X-Ray Crystallographic Determination of the Molecular Structures of the Antibiotic Cyanocycline A and Related Compounds

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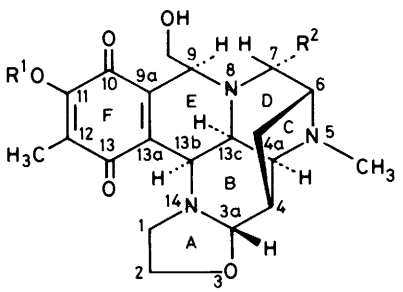
The molecular structures and absolute configurations of cyanocycline A (I) and related compounds have been determined by single crystal *X*-ray diffraction methods using diffractometer-measured data. Compound (I) contains the molecular structure of naphthyridinomycin with a hydroxy-group replacing a cyano-group. When the pH at which crystallization is carried out is changed, the oxazolidine ring of (I) changed reversibly from the closed to the open form in the bis(hydrogen halide) salts. Two nitrogen atoms are quaternized in the bis(hydrogen halide) salts: one forms an ion-pair with a halide anion and the other has a short intramolecular contact with the oxygen of atom the hydroxymethyl group. The remaining halide anion in these salts forms a bifurcated intermolecular hydrogen bond with two hydroxy-groups.

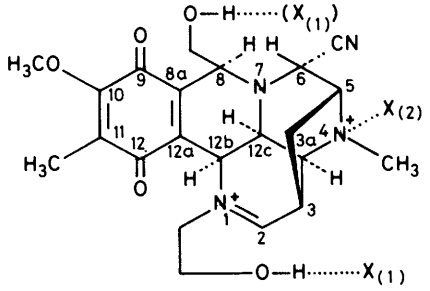
Cyanocycline A (I), produced by *Streptomyces flavogriseus* strain No. 49, is a basic antibiotic with broad antimicrobial spectrum and antitumour activity.[1,2] The definitive structure of this compound had not previously been determined although spectroscopic studies with high resolution m.s., u.v., i.r., and n.m.r. have indicated the chemical composition and the presence of a quinone moiety and hydroxy- and cyano-groups in the molecule. We now report single crystal *X*-ray analyses of (I), cyanocycline F (II) produced by the reaction of (I) with concentrated hydrogen chloride, the bis(hydrogen bromide) salt (III), and the bis(hydrogen chloride) salt (IV). Further, the absolute configurations were also determined by the Bijvoet method. When a hydroxy-group is substituted for the cyano-group in (I) we have the antibiotic naphthyridinomycin; [3] (II) is identical with naphthocyanidine, a semisynthetic antibiotic.[4,5] Although we have previously described [1] (III) as having structure (V), it became clear from the studies of (I) and (II) that this salt has structure (III).[6]

Experimental

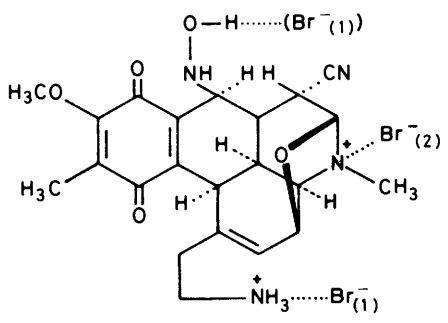
Materials.—Compound (I) was obtained as orange crystals, m.p. 168—170 °C (decomp.); $[\alpha]_D^{25}$ +82° (*c* 1, $CHCl_3$); $\lambda_{max.}$ (EtOH) 268 nm (ε 10 990) (Found: C, 61.9; H, 6.1; N, 13.05. $C_{22}H_{26}N_5O_4$ requires C, 62.0; H, 6.15; N, 13.15%). Single crystals of (I) were grown from ethanol at −20 °C. Samples of (II) were obtained by treatment of (I) with concentrated hydrogen chloride for 24 h at room temperature followed by neutralization with sodium hydrogencarbonate, extraction of (II) with chloroform, and purification on silica gel column chromatography with chloroform–methanol (9 : 1). Single orange-red crystals of (II) were grown from chloroform at



(I) $R^1 = CH_3$, $R^2 = CN$
(II) $R^1 = H$, $R^2 = CN$



(III) X = Br^-
(IV) X = Cl^-



(V)

Table 1. Crystal data and experimental parameters

Sample	Cyanocycline A	Cyanocycline F	Cyanocycline A·2HBr	Cyanocycline A·2HCl
Formula	$C_{22}H_{26}O_5N_4$	$C_{21}H_{24}O_5N_4{\cdot}CHCl_3$	$C_{22}H_{26}O_5N_4{\cdot}2HBr$	$C_{22}H_{26}O_5N_4{\cdot}2HCl$
Formula weight	426.47	531.82	588.30	499.40
Crystal system	Orthorhombic	Orthorhombic	Orthorhombic	Orthorhombic
Space group	$P2_12_12$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
a/Å	16.956(8)	13.802(2)	12.070(6)	11.991(7)
b/Å	20.765(10)	19.251(9)	26.736(13)	26.702(7)
c/Å	5.975(3)	9.269(5)	7.619(4)	7.338(4)
U/Å^3	2 103.7	2 462.8	2 458.7	2 349.3
z	4	4	4	4
λ/Å	1.5418	1.5418	1.5418	1.5418
ρ calc/g cm^{-3}	1.346	1.434	1.589	1.412
μ(Cu-K_α)/cm^{-1}	7.6	37.8	45.5	28.7
Crystal size (mm^3)	0.40 × 0.18 × 0.05	0.40 × 0.10 × 0.08	0.25 × 0.22 × 0.10	0.63 × 0.18 × 0.10
Data measured	$6° \leqslant 2\theta \leqslant 156°$	$6° \leqslant 2\theta \leqslant 156°$	$6° \leqslant 2\theta \leqslant 156°$	$6° \leqslant 2\theta \leqslant 130°$
Scan width (°)	1.0 + 0.35tanθ	1.0 + 0.35tanθ	1.0 + 0.35tanθ	1.0 + 0.30tanθ
Scan speed (° s^{-1} θ^{-1})	0.0668	0.0668	0.1	0.1
Min. counts *	5 000	3 000	3 000	400
Observed data (above 2σ level)	988	1 389	2 477	1 899

* Intensity measurements were repeated twice for the reflexion weaker than the respective preset number of counts.

