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STRUCTURE AND REACTIONS OF PHOTOTHEBAINEHYDROQUINONE

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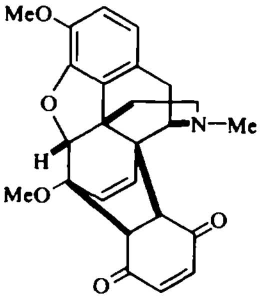
Abstract The structure of photothebainehydroquinone, which was obtained by unsensitized irradiation with UV light of thebainequinone (**1**) or thebainehydroquinone (**2**) has been shown by X-ray crystallography to be **3a**, which arises from **2** through a di-π-methane to vinylcyclopropane rearrangement. Treatment of **3a** with acid gave **5a**, **6a**, **5b** and probably **6b**. Studies using DCl showed that the opening of the cyclopropane in **3a** to give **5a**, **5b**, and **6a** involved 'end-on' approach of the D^+. The mechanisms of the reactions are discussed.

In a study of the photochemistry of some compounds related to morphine‡ we irradiated a solution of thebainquinone (**1**)[3] in dioxan with ultraviolet light and isolated a photoproduct. Our compound (empirical formula $C_{25}H_{25}NO_5$) had no IR absorption in the ketone region. It was therefore not a cage compound corresponding to those prepared by Cookson *et al.*[4] from other Diels–Alder adducts of benzoquinone. Its UV spectrum was similar to that of thebainehydroquinone(**2**).[3] We, therefore, irradiated thebainehydroquinone in dioxan and obtained the same photo



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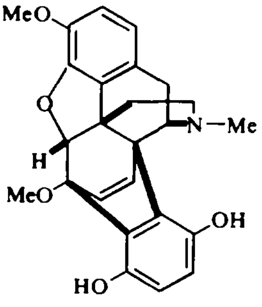

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[†] This work was started at the University of South Carolina, Columbia, S.C.

[‡] There have been scattered accounts of the effect of light on morphine and some of its derivatives.[1] More recently we and other groups (personal communications) find that thebaine does not undergo reaction on irradiation with UV light.[2]

product (which we call photothebainehydroquinone) in yields of up to 65%.* Another product appeared to be present but was not isolated.

The UV, IR, mass, and NMR spectra of photothebainehydroquinone are very similar to those of **2**. The main differences are: the IR spectrum of the photo product has a broad weak peak at 1850 cm^{-1} (attributed to a hydrogen bonded hydroxyl); similarly in the NMR the hydroxyl peak at $\delta = 12{\cdot}34$ in **2** shifts to $\delta = 15{\cdot}00$ ppm in the photo compound; the NMR signals corresponding to vinyl protons at C_7 and C_8 in **2** do not appear in the spectrum of the photo product; and the signal corresponding to C_5 in **2**, which is split ($J = 1{\cdot}5$ Hz)[5] by the proton at C_7 is no longer split in the photo compound. On the basis of molecular weight determinations by the isothermal distillation method, we[6] concluded that the photo compound was a dimer (formed between C_7 and C_8 of two molecules of **2**); however, this formulation did not lead to rational structures for the products obtained from treatment of photothebainehydroquinone with acid (see below) and so we examined crystals of photothebainehydroquinone hydrobromide by X-ray crystallography.

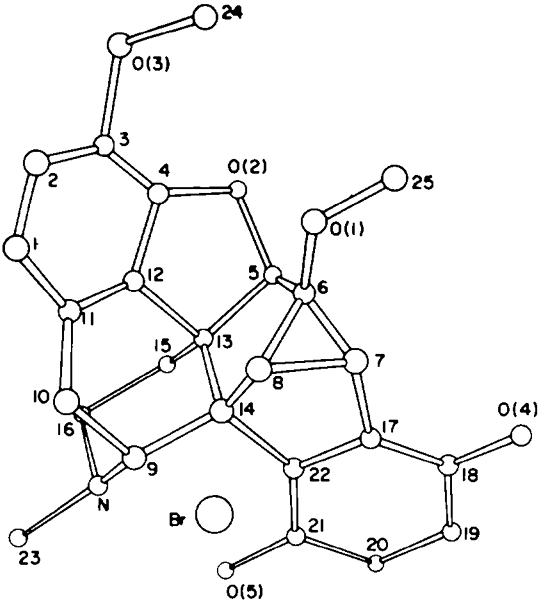

FIG 1. The molecular structure of photothebainehydroquinone hydrobromide.

Structure of photothebainehydroquinone. The results of the X-ray work lead to structure **3a**[7]† (Figs 1 and 2, Tables 1–4). An interesting consequence of the ring fusions is that the benzene ring A is slightly bowed about the line through C_2, C_{12}, and C_{13}, so that the mean plane through atoms O_2, C_4, C_{12}, and C_{13} is inclined by

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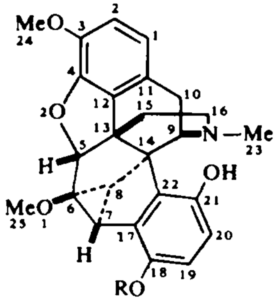
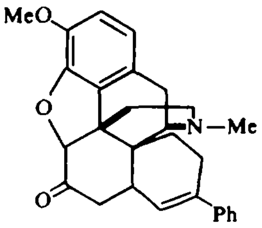
* To obtain good yields of the photo product it is essential that oxygen be rigourlessly excluded.

† We feel that the stereochemical structure in our preliminary communications[7,8] may not have given an unambiguous description of the stereochemistry, hence our new representation.



3a: R = H
3b: R = COMe



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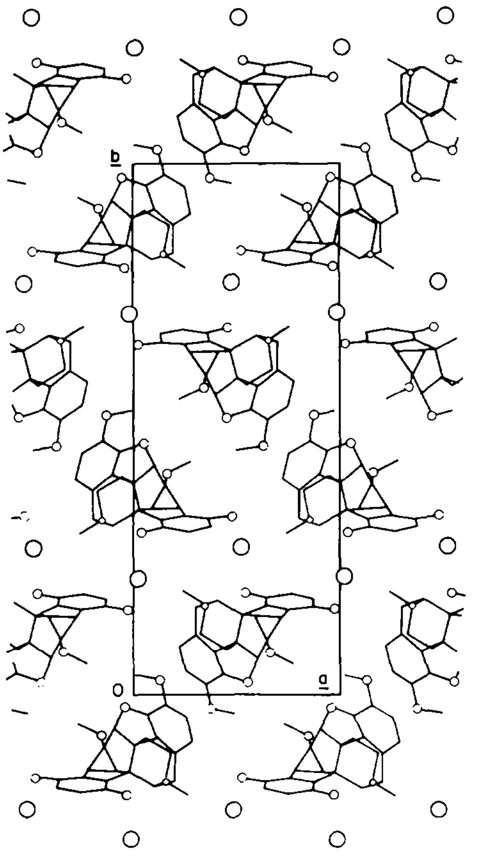

Fig 2. The crystal structure of photothebainehydroquinone hydrobromide, viewed in projection along the *c* axis.

Table 1. Atomic co-ordinates (fractional × 10^4), temperature factors ($Å^2$), and positional standard deviations ($Å \times 10^3$)

	x	y	z	B	$\sigma(X)$	$\sigma(Y)$	$\sigma(Z)$
O(1)	3383	5822	5125	3·69	13	12	16
O(2)	4515	5236	2806	3·22	13	12	13
O(3)	6273	4721	5356	5·42	17	15	18
O(4)	243	6606	1402	3·54	14	13	13
O(5)	4615	6927	−2328	2·28	13	11	12
N	6525	6694	− 484	2·18	14	13	13
C(1)	7791	5931	4494	2·92	19	17	18
C(2)	7515	5448	5071	4·00	20	19	27
C(3)	6500	5195	4621	2·72	18	16	17
C(4)	5676	5389	3403	2·60	19	17	18
C(5)	3968	5669	2090	1·69	16	14	16
C(6)	3522	6037	3549	2·09	13	16	18
C(7)	2749	6476	3106	1·72	16	15	16
C(8)	4142	6509	3363	1·35	15	13	14
C(9)	5984	6793	1325	1·77	17	14	16
C(10)	6994	6667	2763	2·54	19	17	18
C(11)	6990	6129	3226	2·60	19	17	18
C(12)	6037	5827	2640	1·72	16	14	16
C(13)	5004	5984	1268	2·38	18	16	17
C(14)	4710	6521	1529	1·90	17	14	15
C(15)	5545	5861	−543	2·66	18	16	17
C(16)	6772	6151	−848	3·21	20	19	20
C(17)	2502	6623	1272	1·99	17	16	17
C(18)	1333	6674	525	1·82	17	15	15
C(19)	1266	6824	−1222	2·69	20	17	19
C(20)	2384	6908	−2097	2·14	18	16	17
C(21)	3578	6840	−1368	2·50	19	16	18
C(22)	3642	6677	379	1·64	16	14	15
C(23)	7682	6975	−934	3·13	21	19	20
C(24)	5019	4633	6068	7·67	35	32	35
C(25)	2189	5566	5431	6·83	28	28	32
Br	4787	7789	5115	†	2	2	2

