Stereochemical Studies. Part 50.[1] Saturated Heterocycles. Part 29.[2] Synthesis and *X*-Ray Analysis of Stereoisomeric Dodecahydropyrido[2,1-*b*]quinazolin-11-ones

Ferenc Fülöp,[a] Kálmán Simon,[b] Gábor Tóth,[c] István Hermecz,[b] Zoltán Mészáros,[b] and Gábor Bernáth [a]*

[a] *Institute of Pharmaceutical Chemistry, University Medical School, 6720 Szeged, Eötvös u. 6.;*
[b] *Chinoin Pharmaceutical and Chemical Works, 1325 Budapest;*
[c] *Technical University, NMR Laboratory of the Institute for General and Analytical Chemistry, 1111 Budapest, Gellért tér 4., Hungary*

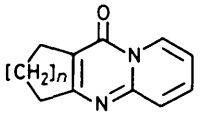
Reductions of *cis*- and *trans*-decahydropyrido[2,1-*b*]quinazolin-11-ones (4), (3) and their quaternary salts (10), (9), prepared by means of dimethyl sulphate, have been investigated. Stereospecific or stereoselective formation of the unsubstituted tricycles was found, whereas the 5-methylperhydropyrido-[2,1-*b*]quinazolines were formed stereospecifically only in the case of the *trans*-derivatives. The relative configurations of the 5-methyl compounds were established by means of configurative correlation, and the steric structures of the *r*-4a,*c*-5a,*t*-11a- and *r*-4a,*c*-6a,*c*-11a-dodecahydropyrido[2,1-*b*]quinazolin-11-ones (5a) and (7a), respectively, were determined by *X*-ray diffraction analysis.

In continuation of our synthetic and stereochemical studies on partly or completely saturated heterocycles containing two hetero-atoms, we recently reported syntheses of multisubstituted tetrahydropyrido[2,1-*b*]quinazolin-11-ones of type (1) and their 5-, 7-, and 8-membered A-ring homologues.[3] Several compounds in this series have very favourable analgesic action.[4]

Stereospecific syntheses of partly saturated analogues of the pyridoquinazolinones of type (1), *i.e.* of decahydropyrido-[2,1-*b*]quinazolin-11-ones (2), have also been reported in a recent publication.[5] In compounds of this type, the stereohomogeneous 5-, 6-, and 7-membered A- and C-ring analogues have been prepared, the A/B ring fusion being *cis* and *trans*. It was found in the *cis*-isomers of the tricycles (2) that, of the two possible conformers, the predominating one contained the C=O group in the equatorial, and the nitrogen atom in the axial position relative to the cycloalkane ring. In that paper [5] the total saturation of these derivatives, by means of sodium borohydride, was also described. However, the relative configuration of the newly introduced asymmetric centre has not been definitively established.

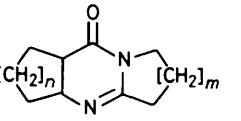
The present paper deals with the synthesis and stereochemical investigation of the perhydro-derivatives (5a)—(8a) obtainable by reduction of the 6-membered tricycles (3) and (4), and with the *N*-methyl derivatives (5b)—(8b) of these perhydro-compounds. In recent years the conformational analysis of saturated heterocycles has been the subject of particular attention (see, *e.g.* refs. 6—8), which lends additional interest to these studies. It is worth noting that the examined perhydropyrido[2,1-*b*]quinazolin-11-ones are the perhydrogenated analogues of the alkaloid [9] 6,7,8,9-tetrahydropyrido[2,1-*b*]quinazolin-11-one, isolated from the plants *Mackinlaya subulata* and *Mackinlaya macrosciadia*. Structure elucidations were effected by ^{1}H and ^{13}C n.m.r. spectroscopy, and also by *X*-ray analysis. The next paper of this series [10] will describe details of the ^{13}C n.m.r. spectroscopic determinations of the relative configurations of the newly synthesised compounds, and their conformational analyses.

Syntheses.—*cis*- and *trans*-Decahydropyrido[2,1-*b*]quinazolin-11-ones, used as the starting materials, were synthesised according to the method described earlier,[5] by condensing *O*-methyl-δ-valerolactim with *cis*- or *trans*-2-amino-1-cyclohexanecarboxylic acid.



