Quinoline Alkaloids. Part XI.[1] A Study of the Claisen Rearrangement of the 3,3-Dimethylallyl Ether of 4-Hydroxy-1-methyl-2-quinolone. Synthesis of Ifflaiamine and the Identification of a New Alkaloid from *Flindersia ifflaiana* F. Muell

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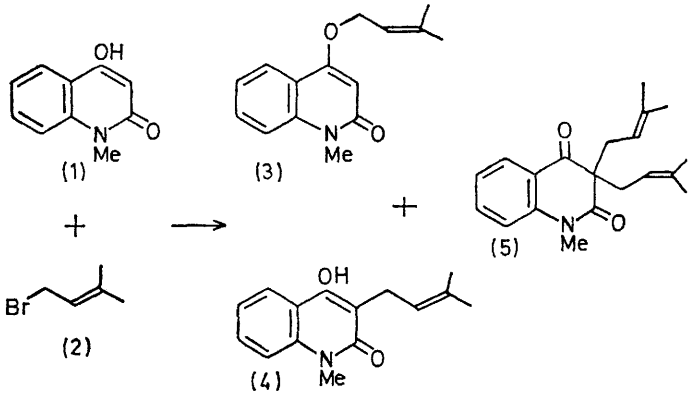
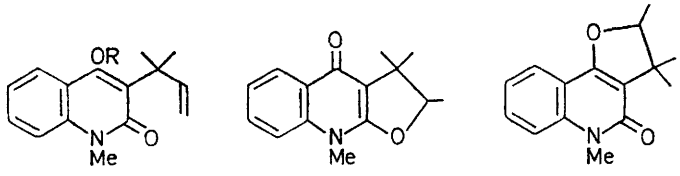
Claisen rearrangement of 1-methyl-4-(3-methylbut-2-enyloxy)-2-quinolone resulted mainly in abnormal reaction to give a 1,2-dimethylallylquinoline and its linear and angular cyclisation products. The intermediate 1,1-dimethylallylquinoline was trapped as its acetate which was cyclised to ifflaiamine with hydrobromic acid. An isomeric furanoquinoline alkaloid is shown to occur with ifflaiamine in *Flindersia ifflaiana* and the biogenesis of the two alkaloids is discussed.

THE alkaloid ifflaiamine was isolated in 1963 from the wood of *Flindersia ifflaiana* F. Muell.[2] It was shown to have a molecular formula of $C_{15}H_{17}NO_2$ and to contain a methylimino- but no methoxy-group. The i.r. and u.v. spectrum of the alkaloid suggested the presence of a



4-quinolone system and the n.m.r. spectrum supported structure (7). In particular, the one-proton quartet at τ 1·56 attributed to the 5-aromatic proton deshielded by the 4-carbonyl group established the linear structure (7) rather than the angular formulation (8). The proposed



'Normal' Claisen products

structure for ifflaiamine is consistent with biogenetic theory in that the furan ring is clearly derived from an isoprene unit; the alkaloid apparently belongs to the rather rare group of natural 1,1-dimethylallyl derivatives. The biogenesis of aryl and heterocyclic compounds of this type (see below) may occur by direct 3-allylation[3] or by Claisen rearrangement of a 3,3-dimethylallyl ether. This biosynthetic problem, prompted us to study the Claisen rearrangement of the 3,3-dimethylallyl ether (3) related to ifflaiamine. We have already reported briefly the successful synthesis of the alkaloid by this method.[4]

The required *O*-3,3-dimethylallyl ether (3) was prepared from 4-hydroxy-1-methyl-2-quinolone (1) and 1-bromo-3-methylbut-2-ene (2). When the components were heated under reflux in acetone in the presence of potassium carbonate, some starting quinolone was recovered and three products were isolated. An acidic compound (3%), $C_{15}H_{17}NO_2$, was shown by its n.m.r. spectrum (Table) to be the 3-(3,3-dimethylallyl)-derivative (4). The *O*-3,3-dimethylallyl ether (3) (22%) was obtained from the neutral fraction; its structure was indicated by i.r. absorption at 1640 cm.$^{-1}$ [N(Me)CO] and by its n.m.r. spectrum (Table), which showed a one-proton singlet at τ 3·97 (3-H). A second neutral product did not crystallise and was not analysed, but it was shown by spectral data to be the bisdimethylallyldione (5). The compound absorbed in the i.r. region at 1695 (ArCO) and 1650 cm.$^{-1}$ [N(Me)CO] and the n.m.r. spectrum (Table) indicated the presence of two equivalent dimethylallyl groups; the proton at C-5 is not profoundly deshielded by the C-4 carbonyl group presumably because the latter does not lie in the plane of the aromatic ring, in contrast to the corresponding group in 4-quinolones. The reaction just described gave a rather poor yield of the required ether (3) (32% based on starting material consumed) but other allylation conditions were no more successful. For instance, reaction of the silver salt of quinolone (1) with 3,3-dimethylallyl bromide in ether at 20°, conditions which generally favour reaction at the more electronegative site in an ambident nucleophile,[5] gave the *O*-dimethylallyl ether (3) in 16% yield, the other products resulting from *C*-allylation.

