

710. Cyclic Amidines. Part XI.¹ Rearrangements of Quinazoline Ethers.

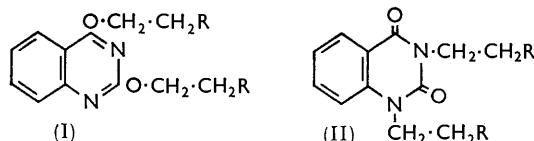
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Certain basic ethers of 2,4-dihydroxyquinazoline have been shown to undergo a thermal rearrangement not hitherto recognised. Evidence has been obtained for a cyclic mechanism for the formally similar rearrangements shown to occur with 2-chloro-4-chloroalkoxyquinazolines on distillation, and with analogous 4-hydroxyalkyl ethers when these were treated with thionyl chloride.

3-Substituted 3,4-dihydro-2-hydroxy-4-oxoquinazolines have been prepared from methyl *o*-ethoxycarbonylamino benzoate and an amine.

QUATERNARY salts of 2,4-di(alkylaminoalkoxy)quinazolines were required for testing as muscle relaxants. Rearrangements observed in syntheses of these and related ethers are now recorded.

2,4-Dichloroquinazoline and sodium 2-diethylaminoethoxide furnished an oil which was evidently 2,4-bis-(2-diethylaminoethoxy)quinazoline (I; R = NEt₂) since, as its dimethiodide, it was readily hydrolysed to 2,4-dihydroxyquinazoline. The isomer obtained on distillation of this ditertiary base was assigned the structure (II; R = NEt₂),



since it was stable to boiling hydrobromic acid and afforded a different dimethiodide (II; R = NEt₂Me}I). Similar results were obtained with the corresponding dimethylamino-derivatives; in one experiment, the distilled ditertiary base gave a mixture of the two dimethiodides, separable by fractional crystallisation.

In previous investigations^{2,3} of these compounds, the isomerisation of the ditertiary bases was not observed, but products described as ethers were apparently identical with the foregoing 1,3-disubstituted quinazolines. Similar thermal isomerisations have been reported for certain 4-alkoxyquinazolines,⁴ but not for 2,4-dialkoxyquinazolines.⁵

The reactivity of both chlorine atoms in 2,4-dichloroquinazoline was insufficient for the production of a bisquaternary ether from a 2-hydroxyethyltrialkylammonium iodide; only one ether link was formed.

Examination of further possible routes to these quaternary compounds disclosed a second type of rearrangement. The product from 2,4-dichloroquinazoline, ethylene chlorohydrin, and potassium carbonate was presumed to be 2-chloro-4-2'-chloroethoxyquinazoline (III; R = R' = Cl) because of the known difference in reactivity of the chlorine atoms in 2,4-dichloroquinazoline,⁶ and since it afforded 2,4-dihydroxyquinazoline on hydrolysis. On distillation, the ether (III; R = R' = Cl) rearranged to its isomer (IV; R = R' = Cl), converted by hydrolysis into the 2-hydroxyquinazoline derivative (IV; R = OH, R' = Cl). The structure of the last compound was unequivocally established by a direct synthesis; it was produced by interaction of thionyl chloride and

¹ Part X, preceding paper.

² Donleavy and Kise, *J. Amer. Chem. Soc.*, 1935, **57**, 753.

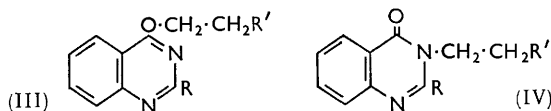
³ Hohmann, *Univ. Microfilms*, Publ. No. 6519, 1953.

⁴ Bogert and Seil, *J. Amer. Chem. Soc.*, 1907, **29**, 517.

⁵ Abt, *J. prakt. Chem.*, 1889, **39**, 140.

