806. *The Synthesis of* Lunasia *Alkaloids. Part II.*[1] *Dihydropyranoquinolines.*

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Acid cyclisations of the 3-methylbut-2-enylquinolones (I; R = H, Me), of the acetamido-derivatives (V; R = H, Me), and of the tertiary alcohol (IV) furnish the angular pyranoquinoline (IX) and the linear pyranoquinoline (VIII; R = H), which equilibrate on prolonged treatment with acid. The mechanisms of the reactions are discussed, and the spectra of the dimethylpyranoquinolines are compared with those of the isomeric isopropylfuranoquinolines. The quinolones (XII; R = H, Me) were also converted into pyranoquinoline derivatives.

In Part I[1] we reported the synthesis of the 3-methylbut-2-enylquinolines (I; R = H) and (XII; R = H), and their conversion through hydroboronation into the *Lunasia* alkaloid, lunacridine (II; R = Me). Acid cyclisation of lunacridine afforded a mixture of lunacrine (III) and the angular tetrahydrofuranoquinoline (VI). In order to confirm that this was indeed an unambiguous synthesis, we decided to prepare the tertiary alcohol (IV), isomeric with lunacridine (II; R = Me), and to study its conversion into pyranoquinolines. Syntheses of the latter compounds are of intrinsic interest because the enantiomeric alkaloids, isobalfourodine[2] and Lunasia II,[3,4] were shown to possess the pyranoquinoline structure (VIII; R = OH).

Markovnikov hydration of the 4-methoxy-3-(3-methylbut-2-enyl)quinolone (I; R = Me) with sulphuric acid in aqueous dioxan at 0° gave the tertiary alcohol (IV) (82%), which was clearly different from (±)-lunacridine (II; R = Me). The product showed hydroxyl absorption in the infrared at 3420 cm.$^{-1}$, and the presence of a 2-quinolone group

Table 1.

Nuclear magnetic resonance spectral assignments (determined in deuteriochloroform solution at 60 Mc./sec.).

(III) * τ Value	(VIII; R = H) τ Value	(VI) τ Value	(IX) τ Value	(XIII) τ Value	(XV) τ Value	Assignment
1·89q	1·97q	2·60q	2·40q	2·50q		arom. 5-*H*
($J_{A,X}$ = 7; $J_{B,X}$ = 2)	($J_{A,X}$ = 7; $J_{BX,}$ = 2)	($J_{A,X}$ = 6; $J_{B,X}$ = 3)	($J_{A,X}$ = 6·5; $J_{B,X}$ = 2·7)	($J_{A,X}$ = 7·5; $J_{B,X}$ = 2)	2·39—3·14	
2·56—3·05	2·66—3·06	2·85—3·03	2·71—3·08	2·75—3·18		arom. 6- and 7-*H*
5·22m	—	5·23m	—	—	—	α-furano-C*H*<
6·12s	6·22s	6·09s	6·08s	—	—	>N·CH_3
6·08s	6·13s	6·13s	6·14s	6·04s	6·04s	—O·CH_3
6·83m	—	6·95m	—	—	—	β-furano-CH_2—
—	7·30t (J = 6·5)	—	7·36t (J = 6·5)	7·33t (J = 6·5)	7·08t (J = 7)	γ-pyrano-CH_2—
—	8·22t (J = 6·5)	—	8·20t (J = 6·5)	8·16t (J = 6·5)	8·18t (J = 7)	β-pyrano-CH_2—
8·01m	—	8·02m	—	—	—	—C*H*Me$_2$
8·98d	8·60s	8·97d	8·61s	8·60s	8·61s	—C(CH_3)$_2$
9·09d		9·10d				

In all cases the integrated areas support the assignments: s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet.

