Tetrahedron Letters No. 16, pp 1447 - 1450, 1978. Pergamon Press. Printed in Great Britain.

SYNTHESIS OF 3,9-DIMETHYLGUANINE AND ITS CONVERSION INTO 3-METHYL-WYE (Yt BASE), A MODEL SUBSTANCE OF WYOSINE, WYBUTOSINE AND WYBUTOXINE.

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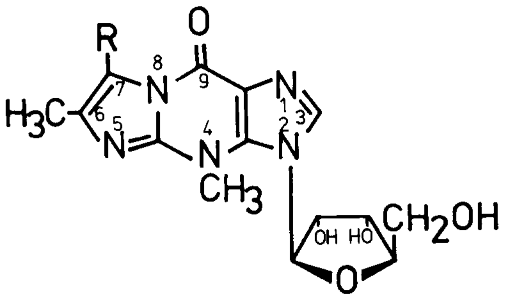
(Received in UK 24 February 1978; accepted for publication 3 March 1978)

Three fluorescent Y nucleosides, wybutosine (1)[1-5], wybutoxine (2)[6-8] and wyosine (3)[9] have been found and isolated as minor components in various tRNAs and unusual structures as 4,6-dimethyl-imidazo[1.2-a]purine-N-3-ribofuranoside derivatives have been proposed.

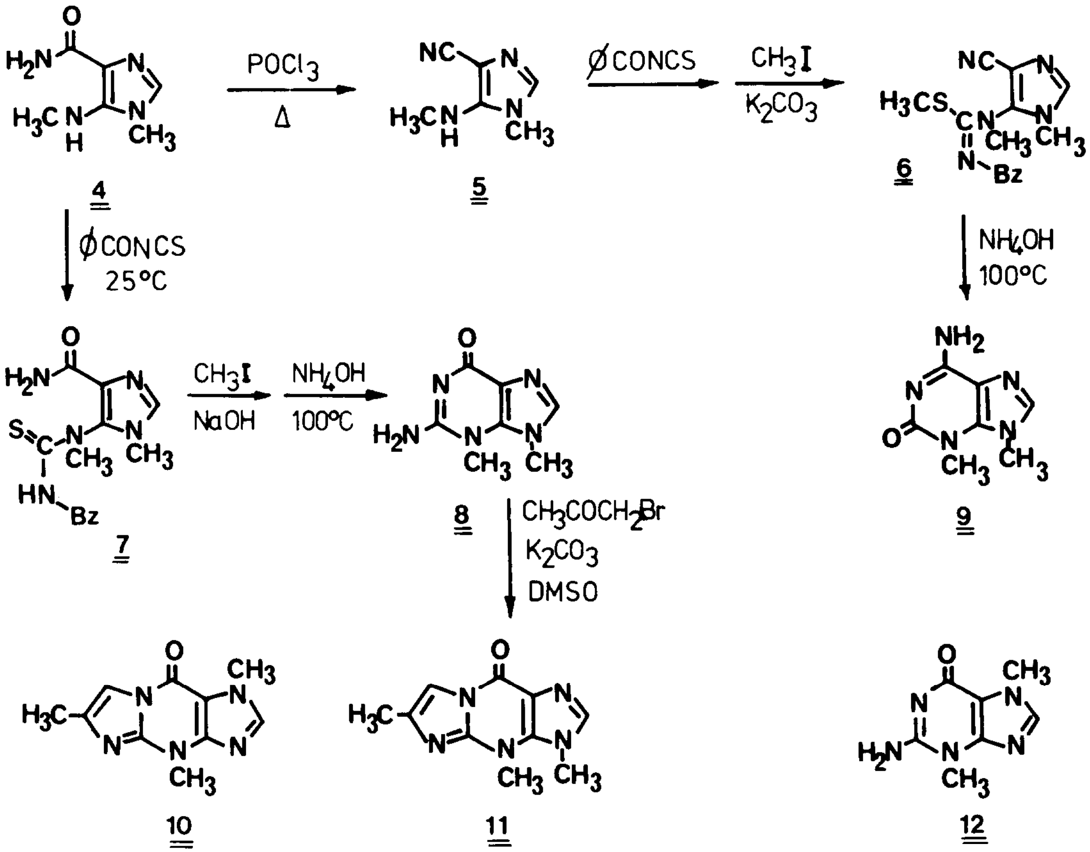


	R
1	$CH_2\text{-}CH_2\text{-}\underset{COOCH_3}{CH}\text{-}NHCOOCH_3$
2	$CH_2\text{-}\underset{OOH}{CH}\text{—}\underset{COOCH_3}{CH}\text{-}NHCOOCH_3$
3	H