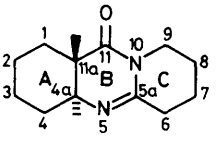
(1)

n = 1, 2, 3, 4

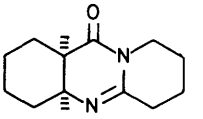


(2)

n = 1, 2; *m* = 1, 2, 3



(3)

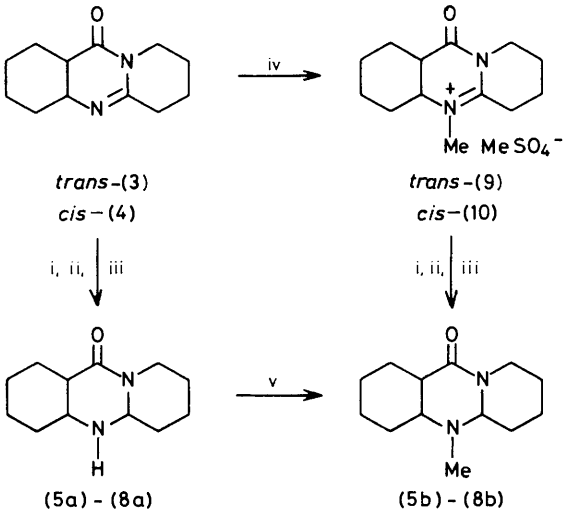


(4)

Owing to the introduction of a new 5a-asymmetric centre as a result of the reduction, when starting from the *cis*- and *trans*-derivatives the formation of two diastereoisomers each, (5) + (6) and (7) + (8), respectively, can be expected. Although our work was carried out with racemic compounds in every case, here only those enantiomers are shown where the configuration of the 4*a*-carbon atom is *S*. Consequently, the possible diastereoisomers in Crabb's notation (see, *e.g.* ref. 11) are the following: (5): *r*-4a, *c*-5a, *t*-11a; (6): *r*-4a, *t*-5a, *t*-11a; (7): *r*-4a, *c*-5a, *c*-11a; (8): *r*-4a, *t*-5a, *c*-11a.

The reductions were accomplished in the ways shown in the Scheme. The 5-methyl derivatives were prepared by two routes. In the first (iv), the tricyclic compounds (3) and (4) were quaternised with dimethyl sulphate in acetone, and the quaternary salts were reduced without isolation. The other way (v), the alkylation of the perhydro-bases of known configuration with methyl iodide in the presence of silver oxide, made possible the determination of the configurative correlations in the compounds, since methylation does not affect any of the asymmetric centres here.

The crude products were analysed by ^{1}H or ^{13}C n.m.r. spectroscopy in each case after the different reductions. The ratio of the diastereoisomers was deduced from the ratio of the ^{13}C signals in the case of the *N*-unsubstituted compounds; for



Scheme. *Reagents*: i, $NaBH_4$; ii, H_2–PtO_2 in EtOH; iii, H_2–PtO_2 in AcOH; iv, Me_2SO_4; v, MeI–Ag_2O

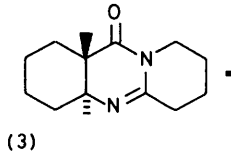
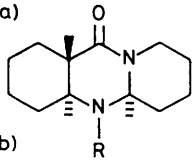
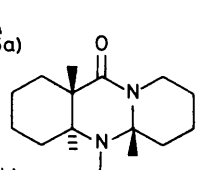
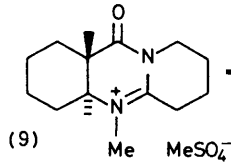
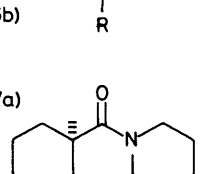
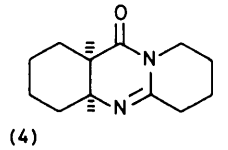
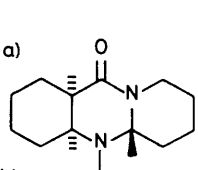
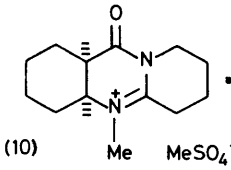
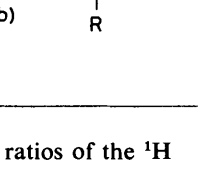
reductions of the *trans*-quaternary salt (9). In all three cases the newly introduced hydrogen—connected carbon 5a—is in the same steric situation as in 4a.

An interesting reversal of selectivity is found in the reduction of the *cis*-quaternary salt (10). In this case the main product of the reduction, (8b), has the hydrogens—connected carbon 4a and 5a—in the opposite steric positions.

