A further observation by Fitzgerald *et al.* (1978) that the magnitude of puckering in unsymmetrically substituted phosphetanes is substantially larger than in symmetrically substituted compounds can probably now be discounted, based on subsequent studies. Thus, to date, the structures of twelve phosphetanes have been determined (Swank & Caughlan, 1968; Moret & Trefonas, 1969; Fitzgerald *et al.*, 1978; Mazhar-ul-Haque, 1970, 1971, 1979; Mazhar-ul-Haque, Horne, Cremer, Kremer & Kafarski, 1981; Mazhar-ul-Haque & Horne, 1982, 1984, unpublished results) with a mean puckering angle of 24·5° ($\sigma = 5\cdot1°$).* Seven of these are symmetrically substituted, with a mean puckering angle of 23·7° ($\sigma = 4\cdot0°$) compared with a mean value of 25·6° ($\sigma = 6\cdot8°$) for the unsymmetrically substituted ones.

The geometry around P in (I) is as expected in the presence of a four-membered ring. The internal angle at P is 81·1 (1)° with adjacent angles 86·1 (1) and 85·8 (1)°. The internal angle opposite to P is 99·2 (2)°. These angles match very well with those found in other substituted phosphetanes. The naphthalene ring is essentially planar [with 0·052 (2) Å maximum deviation, r.m.s.d = 0·035 Å]. The P(1)—O(20) bond is relatively long, but consistent with values observed in other, similar structures (Swank & Caughlan, 1968; Mazhar-ul-Haque, 1970, 1971).

Other bond lengths and angles are comparable with the observed values in related structures (Mazhar-ul-Haque, 1970, 1971). All non-hydrogen intermolecular contacts are larger than the sum of the van der Waals radii of the involved atoms.

* We have excluded from this analysis fused-ring phosphetanes such as, for example, the tetracyclic compound studied by Mazhar-ul-Haque, Rashid & Cremer (1978), due to the different ring constraints in these cases.

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10-Hydroxy-10-methyl-10,11-dihydroquinine, $C_{21}H_{28}N_2O_3$, a New Derivative of Quinine

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Abstract. $M_r = 356\cdot5$, orthorhombic, $P2_12_12_1$, $a = 11\cdot199$ (3), $b = 11\cdot237$ (3), $c = 15\cdot318$ (4) Å, $V = 1927\cdot7$ (9) Å^3, $Z = 4$, $D_x = 1\cdot228$, $D_m = 1\cdot224$ (1) Mg m^{-3}, λ(Mo $K\alpha$) = 0·71069 Å, $\mu = 0\cdot077$ mm^{-1}, $F(000) = 768$, $T = 293$ K, final $R = 0\cdot032$ for 1790 unique reflections. The molecular structure of the title compound is very similar to that of cinchonidine. The packing is determined by intermolecular hydrogen bonds between hydroxyl groups and N atoms of the quinuclidine moiety; this led to the formation of molecular layers parallel to the *ab* plane.

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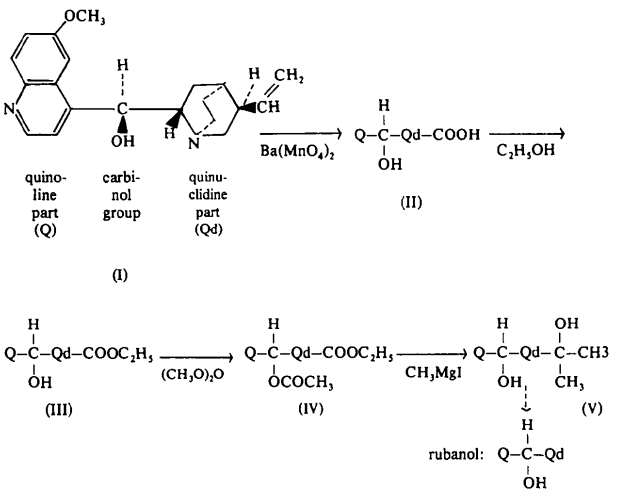
Introduction. The title compound (V) is a new derivative of quinine (I), one of the *Cinchona* alkaloids, whose chemical and structural properties are the subject of our systematic studies. The structure of quinine base in the crystalline state has not yet been determined because of difficulties in the preparation of crystals suitable for X-ray structure analysis. Also, the crystals of most quinine salts are unstable and effloresce in air. Thus we decided to investigate (V), whose crystals appeared to be very well shaped and stable. Compound (V) was obtained at one of the stages of quinine degradation:



which involves elimination of the vinyl chain at C(3) (for numbering of the atoms see Fig. 1). According to the hypothesis given earlier together with a description of a proposed procedure (Suszko-Purzycka, 1963) such a degradation should lead to rubanol (8-quinuclidinyl-4-quinolinylcarbinol).

