CRYSTAL AND MOLECULAR STRUCTURE OF A RIMAZOLIUM® DECOMPOSITION PRODUCT. CALCULATION OF PYRAMIDALITY OF ANALOGOUS CYCLIC AMIDES[1]

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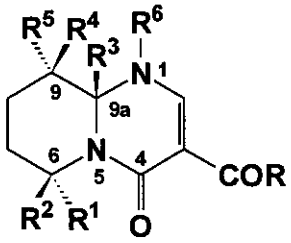
Abstract- The solid state structure of **10** was determined by X-Ray investigations, and stereostructure of 1,6,7,8,9,9*a*-hexahydro-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones were studied by semiempirical quantum chemical calculations at the AM1 level. While 9*a*-unsubstituted 1-methyl-1,6,7,8,9,9*a*-hexahydro-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones adopt a *cis*-fused conformation, 9*a*-ethoxy-1-methyl derivative has a *trans*-fused conformation to avoid a serious non-bonding interaction between 9*a*-ethoxy and 1-methyl groups in *cis*-fused one.

INTRODUCTION

There is a growing awareness of the importance of information on the stereochemistry of organic compounds, not only for understanding their reactivity[2] but also their biological activity.[3] For the determination of the ring junction Bohlmann region in the IR spectra are sometimes useful.[4] However, this phenomenon can not be applied to systems where the bridgehead nitrogen atom is linked up with a carbonyl group as the pyramidality of nitrogen atom is decreased considerable by the conjugation of neighbouring carbonyl group.

We reported earlier the structure of the biologically active[5] 1,6,7,8,9,9*a*-hexahydro-4*H*-pyrido[1,2-*a*]-pyrimidin-4-ones (**1-3**) using X-Ray diffraction and spectroscopic methods.[6, 7] These studies revealed that the ring junction of pyrimidine and piperidine ring is governed primary by the interactions between substituents at N(1), C(4), and C(9), C(6) atoms because the *trans* annelated form can transform into a *cis*

annelated form by inversion of N(5) with low energy barrier.[7, 8] The identity of structures concerning ring



1 R = NH_2, R^1 = H, R^2 = Me, R^3 = H, R^4 = R^5 = R^6 = H;
2a R = NH_2, R^1 = H, R^2 = Me, R^3 = H, R^4 = R^5 = H, R^6 = Me;
2b R = NH_2, R^1 = Me, R^2 = H, R^3 = H, R^4 = R^5 = H, R^6 = Me;
3 R = OEt, R^1 = H, R^2 = Me, R^3 = H, R^4 = R^5 = H, R^6 = Me;

junction in solution and in the solid state was confirmed by the CD investigation of the respective optically active diastereoisomers.[7] Our investigation was extended recently to a tetracyclic pyrimido[1',2':1,2]pyrido[3,2-*b*]indole ring system containing above mentioned pyrido[1,2-*a*]pyrimidin-4-one moiety.[9]

In the present paper we report on (i) the X-Ray structure determination of 9-hydroxy-9*a*-ethoxy-1,6,7,8,9,9*a*-hexahydro-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**10**) obtained as a decomposition product (see Scheme 1) during the investigation of the tautomerism[10] of an analgesic 1,6-dimethyl-3-ethoxycarbonyl-4-oxo-6,7,8,9-tetrahydro-4*H*-pyrido[1,2-*a*]pyrimidinium salt, Rimazolium® (**4**),[11, 12] (ii) the quantum chemical studies of related hexahydropyrido[1,2-*a*]pyrimidin-4-ones(**1- 3**, **10**).