Each spectroscopically detected diastereoisomer has been isolated as a homogeneous product. The reductions gave the NH-derivatives (5a) and (7a), as well as the *N*-methyl derivative (5b), in the pure state. The identical relative configurations of (5a) and (5b) have been confirmed both spectroscopically and chemically. As shown in the Scheme, the *N*-alkylation of (5a) gives (5b). The main product (8b) can be isolated from the mixture resulting from the reductions of the quaternary salt (10) by fractional crystallisation of the hydrochlorides of the crude products. Methylation of (7a) gives the minor component (7b) as a pure compound. All products of the conversions were examined and checked by ^1H and ^{13}C n.m.r. spectroscopy in each case.

The relative steric positions of the annellation hydrogens in (5a) could not be unequivocally decided on the basis of the ^1H and ^{13}C n.m.r. data; therefore, an *X*-ray diffraction structure

Table 1. Diastereoisomeric ratio in the crude products of the reductions

Starting compound	Product *	Method $NaBH_4$	Method H_2–PtO_2 (in EtOH)	Method H_2–PtO_2 (in AcOH)
	 (5a)	100	100	100
		100	100	100
	 (5b)	0	0	0
		0	0	0
	(6a)			
	 (6b)			
	(7a)	100	100	75
		35	25	25
	 (7b)	0	0	25
		65	75	75
	(8a)			
	 (8b)			

* a, R = H; b, R = Me.

the *N*-methyl compounds, the *N*-CH_3 signal ratios of the ^1H spectrum afforded this information.

Table 1 shows that the *trans*- (3) and *cis*- (4) decahydro-compounds are reduced with great selectivity by the methods employed. A similar high selectivity is also obtained in the determination of this compound was performed. In compounds (7), the relative steric positions of the annelation hydrogens can be unambiguously determined by spectroscopic methods.[10] In the present case, however, the existence of a conformational equilibrium in the liquid phase cannot be

Table 2. Fractional co-ordinates and B_{eq} values * of (5a) with e.s.d.s in parentheses

	x/a	y/b	z/c	B_{eq}
C(1)	0.791 0(5)	0.143 2(4)	0.852 7(2)	5.36(15)
C(2)	0.933 0(5)	0.233 5(4)	0.902 5(2)	5.72(15)
C(3)	1.137 5(5)	0.281 1(4)	0.870 6(2)	5.95(16)
C(4)	1.076 3(5)	0.356 3(3)	0.803 5(2)	5.12(14)
C(4a)	0.935 1(4)	0.265 5(3)	0.754 8(1)	3.86(12)
N(5)	0.872 5(3)	0.342 2(2)	0.622 9(1)	4.07(10)
C(5a)	0.734 7(4)	0.259 6(3)	0.645 0(1)	4.10(12)
C(6)	0.656 7(6)	0.345 1(4)	0.583 7(2)	6.16(16)
C(7)	0.503 2(6)	0.265 0(4)	0.533 0(2)	7.62(19)
C(8)	0.316 0(5)	0.202 4(4)	0.566 9(2)	6.93(18)
C(9)	0.395 7(5)	0.116 6(4)	0.627 0(2)	7.21(17)
N(10)	0.547 1(5)	0.198 3(3)	0.675 6(1)	7.90(15)
C(11)	0.567 1(4)	0.156 4(3)	0.744 2(2)	4.21(12)
C(11a)	0.740 9(4)	0.213 1(3)	0.786 8(1)	3.56(11)
O(15)	0.433 1(3)	0.075 2(2)	0.765 8(1)	5.62(9)
H(11)	0.636(1)	0.113(1)	0.876(1)	6.57
H(12)	0.874(1)	0.042(1)	0.846(1)	6.57
H(21)	0.976(1)	0.181(1)	0.950(1)	6.96
H(22)	0.835(1)	0.326(1)	0.913(1)	6.96
H(31)	1.241(1)	0.194(1)	0.864(1)	6.70
H(32)	1.230(1)	0.354(1)	0.906(1)	6.70
H(41)	1.224(1)	0.386(1)	0.778(1)	6.45
H(42)	0.987(1)	0.453(1)	0.810(1)	6.45
H(4a)	1.032(1)	0.174(1)	0.742(1)	4.50
H(5)	0.791(1)	0.445(1)	0.703(1)	5.20
H(5a)	0.837(1)	0.173(1)	0.632(1)	5.17
H(61)	0.570(1)	0.436(1)	0.599(1)	8.04
H(62)	0.800(1)	0.382(1)	0.559(1)	8.04
H(71)	0.445(1)	0.325(1)	0.488(1)	7.77
H(72)	0.594(1)	0.174(1)	0.511(1)	7.77
H(81)	0.224(1)	0.293(1)	0.586(1)	8.43
H(82)	0.202(1)	0.146(1)	0.533(1)	8.43
H(91)	0.260(1)	0.077(1)	0.654(1)	7.81
H(92)	0.483(1)	0.025(1)	0.610(1)	7.81
H(11a)	0.665(1)	0.311(1)	0.802(1)	4.52

