X-Ray Structural and Conformational Analyses of the *Erythrina* Alkaloids Cocculine and Coccutrine

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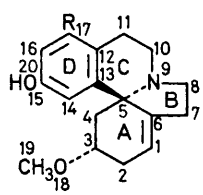
Crystal structures of the title alkaloids have been established by direct phase-determining methods and atomic parameters refined by full-matrix least-squares calculations to R 0.063 (1) and 0.078 (2) over 960 (1) and 1 342 (2) reflections from diffractometer measurements. The non-isomorphous crystals both belong to the orthorhombic system, space group $P2_12_12_1$, with $Z = 4$ in unit cells of dimensions: (1), $a = 10.51(1)$, $b = 15.87(1)$, $c = 8.95(1)$ Å; and (2), $a = 10.69(1)$, $b = 16.65(1)$, $c = 8.80(1)$ Å. Detailed comparisons of the ring conformations are made. Ring A approximates to a half-chair form and ring C to a form intermediate between half-chair and envelope in both compounds. Small variations observed in the ring B conformations are ascribed to different hydrogen-bonded arrangements in the crystals.

In the course of their studies on the constituents of *Cocculus trilobus* D. C. Furukawa and Ju-ichi [1] recently isolated two related *Erythrina* alkaloids. Chemical and spectral data for one of these showed it to be a new



(1) R = H

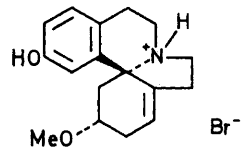
(2) R = OMe

alkaloid with a methoxy-group *meta* to an aromatic hydroxy group, but the exact positions of these two substituents required definition. The other alkaloid possessed spectral and physical data very similar to those reported for cocculine (1) [2] which had been isolated previously from *Cocculus laurifolius* D.C. and for which the structure and absolute stereochemistry had been defined unequivocally by *X*-ray analysis of the hydrobromide salt.† We undertook *X*-ray diffraction studies of both alkaloids in order to establish the structure of the new alkaloid (2), to verify that the other alkaloid was the known cocculine, and to define carefully the conformations of this structurally similar pair of bases as representatives of this class of alkaloid and compare these results with those for the hydrobromide salt of cocculine.[2a] A preliminary account of this work has appeared.[3]

EXPERIMENTAL

Crystal Data.—(*a*) Cocculine (1), $C_{17}H_{21}NO_2$, $M = 271.4$. Orthorhombic, $a = 10.51(1)$, $b = 15.87(1)$, $c = 8.95(1)$ Å, $U = 1\ 493$ Å^3, $D_m = 1.21$ g cm^{-3} (by flotation in chlorobenzene–*p*-bromoanisole), $Z = 4$, $D_c = 1.207$ g cm^{-3}, $F(000) = 584$. Cu-K_α radiation, $\lambda = 1.541\ 8$ Å; μ(Cu-K_α) $= 6.3$ cm^{-1}. Space group $P2_12_12_1$ (D_2^4) from systematic absences: $h00$ when $h \neq 2n$, $0k0$ when $k \neq 2n$, $00l$ when $l \neq 2n$.

(*b*) Coccutrine (2), $C_{13}H_{23}NO_3$, $M = 301.4$. Orthorhombic,



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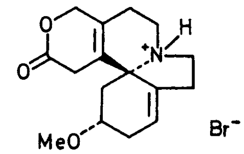

(4)

$a = 10.69(1)$, $b = 16.65(1)$, $c = 8.80(1)$ Å, $U = 1\ 566$ Å^3, $D_m = 1.26$ g cm^{-3} (flotation in aqueous $ZnCl_2$), $Z = 4$, $D_c = 1.278$ g cm^{-3}, $F(000) = 648$. Cu-K_α radiation,

† The representation of (1) in ref. 2*a* shows the enantiomer of the structure defined by the torsion angles reported in this same article and so the absolute stereochemistry is ambiguously presented therein. In addition, the sign of one of the torsion angles is incorrect and the magnitude of another is in error (see Table 5). The stereochemistry shown here accords with the previously defined absolute configuration for *Erythrina* alkaloids and with the torsion angles reported in ref. 2*a*.

[1] H. Furukawa, personal communication.
[2] (*a*) R. Razakov, S. Y. Yunusov, S.-M. Nasyrov, A. L. Chekhlov, V. G. Adrianov, and Y. T. Struchkov, *J.C.S. Chem. Comm.*, 1974, 150; (*b*) S. Y. Yunusov and R. Razakov, *Khim. prirod. Soedinenii*, 1970, 74; (*c*) S. Y. Yunusov, *Zhur. obshchei. Khim.*, 1950, **20**, 368.
[3] A. T. McPhail, K. D. Onan, H. Furukawa, and M. Ju-ichi, *Tetrahedron Letters*, 1976, 485.

μ(Cu-K_α) = 7.0 cm^{-1}. Space group $P2_12_12_1$ (D_4^2) from systematic absences as for (1).

