Stereochemical Studies. Part 92.[1] Nitrogen Bridgehead Compounds. Part 61.[2] Synthesis and *X*-Ray Analysis of 4,8-Dimethylperhydrocyclopenta[*d*]-pyrido[1,2-*a*]pyrimidin-10-one Diastereoisomers†

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Stereoisomeric 4,8-dimethylperhydrocyclopenta[*d*]pyrido[1,2-*a*]pyrimidin-10-ones were prepared by reduction. Two of the eight possible stereoisomers were found in the reaction mixture, and their steric structures were determined by *X*-ray analysis.

Continuing our stereochemical investigations on the conformations and configurations of bicyclic[3–14] and tricyclic[15–19] saturated ring systems containing an amidine moeity, we recently reported the conformational analysis of the perhydropyrido[2,1-*b*]quinazolin-11-ones (**1**) and (**2**) by ^{1}H and ^{13}C n.m.r. spectroscopy.[17]

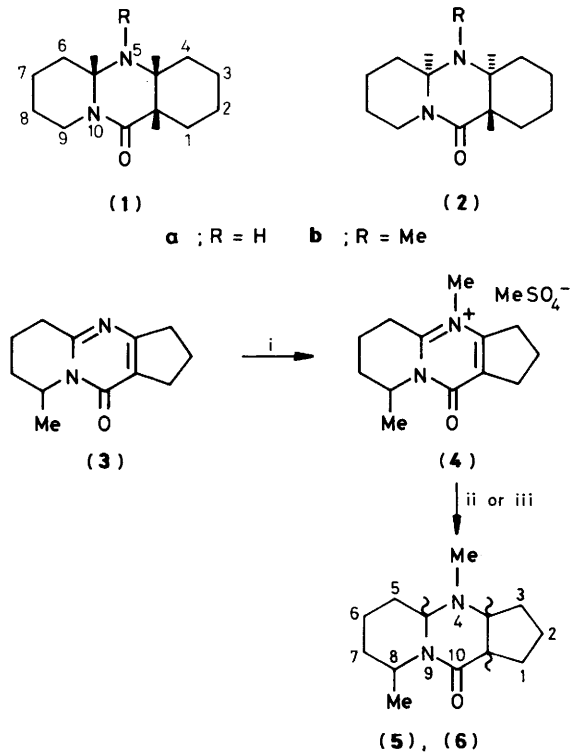
X-Ray analysis of the *N*-demethyl derivatives (**1a**) and (**2a**) revealed[16] that their solid-state conformation is the same as that predominating in solution. Nevertheless, the hydrogen attached to N-5 occupies an axial position in the solid state, whereas in solution it is in the equatorial position. In this paper we give an account of our results with the analogous cyclopenta[*d*]pyrido[1,2-*a*]pyrimidinone system.

As starting material the quaternary salt (**4**) of the 6-methyl derivative (**3**)[20] was selected because of its favourable analgetic properties.[21] The perhydrocyclopentapyridopyrimidinones were obtained from the quaternary salt (**4**) with sodium borohydride in aqueous methanol at 0 °C or −70 °C, and also by catalytic reduction over 5% platinum–carbon in ethanol or glacial acetic acid at ambient temperature. Whereas the cyclopentapyridopyrimidone (**3**) could not be reduced[20] with sodium borohydride (like the 3-methyl- and 2,3-dialkyl-6,7,8,9-tetrahydro-4*H*-pyrido[1,2-*a*]pyrimidinones[22,23]), its quaternary salt (**4**) reacts smoothly. Compound (**3**) also resisted reduction by $NaBH_3CN$ under mildly acidic conditions, and catalytic reduction in the presence of palladium or Raney nickel.

Only two of the eight potential diastereoisomeric reduction products were detected by t.l.c. The ratio of the diastereoisomers (**5**) and (**6**) in the crude product was determined by ^{1}H n.m.r. spectroscopy, from the ratio of the N–CH_3 signals at δ 2.38 and 2.33, respectively.

The ratio of diastereoisomers was only slightly sensitive to the reduction conditions (see Table 1). The major diastereoisomer was separated as the hydrochloride (**7**); the minor component was isolated by preparative t.l.c. (see Experimental section). The structures of these oily products were examined by ^{1}H and ^{13}C n.m.r. spectroscopy; those of the hydrochloride (**7**) of the major isomer and the picrate (**8**) of the minor diastereoisomer were elucidated by *X*-ray diffraction analysis.

† *Supplementary data available* (SUP 56451, 6 pp.): temperature factors, full lists of bond lengths and angles. For details of Supplementary Publications see Instructions for Authors, *J. Chem. Soc., Perkin Trans. 2*, Issue 1, 1986.