Claisen Rearrangement of the Ether (3).—When heated at 130—140° for 5 hr. the ether (3) gave a mixture containing three components one of which was acidic,

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[1] Part X, D. R. Boyd and M. F. Grundon, *J. Chem. Soc.* (*C*), 1970, 556.

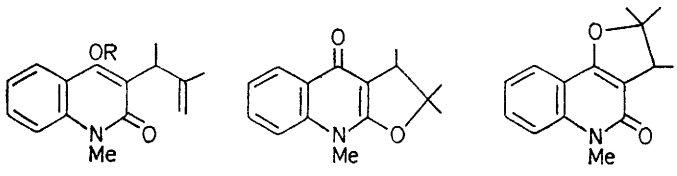
[2] J. Bosson, M. Rasmussen, E. Ritchie, A. V. Robertson, and W. C. Taylor, *Austral. J. Chem.*, 1963, **16**, 480.

[3] W. D. Ollis and I. O. Sutherland in 'Recent Developments in the Chemistry of National Phenolic Compounds,' Pergamon, Oxford, 1961, p. 79.

[4] T. R. Chamberlain and M. F. Grundon, *Tetrahedron Letters*, 1967, 3547.

[5] N. Kornblum, R. A. Smiley, R. K. Blackwood, and D. C. Iffland, *J. Amer. Chem. Soc.*, 1955, **77**, 6269.

one basic, and the third neutral. The acidic compound (20%) was assigned the constitution (9; R = H) on the basis of its n.m.r. spectrum (Table) which in particular established the structure of the side chain; irradiation of the quartet at 5·80 [1H, J = 7·4, CH(CH$_3$)] caused the doublet at 8·60 [3H, J 7·4 Hz, CH(CH_3)] to collapse to a



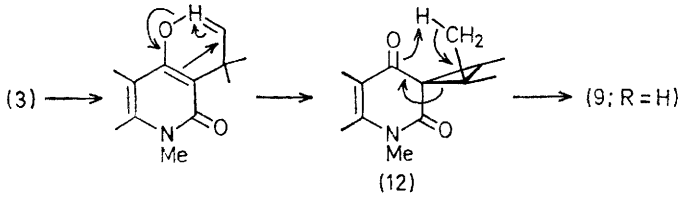
' Abnormal ' Claisen products

singlet and irradiation of the broad vinylic singlets at 4·64 and 4·72 resulted in a sharpening of the singlet at 8·15 [3H, C(CH_3)=CH$_2$]. I.r. absorption at 1640 cm.$^{-1}$ confirmed the presence of a 2-quinolone carbonyl group in the compound.

The n.m.r. spectrum (Table) of the basic product (36%) is consistent with the linear dihydrofuranoquinolone structure (10). Thus, the quartet at 6·64 [1H, J 6·9, –CH(CH$_3$)–] had a chemical shift typical of a β proton in a dihydrofuranoquinoline [6] and was associated with a doublet at τ 8·65 [3H, J 6·9 Hz, CH(CH_3)]. The tricyclic structure was confirmed by the absence of olefinic resonance and the linear 4-quinolone structure (10) is indicated by the quartet at τ 1·54 attributed to the C-5 proton deshielded by the 4-carbonyl group and by the absence of 2-quinolone carbonyl absorption in the i.r. region.

The neutral rearrangement product showed an n.m.r. spectrum (Table) similar to that of the linear dihydrofuranoquinoline (10). The lack of aromatic resonance below τ 2·22 and the presence of i.r. absorption at 1656 cm.$^{-1}$ [N(Me)CO] indicated that the compound had the angular structure (11).