RESULTS AND DISCUSSION

Preparation of 9 and 10

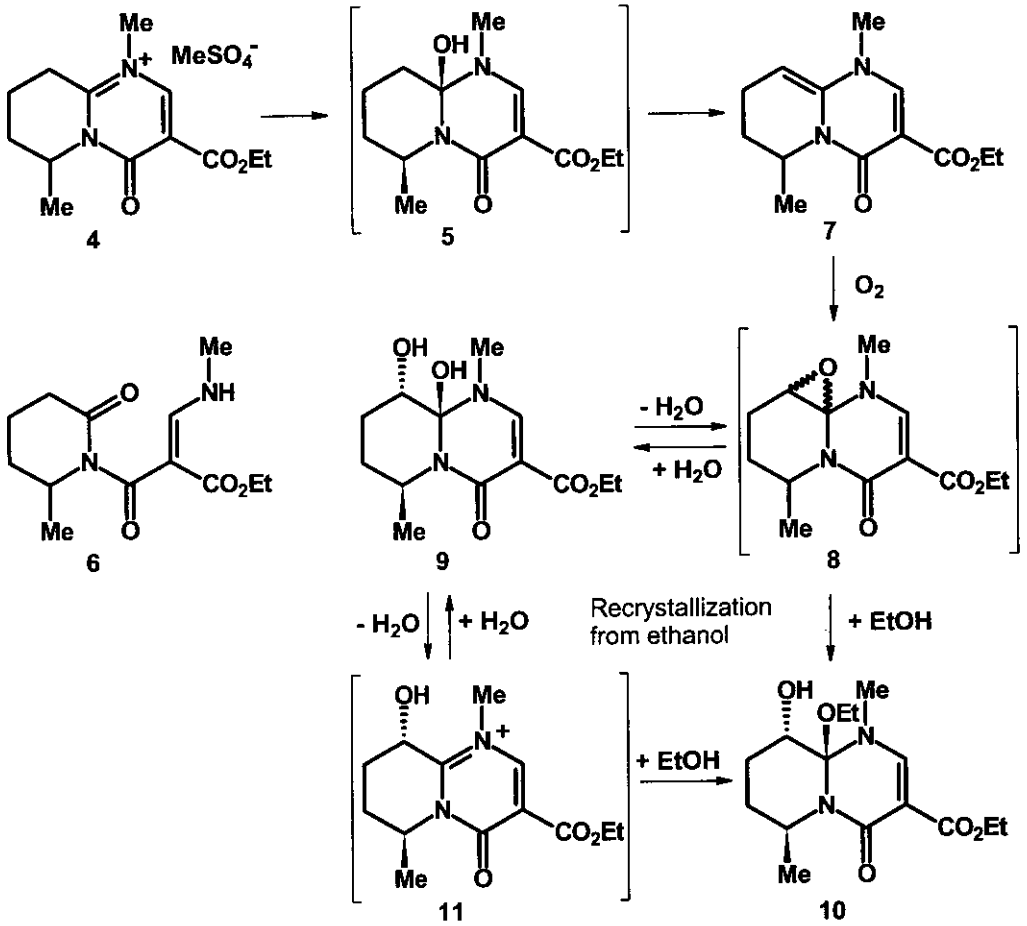
9,9*a*-Dihydroxy compound (**9**) was isolated when quaternary salt (**4**) reacted with 2*N* sodium hydroxide solution, and after the work-up of the reaction mixture (see Experimental) the oily residue was dissolved in acetone and the solution was stored in refrigerator. After 24 hours, two types of crystals **6**[10] and **9** could be isolated. When 9,9*a*-dihydroxy derivative (**9**) was recrystallized from ethanol 9-hydroxy-9*a*-ethoxy derivative (**10**) was obtained.

During the above treatment an epoxy derivative (**8**) is formed by oxidation of 1,6,7,8-tetrahydro derivative (**7**), and regioselective ring opening of the epoxy ring of **8** by the nucleophilic attack of water gave 9,9*a*-dihydroxy derivative (**9**). Ethoxy derivative (**10**) might be formed *via* formally a water-elimination-ethanol-addition process, either *via* epoxide (**8**) or tetrahydro derivative (**11**).