Crystallographic Measurements.—Initial unit-cell dimensions for (1) were obtained from oscillation and Weissenberg photographs taken with Cu-K_α radiation; corresponding information for (2) was obtained from precession photographs taken with Mo-K_α radiation (λ = 0.710 7 Å). Single crystals of dimensions *ca.* 0.22 × 0.26 × 0.66 mm for (1) and *ca.* 0.20 × 0.40 × 1.00 mm for (2) were oriented on glass fibres so that their *b* and *c* axes, respectively, were parallel to the ϕ axis of an Enraf–Nonius CAD 3 diffractometer (Ni-filtered Cu-K_α radiation, 3° take off angle). Refined unit-cell parameters were calculated by least-squares treatment of the θ, χ, and ϕ angles for 36 (1) and 40 (2) high-order reflections, widely separated in reciprocal space. One octant of data to θ 65° was collected from each crystal by use of the θ—2θ scanning technique with scan-widths (1.40 + 0.70tanθ)° for (1) and (1.20 + 0.60tanθ)° for (2). Background measurements were taken at each end of the scan range for times equal to half the duration of the scan. In each case a standard reflection remeasured periodically throughout data collection showed no significant variation in intensity. Of the 1 481 reflections measured for (1) and 1 543 for (2), only those (960 and 1 342) having $I > 2.0\sigma(I)$ [$\sigma^2(I)$ = scan count + total background count] were corrected for the usual Lorentz and polarization effects and used in the structure analysis and refinement. Absorption corrections, established from the ϕ-dependence of the intensity of the 004 reflection measured at χ 90°, were also made to the data from (2); similar measurements on the 080 reflection from (1) showed that no corrections were necessary.

TABLE 1

Fractional atomic co-ordinates (× 10^4) for non-hydrogen atoms, with estimated standard deviations in parentheses

Atom	*x*	*y*	*z*
(*a*) (1) Cocculine			
C(1)	342(9)	3 749(5)	143(9)
C(2)	1 705(9)	3 991(5)	−31(9)
C(3)	2 231(7)	3 805(4)	−1 574(9)
C(4)	1 273(7)	3 985(5)	−2 775(8)
C(5)	33(7)	3 488(5)	−2 555(9)
C(6)	−390(8)	3 513(5)	−962(9)
C(7)	−1 826(9)	3 379(7)	−1 022(11)
C(8)	−2 197(8)	3 535(7)	−2 623(13)
N(9)	−1 050(6)	3 884(4)	−3 311(8)
C(10)	−1 018(8)	3 817(6)	−4 946(10)
C(11)	−1 074(10)	2 892(6)	−5 500(10)
C(12)	−327(8)	2 310(6)	−4 494(8)
C(13)	173(7)	2 548(6)	−3 109(8)
C(14)	765(7)	1 969(5)	−2 206(8)
C(15)	904(7)	1 137(5)	−2 674(9)
C(16)	443(8)	906(5)	−4 032(9)
C(17)	−181(8)	1 488(6)	−4 934(9)
O(18)	3 314(5)	4 304(4)	−1 897(7)
C(19)	4 391(9)	4 065(7)	−1 009(12)
O(20)	1 509(5)	600(4)	−1 719(7)
(*b*) (2) Coccutrine			
C(1)	2 736(4)	3 128(3)	1 594(5)
C(2)	3 740(5)	2 708(3)	2 414(5)
C(3)	5 054(4)	3 046(2)	2 094(4)
C(4)	5 031(4)	3 955(2)	2 037(4)
C(5)	4 144(4)	4 266(2)	790(4)
C(6)	2 917(4)	3 814(2)	852(4)
C(7)	1 946(4)	4 362(3)	179(6)
C(8)	2 539(5)	5 205(3)	274(6)
N(9)	3 706(4)	5 074(2)	1 148(4)
C(10)	4 676(5)	5 690(2)	907(5)
C(11)	5 170(5)	5 727(2)	−708(5)
C(12)	5 267(4)	4 919(2)	−1 430(5)
C(13)	4 757(3)	4 221(2)	−793(4)
C(14)	4 793(3)	3 498(2)	−1 578(4)
C(15)	5 338(3)	3 450(2)	−3 002(4)
C(16)	5 884(4)	4 121(2)	−3 649(4)
C(17)	5 834(4)	4 847(2)	−2 867(4)
O(18)	5 883(3)	2 765(2)	3 266(3)
C(19)	7 130(4)	2 673(3)	2 804(6)
O(20)	5 310(3)	2 722(2)	−3 713(3)
O(21)	6 316(3)	5 540(2)	−3 464(4)
C(22)	6 701(5)	5 545(3)	−5 017(6)

Structure Analyses.—The structures of (1) and (2) were both solved by direct phasing methods by use of MULTAN [4] with the highest 250 $|E|$ values, the program being allowed to select five unknowns in addition to the three origin-defining reflections. In each case an E map calculated with the set of phases producing the highest figure-of-merit and lowest residual revealed positions for all non-hydrogen atoms. Structure-factor calculations gave an initial R 0.239 for (1) and 0.258 for (2). Positional and isotropic

TABLE 2

Hydrogen atom fractional co-ordinates (× 10^3), and distances to their bonded carbon or oxygen atoms, with estimated standard deviations in parentheses