Quinine is a very important antimalarial drug, the most active against malaria parasite, *Plasmodium* sp., of all *Cinchona* alkaloids. Therefore, it seemed interesting to compare the structure of (V), which differs from (I) only in the substituent at C(3), with that of other *Cinchona* alkaloids, especially cinchonidine having the same absolute configuration.

Experimental. The ethyl ester of 9-acetylquitenine (IV) was obtained by transformation of quinine (I) to quitenine (II) and esterification with ethyl alcohol followed by acetylation. The structure of (IV) has been reported (Dupont, Konsur, Lewiński & Oleksyn, 1985). A solution of (IV) in ether was slowly added to a solution of methylmagnesium iodide obtained by boiling a mixture of CH_3I (15·5 ml), anhydrous ether (90 ml), metallic Mg (6 g), and a catalytic amount of I in a water-tight three-necked flask. The reactive solution was extracted three times with ether in the presence of an alkaline solution of sodium versenate (80 g). The ether solutions were dried with anhydrous K_2CO_3 and concentrated. After concentration the product (V) was isolated and crystallized twice from ethanol (30%). The crystals were transparent, slightly yellowish prisms (yield 15%, m.p. 518–519 K); composition, found: C 70·92, H 8·1, N 7·80%; calculated: C 70·78, H 7·86, N 7·80; IR(KBr)(cm^{-1}): 3400–3100*s*, 2960*s*, 2940*s*, 2880*m*, 1620*m*, 1590*m*, 1470*m*, 1430*s*, 1360*m*, 1240*m*, 1200*m*, 1120*s*, 1035*s*, 1020*m*, 860*m*, 835*s*, 765*m*, 715*m*. The molecular weight of (V) was determined from its mass spectrum: *m/e* (% relative abundance): 357 (24), 356 (75), 189 (100), 150 (39), 110 (47), 82 (72), 43 (70). IR spectra were recorded on a Perkin–Elmer 577 spectrometer; the mass spectrum was obtained using an LKB 2091 instrument at 70 e V.

Crystals of (V) were combinations of forms {001}, {101} and {110}. Crystal 0·40 × 0·25 × 0·40 mm. Enraf–Nonius CAD-4 diffractometer. Lattice parameters (determined together with the space group by photographic methods), confirmed and refined in the auto-indexing procedure from setting angles of 15 reflections in the θ range 8–15°. Measurements of reflection intensities carried out in the range $0·5 < \theta < 25°$; $0 < h < 13$, $0 < k < 13$, $0 < l < 18$; $\omega/2\theta$ scanning mode; graphite-monochromated Mo $K\alpha$ radiation; max. value of $(\sin\theta)/\lambda$ 0·595 $Å^{-1}$, scan width $0·70° + 0·42°\tan\theta$. 1999 measured reflections, 1790 unique with $|F_o| > 3\sigma(F_o)$. Intensities of two control reflections, recorded after every 48 reflections, remained constant to within ±2%. The net intensity of a reflection and its standard deviation were calculated according to $I = (T - 2BGL - 2BGR)/NPI$ and $\sigma(I) = [T + 4(BGL + BGR)]^{1/2}/NPI$, where T is the total integrated intensity over the scan range, NPI is proportional to (scan speed)$^{-1}$, and BGL and BGR are respectively left and right backgrounds over $\frac{1}{4}$ of the scan range. Data corrected for Lorentz and polarization effects but not for absorption. Structure solved by direct methods with *SHELX*76 (Sheldrick, 1976) and 352 normalized structure factors having $E > 1·2$. Origin defined with the phases of reflections 3,0,12, 150, 0,13,1, 1,11,0, while 058 and 296, 235 were used as enantiomorph and multisolution phases respectively. The E map with the best consistency revealed the positions of all non-hydrogen atoms, but the configuration at C(8) and C(9) was opposite to that for quinine, known from other methods to be S and R respectively (Lyle & Keefer, 1967). Therefore, a proper enantiomorph was generated by reversal of all the atomic coordinates. In the course of the anisotropic refinement the structure was divided into two segments, *i.e.* the quinoline and quinuclidine parts which had a common fragment consisting of the atoms C(9), H(C9), O(12) and H(O12). Each of the segments was refined separately but together with the common fragment. H-atom positions were found from difference Fourier maps at various stages of the

refinement. Total number of parameters refined: 347. Refinement (on F) was terminated with $\Delta/\sigma < 0{\cdot}1$ for most of the non-hydrogen atoms; average and max. Δ/σ 0·064 and 0·323 [x coordinate for C(24)], respectively. The difference Fourier map had no peaks higher than 0·14 e Å^{-3}. Final $R = wR = 0{\cdot}032$ (unit weights). Atomic scattering factors for O, N, C, and H atoms were those of *SHELX*76. All calculations performed on a Cyber72 computer.