Structure determination of 9 and 10

A band at 3455 cm^{-1} of its IR spectrum suggests the presence of hydroxyl group in **9**. This was confirmed by the ^1H NMR spectrum (Table 4), in which two signals due to hydroxyl groups appear. One of them shows a 5.1 Hz coupling with the signal at 3.8 ppm, which can be assigned to 9-H. In the ^{13}C NMR

spectrum of **9** (Table 4) the signals C-9 and C-9*a* show an upfield shift compared to the values measured in the spectrum of the base (**7**), formed from compound (**4**)[10] where these two atoms are connected with a



Scheme 1

double bond. The chemical shifts of C-9 (64.8 ppm) and C-9*a* (95.7 ppm) in compound (**9**) are in agreement with sp^3 hybrid carbon atoms connected to an oxygen atom, and an oxygen and two nitrogen atoms, respectively. All these data suggest that compound (**9**) is a 9,9*a*-dihydroxy derivative. In order to clarify the stereochemistry we intended to perform X-Ray structure determination. Recrystallization of **9** from ethanol gave 9*a*-ethoxy derivative (**10**) (Scheme 1). Atomic numbering and the conformation of **10** is shown in Figure 1 for the 9*aR* enantiomer. Atomic coordinates are given in Table 1, bond lengths, angles and torsional angles are summarised in Table 2. There is a delocalized bond system in the pyrimidine ring including N(1), C(2), C(3), C(4), N(5), O(17) atoms. The analysis of the endocyclic torsion angles and the ring puckering parameters indicate that the pyrimidine ring has a flat ^{C9a}E envelope conformation while the piperidine ring adopts a $^{C6}C_{C9}$ chair conformation in accordance to similar other

hexahydro derivative (compound **1**) of *trans* type. The sign of the torsion angles of the junction at the N(5)-C(9*a*) bond is opposite corresponding to *trans* ring junction. Based on the sign sequence of the endocyclic torsion angles[13] the O(20) atom is in axial position towards both the piperidine ring and the pyrimidine ring above the bicycle. The O(19) hydroxyl is also in axial position below the piperidine ring. The relative *trans* position of the two oxygen atoms at C(9) and C(9*a*) makes the existence of intermediate product with the epoxy ring plausible.

Table 1. Atomic coordinates and U(eq) values with e.s.d.'s for **10**

Definition of U(eq): U(eq)=[u11+u22+u33++u23.b*.c*.b.c.cosα+u13.a*.c*.cosβ+u12.a*.b*.a.b.cosγ]/3