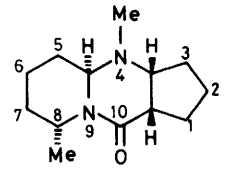


Scheme. *Reagents:* i, Me_2SO_4; ii, $NaBH_4$; iii, PtO_2–H_2

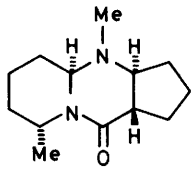
Crystal data of (**7**). $C_{13}H_{23}ClN_2O$, M = 256.8. Monoclinic, a = 12.028(2), b = 6.720(2), c = 17.093(3) Å, β = 96.84(1)°, V = 1 371.9 Å, D_c = 1.24 g cm^{-3}, $F(000)$ = 556. Cu-K_α radiation, λ = 1.5418 Å, μ(Cu-K_α) = 22.46 cm^{-1}, space group $P2_1/c$, Z = 4. Data were collected with a Stoe-Güttinger two-circle diffractometer, with Cu-K_α radiation, up to θ = 75°. 2 218 reflections out of 2 538 were considered observed [$I > 4\sigma(I)$]. Data were corrected for Lorentz and polarization effects. The scattering factors for both non-hydrogen and hydrogen atoms were taken from ref. 24.

The structure was solved by means of the SHELX-76 pro-

Table 1. Diastereoisomer ratios (%) in the crude products of the reductions



(5)



(6)

Method	(5)	(6)
$NaBH_4$ (at 0 °C)	60	40
$NaBH_4$ (at −70 °C)	60	40
H_2–Pt (in EtOH)	65	35
H_2–Pt (in AcOH)*	80	20

* 30% underwent dequaternization

Table 2. Fractional co-ordinates and B_{eq} values of compound (7), with e.s.d.s in parentheses

	x	*y*	*z*	B_{eq}
N(1)	0.717 9(2)	−0.025 2(4)	0.289 7(2)	2.83(12)
C(2)	0.839 7(3)	−0.029 9(5)	0.321 8(2)	3.31(14)
C(3)	0.898 6(3)	0.150 6(5)	0.283 1(2)	3.03(13)
C(4)	0.849 3(3)	0.217 2(5)	0.202 1(2)	3.09(13)
N(5)	0.754 4(2)	0.132 4(4)	0.168 3(2)	2.73(11)
C(6)	0.719 0(3)	0.160 9(6)	0.083 0(2)	3.30(17)
C(7)	0.745 1(4)	−0.031 3(6)	0.039 8(3)	4.47(21)
C(8)	0.697 2(4)	−0.214 0(6)	0.076 1(3)	4.82(22)
C(9)	0.731 2(4)	−0.229 9(6)	0.165 6(3)	3.95(21)
C(9a)	0.698 2(3)	−0.035 3(4)	0.201 8(2)	2.83(13)
C(10)	0.855 4(4)	0.022 4(6)	0.410 8(2)	4.17(17)
C(11)	0.937 1(4)	0.194 5(7)	0.422 0(2)	4.79(21)
C(12)	0.911 3(4)	0.315 4(6)	0.345 6(2)	4.80(22)
C(14)	0.654 9(3)	−0.185 8(5)	0.325 9(2)	4.42(18)
O(15)	0.898 4(2)	0.346 7(4)	0.168 0(2)	5.04(13)
C(16)	0.596 9(4)	0.227 8(7)	0.067 6(3)	4.21(21)
Cl(17)	0.589 3(1)	0.321 7(2)	0.337 6(1)	4.49(06)
H(1)	0.6880	0.1206	0.3036	6.05
H(2)	0.8711	−0.1581	0.3092	6.05
H(3)	0.9835	0.0957	0.2726	6.05
H(6)	0.7737	0.2744	0.0692	6.05
H(71)	0.7063	−0.0066	−0.0202	6.05
H(72)	0.8367	−0.0465	0.0386	6.05
H(81)	0.6167	−0.2196	0.0620	6.05
H(82)	0.7105	−0.3395	0.0541	6.05
H(91)	0.6868	−0.3454	0.1907	6.05
H(92)	0.8055	−0.2590	0.1749	6.05
H(9a)	0.6101	−0.0176	0.1822	6.05
H(101)	0.8844	−0.0959	0.4522	6.05
H(102)	0.7736	0.0792	0.4265	6.05
H(111)	1.0267	0.1422	0.4242	6.05
H(112)	0.9322	0.2922	0.4744	6.05
H(121)	0.9754	0.4330	0.3433	6.05
H(122)	0.8398	0.3963	0.3406	6.05
H(141)	0.6514	−0.1458	0.3891	6.05
H(142)	0.6871	−0.3036	0.3215	6.05
H(143)	0.5738	−0.1905	0.2845	6.05
H(161)	0.5766	0.2744	0.0111	6.05
H(162)	0.5430	0.0910	0.0709	6.05
H(163)	0.5834	0.3405	0.0975	6.05

Table 3. Fractional co-ordinates and B_{eq} values of compound (8), non-hydrogen atoms