† The bromine atom was assigned an anisotropic temperature factor of the form

$$T = \exp[\,-(h^2b_{11} + k^2b_{22} + l^2b_{33} + 2hkb_{12} + 2hlb_{13} + 2klb_{23})]$$

with final parameters

b_{11}	b_{22}	b_{33}	b_{12}	b_{13}	b_{23}
0·00727	0·00114	0·01013	−0·00048	0·00289	0·00036

TABLE 2. MOLECULAR DIMENSIONS

(*a*) Bond lengths (Å)

O(1)—C(6)	1·358 (22)	C(6)—C(8)	1·452 (21)
O(1)—C(25)	1·472 (33)	C(7)—C(8)	1·501 (22)
O(2)—C(4)	1·385 (22)	C(7)—C(17)	1·496 (33)
O(2)—C(5)	1·427 (19)	C(8)—C(14)	1·542 (21)
O(3)—C(3)	1·431 (23)	C((9)—C(10)	1·586 (24)
O(3)—C(24)	1·466 (39)	C(9)—C(14)	1·554 (23)
O(4)—C(18)	1·359 (21)	C(10)—C(11)	1·505 (24)
O(5)—C(21)	1·352 (22)	C(11)—C(12)	1·383 (24)
N—C(9)	1·537 (21)	C(12)—C(13)	1·587 (23)
N—C(16)	1·525 (23)	C(13)—C(14)	1·508 (21)
N—C(23)	1·492 (24)	C(13)—C(15)	1·550 (24)
C(1)—C(2)	1·419 (26)	C(14)—C(22)	1·505 (22)
C(1)—C(11)	1·408 (26)	C(15)—C(16)	1·547 (23)
C(2)—C(3)	1·328 (27)	C(17)—C(18)	1·381 (24)
C(3)—C(4)	1·392 (25)	C(17)—C(22)	1·406 (23)
C(4)—C(12)	1·384 (22)	C(18)—C(19)	1·411 (24)
C(5)—C(6)	1·580 (22)	C(19)—C(20)	1·390 (26)
C(5)—C(13)	1·536 (23)	C(20)—C(21)	1·404 (26)
C(6)—C(7)	1·491 (22)	C(21)—C(22)	1·424 (23)

(*b*) Valency angles (degrees)

C(6)—O(1)—C(25)	116·2 (1·8)	C(1)—C(11)—C(12)	116·6 (1·5)
C(4)—O(2)—C(5)	104·3 (1·2)	C(10)—C(11)—C(12)	120·1 (1·6)
C(3)—O(3)—C(24)	116·8 (1·8)	C(4)—C(12)—C(11)	125·1 (1·5)
C(9)—N—C(16)	113·7 (1·2)	C(4)—C(12)—C(13)	108·9 (1·3)
C(9)—N—C(23)	115·8 (1·3)	C(11)—C(12)—C(13)	124·7 (1·4)
C(16)—N—C(23)	108·0 (1·4)	C(5)—C(13)—C(12)	94·2 (1·2)
C(2)—C(1)—C(11)	116·6 (1·8)	C(5)—C(13)—C(14)	109·6 (1·4)
C(1)—C(2)—C(3)	124·5 (2·0)	C(5)—C(13)—C(15)	121·4 (1·4)
O(3)—C(3)—C(2)	120·0 (1·8)	C(12)—C(13)—C(14)	108·4 (1·3)
O(3)—C(3)—C(4)	120·2 (1·6)	C(12)—C(13)—C(15)	106·7 (1·3)
C(2)—C(3)—C(4)	119·7 (1·7)	C(14)—C(13)—C(15)	114·0 (1·3)
C(3)—C(4)—C(12)	116·0 (1·6)	C(8)—C(14)—C(9)	116·5 (1·3)
O(2)—C(4)—C(3)	132·5 (1·6)	C(8)—C(14)—C(13)	100·6 (1·2)
O(2)—C(4)—C(12)	111·4 (1·5)	C(8)—C(14)—C(22)	104·6 (1·3)
O(2)—C(5)—C(6)	111·7 (1·3)	C(9)—C(14)—C(13)	105·6 (1·3)
O(2)—C(5)—C(13)	109·0 (1·3)	C(9)—C(14)—C(22)	117·9 (1·2)
C(6)—C(5)—C(13)	99·2 (1·2)	C(13)—C(14)—C(22)	110·5 (1·3)
C(5)—C(6)—C(7)	120·6 (1·4)	C(13)—C(15)—C(16)	110·0 (1·4)
C(5)—C(6)—C(8)	110·6 (1·3)	N—C(16)—C(15)	108·7 (1·5)
C(7)—C(6)—C(8)	61·3 (1·1)	C(7)—C(17)—C(18)	125·6 (1·5)
O(1)—C(6)—C(5)	113·6 (1·3)	C(7)—C(17)—C(22)	109·9 (1·4)
O(1)—C(6)—C(7)	119·3 (1·5)	C(18)—C(17)—C(22)	124·4 (1·4)
O(1)—C(6)—C(8)	121·2 (1·4)	O(4)—C(18)—C(17)	123·4 (1·4)
C(6)—C(7)—C(8)	58·0 (1·0)	O(4)—C(18)—C(19)	118·2 (1·6)
C(6)—C(7)—C(17)	121·9 (1·3)	C(17)—C(18)—C(19)	118·4 (1·7)
C(8)—C(7)—C(17)	106·5 (1·3)	C(18)—C(19)—C(20)	118·0 (1·8)
C(6)—C(8)—C(7)	60·6 (1·1)	C(19)—C(20)—C(21)	124·1 (1·6)
C(6)—C(8)—C(14)	106·8 (1·2)	O(5)—C(21)—C(20)	119·9 (1·5)
C(7)—C(8)—C(14)	105·6 (1·3)	O(5)—C(21)—C(22)	122·4 (1·7)
N—C(9)—C(10)	110·2 (1·2)	C(20)—C(21)—C(22)	117·7 (1·6)
N—C(9)—C(14)	109·7 (1·3)	C(14)—C(22)—C(17)	109·6 (1·3)
C(10)—C(9)—C(14)	114·8 (1·2)	C(14)—C(22)—C(21)	133·2 (1·6)

TABLE 2—*continued*

(*b*) Valency angles (degrees) (*contd.*)

C(9)—C(10)—C(11)	111·9 (1·4)	C(17)—C(22)—C(21)	117·2 (1·5)
C(1)—C(11)—C(10)	122·4 (1·6)		

(*c*) Torsion angles (degrees). The angle *A*—*B*—*C*—*D* is defined as positive if, when viewed along the *B*—*C* bond, atom *A* must be rotated clockwise to eclipse atom *D*. The standard deviations of the torsion angles are *ca.* 2°.