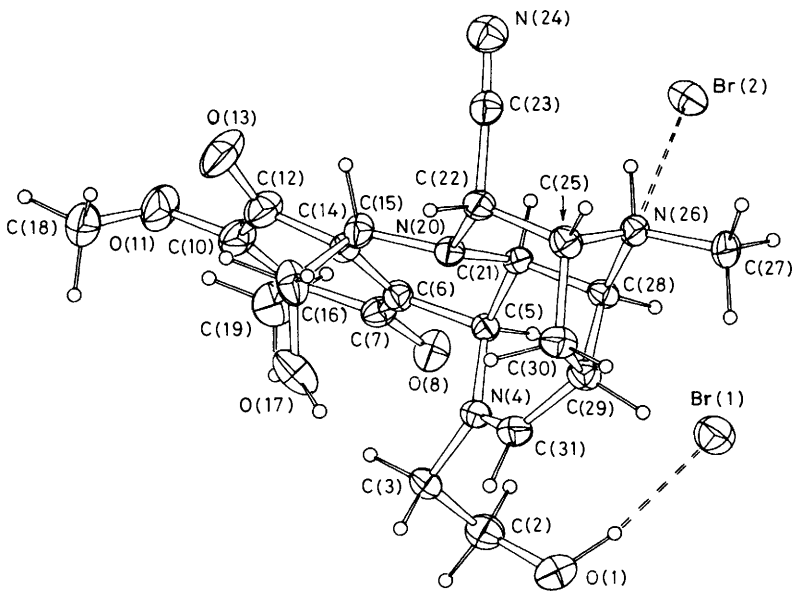


Figure 1. An ORTEP drawing of cyanocycline A·2HBr projected down the [100] direction. Thermal ellipsoids are drawn at the 30% probability level with atom labelling. Hydrogen atoms, calculated stereochemically, are shown as spheres of arbitrary radius

room temperature, m.p. 160 °C (decomp.); $[\alpha]_D^{25}$ +61° (*c* 1, $CHCl_3$), $\lambda_{max.}$ (EtOH) 270 nm (ε 6 969) (Found: C, 48.75; H, 4.75; N, 10.4. $C_{21}H_{24}N_4O_5{\cdot}CHCl_3$ requires C, 49.7; H, 4.75; N, 10.55%). Compounds (III) and (IV) were prepared by dissolving (I) in methanol, and neutralization with 0.1N-HBr or 0.1N-HCl. The solution was concentrated *in vacuo* and stored at 5 °C to give the corresponding crystals.

Analyses.—Preliminary *X*-ray diffraction data were obtained from Weisenberg and precession photographs, then a Philips PW 1100 four-circle diffractometer was employed for successive experiments with Cu-K_α radiation monochromated by a graphite plate. Accurate lattice parameters and the crystal orientation were determined from least-squares refinement of diffractometer co-ordinates of 15—25 standard reflexions. Diffraction intensity data were collected using an ω–2θ scan technique. A periodic check on three selected reflexions showed that no significant crystal decomposition or instrumental instability takes place during data collection. Table 1 summarizes the crystal data and experimental conditions. Lorentz and polarization corrections were applied to the intensity data, but absorption correction was eliminated. Absolute scale and overall temperature factors were calculated by Wilson's statistics.

Structure Analyses.—(a) *Cyanocycline A*·2HBr. The structure was solved by a heavy atom method. In the early stages of analysis, calculations were done by regarding all non-hydrogen atoms except for the bromine ions as carbon atoms. The molecular formula of (I) ($C_{22}H_{26}O_5N_4$) was determined by high resolution mass spectrometry. The assignments of two oxygen atoms [O(8) and O(13)] in the quinone skeleton, an oxygen

Table 2. Final positional parameters ($\times 10^4$) for non-hydrogen atoms with e.s.d.s in parentheses

Atom	*x/a*	*y/b*	*z/c*
(a) Cyanocycline A·2HBr			
Br(1)	2 526(1)	−1 526(0)	2 494(1)
Br(2)	6 782(1)	−2 056(0)	3 202(1)
O(1)	1 193(5)	−939(3)	5 618(10)
C(2)	1 863(7)	−524(3)	5 866(12)
C(3)	2 622(5)	−591(2)	7 463(10)
N(4)	3 356(4)	−1 019(2)	7 195(7)
C(5)	4 409(5)	−941(2)	6 190(8)
C(6)	5 023(5)	−479(2)	6 785(9)
C(7)	4 868(5)	−6(2)	5 749(10)
O(8)	4 248(5)	−5(2)	4 487(8)
C(9)	5 444(6)	454(2)	6 307(10)
C(10)	6 130(6)	430(2)	7 690(12)
O(11)	6 685(5)	842(2)	8 213(10)
C(12)	6 423(6)	−51(3)	8 519(12)
O(13)	7 219(6)	−92(2)	9 493(12)
C(14)	5 750(5)	−502(2)	8 086(10)
C(15)	5 927(6)	−962(2)	9 197(9)
C(16)	5 435(8)	−868(3)	10 998(11)
O(17)	4 319(6)	−714(2)	10 867(9)
C(18)	6 663(8)	949(3)	10 065(15)
C(19)	5 222(8)	925(3)	5 272(14)
N(20)	5 445(4)	−1 405(2)	8 357(7)
C(21)	5 172(4)	−1 387(2)	6 482(8)
C(22)	5 959(5)	−1 871(2)	8 931(9)
C(23)	7 148(6)	−1 914(2)	8 352(10)
N(24)	8 054(5)	−1 922(2)	7 949(9)
C(25)	5 274(5)	−2 315(2)	8 335(10)
N(26)	5 260(4)	−2 315(2)	6 345(8)
C(27)	4 808(6)	−2 791(2)	5 577(11)
C(28)	4 549(5)	−1 862(2)	5 977(9)
C(29)	3 574(5)	−1 937(2)	7 231(9)
C(30)	4 047(6)	−2 243(3)	8 809(11)
C(31)	3 048(5)	−1 450(3)	7 721(10)
(c) Cyanocycline A			
O(1)	5 445(5)	3 993(4)	−3 205(17)
C(2)	5 894(7)	3 425(7)	−3 753(33)
C(3)	5 274(7)	2 858(7)	−3 938(26)
N(4)	4 556(6)	3 157(5)	−2 898(18)
C(5)	4 522(7)	3 065(6)	−439(23)
C(6)	4 332(6)	2 372(6)	135(25)
C(7)	4 956(7)	1 924(6)	888(24)
O(8)	5 640(4)	2 116(4)	889(19)
C(9)	4 761(8)	1 310(7)	1 916(30)
C(10)	3 988(7)	1 137(6)	1 997(29)
O(11)	3 769(5)	559(4)	2 923(22)
C(12)	3 349(7)	1 535(7)	1 100(30)
O(13)	2 670(5)	1 352(4)	1 064(21)
C(14)	3 561(6)	2 189(6)	156(24)
C(15)	2 881(6)	2 614(6)	−592(28)
C(16)	2 614(8)	2 385(7)	−2 933(27)
O(17)	3 220(5)	2 383(5)	−4 500(18)
C(18)	3 351(10)	577(9)	4 998(34)
C(19)	5 403(8)	879(8)	2 761(40)
N(20)	3 133(5)	3 293(5)	−711(21)
C(21)	3 851(6)	3 473(6)	562(23)
C(22)	2 478(7)	3 743(6)	−491(26)
C(23)	2 079(7)	3 717(7)	1 725(25)
N(24)	1 803(7)	3 654(7)	3 417(21)
C(25)	2 804(7)	4 433(7)	−933(27)
N(26)	3 344(6)	4 563(5)	961(20)
C(27)	3 536(8)	5 245(6)	1 252(31)
C(28)	4 065(7)	4 174(6)	226(22)
C(29)	4 148(7)	4 334(6)	−2 267(26)
C(30)	3 282(7)	4 449(7)	−3 138(26)
C(31)	4 619(7)	3 841(7)	−3 582(26)