Atom	*x*	*y*	*z*	*d*/Å
(*a*) (1) Cocculine				
H(1)	−7(7)	383(5)	102(9)	0.91(8)
H(2A)	222(7)	369(4)	59(18)	0.91(7)
H(2B)	180(5)	458(3)	19(5)	0.96(5)
H(3)	250(4)	325(3)	−169(5)	0.92(4)
H(4A)	164(5)	376(3)	−375(6)	1.02(5)
H(4B)	107(4)	456(3)	−285(5)	0.94(4)
H(7A)	−196(8)	298(5)	−52(9)	0.79(8)
H(7B)	−214(9)	369(6)	−20(11)	0.95(9)
H(8A)	−266(9)	282(6)	−328(11)	1.37(10)
H(8B)	−282(6)	386(4)	−276(7)	0.85(6)
H(10A)	−159(12)	412(8)	−545(13)	0.90(12)
H(10B)	−20(5)	399(3)	−523(6)	0.93(5)
H(11A)	−197(6)	268(4)	−562(6)	1.00(6)
H(11B)	−94(8)	285(5)	−643(9)	0.85(8)
H(14)	113(7)	215(4)	−129(8)	0.95(7)
H(16)	56(6)	35(4)	−427(6)	0.91(6)
H(17)	−46(6)	127(4)	−598(7)	1.03(6)
H(19A)	512(8)	445(5)	−164(9)	1.13(8)
H(19B)	409(8)	441(5)	−22(9)	0.95(8)
H(19C)	464(7)	359(5)	−122(8)	0.82(7)
H(20)	126(5)	11(3)	−196(5)	0.85(5)
(*b*) (2) Coccutrine				
H(1)	188(5)	312(3)	190(6)	0.95(5)
H(2A)	385(5)	220(3)	228(6)	0.86(5)
H(2B)	363(4)	277(2)	336(5)	0.85(4)
H(3)	541(3)	286(2)	122(3)	0.91(3)
H(4A)	588(4)	409(2)	195(5)	0.94(4)
H(4B)	469(3)	418(2)	298(4)	0.98(4)
H(7A)	174(9)	403(4)	−95(10)	1.16(9)
H(7B)	130(5)	422(3)	86(6)	0.95(5)
H(8A)	256(10)	523(5)	−87(13)	1.01(11)
H(8B)	198(7)	546(4)	75(9)	0.84(7)
H(10A)	445(4)	618(2)	113(5)	0.87(4)
H(10B)	539(6)	555(3)	161(7)	1.01(6)
H(11A)	462(4)	610(2)	−131(4)	1.01(4)
H(11B)	611(5)	593(3)	−76(6)	1.07(5)
H(14)	454(3)	308(2)	−125(3)	0.80(3)
H(16)	638(3)	424(2)	−473(4)	1.11(3)
H(19A)	763(4)	238(2)	361(6)	1.01(5)
H(19B)	717(7)	204(4)	178(8)	1.39(7)
H(19C)	744(4)	316(3)	249(5)	0.91(4)
H(20)	546(10)	279(5)	−449(12)	0.71(11)
H(22A)	716(5)	595(3)	−546(6)	0.92(5)
H(22B)	691(4)	493(2)	−538(5)	1.10(4)
H(22C)	589(5)	546(3)	−570(6)	1.06(5)

[4] G. Germain, P. Main, and M. M. Woolfson, *Acta Cryst.*, 1971, **A27**, 368.

thermal parameters were then adjusted by full-matrix least-squares calculations to R 0.141 (1) and 0.129 (2) at which point hydrogen atom positions were located in three-dimensional difference-Fourier syntheses and included in

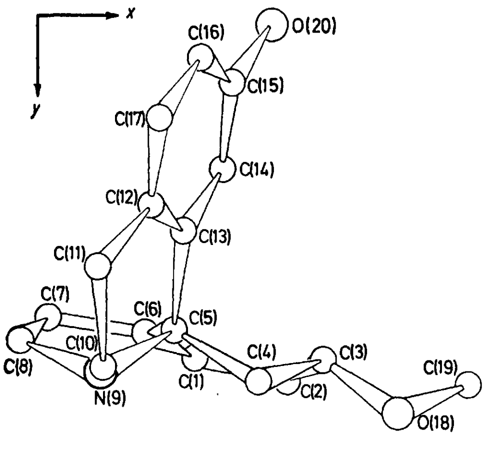

FIGURE 1 Conformation and atom-numbering scheme for cocculine (1); positive z goes away from the viewer

the subsequent structure-factor calculations [R 0.123 (1), 0.120 (2)]. Least-squares refinement of the positional and isotropic thermal parameters of some of the hydrogen atoms led to physically meaningless thermal parameters and so these atoms were all included with fixed values of $B = 4.0$ Å^2 for (1) and 4.5 Å^2 for (2). Subsequent refinement of positional and thermal parameters led to convergence at R 0.063 (1) and 0.078 (2). Final positional parameters are in Tables 1 and 2. Anisotropic thermal parameters for the non-hydrogen atoms have been deposited with Tables of observed and calculated structure amplitudes in Supple-

