).

The oily base, liberated from the hydrochloride (5 g.) by ammonia, effervesced at 140°. After 10 min. at 140°, lactic acid-soluble material was extracted, liberated with ammonia, extracted with ether for 4 days, and recovered. Fractional crystallisation from ethyl acetate then afforded 1,2,3,4-tetrahydro-3-methyl-2,4-dioxoquinazoline,[6] m. p. and mixed m. p. 234—236°, and the *imidazoquinazoline* (I; R = Me) (0·9 g.) which separated from light petroleum as needles, m. p. 172—174°, $\lambda_{max.}$ 230, 266, 273, 326, and 340 (infl.) mμ (ε 51,000, 19,600, 20,200, 3200, and 2700) (Found: C, 65·4; H, 5·4; N, 21·4. $C_{11}H_{11}N_3O$ requires C, 65·7; H, 5·5; N, 20·9%). Its *picrate* separated from water as prisms, m. p. 246° (decomp,) (Found: loss at 120°/vac., 2·1; C, 46·7; H, 3·4. $C_{17}H_{14}N_6O_8,\frac{1}{2}H_2O$ requires H_2O, 2·0; C, 46·5; H, 3·4%). The *hydrochloride* formed prisms, m. p. 265° (decomp.), from ethanol (Found: C, 47·0; H, 5·6; N, 15·0. $C_{11}H_{12}ClN_3O,2\frac{1}{2}H_2O$ requires C, 46·7; H, 6·1; N, 14·9%).

2-*Amino*-3-2′-*diethylaminoethyl*-3,4-*dihydro*-4-*oxoquinazoline* (IV; R = NEt_2, R′ = NH_2) was obtained (2·98 g., 88%) when 2-amino-4-hydroxyquinazoline (2 g.) and 2-diethylaminoethyl chloride hydrochloride (2·4 g.) in ethanol (25 ml.) containing sodium (0·61 g.) and sodium iodide (0·2 g.) was heated to the b. p., then kept overnight and worked up. It formed prisms, m. p. 119—121°, from benzene–light petroleum (Found: C, 64·8; H, 7·7; N, 21·9. $C_{14}H_{20}N_4O$

[6] Bogert and Scatchard, *J. Amer. Chem. Soc.*, 1919, **41**, 2052.

requires C, 64·6; H, 7·7; N, 21·5%). Its *picrate* (prisms from acetone) had m. p. 236—237·5° (decomp.) (Found: N, 19·8. $C_{20}H_{23}N_7O_8$ requires N, 20·0%), and its *methiodide* (prisms from methanol) had m. p. 220° (Found: C, 44·5; H, 5·6. $C_{15}H_{23}IN_4O$ requires C, 44·8; H, 5·8%).

3-2′-Diethylaminoethyl-3,4-dihydro-2-hydroxy-4-oxoquinazoline (IV; R = NEt_2, R′ = OH).—(i) A boiling solution of the foregoing 2-aminoquinazoline (2·6 g.) in 10% hydrochloric acid (60 ml.) was treated during 30 min. with 50% aqueous sodium nitrite (30 ml.), then basified with ammonia. The precipitated *2-hydroxyquinazoline* (IV; R = NEt_2, R′ = OH) (1·5 g.) crystallised from aqueous ethanol as prisms, m. p. 148—149° (Found: C, 64·2; H, 7·5; N, 16·1. $C_{14}H_{19}N_3O_2$ requires C, 64·3; H, 7·3; N, 16·1%). From aqueous acetic acid its *picrate* formed prisms, m. p. 219—220° (decomp.) (Found: C, 49·1; H, 4·7. $C_{20}H_{22}N_6O_9$ requires C, 49·0; H, 4·5%); its *hydrochloride* crystallised from ethanol as needles, m. p. 265—266° (Found: C, 56·7; H, 6·8; N, 14·0. $C_{14}H_{20}ClN_3O_2$ requires C, 56·5; H, 6·8; N, 14·1%), and its *methiodide* formed prisms, m. p. 245° (decomp.), from methanol (Found: C, 44·8; H, 5·5. $C_{15}H_{22}IN_3O_2$ requires C, 44·7; H, 5·5%).