Discussion. Final atomic coordinates are given in Table 1,* while bond distances and angles are listed in Table 2.

The numbering of the atoms is given in Fig. 1, which depicts the molecule projected along the line C(4)···N(1).

The molecular structure of the title compound is in agreement with that proposed for quinine (Turner & Woodward, 1953). The bond lengths and angles are close to those found in other *Cinchona* alkaloids (Oleksyn, 1982; Oleksyn, Lebioda & Ciechanowicz-Rutkowska, 1979; Oleksyn, Stadnicka & Hodorowicz, 1978; Karle & Karle, 1981; Kashino & Haisa, 1983).

The quinoline part of the molecule is not planar, the largest deviations from the least-squares plane being those for C(14) and C(16) [−0·024 (2) and −0·026 (2) Å respectively].

The methoxy group, O(23)—C(24), shows a tendency to be coplanar with the quinoline moiety [deviations from the least-squares plane: −0·054 (2) and −0·040 (2) Å respectively], probably as a consequence of some degree of conjugation between O(23)

* Lists of structure factors, anisotropic thermal parameters, H-atom positions with isotropic thermal parameters, and interatomic bonds and angles involving hydrogen H atoms have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 42090 (17 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

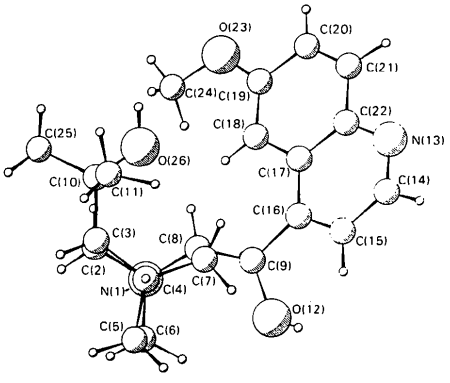


Fig. 1. Projection of the molecule of (V) along the line C(4)···N(1).

Table 1. *Fractional atomic coordinates* (×10^4) *for non-hydrogen atoms and equivalent isotropic thermal parameters* (Å^2 ×10^4) *with e.s.d.'s in parentheses*

$$U_{eq} = \tfrac{1}{3}\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	U_{eq}
N(1)	5776 (2)	9240 (2)	1852 (1)	31
C(2)	4498 (2)	8918 (2)	1938 (2)	37
C(3)	4108 (2)	7969 (2)	1256 (2)	35
C(4)	5150 (2)	7836 (2)	608 (2)	36
C(5)	5413 (2)	9084 (2)	250 (2)	42
C(6)	5943 (2)	9831 (2)	995 (2)	40
C(7)	6288 (2)	7383 (2)	1057 (2)	34
C(8)	6467 (2)	8113 (2)	1899 (1)	29
C(9)	7775 (2)	8287 (2)	2163 (1)	31
C(10)	3619 (2)	6811 (2)	1663 (2)	42
C(11)	3474 (3)	5848 (3)	968 (2)	59
O(12)	8422 (2)	8818 (2)	1467 (1)	42
N(13)	9457 (2)	4926 (2)	2868 (1)	42
C(14)	9573 (2)	5415 (2)	2091 (2)	47
C(15)	9033 (2)	6491 (2)	1852 (2)	42
C(16)	8317 (2)	7099 (2)	2428 (1)	31
C(17)	8133 (2)	6574 (2)	3265 (1)	31
C(18)	7389 (2)	7080 (2)	3920 (2)	37
C(19)	7266 (2)	6528 (2)	4710 (2)	46
C(20)	7883 (3)	5465 (2)	4894 (2)	49
C(21)	8594 (2)	4963 (2)	4283 (2)	42
C(22)	8732 (2)	5493 (2)	3451 (1)	34
O(23)	6570 (2)	6904 (2)	5384 (1)	74
C(24)	5932 (5)	7996 (4)	5277 (3)	96
C(25)	2435 (3)	7058 (3)	2111 (1)	67
O(26)	4456 (2)	6407 (2)	2296 (1)	49