Atom	*x/a*	*y/b*	*z/c*
(b) Cyanocycline A·2HCl			
Cl(1)	2 572(2)	−1 545(1)	2 418(3)
Cl(2)	6 863(1)	−2 054(1)	3 276(2)
O(1)	1 212(4)	−986(2)	5 409(8)
C(2)	1 852(7)	−554(3)	5 720(11)
C(3)	2 575(6)	−615(2)	7 396(10)
N(4)	3 347(4)	−1 040(2)	7 147(7)
C(5)	4 415(5)	−950(2)	6 143(7)
C(6)	5 005(5)	−486(2)	6 788(8)
C(7)	4 847(5)	−10(2)	5 787(9)
O(8)	4 199(4)	−1(2)	4 494(7)
C(9)	5 405(6)	448(2)	6 371(9)
C(10)	6 136(6)	416(2)	7 774(11)
O(11)	6 710(5)	830(2)	8 301(9)
C(12)	6 402(6)	−63(2)	8 634(11)
O(13)	7 211(5)	−102(2)	9 667(10)
C(14)	5 738(5)	−511(2)	8 161(8)
C(15)	5 949(5)	−978(2)	9 274(8)
C(16)	5 410(7)	−904(3)	11 185(9)
O(17)	4 280(6)	−752(2)	11 054(8)
C(18)	6 677(9)	964(3)	10 182(13)
C(19)	5 182(8)	925(3)	5 404(14)
N(20)	5 450(4)	−1 421(2)	8 404(6)
C(21)	5 194(5)	−1 396(2)	6 426(7)
C(22)	5 976(5)	−1 888(2)	8 941(8)
C(23)	7 178(5)	−1 920(2)	8 430(8)
N(24)	8 102(5)	−1 929(2)	8 040(8)
C(25)	5 309(5)	−2 333(2)	8 298(8)
N(26)	5 315(4)	−2 319(2)	6 224(7)
C(27)	4 865(7)	−2 794(2)	5 366(11)
C(28)	4 582(5)	−1 872(2)	5 885(8)
C(29)	3 589(5)	−1 953(2)	7 142(9)
C(30)	4 066(6)	−2 267(2)	8 762(9)
C(31)	3 043(5)	−1 483(2)	7 669(8)
(d) Cycanocycline F			
O(1)	3 207(4)	639(4)	1 831(9)
C(2)	3 398(8)	1 086(6)	3 024(14)
C(3)	4 098(6)	1 644(5)	2 454(11)
N(4)	4 499(5)	1 335(4)	1 095(8)
C(5)	5 370(6)	872(4)	1 450(10)
C(6)	6 229(6)	1 327(4)	1 783(10)
C(7)	6 560(6)	1 413(5)	3 310(11)
O(8)	6 028(5)	1 196(4)	4 284(7)
C(9)	7 478(7)	1 772(5)	3 612(11)
C(10)	7 986(6)	2 019(5)	2 499(11)
O(11)	8 817(5)	2 365(4)	2 728(7)
C(12)	7 660(6)	1 976(4)	990(9)
O(13)	8 128(4)	2 241(3)	38(7)
C(14)	6 743(5)	1 590(4)	691(10)
C(15)	6 462(5)	1 506(4)	−878(10)
C(16)	6 014(6)	2 178(4)	−1 464(10)
O(17)	5 168(4)	2 371(3)	−718(7)
C(19)	7 809(8)	1 809(8)	5 146(12)
N(20)	5 736(4)	945(4)	−1 073(8)
C(21)	5 595(5)	451(4)	105(10)
C(22)	5 739(6)	658(5)	−2 524(10)
C(23)	6 655(7)	257(5)	−2 791(13)
N(24)	7 352(8)	−23(5)	−2 950(13)
C(25)	4 858(7)	175(5)	−2 645(11)
N(26)	5 005(6)	−389(4)	−1 618(9)
C(27)	4 411(8)	−997(5)	−1 940(14)
C(28)	4 767(6)	−41(5)	−249(11)
C(29)	3 836(7)	368(5)	−512(12)
C(30)	3 930(6)	572(5)	−2 140(12)
C(31)	3 656(6)	936(5)	580(11)
C(32)	5 299(8)	3 583(6)	1 432(14)
Cl(1)	4 308(2)	4 141(2)	1 606(5)
Cl(2)	6 297(3)	4 080(3)	918(5)
Cl(3)	5 538(4)	3 191(2)	3 088(5)

[O(11)] in the methoxy-group, a nitrogen [N(24)] in the cyano-group, and a quaternary nitrogen [N(26)] close to a bromine ion [Br(2)] were easily performed (i.r. and n.m.r.). However, the assumption that the bromine ion Br(1) is also in the neighbourhood of the quaternary nitrogen led to an incorrect conclusion. Unusual positive and negative peaks appeared on the difference electron density map, and unusual bond distances were observed in the structure. These crystallographic inconsistencies were circumvented by assuming that Br(1) is not able to form an ion-pair with the quaternary nitrogen in the crystal, whereas it forms a hydrogen bond with the hydroxy-group O(1)H. Thus we could assign all atoms to the structure described below. The structure was refined by the least-squares method of block matrix approximations [7] to a final R value of 4.7%. The function minimized was $\Sigma w(|F_o| - k|F_c|)^2$. The weighting scheme adopted was as follows: $\sqrt{w} = 20.0/|F_o|$ when $|F_o| \geqslant 20.0$, $\sqrt{w} = 1.0$ when $20.0 > |F_o| \geqslant 4.0$, and $\sqrt{w} = 0.8$ when $|F_o| < 4.0$. The positions of the hydrogen atoms were geometrically calculated, and were given with small dump factors during the refinements of the final three cycles. Atomic scattering factors used for the analyses are those listed in ref. 8. The absolute configuration of the molecule was determined by the Bijvoet method taking account the anomalous dispersion effect of bromine atom for Cu-K_α. An ORTEP [9] drawing of the salt is given in Figure 1 (indicating the absolute configuration), the final atomic co-ordinates of non-hydrogen atoms in Table 2(a), the bond distances in Table 3(a), and the bond angles in Table 4(a).