(ii) A solution of 2-diethylaminoethyl chloride hydrochloride (9·5 g.) was boiled for 5 hr. with 2,4-dihydroxyquinazoline (8·1 g.) in aqueous ethanol (250 ml.) containing sodium (3·4 g.) and sodium iodide (0·8 g.), and then concentrated. The basic fraction of the precipitate, after recrystallisation, afforded the same compound (6 g., 46%), m. p. and mixed m. p. 148—149° and the same picrate, m. p. and mixed m. p. 219—220° (decomp.), as above.

(iii) Methyl *o*-ethoxycarbonylaminobenzoate (4·5 g.), when heated at 180° for 2 hr. with 2-diethylaminoethylamine (2·3 g.), diluted with chloroform, extracted with dilute hydrochloric acid, and basified, furnished this 2-hydroxyquinazoline (IV; R = NEt_2, R′ = OH) (1·6 g.), m. p. and mixed m. p. 148—149°; the picrate prepared from this had m. p. and mixed m. p. 219—220° (decomp.).

1,2,3,5-Tetrahydro-5-oxo-1-phenylimidazo[2,1-b]*quinazoline* (I; R = Ph) separated as its *hydrochloride* (2·4 g., 80%) when 2-chloro-3-2′-chloroethyl-3,4-dihydro-4-oxoquinazoline [1] (2·4 g.) was boiled for 1 hr. with aniline (1·9 g.) in ethanol (25 ml.), and crystallised from methanol–ether as prisms, m. p. 230—233° (Found: C, 63·8; H, 4·4; N, 13·8. $C_{16}H_{14}ClN_3O$ requires C, 64·1; H, 4·7; N, 14·0%). The *base* (0·24 g., 9%), precipitated from the mother-liquor with ammonia, separated from ethanol as prisms, m. p. 164—165°, $\lambda_{max.}$ 223, 286, 296, (infl.), and 327 mμ (ε 31,600, 28,100, 23,800, and 3660) (Found: C, 72·9; H, 4·8; N, 15·9. $C_{16}H_{13}N_3O$ requires C, 73·0; H, 5·0; N, 16·0%).

1,2,3,5-Tetrahydro-5-oxoimidazo[2,1-b]*quinazolines* (I) listed in the Table were analogously prepared from the 2-chloro-3-2′-chloroethylquinazoline [1] (IV; R = R′ = Cl) and the appropriate amine.

Interaction of the 2-Chloro-3-2′-chloroethylquinazoline (IV; R = R′ = Cl) *and 2-Aminopyridine.*—These compounds reacted exothermically when heated at 135° for 15 min. The methanol-soluble product (31%), on basification with ammonia, collection in ether, and recovery, formed colourless prisms, m. p. 185—186°, from benzene–light petroleum and was probably the *pyridylimidazo*[2,1-b]*quinazoline* (I; R = C_5H_4N); it had $\lambda_{max.}$ 222, 240, (infl.), 296, and 330 (infl.) mμ (ε 41,400, 26,400, 35,200, and 4900) (Found: C, 67·9; H, 4·5; N, 21·3. $C_{15}H_{12}N_4O$ requires C, 68·2; H, 4·6; N, 21·2%). Its *picrate* separated from aqueous acetic acid as prisms, m. p. 204° (decomp.) (Found: C, 51·2; H, 3·0. $C_{21}H_{15}N_7O_8$ requires C, 51·1; H, 3·1%). The methanol-insoluble product crystallised from methanol as needles, m. p. 352° (decomp.), and was probably *12,13-dihydro-15-oxopyrido*[1,2-a]*quinazo*[2,3-d]-[1,3,5]-*triazepine* (V) *hydrochloride* (Found: C, 53·8; H, 5·1; Cl, 10·7; N, 16·1. $C_{15}H_{12}N_4O,HCl,2H_2O$ requires C, 53·5; H, 5·1; Cl, 10·5; N, 16·6%); the *base* (V) separated from ethanol as yellow prisms, m. p. 264° (decomp.), $\lambda_{max.}$ 215, 304, 365, and 395 (infl.) mμ (ε 37,900, 25,500, 33,800, and 18,500) (Found: C, 67·8; H, 4·5; N, 20·8. $C_{15}H_{12}N_4O$ requires C, 68·2; H, 4·6; N, 21·2%); the *picrate* crystallised from glacial acetic acid as needles, m. p. 249° (decomp.) (Found: C, 51·3; H, 3·2; N, 19·6. $C_{21}H_{15}N_7O_8$ requires C, 51·1; H, 3·0; N, 19·9%).