Atom	*x*	*y*	*z*	B_{eq}
N(1a)	0.601 3(2)	0.868 5(2)	0.343 2(2)	1.9(2)
C(2a)	0.619 4(3)	0.886 4(3)	0.242 5(2)	2.2(3)
C(3a)	0.733 5(3)	0.781 4(3)	0.200 3(2)	2.5(3)
C(4a)	0.715 6(3)	0.673 3(3)	0.222 0(2)	2.8(4)
N(5a)	0.648 6(2)	0.668 9(2)	0.306 6(2)	2.9(3)
C(6a)	0.623 3(4)	0.566 5(3)	0.335 3(3)	3.8(5)
C(7a)	0.662 9(4)	0.514 1(3)	0.426 4(3)	4.6(5)
C(8a)	0.608 4(3)	0.603 9(3)	0.498 1(3)	3.2(4)
C(9a)	0.634 0(3)	0.707 6(3)	0.462 0(2)	2.5(4)
C(9aa)	0.587 2(3)	0.757 8(2)	0.374 9(2)	1.9(3)
C(10a)	0.643 4(4)	0.989 9(3)	0.202 5(3)	3.0(4)
C(11a)	0.704 4(4)	0.955 8(3)	0.102 9(3)	3.3(4)
C(12a)	0.753 6(4)	0.822 4(3)	0.100 0(2)	3.3(5)
C(14a)	0.490 7(3)	0.971 4(3)	0.389 3(2)	3.0(4)
O(15a)	0.758 6(2)	0.595 9(2)	0.168 6(2)	4.1(3)
C(16a)	0.488 5(4)	0.601 4(3)	0.338 4(3)	3.2(5)
C(17a)	0.868 3(3)	0.907 0(3)	0.388 3(2)	2.3(3)
C(18a)	0.993 5(3)	0.815 9(3)	0.368 8(2)	2.4(3)
C(19a)	1.096 1(3)	0.832 2(3)	0.358 9(2)	2.9(4)
C(20a)	1.080 0(3)	0.941 8(3)	0.368 2(2)	2.3(3)
C(21a)	0.963 4(3)	1.036 7(3)	0.387 4(2)	2.6(3)
C(22a)	0.863 3(3)	1.018 7(3)	0.395 8(2)	3.0(4)
O(23a)	0.773 4(2)	0.895 3(2)	0.401 4(2)	3.4(3)
N(24a)	1.018 4(3)	0.695 8(3)	0.358 9(2)	3.4(4)
O(25a)	1.119 7(3)	0.616 8(2)	0.363 1(3)	6.3(4)
O(26a)	0.934 1(3)	0.680 2(2)	0.348 4(3)	4.7(4)
N(27a)	1.187 0(2)	0.961 3(3)	0.355 8(2)	3.1(3)
O(28a)	1.170 0(2)	1.056 4(2)	0.374 3(2)	4.3(3)
O(29a)	1.289 0(2)	0.881 4(2)	0.326 4(2)	4.5(3)
N(30a)	0.742 4(3)	1.120 9(3)	0.416 7(3)	4.9(4)
O(31a)	0.727 7(4)	1.189 0(3)	0.468 4(3)	8.5(6)
O(32a)	0.661 4(3)	1.131 8(4)	0.384 9(4)	11.0(6)
N(1b)	0.156 7(2)	0.386 6(2)	0.157 2(2)	2.3(3)
C(2b)	0.115 3(3)	0.401 2(3)	0.257 4(2)	2.5(3)
C(3b)	0.206 7(3)	0.296 2(3)	0.302 9(2)	2.5(3)
C(4b)	0.332 3(3)	0.287 0(3)	0.273 8(2)	2.6(3)
N(5b)	0.362 7(2)	0.322 7(2)	0.186 3(2)	2.3(3)
C(6b)	0.484 6(3)	0.323 3(3)	0.157 8(3)	2.9(4)
C(7b)	0.541 9(3)	0.291 9(3)	0.058 9(3)	3.7(4)
C(8b)	0.454 7(4)	0.362 4(3)	−0.003 3(3)	3.5(5)
C(9b)	0.336 8(3)	0.350 8(3)	0.029 0(2)	2.8(4)
C(9ab)	0.277 3(3)	0.392 3(3)	0.125 4(2)	2.0(3)
C(10b)	−0.008 7(3)	0.404 4(3)	0.302 3(4)	3.5(4)
C(11b)	0.006 0(4)	0.367 2(4)	0.402 3(3)	4.2(5)
C(12b)	0.144 0(4)	0.315 1(3)	0.403 3(2)	3.4(4)
C(14b)	0.060 8(4)	0.479 1(4)	0.106 9(3)	3.7(5)
O(15b)	0.405 8(2)	0.245 7(2)	0.324 0(1)	3.8(3)
C(16b)	0.471 3(4)	0.440 0(3)	0.178 9(3)	3.4(4)
C(17b)	0.112 9(3)	0.119 1(3)	0.131 8(2)	2.8(4)
C(18b)	0.004 7(3)	0.105 7(3)	0.134 6(3)	3.7(4)
C(19b)	0.003 7(3)	0.002 0(3)	0.133 5(3)	3.3(4)
C(20b)	0.111 6(3)	−0.099 5(3)	0.131 0(3)	2.8(4)
C(21b)	0.221 0(3)	−0.099 0(3)	0.129 1(2)	2.8(4)
C(22b)	0.220 1(3)	0.007 0(3)	0.130 1(2)	2.3(3)
O(23b)	0.108 1(2)	0.216 8(2)	0.129 5(2)	3.7(3)
N(24b)	−0.110 8(4)	0.217 4(4)	0.133 4(4)	10.6(6)
O(25b)	−0.148 9(5)	0.269 0(5)	0.207 1(5)	15(1)
O(26b)	−0.176 9(5)	0.230 1(6)	0.096 8(5)	19(1)
N(27b)	0.112 2(3)	−0.212 2(3)	0.133 3(3)	3.8(4)
O(28b)	0.209 1(3)	−0.301 3(3)	0.131 2(3)	6.5(5)
O(29b)	0.013 6(3)	−0.210 8(3)	0.140 2(3)	6.0(4)
N(30b)	0.339 3(2)	0.000 8(3)	0.127 5(2)	3.0(3)
O(31b)	0.342 2(2)	0.085 2(2)	0.149 9(2)	4.7(3)
O(32b)	0.432 2(2)	−0.089 4(3)	0.104 2(2)	5.2(3)