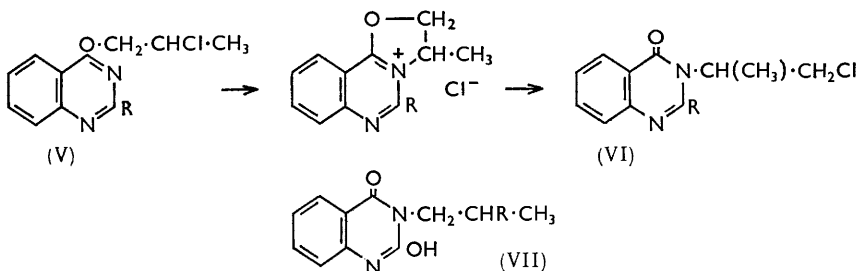
⁶ Lange and Sheibley, *J. Amer. Chem. Soc.*, 1931, **53**, 3867; 1933, **55**, 1188; Curd, Landquist, and Rose, *J.*, 1947, 775.

the 3-2'-hydroxyethylquinazoline (IV; R = R' = OH) that was itself unambiguously obtained from methyl *o*-ethoxycarbonylaminobenzoate and ethanolamine.



2-Chloro-4-2'-hydroxyethoxyquinazoline (III; R = Cl, R' = OH) and the homologous 4-3'-hydroxypropoxy-derivative underwent similar rearrangements when treated with thionyl chloride. In each instance, the 3-chloroalkylquinazoline (*e.g.*, IV; R = R' = Cl) was obtained. 2,4-Di-(2-hydroxyethoxy)quinazoline⁷ (I; R = OH) was readily hydrolysed by dilute acid to 2,4-dihydroxyquinazoline, and likewise gave, with thionyl chloride, a dichloro-derivative which was stable to hydrobromic acid and therefore considered to be the 1,3-disubstituted quinazoline (II; R = Cl). This compound could not be converted into a quaternary salt with triethylamine at temperatures up to 130°. In the reaction of 2-anilino-4-2'-hydroxyethoxyquinazoline (III; R = NHPH, R' = OH) with thionyl chloride to yield the compound (III; R = NHPH, R' = Cl), no rearrangement occurred.

4-Allyloxy-2-chloro-, 4-benzyloxy-2-chloro-, and 2-chloro-4-ethoxy-quinazoline did not undergo isomerisation on being heated. Accordingly, it appeared likely that the isomerisation of 4-chloroalkoxyquinazolines proceeded *via* an oxazolinium chloride analogously to the rearrangement of 2-chloroethyl benzimidate.⁸ Collateral evidence for this was provided by an examination of an unsymmetrically substituted ether. 2-Chloropropan-1-ol with 2,4-dichloroquinazoline gave 2-chloro-4-2'-chloropropoxyquinazoline (V; R = Cl),



which was distilled to effect isomerisation to compound (VI; R = Cl) and then hydrolysed to the corresponding hydroxyquinazoline (VI; R = OH). In agreement with the supposed mechanism (V \rightarrow VI; R = Cl), the compound (VI; R = OH) was shown to be identical with that formed when 2-aminopropan-1-ol was brought into reaction with methyl *o*-ethoxycarbonylaminobenzoate and the product was treated with thionyl chloride; the isomer (VII; R = Cl), analogously synthesised from 1-aminopropan-2-ol, was different.

No muscle-relaxant properties were observed for the bisquaternary compounds.

EXPERIMENTAL

Interaction of 2,4-Dichloroquinazoline and Sodium 2-Diethylaminoethoxide.—2,4-Dichloroquinazoline (10 g.) reacted exothermically when added during 15 min. to a solution of sodium (2.3 g.) in 2-diethylaminoethanol (50 ml.). The mixture was heated at 115° for 90 min. An ethereal extract on evaporation under reduced pressure furnished an oil, converted by methyl iodide into 2,4-bis-2'-diethylaminoethoxyquinazoline dimethiodide (I; R = NMeEt₂); this crystallised from ethanol as needles, m. p. 207—208° (decomp.) (Found: C, 40.7; H, 5.9;

⁷ Lange and Sheibley, *J. Amer. Chem. Soc.*, 1932, **54**, 4305.

⁸ Gabriel and Neumann, *Ber.*, 1892, **25**, 2383; Wislicenus and Korber, *ibid.*, 1902, **35**, 164.