(b) *Cyanocycline A*·2HCl. The compound crystallizes in crystals isomorphous with those of (III). Structure analysis

Table 3. Bond lengths (Å) for non-hydrogen atoms with e.s.d.s in parentheses

(a) Cyanocycline A·2HBr		(b) Cyanocycline A·2HCl	
O(1)–C(2)	1.386(0.011)	O(1)–C(2)	1.404(0.010)
C(2)–C(3)	1.534(0.011)	C(2)–C(3)	1.513(0.011)
C(3)–N(4)	1.462(0.008)	C(3)–N(4)	1.476(0.008)
N(4)–C(5)	1.498(0.008)	N(4)–C(5)	1.497(0.008)
N(4)–C(31)	1.275(0.009)	N(4)–C(31)	1.296(0.008)
C(5)–C(6)	1.510(0.008)	C(5)–C(6)	1.503(0.008)
C(5)–C(21)	1.523(0.008)	C(5)–C(21)	1.528(0.008)
C(6)–C(7)	1.502(0.008)	C(6)–C(7)	1.480(0.008)
C(6)–C(14)	1.325(0.010)	C(6)–C(14)	1.339(0.008)
C(7)–O(8)	1.218(0.009)	C(7)–O(8)	1.227(0.008)
C(7)–C(9)	1.475(0.008)	C(7)–C(9)	1.458(0.008)
C(9)–C(10)	1.342(0.011)	C(9)–C(10)	1.355(0.010)
C(9)–C(19)	1.510(0.011)	C(9)–C(19)	1.482(0.010)
C(10)–O(11)	1.349(0.009)	C(10)–O(11)	1.358(0.008)
C(10)–C(12)	1.476(0.010)	C(10)–C(12)	1.461(0.009)
O(11)–C(18)	1.440(0.014)	O(11)–C(18)	1.426(0.011)
C(12)–O(13)	1.219(0.011)	C(12)–O(13)	1.236(0.010)
C(12)–C(14)	1.491(0.010)	C(12)–C(14)	1.478(0.008)
C(14)–C(15)	1.508(0.009)	C(14)–C(15)	1.512(0.008)
C(15)–C(16)	1.516(0.011)	C(15)–C(16)	1.557(0.009)
C(15)–N(20)	1.467(0.008)	C(15)–N(20)	1.471(0.008)
C(16)–O(17)	1.412(0.012)	C(16)–O(17)	1.418(0.011)
N(20)–C(21)	1.467(0.008)	N(20)–C(21)	1.485(0.007)
N(20)–C(22)	1.459(0.008)	N(20)–C(22)	1.452(0.008)
C(21)–C(28)	1.525(0.008)	C(21)–C(28)	1.520(0.008)
C(22)–C(23)	1.506(0.009)	C(22)–C(23)	1.492(0.008)
C(22)–C(25)	1.516(0.008)	C(22)–C(25)	1.508(0.008)
C(23)–N(24)	1.136(0.009)	C(23)–N(24)	1.145(0.008)
C(25)–N(26)	1.516(0.010)	C(25)–N(26)	1.522(0.008)
C(25)–C(30)	1.536(0.010)	C(25)–C(30)	1.539(0.009)
N(26)–C(27)	1.503(0.008)	N(26)–C(27)	1.515(0.008)
N(26)–C(28)	1.511(0.008)	N(26)–C(28)	1.503(0.008)
C(28)–C(29)	1.529(0.009)	C(28)–C(29)	1.522(0.009)
C(29)–C(30)	1.562(0.010)	C(29)–C(30)	1.563(0.009)
C(29)–C(31)	1.496(0.009)	C(29)–C(31)	1.467(0.008)

Table 3 (*continued*)

(c) Cyanocycline A		(d) Cyanocycline F	
O(1)–C(2)	1.442(0.017)	O(1)–C(2)	1.426(0.015)
O(1)–C(31)	1.453(0.015)	O(1)–C(31)	1.434(0.012)
C(2)–C(3)	1.582(0.019)	C(2)–C(3)	1.538(0.015)
C(3)–N(4)	1.501(0.017)	C(3)–N(4)	1.499(0.012)
N(4)–C(5)	1.483(0.017)	N(4)–C(5)	1.532(0.011)
N(4)–C(31)	1.482(0.018)	N(4)–C(31)	1.474(0.011)
C(5)–C(6)	1.514(0.018)	C(5)–C(6)	1.506(0.012)
C(5)–C(21)	1.539(0.017)	C(5)–C(21)	1.519(0.012)
C(6)–C(7)	1.479(0.017)	C(6)–C(7)	1.496(0.014)
C(6)–C(14)	1.361(0.015)	C(6)–C(14)	1.336(0.012)
C(7)–O(8)	1.226(0.014)	C(7)–O(8)	1.236(0.012)
C(7)–C(9)	1.453(0.020)	C(7)–C(9)	1.470(0.013)
C(9)–C(10)	1.360(0.018)	C(9)–C(10)	1.335(0.014)
C(9)–C(19)	1.497(0.022)	C(9)–C(19)	1.495(0.015)
C(10)–O(11)	1.373(0.016)	C(10)–O(11)	1.343(0.011)
C(10)–C(12)	1.464(0.019)	C(10)–C(12)	1.472(0.013)
O(11)–C(18)	1.429(0.023)	C(12)–O(13)	1.207(0.010)
C(12)–O(13)	1.213(0.015)	C(12)–C(14)	1.494(0.011)
C(12)–C(14)	1.514(0.020)	C(14)–C(15)	1.514(0.013)
C(14)–C(15)	1.519(0.016)	C(15)–C(16)	1.533(0.011)
C(15)–C(16)	1.545(0.022)	C(15)–N(20)	1.484(0.010)
C(15)–N(20)	1.475(0.016)	C(16)–O(17)	1.407(0.010)
C(16)–O(17)	1.390(0.018)	N(20)–C(21)	1.461(0.011)
N(20)–C(21)	1.483(0.015)	N(20)–C(22)	1.454(0.012)
N(20)–C(22)	1.457(0.015)	C(21)–C(28)	1.520(0.012)
C(21)–C(28)	1.514(0.018)	C(22)–C(23)	1.502(0.013)
C(22)–C(23)	1.488(0.021)	C(22)–C(25)	1.535(0.013)
C(22)–C(25)	1.558(0.019)	C(23)–N(24)	1.113(0.014)
C(23)–N(24)	1.122(0.019)	C(25)–N(26)	1.458(0.013)
C(25)–N(26)	1.481(0.018)	C(25)–C(30)	1.563(0.013)
C(25)–C(30)	1.547(0.021)	N(26)–C(27)	1.460(0.013)
N(26)–C(27)	1.463(0.016)	N(26)–C(28)	1.472(0.013)
N(26)–C(28)	1.530(0.016)	C(28)–C(29)	1.527(0.013)
C(28)–C(29)	1.533(0.020)	C(29)–C(30)	1.565(0.016)
C(29)–C(30)	1.576(0.017)	C(29)–C(31)	1.511(0.014)
C(29)–C(31)	1.518(0.019)	C(32)–Cl(1)	1.747(0.012)
		C(32)–Cl(2)	1.743(0.012)
		C(32)–Cl(3)	1.742(0.013)

Table 4. Bond angles (°) for non-hydrogen atoms with e.s.d.s in parentheses

(a) Cyanocycline A·2HBr	
C(3)–C(2)–O(1)	111.30(0.68)
N(4)–C(3)–C(2)	110.04(0.55)
C(5)–N(4)–C(3)	118.46(0.48)
C(5)–N(4)–C(31)	122.25(0.55)
C(3)–N(4)–C(31)	119.13(0.56)
C(6)–C(5)–N(4)	112.13(0.48)
C(6)–C(5)–C(21)	107.45(0.47)
N(4)–C(5)–C(21)	109.23(0.46)
C(7)–C(6)–C(5)	118.01(0.52)
C(7)–C(6)–C(14)	120.96(0.57)
C(5)–C(6)–C(14)	120.77(0.56)
O(8)–C(7)–C(6)	119.53(0.59)
O(8)–C(7)–C(9)	121.00(0.61)
C(6)–C(7)–C(9)	119.44(0.55)
C(10)–C(9)–C(7)	118.51(0.62)
C(10)–C(9)–C(19)	124.03(0.68)
C(7)–C(9)–C(19)	117.46(0.63)
O(11)–C(10)–C(9)	119.95(0.68)
O(11)–C(10)–C(12)	117.77(0.66)
C(9)–C(10)–C(12)	121.72(0.68)
C(18)–O(11)–C(10)	116.26(0.67)
O(13)–C(12)–C(10)	121.86(0.76)
O(13)–C(12)–C(14)	119.44(0.74)
C(10)–C(12)–C(14)	118.65(0.66)
C(15)–C(14)–C(6)	123.46(0.58)
C(15)–C(14)–C(12)	117.27(0.58)
C(6)–C(14)–C(12)	119.26(0.61)