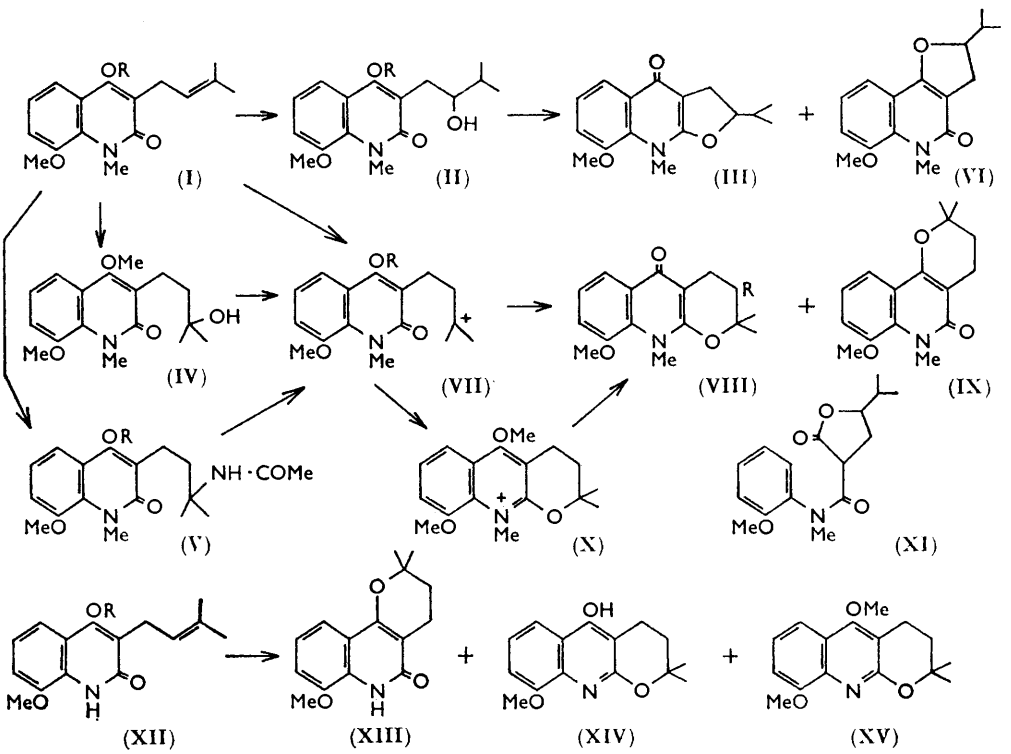
* In the spectrum of (−)-lunacrine that was determined previously,[5] the frequencies given were related to benzene.

was also confirmed spectroscopically (Table 2, and see below). Acid cyclisation of the tertiary alcohol under the conditions used for lunacridine (II; R = Me) afforded a mixture of the isomeric tetrahydropyranoquinolines (VIII; R = H) and (IX). Beyerman and

[1] Part I, *J.*, 1964, 438.
[2] Rapoport and Holden, *J. Amer. Chem. Soc.*, 1960, **82**, 4395.
[3] Beyerman and Rooda, *Proc. k. ned. Akad. Wetenschap.*, 1959, **62**, *B*, 187.
[4] Beyerman and Rooda, *Proc. k. ned. Akad. Wetenschap.*, 1960, **63**, *B*, 154.

Rooda [3] prepared the same compounds by heating the lactone (XI) with polyphosphoric acid.

The structures assigned to the pyranoquinolines are based on the following spectroscopic evidence. The nuclear magnetic resonance (n.m.r.) spectra of the pyranoquinolines (VIII; R = H) and (IX) are very similar in the 4—9 τ region. The group resonances are well separated, and their positions and relative intensities (Table 1) confirm that both compounds are 2,2-dimethyldihydropyrano-derivatives. Comparison with the data for lunacrine (III) and for the angular tetrahydrofuranoquinoline (VI) (Table 1) shows that n.m.r. spectroscopy is an excellent method for distinguishing between pyrano- and furano-isomers in this series: in particular, the pyrano-compounds produce a singlet at *ca.* 8—60 τ ($>CMe_2$), whilst the methyl resonances ($CHMe_2$) of the furano-derivatives appear as a multiplet in this region. Goodwin, Shoolery, and Johnson [5] pointed out that, because of deshielding by the neighbouring 4-carbonyl group, the aromatic protons of lunacrine (III) constitute an ABX system, the proton at position 5 of the quinoline ring producing a quartet at unusually low field (1·89 τ, $J_{A,X} = 7$, $J_{B,X} = 2$). We find that one of the pyranoquinolines behaves similarly, the resonance of the 5-proton occurring at 1·97 τ ($J_{A,X} = 7$, $J_{B,X} = 2$); this is, therefore, the linear 4-quinolone (VIII; R = H). In contrast, the aromatic protons of the angular pyranoquinoline (IX), like those of the angular furanoquinoline (VI), absorb at 2·4—3·1 τ. This difference is of general use for distinguish-