2-Hydroxy-4,5-dihydroimidazo[1,2-c]*quinazoline* (VI).—This *compound* separated (0·53 g.) when methyl *o*-ethoxycarbonylaminobenzoate (5·6 g.) was heated at 180° for 2 hr. with 2-aminoethylammonium toluene-*p*-sulphonate (5·8 g.), the melt was digested with water and chloroform, and the aqueous layer was basified with ammonia. It crystallised from 2-ethoxyethanol as prisms, m. p. 299—300° (decomp.), $\lambda_{max.}$ 250, 305 (infl.), 316, and 330 mμ (ε 8150, 4600, 6800, and 5600) (Found: C, 63·8; H, 4·7; N, 22·5. $C_{10}H_9N_3O$ requires C, 64·2; H, 4·9; N, 22·5%). Its *picrate* formed tablets, m. p. 301° (decomp.), from aqueous acetic acid (Found: C, 46·3;

1,2,3,5-*Tetrahydro*-5-*oxoimidazo*[2,1-b]*quinazolines* (I).

R	M. p.	Yield (%)	Formula	Found (%) C	Found (%) H	Found (%) N	Reqd. (%) C	Reqd. (%) H	Reqd. (%) N
Bu^n	65—66°	25	$C_{14}H_{17}N_3O$	68·8	6·8		69·1	7·0	
picrate	174—174·5		$C_{20}H_{20}N_6O_8$	51·2	4·5		50·9	4·3	
HO·[CH_2]$_2$	138·5—140	54	$C_{12}H_{13}N_3O_2$	62·5	5·4	18·1	62·3	5·7	18·2
picrate	220—221 *		$C_{18}H_{16}N_6O_9$	47·1	3·6		47·0	3·5	
Cyclohexyl	142—143	34	$C_{16}H_{19}N_3O$	71·2	6·9	15·4	71·3	7·1	15·6
picrate	228—229 *		$C_{22}H_{22}N_6O_8$	52·8	4·6		53·0	4·5	
Ph·CH_2	124—124·5	39	$C_{17}H_{15}N_3O$	73·4	5·3		73·6	5·5	
picrate [a]	158—159 *		$C_{23}H_{18}N_6O_8,H_2O$	52·8	3·8		52·7	3·8	
p-C_6H_4Me	198·5	93	$C_{17}H_{15}N_3O$	73·7	5·3	14·9	73·6	5·5	15·2
HCl	231—236		$C_{17}H_{16}ClN_3O$	64·8	5·2		65·1	5·1	
p-MeO·C_6H_4	183—183·5	95	$C_{17}H_{15}N_3O_2$	69·8	5·4	13·9	69·6	5·2	14·3
HCl	240 *.		$C_{17}H_{16}ClN_3O_2$	62·1	4·9	12·5	61·9	4·9	12·7
p-HO·C_6H_4	253—254	85	$C_{16}H_{13}N_3O_2$	68·2	4·8		68·8	4·7	
HCl	280		$C_{16}H_{14}ClN_3O_2$	61·0	4·5	13·0	60·9	4·5	13·3
p-Me_2N·C_6H_4	219—220	92	$C_{18}H_{18}N_4O$	70·3	6·0	18·2	70·6	5·9	18·3
HCl	239 *.		$C_{18}H_{19}ClN_4O$	62·7	5·8		63·1	5·6	
p-Et_2N·C_6H_4	157·5—158	93	$C_{20}H_{22}N_4O$	71·7	6·5	16·9	71·8	6·6	16·8
HCl	282 *.		$C_{20}H_{23}ClN_4O$	64·8	6·5		64·8	6·3	
β-Naphthyl	199—200	95	$C_{20}H_{15}N_3O$	76·7	4·9	13·3	76·7	4·8	13·4
HO [b]	226·5 *	52	$C_{10}H_9N_3O_2$	58·9	4·6	21·0	59·1	4·5	20·7
picrate	194 *.		$C_{16}H_{12}N_6O_9$	44·7	3·2	19·5	44·5	2·8	19·4
HCl	250—251 *		$C_{10}H_{10}ClN_3O_2$			17·8			17·5
H [c]	266—268	50	$C_{10}H_9N_3O$	64·0	4·7	22·7	64·2	4·9	22·5
picrate	269 *.		$C_{16}H_{12}N_6O_8$	46·1	3·2	19·9	46·2	2·9	20·2
acetyl	244—245		$C_{12}H_{11}N_3O_2$	62·6	4·5	18·4	62·9	4·8	18·3
Br [d]	308—309 *		$C_{10}H_8BrN_3O$	44·7	3·1	15·2	45·1	3·0	15·8
Br HBr	346 *		$C_{10}H_9Br_2N_3O$	Br, 45·7		11·6	Br, 46·1		12·1