Table 4 (*continued*)

C(16)-C(15)-C(14)	108.50(0.57)
C(16)-C(15)-N(20)	111.93(0.57)
C(14)-C(15)-N(20)	110.94(0.52)
O(17)-C(16)-C(15)	110.98(0.67)
C(21)-N(20)-C(15)	119.18(0.48)
C(21)-N(20)-C(22)	114.55(0.47)
C(15)-N(20)-C(22)	112.97(0.49)
C(28)-C(21)-C(5)	108.48(0.46)
C(28)-C(21)-N(20)	109.21(0.46)
C(5)-C(21)-N(20)	107.69(0.45)
C(23)-C(22)-N(20)	112.50(0.51)
C(23)-C(22)-C(25)	111.85(0.52)
N(20)-C(22)-C(25)	110.30(0.50)
N(24)-C(23)-C(22)	176.42(0.72)
N(26)-C(25)-C(22)	107.79(0.50)
N(26)-C(25)-C(30)	102.96(0.52)
C(22)-C(25)-C(30)	110.92(0.54)
C(27)-N(26)-C(25)	113.16(0.50)
C(27)-N(26)-C(28)	113.60(0.50)
C(25)-N(26)-C(28)	101.07(0.46)
C(29)-C(28)-C(21)	109.33(0.48)
C(29)-C(28)-N(26)	102.48(0.47)
C(21)-C(28)-N(26)	109.92(0.48)
C(30)-C(29)-C(28)	105.56(0.52)
C(30)-C(29)-C(31)	114.76(0.56)
C(28)-C(29)-C(31)	111.62(0.53)
N(4)-C(31)-C(29)	125.75(0.63)
C(25)-C(30)-C(29)	103.71(0.56)

(b) Cyanocycline A·2HCl

C(3)-C(2)-O(1)	110.90(0.63)
N(4)-C(3)-C(2)	109.96(0.56)
C(5)-N(4)-C(3)	118.30(0.47)
C(5)-N(4)-C(31)	122.19(0.49)
C(3)-N(4)-C(31)	119.27(0.52)
C(6)-C(5)-N(4)	112.33(0.46)
C(6)-C(5)-C(21)	108.18(0.45)
N(4)-C(5)-C(21)	109.33(0.44)
C(7)-C(6)-C(5)	119.42(0.49)
C(7)-C(6)-C(14)	120.02(0.53)
C(5)-C(6)-C(14)	120.32(0.52)
O(8)-C(7)-C(6)	118.80(0.55)
O(8)-C(7)-C(9)	120.10(0.57)
C(6)-C(7)-C(9)	121.03(0.53)
C(10)-C(9)-C(7)	117.85(0.59)
C(10)-C(9)-C(19)	122.32(0.65)
C(7)-C(9)-C(19)	119.81(0.61)
O(11)-C(10)-C(9)	119.53(0.63)
O(11)-C(10)-C(12)	118.60(0.61)
C(9)-C(10)-C(12)	121.64(0.63)
C(18)-O(11)-C(10)	117.74(0.64)
O(13)-C(12)-C(10)	120.67(0.65)
O(13)-C(12)-C(14)	119.92(0.63)
C(10)-C(12)-C(14)	119.29(0.59)
C(15)-C(14)-C(6)	123.89(0.52)
C(15)-C(14)-C(12)	116.77(0.51)
C(6)-C(14)-C(12)	119.34(0.54)
C(16)-C(15)-C(14)	108.21(0.50)
C(16)-C(15)-N(20)	108.91(0.49)
C(14)-C(15)-N(20)	111.14(0.46)
O(17)-C(16)-C(15)	111.84(0.59)
C(21)-N(20)-C(15)	118.16(0.45)
C(21)-N(20)-C(22)	113.18(0.44)
C(15)-N(20)-C(22)	113.33(0.45)
C(28)-C(21)-C(5)	108.73(0.45)
C(28)-C(21)-N(20)	108.51(0.45)
C(5)-C(21)-N(20)	107.11(0.44)
C(23)-C(22)-N(20)	113.62(0.47)
C(23)-C(22)-C(25)	112.87(0.48)
N(20)-C(22)-C(25)	111.19(0.47)
N(24)-C(23)-C(22)	177.92(0.62)
N(26)-C(25)-C(22)	106.91(0.45)
N(26)-C(25)-C(30)	102.88(0.46)

Table 4 (*continued*)

C(22)-C(25)-C(30)	110.74(0.48)
C(27)-N(26)-C(25)	113.15(0.48)
C(27)-N(26)-C(28)	112.81(0.48)
C(25)-N(26)-C(28)	100.50(0.43)
C(29)-C(28)-C(21)	109.77(0.47)
C(29)-C(28)-N(26)	104.15(0.45)
C(21)-C(28)-N(26)	109.78(0.46)
C(30)-C(29)-C(28)	104.53(0.48)
C(30)-C(29)-C(31)	114.94(0.50)
C(28)-C(29)-C(31)	112.79(0.49)
N(4)-C(31)-C(29)	125.27(0.53)
C(25)-C(30)-C(29)	104.33(0.48)