grams.[25] The data set with the best combined figure of merit revealed all non-hydrogen atoms (R = 0.37). Full matrix refinement for non-hydrogen atoms resulted in R = 0.10. The difference Fourier map gave the positions of all hydrogen atoms at this stage and they were included in the final refinement for non-hydrogen atoms with the overall temperature factor. The

refinement concluded with $R = 0.066$ and $R_w = 0.077$ for 2 218 reflections. The weighting scheme was $w = 78/[\sigma^2(F) + 0.0001F^2]$. The atomic co-ordinates are given in Table 2.

Crystal data for (**8**). $C_{13}H_{23}N_2O^+C_6H_2N_3O_7^-$, $M = 451.4$. Triclinic, $a = 12.664(12)$, $b = 13.034(9)$, $c = 15.299(3)$ Å, $\alpha = 80.56(4)$, $\beta = 74.93(4)$, $\gamma = 61.24(6)°$, $V = 2\,135.4$ Å^3, $D_c = 1.40$ g cm^{-3}, Mo-K_α radiation, $\lambda = 0.7107$ Å, μ(Mo-K_α) = 1.20 cm^{-1}, space group $P\bar{1}$, $Z = 4$. Intensities up to $\theta = 25°$ were collected with an Enraf–Nonius CAD-4 diffractometer, with monochromated Mo-K_α radiation. 5 174 reflections out of 7 449 were considered observed [$I > 3\sigma(I)$]. The scattering factors for both non-hydrogen and hydrogen atoms were taken from ref. 24. All calculations were carried out with a PDP 11/34 minicomputer, by use of the Enraf-Nonius SDP program package with local modification.

Many attempts to solve the structure with MULTAN 78 and with SHELX 76 programs failed. Interpretation of the Patterson function revealed only the orientation of the two symmetrically independent picrate molecules, but determination of the translation vectors by residual analysis was unsuccessful. All direct-method solutions gave 'chicken-wire' patterns. Fitting the two picrate molecules somewhat arbitrarily to this E-map, we modified our E values according to the formula[26] $|E_{mod.}| = (|E_{obs.}|^2 - c|E_{calc.}|^2)^{\frac{1}{2}}$, with $c = 0.2$. With 346 modified E values, $E_{min.} > 1.40$, and 1 500 phase relationships using 7 starting sets (128 solutions), the set with the best ABSFOM and RESID parameters revealed 63 atoms.

In parallel to this, 25 atoms could be found after improving the PSIZRO test in our MULTAN version.[27] In the original version, depending on the sorting of the reflections, the last 50 reflections with $F_o = 0$ were kept for the PSIZRO test. In the usual data collection mode, these are the reflections that have high θ values, which are weak because the scattering values are small. For the PSIZRO test, therefore, we chose reflections with low θ values by setting F_o to 0.1 if θ was above a given value. With the corrected PSIZRO test, a fragment containing 25 atoms could be gained using the solution with the best combined figure of merit (400 E values, $E > 1.4$, 5 starting reflections, 2 242 phase relationships, $R = 0.39$). The remaining atoms were obtained from subsequent structure factor–electron density calculations. The non-hydrogen atom positions were refined by block-diagonal least-squares calculations ($R = 0.126$). One hydrogen atom in each methyl group was located from difference Fourier synthesis, and the remaining hydrogen atoms were entered in calculated positions. Further anisotropic refinement of the non-hydrogen atoms revealed that O(25) and O(26) of picrate molecule B (see Figure 4) were disordered. Their positions were redetermined from a subsequent difference Fourier map, but the thermal parameters of these atoms remained high in the final stage ($R = 0.069$, $R_w = 0.063$ for 5 174 reflections using unit weight). The atomic co-ordinates are given in Tables 3 and 4.

Table 4. Fractional co-ordinates and B values of compound (**8**), hydrogen atoms