ing 1-methyl-2-quinolones from their 4-quinolone isomers (Table 1). For instance, the resonances at 2·5—3·1 τ (3 aromatic protons) in the spectrum of the 4-methoxyquinolone (I; R = Me) further confirms that the reaction of the 4-hydroxy-2-quinolone (I; R = H) with diazomethane [1] affords the 4- rather than the 2-methyl ether; recent independent studies provide further examples.[6]

[5] Goodwin, Shoolery, and Johnson, *J. Amer. Chem. Soc.*, 1959, **81**, 3065.
[6] Robertson, *Austral. J. Chem.*, 1963, **16**, 451; Bosson, Galbraith, Ritchie, and Taylor, *ibid.*, p. 491.

TABLE 2.

Infrared and ultraviolet absorption maxima of 2- and 4-quinolones.

Compound	$\nu_{max.}$	$\varepsilon_{max.}$	$\lambda_{max.}$	ε	$\lambda_{max.}$	ε	$\lambda_{max.}$	ε	Solvent
(I; R = Me) [1]	1645	—	258	25,700	286	8700	331	3500	A
(XII; R = Me) [1] ...	1640	1446	254	28,800	282	9100	331	4200	A
(II; R = Me) [1] ...	1635	8182	258	26,300	285	8300	333	3100	A
(IV)	1635	878	258	25,100	285	8100	332	3300	A
(V; R = Me)	1640	—	257	26,900	283	8500	332	3700	A
(III)	1615	630	242	40,700	—	—	313	10,200	A
			256	33,100	—	—	299	7100	B
(VIII; R = H) ...	1610	340	244	39,800	—	—	322	9600	A
			255	43,700	—	—	306	7200	B
(VI)	1660	934	239	26,300	301	6900	326	2300	A
			248	30,900	301	7400	327	3100	B
(IX)	1635	897	237	27,500	281	6600	323	2500	A
			238	27,500	281	6800	322	2500	B
(XIII)	1635	1324	245	28,200	277	8100	319	3200	A
			248	35,500	288	6000	317	3100	B
(XIV)	1625	604	239	50,100	—	—	313	9600	A
			253	41,700	—	—	302	7900	B

A = Methanol, B = 0·2N-methanolic hydrochloric acid. Infrared data were obtained with 0·027—0·054M-solutions in chloroform, with 0·1 mm. cells.

Examination of the ultraviolet spectra of a large number of 2- and 4-quinolones led to the following generalisations: [2,7] (*a*) 2-quinolones show maxima at 263—298 mμ, usually absent from the spectra of 4-quinolones; (*b*) the long-wavelength band is more intense in 4-quinolones; (*c*) the greater basicity of 4-quinolones is reflected in a shift in acid solution, which is not observed with 2-quinolones. The ultraviolet data for compounds discussed in this Paper and in Part I (Table 2) support the postulated structures and, in particular, distinguish between the pyrano-compounds (VIII; R = H) and (IX). Infrared absorption in the carbonyl region (attributable to amide-carbonyl stretching or to a ring mode) occurs at 1660—1640 cm.$^{-1}$ in most 2-quinolones and at lower frequency (1630—1620 cm.$^{-1}$) in many 4-quinolones.[7,8] This distinction must be employed cautiously in assigning structures, because some exceptions have been reported.[9] For example, intramolecular hydrogen bonding is apparently responsible for the low frequency (1635 cm.$^{-1}$) of the band in the spectrum of lunacridine (II; R = Me);[9] the tertiary alcohol (IV) also absorbs at 1635 cm.$^{-1}$, presumably for the same reason. 2-Quinolones possess stronger carbonyl absorption than 4-quinolones, and McCorkindale [10] showed that the difference in integrated intensity provides a reliable method of diagnosis; the apparent extinction coefficients were less consistent. We find that the position of the peak and its apparent extinction coefficient are useful criteria when both isomers are available, and the infrared data given in Table 2 clearly differentiate between the furano-compounds (III) and (VI), and between the pyrano-derivatives (VIII; R = H) and (IX).