C(25)—O(1)—C(6)—C(5)	−83	O(2)—C(5)—C(6)—C(8)	121
C(25)—O(1)—C(6)—C(7)	69	C(13)—C(5)—C(6)—O(1)	−134
C(25)—O(1)—C(6)—C(8)	142	C(13)—C(5)—C(6)—C(7)	75
C(5)—O(2)—C(4)—C(3)	159	C(13)—C(5)—C(6)—C(8)	7
C(5)—O(2)—C(4)—C(12)	−19	O(2)—C(5)—C(13)—C(12)	−33
C(4)—O(2)—C(5)—C(6)	−74	O(2)—C(5)—C(13)—C(14)	−144
C(4)—O(2)—C(5)—C(13)	35	O(2)—C(5)—C(13)—C(15)	79
C(24)—O(3)—C(3)—C(2)	131	C(6)—C(5)—C(13)—C(12)	84
C(24)—O(3)—C(3)—C(4)	−51	C(6)—C(5)—C(13)—C(14)	−28
C(16)—N—C(9)—C(10)	67	C(6)—C(5)—C(13)—C(15)	−164
C(16)—N—C(9)—C(14)	−60	O(1)—C(6)—C(7)—C(8)	112
C(23)—N—C(9)—C(10)	−59	O(1)—C(6)—C(7)—C(17)	−158
C(23)—N—C(9)—C(14)	174	C(5)—C(6)—C(7)—C(8)	−98
C(9)—N—C(16)—C(15)	55	C(5)—C(6)—C(7)—C(17)	−8
C(23)—N—C(16)—C(15)	−175	C(8)—C(6)—C(7)—C(17)	90
C(11)—C(1)—C(2)—C(3)	−7	O(1)—C(6)—C(8)—C(7)	−109
C(2)—C(1)—C(11)—C(10)	167	O(1)—C(6)—C(8)—C(14)	153
C(2)—C(1)—C(11)—C(12)	−2	C(5)—C(6)—C(8)—C(7)	115
C(1)—C(2)—C(3)—O(3)	−176	C(5)—C(6)—C(8)—C(14)	16
C(1)—C(2)—C(3)—C(4)	5	C(7)—C(6)—C(8)—C(14)	−99
O(3)—C(3)—C(4)—O(2)	8	C(6)—C(7)—C(8)—C(14)	101
O(3)—C(3)—C(4)—C(12)	−174	C(17)—C(7)—C(8)—C(6)	−118
C(2)—C(3)—C(4)—O(2)	−173	C(17)—C(7)—C(8)—C(14)	−17
C(2)—C(3)—C(4)—C(12)	5	C(6)—C(7)—C(17)—C(18)	122
O(2)—C(4)—C(12)—C(11)	165	C(6)—C(7)—C(17)—C(22)	−55
O(2)—C(4)—C(12)—C(13)	−3	C(8)—C(7)—C(17)—C(18)	−176
C(3)—C(4)—C(12)—C(11)	−14	C(8)—C(7)—C(17)—C(22)	8
C(3)—C(4)—C(12)—C(13)	179	C(6)—C(8)—C(14)—C(9)	−145
O(2)—C(5)—C(6)—O(1)	−19	C(6)—C(8)—C(14)—C(13)	−32
O(2)—C(5)—C(6)—C(7)	−171	C(6)—C(8)—C(14)—C(22)	83
C(7)—C(8)—C(14)—C(9)	152	C(15)—C(13)—C(14)—C(9)	−61
C(7)—C(8)—C(14)—C(13)	−95	C(15)—C(13)—C(14)—C(22)	67
C(7)—C(8)—C(14)—C(22)	20	C(5)—C(13)—C(15)—C(16)	−166
N—C(9)—C(10)—C(11)	−85	C(12)—C(13)—C(15)—C(16)	−60
C(14)—C(9)—C(10)—C(11)	40	C(14)—C(13)—C(15)—C(16)	59
N—C(9)—C(14)—C(8)	170	C(8)—C(14)—C(22)—C(17)	−16
N—C(9)—C(14)—C(13)	60	C(8)—C(14)—C(22)—C(21)	167
N—C(9)—C(14)—C(22)	−64	C(9)—C(14)—C(22)—C(17)	−147
C(10)—C(9)—C(14)—C(8)	45	C(9)—C(14)—C(22)—C(21)	36
C(10)—C(9)—C(14)—C(13)	−65	C(13)—C(14)—C(22)—C(17)	92
C(10)—C(9)—C(14)—C(22)	171	C(13)—C(14)—C(22)—C(21)	−86
C(9)—C(10)—C(11)—C(1)	−179	C(13)—C(15)—C(16)—N	−52
C(9)—C(10)—C(11)—C(12)	−11	C(7)—C(17)—C(18)—O(4)	2
C(1)—C(11)—C(12)—C(4)	12	C(7)—C(17)—C(18)—C(19)	179
C(1)—C(11)—C(12)—C(13)	178	C(22)—C(17)—C(18)—O(4)	178
C(10)—C(11)—C(12)—C(4)	−157	C(22)—C(17)—C(18)—C(19)	−5
C(10)—C(11)—C(12)—C(13)	9	C(7)—C(17)—C(22)—C(14)	5

TABLE 2— *continued*

(*c*) Torsion angles (degrees) (*contd.*)

C(4)—C(12)—C(13)—C(5)	21	C(7)—C(17)—C(22)—C(21)	−177
C(4)—C(12)—C(13)—C(14)	133	C(18)—C(17)—C(22)—C(14)	−172
C(4)—C(12)—C(13)—C(15)	−103	C(18)—C(17)—C(22)—C(21)	6
C(11)—C(12)—C(13)—C(5)	−146	O(4)—C(18)—C(19)—C(20)	178
C(11)—C(12)—C(13)—C(14)	−34	C(17)—C(18)—C(19)—C(20)	0
C(11)—C(12)—C(13)—C(15)	89	C(18)—C(19)—C(20)—C(21)	2
C(5)—C(13)—C(14)—C(8)	37	C(19)—C(20)—C(21)—O(5)	179
C(5)—C(13)—C(14)—C(9)	159	C(19)—C(20)—C(21)—C(22)	0
C(5)—C(13)—C(14)—C(22)	−73	O(5)—C(21)—C(22)—C(14)	−6
C(12)—C(13)—C(14)—C(8)	−64	O(5)—C(21)—C(22)—C(17)	177
C(12)—C(13)—C(14)—C(9)	57	C(20)—C(21)—C(22)—C(14)	174
C(12)—C(13)—C(14)—C(22)	−174	C(20)—C(21)—C(22)—C(17)	−4
C(15)—C(13)—C(14)—C(8)	177		

TABLE 3. DISPLACEMENTS (Å) OF THE ATOMS FROM VARIOUS MEAN PLANES IN THE MOLECULE. ATOMS NOT INCLUDED IN THE DERIVATION OF A PLANE ARE IN ITALICS

(*a*)	C(1)	−0·03	C(12)	0·08
	C(2)	0·05	*O(3)*	*−0·00*
	C(3)	−0·01	*O(2)*	*−0·24*
	C(4)	−0·05	*C(13)*	*0·04*
	C(11)	−0·03	*C(10)*	*−0·40*
(*b*)	O(2)	−0·01	C(13)	0·01
	C(4)	0·02	*C(5)*	*−0·51*
	C(12)	−0·01		
(*c*)	C(10)	−0·02	C(13)	0·02
	C(11)	0·04	*C(9)*	*0·11*
	C(12)	−0·04	*C(14)*	*−0·66*
(*d*)	C(15)	−0·03	C(9)	−0·03
	C(16)	0·03	*N*	*0·67*
	C(14)	0·03	*C(13)*	*−0·69*
(*e*)	C(17)	−0·03	C(22)	0·03
	C(18)	0·01	*O(4)*	*−0·01*
	C(19)	0·01	*O(5)*	*−0·02*
	C(20)	−0·01	*C(7)*	*−0·06*
	C(21)	−0·01	*C(14)*	*0·17*
(*f*)	C(6)	0	*C(13)*	*−0·17*
	C(5)	0	*C(14)*	*0·40*
	C(8)	0		
(*g*)	C(6)	0	*C(8)*	*−0·19*
	C(17)	0	*C(14)*	*0·13*
	C(22)	0		

TABLE 4. INTERMOLECULAR CONTACTS (Å)

Br ··· O(5$^{\mathrm{I}}$)	3·07	O(3) ··· C(1$^{\mathrm{V}}$)	3·79
Br ··· C(21$^{\mathrm{I}}$)	3·96	O(3) ··· C(2$^{\mathrm{V}}$)	3·89
O(1) ··· O(5$^{\mathrm{I}}$)	3·82	O(3) ··· C(11$^{\mathrm{V}}$)	3·70
O(1) ··· C(20$^{\mathrm{I}}$)	3·80	O(3) ··· C(12$^{\mathrm{V}}$)	3·68
O(1) ··· C(21$^{\mathrm{I}}$)	3·88	O(3) ··· C(15$^{\mathrm{V}}$)	3·81
C(1) ··· C(16$^{\mathrm{I}}$)	3·81	O(3) ··· C(16$^{\mathrm{V}}$)	3·29
C(2) ··· C(16$^{\mathrm{I}}$)	3·77	C(2) ··· C(4$^{\mathrm{V}}$)	3·94
C(7) ··· C(20$^{\mathrm{I}}$)	3·91	C(24) ··· C(1$^{\mathrm{V}}$)	3·85
C(8) ··· O(5$^{\mathrm{I}}$)	3·56	Br ··· C(19$^{\mathrm{VI}}$)	3·56
C(1) ··· O(4$^{\mathrm{II}}$)	3·99	Br ··· C(20$^{\mathrm{VI}}$)	3·71
C(10) ··· O(4$^{\mathrm{II}}$)	3·63	C(9) ··· C(19$^{\mathrm{VI}}$)	3·78
C(11) ··· O(4$^{\mathrm{II}}$)	3·96	C(9) ··· C(20$^{\mathrm{VI}}$)	3·88
C(23) ··· O(4$^{\mathrm{II}}$)	3·42	C(10) ··· C(20$^{\mathrm{VI}}$)	3·93
C(23) ··· C(19$^{\mathrm{II}}$)	3·85	C(23) ··· Br$^{\mathrm{VI}}$	3·99
C(24) ··· O(4$^{\mathrm{III}}$)	3·39	C(23) ··· C(17$^{\mathrm{VI}}$)	3·83
C(24) ··· C(18$^{\mathrm{III}}$)	3·86	C(23) ··· C(18$^{\mathrm{VI}}$)	3·96
C(25) ··· O(2$^{\mathrm{III}}$)	3·81	C(23) ··· C(19$^{\mathrm{VI}}$)	3·97
C(25) ··· C(5$^{\mathrm{III}}$)	3·80	C(23) ··· C(20$^{\mathrm{VI}}$)	3·85
Br ··· O(4$^{\mathrm{IV}}$)	3·19	C(23) ··· C(21$^{\mathrm{VI}}$)	3·80
Br ··· C(7$^{\mathrm{IV}}$)	3·98	C(23) ··· C(22$^{\mathrm{VI}}$)	3·83
C(10) ··· Br$^{\mathrm{IV}}$	3·71		

The superscripts refer to the following transformations of the atomic co-ordinates:

I	x,	y,	$1 + z$	IV	$\frac{1}{2} + x$,	$1\frac{1}{2} - y$,	$1 - z$
II	$1 + x$,	y,	z	V	$1\frac{1}{2} - x$,	$1 - y$,	$\frac{1}{2} + z$
III	$\frac{1}{2} - x$,	$1 - y$,	$\frac{1}{2} + z$	VI	$\frac{1}{2} + x$,	$1\frac{1}{2} - y$,	$- z$

19° to that through C_{10}, C_{11}, C_{12} and C_{13}. Atoms C_1, C_3, C_4, and C_{11} are a little below the mean plane of the aromatic ring (by an average of 0·03 Å), atoms C_2, C_{12} and C_{13} are a little above (by an average of 0·05 Å), and substituents O_2 and C_{10} are displaced below by 0·23 and 0·40 Å. In codeine, on the other hand, atoms O_2 and C_{10} are displaced from the plane of ring A by only 0·03 and 0·09 Å.[9]

The five-membered ring defined by atoms O_2, C_4, C_{12}, C_{13} and C_5 adopts an envelope conformation with C_5 displaced by 0·51 Å from the mean plane of the other four atoms. The cyclopentane ring comprising atoms C_5, C_6, C_8, C_{14} and C_{13} adopts a conformation intermediate between envelope and half-chair forms: C_{13} and C_{14} are displaced by $-0·17$ and 0·40 Å from the plane of the other atoms. The other five-membered ring comprising atoms C_7, C_8, C_{14}, C_{22} and C_{17} is somewhat flatter, and approximates to a half-chair form with C_8 and C_{14} deviating by $-0·19$ and 0·13 Å from the plane of the other three atoms.

The six-membered ring comprising atoms C_9, C_{10}, C_{11}, C_{12}, C_{13} and C_{14} has atoms C_9 and C_{14} displaced by 0·11 and $-0·66$ Å from the mean plane through the other four atoms, and the half-chair conformation is therefore considerably distorted. The piperidine ring adopts a normal chair conformation, with atoms C_9, C_{14}, C_{15} and C_{16} closely coplanar and atoms N and C_{13} displaced by 0·67 and $-0·69$ Å to opposite sides of the plane; the *N*-methyl group occupies an equatorial position. The hydroquinone ring is planar, the maximum deviation from the mean plane of the ring being 0·03 Å by C_{17}. The cyclopropane appears to be subjected to considerable strain from the two fused five-membered rings, for the torsion angles C_5-C_6-C_7-C_{17}, −8°, C_5-C_6-C_8-C_{14}, 16°, and C_{17}-C_7-C_8-C_{14}, −17°, show large departures from 0°.

The average sp^3-sp^3 carbon–carbon single bond length is 1·545 Å and the average benzene carbon–carbon bond length is 1·395 Å. The average sp^3-carbon–oxygen and sp^2-carbon–oxygen distances are 1·431 and 1·382 Å, respectively.

The hydroxyl oxygen O_5 of the hydroquinone ring and the quarternary $\rightarrow$NH group are associated by an intramolecular NH … O hydrogen bond of length 2·57 Å. The mean value of the C—N … O angles is 105·2°, which is not far from tetrahedral and indicates that the N—H bond must be close to the N … O line. The closeness of O_5 and N accounts for the strength of the O_5-H … N hydrogen bond which is indicated by the IR and NMR spectra of **3a**. The bromide ions and the positively charged alkaloid cations are held together by hydrogen bonds and weak ionic forces. The closest $N^+ \ldots Br^-$ approaches are 4·89 and 5·19 Å whereas the $O \ldots Br^-$ distances involving the hydroquinone hydroxyl groups are 3·07 and 3·19 Å, indicative of hydrogen bonding. The $Br' \ldots O_5$-C_{21} and $Br'' \ldots O_4$-C_{18} angles of 110 and 119° do not differ greatly from the expected value of 120° for the C-O-H angle at an sp^2-oxygen atom and, accordingly, the O—H … Br hydrogen bonds probably deviate only slightly from linearity. The hydrogen-bonded bromide ions are displaced by 1·69 and 2·36 Å from the plane of the hydroquinone ring, and the angles subtended at this plane by the bromine … hydroxyl lines are 29° and 37°. Assuming that the hydrogen atoms of the hydroxyl groups lie along these directions, and that the atoms O_4 and O_5 are sp^2-hybridized with the lone pair of electrons in the p_z orbital then these orbitals would still be able to overlap to a considerable extent with the π-cloud of the hydroquinone ring.

Mechanism of photoreactions. Our rearrangement of **2** to **3a** is interesting because it involves a bridged bicyclic di-π-methane rearranging without a sensitiser to a vinylcyclopropane rather than a cyclooctatetraene.[7, 10–13]* In accord with the accepted mechanism of di-π-methanevinyl cyclopropane rearrangements[7, 10, 14] the stereochemistry of C_6 is inverted in going from **2** to **3a**. The main difference in our system and those studied by others is that the light is absorbed by a hydroquinone system in **2**. We defer further discussion of the mechanism to a later paper in which we shall discuss our work on some simple models for **2**[7, 13]

In addition to the rearrangement of **2** to **3a** we also observed the rearrangement of **1** to **3a**. This reaction must involve a photochemical equilibrium between an enedione and the corresponding hydroquinone and raises the possibility that the conversion of **2** to **3a** may be sensitized by the presence of **1**. Our results with bridged bicyclic dihydronaphthalene diols[7] show[13] that the presence of the enedione does not sensitize the rearrangement of the hydroquinone; we thus think that **1** enolises to **2** which then undergoes unsensitized rearrangement to **3a**.

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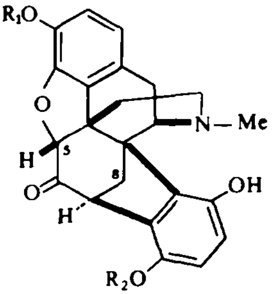
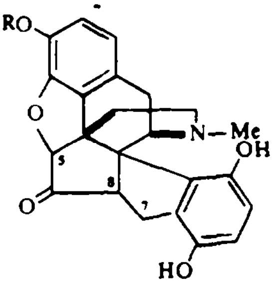
* The other reported photo rearrangement of a Diels–Alder adduct of thebaine involved the adduct with dimethyl acetylenedicarboxylate and resulted in a migration of the C_{17} bond from C_6 to C_5 and the oxygen bridge from C_5 to C_6.[11] Other examples of an unsensitised rearrangement of a bridged bicyclic di-π-methane to a vinylcyclopropane are known.

Reaction of **3a** *with acid.* When **3a** was refluxed with concentrated hydrochloric acid 4 products (as determined by TLC), A, B, C and D, were formed. Two of these, C and D, predominate with short times (3 hr) of reflux; and the other two, A and B, appear after longer periods (24 hr). We have isolated A, C and D. The compounds C and D each have molecular weights 405 ($C_{24}H_{23}NO_5$), one ketonic group (ν_{max} 1745 cm^{-1} with D and 1725 cm^{-1} with C) and one methoxyl group; A has a molecular weight of 391 ($C_{23}H_{21}NO_5$), no methoxyl and one ketonic group (ν_{max} 1725 cm^{-1}); B was not isolated but mixtures of A and B have a peak in the IR at 1745 cm^{-1} which we attribute to B. Methylation of A gave a dimethyl ether which is identical with the monomethyl ether of C; thus A is C demethylated at C_3 (see below). We believe that B has the same relation to D that A has to C.



5a: R_1 = Me, R_2 = H
5b: R_1 = R_2 = H
5c: R_1 = R_2 = Me
5d: R_1 = Me, R_2 = COMe



6a: R = Me
6b: R = H

There are a large number of structures that can be derived for C on the basis that its formation involved opening of the ether bridge followed by a migration analogous to that in the formation of flavothebaone[15] and opening of the cyclopropane. However none of these structures explains the experimental facts about C, in particular that C contains *only one proton* (that giving an NMR signal at δ 4·67 ppm) which is exchangeable with deuterium in base. An analogous exchange of only one proton (NMR signal at 4·50 ppm) occurred with A. Similar treatment of the model compound **4*** led to exchange of the C_5 proton (peak at 4·50 ppm), (and probably the two C_7 protons). We concluded that the C_5 proton in C and A was the one that exchanged and that in the conversion of **3a** to C and A the ether had not opened. This conclusion was confirmed by the observation that (in contrast to flavothebaone) neither C nor A coupled with diazotized sulphanilic acid. These results lead to structures **5a** for C, **5b** for A and **5c** for the dimethyl ether of A.†

Compound D did not couple with diazotized sulphanilic acid. With sodium in D_2O or MeOD, D exchanged 2 protons. These results and the spectral evidence lead to structure **6a** for D (and probably **6b** for B).

* Kindly supplied by Dr. K. W. Bentley.

† The NMR spectrum of C has a peak at 13·80 ppm; a similar peak appears in the spectrum of the dimethyl ether of A at 13·98 ppm. On the basis of earlier work[16] we attribute this peak to the C_{21} hydroxyl; hence methylation of **5a** took place on the C_{18} hydroxyl.