The 4-hydroxyquinoline (9; R = H) apparently arises by ' abnormal ' Claisen rearrangement of the *O*-allyl ether (3) and in accord with the established mechanism of the reaction [7] the ' normal ' rearrangement product (6; R = H) and the spirodione (12) are presumably intermediates as in the following scheme:



The furanoquinolones (10) and (11) are also ' abnormal ' products formed by cyclisation of the 4-hydroxyquinolone (9; R = H) involving, respectively, the 2- and 4-oxygen atoms. The approximately equal yields of furano-products implied that the rates of cyclisation of the 4-hydroxyquinoline (9; R = H) at the two sites were almost identical. When the ether (3) was pyrolysed for a longer time (20 hr.), the ratio of furano-products was different, the angular isomer (11) being formed in 63% yield and the linear product (10) in 31% yield. The new ratio suggests that the linear derivative is isomerised thermally to the angular compound and this was confirmed by pyrolysing the furano-compounds separately for 20 hr. under the original rearrangement conditions; the angular isomer (11) was essentially unchanged but approximately 50% of the linear isomer was isomerised, mainly to the angular compound (11).

In the rearrangement of the ether (3) conducted for 20 hr. a new product (3%) was isolated and the same compound was detected by t.l.c. in the rearrangement of the linear furano-derivative (10). Spectroscopic studies showed that it was the ' normal ' angular furanoquinoline (8). Thus, i.r. absorption at 1653 cm.$^{-1}$ was characteristic of a 2-quinolone carbonyl group and the n.m.r. spectrum (Table) established the presence of a 2,3,3-trimethyldihydrofuran ring; the quartet at 5·43 (1H, J 6·7) [O–CH(CH$_3$)] had a chemical shift typical of an α-proton in a dihydrofuranoquinoline and was associated with a doublet at τ 8·60 (3H, J 6·7 Hz) [O–CH(CH_3)]. The striking non-equivalence of the *gem*-dimethyl group, resonating at τ 8·55 and 8·75, is consistent with its position adjacent to the aromatic system in a rigid environment. The formation of the ' normal ' Claisen product (8) in pyrolyses conducted for 20 hr. but not in the shorter experiment may be a manifestation of the reported reversibility of the abnormal Claisen rearrangement.[8]

When the ether (3) was heated under reflux in *N*-methylpiperidine (b.p. 107°) abnormal Claisen rearrangement products were formed exclusively; the 4-hydroxyquinolone (9; R = H) was isolated in 57% yield and the furano-derivatives (10) and (11) were detected by t.l.c.

The mechanism of the rearrangement of the normal Claisen product to the abnormal compound (see Scheme above) involves the transfer of a proton from the acidic 4-hydroxy-group and it appeared that conversion of this group into the corresponding anion by addition of base might inhibit the abnormal reaction. Accordingly, we heated the ether (3) at 140—145° for 4½ hr. in the presence of anhydrous sodium carbonate, conditions already employed by Claisen [9] for the rearrangement of 3,3-dimethylallylphenyl ether. The main product from our reaction was the ' normal ' angular furano-derivative (8) (89%). The ' abnormal ' products (9; R = H) (4%), (10) (<1%), and (11) (1%) were also formed and an isomer not hitherto encountered in this work was isolated in 6% yield. The new compound was clearly ifflaiamine (7) since its n.m.r. spectrum showed the presence of a 2,3,3-trimethyldihydrofuran ring and was

[6] A. V. Robertson, *Austral. J. Chem.*, 1963, **16**, 451.

[7] E. N. Marvell, D. R. Anderson, and J. Ong, *J. Org. Chem.*, 1962, **27**, 1109; A. von Habich, R. Barner, R. M. Roberts, and H. Schmid, *Helv. Chem. Acta*, 1962, **45**, 1943.

[8] R. M. Roberts and R. G. Landolt, *J. Org. Chem.*, 1966, **31**, 2699.

[9] F. Kremers, F. Roth, E. Tietze, and L. Claisen, *J. prakt. Chem.*, 1922, **105** (2), 65.

essentially identical with the published spectrum [2] of the natural alkaloid. It is clear that addition of base in the Claisen rearrangement led to 'normal' products almost exclusively but at the same time promoted cyclisation of the primary product.