I, 39.4. $C_{22}H_{38}I_2N_4O_2$ requires C, 41.0; H, 5.9; I, 39.4%). Hohmann³ cites m. p. 247—248° for the dimethiodide said to be this compound. This dimethiodide when boiled for 1 hr. with concentrated hydrochloric acid gave 2,4-dihydroxyquinazoline, m. p. and mixed m. p. 350°.

The foregoing oil distilled as 1,2,3,4-tetrahydro-1,3-bis-2'-diethylaminoethyl-2,4-dioxoquinazoline (II; R = NEt₂) (13.6 g., 75%), b. p. 227°/1.5 mm. (Found: C, 66.4; H, 9.1; N, 15.6. $C_{20}H_{32}N_4O_2$ requires C, 66.6; H, 9.0; N, 15.5%); Hohmann³ records b. p. 225—226°/4 mm., and Donleavy and Kise² record b. p. 209—210°/5 mm. for the compound said to be the diether. Its *dipicrate* separated from 2-ethoxyethanol as prisms, m. p. 212° (decomp.) (Found: C, 46.9; H, 4.9; N, 16.8. $C_{32}H_{38}N_{10}O_{16}$ requires C, 46.9; H, 4.7; N, 17.1%). The same dipicrate, m. p. and mixed m. p. 212° (decomp.), was prepared from the distilled ditertiary base which had been boiled for 4 hr. with hydrobromic acid (47.5%). The *dimethiodide* of the distilled ditertiary base crystallised from methanol as needles, m. p. 254—255° (decomp.) (Found: C, 41.2; H, 5.8; N, 8.2. $C_{22}H_{38}I_2N_4O_2$ requires C, 41.0; H, 5.9; N, 8.7%).

2,4-Dichloroquinazoline and sodium 2-dimethylaminoethoxide, when treated as in the above experiment, afforded an oil whose *dimethiodide* (I; R = NMe₃I) crystallised as prisms (from methanol), m. p. 242° (decomp.) [Hohmann³ gives m. p. 299—301°] (Found: C, 36.6; H, 5.3. $C_{18}H_{30}I_2N_4O_2$ requires C, 36.7; H, 5.1%); on acid hydrolysis, this dimethiodide afforded 2,4-dihydroxyquinazoline, m. p. and mixed m. p. 350°.

The foregoing oil (9.3 g., 62%) distilled mainly as 1,3-bis-2'-dimethylaminoethyl-1,2,3,4-tetrahydro-2,4-dioxoquinazoline (II; R = NMe₂) at 202°/1 mm. (lit.,³ b. p. 234—236°/9 mm.) (Found: C, 62.8; H, 7.8; N, 18.2. $C_{16}H_{24}N_4O_2$ requires C, 63.1; H, 8.0; N, 18.4%). This distillate (3 g.) in ethanol (25 ml.) furnished with methyl iodide (3.2 g.), after 1 hr. at room temperature, a solid (5.5 g.) which, by fractional crystallisation from aqueous ethanol, was separated into the same dimethiodide, m. p. and mixed m. p. 242° (decomp.) (Found: C, 36.3; H, 5.3; I, 44.0. Calc. for $C_{18}H_{30}I_2N_4O_2$: C, 36.7; H, 5.1; I, 43.1%), and 1,3-bis-2'-dimethylaminoethyl-1,2,3,4-tetrahydro-2,4-dioxoquinazoline *dimethiodide*, prisms, m. p. 305° (decomp.) (Found: C, 36.8; H, 4.8; I, 44.8; N, 9.6. $C_{18}H_{30}I_2N_4O_2$ requires C, 36.7; H, 5.1; I, 43.1; N, 9.5%).

In other experiments the distillate behaved as a single compound. It furnished a single *dipicrate*, which crystallised from glacial acetic acid as prisms, m. p. 213—214° (Found: C, 44.4; H, 4.0. $C_{28}H_{30}N_{10}O_{16}$ requires C, 44.1; H, 4.0%), and a *dihydrobromide* as hygroscopic prisms (from acetonitrile), m. p. 124° (effervescence) (Found, on dried material: Br, 34.0. $C_{16}H_{26}Br_2N_4O_2$ requires Br, 34.3%). On being boiled for 4 hr. with hydrobromic acid (47.5%), the distilled oil furnished the same dihydrobromide, m. p. and mixed m. p. 124° (effervescence).