Atom	x	y	z	B_{eq}
H(1a)	0.676	0.859	0.360	4.3
H(2a)	0.531	0.902	0.231	4.5
H(3a)	0.817	0.756	0.224	4.4
H(4a)	0.673	0.501	0.287	6.4
H(5a)	0.762	0.476	0.415	6.3
H(6a)	0.634	0.447	0.452	6.3
H(7a)	0.647	0.565	0.558	6.2
H(8a)	0.509	0.636	0.517	6.2
H(9a)	0.733	0.677	0.447	5.9
H(10a)	0.590	0.774	0.511	5.9
H(11a)	0.490	0.783	0.386	4.3
H(12a)	0.702	0.803	0.064	5.5
H(13a)	0.850	0.780	0.067	5.5
H(14a)	0.636	1.002	0.060	5.9
H(15a)	0.778	0.979	0.079	5.9
H(16a)	0.559	1.071	0.207	5.8
H(17a)	0.705	0.996	0.235	5.8
H(18a)	0.480	0.959	0.459	5.2
H(19a)	0.410	0.983	0.369	5.2
H(20a)	0.503	1.050	0.367	5.2
H(21a)	0.479	0.520	0.354	8.7
H(22a)	0.462	0.645	0.278	8.7
H(23a)	0.429	0.659	0.396	8.7
H(24a)	1.187	0.761	0.341	5.2
H(25a)	0.948	1.125	0.396	5.0
H(1b)	0.168	0.307	0.145	4.6
H(2b)	0.109	0.487	0.264	4.5
H(3b)	0.223	0.212	0.286	4.5
H(4b)	0.547	0.255	0.197	5.7
H(5b)	0.623	0.306	0.038	6.3
H(6b)	0.570	0.200	0.052	6.3
H(7b)	0.497	0.336	−0.074	5.9
H(8b)	0.432	0.457	−0.004	5.9
H(9b)	0.361	0.259	0.029	5.8
H(10b)	0.273	0.400	−0.015	5.8
H(11b)	0.257	0.484	0.126	4.7
H(12b)	0.159	0.377	0.430	5.3
H(13b)	0.175	0.234	0.443	5.3
H(14b)	−0.049	0.441	0.444	5.8
H(15b)	−0.025	0.300	0.427	5.8
H(16b)	−0.084	0.488	0.297	5.8
H(17b)	−0.019	0.339	0.273	5.8
H(18b)	0.041	0.562	0.125	6.5
H(19b)	0.095	0.509	0.040	6.5
H(20b)	0.000	0.440	0.115	6.4
H(21b)	0.437	0.500	0.125	7.7
H(22b)	0.558	0.432	0.183	7.7
H(23b)	0.405	0.473	0.242	7.7
H(24b)	−0.083	0.003	0.133	6.2
H(25b)	0.306	−0.180	0.125	5.3

Discussion

Diagrams of the cations of (**7**) and (**8A** and **B**) are illustrated in Figures 1—3, respectively, which also show the crystallographic numbering scheme (based on pyrido[1,2-*a*]pyrimidine numbering). Endocyclic torsion angles are also given. The configurations of the chiral centres (crystallographic numbering) are for (**7**) *r*-9a,*t*-2,*t*-3,*t*-6; and for (**8**) *r*-9a,*c*-2,*t*-3,*t*-6 (for both A and B); the structures thus differ at C(2). Characteristic bond

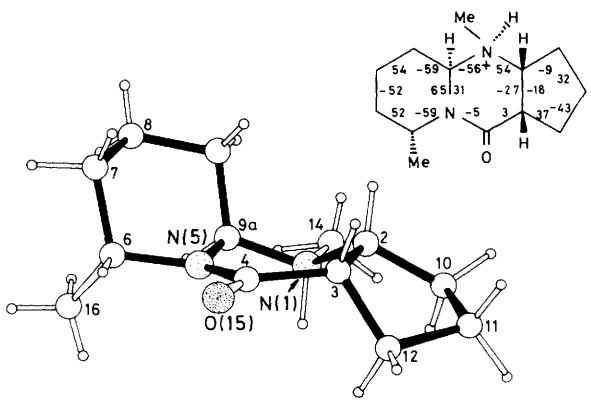


Figure 1. A molecular diagram of the cation of (**7**), showing the crystallographic numbering scheme. The inclination angle between N(5)–C(9a) and the plane of the paper is 40°. Endocyclic torsion angles are given in the line drawing

Table 5. Selected bond lengths of the cations (crystallographic numbering)

	(7)	(8A)	(8B)
N(1)–C(2)	1.502(4)	1.493(7)	1.498(7)
N(1)–C(9a)	1.495(4)	1.523(7)	1.511(5)
N(1)–C(14)	1.494(5)	1.499(6)	1.514(7)
C(3)–C(4)	1.508(5)	1.503(9)	1.486(6)
C(4)–N(5)	1.344(4)	1.361(7)	1.362(7)
C(4)–O(15)	1.236(4)	1.221(7)	1.226(6)
N(5)–C(6)	1.482(5)	1.490(9)	1.495(6)
N(5)–C(9a)	1.465(4)	1.465(7)	1.472(6)
C(6)–C(7)	1.538(6)	1.543(11)	1.526(9)
C(*sp*3)–C(*sp*3) (average)	1.529(6)	1.528(10)	1.528(10)

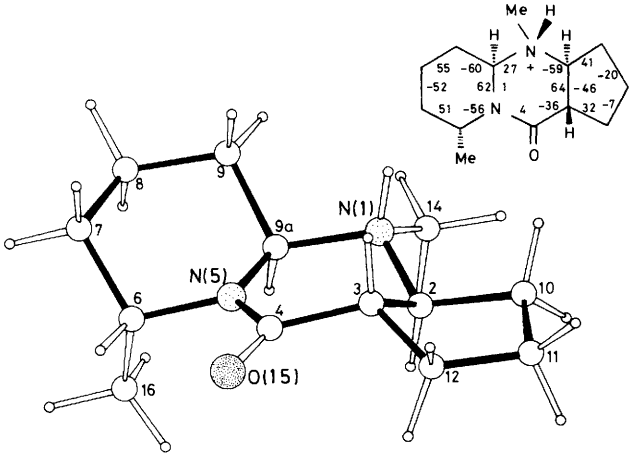


Figure 2. A molecular diagram of the cation of (**8A**), showing the crystallographic numbering scheme. The inclination angle between N(5)–C(9a) and the plane of the paper is 40°. Endocyclic torsion angles are given in the line drawing