Table 2. *Bond distances* (Å) *and angles* (°) *involving non-hydrogen atoms with e.s.d.'s in parentheses*

N(1)—C(2)	1·483 (3)	C(10)—O(26)	1·423 (3)
N(1)—C(6)	1·483 (3)	N(13)—C(14)	1·317 (3)
N(1)—C(8)	1·486 (3)	N(13)—C(22)	1·365 (3)
C(2)—C(3)	1·555 (3)	C(14)—C(15)	1·400 (4)
C(3)—C(4)	1·540 (3)	C(15)—C(16)	1·373 (3)
C(3)—C(10)	1·542 (3)	C(16)—C(17)	1·426 (3)
C(4)—C(5)	1·535 (4)	C(17)—C(18)	1·423 (3)
C(4)—C(7)	1·534 (3)	C(17)—C(22)	1·417 (3)
C(5)—C(6)	1·536 (4)	C(18)—C(19)	1·368 (3)
C(7)—C(8)	1·542 (3)	C(19)—C(20)	1·407 (4)
C(8)—C(9)	1·533 (3)	C(19)—O(23)	1·361 (3)
C(9)—O(12)	1·421 (3)	C(20)—C(21)	1·352 (3)
C(9)—C(16)	1·522 (3)	C(21)—C(22)	1·415 (3)
C(10)—C(11)	1·526 (4)	O(23)—C(24)	1·429 (6)
C(10)—C(25)	1·519 (4)		

C(2)—N(1)—C(6)	108·0 (2)	C(11)—C(10)—C(25)	110·6 (2)
C(2)—N(1)—C(8)	106·8 (2)	C(11)—C(10)—O(26)	108·6 (2)
C(6)—N(1)—C(8)	111·0 (2)	C(25)—C(10)—O(26)	109·0 (2)
N(1)—C(2)—C(3)	112·3 (2)	C(14)—N(13)—C(22)	117·1 (2)
C(2)—C(3)—C(4)	106·6 (2)	N(13)—C(14)—C(15)	123·6 (2)
C(2)—C(3)—C(10)	114·0 (2)	C(14)—C(15)—C(16)	120·9 (2)
C(4)—C(3)—C(10)	116·6 (2)	C(9)—C(16)—C(15)	119·9 (2)
C(3)—C(4)—C(5)	106·7 (2)	C(9)—C(16)—C(17)	123·0 (2)
C(3)—C(4)—C(7)	111·9 (2)	C(15)—C(16)—C(17)	117·1 (2)
C(5)—C(4)—C(7)	107·7 (2)	C(16)—C(17)—C(18)	123·6 (2)
C(4)—C(5)—C(6)	107·9 (2)	C(16)—C(17)—C(22)	117·9 (2)
N(1)—C(6)—C(5)	111·4 (2)	C(18)—C(17)—C(22)	118·5 (2)
C(4)—C(7)—C(8)	107·8 (2)	C(17)—C(18)—C(19)	120·1 (2)
N(1)—C(8)—C(7)	110·2 (2)	C(18)—C(19)—C(20)	120·8 (2)
N(1)—C(8)—C(9)	113·7 (2)	C(18)—C(19)—O(23)	126·0 (2)
C(7)—C(8)—C(9)	114·4 (2)	C(20)—C(19)—O(23)	113·2 (2)
C(8)—C(9)—O(12)	110·1 (2)	C(19)—C(20)—C(21)	120·4 (2)
C(8)—C(9)—C(16)	109·9 (2)	C(20)—C(21)—C(22)	120·8 (2)
O(12)—C(9)—C(16)	111·4 (2)	N(13)—C(22)—C(17)	123·3 (2)
C(3)—C(10)—C(11)	110·8 (3)	N(13)—C(22)—C(21)	117·3 (2)
C(3)—C(10)—C(25)	109·8 (2)	C(17)—C(22)—C(21)	119·4 (2)
C(3)—C(10)—O(26)	108·1 (2)	C(19)—O(23)—C(24)	117·8 (3)

and the quinoline system. This tendency causes an enlargement of C(18)—C(19)—O(23) [126·0 (2)°], a narrowing of C(20)—C(19)—O(23) [113·2 (2)°] and a shortening of C(19)—O(23) [1·361 (3) Å], as observed in 9-acetylquitenine ethyl ester in which these values are 125·5 (3)°, 114·4 (2)° and 1·358 (3) Å respectively (Dupont, Konsur, Lewiński & Oleksyn, 1985) as well as in other cases (Domiano, Nardelli, Balsamo, Macchia & Macchia, 1979).