Diethyl-2-hydroxyethylmethylammonium iodide had m. p. 269° (decomp.); Emde and Runne⁹ record m. p. 249°. Its *picrate* crystallised from ethanol as needles, m. p. 239—241° (Found: C, 43.4; H, 5.5. $C_{13}H_{20}N_4O_8$ requires C, 43.3; H, 5.6%).

2-(2-Chloro-4-quinazolinyl-oxy)ethyl-diethylmethylammonium Iodide (III; R = Cl, R' = NMeEt₂I).—The solid obtained by boiling together 2,4-dichloroquinazoline (1.95 g.), diethyl-2-hydroxyethylmethylammonium iodide (5 g.) and triethylamine (2 g.) in acetone (100 ml.) for 5 days furnished this ether (2.2 g., 52%) as prisms, m. p. 200° (decomp.) (from ethanol) (Found: C, 42.7; H, 4.8; N, 9.7. $C_{15}H_{21}ClN_3O$ requires C, 42.7; H, 5.0; N, 10.0%).

2-Chloro-4-2'-hydroxyethoxyquinazoline (III; R = Cl, R' = OH).—2,4-Dichloroquinazoline (25 g.) and ethylene glycol (15.5 g.) were boiled in acetone (350 ml.) for 4 hr. with potassium carbonate (35 g.). The acetone-soluble *ether* (III; R = Cl, R' = OH) (24.6 g., 87%), precipitated by water, crystallised from benzene as needles, m. p. 125° (Found: C, 53.7; H, 3.8; N, 12.5. $C_{10}H_9ClN_2O_2$ requires C, 53.5; H, 4.0; N, 12.5%). 1,2-Di-(2-chloro-4-quinazolinyl-oxy)-ethane (1.6 g.), needles, m. p. 208°, from 2-ethoxyethanol, was the acetone-insoluble product [Found: C, 56.2; H, 3.3; N, 14.1%; M (Rast), 356. $C_{18}H_{12}Cl_2N_4O_2$ requires C, 55.8; H, 3.1; N, 14.5%; M, 387].

2-Chloro-4-2'-chloroethoxyquinazoline (III; R = R' = Cl).—A solution of 2,4-dichloroquinazoline (25 g.) and ethylene chlorohydrin (20 g.) in acetone (350 ml.) was boiled for 5 hr. with potassium carbonate (35 g.), filtered, evaporated, and diluted with water. The precipitated *ether* (25.4 g., 84%) crystallised from light petroleum as plates, m. p. 101—103° (Found: C, 49.8; H, 3.6; N, 11.1. $C_{10}H_8Cl_2N_2O$ requires C, 49.4; H, 3.3; N, 11.5%). When boiled with concentrated hydrochloric acid for 1 hr., this compound gave 2,4-dihydroxyquinazoline, m. p. and mixed m. p. 349°.

⁹ Emde and Runne, *Arch. Pharm.*, 1911, **249**, 371.

2-Chloro-3-2'-chloroethyl-3,4-dihydro-4-oxoquinazoline (IV; R = R' = Cl).—(i) 2-Chloro-4-2'-chloroethoxyquinazoline when distilled at 166°/1.1 mm. yielded the isomeric 3-2'-chloroethyl derivative which crystallised from light petroleum as needles, m. p. 91—92° (Found: C, 49.5; H, 3.6; Cl, 29.4; N, 11.3. C₁₀H₈Cl₂N₂O requires C, 49.4; H, 3.3; Cl, 29.2; N, 11.5%). This compound, when boiled for 30 min. with concentrated hydrochloric acid, gave the 2-hydroxyquinazoline (IV; R = OH, R' = Cl), m. p. 195.5—196°, not depressed by an unambiguously synthesised specimen (see below) (Found: C, 53.1; H, 4.4; Cl, 16.3; N, 12.2. C₁₀H₉ClN₂O₂ requires C, 53.5; H, 4.4; Cl, 15.8; N, 12.5%).

