Quinoline Alkaloids. Part 24.[1,2] Dimerization of *N*-Methylflindersine[2]

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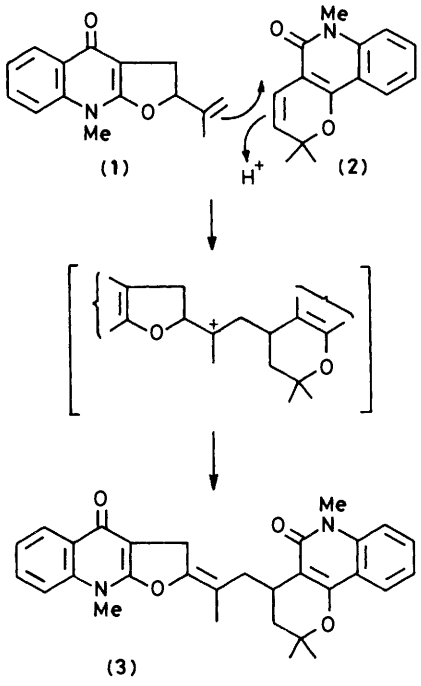
Reaction of 2,6-dihydro-2,2,6-trimethyl-5*H*-pyrano[3,2-*c*]quinolin-5-one (*N*-methylflindersine) with acid gave the dimer (**5**) which was converted into its dehydro derivative (**4**). The biogenesis of the dimeric quinolinone alkaloid, pteledimerine (**3**) is discussed.

A plausible biosynthetic pathway to pteledimerine (**3**), a dimeric quinolinone alkaloid isolated from *Ptelea trifoliata*,[3] involves acid-catalysed addition of the olefin (**1**) to *N*-methylflindersine (**2**) (Scheme 1). The co-occurrence in *P. trifoliata* of the latter alkaloid and of terminal olefins of type (**1**) provides chemotaxonomic support for this proposal and prompted us to study the reactions of *N*-methylflindersine with acids.



Scheme 1.

N-Methylflindersine was unaffected by hot acetic acid but on being heated under reflux with formic acid or with trifluoroacetic acid a crystalline compound was formed (57—68% yield). The mass spectrum showed a molecular ion peak at *m/z* 482 (100%) corresponding to a dimer of *N*-methylflindersine of molecular formula $C_{30}H_{30}N_2O_4$; the presence of dihydrodimethyl- and dimethyl-pyranoquinolinone portions was indicated by fragment ions at *m/z* 242 (9) and 241, *cf.* (**2**), respectively. On this basis, the four structures (**5**)—(**8**) for the dimer should be considered.

In the high frequency (270 MHz) ^{1}H n.m.r. spectrum of the dimer, the resonance at 3.58 p.p.m. (1 H, dd) is assigned to a benzylic CH group as in structures (**5**) or (**8**); the resonances at 2.24 (1 H, dd) and 2.02 p.p.m. (1 H, dd) for the CH_2 group also favour structures (**5**) or (**8**) and are comparable in chemical shift with that recorded[3] (δ 2.16) for the corresponding methylene group in pteledimerine (**3**). A one-proton singlet at δ 6.35 in the n.m.r. spectrum is due to the olefinic proton of the dimethylpyrano ring of the dimer and comparison with the spectra of *N*-methylflindersine and its derivatives in which C-4 protons occur at δ 6.84—6.65 and C-3 protons at 5.60—5.46[4,5] suggests that the dimer has structure (**5**) rather than structure (**8**).

Table. ^{13}C N.m.r. chemical shifts of compounds (**2**), (**4**) and (**5**) (δ values)