	x/a	y/b	z/c	U(eq)		x/a	y\b	z/c	U(eq)
N1	.0759(3)	-.3966(3)	.2218(2)	.045(2)	H6	.3887	-.1875	.2207	.0574
C2	.0954(3)	-.4075(3)	.3378(3)	.041(3)	H71	.3594	-.1465	.0273	.0647
C3	.1959(3)	-.3729(3)	.4027(3)	.036(2)	H72	.2359	-.1144	.1040	.0648
C4	.2880(3)	-.3171(3)	.3445(3)	.036(2)	H81	.2500	-.2930	-.0566	.0643
N5	.2617(3)	-.3007(2)	.2253(2)	.035(1)	H82	.1675	-.1836	-.0809	.0644
C6	.3534(4)	-.2393(3)	.1670(3)	.045(2)	H9	.0547	-.3320	.0000	.0593
C7	.2903(4)	-.1740(3)	.0696(3)	.053(2)	H141	.3594	-.3125	.7500	.0944
C8	.2048(4)	-.2361(3)	-.0149(3)	.056(2)	H142	.2158	-.3684	.7632	.0944
C9	.1099(4)	-.2885(3)	.0514(3)	.046(2)	H151	.4434	-.4590	.7207	.1310
C9a	.1697(3)	-.3563(3)	.1506(3)	.036(2)	H152	.3582	-.4868	.8340	.1310
C11	.1985(4)	-.3938(3)	.5280(3)	.049(2)	H153	.3105	-.5236	.6890	.1310
O12	.1214(2)	-.4396(2)	.5751(2)	.058(2)	H161	.5000	-.3320	.1934	.0679
O13	.2930(3)	-.3512(3)	.5910(2)	.085(2)	H162	.5273	-.2500	.1094	.0679
C14	.3007(5)	-.3687(5)	.7200(4)	.089(3)	H163	.4160	-.3535	.0547	.0679
C15	.3564(6)	-.4625(6)	.7434(6)	.136(5)	H181	-.0840	-.4785	.2207	.0880
C16	.4570(4)	-.3032(4)	.1259(4)	.058(2)	H182	.0000	-.5000	.1094	.0880
O17	.3820(2)	-.2809(2)	.3944(2)	.051(1)	H183	-.0840	-.3945	.1094	.0880
C18	-.0349(4)	-.4411(5)	.1608(4)	.077(3)	H19	-.0293	-.1875	.0547	.0809
O19	.0351(3)	-.2172(2)	.1044(2)	.067(2)	H211	.227	-.5625	.1953	.0657
O20	.2208(2)	-.4368(2)	.0884(2)	.039(1)	H212	.3320	-.4785	.2207	.0657
C21	.2771(4)	-.5176(3)	.1588(4)	.051(2)	H221	.4180	-.5410	.0566	.0776
C22	.3399(4)	-.5874(3)	.0799(4)	.064(3)	H222	.3734	-.6559	.1238	.0776
H2	.0273	-.4375	.3887	.0547	H223	.2831	-.6070	.0018	.0776

The atoms N(1), C(2), C(4) and N(5) are sp^2 in character. The H(19) atom form bifurcated hydrogen bonds with two symmetry transformed oxygen:

H(19)...O(13) [x+1/2,1/2-y,1/2+z] 2.09 Å, O(19)...O(13) 2.794 Å, O(19)-H(19)...O(13) 130°,

H(19)...O(17) [x+1/2,1/2-y,1/2+z] 2.04 Å, O(19)...O(17) 2.811 Å, O(19)-H(19)...O(17) 135°.

The piramidality parameters defined by Dunitz and his coworkers for the characterization of enamines and amides[14] have been applied and slightly modified by us in order to use them for the description of the pyramidality of the bridgehead atoms (χN5 and χC9*a*). For the characterisation of the type of ring

junction we introduced parameter JUN:

$$\chi N5 = \tau 9,9a,5,6 - \tau 9,9a,5,4 + 180$$

$$\chi C9a = \tau 1,9a,5,4 - \tau 9,9a,5,4 + 180$$

$$\tau N5,C9a = (\tau 1,9a,5,4 + \tau 9,9a,5,6)/2$$

$$JUN = \sin(\chi N5) * \sin(\chi C9a)$$

In the case of *cis* juction JUN > 0, for *trans* JUN <= 0. The adventage of the use of JUN is that its value is independent of the chirality of the molecule.

In our previous paper[7] on the hexahydropyrido[1,2-*a*]pyrimidin-4-ones we have analysed the influence of the substituents at the 1,9 positions on the type of ring junction of the hexahydropyrido[1,2-*a*]pyrimidine ring. *trans*-Type junctions was found only in the case of 1-desmethyl derivative. We explained this with 1,3-*syn*-diaxial interactions of substituents at positions 1 and 9. Although compound (**10**) is an 1-methyl derivative a *trans*-type junction was observed.

Quantum chemical studies

In order to clarify the mode of junction in **10** and related compounds, semiempirical calculations were performed at the AM1 level within the MOPAC suite of programs.[15] Model structures were optimised using a gradient algorithm. The calculated equilibrium structures reproduce the experimental trends from X-Ray crystallography, as documented (Table 3). Except of compound (**1**) the calculated torsional angles agree with the experimental values to within about ±15°. This small discrepancy is thought to arise as a result of the approximations, inherent in semiempirical theory, as well as the neglect of intermolecular interactions and hydrogen bonds. The latter may be the cause of substancial difference found at compound **1**. X-Ray studies revealed a *trans*-type junction with an intermolecular hydrogen bond of N-H...O type. Quantum chemical studies not taking into account the hydrogen bonding indicates a flact *cis*-type junction.