* With decomp.

[a] Found: loss at 100°/vac., 3·2. $C_{23}H_{18}N_6O_8,H_2O$ requires H_2O, 3·4%. [b] $\lambda_{max.}$ 233, 267, and 318 mμ (ε 34,200, 12,900, and 3060); this compound gave a blue-green colour with ferric chloride. [c] $\lambda_{max.}$ 230, 270, and 327 mμ (ε 45,200, 14,000, and 3400). [d] Found: Br, 31·8. $C_{10}H_8BrN_3O$ requires Br, 30·0%.

H, 3·0; N, 20·2. $C_{16}H_{12}N_6O_8$ requires C, 46·2; H, 2·9; N, 20·2%). The water- and chloroform-insoluble product was *NN'*-di-*o*-aminobenzoylethylenediamine, m. p. 244° (Found: C, 64·0; H, 6·1; N, 18·8. Calc. for $C_{16}H_{18}N_4O_2$: C, 64·4; H, 6·1; N, 18·8%); Finger [7] records m. p. 245°; the isomeric 1,2-bis-3-phenylureidoethane,[8] m. p. 245°, depressed its m. p. to 230°.

Interaction of Ethyl Hydantoate, Methyl Anthranilate, and Benzenesulphonyl Chloride.—Ethyl hydantoate (14·6 g.) and benzenesulphonyl chloride (17·7 g.) were kept in pyridine (35 ml.) overnight and heated on a steam-bath for 4 hr. with methyl anthranilate (15·1 g.). The solid which separated, crystallised, after purification *via* its sodium salt, from dimethylformamide as needles, m. p. 350° (decomp.) (Found: C, 59·5; H, 3·1; N, 20·3. $C_{10}H_7N_3O_2$ requires C, 59·7; H, 3·5; N, 20·9%). With phosphoryl chloride this compound was completely carbonised.

1,5-*Dihydro*-5-*oxoimidazo*[2,1-b]*quinazoline* (VII).—1,2,3,5-Tetrahydro-1-hydroxy-5-oxoimidazo[2,1-*b*]quinazoline (4·5 g.) was kept for 70 hr. in pyridine (100 ml.) with benzenesulphonyl chloride (3·9 g.) to give the *dihydroimidazoquinazoline* (2·85 g.) which sublimed at 210°/0·02 mm. and had m. p. 302° (decomp.), $\lambda_{max.}$ 236, 256, 285, 295, and 354 mμ (ε 35,000, 14,600, 5700, 5400, and 5400) (Found: C, 64·5; H, 3·8; N, 22·5. $C_{10}H_7N_3O$ requires C, 64·9; H, 3·8; N, 22·7%). This compound was alkali-soluble and furnished a *picrate* (needles from glacial acetic acid), m. p. 256—259° (decomp.) (Found: N, 19·9. $C_{16}H_{10}N_6O_8$ requires N, 20·3%), and an *acetyl derivative* (needles from ethanol), m. p. 191° (decomp.) [Found: C, 63·3; H, 4·3; N, 18·0%; *M* (Rast), 223. $C_{12}H_9N_3O_2$ requires C, 63·4; H, 4·0; N, 18·5%; *M*, 227].

In less pyridine (60 ml.), these reagents furnished, in addition, an alkali-insoluble *benzenesulphonyl derivative* (8%), m. p. 231° (decomp.) (from 2-ethoxyethanol) (Found: C, 58·9; H, 3·8. $C_{16}H_{11}N_3O_3S$ requires C, 59·1; H, 3·4%).