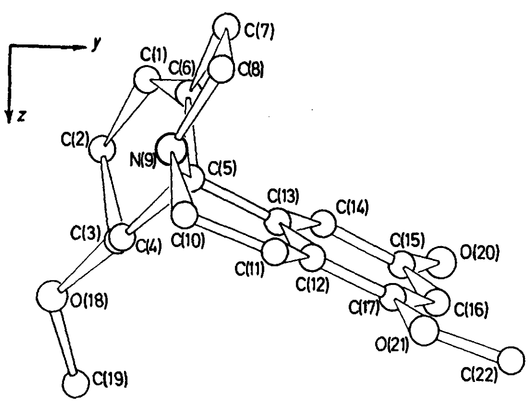

FIGURE 2 Conformation and atom numbering scheme for coccutrine (2); positive x goes away from the viewer

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Atomic scattering factors for oxygen, nitrogen, and carbon were from ref. 5, and for hydrogen from ref. 6. In the least-squares calculations the function minimized was $\Sigma w\Delta^2$, weights being assigned according to $\sqrt{w} = 1$ for $|F_o| \leqslant K$ and $\sqrt{w} = K/|F_o|$ for $|F_o| > K$ [$K = 8.4$ for (1), $K = 8.6$ for (2)]; there was then no systematic dependence of $\Sigma w\Delta^2$ on $|F_o|$.

RESULTS AND DISCUSSION

The results of these studies confirm that (1) is indeed cocculine and that the new alkaloid is its C(17)-methoxy derivative, coccutrine (2). The absolute stereochemistries as represented by (1) and (2) follow from the investigations on cocculine hydrobromide [2a] and other *Erythrina* alkaloids.[7-10] Views of the molecular conformations and atom numbering schemes are shown in Figures 1 and 2. The packing arrangements of (1) and

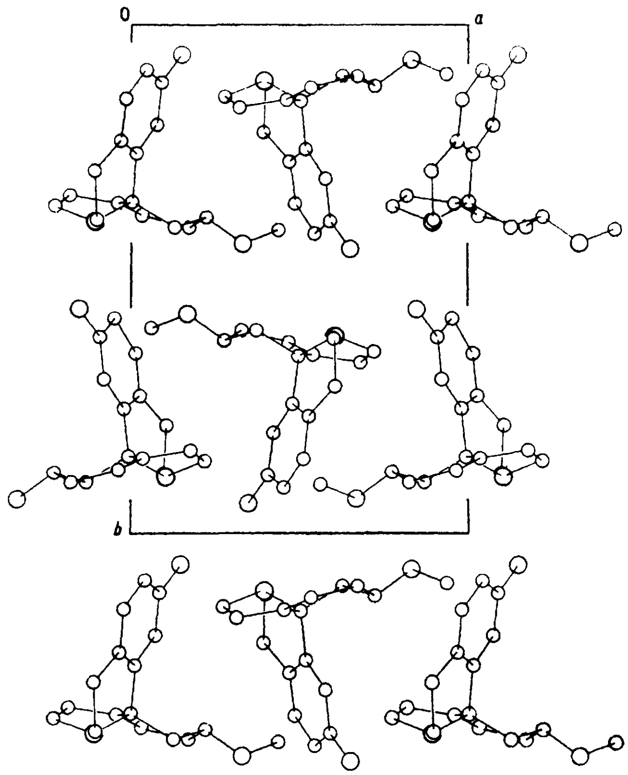

FIGURE 3 Packing of cocculine molecules in the crystal, viewed in projection along the c axis; positive direction goes away from the viewer

(2) in the crystals are illustrated in Figures 3 and 4. Corresponding interatomic distances and valency angles for (1) and (2) are listed in Table 3; torsion angles are in Table 4.

The ring conformations of (1) and (2) would be expected to be very similar and analysis of the torsion angles (Table 5) bears this out. The only significant differences occur in the heterocyclic B rings, and may be ascribed to different crystal-packing forces.

Cyclohexene ring A, with ΔC_2-HC 14 in (1), 11.7° in (2), and ΔC_s-E 39 in (1), 52.0° in (2), lies nearer to a half-

* See Notice to Authors No. 7 in *J.C.S. Perkin II*, 1975, Index issue.

[5] D. T. Cromer and J. T. Waber, *Acta Cryst.*, 1965, **18**, 104.

[6] R. F. Stewart, E. R. Davidson, and W. T. Simpson, *J. Chem. Phys.*, 1965, **42**, 3175.

[7] D. H. R. Barton, R. James, G. W. Kirby, D. W. Turner, and D. A. Widdowson, *J. Chem. Soc. (C)*, 1968, 1529.

[8] V. Boekelheide and G. R. Wenzinger, *J. Org. Chem.*, 1964, **29**, 1307.

[9] A. W. Hanson, *Proc. Chem. Soc.*, 1963, 52; A. W. Hanson, *Acta Cryst.*, 1963, **16**, 939.

[10] D. H. R. Barton, P. N. Jenkins, R. Letcher, D. A. Widdowson, E. Hough, and D. Rogers, *Chem. Comm.*, 1970, 391.