Normally the action of acid on derivatives of thebaine leads to opening of the ether bridge as the initial reaction.[17] However, inspection of models shows that the ether bridge in **3a** is less strained than in **2**: once the ketone is formed at C_6 opening of the ether ring with acid is unlikely. The formation of **5a** and **6a** results from different modes of opening of the cyclopropane ring, with that to **5a** being more favoured.

NMR spectra of **5a**, **5b** *and* **6a**. The NMR spectra of A, C and D are clearly in accord with structures **5b**, **5a** and **6a**. The doublet at 4·10 ppm ($J = 5$ Hz) in the spectrum of C (4·05 in A) is attributed to the nonexchangeable C_7 proton. Examination of a model of **5a** reveals that the dihedral angles between the C_7 proton and those at C_8 are 40° (H_a) and 80° (H_b). These correspond to coupling constants of 5–6 and 0–1 Hz:[18] and so the doublet is the result of coupling between H_a and C_7-H.

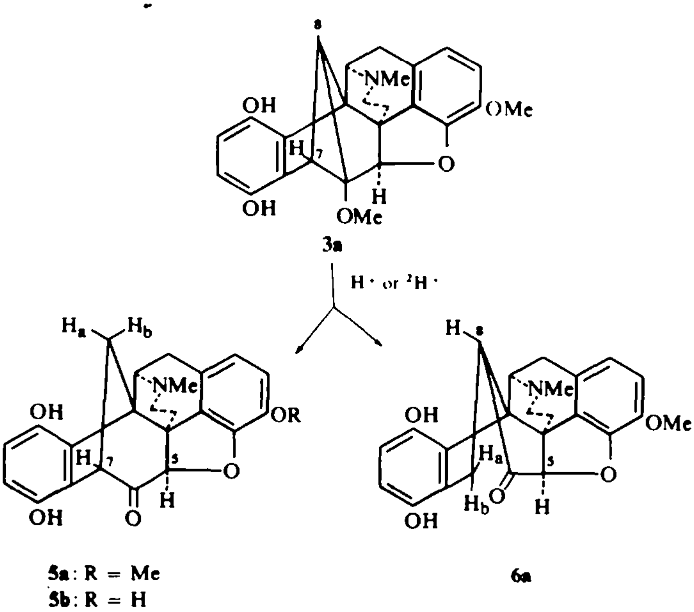


FIG 3.

In the spectrum of D the signal for the C_5 proton (4·54 ppm) is split ($J = 1{\cdot}5$ Hz), presumably, by the C_8 proton. The C_8 proton appears as a doublet ($J = 8$ Hz, signals are broadened) at 2·36 ppm. Both these protons exchange with deuterium under basic conditions. The benzylic protons at C_7 appear as a doublet (H_b) at 3·73 ppm ($J = 16$ Hz) and a doublet of doublets (H_a) at 2·97 ppm ($J = 8$ and 16 Hz). Thus H_b is split only by the geminal H_a, while H_a is also split by C_8-H. Inspection of models shows that the dihedral angle between C_8-H and H_a is 0–10° ($J = 9$–10 Hz)[18] and that between C_8-H and H_b is 110–120° ($J = 2$–4 Hz).[18] When the C_5 and C_8 protons are exchanged with deuterium the signal for H_a collapses to a doublet.

Stereochemistry of opening of cyclopropane ring. We examined the stereochemistry of the opening of the cyclopropane ring in **3a** by refluxing **3a** with PCl_3 and D_2O. From this reaction we isolated C(d_{5-6}), A(d_{5-6}) and D(d_6). The NMR spectrum of C(d_{5-6}) no longer showed peaks corresponding to the 4 aromatic protons, the signal at $\delta = 4.67$ was reduced in intensity, the integration indicated one proton less absorbing in the region $\delta = 1.65$–2.30 ppm and the doublet at 4·10 ppm had become a singlet. Similar results were obtained from the spectrum of A(d_{5-6}) (except that this spectrum was done in C_5H_5N and so the aromatic region was not studied). These results show that in **5a** and **5b** the proton H_a was replaced by deuterium and this indicates that deuterium attacked the ring at C_8 by an 'end-on' approach (Fig. 3 and below), with inversion of configuration at C_8.

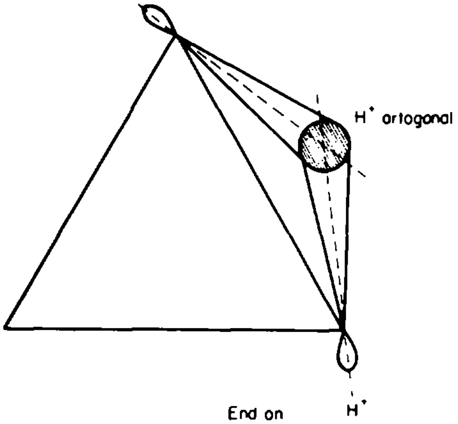


FIG 4.

Similarly the NMR spectrum of D(d_6) was the same as that for D except that the signals for the aromatic protons had lessened markedly in intensity, the doublet of doublets at 2·97 (H_a) and the doublet at 2·20 ppm (C_8-H) had disappeared, the signal at 4·54 ppm no longer showed long range splitting (confirming that it has been split by C_8-H) and the doublet at 3·73 ppm had collapsed to a singlet. These results show that in the formation of D the proton H_a was replaced with deuterium and that the cyclopropane has been deuterated at C_7 by an 'end-on' attack (Fig. 3), and inversion of C_7.

There are two ways (Fig. 4)[19] by which a proton may attack a cyclopropane: an orthogonal approach to a bond (edge-protonation), leading to retention of configuration at the carbon accepting the proton: and 'end-on' approach (corner-protonation), in which the proton attacks a bond along an extended axis joining two carbon atoms, thus leading to an inversion of configuration of the carbon receiving the proton. Although theoretical studies[20] disagree about the relative stabilities of the various forms of protonated cyclopropane, openings of cyclopropanes usually involve orthogonal approach of the proton, with retention of configuration.[21] The previously reported exceptions to this behavior[22] probably result from steric hindrance to the orthogonal approach of the proton.

Our results show that protonation at C_7 and C_8 in **3a** takes place with inversion of configuration by the unusual 'end-on' approach. A study of models indicates that orthogonal approach to the C_6—C_8 bond (to give **5a**) is hindered sterically; but, there appears to be little steric hindrance to orthogonal approach to the C_6–C_7 bond (to give **6a**). So the major factor controlling the stereochemistry of proton attack may not be steric but may result from the electronic effect of the methoxyl group. Orthogonal attack involves an equal distribution of positive charge between the ends of the bond being attacked. As **3a** reacts a positive charge developing at C_6 is stabilized by the methoxyl group; perhaps this stabilization will promote the formation of a distorted corner-substituted cyclopropane,[20b] which would be formed by end-on attack. Some support for this view comes from the finding that the opening of arylcyclopropanes does not proceed through an edge protonated cyclopropane.[23] However, the factors governing the stereochemistry of opening of cyclopropane rings still seem obscure.[22b]

EXPERIMENTAL

Unless otherwise specified UV spectra were taken in EtOH soln, IR spectra in CH_2Cl_2 solns and NMR spectra in $CDCl_3$ solns on a 60 MHz Varian spectrometer, s = singlet; d = doublet; t = triplet; qu = quartet; m = multiplet. Mass spectra were determined by direct sample introduction on (a) an Atlas CH_4 mass spectrometer with an ionising potential of 70 eV, and (b) a Hitachi RMU-6D spectrometer operated at an ionising potential of 70 eV, M.p.s. are uncorrected.

Thebainequinone (**1**).[3] Thebainequinone m.p. 249° had mass spectrum *m/e* (rel. intensity) 420(23), 419(84), 376(11), 312(20), 311(100), 310(23), 296(22), 255(45), 253(13), 230(14), 229(13), 218(11), 202(24), 201(70), 189(15), 187(12), 174(13), 152(15), 110(13), 108(34), 82(15), 55(12), and 54(28), metastable peaks at: 337·2 (M^{*}_{calc} 419 → 376 = 337·4), 281·5 (M^{*}_{calc} 311 → 296 = 281·7), 139·5 (M^{*}_{calc} 218 → 174 = 138·9, 376 → 229 = 139·5 and 255 → 189 = 140·1), and 125 (M^{*}_{calc} 419 → 230 = 126·2).

Thebainehydroquinone (**2**).[3] Thebainehydroquinone m.p. 273° had mass spectrum *m/e* (rel. intensity) 420(10), 419(40), 402(5), 376(8), 230(5), 229(5), 228(7), 218(14), 216(8), 215(4), 214(8), 203(14), 202(40), 201(100), 189(8), 188(5), 187(14), 186(10), 175(5), 160(8), 131(6), 115(5), 59(9·0), and 58(14); metastable peaks at: 386 (M^{*}_{calc} 419 → 402 = 385·7); 337·2 (M^{*}_{calc} 419 → 376 = 337·4); and 172·6 (M^{*}_{calc} 201 → 187 = 174·0).