With methyl sulphate and alkali two N-*methyl derivatives*, stable to hydriodic acid and separable by ethanol, were obtained. After basification the ethanol-soluble compound (47%)

[7] Finger, *J. prakt. Chem.*, 1893, **48**, 92.
[8] Curtius and Hechtenburg, *J. prakt. Chem.*, 1923, **105**, 289.

crystallised from benzene–light petroleum as prisms, m. p. 174—175° (Found: N, 21·0. $C_{11}H_9N_3O$ requires N, 21·1%), and the ethanol-insoluble isomer (28%) (needles from light petroleum) had m. p. 182—183° (Found: C, 66·3; H, 4·8; N, 20·9. $C_{11}H_9N_3O$ requires C, 66·3; H, 4·6; N, 21·1%).

2,3-*Dihydro*-5-*oxo*-*oxazolo*[2,3-b]*quinazoline* (II).—(i) A solution of the 3-2′-chloroethylquinazoline (IV; R = Cl, R′ = OH) (6·7 g.) in dry acetone (100 ml.) was boiled with potassium carbonate (8·4 g.) for 3 hr., filtered, concentrated, and poured into water. The precipitated *oxazoloquinazoline* (5·4 g., 95%) had m. p. 165° (from ethanol), $\lambda_{max.}$ 222, 246, 254, 262, 308, and 320 (infl.) mμ (ε 36,700, 6300, 6450, 5800, 3300, and 2800) (Found: C, 63·6; H, 4·4; N, 15·0. $C_{10}H_8N_2O_2$ requires C, 63·8; H, 4·3; N, 14·9%). The yield on cyclisation with sodium ethoxide was 55%.

(ii) 2,4-Dihydroxyquinazoline (8·1 g.) when boiled with ethylene dibromide (20 g.) in ethanol (200 ml.) containing sodium (2·3 g.) gave the same compound (1·9 g.), m. p. and mixed m. p. 164—165°.

(iii) This oxazoloquinazoline (1·4 g.) separated when 2-chloro-4-hydroxyquinazoline [2] (1·8 g.) and ethylene oxide (30 ml.) in 0·4N-sodium hydroxide (25 ml.) were kept for 24 hr.; it had m. p. and mixed m. p. 163—165°, $\lambda_{max.}$ 222, 246, 254, 262, 309, and 320 (infl.) (ε 37,000, 6550, 6720, 6080, 3430, and 2820) (Found: C, 63·5; H, 4·2; N, 14·9%).

Hydrolysis to 3,4-dihydro-2-hydroxy-3-2′-hydroxyethyl-4-oxoquinazoline,[1] m. p. and mixed m. p. 254°, was effected by boiling 2N-sodium hydroxide (1½ hr.).

2,3-*Dihydro*-2-*methyl*-5-*oxo*-*oxazolo*[2,3-b]*quinazoline* was similarly obtained (60%) from the analogous 3-2′-chloropropyl derivative [1] and sodium ethoxide, and separated from light petroleum as prisms, m. p. 136° (Found: C, 65·0; H, 4·5; N, 13·8. $C_{11}H_{10}N_2O_2$ requires C, 65·3; H, 5·0; N, 13·9%).

2,3-*Dihydro*-3-*methyl*-5-*oxo*-*oxazolo*[2,3-b]*quinazoline*, analogously prepared (75%) from the 3-(2-chloro-1-methylethyl) derivative [1] and potassium carbonate in acetone, had m. p. 68—70° (from ether) (Found: loss at 50°/vac., 4·4. Found, on dried material: C, 65·7; H, 4·9; N, 14·3. $C_{11}H_{10}N_2O_2,\frac{1}{2}H_2O$ requires H_2O, 4·3. $C_{11}H_{10}N_2O_2$ requires C, 65·3; H, 5·0; N, 13·9%).

3-2′-*Chloroethyl*-2-*ethoxy*-3,4-*dihydro*-4-*oxoquinazoline*.—This base (IV; R = Cl, R′ = OEt) was formed (4·8 g.) when its 2-chloro-analogue (4·9 g.) was refluxed for 15 min. in ethanol (30 ml.) containing sodium (0·46 g.) and water was added. It crystallised from light petroleum as prisms, m. p. 104—105° (Found: N, 11·1. $C_{12}H_{13}ClN_2O_2$ requires N, 11·1%).

