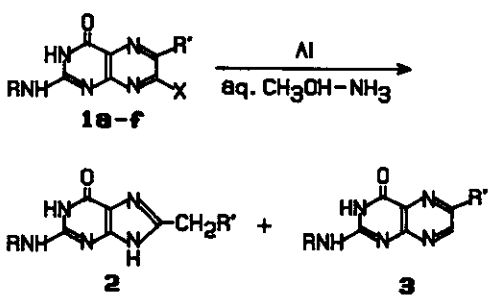
RING TRANSFORMATION OF PTERINS TO GUANINES

Takashi Sugimoto*, Noriko Nishioka, Shizuaki Murata,
and Sadao Matsuura
Department of Chemistry, College of General Education,
Nagoya University, Chikusa-ku, Nagoya 464, Japan

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 pterins[3] 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

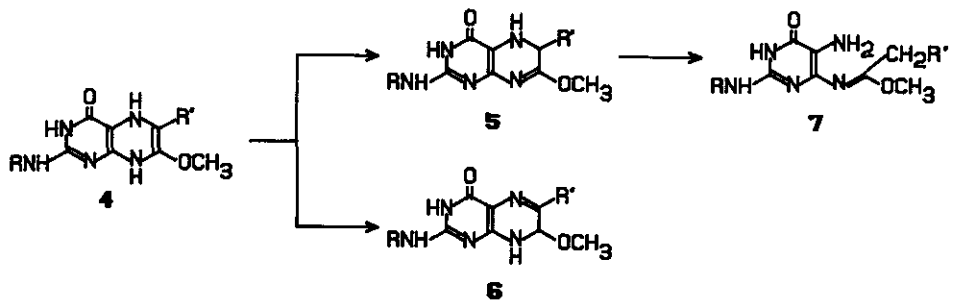


2a and **3a**: R = R´ = H; **2b** and **3b**: R = H, R´ = CH_3; **2c** and **3c**: R = CH_3, R´ = H

Table 1. Reaction of Pterin (1) with Al

1	R	R´	X	product[a] (yield/%)
a	H	H	CH_3O	**2a** (73), **3a** (8)
b	H	H	C_2H_5O	**2a** (34), **3a** (12)
c	H	H	i-C_3H_7O	**2a** (45), **3a** (10)
d	H	H	CH_3S	**2a** (55), **3a** (8)
e	H	CH_3	CH_3O	**2b** (42), **3b** (14)
f	CH_3	H	CH_3O	**2c** (38), **3c** (22)

[a]The structures were confirmed by direct comparison with authentic samples.



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 adduct[4] of **3a**, and is expected to easily generate **3a** by elimination of methanol.

A mixture of **1a** (450 mg) and activated Al[2] (3 g) in 50 % aq. CH_3OH (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. Pfleiderer, Chem. Ber., 1973, **106**, 1389; (c) K. Eistetter and W. Pfleiderer, 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.

Received, 30th April, 1987