

RING TRANSFORMATION OF PTERINS TO GUANINES

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Abstract — 7-Alkoxypterins undergo a ring contraction into
guanine derivatives and demethoxylation by activated aluminum.

The interconversion between guanine and pterin is of particular interest because the ring conversion of guanosine triphosphate to 7,8-dihydroneopterin triphosphate is the common and key step in the biosynthesis of tetrahydrofolic acid and tetrahydrobiopterin. An analogous transformation of a purine to a pteridine has been affected chemically,¹ but the reverse ring contraction has been reported only a little.² Described herein is a new ring contraction of pterins³ to guanines. Treatment of 7-methoxypterin (1a) with aluminum activated by mercuric chloride in aqueous methanol containing ammonia gave 8-methylguanine (2a) together with a small amount of demethoxylated pterin 3a. 7-Ethoxy- and 7-isopropoxypterins (1b and 1c) and 7-methylthiopterin (1d) were employable to the reaction, but 7-hydroxypterin, isoxanthopterin, was intact under these conditions. Reactions of

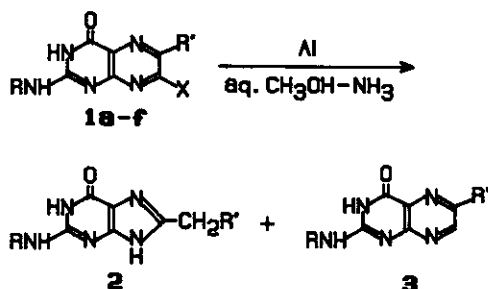
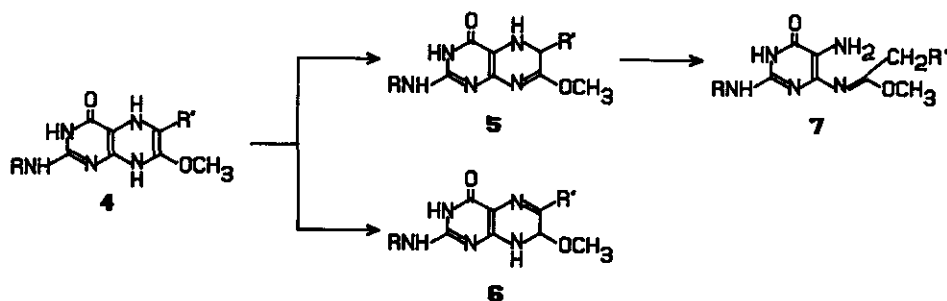


Table 1. Reaction of Pterin (1) with Al

1	R	R'	X	product ^a (yield%)
a	H	H	CH ₃ O	2a (73), 3a (8)
b	H	H	C ₂ H ₅ O	2a (34), 3a (12)
c	H	H	i-C ₃ H ₇ O	2a (45), 3a (10)
d	H	H	CH ₃ S	2a (55), 3a (8)
e	H	CH ₃	CH ₃ O	2b (42), 3b (14)
f	CH ₃	H	CH ₃ O	2c (38), 3c (22)

^aThe structures were confirmed by direct comparison with authentic samples.

2a and 3a: R = R' = H; 2b and 3b: R = H,
R' = CH₃; 2c and 3c: R = CH₃, R' = H



7-methoxy-6-methylpterin (1e) and 2-methylamino derivative 1f gave the corresponding mixture of guanine and demethoxylated pterin, respectively. Results are summarized in Table 1. Other metals, e.g. sodium, magnesium, and zinc, did not give the ring contracted products under similar conditions.

The conversion seems to proceed by the initial formation of 5,8-dihydropterin (4) as the common intermediate, which isomerizes to give 5,6-dihydro (5) and 7,8-dihydro derivatives 6. The former may be further reduced to a ring opened iminoether 7 and then cyclized to furnish 2a with elimination of methanol. The latter 6 is a methanol adduct⁴ of 3a, and is expected to easily generate 3a by elimination of methanol.

A mixture of 1a (450 mg) and activated Al² (3 g) in 50 % aq. CH₃OH (150 ml) containing 28 % aq. ammonia (5 ml) was stirred at room temperature for 10 h. The mixture was filtered and the solid was washed with 1 % aq. ammonia (50 ml). The combined filtrate and washing were concentrated to a volume of 50 ml and acidified by addition of formic acid. This was fractionated on a Florisil column by elution with 0.5 % aq. ammonia to give 2a (260 mg) and 3a (30 mg).

REFERENCES

1. (a) A. Albert, Biochem. J., 1957, **65**, 124; (b) K. Eistetter and W. Pfeleiderer, Chem. Ber., 1973, **106**, 1389; (c) K. Eistetter and W. Pfeleiderer, Chem. Ber., 1974, **107**, 575.
2. T. Sugimoto, N. Nishioka, S. Murata, and S. Matsuura, Heterocycles, 1986, **24**, 1565. The preparation of activated aluminum is described in this paper.
3. 2-Amino-4-oxo-(3H)-pteridine is abbreviated as pterin.
4. A. Albert and W. L. F. Armarego, in "Advances in Heterocyclic Chemistry", eds by A. R. Katritzky, A. J. Bourton, and J. M. Lagowski, Academic Press, New York, 1965, Vol. 4, pp. 1-42.

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