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RING TRANSFORMATION OF 4-OXO-1,6,7,8-TETRAHYDRO-4H-PYRIDO-[1,2-a]PYRIMIDINE-3-CARBOXAMIDE[1]

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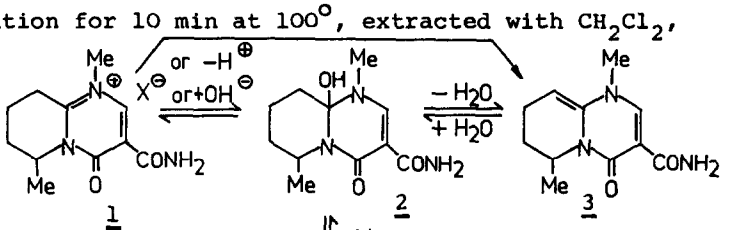
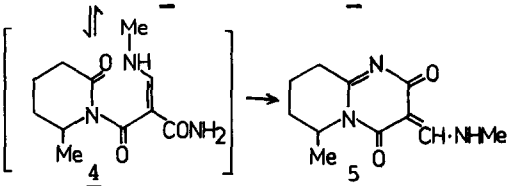
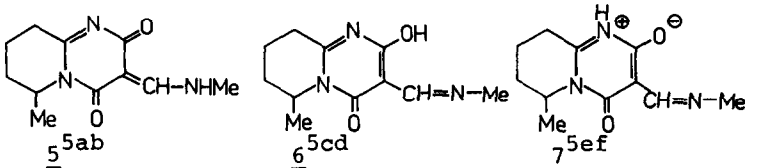
The title compound /3/ may be transformed into the 3-/methylaminomethylene/--2,3,6,7,8,9-hexahydro-4H-pyrido[1,2-a]pyrimidine-2,4-dione /5E, 5Z/ which is in equilibrium with the 1,2,3,6,7,8-hexahydro tautomer /8E, 8Z/ in DMSO-d_6.

We have observed a novel rearrangement of the pyrido[1,2-a]pyrimidines when 1[2] or 3 /which have analgetic, and trombocita aggregation inhibiting effects[3]/ was heated in aqueous $NaHCO_3$ solution for 10 min at 100°, extracted with CH_2Cl_2, [Y:94%, mp. 157-9°C /EtOAc/]



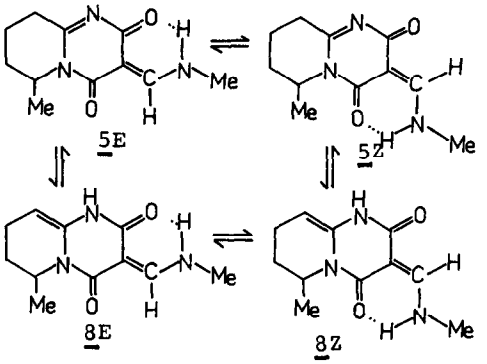
Knowing[4] the behaviour of the quaternary salts of type 1 the new compound 5 was proposed to form in an irreversible water elimination from the amino-ketone 4. Based on earlier studies[5] three tautomers /5-7/ were considered. The low mp. of the product rendered form 7 improbable, while 5 and 6 could readily be distinquished by ^1H n.m.r.





In $CDCl_3$ the N-Me signal /δ=3.42/ appeared as a doublett indicating the predominance of 5. Duplication of both the =CH-NH /8.28d and 8.30d/ and =CH-NH signals /10.35m and 11.40m/ suggested a mixture of Z and E isomers /ratio 1:4/. The value of $J_{=CH-NH-}$=13.5Hz indicated an antiperiplanar disposition of these coupled protons in both 5Z and 5E. The large shifts for the NH protons suggest hydrogen bonding with the C(2)=O and C(4)=O oxygens, respectively. Since due to conjugation the negative polarization of the C(2)=O oxygen is higher, a stronger hydrogen bonding and hence larger chemical shift for NH is expected in 5E.

The 6-Me group is quasi-axial as shown by the large shift of 6-H /δ 4.87m/ and by the coupling constants /$J_{6e7e} \approx J_{6e7a} \approx 3$Hz/. The quasi-equatorial position is disfavoured by A/1-3/ type allylic strain[6] caused by the C(4)=O group. The C(9) methylene protons are mobile[4a] and can be exchanged for deuterium with D_2O.



In DMSO-d_6 beside the 2,3,6,7,8,9-hexahydro tautomeric form /5E, 5Z/ signals associated with the 1,2,3,6,7,8-hexahydro tautomer /8E, 8Z/ can be identified: broad N(1)-H singlets at 9.31 and 9.39; and a multiplet for C(9)-H at 4.20[7]. Based on the intensities of the signals for C(9)methylene /in 5/ and C(9)methine /in 8/ the ratio of 5 and 8 is 75:25. Both tautomers show E-Z isomerism, ratio in 5 is 4:1; in 8 1:1. Because of the similar polarization of the two carbonyls of 8 the assignment of 8E and 8Z becomes problematic. The enamine 8 is probably stabilized by hydrogen bonding with the solvent.

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^{1}H n.m.r. Chemical shifts, ppm, /Intensity/ JEOL-PS-100 /in $CDCl_3$-TMS/

	6-CH	7- and 8-CH_2	9-CH_2	6-Me	=CH-NH-	=CH-NH-	N-Me	9-CH=	1-NH	ratio
5E	4,87m /1H/	1,85-2,15m /4H/	2,85-3,00m /2H/	1,35d /3H/	8,28d /0,8H/	11,40m /0,8H/	3,42d /3H/	-	-	80
5Z					8,30d /0,2H/	10,35m /0,2H/				20

/in DMSO-d_6-TMS/

5E	4,72m /1H/	1,50-2,35m /4H/	2,65-2,90m /0,75 x2H/	1,25d /0,75 x3H/	8,29d /0,6H/	11,15m /0,6H/	3,35d /0,75 x3H/	-	-	60
5Z					8,23d /0,15H/	10,35m /0,15H/				15
8E and 8Z				1,06d and 1,09d /0,25 x3H/	7,76d /0,12H/ and 7,80d /0,12H/	9,30m /0,25H/	3,19d /0,25 x3H/	4,20m /0,25H/	9,31s /0,12H/ and 9,39s /0,12H/	12,5 ----- 12,5

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