* B_{eq} Values are defined as: $B_{eq} = 4[b_{11}/a^{*2} + b_{22}/b^{*2} + b_{33}/c^{*2}]^{1/3}$.

Table 3. Fractional co-ordinates and B_{eq} values * of (7a) with e.s.d.s in parentheses

	x/a	y/b	z/	B_{eq}
C(1)	0.785 7(3)	0.170 8(2)	0.657 7(1)	3.95(7)
C(2)	0.597 8(3)	0.212 0(3)	0.603 6(1)	4.93(9)
C(3)	0.440 5(3)	0.292 6(2)	0.643 4(1)	4.86(8)
C(4)	0.365 6(3)	0.211 5(2)	0.706 0(1)	4.56(8)
C(4a)	0.545 3(3)	0.163 4(2)	0.760 9(1)	3.75(7)
N(5)	0.636 9(2)	0.272 8(2)	0.807 3(1)	3.68(6)
C(5a)	0.781 1(3)	0.221 8(2)	0.866 5(1)	3.72(7)
C(6)	0.896 9(4)	0.336 7(2)	0.906 7(1)	4.93(9)
C(7)	1.065 5(4)	0.290 0(3)	0.966 5(1)	5.84(10)
C(8)	1.215 9(4)	0.194 2(3)	0.933 8(1)	6.02(10)
C(9)	1.097 4(3)	0.077 9(3)	0.897 1(1)	5.35(9)
N(10)	0.934 3(2)	0.123 7(2)	0.840 5(1)	3.86(6)
C(11)	0.905 1(3)	0.056 4(2)	0.776 1(1)	3.61(6)
C(11a)	0.715 8(3)	0.090 7(2)	0.722 5(1)	3.61(6)
O(15)	1.030 0(2)	−0.030 7(1)	0.759 6(1)	4.81(6)
H(11)	0.867(1)	0.261(1)	0.678(1)	4.66
H(12)	0.895(1)	0.111(1)	0.629(1)	4.66
H(21)	0.522(1)	0.122(1)	0.579(1)	5.55
H(22)	0.652(1)	0.271(1)	0.558(1)	5.55
H(31)	0.307(1)	0.321(1)	0.605(1)	5.57
H(32)	0.516(1)	0.384(1)	0.666(1)	5.57
H(41)	0.277(1)	0.126(1)	0.683(1)	5.18
H(42)	0.259(1)	0.274(1)	0.735(1)	5.18
H(4a)	0.480(1)	0.091(1)	0.797(1)	4.56
H(5)	0.722(1)	0.339(1)	0.774(1)	4.40
H(5a)	0.689(1)	0.166(1)	0.904(1)	4.54
H(61)	0.784(1)	0.400(1)	0.932(1)	5.63
H(62)	0.971(1)	0.398(1)	0.867(1)	5.63
H(71)	0.991(1)	0.237(1)	1.010(1)	6.30
H(72)	1.151(1)	0.375(1)	0.992(1)	6.30
H(81)	1.335(1)	0.159(1)	0.976(1)	6.18
H(82)	1.296(1)	0.249(1)	0.892(1)	6.18
H(91)	1.024(1)	0.021(1)	0.939(1)	5.72
H(92)	1.205(1)	0.011(1)	0.872(1)	5.72
H(11a)	0.644(1)	−0.003(1)	0.700(1)	4.32

* The definition of B_{eq} is given in Table 2.

excluded. The *X*-ray analysis of compound (7a) was intended to establish what kind of conformer is present in the solid state and whether it is identical with that existing in the liquid phase.

Crystal Data.—(5a). $C_{12}H_{20}N_2O$, $M = 208.3$. Monoclinic, $a = 6.160(1)$, $b = 9.640(a)$, $c = 19.927(3)$ Å, $\beta = 95.32(1)°$, $V = 1\,172.4$ Å^3, $D_c = 1.18$ g cm^{-3}, $F(000) = 456$. Mo-K_α radiation, $\lambda = 0.710\,73$ Å, μ(Mo-K_α) = 0.82 cm^{-1}, space group $P2_1/c$, $Z = 4$.