(ii) 2-Chloro-4-2'-hydroxyethoxyquinazoline (1 g.) was boiled for 30 min. with thionyl chloride (10 ml.) and poured on ice. The precipitate was the same 3-2'-chloroethyl derivative, m. p. and mixed m. p. 91—92°.

Methyl *o*-Ethoxycarbonylamino benzoate.—A mixture of methyl anthranilate (30.2 g.) and ethyl chloroformate (21.7 g.), after the initial exothermic reaction, was heated on a steam-bath for 15 hr. and distilled at 172°/14 mm., m. p. 62° (yield 43 g., 97%). Heller¹⁰ gives m. p. 62°.

3,4-Dihydro-2-hydroxy-3-2'-hydroxyethyl-4-oxoquinazoline (IV; R = R' = OH).—Methyl *o*-ethoxycarbonylamino benzoate (11.2 g.) and ethanolamine (6.2 g.) were heated together at 160° for 40 min. The paste resulting furnished the quinazoline (7.4 g., 72%) when digested with chloroform; it crystallised as prisms, m. p. 253.5—254°, from aqueous acetic acid (Found: C, 58.6; H, 5.0; N, 13.5. C₁₀H₁₀N₂O₃ requires C, 58.3; H, 4.9; N, 13.6%). With 1 mol. of ethanolamine the yield was 54%.

3-2'-Chloroethyl-3,4-dihydro-2-hydroxy-4-oxoquinazoline (IV; R = OH, R' = Cl) was quantitatively produced when the foregoing alcohol was refluxed with thionyl chloride for 30 min., and crystallised from methanol as plates, m. p. and mixed m. p. 195.5—196°.

2-Chloro-4-3'-hydroxypropoxyquinazoline (III; R = Cl, R' = CH₂·OH), prepared from trimethylene glycol and 2,4-dichloroquinazoline, crystallised from benzene-light petroleum as prisms, m. p. 99—100° (Found: C, 55.4; H, 4.4; N, 11.6. C₁₁H₁₁ClN₂O₂ requires C, 55.4; H, 4.6; N, 11.7%), and gave 2,4-dihydroxyquinazoline when boiled for 2 hr. with concentrated hydrochloric acid.

2-Chloro-3-3'-chloropropyl-3,4-dihydro-4-oxoquinazoline (IV; R = Cl, R' = CH₂Cl) was obtained (28%) by interaction of the foregoing hydroxy-ether and thionyl chloride; it crystallised from light petroleum as needles, m. p. 114.5—115° (Found: C, 51.2; H, 4.1; N, 10.7. C₁₁H₁₀Cl₂N₂O requires C, 51.4; H, 3.9; N, 10.9%). Hydrolysis (0.5 g.) with boiling concentrated hydrochloric acid furnished the corresponding 2-hydroxyquinazoline (IV; R = OH, R' = CH₂Cl) (0.4 g.) which formed plates, m. p. 176—177°, from ethanol (Found: C, 55.4; H, 4.7; N, 11.7. C₁₁H₁₁ClN₂O₂ requires C, 55.4; H, 4.6; N, 11.7%).

1,3-Di-(2-chloroethyl)-1,2,3,4-tetrahydro-2,4-dioxoquinazoline (II; R = Cl).—2,4-Di-(2-hydroxyethoxy)quinazoline⁷ (3 g.) was boiled with thionyl chloride (20 ml.) for 45 min. An ethanol solution of the residue obtained on removal of the excess of thionyl chloride *in vacuo* deposited the 1,3-di-(2-chloroethyl) derivative as prisms, m. p. 127—128° (Found: C, 50.6; H, 4.4; Cl, 25.1; N, 9.9. C₁₂H₁₂Cl₂N₂O₂ requires C, 50.2; H, 4.2; Cl, 24.7; N, 9.8%). This compound was inert to boiling hydrobromic acid (47.5%).