The structural elucidations have been based on chemical degradations to the corresponding supermodified bases and their investigations by physical means such as u.v., n.m.r. and mass spectra. The synthesis, however, of neither of these Y nucleosides nor of any N-3 substituted structural analog has yet been reported due to the synthetic difficulties in principle encountered by a strong steric interference of 3,9-disubstituted purine derivatives in general

3,9-Dimethylguanine (8) is therefore an unknown compound since methylation of the 3-methylguanine will proceed at N-7 whereas the 9-methylguanine will react at N-1 and N-7 respectively.

In order to rationalize the synthesis of 8 we started from 1-methyl-5-methylamino-imidazole-4-carboxamide (4)[10] and followed a reaction sequence ana-



Physical Data

	NMR-Spectra in DMSO-d_6 or $CDCl_3$ *)						UV-Spectra at pH 7					
	7-CH_3 1-CH_3	9-CH_3 3-CH_3	3-CH_3 4-CH_3	6-CH_3	8-H 2-H	7-H	λ_{max} (nm)			lg ε		
8		3.87	3.64		7.49			265			4.04	
9		3.98	3.68		7.94			279			4.07	
12	3.92		3.58		8.04			270			3.76	
10 *)	4.18		3.90	2.33	7.61	7.35	233	265	311	4.48	3.72	3.79
11 *)		4.10	4.00	2.30	7.23	7.37	233	262	295	4.54	3.62	3.88
3[9]							236		295			

logous to the synthesis of guanine from AICA (5-amino-imidazole-4-carboxamide)[11]. Treatment of 4 with benzoylisothiocyanate led to the thiourea derivative 7 which after alkylation by methyl iodide at the sulfur atom reacted with ammonia at 100° for 2 h with cyclization giving 3,9-dimethylguanine (8) in an overall yield of 59 %. 8 crystallizes with 1/2 H_2O and melts with decomposition at 326°. The conversion of 3,9-dimethylguanine (8) into 10 could be achieved by bromoacetone in DMSO in presence of potassium carbonate forming the fluorescent 3-methyl-wye (11) (m.p. 296-297°) in 76 % yield.

4 is also a good starting material for the synthesis of 3,9-dimethylisoguanine (9), which has previously been obtained by a different route[12]. On treatment of 4 with phosphorous oxychloride a quantitative dehydration to 1-methyl-5-methylamino-imidazole-4-carbonitrile (5) is observed. Further reaction with benzoylisothiocyanate led to the corresponding thiourea derivative, which was methylated by methyl iodide to give 6. Subsequent treatment with 25 % ammonia at 100° over night afforded 3,9-dimethylisoguanine (9) which could be isolated in 65 % overall yield (m.p. $>$ 350°) and was proved to agree in its physical properties with the reported data[12].

It is noticed from n.m.r.-spectra that in 3,9-dimethylguanine (8) and 3-methyl wye (11) respectively the proton signals of the imidazole rings occur at fairly high field in comparison to the corresponding 3,7-(12)[13,14] and 1,4-dimethyl derivatives (10) probably due to a stronger mesomeric interaction of the CO-group and the imidazole moiety in the latter compounds. Furthermore the signals of the peri-located N-methyl groups are shifted towards each others showing much smaller $\Delta\delta$ values than any other isomer.

A comparison of the u.v.-spectra of 3, 10 and 11 reveals a close similarity of 3 and 11 whereas 10 shows a bathochromic shift of the longwave absorption band and a lower extinction coefficient as also seen in the 3,9-(8), 3,7-dimethylguanine (12) pair. These results may be regarded as evidence for attachment of the ribofuranosyl moiety at N-3 in wyosine (3) and its analogs 1 and 2 respectively. However, conclusive proof of these structures must await a total synthesis which is already under progress for 3.

ACKNOWLEDGEMENT

We thank Drs. M. Hattori, R.L.N. Harris and J. Engels for valuable discussions and the Deutsche Forschungsgemeinschaft for supporting this project.

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