Data were collected on an ENRAF-NONIUS CAD-4 diffractometer with monochromated Mo-K_α radiation up to σ-30°; 1 423 out of 3 409 reflections were considered observed [$I > \sigma(I)$]. Data were corrected for Lorentz and polarisation effects. The scattering factors for non-hydrogen and for hydrogen atoms were taken from ref. 12. All calculations were carried out on a PDP 11/34 minicomputer by the use of the Enraf-Nonius SDP programme package with local modification.

The structure was solved with programme MULTAN-78,[13] applying 204 *E* values, 1 446 phase relations and 4 starting reflections. The set with the best combined figure of merit revealed all non-hydrogen atoms ($R = 0.26$ for 912 observations). Full matrix refinement for the non-hydrogen atoms gave $R = 0.12$. A difference Fourier map revealed 14 hydrogen atoms out of 20. Among the missing hydrogen atoms was the critical H atom belonging to the atom C(11a). This fact and the abnormally high thermal motion of the atoms N(10) and C(11a) perpendicular to the best plane of the molecule indicated that the molecule and its mirror image through the atoms N(5), C(11), and C(15) takes up the same position in such a way that the atoms N(10) and C(11a) nearly coincide. A difference Fourier map revealed elongated maxima perpendicular to the plane formed by C(4a), C(5a), C(11) atoms for the atomic positions of N(10) and C(11a). Using the shape of these maxima, the positions of N(10) and N(11a) were generated in the plane, while the positions of C(10) and C(11a), 0.3 Å above it. The parameters and the multiplicity of these atoms were refined. Refinement concluded with $R = 0.087$ and $R_w = 0.077$ for 1 423 reflections. The weighting scheme was: $w = 1/[\sigma^2(F_0) + pF_0^2]$, where p was 0.010. The final multiplicity for model A with atoms N(10) and C(11a) was 0.75 while for model B with atoms C(10) and N(11a) it was 0.25.

Crystal Data.—Compound (7a). $C_{12}H_{20}N_2O$, $M = 208.3$. Monoclinic, $a = 6.390(1)$, $b = 9.975(1)$, $c = 18.229(1)$ Å, $\beta = 95.69(1)°$, $V = 1156.2$ Å^3, $D_c = 1.20$ g cm^{-3}, Cu-K_α radiation, $\lambda = 1.5418$ Å, μ(Cu-K_α) = 6.1 cm^{-1}, space group $P2_1/c$, $Z = 4$. Intensity data up to $\nu = 76°$ were collected on an ENRAF-NONIUS CAD-4 diffractometer with monochromated Cu-K_α radiation. 2 165 Reflections out of 2 600 were considered observed [$I > 3\sigma(I)$]. Form factors and computational details were the same as described for (5a).

The structure was solved with MULTAN-78 [13] using 160 largest *E* values and 827 phase relationships. The set with the

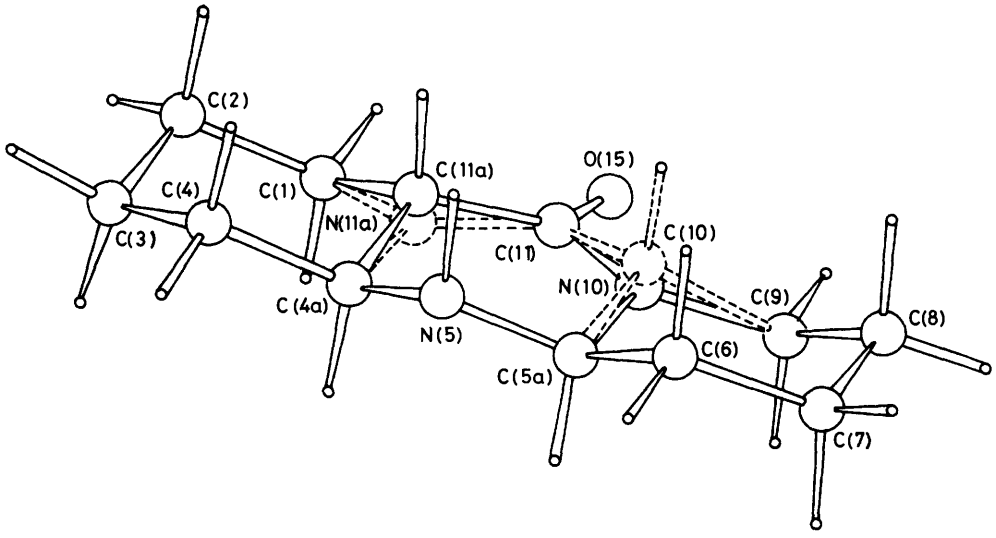


Figure 1. A molecular diagram of (5a). The inclination angle between bond C(4a)–C(11a) and the plane of the drawing is 41°. Dotted lines represent atoms of model B with a multiplicity factor of 0.25. Solid lines represent model B with a multiplicity factor of 0.75. The two models are statistically disordered in the crystal

