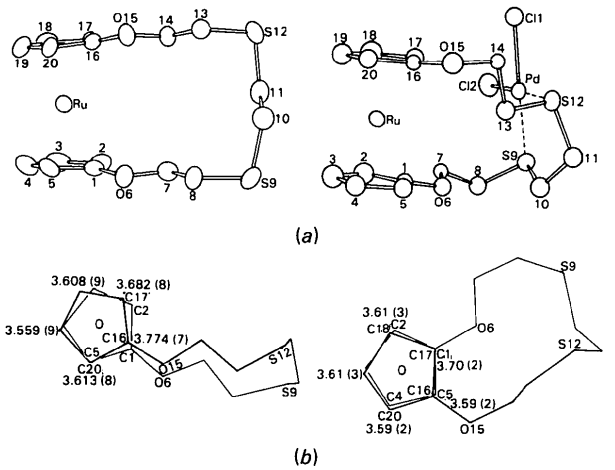

Fig. 1. (*a*) *ORTEP* (Johnson, 1965) drawings of the molecules [(I) on the left] with atom-numbering scheme. (*b*) Projections of the organic ligand moieties on the Cp ring containing the C(1) atom with the C···C distances (Å) between the rings. An open circle denotes the Ru atom.

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Structural Identification of a Purple Product (5,6-Dihydro-10-hydroxy-6-methyl-4*H*-dibenzo[*de*,*g*]quinoline-8,11-dione) of the Reaction of Froehde Reagent and Morphine

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Abstract. The single-crystal X-ray structure of a purple material isolated from the chloroform extraction of the reaction of morphine and Froehde reagent in aqueous sulfuric acid has been identified as $C_{17}H_{13}NO_3$, 5,6-dihydro-10-hydroxy-6-methyl-4*H*-dibenzo[*de*,*g*]quinoline-8,11-dione. $M_r = 279{\cdot}29$, monoclinic, $P2_1/n$, $a = 18{\cdot}591\ (12)$, $b = 7{\cdot}774\ (4)$, $c = 8{\cdot}762\ (5)$ Å, $\beta = 96{\cdot}60\ (5)°$, $V = 1258{\cdot}0\ (13)$ Å^3, $Z = 4$, $D_x = 1{\cdot}474$ g cm^{-3}, λ(Mo $K\alpha$) = 0·71069 Å, μ(Mo $K\alpha$) = 0·951 cm^{-1}, $F(000) = 584$, room temperature, final $R = 5{\cdot}8\%$ for 1528 reflections with $I > 3\sigma(I)$. The morphine molecule undergoes a rearrangement to the apomorphine skeleton by breaking an ether linkage; after further dehydration a hydroxyquinone system is formed in place of the phenolic morphine ring to give a highly conjugated product. The molecule shows coplanarity of the aromatic rings. The quinone ring has typical bond lengths.

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Introduction. Color reactions of morphine and its derivatives, of cholesterol, and of other biologically significant compounds with a variety of test reagents have been used extensively for rapid screening of unknown compounds in clinical and forensic situations (Clarke, 1978). A number of tests are available. Most reagents involve complex inorganic ions with the inorganic element present in its highest valence state, dissolved in concentrated sulfuric acid: for example, the Froehde (ammonium molybdate), the Mecke (selenous acid), and the Mandelin (ammonium vanadate) reagents (Stewart & Stohlman, 1961; Fulton & Nebraska, 1928). The principal reaction is believed to be oxidation–reduction with the reagent oxidizing the drug in some specific way.

The chemistry of the progressive color changes which occur with time for the morphine alkaloids is very complex and not fully understood. Akin to the color reaction of cholesterol with ferric ion in concentrated sulfuric acid solution (Burke, Diamondstone,

Velapoldi & Menis, 1974), it is believed that extensive conjugation is produced in the organic molecules, as evidenced by the displacement of the absorption maxima from the ultraviolet into the visible range (Ahlers & Auterhoff, 1975). Accompanying the change in absorption maxima is the ultimate loss of chirality as determined by circular dichroism (CD) spectropolarimetry (Wongwiechintana, 1983). The loss of optical activity is preceded by an interesting inversion of the CD spectrum from that in aqueous acid immediately after mixing. The associated conformational change which occurs is not reversed on careful addition of water.