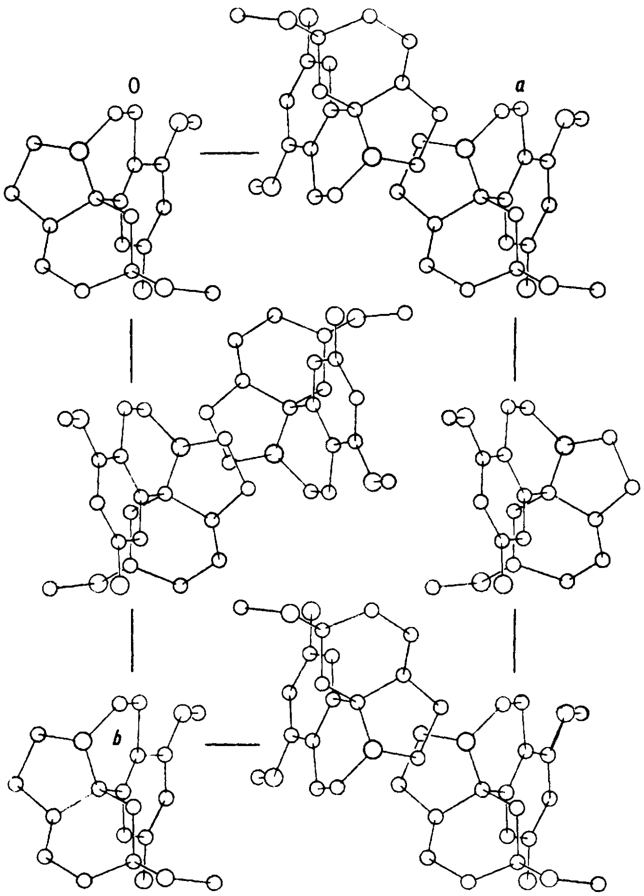

FIGURE 4 Packing of coccutrine molecules in the crystal, viewed in projection along the c axis; positive direction goes away from the viewer.

TABLE 3

Interatomic distances (Å) and angles (°), with estimated standard deviations in parentheses

	(1)	(2)
(*a*) Bond lengths		
C(1)–C(2)	1.491 (14)	1.471 (6)
C(1)–C(6)	1.308 (12)	1.330 (6)
C(2)–C(3)	1.517 (11)	1.538 (6)
C(3)–C(4)	1.500 (10)	1.515 (5)
C(3)–O(18)	1.417 (9)	1.438 (4)
C(4)–C(5)	1.537 (11)	1.540 (5)
C(5)–C(6)	1.494 (12)	1.513 (6)
C(5)–N(9)	1.465 (10)	1.459 (5)
C(5)–C(13)	1.579 (12)	1.541 (5)
C(6)–C(7)	1.525 (13)	1.503 (6)
C(7)–C(8)	1.505 (15)	1.542 (7)
C(8)–N(9)	1.463 (11)	1.482 (6)
N(9)–C(10)	1.467 (12)	1.474 (6)
C(10)–C(11)	1.550 (14)	1.517 (7)
C(11)–C(12)	1.510 (13)	1.492 (5)
C(12)–C(13)	1.399 (11)	1.400 (5)
C(12)–C(17)	1.371 (13)	1.407 (6)
C(13)–C(14)	1.373 (11)	1.390 (5)
C(14)–C(15)	1.393 (11)	1.384 (5)
C(15)–C(16)	1.359 (11)	1.383 (5)
C(15)–O(20)	1.365 (10)	1.364 (5)
C(16)–C(17)	1.390 (12)	1.392 (5)
C(17)–O(21)		1.369 (5)
O(18)–C(19)	1.435 (12)	1.403 (6)
O(21)–C(22)		1.428 (6)

TABLE 3 (*Continued*)

	(1)	(2)
(*b*) Valency angles		
C(2)–C(1)–C(6)	124.1(8)	122.9(4)
C(1)–C(2)–C(3)	113.3(7)	113.8(4)
C(2)–C(3)–C(4)	111.7(6)	110.9(3)
C(2)–C(3)–O(18)	111.7(6)	108.2(3)
C(4)–C(3)–O(18)	106.6(6)	111.0(3)
C(3)–C(4)–C(5)	112.3(6)	111.7(3)
C(4)–C(5)–C(6)	111.2(7)	109.9(3)
C(4)–C(5)–N(9)	112.3(6)	110.7(3)
C(4)–C(5)–C(13)	111.4(6)	111.5(3)
C(6)–C(5)–N(9)	101.5(6)	99.9(3)
C(6)–C(5)–C(13)	110.6(6)	112.1(3)
N(9)–C(15)–C(13)	109.4(6)	112.1(3)
C(1)–C(6)–C(5)	123.6(8)	124.8(4)
C(1)–C(6)–C(7)	130.5(8)	127.9(4)
C(5)–C(6)–C(7)	104.9(7)	106.4(3)
C(6)–C(7)–C(8)	105.5(7)	104.3(4)
C(7)–C(8)–N(9)	104.5(7)	103.9(4)
C(5)–N(9)–C(8)	106.5(7)	107.1(3)
C(5)–N(9)–C(10)	114.3(6)	112.6(3)
C(8)–N(9)–C(10)	114.3(7)	114.6(3)
N(9)–C(10)–C(11)	112.8(7)	114.1(4)
C(10)–C(11)–C(12)	111.6(7)	112.7(3)
C(11)–C(12)–C(13)	123.9(8)	123.4(4)
C(11)–C(12)–C(17)	118.0(7)	119.3(3)
C(13)–C(12)–C(17)	118.0(8)	117.2(3)
C(5)–C(13)–C(12)	119.9(7)	119.2(3)
C(5)–C(13)–C(14)	119.4(7)	120.2(3)
C(12)–C(13)–C(14)	120.7(8)	120.6(3)
C(13)–C(14)–C(15)	120.4(7)	120.8(3)
C(14)–C(15)–C(16)	119.1(7)	120.3(3)
C(14)–C(15)–O(20)	116.9(7)	117.2(3)
C(16)–C(15)–O(20)	123.9(7)	122.5(3)
C(15)–C(16)–C(17)	120.6(7)	118.8(3)
C(12)–C(17)–C(16)	121.2(7)	122.4(3)
C(12)–C(17)–O(21)		115.8(3)
C(16)–C(17)–O(21)		121.9(3)
C(3)–O(18)–C(19)	111.9(7)	114.4(3)
C(17)–O(21)–C(22)		118.8(3)