Synthesis of Ifflaiamine.—The foregoing results indicated that a Claisen rearrangement of the 3,3-dimethylallyl ether (3) was unlikely to lead directly to an efficient synthesis of ifflaiamine; even when the abnormal reaction is inhibited, cyclisation of the 4-hydroxyquinolone (6; R = H) favours formation of the angular isomer (8). A new approach to the synthesis of the alkaloid was therefore adopted involving trapping of the intermediate 4-hydroxyquinolone (6; R = H) as its acetate during Claisen rearrangement of ether (3). (Table) which indicated the presence of 1,1-dimethylallyl side-chains as in the acetate.

In planning the synthesis of ifflaiamine by cyclisation of a 1,1-dimethylallyl derivative we expected that the absence of phenolic hydrogen in the acetate (6; R = Ac) and the methyl ether (6; R = Me) would preclude the rearrangement of the side-chain and avoid formation of angular cyclic products. The two compounds were accordingly treated with hydrogen bromide in acetic acid at room temperature. The acetate (6; R = Ac) gave ifflaiamine (56%), the 'abnormal' linear furano-derivative (10) (3%) and the 'abnormal' angular isomer (11) (25%). The 4-methoxy-derivative (6; R = Me) was converted into ifflaiamine (60%) but the angular isomers (8) and (11) were also formed. Thus, although

N.m.r. spectral assignments (τ values) (determined in deuteriochloroform solution at 100 MHz)

Compound	Arom. 5-H	Arom. 6-, 7-, and 8-H	=CH–	$=CH_2$	$-CH_2-$	–CH<	–OMe and >NMe	=C(Me)–	$>CMe_2$	>C–Me
(3)	2·01q	2·42—2·90	4·48t		5·37d		6·35s		8·16s 8·22s	
(4)	2·06q	2·42—2·86	4·30t		6·46d		6·30s		8·15s 8·20s	
(5)	2·00q	2·38—2·94	5·15t		7·25d		6·50s		8·40s 8·50s	
(6; R = H)	2·02q	2·46—2·96	3·42q	4·40q 4·56q			6·34s		8·35s	
(6; R = Ac) [a]	←2·40—2·90→		3·67q	5·03d 5·09d			6·32s		8·44s	
(6; R = Me)	2·15q	2·46—2·88	3·54q	4·99q 5·14q			6·29s 6·34s		8·40s	
(7)	1·54q	2·39—2·76				5·80q	6·32s		8·45s 8·66s	8·56d
(8)	2·22q	2·45—2·90				5·43q	6·36s		8·55s 8·75s	8·60d
(9; R = H)	2·06q	2·42—2·88		4·64s 4·75s		5·80q	6·25s	8·15s		8·60d
(9; R = Ac) [b]	←2·32—2·85→			5·05s		5·95q	6·25s	8·30s		8·60d
(10)	1·54q	2·39—2·73				6·64q	6·35s		8·49s 8·65s	8·65d
(11)	2·22q	2·41—2·90				6·74q	6·30s		8·60s	8·60d

In all cases the integrated areas support the assignments: s = singlet, d = doublet, t = triplet and q = quartet.
[a] OCOMe at 7·65s. [b] OCOMe at 7·68s.

Heating the ether under reflux in acetic anhydride gave the acetate of the 'abnormal' Claisen rearrangement product (9; R = Ac); its structure was established by the n.m.r. spectrum (Table), by i.r. absorption at 1761 $cm.^{-1}$ (OCOMe) and by its conversion by basic hydrolysis into the 4-hydroxyquinolone (9; R = H). When the ether was heated in *N*-methylpiperidine containing acetic anhydride a new acetate was formed in quantitative yield and was shown to be the 'normal' rearrangement product (6; R = Ac) by its n.m.r. spectrum (Table). Thus, the three vinylic protons constituted an ABX system (H_A, doublet at τ 5·03; H_B doublet at τ 5·09; H_X quartet at τ 3·67; J_{AX} = 18, J_{BX} 10 Hz), and the adjacent *gem*-dimethyl group produced a sharp singlet at τ 8·44.

Hydrolysis of the acetate (6; R = Ac) with ethanolic sodium hydroxide at 20° furnished the 'normal' 4-hydroxyquinolone (6; R = H) quantitatively, and this compound was converted into the methyl ether (6; R = Me) with diazomethane. The structures of the new products were confirmed by their n.m.r. spectra rearrangement and angular cyclisation did occur presumably *via* the 4-hydroxy-compound (6; R = H), these reactions constitute efficient synthesis of ifflaiamine; the route through the acetate (6; R = Ac) is preferred since fewer stages are involved and the acetate is purified more readily than the 4-methoxy-derivative.