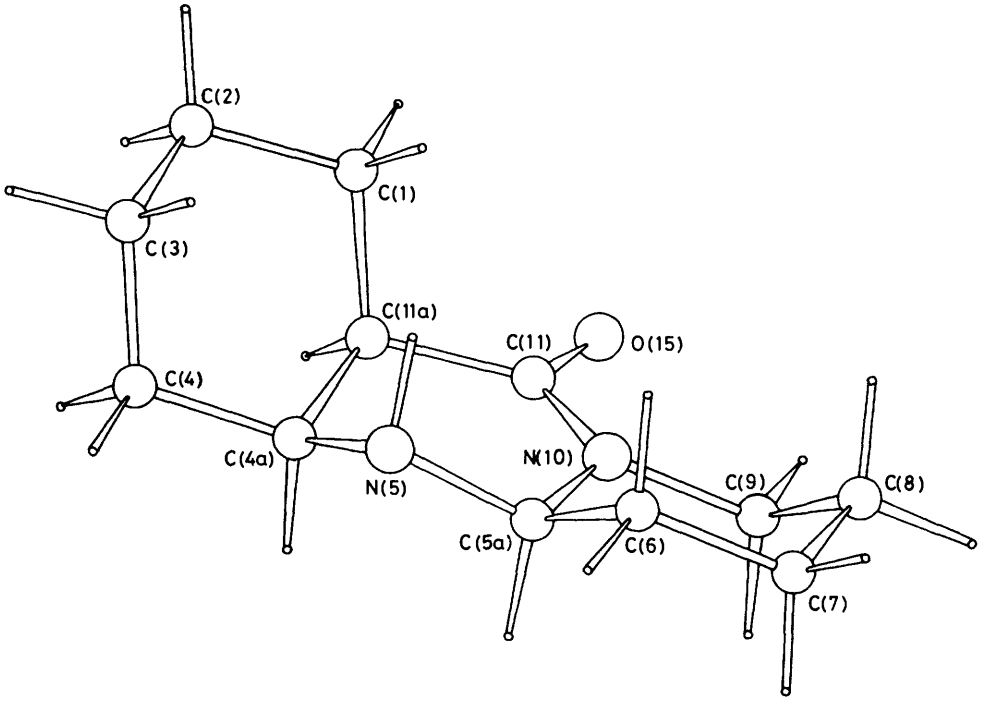


Figure 2. A molecular diagram of (7a). The inclination angle between bond C(4a)–C(11a) and the plane of the drawing is 41°

best combined figure of merit revealed all non-hydrogen atoms; $R = 0.34$. Full matrix refinement for the non-hydrogen atoms resulted in $R = 0.12$. 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 which concluded with $R = 0.054$ and $R_w = 0.047$ for 2 165 reflections using unit weighting throughout the refinement. The atomic co-ordinates are given in Tables 2 and 3 and the anisotropic thermal parameters and the structure factors are listed in Supplementary Publication No. 23405 (29 pages).*

Discussion

Molecular diagrams of compounds (5a) and (7a) are illustrated in Figures 1 and 2; the C(4a)–C(11a) vector is tilted in the same manner in both Figures. The packing of compound (5a) is disordered. The atoms and the bonds of model B are represented with dotted lines in Figure 1. Bond lengths and angles as well as torsion angles describing the geometry of the middle

* For details of the Supplementary publications scheme, see Notice to Authors No. 7, *J. Chem. Soc., Perkin Trans. 1*, 1981, Index issue.