(*c*) Intermolecular distances <3.70 Å

(i) For (1)

N(9) · · · O(20$^{\mathrm{I}}$)	2.76	C(19) · · · C(14$^{\mathrm{II}}$)	3.61
C(10) · · · O(20$^{\mathrm{I}}$)	3.23	C(1) · · · C(16$^{\mathrm{I}}$)	3.66
C(19) · · · O(20$^{\mathrm{II}}$)	3.35	C(19) · · · C(15$^{\mathrm{II}}$)	3.67
C(8) · · · O(20$^{\mathrm{I}}$)	3.39	N(9) · · · C(15$^{\mathrm{I}}$)	3.68
O(20) · · · C(7$^{\mathrm{II}}$)	3.42		

(ii) For (2)

O(18) · · · O(20$^{\mathrm{III}}$)	2.73	C(19) · · · O(20$^{\mathrm{III}}$)	3.55
O(20) · · · C(1$^{\mathrm{II}}$)	3.49	C(19) · · · C(14$^{\mathrm{II}}$)	3.61
O(18) · · · C(15$^{\mathrm{III}}$)	3.53	C(19) · · · O(20$^{\mathrm{III}}$)	3.63
O(18) · · · C(16$^{\mathrm{II}}$)	3.53		

Roman numeral superscripts refer to the following transformations of the co-ordinates of Table 1:

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

chair (C_2) than an envelope (C_s) form. The methoxy-substituent is pseudo-equatorially oriented as in other *Erythrina* alkaloids.[7-11] The conformation adopted by the methoxy-group would be expected to be close to one of the two forms in which the methyl group is approximately gauche to either C(2) or C(4) and the actual form found in the solid state would then depend on crystal-packing forces which are distinctly different in (1) and (2). In (1) the C(2)–C(3)–O(18)–C(19) torsion angle (69.4°) corresponds to the first of these forms whereas in (2) C(4)–C(3)–O(18)–C(19) (−87.8°) is indicative of the second form. Both angles exceed the ideal 60° value in order to minimize non-bonding interactions between the

[11] D. S. Bhakuni, H. Uprety, and D. A. Widdowson, *Phytochemistry*, 1976, **15**, 739.

methyl and ring methylene groups; this effect is also responsible for the small inequalities in the exocyclic valency angles at C(3). The much larger torsion angle in (2) may be required to optimise the intermolecular hydrogen-bonding interaction involving the methoxy-oxygen atom (*vide infra*).