Isolation of a New Alkaloid from Flindersia ifflaiana *and the Biogenesis of* 1,1- *and* 1,2-*Dimethylallyl Derivatives.*—A sample of crude alkaloid extract from *Flindersia ifflaiana* F. Muell * was separated into two crystalline components. One was shown by comparison with a synthetic sample to be (—)-ifflaiamine (7), although its properties did not correspond with those reported for the alkaloid [2] (see Experimental section). The second alkaloid, which had not been described previously, was shown by comparison with the synthetic compound to be the 'abnormal' linear isomer (10); it was optically active and therefore was unlikely to be an artefact arising from the isolation procedure.

* We are grateful to Dr. E. Ritchie for the sample of alkaloid extract.

After the completion of this work Paul and Bose [10] established the structures of the alkaloids of the rutaceous plant, *Ravenia spectabilis* Engl.; ravenine was the 3,3-dimethylallyl ether (3) and ravenoline was shown to be the 1,2-dimethylallyl derivative (9; R = H). It has been reported recently [11] that alkaloid (10), named spectabiline, is also a component of *R. spectabilis*. The recognition of 'normal' and 'abnormal' Claisen products as constituent of the *Flindersia* species and the isolation from *Ravenia spectabilis* of an 'abnormal' product together with the Claisen precursor suggests that the biosynthesis of 1,1-dimethylallyl derivatives can occur by Claisen rearrangement. Our recent ^{14}C-feeding experiments [12] with *Ravenia spectabilis* establishes that the 3,3-dimethylallyl ether (3) is indeed a precursor of ravenoline (9; R = H). It is therefore probable that the alkaloids (7) and (10) from *Flindersia ifflaiana* are also formed by Claisen rearrangement of ether (3) by 'normal' and 'abnormal' reactions, respectively, followed by cyclisation.

EXPERIMENTAL

The n.m.r. spectra were determined with a Varian HR-100 spectrometer using tetramethylsilane as an internal standard. Optical rotations were measured with a Bendix Ericsson Automatic Polarimeter (type 143A). T.l.c. was on silica gel 41 in chloroform (system A), in ethyl acetate (system B) or in chloroform–ethyl acetate (2 : 1) (system C) or on Merck S. G. in chloroform (system D) or in chloroform–ethyl acetate (2 : 1) (system E).

1-Methyl-4-(3-methylbut-2-enyloxy)-2-quinolone (3).—(*a*) 4-Hydroxy-1-methyl-2-quinolone [2] (7·8 g.) and powdered anhydrous potassium carbonate (6·2 g.) in acetone (120 ml.) were stirred and heated under reflux for 1 hr. 1-Bromo-3-methylbut-2-ene [13] (7·3 g.) in acetone (10 ml.) was added during 30 min. to the suspension and after 60 hr. the white solid was filtered off. The filtrate was concentrated, digested with 2N-aqueous sodium hydroxide (25 ml.) for 15 min., and extracted with ether. The solid obtained by acidification of the aqueous alkaline layer was extracted with boiling chloroform, leaving starting material (2·4 g., 32%); evaporation of the chloroform solution yielded 4-hydroxy-1-methyl-3-(3-methylbut-2-enyl)-2-quinolone (4) (0·29 g., 3%), m.p. 156—159° (from benzene–light petroleum) (lit.,[14] m.p. 162—163°), $\nu_{max.}$ (KBr) 3100 and 1640 cm.$^{-1}$.

Evaporation of the original ether solution and trituration of the residue with light petroleum (b.p. 40—60°) gave the *quinolone* (3) as a colourless solid (1·6 g., 22%) which separated from light petroleum (b.p. 60—80°) as needles, m.p. 118—119·5° (Found: C, 74·4; H, 7·0; N, 5·9. $C_{15}H_{17}NO_2$ requires C, 74·1; H, 7·0; N, 5·8%).

After separation of the ether (3), the residue was chromatographed on alumina. Elution with light petroleum (b.p. 60—80°) afforded a gum, R_F 0·6 (system A), shown by its n.m.r. spectrum (Table) to be the bisdimethylallyl dione (5).

(*b*) The silver salt of the hydroxyquinolone (1) (1·2 g.) [prepared by adding 0·58N-aqueous silver nitrate (10 ml.) to the quinolone (1 g.) in 0·58N aqueous sodium hydroxide] and 1-bromo-3-methylbut-2-ene (0·71 g.) in ether (15 ml.) was stirred in the dark at 20° for 40 hr. A similar work-up to that described in (*a*) gave starting material (0·30 g., 40%), the 4-hydroxyquinolone (4) (0·11 g., 18%), and the ether (3) (0·1 g., 16%), m.p. 118—119·5°.