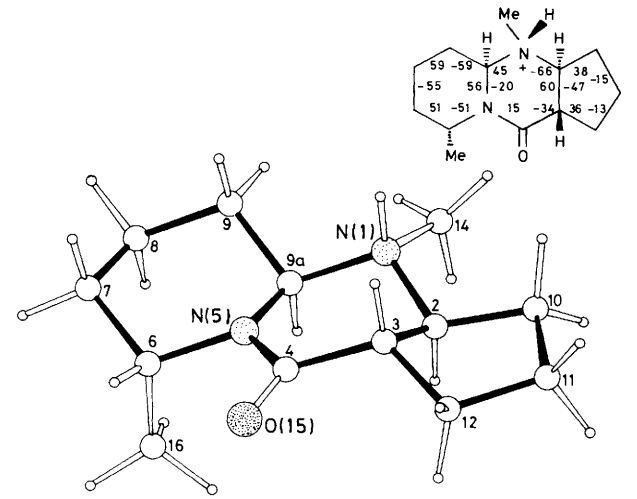


Figure 3. A molecular diagram of the cation of (**8B**), showing the crystallographic numbering scheme. The inclination angle between N(5)–C(9a) and the plane of the paper is 40°. Endocyclic torsion angles are given in the line drawing.

Table 6. Puckering parameters[28] of the individual rings, together with the parameters of ideal rings[29] (crystallographic numbering)

	Ring *A* [N(5)/6/7/8/9/9a]			Ring *B* [N(1)/2/3/4/N(5)/9a]			Ring *C* [2/10/11/12/3]	
	Q	Θ	φ	*Q*	Θ	φ	*Q*	φ
(7)	0.58 Å	6°	48°	0.46 Å	129°	177	0.42	96
Ideal	$^{N5}C_8$	0°	undetermined	E_{N1}	125°	180	$^{11}H_{12}$	90
(**8A**)	0.57	5	299	0.53	52	68	0.43	171
(**8B**)	0.56	7	239	0.53	41	48	0.45	163
Ideal	$^{N5}C_8$	0	undetermined	E_2	55	60	$^3H_2$	162

Table 7. Conformational parameters for the amide group

Compound	(7)	(8A)	(8B)
$\chi_{N(5)}$	−19.4	+4.9	+19.4
$\tau_{N(5)-C(4)}$	+7.5	+2.6	+7.1
$\chi_{C(4)}$	+1.1	+0.7	+2.7

Definition of the parameters according to ref. 30.

$\chi_N = \omega_2 - \omega_3 + 180°$
$\chi_C = \omega_1 - \omega_3 + 180°$
$\tau_{C-N} = \omega_1 + \omega_2$

ω_1 = C(9a)–N(5)–C(4)–C(3)
ω_2 = O(15)–C(4)–N(5)–C(6)
ω_3 = O(15)–C(4)–N(5)–C(9a)
ω_4 = C(6)–N(5)–C(4)–C(3)

lengths are given in Table 5. The lone pair of N(5) is delocalized toward the carbonyl group: the N(5)–C(4) bond length is 1.34–1.36 Å, similar to that in the six-membered dodecahydropyrido[2,1-*b*]quinazolin-11-one analogues.[16] The geometry of the individual rings is described in Table 6, by use of Cremer-Pople puckering parameters.[28] For comparison, the numerical values for the ideal conformers are also listed, together with the nomenclature of the canonic conformers.[29] The piperidine ring has a chair conformation in all cases. As a result of the different configuration at C(2), the conformation of ring *B* is E_{N1} envelope in (**7**), but E_2 in (**8**). Nevertheless, ring *B* of (**8B**) is distorted ($\Delta\Theta = -11°$, $\Delta\varphi = -20°$) towards an $^{N1}C_4$ chair, owing to packing forces. The half-chair conformation is characteristic of all five-membered rings, though with different φ parameters. In (**7**) the *A*/*B* junction is of *cisoid* type, and the *B*/*C* junction of *cis* type, whereas in (**8**) the *A*/*B* junction is of *transoid* type, and the *B*/*C* junction of *trans* type. Conformational parameters for the amide group[30] are given in Table 7. In comparison with the situation in the bicyclic hexahydropyrido[1,2-*a*]pyrimidinones, the bridgehead nitrogen atom is flattened, especially in (**8A**): $\chi_N = 4.9°$. The signs of the pyramidality parameters of the bridgehead nitrogen atom are opposite in (**7**) and (**8**).