Table 4. Selected bond lengths, bond angles, and torsion angles describing the geometry of the middle ring

Bond lengths	(5a) Model A	(5a) Model B	(7a)
	max. e.s.d. 0.006 Å		max. e.s.d. 0.003 Å
C(4a)-N(5)	1.453 Å		1.467 Å
C(4a)-C11(a)/N(11a)	1.513	1.481	1.534
N(5)-C(5a)	1.447		1.441
C(5a)-N(10)/C(10)	1.476	1.505	1.494
N(10)/C(10)-C(11)	1.405	1.436	1.349
C(11)-C(11a)/N(11a)	1.427	1.398	1.517
C(11)-O(15)	1.246		1.237

Bond angles	(5a) Model A	(5a) Model B	(7a)
	max. e.s.d. 0.7°		max. e.s.d. 0.3°
N(5)-C(4a)-C(11a)/N(11a)	110.0°	115.3°	110.7°
C(4a)-N(5)-C(5a)	111.7		111.0
N(5)-C(5a)-N(10)/C(10)	113.9	109.3	112.6
C(5a)-N(10)/C(10)-C(9)	115.9	108.6	115.1
C(5a)-N(10)/C(10)-C(11)	121.0	116.9	124.3
C(9)-N(10)/C(10)-C(11)	119.3	111.3	119.0
N(10)/C(10)-C(11)-C(11a)/N(11a)	117.7	118.0	118.7
N(10)/C(10)-C(11)-O(15)	120.3	121.9	121.6
C(11a)/N(11a)-C(11)-O(15)	122.0	120.0	119.6
Torsion angles			
C(11a)/N(11a)-C(4a)-N(5)-C(5a)	−59°	−48°	−64°
C(4)-C(4a)-C(11a)/N(11a)-C(1)	−59	−37	50
N(5)-C(4a)-C(11a)/N(11a)-C(11)	49	25	48
C(4a)-N(5)-C(5a)-N(10)/C(10)	49	58	49
N(5)-C(5a)-N(10)/C(10)-C(11)	−27	−48	−20
C(6)-C(5a)-N(10)/C(10)-C(9)	49	65	51
C(5a)-N(10)/C(10)-C(11)-C(11a)/N(11a)	17	39	6
N(10)/C(10)-C(11)-C(11a)-C(4a)	−28	−39	−20

ring are summarized in Table 4. The lone pair of the bridgehead nitrogen atom is delocalised toward the carbonyl group, especially in the case of compound (7a). The numerical values related to (5a) have to be considered with care because of the disorder.

All rings in both molecules have a chair conformation; nevertheless, the conformation of the middle ring is distorted especially in the case of compound (7a).

An A/B *trans*, B/C *transoid* type junction can be observed in the case of (5a), in complete accordance with the configuration of the minor component of the reduction with $NaBH_4$ of 2,3-trimethylene-6-methyl-6,7,8,9-tetrahydro-4*H*-pyrido[1,2-*a*]-pyrimidin-4-one.[14] An A/B *cis*, B/C *transoid* type junction is characteristic for (7a). A comparison of C(4a) in both cases, shows that the configuration of all other centres of chirality is the same. The configuration of (7a) differs at position C(5a) in relation to the major component of the reduction of 2,3-trimethylene-6-methyl-6,7,8,9-tetrahydro-5*H*-pyrido[1,2-*a*]-pyrimidin-4-one.[14] It is worth mentioning that the hydrogen atom attached to atom N(5) is always in the axial position, maintaining an intermolecular hydrogen bond with O(15); (5a): N(5)–H(5) · · · O [1-*x*, *y*-1/2, −*z* + 3/2] H · · · O 2.000 Å, N–H · · · O 158°; (7a): N(5)–H(5) · · · O [2-*x*, *y*-1/2, *z* + 3/3] (H · · · O 2.18 Å, N–H · · · O 160°).

Experimental

M.p.s were determined with a Boetius M. hot-stage apparatus. The ^1H and ^{13}C n.m.r. spectra were recorded in PFT mode (16K data points for the FID) at ambient temperature with 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, using tetramethylsilane as internal standard.

Reductions of cis- *and* trans-1,2,3,4,4a,6,7,8,9,11a-*Decahydropyrido*[2,1-b]*quinazolin*-11-*one*.—(*a*) *With sodium borohydride*. The reductions of (3) or (4) under conditions described in our earlier paper[5] gave a white crystalline residue.

(*b*) *With platinum oxide in ethanol*. Platinum oxide (10 mg) in ethanol (20 ml) was pre-hydrogenated at room temperature and atmospheric pressure for 1 h in a shaker flask, the decahydro-compound (3) or (4) (0.2 g, 1 mmol) was then added, and hydrogenation was continued for 5 h. Removal of the catalyst by filtration and evaporation of the reaction mixture gave a white, crystalline substance.