2-Anilino-4-2'-hydroxyethoxyquinazoline (III; R = NHPH, R' = OH).—(i) 2-Anilino-4-ethoxyquinazoline¹¹ (5.3 g.) was kept for 42 hr. in ethylene glycol (60 ml.) containing sodium (0.46 g.). The material precipitated by the addition of water afforded the hydroxyethyl ether (2.2 g., 39%) as prisms, m. p. 116—116.5° (from propan-2-ol) (Found: C, 68.8; H, 5.7; N, 14.7. C₁₆H₁₅N₃O₂ requires C, 68.3; H, 5.4; N, 14.9%). Its picrate, prisms from ethanol, had m. p. 188—188.5° (Found: N, 16.2. C₂₂H₁₈N₆O₉ requires N, 16.5%). When the reaction was performed in boiling ethylene glycol, the product was 2-anilino-4-hydroxyquinazoline.

(ii) 2-Chloro-4-2'-hydroxyethoxyquinazoline (III; R = Cl, R' = OH) (4.5 g.) and aniline (1.9 g.), when boiled in ethanol (30 ml.) for 1 hr., furnished the hydrochloride (6 g., 94%) which crystallised from methanol as prisms, m. p. 187° (Found: C, 60.3; H, 5.2. C₁₅H₁₅ClN₃O₂ requires C, 60.5; H, 5.1%). The liberated base had m. p. and mixed m. p. 116—117°.

2-Anilino-4-2'-chloroethoxyquinazoline (III; R = NHPH, R' = Cl). The foregoing hydrochloride (2 g.) was boiled in thionyl chloride (15 ml.) for 15 min. and the solution was evaporated under reduced pressure. Crystallisation of the residue from methanol gave the chloroethoxyhydrochloride (1.6 g., 76%), m. p. 169—170° (effervescence) (Found: C, 54.7; H, 4.6; N, 11.7.

¹⁰ Heller, *Ber.*, 1918, **51**, 424; Heller and Lauth, *J. prakt. Chem.*, 1928, **113**, 226.

¹¹ Lange and Sheibley, *J. Amer. Chem. Soc.*, 1932, **54**, 1994.

$C_{16}H_{15}Cl_2N_3O \cdot H_2O$ requires C, 54.2; H, 4.8; N, 11.9%). Its *picrate* separated as prisms, m. p. 196—197° (decomp.), from glacial acetic acid (Found: C, 49.9; H, 3.1. $C_{22}H_{17}ClN_6O_8$ requires C, 50.0; H, 3.2%). This hydrochloride, on hydrolysis, yielded 2-anilino-4-hydroxyquinazoline, m. p. and mixed ¹¹ m. p. 261°, characterised as its acetyl derivative, m. p. and mixed ¹ m. p. 202—204°.

4-Benzoyloxy-2-chloroquinazoline (6.6 g., 98%) was obtained when 2,4-dichloroquinazoline (5 g.) was added during 15 min. to sodium (0.58 g.) in benzyl alcohol (50 ml.) at below 10°, and the mixture was kept for 2 hr., evaporated, and treated with water. It formed prisms (from light petroleum), m. p. 95—97°, b. p. 202°/1.5 mm. (Found: C, 66.6; H, 4.1; N, 10.3. $C_{15}H_{11}ClN_2O$ requires C, 66.5; H, 4.1; N, 10.4%). The distilled material furnished 2,4-dihydroxyquinazoline, m. p. and mixed m. p. 350°, when boiled for 1 hr. with concentrated hydrochloric acid.

4-Allyloxy-2-chloroquinazoline, prepared analogously from sodium allyloxide, crystallised from light petroleum as laths, m. p. 76.5—77°, b. p. 220°/54 mm. (Found: C, 60.1; H, 4.4; N, 12.1. $C_{11}H_9ClN_2O$ requires C, 59.9; H, 4.1; N, 12.7%). The distilled compound was later hydrolysed to 2,4-dihydroxyquinazoline.