Photothebainehydroquinone (**3a**). A soln of thebainehydroquinone (1·5 g) in purified *p*-dioxan (450 ml) was purged for 2 hr with O_2 free N_2. The soln was irradiated for 1 hr under a N_2 atmosphere with light from a 450 watt medium pressure Hanovia mercury lamp. The solvent was removed under reduced pressure at about 90° and the residue dissolved in CH_2Cl_2(150 ml). The CH_2Cl_2 soln was shaken with 6N HCl (4 × 50 ml); a precipitate separated and the mixture was divided into three portions, the precipitate (A), the portion soluble in acid (B) and that soluble in CH_2Cl_2 (C).

A. *Precipitate.* The precipitate was shaken with a mixture of NH_4OH and CH_2Cl_2 until it dissolved. The ammonical layer was extracted with CH_2Cl_2 and the combined CH_2Cl_2 extracts were water washed, dried (Na_2SO_4), and evaporated to dryness under reduced pressure. The residue was shown by IR to be identical with the product from B (below).

B. *Material soluble in acid.* The HCl soln was made basic with NH_4OH and then extracted several times with CH_2Cl_2. The combined CH_2Cl_2 extracts were water washed, dried (Na_2SO_4), and evaporated to dryness under reduced pressure. The residue was combined with the product obtained from A.

C. CH_2Cl_2 *solution.* The CH_2Cl_2 soln left after extraction with 6N HCl was washed with water, dried (Na_2SO_4) and evaporated to dryness under reduced pressure to give an unidentified material (71·4 mg).

The combined materials (1·5 g) from A and B were chromatographed on Florisil (40 g). The CH_2Cl_2-EtOAc (1:1) fraction crystallized from CH_2Cl_2-light petroleum to give photothebainehydroquinone (**3a**) as prisms, m.p. 156–157° (0·9 g): (Found: C, 72·16; H, 5·72; O, 18·11; N, 3·93. $C_{25}H_{25}O_5N$ requires: C, 71·58; H, 6·01, O, 19·07; N, 3·34%): ν_{max} 3590, 1900–1850, 1660 and 1600 cm^{-1}; λ_{max} 309 nm (ε 5,500); NMR peaks at δ: 15·00 (1H, s), 6·80 (2H, d), 6·65 (2H, s), 5·85 (1H, m), 4·65 (1H, s), 3·92 (3H, s), 3·58 (1H, d, J = 4·5 Hz), 3·40 (3H, s), 1·70–3·30 (11H, m with strong s at 2·52), ppm: *m/e* (rel. intensity) (sample had to be strongly heated to obtain spectrum) 420 (18), 419(64), 418(8), 402(5), 376(8), 218(8), 203(7), 202(19), 201(45), 86(73), 85(6), 84(100), 83(6), 57(9), 55(5), 51(14), 50(7), and 49(14); metastable peaks at: 386 (M^{*}_{calc} 419 → 402 = 385·7), 337·5 (M^{*}_{calc} 419 → 376 = 337·4). Elution of the column with $CHCl_3$ – EtOH (9:1) gave a second material (0·22 g) which was not purified.

Irradiation of thebainequinone under the same conditions gave identical results. In an irradiation of thebainequinone with a 100W lamp samples were taken at suitable intervals. The solvent was removed and the crude products examined by TLC. In this experiment photothebainehydroquinone was detected immediately on irradiation, the starting material had disappeared after about 7 hr and the second product was detected after 14 hr.

Photothebainehydroquinone can crystallize with C_6H_6 or CH_2Cl_2 of crystallization. Occasionally after crystallization from CH_2Cl_2 it had m.p. about 250°; drying this material *in vacuo* gave photoethebainehydroquinone with m.p. 156°.

Photothebainehydroquinone hydrochloride. The hydrochloride, which was prepared by passing HCl through a soln of the photo compound in acetone, crystallized from acetone in prisms, m.p. 285°; (Found: C, 66·57; H, 5·91; O, 17·04; N, 3·00; Cl, 7·57. $C_{25}H_{26}ClNO_5$ requires C, 65·91; H, 5·71; O, 17·54; N, 3·08; Cl, 7·80%).

Photothebainehydroquinone hydrobromide. HBr gas was passed through a soln of photothebainehydroquinone (570 mg) in CH_2Cl_2 (35 ml) at −78°. Removal of the solvent gave a residue which crystallized from MeOH-ether to give the hydrobromide (400 mg) as prisms, m.p. 255–257·5°. (Found: C, 59·81; H, 5·37; Br, 16·16; N, 2·81. $C_{25}H_{26}BrNO_5$ requires: C, 60·01; H, 5·24; Br, 15·97; N, 2·80%); ν_{max}^{KBr}: 1900, 1760, 1740, 1650 and 1620 cm^{-1}; main NMR peaks (in D_2O) at δ: 6·81 (2H, s), 6·66 (2H, d, J = 1 Hz) 4·52 (1H, s), 3·94 (1H, d, J = 3 Hz), 3·82 (3H, s), 3·27 (3H, s), and 2·98 (3H, s). The NMR spectrum in pyridine was the same as that of photothebainehydroquinone. Crystals of the hydrobromide were used for X-ray crystallography.

Crystal data. $C_{25}H_{26}BrNO_5$, $M = 500{\cdot}4$, Orthorhombic, $a = 10{\cdot}67$, $b = 27{\cdot}20$, $c = 7{\cdot}73$ Å, $U = 2242$ Å^3, $D_m = 1{\cdot}46$, $Z = 4$, $D_c = 1{\cdot}48$ g cm^{-3}. Space group $P2_12_12_1$ (D_2^4), $F(000) = 1032$, μ(Mo–K_α) = 19·8 cm^{-1}.

Crystallographic measurements. Cell dimensions were initially obtained from precession photographs, and subsequently modified slightly to comply with the θ, χ, ϕ setting angles of a number of reflections measured with Mo-K_α radiation on a Hilger and Watts' Y290 automatic diffractomer. The intensity data were collected by the balanced-filter method (Zr and Y filters) for reflections with $\theta \leqslant 30°$. Each reflection was scanned by the $\theta - 2\theta$ procedure in 60 steps of 0·01° (θ), counting for two seconds at each step, and the intensity was taken as the difference between the total counts obtained in the separate scans with the Zr and Y filters. The intensities were corrected for Lorentz and polarization effects, but absorption was neglected. After rejecting those weak reflections which were not considered to have significant intensities, a total of 1879 reflections was used in the structure analysis.

Structure analysis. Initial co-ordinates for the bromide ion were obtained from the three-dimensional Patterson synthesis. Structure amplitudes and phases were then calculated (R = 44·9%), weights assigned to the measured $|F_0|$ values according to the procedure described by Sim,[24] and a modified three-dimensional electron-density distribution derived. The function was displayed as contoured sections drawn on sheets of glass. Since the z-co-ordinate of the bromide ion is approximately zero, interpretation was complicated by false mirror planes at $z = 0$ and $z = 0{\cdot}5$, nevertheless positions were deduced for most of the carbon, nitrogen, and oxygen atoms, only the carbon atoms of the two methoxy groups remaining undetermined. When the additional atoms were included in a second structure-factor calculation R was 34·5% and the subsequent Fourier calculation yielded the positions of the methoxy carbon atoms.

The adjustment of the positional and thermal parameters of the atoms was accomplished by a series of least-squares calculations with the full-matrix programme ORFLS. The established absolute configuration of the morphine alkaloids[25] was adopted, and anomalous dispersion corrections incorporated for the bromide ion. Isotropic thermal parameters were employed initially for all the atoms and R converged to 12·3%, at which stage the bromide ion was assigned an anisotropic temperature factor and after two more rounds of least-squares refinement R converged to 10·9%. Since the main features of the molecular geometry had now been firmly established and available computing time was limited, further refinement with anisotropic thermal parameters for the light atoms was not undertaken. The weighting scheme employed in the least-squares calculations was $w = (a + b|F_0|)^{-1}$, where a and b were adjusted during the analysis so as to make Δw^2 approximately constant over various ranges of $|F_0|$ and sin; the final values of these parameters are $a = 7{\cdot}83$ and $b = 0{\cdot}313$.