(*c*) *With platinum oxide in acetic acid*. Platinum oxide (10 mg) in glacial acetic acid (20 ml) was pre-reduced as described above; compound (3) or (4) (0.2 g, 1 mmol) was then added and the hydrogenation was continued for 4 h. The catalyst was removed by filtration and the mixture evaporated to dryness. The residue was suspended in ice-water (15 ml) and neutralised with sodium hydrogen carbonate. Extraction with chloroform, drying, and evaporation of the solvent gave a white, crystalline product.

The perhydro-derivatives prepared according to methods (*a*), (*b*), and (*c*) were shown to be identical on the basis of their ^1H and ^{13}C n.m.r. spectra. Their physical properties are listed in Table 5.

Stereoisomeric 5-*Methyl*-1,2,3,4,4a,5,5a,6,7,8,9,11a-*dodecahydropyrido*[2,1-b]*quinazolin*-11-*ones*.—The tricyclic compound (3) [or (4)] (1.03 g, 5 mmol) was dissolved in acetone

Table 5. Physical and analytical data for the tricycles (5)—(8)

Compound	Cryst. solvent	M.p. (°C)	Found (%)			Formula	Required (%)		
			C	H	N		C	H	N
(5a) [a]	Ether	175.5	69.1	9.5	13.4	$C_{12}H_{20}N_2O$	69.2	9.7	13.4
(7a) [a]	Ether	112—113	69.2	9.7	13.3	$C_{12}H_{20}N_2O$	69.2	9.7	13.4
(5b) [b]	Ethanol	218—221	50.7	5.5	15.3	$C_{19}H_{25}N_5O_8$	50.6	5.6	15.5
(7b) [b]	Ethanol–ether	166—168	50.7	5.6	15.3	$C_{19}H_{25}N_5O_8$	50.6	5.6	15.5
(8b) [c]	Ethanol–ether	229—231	60.4	9.0	11.0	$C_{13}H_{23}ClN_2O$	60.3	9.0	10.8

[a] Compound prepared by us earlier,[5] but with insufficient proof of the relative configuration. [b] Picrate; the base liberated from it is a slowly, crystallising oil. [c] Hydrochloride; the base liberated is a colourless, viscous oil.

(30 ml), dimethyl sulphate (0.63 g, 5 mmol) was added, and the mixture was refluxed for 12 h. Evaporation of the mixture to dryness gave a yellow, viscous oil, which was reduced, without isolation, according to methods (*a*), (*b*), and (*c*). The isomeric ratios of the crude reduction products are shown in Table 1.

5-*Methyl*-r-4a,t-5a,c-11a-1,2,3,4,4a,5,5a,6,7,8,9,11a-*dodecahydropyrido*[2,1-b]*quinazolin*-11-*one* (8b).—The crude products obtained on reduction of the quaternary salt (10) of the tricyclic compound (4) were combined, and the hydrochloride was prepared with ethanolic hydrogen chloride. Recrystallisation from acetone, repeated three times, gave compound (8b) with stable m.p.; its physical properties are shown in Table 5. The base liberated for the purpose of spectroscopic examination was a colourless, viscous oil.

5-*Methyl*-r-4a,c-5a,c-11a-1,2,3,4,4a,5,5a,6,7,8,9,11a-*dodecahydropyrido*[2,1-b]*quinazolin*-11-*one* (7b).—The stereohomogeneous compound (7a) (0.42 g, 2 mmol), obtained by the reduction of the tricycle (4), was stirred in acetone (20 ml) in the presence of silver oxide (1 g) and methyl iodide (1 g) at room temperature for 5 h. The reaction mixture was filtered and evaporated, to yield (7b) as a pale-yellow, viscous oil, which was identified as its picrate. Data for the picrate are shown in Table 5.

5-*Methyl*-r-4a,c-5a,t-11a-1,2,3,4,4a,5,5a,6,7,8,9,11a-*dodecahydropyrido*[2,1-b]*quinazolin*-11-*one* (5b).—Stereohomogeneous (5a), obtained from the reduction of the tricycle (3), was alkylated with methyl iodide in the presence of silver oxide, as described above, to yield compound (5b) as a viscous oil, which was identified as its picrate (see Table 5). The derivative (5b) prepared in this way and the compound resulting from the sodium borohydride reduction of the quaternary salt (9) were found by ^1H and ^{13}C n.m.r. spectroscopy to be identical; the picrates prepared from them gave no depression on mixed m.p. determination.

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