TABLE 4

Torsion angles (°); 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

	(1)	(2)
C(6)–C(1)–C(2)–C(3)	−9	−10.7
C(2)–C(1)–C(6)–C(5)	−3	−2.1
C(2)–C(1)–C(6)–C(7)	−169	−169.9
C(1)–C(2)–C(3)–C(4)	39	40.9
C(1)–C(2)–C(3)–O(18)	158	162.8
C(2)–C(3)–C(4)–C(5)	−57	−59.5
O(18)–C(3)–C(4)–C(5)	−179	−179.8
C(2)–C(3)–O(18)–C(19)	69	150.3
C(4)–C(3)–O(18)–C(19)	−168	−87.8
C(3)–C(4)–C(5)–C(6)	44	45.7
C(3)–C(4)–C(5)–N(9)	157	155.2
C(3)–C(4)–C(5)–C(13)	−79	−79.3
C(4)–C(5)–C(6)–C(1)	−15	−15.5
C(4)–C(5)–C(6)–C(7)	155	154.4
N(9)–C(5)–C(6)–C(1)	−135	−132.0
N(9)–C(5)–C(6)–C(7)	35	38.0
C(13)–C(5)–C(6)–C(1)	109	109.1
C(13)–C(5)–C(6)–C(7)	−81	−81.0
C(4)–C(5)–N(9)–C(8)	−161	−158.9
C(4)–C(5)–N(9)–C(10)	72	74.3
C(6)–C(5)–N(9)–C(8)	−42	−43.0
C(6)–C(5)–N(9)–C(10)	−170	−169.8
C(13)–C(5)–N(9)–C(8)	74	76.0
C(13)–C(5)–N(9)–C(10)	−53	−50.8
C(4)–C(5)–C(13)–C(12)	−102	−100.3
C(4)–C(5)–C(13)–C(14)	80	80.1
C(6)–C(5)–C(13)–C(12)	134	135.9
C(6)–C(5)–C(13)–C(14)	−44	−43.7
N(9)–C(5)–C(13)–C(12)	23	24.4
N(9)–C(5)–C(13)–C(14)	−155	−155.2
C(1)–C(6)–C(7)–C(8)	153	150.1
C(5)–C(6)–C(7)–C(8)	−16	−19.4
C(6)–C(7)–C(8)–N(9)	−10	−6.6
C(7)–C(8)–N(9)–C(5)	33	31.7
C(7)–C(8)–N(9)–C(10)	160	157.3
C(5)–N(9)–C(10)–C(11)	63	59.1
C(8)–N(9)–C(10)–C(11)	−60	−63.6
N(9)–C(10)–C(11)–C(12)	−37	−36.8
C(10)–C(11)–C(12)–C(13)	10	10.6
C(10)–C(11)–C(12)–C(17)	−173	−173.3
C(11)–C(12)–C(13)–C(5)	−3	−4.7
C(11)–C(12)–C(13)–C(14)	175	174.9
C(17)–C(12)–C(13)–C(5)	180	179.1
C(17)–C(12)–C(13)–C(14)	−2	−1.3
C(11)–C(12)–C(17)–C(16)	−177	−175.7
C(11)–C(12)–C(17)–O(21)		3.1
C(13)–C(12)–C(17)–C(16)	0	0.7
C(13)–C(12)–C(17)–O(21)		179.5
C(5)–C(13)–C(14)–C(15)	180	179.8
C(12)–C(13)–C(14)–C(15)	2	0.2
C(13)–C(14)–C(15)–C(16)	0	1.7
C(13)–C(14)–C(15)–O(20)	180	−178.5
C(14)–C(15)–C(16)–C(17)	−1	−2.3
O(20)–C(15)–C(16)–C(17)	179	177.9
C(15)–C(16)–C(17)–C(12)	1	1.2
C(15)–C(16)–C(17)–O(21)		−177.6
C(12)–C(17)–O(21)–C(22)		−168.9
C(16)–C(17)–O(21)–C(22)		9.9

Dreiding molecular models of (1) and (2) reveal severe H(3) · · · H(14) and H(8A) · · · H(11A) non-bonded interactions. The results of the present studies show that relief from these interactions is achieved principally by anticlockwise rotation about the C(5)–C(13) bond to give an orientation wherein the H(3) · · · H(14) and H(8A) · · · H(11A) model distances (1.2 and 1.7 Å) are increased to more acceptable values [2.30(8) and 2.23(11) in (1), and 2.40(4) and 2.65(11) Å in (2)]. Further rotation about this bond is restricted by the introduction of non-bonded interactions between H(14) and the π-electrons in the C(1)–C(6) double-bond resulting in the adoption by ring C of a form intermediate between half-chair and envelope conformations (see Table 5). In addition to this rotation there appears to be slight elongation of the C(5)–C(13) bond, not dissimilar to that encountered in mesembrine alkaloids,[12–15] where an axial phenyl substituent is also present but the constraining ethano-bridge of the *Erythrina* alkaloids is absent.

TABLE 5

Endocyclic torsion angles for the A, B, and C rings of some *Erythrina* alkaloids

	(1) [a]	(2) [a]	(3) [b]	(4) [c]
Ring A				
$\omega_{1.2}$	−9	−10.7	4	−1
$\omega_{2.3}$	39	40.9	29	33
$\omega_{3.4}$	−57	−59.5	−55	−57
$\omega_{4.5}$	44	45.7	53	49
$\omega_{5.6}$	−15	−15.5	−26 [g]	−21
$\omega_{1.6}$	−3	−2.1	−3	−3
ΔC_2 − HC [d]	14	11.7	49	39
ΔC_s − E [d]	39	52.0	6	24
Ring B				
$\omega_{5,6}$	35	38.0	35	37
$\omega_{6.7}$	−16	−19.4	−16	−18
$\omega_{7.8}$	−10	−6.6	−11	−8
$\omega_{8.9}$	33	31.7	34 [h]	33
$\omega_{5.9}$	−42	−43.0	−42	−41
ΔC_2 − HC [e]	8	19.1	6	14
ΔC_s − E [e]	34	23.9	36	27
Ring C				
$\omega_{5.9}$	−53	−50.8	−54	−50
$\omega_{9.10}$	63	59.1	62	62
$\omega_{10.11}$	−37	−36.8	−36	−39
$\omega_{11.12}$	10	10.6	9	11
$\omega_{12,13}$	−3	−4.7	−4	−2
$\omega_{5.13}$	23	24.4	26	21
ΔC_2 − HC [f]	32	32.5	39	22
ΔC_s − E [f]	31	26.6	23	42