In order to estimate individually the influence of the 9-hydroxy and 9*a*-ethoxy groups for the ring junction, the lowest energy conformers for the hypotetic 9-hydroxy-**3** and 9*a*-ethoxy-**3** derivatives were determined. At 9-hydroxy-**3** derivative *cis* ring junction was found, while at 9*a*-ethoxy-**3** derivatives *trans*-type junction indicating that for the 9*a*-ethoxy is responsible the *trans*-type junction of **10**. The type of R^2 substituent had no effect on the conformational behaviour.

When 9*a*-H atom of 1-methyl-1,6,7,8,9,9*a*-hexahydro derivative (**2a**) was changed for an ethoxy group with appropriate bond length in its *cis*-fused X-Ray structure,[7] an unfavourable non-bonding interaction developed between 9*a*-ethoxy and 1-methyl groups, as their distance (2.731Å) was shorter, than the sum of their Van der Waals values.To avoid this interaction **10** adopts a *trans*-fused conformation where this distances increase to 2.987Å.

Table 2. Bond lengths (Å), angles (°) and torsion angles (°) for **10**.

N(1)-C(2)	1.333(4)	C(2)-N(1)-C(9*a*)	122.1(5)	C(4)-C(3)-C(2)-N(1)	2.1(5)
N(1)-C(9*a*)	1.464(4)	C(2)-N(1)-C(18)	119.1(6)	C(4)-N(5)-C(9*a*)-N(1)	24.9(5)
N(1)-C(18)	1.470(5)	C(9*a*)-N(1)-C(18)	118.1(5)	N(5)-C(4)-C(3)-C(2)	2.4(5)
C(2)-C(3)	1.354(5)	N(1)-C(2)-C(3)	124.3(6)	N(5)-C(9*a*)-N(1)-C(2)	-19.3(5)
C(3)-C(4)	1.453(5)	C(2)-C(3)-C(4)	118.9(5)	C(6)-N(5)-C(9*a*)-N(1)	-169.9(5)
C(3)-C(11)	1.457(5)	C(2)-C(3)-C(11)	115.0(5)	C(8)-C(7)-C(6)-N(5)	-51.4(5)
C(4)-N(5)	1.385(4)	C(4)-C(3)-C(11)	126.1(5)	C(8)-C(9)-C(9*a*)-N(5)	51.2(5)
C(4)-O(17)	1.231(4)	C(3)-C(4)-N(5)	115.7(5)	C(9)-C(8)-C(7)-C(6)	57.8(6)
N(5)-C(6)	1.490(5)	C(3)-C(4)-O(17)	124.7(5)	C(9)-C(9*a*)-N(5)-C(4)	147.3(6)
N(5)-C(9*a*)	1.462(4)	N(5)-C(4)-O(17)	119.5(5)	C(9)-C(9*a*)-N(5)-C(6)	-47.6(5)
C(6)-C(7)	1.462(4)	C(4)-N(5)-C(6)	115.6(5)	C(9*a*)-N(1)-C(2)-C(3)	7.6(6)