The title compound (I) was isolated from a morphine–Froehde reagent reaction mixture which was allowed to stand for three weeks. A chloroform extract of the mixture was separated into three components by preparative thin-layer chromatography. The principal component crystallized as purple crystals. The solid-state structure of this material was determined by single-crystal X-ray diffraction techniques after NMR, IR and UV studies had failed to establish its identity.

A parallel study was done on the reaction of apomorphine with Froehde reagent. The CD spectrum taken immediately after mixing was essentially the same as the spectrum from apomorphine in aqueous acid. There was no ESR evidence for the production of free radicals. Chloroform extraction of the reaction mixture after three weeks yielded component (I) as confirmed by a comparison of the UV–visible spectrum with that for (I) and the identical TLC behavior of both extracts. Thus, apomorphine appears to be a possible intermediate in the reaction of morphine with inorganic oxidizing agents in concentrated sulfuric acid which results in the formation of (I).

Experimental. Crystal of $C_{17}H_{13}NO_3$ ($0{\cdot}2 \times 0{\cdot}3 \times 0{\cdot}25$ mm) sealed in capillary, mounted on Syntex *P*3 automated diffractometer. Tendency of crystals to decompose in air precluded measurement of density. Unit-cell dimensions determined by least-squares refinement of best angular positions for fifteen independent reflections ($2\theta > 15°$) during normal alignment procedures using Mo radiation ($\lambda = 0{\cdot}71069$ Å). Data (3476 points, $\pm h, k, l$; $h = -10$ to 10, $k = 0$ to 10, $l = 0$ to 20) collected at room temperature using variable scan rate, θ–2θ scan mode and scan width 1·2° below $K\alpha_1$ and 1·2° above $K\alpha_2$ to max. 2θ of 116°. Backgrounds measured at each side of the scan for combined time equal to total scan time. Intensities of three standard reflections remeasured after every 97 reflections showed less than 8% variation, corrections for decomposition deemed unnecessary. Data corrected for Lorentz, polarization and background effects. No absorption corrections. After removal of redundant and space-group-forbidden data, 1529 reflections considered observed [$I > 3{\cdot}0\sigma(I)$]. Structure solved by direct methods using *MULTAN*80 (Main *et al.*, 1980). Refinement of scale factor, positional and anisotropic thermal parameters for all nonhydrogen atoms carried out to convergence (Stewart, 1978). Hydrogen positional parameters determined from difference Fourier synthesis. These parameters and associated isotropic thermal parameters for hydrogen atoms refined with nonhydrogen parameters in final cycles of refinement. Final cycle of refinement [function minimized $\sum w(|F_o| - |F_c|)^2$] led to final agreement factor $R = 5{\cdot}8$, $wR = 6{\cdot}0\%$, $S = 1{\cdot}21$, max. shift/e.s.d. 0·18, max. peak height in final difference Fourier map 0·4 e Å^{-3}. $w = 1/\sigma(F)^2$ used in final cycles of refinement. Scattering factors from Cromer & Mann (1968).* The atomic parameters are given in Table 1 and bond lengths and angles in Table 2.

Discussion. Compound (I) has been determined to be 5,6-dihydro-10-hydroxy-6-methyl-4*H*-dibenzo[*de,g*]-quinoline-8,11-dione (Fig. 1). It thus shows a strong structural similarity to apomorphine, which may be the precursor to (I) in the sequence of reactions of Froehde reagent with morphine in sulfuric acid which leads to (I). Compound (I) displays the result of ring rearrangement and opening of the apomorphine furan ring with further dehydration and production of a hydroxyquinone system on the aromatic morphine ring. This highly conjugated ring system absorbs in the visible region and the compound's lack of optical activity stems from the loss of the five chiral centers of morphine. The molecule shows virtual coplanarity (Fig. 2) of all nonhydrogen atoms except C(4), C(5) and C(12) [deviation from plane determined by C(1)–C(3), C(6)–C(11), C(13), C(14), N(1), O(1)–O(3) is 0·04 Å]. The quinone ring displays the anticipated bond fixation with C(9)–C(10) [1·345 (7) Å] and C(7a)–C(11a) [1·396 (6) Å] showing typical double-bond distances, whereas C(7a)–C(8) [1·505 (8) Å] and C(10)–C(11) [1·493 (8) Å] are more like normal normal C–C single bonds. C–O bond distances are consistent with C=O groups on C(8) and C(11) [C(8)–O(1), 1·233 (6), C(11)–O(3), 1·238 (8) Å] and OH at C(10) [C(10)–O(2), 1·337 (6) Å].