Since the quinolone (IV) is a tertiary alcohol its cyclisation to the pyranoquinolines (VIII; R = H) and (IX) might be expected to proceed by an S_N1 reaction involving a carbonium ion (VII). On this basis, 3-methylbut-2-enylquinolines and also compounds containing different leaving groups in the tertiary position should behave similarly, and we find, indeed, that the pyranoquinolines are also formed by acid cyclisation of the 3-methylbut-2-enylquinolones (I; R = H, Me) and of the acetamido-derivatives (V; R = H, Me). The latter compounds were prepared by the Ritter reaction.[11] With acetonitrile and concentrated sulphuric acid, the 3-methylbut-2-enylquinolone (I; R = H) afforded the acetamido-compound (V; R = H), which with diazomethane was converted into the 4-methoxyquinolone (V; R = Me); the infrared absorptions at 1680 (NH·CO·CH_3) and at

[7] Grundon, McCorkindale, and (in part) Rodger, *J.*, 1955, 4284; Grundon and McCorkindale, *J.*, 1957, 2177.
[8] Witkop, Patrick, and Rosenblum, *J. Amer. Chem. Soc.*, 1951, **73**, 2641.
[9] Price and Willis, *Austral. J. Chem.*, 1959, **12**, 589.
[10] McCorkindale, *Tetrahedron*, 1961, **14**, 223.
[11] Ritter and Minieri, *J. Amer. Chem. Soc.*, 1948, **70**, 4045.

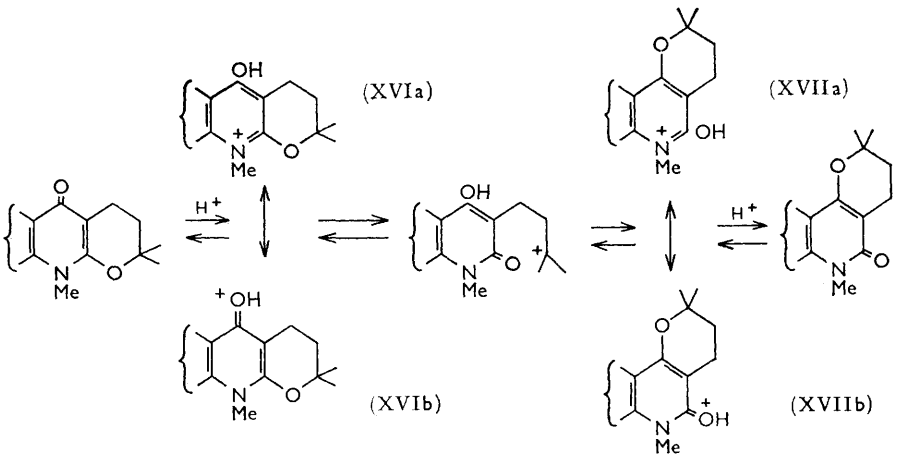
TABLE 3.

Formation and isomerisation of the tetrahydropyranoquinolines (VIII; R = H) and (IX) in refluxing 6N-hydrochloric acid.

No.	Starting compound	Time (hr.)	Total yield (%) of tetrahydropyranoquinolines	Ratio (%) of (VIII; R = H)	Ratio (%) of (IX)
1	(I; R = H)	6	94	42	58
2	,,	24	88	27	73
3	(V; R = H)	6	99	41	59
4	(IV)	6	98	76	24
5	(I; R = Me)	6	86	77	23
6	(VIII; R = H)	6	92	43	57
7	(IX)	6	99	22	78
8	,,	72	80	28	72

1640 cm.$^{-1}$ (NH·CO in a 2-quinolone) were in accord with this structure. The compound (V; R = Me) was obtained in higher yield by applying the Ritter procedure to the 4-methoxy-3-(3-methylbut-2-enyl)quinolone (I; R = Me).