Claisen Rearrangement of 1-Methyl-4-(3-methylbut-2-enyloxy)-2-quinolone (3).—(a) *By pyrolysis for 5 hr.* The ether (3) (0·95 g.) was heated at 130—140° for 5 hr. under nitrogen, and the products in chloroform were extracted with 2N-aqueous sodium hydroxide. Acidification of the aqueous layer followed by extraction with ether afforded *4-hydroxy-1-methyl-3-(1,2-dimethylprop-2-enyl)-2-quinolone* (9; R = H) (0·18 g., 20%) as needles (from isopropyl ether), m.p. 140—142° (Found: C, 74·2; H, 7·2; N, 5·9. $C_{15}H_{17}NO_2$ requires C, 74·1; H, 7·0; N, 5·8%).

The chloroform solution was evaporated, and the residue in ether was extracted with 2N-aqueous hydrochloric acid. Neutralisation of the acid solution followed by extraction with ether gave *2,3,4,9-tetrahydro-2,2,3,9-tetramethyl-4-oxofurano[2,3-b]quinoline* (10) (0·32 g., 36%) which separated from light petroleum (b.p. 40—60°) as prisms, m.p. 106—108°, R_F 0·15 (system B) (Found: C, 64·5; H, 7·5; N, 5·0. $C_{15}H_{17}NO_2,2H_2O$ requires C, 64·5; H, 7·5; N, 5·0%). The *picrate* crystallised from ethyl acetate as prisms, m.p. 186—190° (Found: C, 53·4; H, 4·2; N, 12·0. $C_{21}H_{20}N_4O_9$ requires C, 53·4; N, 4·2; N, 11·9%).

The ether solution containing the neutral product was evaporated to give *2,3,4,5-tetrahydro-2,2,3,5-tetramethyl-4-oxofurano[3,2-c]quinoline* (11) (0·39 g., 44%) which separated from light petroleum (b.p. 30—40°) as prisms, m.p. 87—88°, R_F 0·37 (system B) (Found: C, 73·9; H, 7·2; N, 5·8. $C_{15}H_{17}NO_2$ requires C, 74·1; H, 7·0; N, 5·8%).

(b) *By pyrolysis for 20 hr.* The ether (3) (0·33 g.) was heated at 140° for 20 hr. under nitrogen. With the isolation procedure described in (a), the 4-hydroxyquinolone (9; R = H) (3%) and the linear furanoquinoline (10) (31%) were obtained. The neutral fraction contained two components, R_F 0·45 and 0·37 (system B), and was chromatographed on alumina. Elution with light petroleum (b.p. 40—60°)–ether (40 : 1) gave a gum (0·011 g., 3%), R_F 0·45, shown by t.l.c. and i.r. comparison to be identical with the angular isomer (8) (see below). Elution with light petroleum (b.p. 40—60°)–ether (33 : 1) afforded the furano-quinoline (11) (0·20 g., 63%), R_F 0·37, m.p. and mixed m.p. 87—88°.

(c) *By pyrolysis with base.* A mixture of the ether (3) (0·40 g.) and anhydrous potassium carbonate (0·046 g.) was heated at 140—145° for 4·5 hr. under nitrogen. The acidic fraction was isolated as described in (a), and yielded the 4-hydroxyquinolone (9; R = H) as needles (0·018 g., 4%), m.p. and mixed m.p. 120—125°.

The nonacidic fraction, which was shown by t.l.c. (system B) to contain four components, R_F 0·45, 0·37, 0·24, and 0·11, was chromatographed on alumina. Elution with benzene gave *2,3,4,5-tetrahydro-2,3,3,5-tetramethyl-4-oxofurano[3,2-c]quinoline* (8) as a solid (0·329 g., 89%), R_F 0·45, which separated from light petroleum (b.p. 30—40°) as needles, m.p. 88—89° (Found: C, 74·0; H, 7·2; N, 5·9. $C_{15}H_{17}NO_2$ requires C, 74·1; H, 7·0; N, 5·8%). Further elution with benzene gave a gum (0·004 g., 1%), R_F 0·37, shown by i.r.