The molecules pack in the crystal with a hydrogen bond between hydroxyl hydrogen, H(102), and carbonyl oxygen, O(3), of another molecule [O···H 2·09 (6) Å].

The unexpected appearance of a carbonyl moiety at C(8) in (I) may be pertinent to the mode of coupling involved when morphine dimerizes to form pseudomorphine in aqueous neutral and basic solutions in the

* Lists of structure factors, anisotropic thermal parameters and H-atom coordinates have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 42698 (23 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

presence of oxidizing agents such as $K_3Fe(CN)_6$, $KMnO_4$ or other metal ions. The identity of the dimer has not been established; however, the aromatic rings of morphine are believed to undergo a symmetric coupling reaction, perhaps at C(9) (Wongwiechintana, 1983), a position which in (I) must be attractive to nucleophiles.

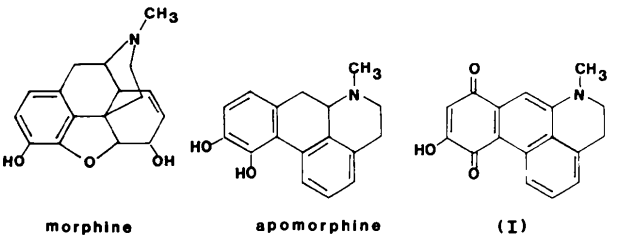

Fig. 1. Structure of morphine and derivatives.

Table 1. *Positional parameters for* $C_{17}H_{13}NO_3$ *with e.s.d.'s in parentheses*

U_{eq} = 1/3 the trace of the diagonalized U_{ij} matrix.

	x	y	z	U_{eq}(Å^2 × 10^2)
C(1)	0·1607 (3)	−0·1101 (6)	0·5335 (5)	3·63
C(2)	0·2248 (4)	−0·0499 (6)	0·6082 (5)	3·90
C(3)	0·2491 (3)	0·1166 (6)	0·5837 (5)	3·43
C(3a)	0·2089 (3)	0·2231 (6)	0·4822 (5)	3·33
C(4)	0·2303 (4)	0·4074 (6)	0·4632 (6)	4·53
C(5)	0·2079 (3)	0·4689 (6)	0·3019 (6)	4·43
N(6)	0·1326 (2)	0·4277 (5)	0·2505 (4)	3·60
C(6a)	0·1050 (3)	0·2720 (5)	0·2844 (5)	3·03
C(7)	0·0395 (3)	0·2159 (6)	0·2109 (5)	3·27
C(7a)	0·0119 (3)	0·0555 (6)	0·2427 (4)	3·13
C(8)	−0·0591 (3)	0·0064 (6)	0·1530 (5)	3·87
C(9)	−0·0908 (3)	−0·1599 (6)	0·1784 (5)	3·60
C(10)	−0·0556 (3)	−0·2655 (6)	0·2834 (5)	3·70
C(11)	0·0147 (3)	−0·2213 (6)	0·3746 (5)	3·30
C(11a)	0·0487 (3)	−0·0578 (5)	0·3478 (4)	2·63
C(11b)	0·1175 (3)	−0·0044 (5)	0·4268 (4)	2·93
C(11c)	0·1445 (3)	0·1637 (6)	0·3986 (5)	2·87
C(12)	0·0963 (5)	0·5334 (7)	0·1262 (6)	4·80
O(1)	−0·0894 (2)	0·1079 (5)	0·0584 (4)	5·50
O(2)	−0·0828 (2)	−0·4205 (4)	0·3100 (4)	4·83
O(3)	0·0394 (2)	−0·3324 (4)	0·4674 (4)	4·77