The atomic co-ordinates and thermal parameters are listed in Table 1, molecular dimensions in Table 2, and deviations of the atoms from various planes in Table 3. The shorter intermolecular contacts are tabulated in Table 4. Fig. 1 gives a view of the molecular structure, and Fig. 2 shows the crystal structure. Values of $|F_o|$ and $|F_c|$ are tabulated elsewhere.[26]

Photothebainehydroquinone-18-acetate (**3b**). A soln of photothebainehydroquinone (500 mg) and sodium acetate (600 mg) in Ac_2O (15 ml) was refluxed for 24 hr. The soln was cooled and aq Na_2CO_3 was added until the soln was basic. The precipitate crystallized from EtOH to give the acetate (**3b**), m.p. 249° (223 mg); (Found: C, 69·61; H, 6·09; O, 21·18; N, 3·14. $C_{27}H_{27}O_6N$ requires C, 70·27; H, 5·90; O, 20·80; N, 3·04%); ν_{max}: 1850–1800, 1770, 1625 and 1600 cm^{-1}; NMR peaks at δ: 15·0 (1H, s), 6·65 (4H, m), 4·72 (1H, s), 3·90 (3H, s), 3·52 (1H, m), 3·33 (3H, s), 3·15 (1H, m), 2·40–2·90 (7H, m with s, 3H at 2·55), 2·30 (3H, s), and 2·1–1·7 (3H, m) ppm; *m/e* (rel. intensity) 462(18), 461(60), 419(8), 418(16), 244(10), 203(6), 202(10), 89(43), 74(21), 72(6), 71(34), 63(36), 62(26), 59(8), and 46(100); metastable peaks at: 380 (M^*_{calc} 461 → 419 = 380); 178·5, 167·5 (M^*_{calc} 244 → 202 = 167·2); 164, 129 (M^*_{calc} 461 → 244 = 129·1). The assignment of the acetoxy group to the 18 position was based on the presence of the NMR peak at 15·00 ppm, which indicated a C_{21} hydroxyl group.

Treatment of photothebainehydroquinone with acid. (a) *Product A.* A solution of photothebainehydroquinone (2·78 g) in conc HCl (50 ml) was refluxed for 24 hr. The resultant precipitate was treated with Na_2CO_3 aq to give a product (**5b**) which crystallized from i-PrOH-hexane in needles, m.p. 331–332° (578 mg); (Found: C, 71·06; H, 5·43; N, 3·68. $C_{23}H_{21}NO_5$ requires: C, 70·80; H, 5·54; N, 3·57%). ν_{max}: 3500, 2940, 2920, 1720 and 1680, cm^{-1}; λ_{max} 308 nm (ε 3660) and 290 nm (sh, ε 2795), NMR peaks (in C_5H_5N) at δ: 13·56 (1H, s), 10·00 (1H), 9·25 (1H), 6·5–9·0 (blocked by C_5H_5N absorption), 4·50 (1H, s), 4·05 (1H, d, J = 5 Hz), 2·85–3·40 (2H, m), and 1·20–2·70 (10H, m, 3H, s at 2·37) ppm; *m/e* (rel. intensity) 391 (100), 307(3), 297(5), 216(8), 215(11), 202(13), 190(5), 189(5), 175(3), 174(6), 161(6), 148(4), 147(4), 131(6), 115(5), 91(5), and 77(5).

(b) *Product B.* Although this product was not isolated, its presence was indicated on TLC plates. Further the IR spectrum of crude A showed an additional peak at 1745 cm^{-1}; this suggests that B is probably D demethylated at C_3.

(c) *Products C and D.* A solution of photothebainehydroquinone (3·6 g) in conc HCl (30 ml) was refluxed for 1½ hr. The cooled soln was made basic with conc NH_4OH. Crystallization of the crude precipitate from MeOH gave a mixture of products C and D. Separation of these compounds was effected by treating the mixture with MeOH or CH_2Cl_2. (i) *MeOH or CH_2Cl_2 soluble fraction.* The soln was evaporated to give a residue which crystallized from MeOH in plates to give product C (**5a**) (m.p. 239–240°) (496 mg): (Found: C, 70·83; H, 5·82; O, 19·11; N, 4·06. $C_{24}H_{23}O_5N$ requires C, 71·10; H, 5·72; O, 19·73; N, 3·45%); ν^{KBr}_{max}: 3585, 3000, 2840, 2740, 1885 and 1725 cm^{-1}; λ_{max} 310 nm (ε 3750) and 291 nm (ε 2700); NMR peaks at δ: 6·60–6·80 (4H, d, J = 4 Hz), 4·43 (1H, s), 3·90 (3H, s), 3·75 (1H, d, J = 5 Hz) 2·90–3·50 (2H, m), and 1·50–2·90 (10H, m, with s, 3H at 2·57) ppm; (in C_5D_5N) δ: 13·80 (1H, s), 8·73 (1H, s), 6·85–7·50 (4H, m), 4·67 (1H, s), 4·10 (1H, d, J = 5 Hz), 3·87 (3H, s), 2·90–3·50 (2H, m), and 1·40–2·90 (10H, m with s, 3H at 2·40) ppm. The spectrum showed the presence of methanol of crystallization; *m/e* (rel. intensity) 407(5), 406(26), 405(100), 404(18), 403(5), 305(6), 231(5), 230(19), 229(36), 216(6), 215(6), 214(13), 202(42), 189(17), 175(14), 174(13), 161(9), 160(8), 159(8), 148(18), 147(14), 144(9), 131(17), 128(11), 115(28), 103(16), 91(23) and 77(22). (ii) *Fraction less soluble in* CH_2Cl_2 *and* MeOH. The solid left after treatment with MeOH or CH_2Cl_2 (226 mg) crystallized from MeOH in prisms to give product D (**6a**), m.p. 287–289° (100 mg); (Found: C, 70·58; H, 5·73; N, 3·41. $C_{24}H_{23}NO_5$ requires: C, 71·10; H, 5·72; N, 3·45%). ν^{KBr}_{max}: 3400 to 2850, 1745 and 1625 cm^{-1}; $\lambda^{dioxane}_{max}$ 302 nm (ε 4360); NMR peaks (in C_5D_5N) at δ: 13·28 (1H, s), 6·87 (2H, s), 6·75 (2H, s), 4·28 (1H, d, J = 1·5 Hz), 3·77 (3H, s), 2·50–3·67 (8H, m), 2·40 (3H, s), 2·20 (1H, d, J = 8 Hz) and 1·45–1·90 (1H, m) ppm; 100 MHz in C_5D_5N; 4·54 (1H, d, J = 1·5 Hz), 3·85 (s, 3H), 3·73 (1H, d, J = 16 Hz), 3·64 (1H, s), 3·52 (1H, t, J = 5 Hz), 3·27 (1H, broad s) 2·97 (1H, d of d, J = 8 and 16 Hz), 2·57–2·80 (3H, m), 2·39 (3H, s), 2·35 (1H, d, J = 8 Hz) and 1·75 (1H, m) ppm. *m/e* (rel. intensity) 404(24), 405(100), 305(4), 230(22), 229(98), 214(18), 202(10), 190(6), 189(6), 188(9), 149(10), 148(6), 147(5), 131(5), 115(7), 105(5), 91(6), 83(8), 77(5), 71(6), 70(6), 69(7), 57(10) and 55(14).

Determination of the course of the reaction of photothebainehydroquinone with acid. A soln of photothebainehydroquinone (1·77 g) in conc HCl was heated under reflux. One ml aliquots were removed every hr., made basic with conc NH_4OH and the products were isolated *via* extraction with CH_2Cl_2. The TLCs (Eastman silica gel chromatograms) of the crude product were developed with EtOAc. The following results were obtained: Products **5a** and **6a** had appeared after 1 hr; by 2 hr. **3a** had disappeared and **5a** and **6a** were at their maximum concentration; products **5b** and **6b** were present after 3 hr; after 24 hr. the four products were present in approximately equal concentrations.

Hydrobromide of A. The hydrobromide of A, which was prepared by passing HBr gas through a methanolic solution of A, crystallized from MeOH–ether in prisms m.p. *ca.* 350° (decomp) (Found: C, 56·47; H, 5·28; Br, 16·38; N, 2·91. $C_{23}H_{22}BrNO_5 \ H_2O$ requires: C, 56·34; H, 4·93; Br, 16·30; N, 2·86%.)

Compound C-18-Acetate (**5d**). A mixture of compound **5a** (100 mg) and NaOAc (200 mg) in Ac_2O (10 ml) was refluxed for four hr. Saturated Na_2CO_3 was added until the solution was basic. The mixture was extracted with CH_2Cl_2 and the combined CH_2Cl_2 extracts were dried (Na_2SO_4) and evaporated under reduced pressure; the residue crystallized from MeOH to give the acetate (**5d**) as needles; m.p. 252° (70 mg); (Found: C, 69·45; H, 5·67; O, 21·12; N, 3·57. $C_{26}H_{25}O_6N$ requires: C, 69·82. H, 5·59; O, 21·48; N, 3·13%; ν_{max}: 1850, 1755, 1730, 1625 and 1600 cm^{-1}; NMR peaks at δ: 14·47 (1H, s), 6·80 (4H, d), 4·52 (1H, s), 3·97 (3H, s), 3·52 (1H, d, $J = 5$ Hz), 3·00–3·40 (2H, m), and 1·20–2·90 (13H, m with strong singlets at 2·58 and 2·23) ppm; *m/e* (rel. intensity) 448(12), 447(52), 419(6), 405(25), 404(100), 403(10), 233(4), 232(4), 205(4), 152(5), 126(5), 111(8), 109(6), 98(4), 97(13), 96(5), 95(7), 86(6), 85(12), 84(8), 83(13), 82(6), 81(8), 71(15), 70(8), 69(14), 60(5), 57(16), 56(8) and 55(14), metastable peak at 369 (M^{*}_{calc} 447 → 405 = 367·0). The NMR peak at $\delta = 14·47$ ppm shows the presence of a C_{21} hydroxyl; hence the acetate is at C_{18}.