The quinuclidine moiety has a skew conformation, very similar to those found in other *Cinchona* alkaloids. Its three fused rings are all boats with all the C—N(1) bonds nearly eclipsed, as shown in Fig. 1 and by the values of the torsion angles around the line C(4)···N(1): C(3)—C(4)···N(1)—C(2) −5·76 (2), C(5)—C(4)···N(1)—C(6) −7·98 (2) and C(7)—C(4)···N(1)—C(8) −11·72 (2)°. The substituents at C(8) and C(3) are in *exo* and *endo* orientations respectively.

No intramolecular hydrogen bond is observed, contrary to the suggestion of Cheng (1971) and Loew & Sahakian (1977) that such a bond should be present between O(12) and N(1) in the antimalarial compounds of this type (aminoalcohols).

Table 3. *Comparison of the conformation of the title compound* (V) *and cinchonidine*

	(V)	Cinchonidine
C(16)—C(9)—C(8)—N(1)	165·0 (2)°	158·0 (6)°
C(16)—C(9)—C(8)—C(7)	−67·2 (2)	−76·1 (4)
O(12)—C(9)—C(8)—C(7)	55·8 (2)	48·0 (7)
O(12)—C(9)—C(8)—N(1)	−71·9 (2)	−77·9 (4)
O(12)—C(9)—C(16)—C(17)	157·9 (3)	159·1 (7)
O(12)—C(9)—C(16)—C(15)	−21·2 (2)	−22·6 (9)
C(8)—C(9)—C(16)—C(15)	101·0 (2)	101·5 (7)
C(8)—C(9)—C(16)—C(17)	−79·0 (2)	−76·8 (7)

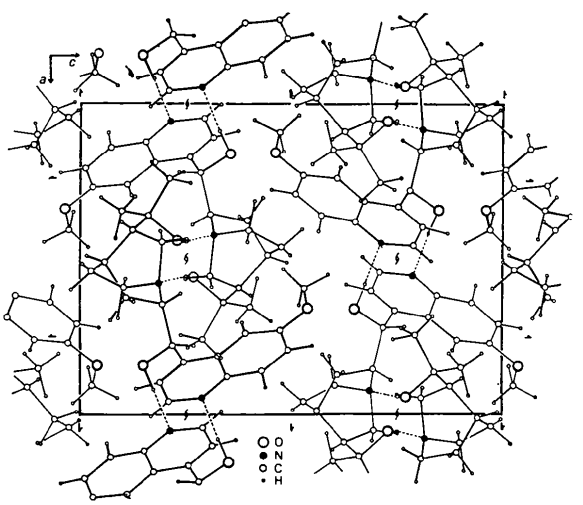


Fig. 2. The packing in the unit cell of the title compound projected along **b**. Hydrogen bonds are indicated with dashed lines.

Table 4. *Hydrogen-bond distances* (Å) *and angles* (°) *with e.s.d.'s in parentheses*

D H *A*	H···*A*	*D*···*A*	*D*—H···*A*
O(26)—H(O26)···N(1^{ii}) O(26^{i})—H(O26^{i})···N(1)	1·83 (3)	2·775 (5)	159 (1)
O(12)—H(O12)···N(13^{iii}) O(12^{iv})—H(O12^{iv})···N(13)	1·89 (3)	2·869 (5)	174 (1)

Symmetry code: (i) $1-x, 0{\cdot}5+y, 0{\cdot}5-z$; (ii) $1-x, y-0{\cdot}5, 0{\cdot}5-z$; (iii) $2-x, 0{\cdot}5+y, 0{\cdot}5-z$; (iv) $2-x, y-0{\cdot}5, 0{\cdot}5-z$.

The overall shape of the molecule is very similar to that of cinchonidine (Table 3) and of other *Cinchona* alkaloids, which indicates a high stability for their conformation in various crystalline environments.

The packing of the molecules in the structure is depicted in Fig. 2, which shows the unit-cell contents projected along **b**.

Each molecule takes part in four intermolecular hydrogen bonds in which O(12) and O(26) are donors while N(1) and N(13) are acceptors of protons. This leads to the formation of molecular layers parallel to the *ab* plane. The layers consist of molecules linked to each other by hydrogen bonds, two systems of which climb helically along consecutive twofold axes parallel to **b**. Between the layers only van der Waals interactions are present. Details concerning the hydrogen-bond lengths and angles are given in Table 4.

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