In order to study the cyclisation further, the 4-hydroxyquinolones (I; R = H) and (V; R = H), and the 4-methoxyquinolones (I; R = Me) and (IV) were heated with acid under standard conditions. The pyranoquinolines (VIII; R = H) and (IX), which were obtained in high yield, were separated by chromatography on alumina. Thin-layer chromatography indicated that these products were homogeneous, and that the isomeric furanoquinolines (III) and (VI) were absent from the reaction mixtures. The product ratios (±3%) are presented in Table 3. The interpretation of this data is complicated, however, by the further observations (Table 3, nos. 6 and 7) that the pyranoquinolones are interconverted when heated with hydrochloric acid. This contrasts with the behaviour of the furanoquinolones (III) and (VI), which were stable to acid.[1] Prolonged treatment of the quinolone (I; R = H) and of the angular pyranoquinoline (IX) with acid (Table 3, nos. 2 and 8) gave an equilibrium mixture of the products, in which the angular isomer predominated. The equilibration may proceed as shown. Both pyranoquinolones are soluble in the strongly acidic medium, and are probably extensively protonated; the relative stabilities of the protonated species therefore determine the composition of the equilibrium mixture. The mesomeric form (XVIIb) has a more extended conjugated system than (XVIb), and the greater stability of the angular isomer (XVII) may be attributed, therefore,



to a greater contribution of the mesomeric form (XVIIb) to the hybrid (XVII) compared with the contribution of (XVIb) to the hybrid (XVI). This argument assumes that the mesomeric forms (XVIa) and (XVIIa) have approximately the same energy content, and that protonation of the amide group occurs on oxygen rather than on nitrogen. Although

the latter assumption has been disputed recently,[12] evidence for related systems seems to be overwhelmingly in favour of oxygen protonation.[13]

Formation of a carbonium ion (VII) during the cyclisations is the most plausible explanation of the results, but the data given in Table 3 indicate that the reactions are partly under kinetic control and partly under thermodynamic control; further conclusions, therefore, can be only tentative. After 6 hours, the 4-hydroxyquinolones (I; R = H) and (V; R = H) yield more linear pyranoquinoline than is present in the equilibrium mixture (Table 3, nos. 1 and 3); this suggests that the 2-amido-oxygen is at least as nucleophilic as the phenolic oxygen at position 4. In contrast, S_N2 cyclisation of the secondary alcohol (II; R = H), in which equilibration of the products does not occur, involved the 4-hydroxyl group predominantly.[1] Acid treatment of the 4-methoxyquinolones (I; R = Me) and (IV) for 6 hours gave the linear pyranoquinoline as the principal product (Table 3, nos. 5 and 4). This suggests that protonation to a carbonium ion (VII; R = Me) proceeds faster than cleavage of the methoxy group; cyclisation should then favour the formation of the linear isomer through the quinolinium ion (X).

The investigation was extended to compounds which did not possess an *N*-methyl group. Acid cyclisation of the 4-hydroxy-3-(3-methylbut-2-enyl)quinolone (XII; R = H) gave a single compound, which was shown by ultraviolet, infrared, and n.m.r. spectroscopy (Tables 1 and 2) to be the angular pyranoquinoline (XIII). Unlike the corresponding compound in the *N*-methyl series, the pyranoquinoline (XIII) was sparingly soluble in refluxing acid solution, and this property may be responsible for the isolation of one isomer only. When sufficient ethanol was added to keep the products in solution, a mixture of the angular pyranoquinoline (XIII) (59%) and the linear isomer (XIV) (34%) was obtained. The constitution of the latter compound was indicated by its ultraviolet and infrared spectra (Table 2), and by its solubility in aqueous alkali. Acid treatment of the 4-methoxyquinoline (XII; R = Me) furnished the angular pyranoquinoline (XIII) (33%) and the linear isomer (XIV) (33%). A third product, $C_{16}H_{19}NO_3$, characterised as its perchlorate and as its picrate, was also isolated, and was assigned structure (XV) on the basis of its ultraviolet, infrared, and n.m.r. spectra (Tables 1 and 2), and because it dissolved in 2N-hydrochloric acid. The 4-methoxy-group is retained in this compound, and, when the cyclisation was performed with polyphosphoric acid (which is unlikely to effect cleavage of the ether group [2]), the same pyranoquinoline (XV) was obtained in much higher yield (69%).