A common feature of (**7**) and (**8**) is that the *N*-methyl groups are in equatorial positions, and the *C*-methyl groups in axial positions. The hexahydropyridopyrimidinones formed by catalytic reduction possess with equatorial C(6)-methyl groups.[5] In (**8**), as a consequence of the *transoid-trans* ring junctions all bridgehead hydrogen atoms are axial to each ring. In (**7**) H-2 and H-3 are axial to ring *B*, but equatorial to ring *C*; H-9a is axial to ring *A* and equatorial to ring *B*. The cations are hydrogen-bonded to the anions, with the parameters (**7**): N(1)–H(1) · · · Cl(17) H · · · Cl 1.93 Å, N–H · · · Cl 161°, N · · · Cl 2.97 Å; (**8A**): N(1)–H(1) · · · O(23) H · · · O 1.78 Å, N–H · · · O 159°, N · · · O 1.78 Å; (**8B**): N(1)–H(1) · · · O(23) H · · · O 1.75 Å, N–H · · · O 151°, N · · · O 1.75 Å.

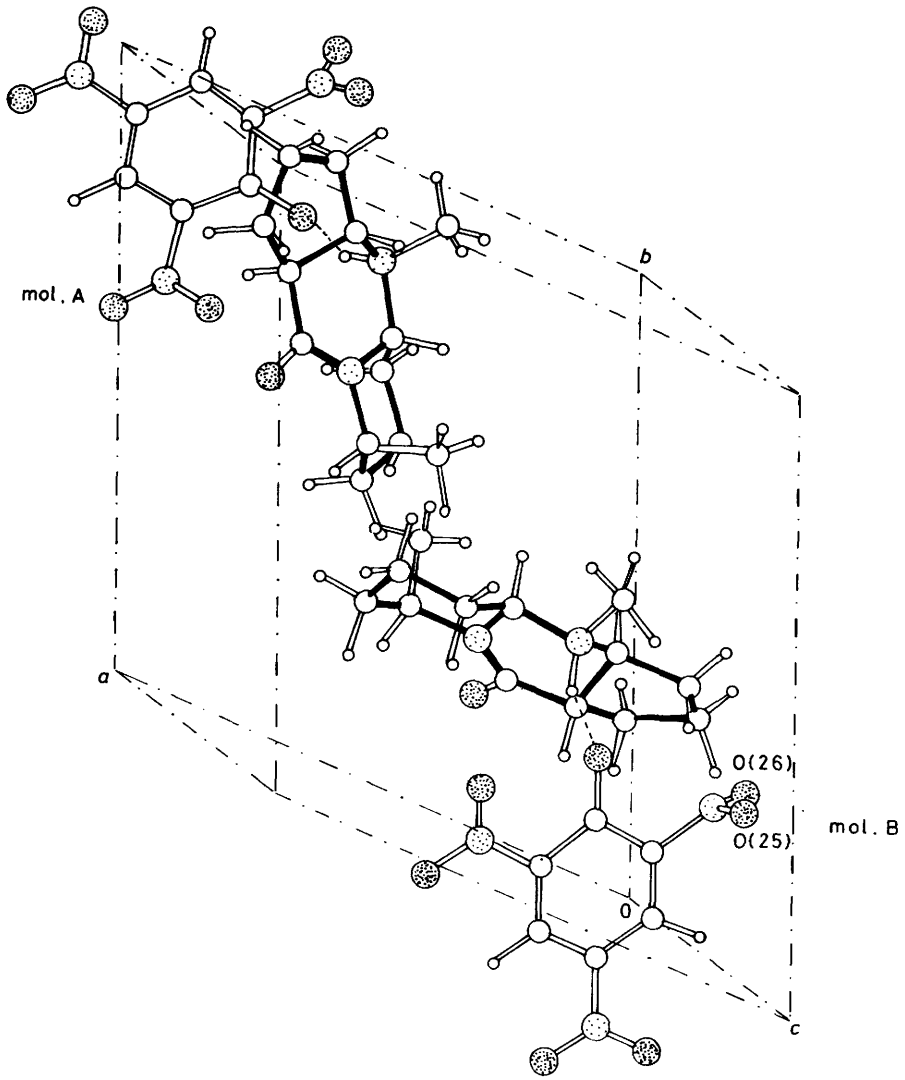


Figure 4. Diagram showing the relative positions of the two counter-ions in the structure of (**8**)

The packing of (**8**) is illustrated in Figure 4. The best mean planes P1 and P2 of the independent picrate anions are almost parallel to each other (P1,P2 angle 10°) and perpendicular to c^*, with $z = 0.37$ for picrate A, and $z = 0.13$ for picrate B. If we disregard the phenolic oxygen atoms, the picrate molecules are related by a pseudo-centre of symmetry. A very similar arrangement was found in a hexahydropyrido[2,1-*b*]quinazolinium picrate.[31] This pseudo-symmetry might have caused the difficulties in the application of direct methods.

The best mean planes of the carbamoyl groups C(3),C(4),-N(5),O(15) (P3 and P4) are almost perpendicular to each other (P3,P4 angle −81°). The crystallographically independent counter-ion pairs are angled differently: P1,P3 58°, P2,P4 73°. This might explain the difference found in the conformations of the cations.

Experimental

M.p.s were determined with a Boetius micro hot-stage apparatus. The ^1H and ^{13}C n.m.r. spectra were recorded in pulsed Fourier transform mode (16 K data points for the free induction decay) at ambient temperature, with an internal deuterium lock, at 99.6 and 25.0 MHz, using a JEOL FX-100 spectrometer. The chemical shifts were determined on the δ scale, with tetramethylsilane as internal standard.