[10] B. D. Paul and P. K. Bose, *J. Indian Chem. Soc.*, 1968, **45**, 552; 1969, **46**, 678.
[11] S. B. Talapatra, B. C. Maiti, B. Talapatra, and B. C. Das, *Tetrahedron Letters*, 1969, 4789.
[12] T. R. Chamberlain, J. F. Collins, and M. F. Grundon, *Chem. Comm.*, 1969, 1269.
[13] H. Staudinger, W. Kreis, and W. Schilt, *Helv. Chem. Acta*, 1922, **5**, 743.
[14] R. A. Corral and D. O. Orazi, *Tetrahedron Letters*, 1967, 583.

and t.l.c. comparison to be the furanoquinoline (11). Elution with benzene–ether (12 : 1) gave ifflaiamine (7) as needles (0·021 g., 6%), m.p. 115—120°, R_F 0·25, identical with a sample prepared by another route (see below). Further elution with the same solvent afforded a trace of the furanoquinoline (10), R_F 0·15 (picrate, m.p. and mixed m.p. 186—190°).

(d) *By heating under reflux in* N-*methylpiperidine*. A solution of the ether (3) (70 mg.) in *N*-methylpiperidine (10 ml.) was heated under reflux for 16 hr. after which the mixture was evaporated to dryness. The residue in ether was shaken successively with 2N-aqueous hydrochloric acid and 2N-aqueous sodium hydroxide. Acidification of the alkaline solution afforded the 4-hydroxyquinolone (9; R = H) (40 mg., 57%), m.p. and mixed m.p. 120—126°. Evaporation of the ether solution gave a gum shown by t.l.c. comparison with authentic samples to contain starting material (3), and the furano-derivatives (10) and (11).

Pyrolysis of the Furanoquinolines (10) *and* (11).—The linear furanoquinoline (10) (25 mg.) was heated at 140° for 20 hr. under nitrogen. Unchanged furanoquinoline (10) (*ca.* 50%) was separated as its picrate and the residue was shown by t.l.c. comparison with authentic samples (system E) to consist of the angular furanoquinolines (8), R_F 0·60 and (11), R_F 0·47.

Similar pyrolysis of the angular furanoquinoline (11) was shown by t.l.c. (system E) to give unchanged material, R_F 0·47, with traces of ifflaiamine (7), R_F 0·31 and its linear isomer (10), R_F 0·19.

4-*Acetoxy*-1-*methyl*-3-(1,2-*dimethylprop*-2-*enyl*)-2-*quinolone* (9; R = Ac).—A solution of the ether (3) (0·12 g.) in acetic anhydride (25 ml.) was heated under reflux for 20 hr. after which the mixture was evaporated to dryness. Crystallisation of the solid residue from light petroleum (b.p. 40—60°) afforded the *acetate* as prisms, m.p. 104—105°, R_F 0·71 (system D) (Found: C, 71·8; H, 6·9. $C_{17}H_{19}NO_3$ requires C, 71·6; H, 6·7%).

The crude product was shown by t.l.c. (system D) to contain traces of the angular furanoquinolines (8), R_F 0·60 and (11), R_F 0·48.

Hydrolysis of the acetate with sodium hydroxide in aqueous ethanol at 20° gave the 4-hydroxyquinolone (9; R = H), m.p. and mixed m.p. 125—128°, quantitatively.

4-*Acetoxy*-1-*methyl*-3-(1,1-*dimethylprop*-2-*enyl*)-2-*quinolone* (6; R = Ac).—A solution of the ether (3) (1·4 g.) and acetic anhydride (5·7 ml.) in *N*-methylpiperidine (5 ml.) was heated under reflux for 26 hr. after which the mixture was evaporated to dryness. The residue in ether was washed with 2N-aqueous hydrochloric acid and then passed through a short column of neutral alumina. Evaporation gave the *acetate* as a solid (1·7 g., 98%), showing a single spot, R_F 0·54 on t.l.c. (system E), which separated from light petroleum (b.p. 40—60°) as prisms, m.p. 123—124·5°, $\nu_{max.}$ (KBr) 1761 and 1642 cm.$^{-1}$ (Found: C, 71·8; H, 6·8; N, 4·9. $C_{17}H_{19}NO_3$ requires C, 71·6; H, 6·7; N, 4·9%).