[a] Present work. [b] Ref. 2(*a*). [c] Ref. 9. [d] $\Delta C_2 - \mathrm{HC} = |\omega_{1.6}| + |\omega_{1.2} - \omega_{5.6}| + |\omega_{2.3} - \omega_{4.5}|$, $\Delta C_s - \mathrm{E} = |\omega_{1.2} + \omega_{1.6}| + |\omega_{2.3} + \omega_{5.6}| + |\omega_{3.4} + \omega_{4.5}|$. [e] $\Delta C_2 - \mathrm{HC} = |\omega_{5.6} - \omega_{8.9}| + |\omega_{6.7} - \omega_{7.8}|$, $\Delta C_s - \mathrm{E} = |\omega_{7.8}| + |\omega_{6.7} + \omega_{8.9}| + |\omega_{5.6} + \omega_{5.9}|$. [f] $\Delta C_2 - \mathrm{HC} = |\omega_{12.13}| + |\omega_{5.13} - \omega_{11.12}| + |\omega_{5.9} - \omega_{10,11}|$, $\Delta C_s - \mathrm{E} = |\omega_{11.12} + \omega_{12.13}| + |\omega_{5.13} + \omega_{10.11}| + |\omega_{5.9} + \omega_{9.10}|$. [g] Sign reported incorrectly in ref. 2*a*. [h] Magnitude reported incorrectly in ref. 2*a*, but deduced from the fact that $\Sigma\omega = 0$ for a ring.

The five-membered heterocyclic ring in (1), characterized by ΔC_2-HC 8, ΔC_s-E 34°, clearly lies close to a half-chair form whereas the corresponding values in (2) (19.1 and 23.9°), indicate that a form intermediate between a half-chair and envelope is adopted. This conformational difference undoubtedly originates from the involvement of the nitrogen lone-pair in a strong

[12] P. Coggon, D. S. Farrier, P. W. Jeffs, and A. T. McPhail, *J. Chem. Soc.* (*B*), 1970, 1267.
[13] P. A. Luhan and A. T. McPhail, *J.C.S. Perkin II*, 1972, 2006.
[14] P. A. Luhan and A. T. McPhail, *J.C.S. Perkin II*, 1973, 51.
[15] T. M. Capps, K. D. Hargrave, P. W. Jeffs, and A. T. McPhail, *J.C.S. Perkin II*, 1977, 1098.

N ••• H–O hydrogen-bond in crystals of (1) while no such interaction is present in (2).

The phenyl-ring atoms, their oxygen substituents, and C(5) are all approximately coplanar in both molecules, but C(11) is displaced significantly [Δ 0.091 in (1) and 0.117 Å in (2)] from the least-squares plane through the phenyl-ring atoms as a further consequence of the C(5)–C(13) rotation already described. The valency angles and the small out-of-plane displacement of the C(17) methoxy-methyl in (2) are all quite normal.[12-16]

In crystals of cocculine the molecules are held together by O–H ··· N hydrogen bonds [O(20) ··· N(9) 2.76 Å] between molecules related by the 2_1 screw axis along the *b* direction. Coccutrine molecules are also held by hydrogen bonds but these do not involve the nitrogen lone-pair; instead O–H ··· O(methoxy) hydrogen bonds [O(20) ··· O(18) 2.73 Å] are present between molecules related by unit translation along the *c* axis. Other intermolecular distances <3.70 Å (Table 3) correspond to normal van der Waals interactions.

Endocyclic torsion angles defining the non-aromatic ring conformations in cocculine hydrobromide (3) and dihydro-β-erythroidine hydrobromide (4) are included for comparison in Table 5. These show that whereas protonation of the nitrogen atom results in only minor changes in the B and C ring conformations from those for (1) and (2), there is a more significant alteration in cyclohexene ring A which is modified from the approximately half-chair form of (1) and (2) to an envelope form in (3). Further, replacement of the phenyl ring D by the βγ-unsaturated δ-lactone ring in (4) also results in only small changes in the ring conformations from those in (1) and (3). The torsion angles for (4) indicate intermediate forms for all three rings, with B and C lying closer to half-chair forms while A is closer to an envelope form. These conformational differences are all quite small, as would be expected in such fused polycyclic structures. However, in view of the differences already noted for (1) and (2) it is not possible unequivocally to resolve to what extent they are due to intramolecular interactions or to variations in crystal-packing forces, especially hydrogen bonding, which can result in the existence of less-energetically favoured conformers in the solid state.[14,17]

Lack of an oxygenated function at C(16) in the phenyl rings of cocculine, coccutrine, as well as cocculidine,[2a,11] isococculidine,[11] and coccoline [11] from *Cocculus laurifolius* D. C. is biogenetically intriguing, since it has been shown that aromatic *Erythrina* alkaloids are biogenetically derived from suitably oxidised benzylhydroisoquinoline precursors,[18] and all *Erythrina* alkaloids from *Erythrina* species (*Leguminosae*) bear such a function.

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