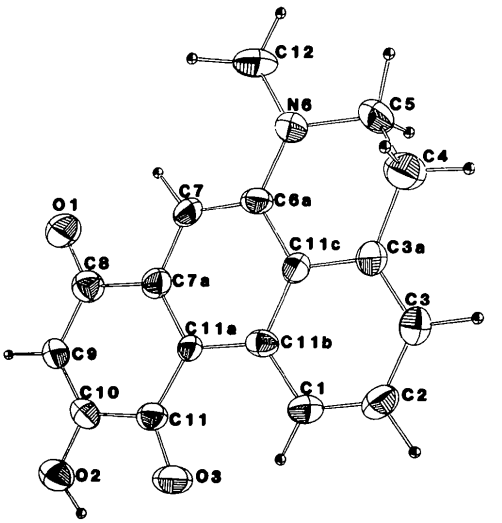

Fig. 2. Projection of a purple product of the reaction of morphine and Froehde reagent. [Drawn using *ORTEP* (Johnson, 1965).]

Table 2. *Bond distances* (Å) *and angles* (°) *for* $C_{17}H_{13}NO_3$

C(1)–C(2)	1·374 (8)	C(7a)–C(11a)	1·396 (6)
C(2)–C(3)	1·396 (7)	C(7a)–C(8)	1·505 (8)
C(3)–C(3a)	1·372 (7)	C(8)–O(1)	1·233 (6)
C(3a)–C(4)	1·502 (7)	C(8)–C(9)	1·448 (7)
C(3a)–C(11c)	1·407 (7)	C(9)–C(10)	1·345 (7)
C(4)–C(5)	1·505 (7)	C(10)–O(2)	1·337 (6)
C(5)–N(6)	1·457 (8)	C(10)–C(11)	1·493 (8)
N(6)–C(12)	1·466 (7)	C(11)–O(3)	1·238 (8)
N(6)–C(6a)	1·360 (6)	C(11)–C(11a)	1·450 (7)
C(6a)–C(11c)	1·443 (6)	C(11a)–C(11b)	1·443 (8)
C(6a)–C(7)	1·381 (8)	C(11b)–C(1)	1·421 (6)
C(7)–C(7a)	1·389 (7)	C(11b)–C(11c)	1·432 (6)
C(1)–C(2)–C(3)	121·4 (5)	C(8)–C(9)–C(10)	118·4 (5)
C(2)–C(3)–C(3a)	119·8 (5)	C(9)–C(10)–O(2)	120·4 (5)
C(3)–C(3a)–C(11c)	120·4 (4)	C(9)–C(10)–C(11)	123·6 (5)
C(3)–C(3a)–C(4)	121·0 (5)	O(2)–C(10)–C(11)	116·0 (4)
C(3a)–C(4)–C(5)	111·0 (4)	C(10)–C(11)–O(3)	115·2 (4)
C(4)–C(5)–N(6)	111·9 (5)	C(10)–C(11)–C(11a)	119·1 (4)
C(5)–N(6)–C(12)	116·8 (4)	O(3)–C(11)–C(11a)	125·7 (5)
C(5)–N(6)–C(6a)	120·0 (4)	C(11)–C(11a)–C(7a)	118·0 (5)
C(12)–N(6)–C(6a)	120·6 (4)	C(11)–C(11a)–C(11b)	123·5 (4)
N(6)–C(6a)–C(11c)	119·8 (4)	C(7a)–C(11a)–C(11b)	118·4 (4)
N(6)–C(6a)–C(7)	120·9 (4)	C(11a)–C(11b)–C(11c)	119·3 (4)
C(7)–C(6a)–C(11c)	119·4 (4)	C(11a)–C(11b)–C(1)	123·5 (4)
C(6a)–C(7)–C(7a)	121·1 (4)	C(1)–C(11b)–C(11c)	117·2 (5)
C(7)–C(7a)–C(11a)	122·3 (5)	C(11b)–C(11c)–C(6a)	119·4 (4)
C(7)–C(7a)–C(8)	116·4 (4)	C(11b)–C(11c)–C(3a)	120·3 (4)
C(8)–C(7a)–C(11a)	121·2 (4)	C(3a)–C(11c)–C(6a)	120·3 (4)
C(7a)–C(8)–O(1)	119·6 (4)	C(11b)–C(1)–C(2)	120·7 (4)
C(7a)–C(8)–C(9)	119·6 (4)	C(11c)–C(3a)–C(4)	118·4 (4)
C(9)–C(8)–O(1)	120·8 (5)		

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