(c) Cyanocycline A

C(2)-O(1)-C(31)	107.22(1.01)
C(3)-C(2)-O(1)	105.89(1.14)
N(4)-C(3)-C(2)	101.66(1.07)
C(5)-N(4)-C(3)	112.86(0.99)
C(5)-N(4)-C(31)	113.55(1.00)
C(3)-N(4)-C(31)	102.93(0.99)
C(6)-C(5)-N(4)	110.81(1.02)
C(6)-C(5)-C(21)	106.13(1.01)
N(4)-C(5)-C(21)	110.05(1.00)
C(7)-C(6)-C(5)	120.97(1.09)
C(7)-C(6)-C(14)	120.57(1.15)
C(5)-C(6)-C(14)	118.14(1.12)
O(8)-C(7)-C(6)	118.18(1.15)
O(8)-C(7)-C(9)	120.01(1.22)
C(6)-C(7)-C(9)	121.17(1.18)
C(10)-C(9)-C(7)	117.78(1.33)
C(10)-C(9)-C(19)	122.07(1.43)
C(7)-C(9)-C(19)	120.11(1.36)
O(11)-C(10)-C(9)	120.40(1.29)
O(11)-C(10)-C(12)	116.16(1.21)
C(9)-C(10)-C(12)	123.44(1.34)
C(18)-O(11)-C(10)	117.46(1.19)
O(13)-C(12)-C(10)	122.15(1.35)
O(13)-C(12)-C(14)	120.00(1.29)
C(10)-C(12)-C(14)	117.84(1.23)
C(15)-C(14)-C(6)	124.33(1.15)
C(15)-C(14)-C(12)	116.78(1.10)
C(6)-C(14)-C(12)	118.81(1.16)
C(16)-C(15)-C(14)	108.05(1.09)
C(16)-C(15)-N(20)	109.60(1.08)
C(14)-C(15)-N(20)	110.46(1.05)
O(17)-C(16)-C(15)	113.21(1.16)
C(21)-N(20)-C(15)	116.99(0.99)
C(21)-N(20)-C(22)	114.69(0.99)
C(15)-N(20)-C(22)	112.82(1.01)
C(28)-C(21)-C(5)	107.49(1.00)
C(28)-C(21)-N(20)	111.78(0.99)
C(5)-C(21)-N(20)	105.59(0.97)
C(23)-C(22)-N(20)	113.80(1.10)
C(23)-C(22)-C(25)	110.21(1.12)
N(20)-C(22)-C(25)	107.69(1.06)
N(24)-C(23)-C(22)	174.88(1.50)
N(26)-C(25)-C(22)	104.92(1.07)
N(26)-C(25)-C(30)	108.84(1.11)
C(22)-C(25)-C(30)	110.48(1.12)
C(27)-N(26)-C(25)	113.88(1.08)
C(27)-N(26)-C(28)	111.55(1.02)
C(25)-N(26)-C(28)	100.28(0.96)
C(29)-C(28)-C(21)	111.06(1.03)
C(29)-C(28)-N(26)	103.77(0.98)
C(21)-C(28)-N(26)	106.15(0.97)
C(30)-C(29)-C(28)	105.56(1.05)
C(30)-C(29)-C(31)	114.93(1.11)
C(28)-C(29)-C(31)	113.91(1.10)
O(1)-C(31)-N(4)	103.59(1.02)
O(1)-C(31)-C(29)	106.28(1.07)
N(4)-C(31)-C(29)	117.76(1.12)
C(25)-C(30)-C(29)	101.75(1.08)

Table 4 (*continued*)

(d) Cyanocycline F

C(2)-O(1)-C(31)	107.86(0.77)
C(3)-C(2)-O(1)	105.74(0.86)
N(4)-C(3)-C(2)	104.09(0.77)
C(5)-N(4)-C(3)	109.88(0.66)
C(5)-N(4)-C(31)	112.69(0.67)
C(3)-N(4)-C(31)	100.81(0.67)
C(6)-C(5)-N(4)	108.86(0.67)
C(6)-C(5)-C(21)	108.52(0.68)
N(4)-C(5)-C(21)	107.13(0.65)
C(7)-C(6)-C(5)	119.90(0.74)
C(7)-C(6)-C(14)	120.84(0.78)
C(5)-C(6)-C(14)	118.90(0.75)
O(8)-C(7)-C(6)	118.16(0.82)
O(8)-C(7)-C(9)	122.11(0.86)
C(6)-C(7)-C(9)	119.68(0.80)
C(10)-C(9)-C(7)	118.23(0.88)
C(10)-C(9)-C(19)	123.88(0.95)
C(7)-C(9)-C(19)	117.83(0.89)
O(11)-C(10)-C(9)	120.20(0.87)
O(11)-C(10)-C(12)	116.05(0.78)
C(9)-C(10)-C(12)	123.63(0.86)
O(13)-C(12)-C(10)	120.50(0.77)
O(13)-C(12)-C(14)	121.89(0.74)
C(10)-C(12)-C(14)	117.61(0.72)
C(15)-C(14)-C(6)	123.47(0.74)
C(15)-C(14)-C(12)	116.65(0.68)
C(6)-C(14)-C(12)	119.87(0.74)
C(16)-C(15)-C(14)	110.70(0.66)
C(16)-C(15)-N(20)	107.37(0.64)
C(14)-C(15)-N(20)	111.57(0.65)
O(17)-C(16)-C(15)	112.54(0.67)
C(21)-N(20)-C(15)	118.20(0.64)
C(21)-N(20)-C(22)	116.38(0.66)
C(15)-N(20)-C(22)	112.78(0.65)
C(28)-C(21)-C(5)	110.85(0.69)
C(28)-C(21)-N(20)	110.15(0.67)
C(5)-C(21)-N(20)	107.06(0.65)
C(23)-C(22)-N(20)	110.50(0.76)
C(23)-C(22)-C(25)	110.09(0.78)
N(20)-C(22)-C(25)	107.19(0.72)
N(24)-C(23)-C(22)	177.17(1.15)
N(26)-C(25)-C(22)	107.05(0.76)
N(26)-C(25)-C(30)	106.41(0.77)
C(22)-C(25)-C(30)	109.33(0.77)
C(27)-N(26)-C(25)	112.67(0.79)
C(27)-N(26)-C(28)	114.57(0.78)
C(25)-N(26)-C(28)	101.12(0.72)
C(29)-C(28)-C(21)	110.24(0.76)
C(29)-C(28)-N(26)	106.55(0.76)
C(21)-C(28)-N(26)	107.57(0.73)
C(30)-C(29)-C(28)	102.34(0.77)
C(30)-C(29)-C(31)	118.57(0.82)
C(28)-C(29)-C(31)	113.88(0.82)
Cl(1)-C(32)-Cl(2)	107.84(0.66)
Cl(1)-C(32)-Cl(3)	109.47(0.67)
Cl(2)-C(32)-Cl(3)	109.20(0.68)
O(1)-C(31)-N(4)	106.69(0.72)
O(1)-C(31)-C(29)	108.93(0.77)
N(4)-C(31)-C(29)	117.68(0.78)
C(25)-C(30)-C(29)	103.53(0.76)

was carried out on the basis of the result obtained in (a), and refined to a final R value of 6.2% by the least-squares techniques described in (a). The weighting scheme adopted was that used for (III). Tables 2(b), 3(b), and 4(b) give the final atomic co-ordinates of the non-hydrogen atoms, the bond distances, and the bond angles, respectively.

(c) *Cyanocycline A*. This compound was obtained as orthorhombic crystals. Systematic absence ($h00$ with h odd) and Laue symmetry (*mmm*) indicated the space group $P2_12_12$. The structure was analysed by the conventional application of MULTAN [10] using 151 reflexions ($|E_o| \geq 1.30$); however this did not give the correct solution. Therefore the analysis was tried on another space group ($P2_12_12$) obtained by omitting three $0k0$ reflexions with k odd from the data. In this trial, the correct structure was found on the E-map synthesized with the phase set for which the most appropriate values of R(Karle) and absolute figure of merit were given. The structure was refined by the least-squares method to a final R value of 7.7%. The weighting scheme was as follows: $\sqrt{w} = 40.0/|F_o|$ when $|F_o| \geq 40.0$, $\sqrt{w} = 1.0$ when $40.0 > |F_o| \geq 4.0$, and $\sqrt{w} = 0.8$ when $|F_o| < 4.0$. Figure 2 and Tables 2(c), 3(c), and 4(c) give the structure of (I), the final atomic co-ordinates of non-hydrogen atoms, the bond distances, and the bond angles, respectively.