1,2,3,5,6,7,8,10-*Octahydro*-4,8-*dimethyl*-10-*oxopyrido*[1,2-a]-*pyrimidin*-4-*ium Methosulphate* (**4**).—A solution of the 8-methylcyclopenta[*d*']pyrido[1,2-*a*]pyrimidone (**3**)[20] (2.04 g, 10 mmol) and dimethyl sulphate (1.31 g, 10 mmol) in acetone (30 ml) was refluxed for 8 h. After reduction of its volume to half, the reaction mixture set aside overnight. The precipitated *quaternary salt* (**4**) (2.4 g, 75%) was filtered off, washed with acetone, dried, and recrystallized from acetone–diethyl ether; m.p. 129—132 °C (Found: C, 50.5; H, 6.8; N, 8.3. $C_{14}H_{22}N_2O_5S$ requires C, 50.9; H, 6.7; N, 8.5%).

Reduction of the Quaternary Salt (**4**).—(a) *With sodium borohydride.* To a solution of the quaternary salt (**4**) (0.65 g, 2 mmol) in methanol (5 ml) at 0 or −70 °C, sodium borohydride (0.3 g, 8 mmol) in water (5 ml) was added dropwise. The mixture was stirred for 2 or 6 h at the given temperature, respectively, then evaporated to dryness, and the residue was extracted with chloroform (3 × 10 ml). The combined and dried (Na_2SO_4) extracts were evaporated to dryness *in vacuo* to give a

diastereoisomeric mixture of perhydrocyclopentapyrido[1,2-*a*]-pyridinones (**5**) and (**6**).

(b) *With platinum oxide in ethanol or in glacial acetic acid.* The quaternary salt (**4**) (0.65 g, 2 mmol) in ethanol (20 ml) or in glacial acetic acid (20 ml) was hydrogenated over 5% platinum–carbon (10 mg) for 4 h at ambient temperature and atmospheric pressure. The catalyst was filtered off, and the solution evaporated to dryness *in vacuo*. The residue was dissolved in water (15 ml) and the pH of the aqueous solution adjusted to 7 with 5% sodium hydrogen carbonate solution. The neutralized aqueous mixture was extracted with chloroform (3 × 10 ml). The combined and dried (Na_2SO_4) extracts were evaporated to dryness *in vacuo* to give a diastereoisomeric mixture of perhydrocyclopentapyrido[1,2-*a*]pyrimidinones (**5**) and (**6**) as an oil.

2,3,r-3a,4,t-4a,5,6,7,8,c-10a-*Decahydro*-4,t-8-*dimethylcyclopenta*[d]*pyrido*[1,2-a]*pyrimidin*-10(1H)-*one Hydrochloride* (**7**).—The crude products obtained according to methods (a) and (b) were combined and converted into the hydrochlorides with hydrogen chloride dissolved in ethanol. Recrystallization from acetone, repeated three times, gave *compound* (**7**) with stable m.p. 225—227 °C (Found: C, 60.4; H, 9.1; Cl, 13.3. $C_{13}H_{23}ClN_2O$ requires C, 60.3; H, 9.0; Cl, 13.7%). The base (**5**), liberated for spectroscopic examination, was distilled from a Hickmann flask. The colourless, viscous oil crystallized slowly: δ_C ($CDCl_3$; 25.0 MHz) C-3a, 60.5; C-10a, 44.2; C-10, 170.8; C-8, 44.8; C-7, 27.8; C-6, 18.6; C-5, 29.5; C-4a, 69.1; C-3, 29.5; C-2, 22.8; C-1, 27.6; 8-CH_3, 16.3; N-CH_3, 38.1; $^1J_{C-H}$ (Hz): $^1J_{3a,3a-H}$ 139.2; $^1J_{10a,10a-H}$ 128.2; $^1J_{8,8-H}$ 146; $^1J_{4,4a-H}$ 145.9.

2,3,r-3a,4,c-4a,5,6,7,8,t-10a-*Decahydro*-4,c-8-*dimethylcyclopenta*[d]*pyrido*[1,2-a]*pyrimidin*-10(1H)-*one Picrate* (**8**).—From the mother liquor obtained in the purification of (**7**) the base was liberated with sodium hydrogencarbonate. T.l.c. on a preparative plate (Merck) with benzene–ethanol (4:1) gave the minor component (**6**) as a pale yellow oil, which afforded the *picrate* (**8**), m.p. 161—163 °C (Found: C, 50.4; H, 5.6; N, 15.3. $C_{19}H_{25}N_5O_8$ requires C, 50.55; H, 5.6; N, 15.5%). The base (**6**), liberated for spectroscopic examination, was a colourless, viscous oil, δ_C ($CDCl_3$; 25.0 MHz) C-3a, 64.9; C-10a, 47.7; C-10, 165.0; C-8, 44.0; C-7, 29.3; C-6, 18.6; C-5, 30.3; C-4a, 76.8; C-3, 32.5; C-2, 20.5; C-1, 23.4; 8-CH_3, 16.3; N-CH_3, 39.7; $^1J_{C-H}$ (Hz): $^1J_{3a,3a-H}$ 131.8; $^1J_{10a,10a-H}$ 128.9; $^1J_{8,8-H}$ 142.1; $^1J_{4a,4a-H}$ 140.7.

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