(±)-*Ifflaiamine* (7).—(*a*) The acetate (6; R = Ac) (0·7 g.) in a 12·5% solution of hydrobromic acid in acetic acid (14 ml.) was kept at 20° for 26 hr., after which the mixture was evaporated to dryness. An aqueous solution of the residue was made alkaline with sodium hydroxide and extracted with ether. The product was shown by t.l.c. (system B) to contain four components, R_F 0·49, 0·43, 0·24, and 0·08. The following components were obtained by preparative t.l.c.: (i) the angular furanoquinoline (8) (0·14 g., 28%), R_F 0·43, separating from light petroleum (b.p. 30—40°) as needles, m.p. and mixed m.p. 88—89°; (ii) (±)-*ifflaiamine* (0·28 g., 56%), R_F 6·24, separating from light petroleum (b.p. 40—60°) as needles, m.p. 128—129° (Found: C, 73·9; H, 7·0; N, 5·5. $C_{15}H_{17}NO_2$ requires C, 74·1; H, 7·0; N, 5·8%). The i.r. spectrum was almost identical with that of natural (−)-ifflaiamine,[2] m.p. 122—125° (see below) and the two samples gave identical spots, R_F 0·24, on t.l.c. The *picrate* of (±)-ifflaiamine crystallised from ethyl acetate as yellow prisms, m.p. 179—182° (Found: C, 53·6; H, 4·4; N, 11·8. $C_{21}H_{20}N_4O_9$ requires C, 53·4; H, 4·2; N, 11·8%) and its i.r. spectrum was identical with that of (−)-ifflaiamine picrate,[2] m.p. 189—192° (see below); (iii) the linear furanoquinoline (10) (0·013 g., 3%), R_F 0·08 was identified as its picrate, m.p. and mixed m.p. 186—190°.

A more convenient but less efficient method of isolating ifflaiamine is described in (*b*) below.

(*b*) The acetate (6; R = Ac) (2·5 g.) was hydrolysed with sodium hydroxide in aqueous enthanol at 20° to the 4-hydroxyquinolone (6; R = H) which was obtained as a gum (2·1 g., 98%) showing a single spot, R_F 0·52, on t.l.c. (system B). Its structure was confirmed by n.m.r. spectroscopy (Table). The gum (2·1 g.) in methanol–ether (1 : 1) was treated with an excess of ethereal diazomethane. After 24 hr., the solution was evaporated to dryness and the residue, which was shown by t.l.c. (system B) to contain a major component, R_F 0·60, and minor fractions, R_F 0·45 and 0·37, was chromatographed on alumina. Elution with light petroleum (b.p. 60—88°)–ether (50 : 1) gave the methyl ether (6; R = Me) (1·5 g., 67%), m.p. 63—66°, R_F 0·60, which was identified by its n.m.r. spectrum.

The methyl ether (0·13 g.) was cyclised with hydrobromic acid as described in (*a*). The product in acid solution was extracted with ether and the aqueous solution was made alkaline with sodium hydroxide and again extracted with ether. Evaporation of the ether solution and crystallisation of the residue from light petroleum (b.p. 40—60°) gave (±)-ifflaiamine (0·08 g., 60%), m.p. and mixed m.p. 128—129°. It was shown by t.l.c. that the isomers (8) (10), and (11) were also formed.

Alkaloids of Flindersia ifflaiana *F. Meull.*—A sample * (71 mg.), m.p. 38—47°, of the basic extract of *Flindersia ifflaiana* F. Meull., which was shown by t.l.c. (system B) to contain two main components, R_F 0·25 and 0·11, was chromatographed on alumina. Elution with benzene furnished (−)-ifflaiamine (42 mg.), m.p. 116—120°, R_F 0·25, which separated from light petroleum (b.p. 40—60°) as needles, m.p. 122—125°, $[\alpha]_D$ −6·20° (MeOH) and −9·15° ($CHCl_3$) (lit.,[2] gum, $[\alpha]_D$ −0·6°, dihydrate, m.p. 62—63°).

The picrate separated from ethyl acetate as prisms, m.p. 189—192°.

Elution with benzene–chloroform (20 : 1) gave a new *alkaloid* (18 mg.), m.p. 47—50°, R_F 0·11, $[\alpha]_D$ −0·91° ($CHCl_3$) and −1·62° (MeOH), which after crystallisation from light petroleum (b.p. 40—60°) had m.p. 53—54°. The *picrate* separated from ethyl acetate as prisms, m.p. 188—191°. The alkaloid was shown to have structure (10) by comparison with the racemate, m.p. 106—108° (picrate, m.p. 186—190°).

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