Table 5. Distances (Å) of hydrogen bond, ion-pair, and intramolecular short contacts

Cyanocycline A·2HBr		Cyanocycline A·2HCl	
Br(1) · · · O(1)	3.274(7)	Cl(1) · · · O(1)	3.115(6)
Br(1) · · · O(17)^{i}	3.307(6)	Cl(1) · · · O(17)^{i}	3.111(7)
(Br(1) · · · N(4)	3.958(5))	(Cl(1) · · · N(4)	3.837(6))
Br(2) · · · N(26)	3.097(6)	Cl(2) · · · N(26)	2.937(5)
N(4) · · · O(17)	3.137(9)	N(4) · · · O(17)	3.172(8)
Cyanocycline A:		N(4) · · · O(17)	2.938(14)
Cyanocycline F:		N(4) · · · O(17)	2.767(10)
Naphthyridinomycin:		N(4) · · · O(17)	2.832(2)

i = lattice translation 001.

(d) *Cyanocycline F*. The structure analysis was performed by the method described in (c) using 213 reflexions ($|E_o| \geq 1.30$). In the course of analysis, a small fragment (presumed to be solvated $CHCl_3$ or CO_3^{2-}) appeared on the Fourier map close to molecule (II). Accordingly, taking this fragment into account, the refinements were done for both cases, and in the former the R factor converged to 5.9%. The weighting scheme was that described in (c). The structure of (II), the final atomic co-ordinates of the non-hydrogen atoms, the bond distances, and bond angles are in Figure 3 and Tables 2(d), 3(d), and 4(d), respectively.

Structure and temperature factors are in Supplementary Publication No. SUP 23513 (38 pp.).*

Results and Discussion

Compounds (I)—(IV) are complicated molecules containing four six-membered rings and one or two five-membered rings which are condensed with each other through *ortho* or *ortho-peri* junctions. In these compounds, ring D adopts a distorted chair conformation, ring E a distorted sofa, and ring F is planar (Table 6). However, ring B in (I) and (II) is a distorted chair, in contrast to a distorted sofa in (III) and (IV), in which oxazolidine ring (A) is opened. On the other hand, ring C is in a distorted envelope conformation. It is notable that ring A in (I) is in a twist form and that of (II) is a distorted envelope. In these molecules, the thermal motions of the atoms are locally restricted: the equivalent isotropic temperature factors for atoms of (I) at the ring junctions are 2.1—5.0 Å^2, and those for atoms at the periphery are 3.0—11.2 (Å^2).

Naphthyridinomycin and naphthocyanidine are known to have the same basic structure as (I). The former has a hydroxy-group instead of the cyano-group of (I) and the latter is

* For details of Supplementary Publications see Notice to Authors in *J. Chem. Soc., Perkin Trans. 2*, 1981, Index Issue.

Table 6. Least-squares planes

(a) Parameters for the planes $LX + MY + NZ = D$, where X, Y, Z, and D are in Å.

	L	M	N	D
Ring A				
Cyanocycline A	0.116	−0.195	0.974	−2.409
Cyanocycline F	0.797	−0.572	0.193	3.118
Ring B				
Cyanocycline A	0.755	0.398	0.521	8.078
Cyanocycline F	−0.170	−0.774	0.610	−1.829
Cyanocycline A·2HBr	0.580	0.028	0.814	6.799
Cyanocycline A·2HCl	0.564	0.023	0.826	6.593
Ring C				
Cyanocycline A	0.157	0.971	0.179	9.556
Cyanocycline F	0.520	0.829	0.209	3.278
Cyanocycline A·2HBr	0.229	0.854	0.467	−0.868
Cyanocycline A·2HCl	0.216	0.847	0.486	−0.945
Ring D				
Cyanocycline A	−0.225	0.224	0.948	0.496
Cyanocycline F	0.630	−0.771	−0.090	4.208
Cyanocycline A·2HBr	−0.761	0.292	0.579	−2.984
Cyanocycline A·2HCl	−0.768	0.275	0.578	−3.091
Ring E				
Cyanocycline A	−0.082	0.204	0.976	0.463
Cyanocycline F	0.635	−0.772	0.029	3.504
Cyanocycline A·2HBr	−0.755	0.176	0.631	−1.529
Cyanocycline A·2HCl	−0.759	0.158	0.632	−1.608
Ring F				
Cyanocycline A	−0.087	0.417	0.905	1.458
Cyanocycline F	−0.499	0.862	0.079	−1.948
Cyanocycline A·2HBr	−0.727	0.228	0.647	−1.391
Cyanocycline A·2HCl	−0.724	0.217	0.655	−1.389

(b) Distances (Å) of atoms from the least-squares planes

Ring A	
Cyanocycline A (twist)	O(1), 0.000; C(2), 0.000; C(3), 0.000; N(4)*, 0.342; C(31)*, −0.321
Cyanocycline F (envelope)	O(1), 0.035; C(2), −0.033; C(3), 0.020; C(31), −0.022; N(4)*, 0.588
Ring B	
Cyanocycline A (chair)	C(5), 0.106; C(21), −0.104; C(29), 0.106; C(31), −0.108; N(4)*, −0.541; C(28)*, 0.644
Cyanocycline F (chair)	C(5), 0.093; C(21), −0.093; C(29), 0.093; C(31), −0.093; N(4)*, −0.594; C(28)*, 0.633
Cyanocycline A·2HBr (sofa)	N(4), −0.064; C(5), 0.055; C(28), −0.048; C(29), 0.042; C(31), 0.015; C(21)*, 0.737
Cyanocycline A·2HCl (sofa)	N(4), −0.065; C(5), 0.055; C(28), −0.046; C(29), 0.039; C(31), 0.018; C(21)*, 0.725
Ring C	
Cyanocycline A (envelope)	C(25), 0.031; C(28), −0.032; C(29), 0.046; C(30), −0.046; N(26)*, 0.640
Cyanocycline F (envelope)	C(25), −0.027; C(28), −0.027; C(29), −0.039; C(30), 0.039; N(26)*, −0.622
Cyanocycline A·2HBr (envelope)	C(25), 0.002; C(28), −0.002; C(29), 0.003; C(30), −0.003; N(26)*, −0.710
Cyanocycline A·2HCl (envelope)	C(25), 0.003; C(28), −0.003; C(29), 0.005; C(30), −0.004; N(26)*, −0.703
Ring D	
Cyanocycline A (chair)	C(21), −0.026; C(22), 0.026; C(25), −0.028; C(28), 0.028; N(20)*, −0.558; N(26)*, 0.900
Cyanocycline F (chair)	C(21), −0.019; C(22), 0.019; C(25), −0.021; C(28), 0.021; N(20)*, −0.531; N(26)*, 0.859
Cyanocycline A·2HBr (chair)	C(21), 0.010; C(22), −0.010; C(25), 0.011; C(28), −0.011; N(20)*, 0.572; N(26)*, −0.855
Cyanocycline A·2HCl (chair)	C(21), 0.007; C(22), −0.007; C(25), 0.008; C(28), −0.008; N(20)*, 0.592; N(26)*, −0.867
Ring E	
Cyanocycline A (sofa)	C(5), −0.052; C(6), 0.016; C(14), 0.058; C(15), −0.103; N(20), 0.080; C(21)*, 0.798
Cyanocycline F (sofa)	C(5), −0.059; C(6), 0.026; C(14), 0.056; C(15), −0.108; N(20), 0.086; C(21)*, 0.728
Cyanocycline A·2HBr (sofa)	C(5), 0.046; C(6), −0.011; C(14), −0.059; C(15), 0.098; N(20), −0.074; C(21)*, −0.719
Cyanocycline A·2HCl (sofa)	C(5), 0.035; C(6), −0.007; C(14), −0.048; C(15), 0.078; N(20), −0.058; C(21)*, −0.731
Ring F	
Cyanocycline A (plane)	C(6), 0.033; C(7), −0.040; C(9), 0.013; C(10), 0.020; C(12), −0.026; C(14), −0.001
Cyanocycline F (plane)	C(6), −0.011; C(7), 0.015; C(9), 0.001; C(10), −0.020; C(12), 0.023; C(14), −0.008
Cyanocycline A·2HBr (plane)	C(6), 0.037; C(7), −0.050; C(9), −0.001; C(10), 0.065; C(12), −0.076; C(14), 0.026
Cyanocycline A·2HCl (plane)	C(6), 0.022; C(7), −0.046; C(9), 0.016; C(10), 0.037; C(12), −0.059; C(14), 0.030