2-o-*Ethoxycarbonylaminophenyloxazoline* (IX; R = Et).—This product separated when 2-(*o*-aminophenyl)oxazoline [9] (6·7 g.), ethyl chloroformate (8·3 g.), 2N-sodium hydroxide (41 ml.), and water (150 ml.) were stirred together for 15 min. From light petroleum it crystallised as prisms, m. p. 98—99·5° (Found: C, 61·4; H, 6·0; N, 11·9. $C_{12}H_{14}N_2O_3$ requires C, 61·5; H, 6·0; N, 12·0%).

2-o-*Phenoxycarbonylaminophenyloxazoline* (IX; R = Ph) (1 g.) resulted when the foregoing compound was refluxed in phenol (10 g.) for 90 min. and the excess of phenol was removed in steam; it formed needles, m. p. 170—172°, from ethanol (Found: C, 68·0; H, 5·3; N, 9·6. $C_{16}H_{14}N_2O_3$ requires C, 68·1; H, 5·0; N, 9·9%).

Methyl 5-*Bromo*-2-*ethoxycarbonylaminobenzoate*.—This *ester* (9·8 g.) was prepared by heating methyl 5-bromoanthranilate (9·2 g.) with ethyl chloroformate (6 g.) at 120—130° for 8 hr. and, isolated by distillation, had b. p. 136—142°/0·1 mm., m. p. 94° (from light petroleum) (Found: N, 4·7. $C_{11}H_{12}BrNO_4$ requires N, 4·6%).

6-*Bromo*-3,4-*dihydro*-2-*hydroxy*-3-2′-*hydroxyethyl*-4-*oxoquinazoline* (X; R = OH).—This *quinazoline* resulted (6 g.) when the foregoing urethane (8·3 g.) was heated for 40 min. at 160° with ethanolamine (3·3 g.), and the product was digested with chloroform. It crystallised from 2-ethoxyethanol as needles, m. p. 270—272° (Found: C, 42·3; H, 3·4. $C_{10}H_9BrN_2O_3$ requires C, 42·1; H, 3·2%).

Its 3-2′-*bromoethyl analogue* (X; R = Br) (3·5 g.) separated after the oxo-oxazolo[2,3-*b*]-quinazoline (II) (3·8 g.) had been boiled with bromine (3·2 g.) in glacial acetic acid (40 ml.) for 2 hr., and crystallised from 2-ethoxyethanol as plates, m. p. 287—290° (decomp.) (Found: C, 34·5; H, 2·5; Br, 45·4; N, 7·6. $C_{10}H_8Br_2N_2O_2$ requires C, 34·5; H, 2·3; Br, 45·9; N, 8·1%). This was soluble in alcoholic sodium hydroxide, and in boiling 2N-sodium hydroxide afforded the foregoing 3-2′-hydroxyethyl derivative (X; R = OH), m. p. and mixed m. p. 269—271°. When boiled with an excess of dimethylaniline, it gave the 3-(2-*methylanilinoethyl*) *derivative*

[9] Leffler and Adams, *J. Amer. Chem. Soc.*, 1937, **59**, 2252.

(X; R = NMePh), which crystallised from dimethylformamide as prisms, m. p. 228—229° (Found: C, 54·4; H, 4·2; N, 10·7. $C_{17}H_{16}BrN_3O_2$ requires C, 54·6; H, 4·3; N, 11·2%).

6-*Bromo*-3-2′-*chloroethyl*-3,4-*dihydro*-2-*hydroxy*-4-*oxoquinazoline* (X; R = Cl).—The foregoing 3-2′-hydroxyethylquinazoline (5·5 g.) was refluxed in thionyl chloride (35 ml.) for 1 hr., and the solution was evaporated to dryness. The *chloro-derivative* (5·5 g.), obtained by treating the residue with water and crystallising it from glacial acetic acid, had m. p. 273—274° (Found: C, 39·6; H, 2·9. $C_{10}H_8BrClN_2O_2$ requires C, 39·6; H, 2·7%). This compound was recovered after being boiled with phosphoryl chloride for 2 days.

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