3,18-*Dimethyl ether of product* A (**5c**). (a) *From* A. Methyl sulphate (0·5 ml) was added to a soln of **5b** (185 mg) and KOH (500 mg) in 50% aq 2-ethoxyethanol (5 ml) at reflux. Addition of water and cooling gave a precipitate which crystallized from MeOH in plates m.p. 279–281° (65 mg). The product (**5c**) was shown by m.p., mixed m.p., IR, NMR, and TLC, to be identical with that prepared from C.

(b) *From* C. Methyl sulphate (1 ml) was added to a soln of **5a** (320 mg) and KOH (1 g) in 50% aq 2-ethoxyethanol (5 ml) at reflux. The precipitate obtained on addition of water to the cooled soln crystallized from MeOH in plates, m.p. 279° (163 mg); (Found: C, 71·25; H, 6·03; N, 3·39. $C_{25}H_{25}NO_5$ requires: C, 71·58; H, 6·01; N, 3·34%); ν_{max}^{KBr}: 3435, 2955, 1840, 1730, 1635 and 1610 cm^{-1}; NMR peaks at δ: 13·98 (1H, s), 6·76 (2H, s), 6·75 (2H, s), 4·40 (1H, s), 3·90 (3H, s), 3·74 (3H, s), *ca.* 3·6 (1H, m), *ca.* 3·4 (1H, m), 3·27 (1H, d, $J = 10$ Hz), and 2·7–1·5 (10H, m with a singlet at 2·58) ppm; *m/e* (rel. intensity) 420(29), 419(100), 406(12), 405(35), 319(4), 297(4), 230(10), 229(14), 216(11), 214(5), 202(5), 189(6), 188(8), 175(8), 173(5), 165(5), 131(7), 115(11), 105(7), 103(6), 91(7), 77(10), 69(8), 57(8) and 55(9); metastable peak at 392 (M^{*}_{calc} 419 → 405 = 391·5).

Reactions with diazotized sulphanilic acid. Photothebainehydroquinone, acid products A, C, and D, and flavothebaone were treated with diazotized sulphanilic acid according to the following procedure. A dilute acidic aq soln of sulphanilic acid which had been treated with $NaNO_2$ at 0° was added to a soln of about 5 mg of sample and 2 pellets of KOH in 3 ml of water. The immediate development of a red color indicated coupling. Only flavothebaone coupled; the other solns remained light orange.

Deuteration Experiments. (a) *Deuteration of product* A. A mixture of A (93 mg), sodium (6·9 mg) and D_2O (5 ml) was warmed on a steam bath for 6 hr in a N_2 atmosphere. The cooled solution was saturated with CO_2 and extracted with CH_2Cl_2. The extract was washed with water, dried (Na_2SO_4) and evaporated to give a residue which crystallized from I-PrOH to give the deuterated product (30 mg) A(d_1). The NMR spectrum was identical with that of A, except that the peak at 4·50 ppm had disappeared. The mass spectrum had *m/e* (rel intensity) 394(17), 393(64), 392(100), 391(60), 390(7), 307(6), 292(8), 218(7), 217(21), 216(26), 215(11), 214(5), 204(7), 203(17), 202(42), 201(5), 191(6), 190(12), 189(11), 176(6), 175(9), 174(13), 173(5), 172(5), 161(5), 160(7), 149(21), 148(13), 147(8), 132(7), 131(11), 128(6), 119(5), 118(5), 117(5), 116(6), 115(8), 107(6), 105(9), 104(6), 103(5), 95(5), 91(10), 83(6), 77(7), 71(5), 70(7), 69(6), 64(5), 58(5), 57(10) and 55(7).

(b) *Deuteration of product* C. A mixture of **5a** (106 mg), sodium 5·5 mg) and D_2O (5 ml) was heated on a steam bath for 6 hr in a N_2 atmosphere. The cooled solution was saturated with CO_2 and extracted with CH_2Cl_2. The extract was washed with water, dried (Na_2SO_4), and evaporated to give a residue which crystallized from MeOH to give the deuterated product (20 mg) **5a**-d_1. The NMR spectrum was identical with that of the undeuterated material except that the peak at 4·43 ppm has disappeared. The mass spectrum had *m/e* (rel. intensity) 408(22), 407(32), 406(100), 405(15), 378(8), 231(8), 230(12), 221(7), 215(5), 203(8), 202(15), 190(8), 189(9), 185(8), 176(7), 149(19), 129(15), 111(17), 98(26), 97(27), 95(24), 91(18) and 83(31).

(c) *Deuteration of product* D. A mixture of product **6a** (100 mg), sodium (13 mg) and MeOD (7·5 ml) was heated at 60° in a N_2 atmosphere for 11 hr. The cooled solution was saturated with CO_2 and extracted with EtOAc. The extract was water washed, dried (Na_2SO_4), and evaporated to give the deuterated **6a** (50 mg). The NMR spectrum was identical with that of the undeuterated material except that the signal at 4·28 ppm had disappeared, the doublet of doublets at 2·80 ppm had simplified to a doublet (this is partially masked by other peaks in the 60 MHz spectrum but is clear in the 100 MHz spectrum), and the doublet at 2·20 had disappeared. The mass spectrum had *m/e* (rel. intensity) 409(11), 408(43), 407(72), 406(8), 231(12), 230(57), 229(100), 215(13), 214(19), 191(6), 190(6), 189(8), 188(11), 149(22), 115(7), 105(7), 91(7), 85(6), 83(13), 77(6), 71(8) 70(8), 69(9), 57(18), 56(10) and 55(16).

(d) *Products* **5a**(d_{5-6}) **5b**(d_{5-6}). A mixture of photothebainehydroquinone (2·2 g), PCl_3 (20 ml), and D_2O (25 ml) was heated just below reflux for 24 hr in an atmosphere protected by a $CaCl_2$ drying tube. Cooling the mixture to room temp gave a precipitate thus separating the mixture into two fractions.

(i) *Precipitate.* Addition of aq Na_2CO_3 to an aq soln of the precipitate gave the free base which crystallized from i-PrOH-hexane to give **5b**(d$_{5-6}$) (87·5 mg). The NMR spectrum (in C_5H_5N) was identical with that of undeuterated acid product A except that the doublet at 4·05 ppm had collapsed to a singlet, the signal at 4·50 integrated to about 0·3 of 1H and the integration appeared to indicate one less proton absorbing in the region 1·00–2·00 ppm; *m/e* (rel intensity) 399(24), 398(80), 397(100), 396(62), 395(74), 219(13), 218(24), 217(19), 206(16), 205(28), 204(22), 192(13) and 176(13).

(ii) *Soluble fraction.* The acid soln was neutralized with conc NH_4OH to give a solid which crystallized from MeOH to yield **5a**(d$_{5-6}$) (212 mg). The NMR spectrum ($CDCl_3$) was identical with that of undeuterated product C except that the doublet at 3·75 ppm had collapsed to a singlet, the singlet at 4·43 had weakened in intensity to *ca.* 0·5H, the signals for the aromatic protons had almost disappeared, and the integration indicated one less proton absorbing in the region 1·65–2·60 ppm. Similarly in C_5H_5N the doublet at 4·10 had become a singlet and the signal at 4·65 ppm was reduced in intensity; *m/e* (rel. intensity): 412(22), 411(82), 410(100), 409(60), 310(5), 309(4), 233(8), 232(17), 231(22), 230(6), 219(5), 218(3), 217(4), 216(5), 205(19), 204(10), 193(6), 192(6), 191(7), 190(6), 177(5) and 150(7).

(e) *Product* **6a**(d$_6$). A soln of photothebainehydroquinone (3 g) in D_2O (30 ml) to which had been added PCl_3 (25 ml) (over 1 hr with cooling), was kept at room temp for 2 hr. and then heated at reflux for 4 hr (until a TLC of an EtOAc extract of a basified aliquot no longer indicated starting material). After cooling conc NH_4OH was added. Addition of Na_2CO_3 aq to an aq soln of the precipitate gave a product which crystallized from MeOH to give **6a** (d$_6$) (124 mg) m.p. 280° (identity shown by TLC and spectrum). The NMR spectrum (100 MHz) was identical with that of undeuterated product **6a** except that the absorption in the aromatic region was reduced markedly, the doublets at 4·54 and 3·73 ppm had collapsed to singlets, and the doublet of doublets at 2·97 and the doublet at 2·35 ppm had disappeared, *m/e* (rel. intensity): 412(28), 411(88), 410(69), 409(18), 232(25), 231(100), 230(16), 216(16) and 190(26).

Deuteration of 4. A soln of **4** (114 mg) and Na (6·9 mg) in dioxan (20 ml) and D_2O (5 ml) was heated for 7 hr on a steam-bath. The cooled soln was extracted with CH_2Cl_2 (3 × 30 ml) and the combined extracts were dried (Na_2SO_4). Removal of the solvent gave deuterated **4** (75 mg) which had an NMR identical with **4** except that the peak at 4·5 ppm was markedly reduced in intensity and there was some change in the methylene region.

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