* Atoms not included in the calculation of the plane.

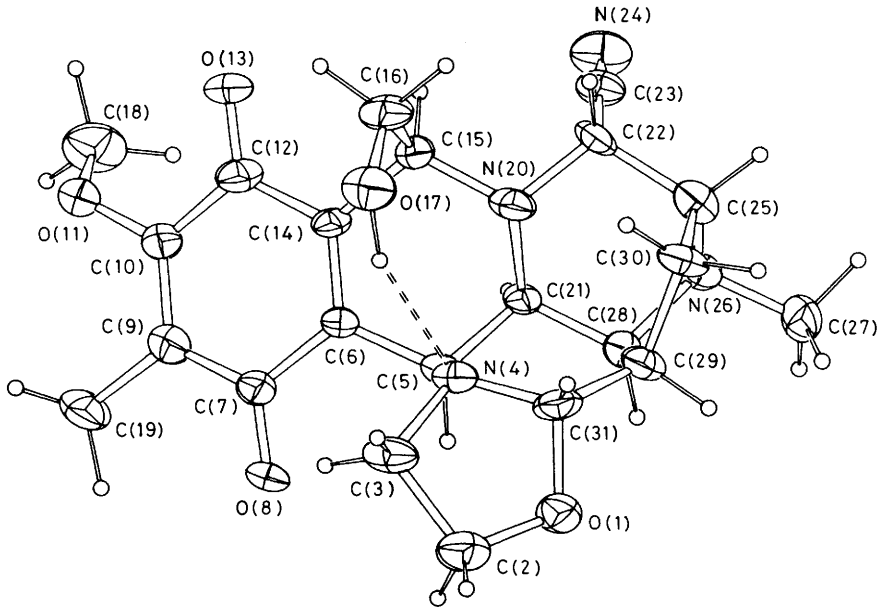


Figure 2. An ORTEP drawing of cyanocycline A projected down the [100] direction. Thermal ellipsoids are drawn at the 30% probability level with atom labelling. Hydrogen atoms, calculated stereochemically, are shown as spheres of arbitrary radius

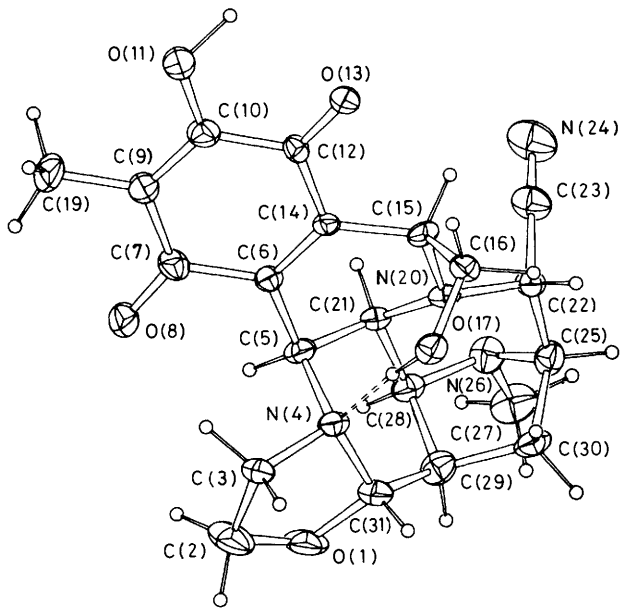


Figure 3. An ORTEP drawing of cyanocycline F projected down the [010] direction. Thermal ellipsoids are drawn at the 30% probability level with atom labelling. Hydrogen atoms, calculated stereochemically, are shown as spheres of arbitrary radius

identical with (II). An examination of ORTEP drawings in the literature indicates that both naphthyridinomycin and naphthocyanidine have the same absolute configuration as (I). Compound (II) (naphthocyanidine) as a hydroxy-group instead of the methoxy-group of (I). As the crystals of (II) contain one molecule of solvated chloroform per asymmetric unit, the actual crystal is not identical with that of naphthocyanidine with no solvent molecule. However, the crystals of (II) belong to the same space group as those of naphthocyanidine and the lattice constants of both crystals are almost identical. At present, it is unclear whether or not the molecular packing in both crystals is similar. When (I) was converted into the bis(hydrogen halide) salts (III) or (IV), the oxazolidine ring opened and when the salts was reconverted into (I), ring closure took place reversibly. Thus the conditions for crystallization change the structural state. In bis(hydrogen halides) obtained by this way, only two nitrogen atoms can quaternize, and the remaining N(20) cannot accept a proton owing to the influence of the cyano-group attached to the adjacent C(22). When the oxazolidine ring in (I) opened, N(4) is quaternized to form an sp^2 bond with one of the three adjacent carbons: the total value of the bond angles around N(4) is 359.9° in (II) and 359.8° in (III). The N(4) atom is not close to bromide ion but is close to O(17) of the hydroxymethyl group, so that an intramolecular ion–dipole interaction exists between these two atoms. On the other hand, Br(1) is near both oxygen O(1) and O(17) (lattice translation 001) and forms a bifurcated intermolecular hydrogen bond. However, Br(2) is close to N(26) and forms an ion-pair (Table 5). The fact that the same negative ion forms different structures in different crystals is related to the strength of the electron-withdrawing substituent. During the crystallization of the bis(hydrogen halide) salt, the quaternized N(4) is considered to be the cation strongly attracted to O(17) as the counterion. Further, O(17) is close to N(4) in (I), (II) (naphthocyanidine), and naphthyridinomycin to produce intramolecular hydrogen bonds. It seems to be reasonable that, when N(4) is in the oxazolidine ring, the atom polarizes strongly under the influence of O(1) and withdraws the hydrogen atom attaching to the polar O(17).

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