Experimental

Thin-layer chromatography was on alumina G in benzene–chloroform (1 : 1) (system A) or on silica gel G in methanol–hydrochloric acid–water (10 : 1 : 2) (system B). The spots were detected by spraying with the Dragendorff reagent.[14]

3-(3-*Hydroxy*-3-*methylbutyl*)-4,8-*dimethoxy*-1-*methyl*-2-*quinolone* (IV).—A mixture of 4,8-dimethoxy-1-methyl-3-(3-methylbut-2-enyl)-2-quinolone (157 mg.), dioxan (4·5 c.c.) and 35% aqueous sulphuric acid (30 c.c.) was kept at 0° for 15 min., diluted with water (50 c.c.), and made alkaline with 10% aqueous sodium hydroxide. Extraction with methylene chloride (3 × 30 c.c.), evaporation of the solvent, and crystallisation of the residue from light petroleum (b. p. 60—80°) gave the *tertiary alcohol* in prisms (136 mg., 82%), m. p. 108—113°, raised by recrystallisation from the same solvent to 115—117°, $\nu_{max.}$ 3420 and 1635 cm.$^{-1}$, $\lambda_{max.}$ (MeOH) 240 (ε 25,100), 258 (ε 25,100), 285 (ε 8100), 292 (ε 7800), and 332 mμ (ε 3300) (Found: C, 66·8; H, 7·7; N, 5·0. $C_{17}H_{23}NO_4$ requires C, 66·9; H, 7·6; N, 4·6%).

3-(3-*Acetamido*-3-*methylbutyl*)-4-*hydroxy*-8-*methoxy*-1-*methyl*-2-*quinolone* (V; R = H).—A solution of the quinolone (I; R = H) (1·9 g.) in acetonitrile (200 c.c.) containing concentrated sulphuric acid (5 c.c.) was kept at 20° for 12 hr., and then concentrated to 20 c.c. under reduced pressure. Water (50 c.c.) was added, the residual acetonitrile was removed by evaporation, and an excess of 2N-sodium hydroxide was added. After extraction of the mixture with

[12] Spinner, *J.*, 1960, 1226.

[13] Katritzky and Reavill, *J.*, 1963, 753; Bell, Shoffner, and Bauer, *Chem. and Ind.*, 1963, 1353; Cook, *Canad. J. Chem.*, 1963, **41**, 515.

[14] Munier and Macheboeuf, *Bull. Soc. Chim. biol.*, 1949, **31**, 1144.

methylene chloride, the aqueous solution was acidified, and again extracted with methylene chloride. The residue, obtained by evaporating the organic solution, was triturated with ethyl acetate to give the *acetamido-compound* (0·64 g., 28%), crystallising from aqueous ethanol in prisms, m. p. 196—198°, $\lambda_{max.}$ (MeOH) 216 (ε 22,400), 238 (ε 30,200), 253 (ε 27,500), 284 (ε 8100), 293 (ε 8700), and 319 mμ (ε 4000) (Found: C, 64·8; H, 7·2; N, 8·6. $C_{18}H_{24}N_2O_4$ requires C, 65·0; H, 7·3; N, 8·4%).

3-(3-*Acetamido*-3-*methylbutyl*)-4,8-*dimethoxy*-1-*methyl*-2-*quinolone* (V; R = Me).—(*a*) The foregoing hydroxy-compound (V; R = H) (321 mg.) in methanol (50 c.c.) at 0° was treated with an excess of diazomethane in ether. After 5 min. the solution was evaporated, and the residue, in methylene chloride, was washed with 2N-sodium hydroxide. Evaporation of the solvent and crystallisation of the residue from light petroleum (b. p. 40—60°) gave the *dimethoxyquinolone* (269 mg., 81%), m. p. 156—158°, $\lambda_{max.}$ (MeOH) 239 (ε 25,100), 257 (ε 26,900), 283 (ε 8500), 292 (ε 7900), and 332 mμ (ε 3700) (Found: C, 65·8; H, 7·4; N, 8·4. $C_{19}H_{26}N_2O_4$ requires C, 65·9; H, 7·6; N, 8·1%).

(*b*) Reaction of the dimethoxy-compound (457 mg.) with acetonitrile and concentrated sulphuric acid, as described above for the corresponding 4-hydroxyquinolone, gave the acetamido-derivative (242 mg., 44%), m. p. and mixed m. p. 156—158°.