C(6)-C(16)	1.518(5)	C(4)-N(5)-C(9*a*)	124.9(5)	C(9*a*)-N(5)-C(4)-C(3)	-17.4(5)
C(7)-C(8)	1.524(6)	C(6)-N(5)-C(9*a*)	117.9(5)	C(9*a*)-N(5)-C(6)-C(7)	47.7(5)
C(8)-C(9)	1.505(6)	N(5)-C(6)-C(7)	110.5(5)	C(9*a*)-C(9)-C(8)-C(7)	-56.7(5)
C(9)-C(9*a*)	1.544(5)	N(5)-C(6)-C(16)	112.8(5)	O(12)-C(11)-C(3)-C(2)	1.5(7)
C(9)-O(19)	1.415(5)	C(7)-C(6)-C(16)	113.0(6)	O(13)-C(11)-C(3)-C(4)	3.8(5)
C(9*a*)-O(20)	1.417(4)	C(6)-C(7)-C(8)	112.2(6)	C(14)-O(13)-C(11)-O(12)	3.4(6)
C(11)-O(12)	1.201(5)	C(7)-C(8)-C(9)	109.9(6)	C(15)-C(14)-O(13)-C(11)	83.1(8)
C(11)-O(13)	1.335(5)	C(8)-C(9)-C(9*a*)	111.5(5)	O(17)-C(4)-N(5)-C(6)	0.5(5)
O(13)-C(14)	1.488(6)	C(8)-C(9)-O(19)	111.1(5)	C(18)-N(1)-C(9*a*)-N(5)	170.5(6)
C(14)-C(15)	1.39(1)	C(9*a*)-C(9)-O(19)	107.1(5)	C(18)-N(1)-C(9*a*)-C(9)	47.3(6)
O(20)-C(21)	1.441(5)	N(1)-C(9*a*)-N(5)	109.8(5)	O(19)-C(9)-C(8)-C(7)	62.7(5)
C(21)-C(22)	1.495(6)	N(1)-C(9*a*)-C(9)	110.1(5)	O(19)-C(9)-C(9*a*)-N(1)	51.6(5)
		N(1)-C(9*a*)-O(20)	109.5(5)	O(19)-C(9)-C(9*a*)-N(5)	-70.5(5)
		N(5)-C(9*a*)-C(9)	111.7(5)	O(20)-C(9*a*)-N(1)-C(2)	104.8(5)
		N(5)-C(9*a*)-O(20)	112.7(5)	O(20)-C(9*a*)-N(1)-C(18)	-65.3(5)
		C(9)-C(9*a*)-O(20)	103.0(5)	O(20)-C(9*a*)-N(5)-C(4)	-97.4(5)
		C(3)-C(11)-O(12)	125.4(6)	O(20)-C(9*a*)-N(5)-C(6)	67.8(5)
		C(3)-C(11)-O(13)	113.6(6)	O(20)-C(9a)-C(9)-C(8)	-70.0(5)
		O(12)-C(11)-O(13)	120.8(6)	O(20)-C(9*a*)-C(9)-O(19)	168.3(5)
		C(11)-O(13)-C(14)	116.6(6)	C(210-O(20)-C(9*a*0-N(1)	-58.9(5)
		O(13)-C(14)-C(15)	108.4(8)	C(21)-O(20)-C(9*a*)-N(5)	63.6(5)
		C(9*a*)-O(20)-C(21)	116.1(4)	C(21)-O(20)-C(9*a*)-C(9)	-176.0(5)
		O(20)-C(21)-C(22)	108.3(5)	C(22)-C(21)-O(20)-C(9*a*)	-172.4(7)

EXPERIMENTAL

The UV spectrum was recorded in ethanol with a Unicam SP-800 spectrometer, and the IR spectrum was recorded with a Pye Unicam SP-1100 IR apparatus in potassium bromide disk. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker WP-80 instrument at 80 and 20.1 MHz respectively (Table 4).