2-Chloro-4-2'-chloropropoxyquinazoline (V; R = Cl).—2,4-Dichloroquinazoline (10 g.), 2-chloropropan-1-ol ¹² (9.5 g.), potassium carbonate (14 g.), and acetone (140 ml.) were boiled together for 5½ hr. The filtered suspension on evaporation *in vacuo* gave an oil which partly solidified. By recrystallisation of the solid from light petroleum below room temperature the *quinazoline ether* (4.7 g.) was obtained as prisms, m. p. 64° (Found: C, 51.3; H, 4.1; N, 10.6. $C_{11}H_{10}Cl_2N_2O$ requires C, 51.4; H, 3.9; N, 10.9%).

2-Chloro-3-(2-chloro-1-methylethyl)-3,4-dihydro-4-oxoquinazoline (VI; R = Cl) was formed when the foregoing ether was heated at 200° for 5 min., then distilled at 130°/0.1 mm., and crystallised from light petroleum as prisms, m. p. 98° (Found: C, 51.4; H, 3.9; N, 10.9. $C_{11}H_{10}Cl_2N_2O$ requires C, 51.4; H, 3.9; N, 10.9%). On acid-hydrolysis, it afforded the corresponding 2-hydroxyquinazoline (VI; R = OH), m. p. 183—184°, undepressed by an unambiguously synthesised specimen (see below) (Found: C, 55.2; H, 4.5; N, 11.9. $C_{11}H_{11}ClN_2O_2$ requires C, 55.4; H, 4.6; N, 11.7%).

3,4-Dihydro-2-hydroxy-3-(2-hydroxy-1-methylethyl)-4-oxoquinazoline.—Methyl *o*-ethoxycarbonylaminobenzoate (11.2 g.) and 2-aminopropan-1-ol ¹³ (7.5 g.), heated together at 140° for 75 min., gave a gum from which the *quinazoline* was extracted with benzene (4 × 20 ml.) (0.75 g.) and with ethyl acetate (20 ml.) (1.75 g.); it formed prisms, m. p. 214.5°, from aqueous ethanol (Found: C, 59.7; H, 5.6; N, 13.0. $C_{11}H_{12}N_2O_3$ requires C, 60.0; H, 5.5; N, 12.7%).

3-(2-Chloro-1-methylethyl)-3,4-dihydro-2-hydroxy-4-oxoquinazoline (VI; R = OH) was formed quantitatively from the foregoing alcohol and thionyl chloride, and crystallised from methanol as prisms, m. p. and mixed m. p. 182—183°.

3,4-Dihydro-2-hydroxy-3-2'-hydroxypropyl-4-oxoquinazoline (VII; R = OH).—(i) Heating methyl *o*-ethoxycarbonylaminobenzoate and 1-aminopropan-2-ol (2 mol.) at 160° for 75 min. afforded this *quinazoline* (50%) which formed prisms, m. p. 205—206°, from ethanol (Found: C, 59.8; H, 5.4; N, 12.4. $C_{11}H_{12}N_2O_3$ requires C, 60.0; H, 5.5; N, 12.7%).

(ii) 2,4-Dihydroxyquinazoline (8.1 g.) in 50% aqueous ethanol (150 ml.) containing sodium (1.2 g.) was boiled with 1-chloropropan-2-ol (4.7 g.) for 4 hr. The solid (0.8 g.) obtained on filtration and concentration of the suspension yielded the same compound, having m. p. and mixed m. p. 205—206° on crystallisation first from water and then from ethyl acetate.

3-2'-Chloropropyl-3,4-dihydro-2-hydroxy-4-oxoquinazoline (VII; R = Cl) was prepared (94%) by refluxing the foregoing alcohol with thionyl chloride and crystallised from ethanol as plates, m. p. 205.5—206°, depressed to 190° by the original alcohol (Found: C, 55.1; H, 4.7; N, 11.7. $C_{11}H_{11}ClN_2O_2$ requires C, 55.4; H, 4.6; N, 11.7%).

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¹² Fickett, Garner, and Lucas, *J. Amer. Chem. Soc.*, 1951, **73**, 5063.

¹³ Attenburrow, Elks, Hems, and Speyer, *J.*, 1949, 510.