3,4,5,10-*Tetrahydro*-9-*methoxy*-2,2,10-*trimethyl*-5-*oxo*-2H-*pyrano*[2,3-b]*quinoline* (VIII; R = H) *and* 3,4,5,6-*tetrahydro*-7-*methoxy*-2,2,6-*trimethyl*-5-*oxo*-2H-*pyrano*[3,2-c]*quinoline* (IX).—A mixture of the quinolone (I; R = H) (300 mg.) and 6N-hydrochloric acid was refluxed for 6 hr., and an excess of 2N-sodium hydroxide was added. Extraction with methylene chloride gave a semi-solid (284 mg.). Thin-layer chromatography with system A or system B gave only two spots. The crude product was chromatographed on neutral alumina. Elution with light petroleum (b. p. 40—60°)–benzene (1 : 2), evaporation of the eluate, and drying of the residue under vacuum gave the angular pyranoquinoline (IX) as a gum (164 mg., 55%). Thin-layer chromatography gave a single spot, R_F 0·63, in system A and a single spot, R_F 0·76, in system B. The compound separated from light petroleum (b. p. 40—60°) in prisms, m. p. 74—76° (lit.,[3] 80—81°), $\lambda_{max.}$ (MeOH) 237 (ε 27,500), 248 (ε 24,000), 253 (ε 24,000), 281 (ε 6600), 291 (ε 6500), and 323 mμ (ε 2500) (Found: C, 70·5; H, 7·1. Calc. for $C_{16}H_{19}NO_3$: C, 70·3; H, 7·0%).

Elution of the column with ethyl acetate, evaporation of the eluate, and drying of the residue under vacuum gave the linear pyranoquinoline (VIII; R = H) as a solid (118 mg., 39%). Thin-layer chromatography gave a single spot, R_F 0·27, in system A and a single spot, R_F 0·67, in system B. Crystallisation from light petroleum (b. p. 40—60°)–ethyl acetate gave prisms, m. p. 129° (lit.,[3] 126—127°), $\lambda_{max.}$ (MeOH) 220 (ε 15,500), 244 (ε 39,800), 302 (ε 6300), 322 (ε 9600), and 333 mμ (ε 8100) (Found: C, 69·9; H, 6·9; N, 5·3. Calc. for $C_{16}H_{19}NO_3$: C, 70·3; H, 7·0; N, 5·1%).

The preparations and isomerisations of the pyranoquinolines in 6N-hydrochloric acid are summarised in Table 3. The acetamidoquinolone (V; R = Me) also gave a mixture of the linear and angular pyranoquinolines but the ratio was not determined.

Cyclisation of 4-*Hydroxy*-8-*methoxy*-3-(3-*methylbut*-2-*enyl*)-2-*quinolone* (XII; R = H).—(*a*) A mixture of the quinolone (XII; R = H) (100 mg.) and 6N-hydrochloric acid (25 c.c.) was refluxed for 6 hr., an excess of a 10% aqueous sodium hydroxide was added, and the mixture was extracted with methylene chloride. Evaporation of the solvent and thin-layer chromatography of the residue in system A gave a single spot, R_F 0·25 (starting material, R_F 0·10). Crystallisation from light petroleum (b. p. 40—60°) afforded 3,4,5,6-*tetrahydro*-7-*methoxy*-2,2-*dimethyl*-5-*oxo*-2H-*pyrano*[3,2-c]*quinoline* (XIII), prisms (89 mg., 89%), m. p. 134—135°, $\lambda_{max.}$ (MeOH) 245 (ε 28,200), 277 (ε 8100), 287 (ε 7800), 319 (ε 3200), and 330 mμ (ε 2300) (Found: C, 69·2; H, 6·7. $C_{15}H_{17}NO_3$ requires C, 69·5; H, 6·6%). The *picrate* separated from ethanol–ether, prisms, m. p. 213—214° (Found: C, 51·3; H, 4·0. $C_{21}H_{20}N_4O_{10}$ requires C, 51·6; H, 4·1%). No product soluble in alkali was obtained.