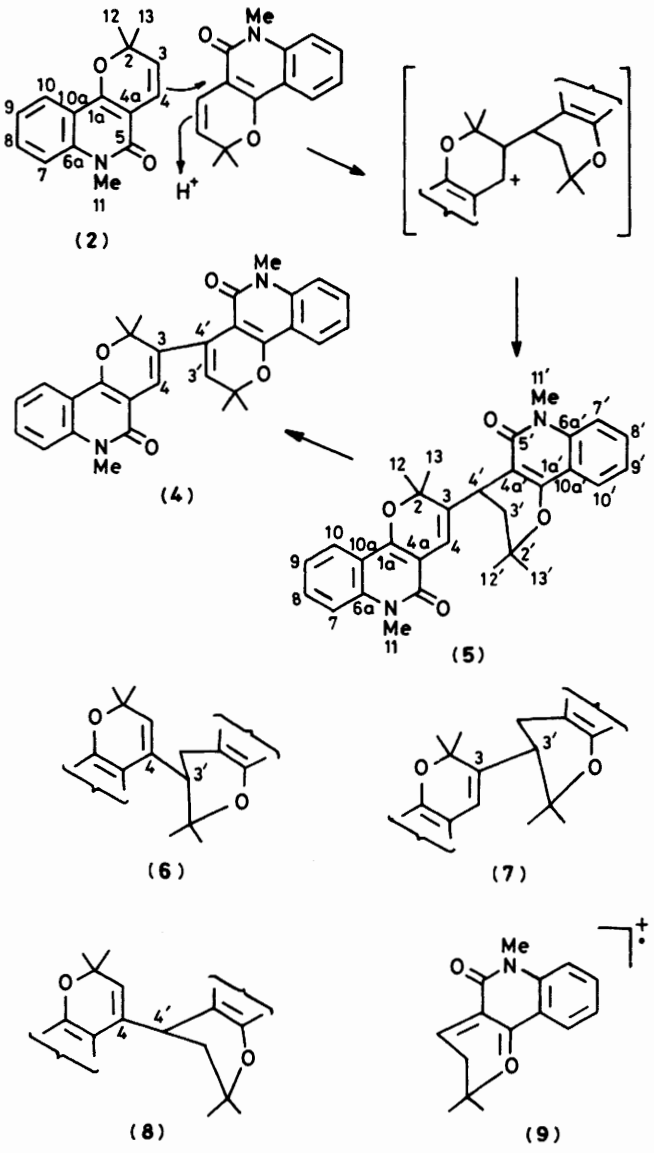
Carbon	(5)	(2)	(4)
1a,1a′	157.0, 153.6	151.9	156.0, 154.4
2	81.9	79.5	81.1, 78.0
2′	76.9		
3	141.9	117.0	130.8
3′	43.7		123.1
4	112.5	126.8	131.2
4′	24.3		137.9
4a,4a′	116.7, 116.3	115.7	116.1
5,5′	162.1, 161.0	162.9	161.1, 160.2
6a,6a′	139.1, 138.9	138.3	139.2, 139.1
7,7′	113.9, 113.8	118.5	113.8
8,8′	130.4, 130.3	130.9	130.4, 128.6
9,9′	123.1	122.6	123.6, 123.4
10,10′	121.6, 121.4	122.0	121.5
10a,10a′	108.3, 107.7	106.7	108.0
11,12	29.2, 29.1	28.7	29.7, 28.2
11′,12′	27.4, 26.7		27.2, 25.1
13,13′	31.9, 29.4	29.1	29.3

Reaction of the dimer with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in benzene gave a dehydro derivative. The mass spectrum of the new compound showed a molecular ion peak at *m/z* 480 ($C_{30}H_{28}N_2O_4$) and a prominent fragment ion at *m/z* 241 representing cleavage of the molecule into *N*-methylflindersine (**2**); the base peak at *m/z* 226 ($C_{14}H_{12}NO_2$) is attributed to loss of a methyl group from the *N*-methylflindersine fragment ion. The ^{1}H n.m.r. spectrum shows that the dehydro compound has the 'unsymmetrical' structure (**4**) containing a C(3)–C(4′) bond. Thus, there are olefinic signals at δ 6.61 (1 H, s, 4-H) and 5.50 (1 H, s, 3′-H) and two *N*-methyl resonances are distinguishable at δ 3.70 and 3.65. The identification of the dehydro derivative confirms structure (**5**) for the dimer of *N*-methylflindersine.

The ^{13}C n.m.r. spectra of the dimer (**5**) and its dehydro derivative (**4**) were assigned by comparison with that of *N*-methylflindersine (**2**) (see Table); the spectrum of the latter apparently has not been recorded previously, although the ^{13}C n.m.r. spectra of related alkaloids with oxygen substituents in the homocyclic ring have been reported.[5] The off-resonance spectrum of the dehydro compound is in accord with the 'unsymmetrical' structure (**4**) in showing doublets at δ 131.2 (C-4) and 123.1 (C-3′) and separate resonances for 20 of the 30 carbon atoms. The ^{13}C n.m.r. spectrum of the dimer (**5**) is more

difficult to assign, partly because of the lack of suitable model compounds, and is less useful than the ^{1}H n.m.r. spectrum in determining the structure of the compound.