Rimazolium® (**4**) (40 g) was dissolved in 2*N* sodium hydroxide (400 mL) and was left to stand for 30 min. The solution was mixed with chloroform (5 x 40 mL) in separating funnel. The combined chloroform phase was dried over anhydrous sodium sulphate then the solution was condensed in vacuum to 50 mL. Following addition of water (50 mL) the two phases are mixed and separated. The chloroform phase was allowed to stand for 5 min at 30 °C and condensed in vacuum again. The residual oil was dissolved in acetone (15 mL) and was allowed to stand for for one day in refrigerator. Two types of

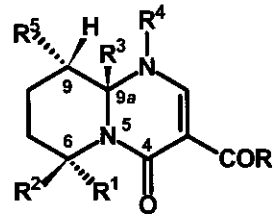


Table 3. Experimental (bold) and calculated torsion angle values of **1**, **2a**, **2b**, **3**, and **10**.

	R	R^1	R^2	R^3	R^4	R^5	C(9)-C(9a)-N(5)-C(6)	C(9)-C(9a)-N(5)-C(4)	N(1)-C(9a)-N(5)-C(4)	R^5-C(9a)-N(1)-R^4	χN(5)	χC(9a)	JUN
2a	**NH_2**	**H**	**Me**	**H**	**Me**	**H**	**-62.3**	**91.3**	**-33.8**	**-44.1**	**26.4**	**54.9**	**0.364**
							-54.2	107.5	-20.0	-55.9	18.3	52.5	0.249
2b	**NH_2**	**Me**	**H**	**H**	**Me**	**H**	**-65.9**	**80.3**	**-44.1**	**-32.9**	**33.8**	**55.6**	**0.459**
							-57.7	93.5	-32.9	-31.8	28.8	53.6	0.388
3	**OEt**	**H**	**Me**	**H**	**Me**	**H**	**-64.0**	**95.2**	**-30.4**	**-39.6**	**20.8**	**54.6**	**0.289**
							-53.9	103.8	-23.6	-53.4	22.3	52.6	0.301
	OEt	H	H	H	Me	OH	-52.4	101.6	-25.8	-27.0	26.0	52.6	0.348
	OEt	H	Me	H	Me	OH	-53.8	103.7	-23.6	-27.5	22.5	52.7	0.304
	OEt	H	H	OEt	Me	H	-52.1	159.5	35.4	-96.2	-31.5	55.9	-0.433
	OEt	H	Me	OEt	Me	H	-49.4	159.8	36.1	-96.1	-29.2	56.3	-0.406
10	**OEt**	**H**	**Me**	**OEt**	**Me**	**OH**	**-47.6**	**147.3**	**24.9**	**-65.3**	**-14.9**	**57.6**	**-0.217**
							-51.7	159.5	35.1	-95.2	-31.2	55.6	-0.427
1	**NH_2**	**H**	**Me**	**H**	**H**	**H**	**-54.4**	**146.4**	**24.1**	**-82**	**-20.8**	**57.7**	**-0.300**
							-53.1	116.6	-10.7	-74.3	10.3	52.7	0.142

crystals was formed [**6**[10] and **9**]. **9**: UV (96% Ethanol): 290 nm and 225 nm; IR (KBr disc): 3455 cm $^{-1}$ [m, ν_{OH}], 3210 cm^{-1} [br, ν_{NH}], 1722 cm^{-1} [s, $\nu_{C=O}$ (COO)], 1633 cm $^{-1}$ [s, $\nu_{C=O}$ (C4=O)]. Compoud (**9**) was purified by recrystallization from acetone. Recrystallization of **9** from ethanol resulted in good quality single crystals of **10**.