(*b*) A solution of the quinolone (XII; R = H) (100 mg.) in 8N-hydrochloric acid (30 c.c.) and ethanol (10 c.c.) was refluxed for 3 hr., and then treated as in (*a*). The angular pyranoquinoline (XIII) (59 mg., 59%), m. p. 133—134°, was identical (infrared spectrum and mixed m. p.) with a sample obtained in (*a*). The alkaline solution was acidified with hydrochloric acid, and the mixture was extracted with methylene chloride. Evaporation of the solvent gave 3,4-*dihydro*-5-*hydroxy*-9-*methoxy*-2,2-*dimethyl*-2H-*pyrano*[2,3-b]*quinoline* (XIV) (34 mg., 34%), which gave a single spot, R_F 0·19, on thin-layer chromatography in system A, and which separated from ethyl acetate–light petroleum (b. p. 40—60°) in prisms, m. p. 224—226°, $\lambda_{max.}$

(MeOH) 239 (ε 50,100), 298 (ε 8300), 313 (ε 9600), and 325 mμ (ε 7600) (Found: C, 69·5; H, 6·7. $C_{15}H_{17}NO_3$ requires C, 69·5; H, 6·6%).

Cyclisation of 4,8-*Dimethoxy*-3-(3-*methylbut*-2-*enyl*)-2-*quinolone* (XII; R = Me).—(*a*) A mixture of the quinolone (200 mg.) and polyphosphoric acid (15 c.c.) was heated at 115° for 1 hr. under nitrogen, added to ice, made alkaline with aqueous sodium carbonate, and extracted with methylene chloride. The solvent was evaporated and the residue was chromatographed on neutral alumina. Elution with light petroleum (b. p. 40—60°)–benzene (3 : 1) gave 3,4-*dihydro*-5,9-*dimethoxy*-2,2-*dimethyl*-2H-*pyrano*[2,3-b]*quinoline* (XV) (139 mg., 69%), which, on thin-layer chromatography in system A, gave a single spot, R_F 0·72. Crystallisation from light petroleum (b. p. 60—80°) afforded prisms, m. p. 71—73°, $\lambda_{max.}$ (MeOH) 250 (ε 47,900), 289 (ε 4600), 298 (ε 4100), 322 (ε 3000), and 335 mμ (ε 2800). A good analysis was not obtained, but the compound was satisfactorily characterised as its *perchlorate*, prisms, m. p. 203—205° (from ethanol–ether) (Found: C, 51·2; H, 5·5. $C_{16}H_{20}ClNO_7$ requires C, 51·3; H, 5·4%) and as its *picrate*, prisms, m. p. 175—176° (from ethanol–ether) (Found: C, 52·7; H, 4·4. $C_{22}H_{22}N_4O_{10}$ requires, C, 52·6; H, 4·4%).

(*b*) A solution of the quinolone (XII; R = Me) (204 mg.) in 6N-hydrochloric acid (25 c.c.) was refluxed for 6 hr., water (50 c.c.) was added, and the mixture was extracted with methylene chloride. The organic solution was washed with 2N-sodium hydroxide (3 × 20 c.c.), and then evaporated. The residue was chromatographed on alumina. Elution with benzene–methylene chloride (1 : 1) furnished the angular pyranoquinoline (XIII) (64 mg., 33%) which gave a single spot, R_F 0·25, on thin-layer chromatography in system A, and which separated from light petroleum (b. p. 40—60°) in prisms, m. p. 133—134°, identical (mixed m. p. and infrared spectrum) with an authentic sample.

The alkaline washings were acidified with 2N-hydrochloric acid and extracted with methylene chloride. Evaporation of the solvent yielded the linear pyranoquinoline (XIV) (65 mg., 33%). Thin-layer chromatography in system A gave a single spot, R_F 0·19, and crystallisation from ethyl acetate–light petroleum (b. p. 40—60°) afforded prisms, m. p. and mixed m. p. 224—226°.

The original acid solution was made alkaline, and the mixture was extracted with methylene chloride. Evaporation of the solvent gave the dimethoxypyranoquinoline (XV) (22 mg., 11%). Thin-layer chromatography in system A gave a single spot, R_F 0·72, and crystallisation from light petroleum (b. p. 40—60°) gave prisms, m. p. 68—70°, identical (mixed m. p. and infrared spectrum) with an authentic sample.

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