Compound (**5**) can be regarded as the Markovnikov dimer of *N*-methylflindersine; its formation by the mechanism indicated in Scheme 2 thus supports the proposed analogous route to the alkaloid pteledimerine (Scheme 1).



Scheme 2.

Experimental

^{1}H N.m.r. spectra were determined with JEOL FX (270 MHz) and Perkin-Elmer R12 (60 MHz) spectrometers, ^{13}C n.m.r. spectra with a JEOL spectrometer (tetramethylsilane as an internal standard), mass spectra with an AE1 MS9 instrument, and i.r. spectra with a Perkin-Elmer 457 spectrometer.

Dimerization of N-*Methylflindersine.*—(*a*) A solution of *N*-methylflindersine (0.2 g) (prepared from *N*-methyl-4-hydroxyquinolin-2-one and 3-methylbut-2-enal [1]) in formic acid (50 ml) was refluxed for 1 h. Evaporation of the solution, trituration of the residue with light petroleum (b.p. 40—60 °C), then with ether and crystallisation from methanol gave 2,2′,3,4′,6,6′-*hexahydro*-2,2,2′,2′,6,6′-*hexamethyl*(3,4′-*bi*-5H-*pyrano*[3,2-*c*]-*quinolin*)-5-*one* (**5**) as prisms (0.12 g), m.p. 257—258 °C; $\nu_{max.}$(KBr) 1 635 cm^{-1} (C=O in quinolin-2-one); δ_H ($CDCl_3$, 270 MHz) 8.01—7.95 (2 H, m, 10-H, 10′-H), 7.57—7.18 (6 H, m, 7-H, 7′-H, 8-H, 8′-H, 9-H, 9′-H), 6.35 (1 H, s, 4-H), 3.62 and 3.615 (6 H, two NMe), 3.58 (1 H, dd, J_{AX} 10, J_{MX} 7 Hz) (C*H*CH_2), 2.24 (1 H, dd, J_{AM} 14 Hz, CHC*H*$_2$), 2.02 (1 H, dd, CHC*H*$_2$), 1.96 (3 H, s, Me), 1.62 (3 H, s, Me), 1.54 (3 H, s, Me), and 1.31 (s, 3 H, Me); *m/z* 482.2212 (M^+, 100%; $C_{30}H_{30}N_2O_4$ requires 482.2205), 467 (M^+ − Me, 20), 308 (M^+ − $C_{10}H_8NO_2$, 23), 295 (62), 294 (3), 242 (39), and 241 (21).

(*b*) A solution of *N*-methylflindersine (0.2 g) in trifluoroacetic acid (50 ml) was refluxed for 24 h. Evaporation, followed by trituration of the residue with di-isopropyl ether gave the dimer (0.14 g) (from methanol), m.p. and mixed m.p. 257—258 °C.

Reaction of the Dimer (**5**) *with DDQ.*—A mixture of the dimer (**5**) (0.15 g), DDQ (0.1 g), and benzene (50 ml) was refluxed for 24 h and filtered. The solution was washed with 2M-sodium hydroxide solution and evaporated. Crystallisation of the residue from methanol gave 2,2,2′,2′,6,6′-*hexamethyl*-2,2′,6,6′-*tetrahydro*(3,4′-*bi*-5H-*pyrano*[3,2-*c*]*quinolin*)-5-*one* (**4**) as yellow prisms (77 mg), m.p. 265—267 °C; $\nu_{max.}$(KBr) 1 640 cm^{-1}; δ_H ($CDCl_3$, 60 MHz) 8.02 (2 H, d, *J* 6 Hz, 10-H, 10′-H), 7.75—7.07 (6 H, m, 7-H, 7′-H, 8-H, 8′-H, 9-H, 9′-H), 6.61 (1 H, s, 4-H), 5.50 (1 H, s, 3′-H), 3.70 and 3.65 (6 H, two NMe), and 1.55 (12 H, s, four Me); *m/z* 480.2030 (M^+, 8%; $C_{30}H_{28}N_2O_4$ requires 480.2049), 465 (M^+ − Me, 4), 241 (62), 240 (57), and 226 (100).

Acknowledgements

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