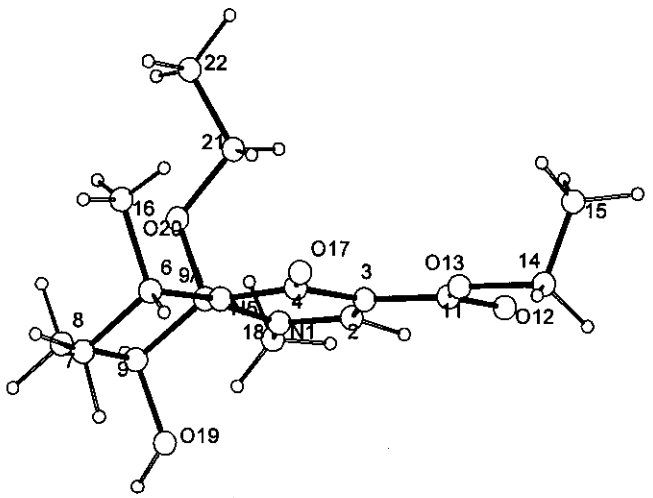


Figure 1. PLUTO diagram for the 9*aR* enantiomer of **10** with crystallographic atomic numbering. The plane of the C(3), N(5),and C(9*a*) atoms is perpendicular to the plain of the drowing. The N(5)-C(9*a*) bond is at an angle of 10° to the normal to the plane of the drowing.

Table 4. NMR parameters for compounds (**9**) and (**10**) in DMSO-d_6

Proton	**9**	**10**	Carbon-13	**9**
2-H	7.90 s	8.05 s	C-2	153.7
6-H	4.70 m	4.77 m	C-3	90.9
7,8-H_2	2.20-1.25 m	2.25-1.30 m	C-4	159.1
9-H	3.80 m	3.85 m	C-6	42.7
N-CH_3	3.18 s	3.12 s	C-7	22.2
6-CH_3	1.13 d	1.15 d	C-8	22.2
$COOCH_2$	4.05 q	4.05 q	C-9	64.8
OCH_2CH_3	1.12 t	1.18 t	C-9*a*	95.7
9-OH	4.97 d	5.15 d	3-COO	164.3
9*a*-OH	7.04 s		OCH_2	58.2
9*a*-OCH_2		3.05 q	CH_3	14.5
9*a*-OCH_2CH_3		1.10 t	6-CH_3	20.5
			N(1)-CH_3	36.2

Crystallography

Appropriate single crystals of compound (**10**) were obtained after recrystallizing from ethanol, and the crystal data are as follows: monoclinic, a = 10.957(1), b = 13.161(4), c = 11.431(1) Å, β = 94.81(1)°, de-

termined from the angular settings of 25 reflections, V = 1642.6 $Å^3$, D_X = 1.263 g, cm^{-3}, Z = 4, (μMoKα = 0.7107 Å) = 1.021 cm^{-1}, space group $P2_1/n$ from systematic absences; 2875 independent reflections were collected on an ENRAF-NONIUS CAD/4 four-circle diffractometer using monochromated Mo-Kα radiation. After conventional data reduction, 2102 reflections with I)2σ (I), all atoms were found by direct methods and refined by the ENRAF-NONIUS SDP program package. After two cycles of anisotropic refinement, the hydrogen atom positions were determined from difference Fourier map, but their positions were not refined. The final R-values for the 2102 observed reflections are R = 0.073, R_W = 0.099, (fudge factor, p = 0.01). The final coordinates are given in Table 1.

Table 4. NMR parameters for compounds (**9**) and (**10**) in DMSO-d_6

Proton	**9**	**10**	Carbon-13	**9**
2-H	7.90 s	8.05 s	C-2	153.7
6-H	4.70 m	4.77 m	C-3	90.9
7,8-H_2	2.20-1.25 m	2.25-1.30 m	C-4	159.1
9-H	3.80 m	3.85 m	C-6	42.7
N-CH_3	3.18 s	3.12 s	C-7	22.2
6-CH_3	1.13 d	1.15 d	C-8	22.2
$COOCH_2$	4.05 q	4.05 q	C-9	64.8
$OCH_2\underline{CH_3}$	1.12 t	1.18 t	C-9*a*	95.7
9-OH	4.97 d	5.15 d	3-COO	164.3
9*a*-OH	7.04 s		OCH_2	58.2
9*a*-OCH_2		3.05 q	CH_3	14.5
9*a*-$OCH_2\underline{CH_3}$		1.10 t	6-CH_3	20.5
			N(1)-CH_3	36.2

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Received, 10th July, 1997