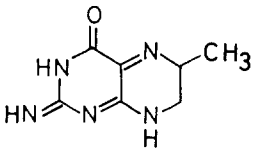
Tetrahedron Letters,Vol.26,No.33,pp 4003-4004,1985 0040-4039/85 $3.00 + .00
Printed in Great Britain

SYNTHESIS OF QUINONOID 6-METHYL- AND 6,7-DIMETHYLDIHYDROPTERINS[1]

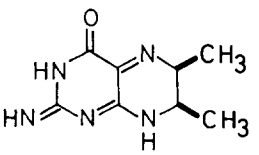
Sadao Matsuura*, Takashi Sugimoto, and Shizuaki Murata
Department of Chemistry, College of General Education, Nagoya University
Chikusa-ku, Nagoya, 464 JAPAN

Abstract: Quinonoid 6-methyl- and 6,7-dimethylpterins were synthesized by the chemical oxidation. Some of their properties are described.

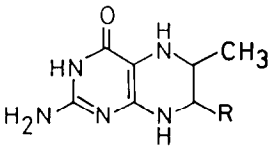
Quinonoid 6-methyl- and 6,7-dimethyldihydropterins (1 and 2) are important metabolic intermediates of the pseudocofactors in the enzymatic hydroxylation of phenylalanine, tyrosine, and tryptophan.[2] These compounds should be the key components to resolve the biosynthetic routes of the neurotransmitting substances, but their properties have been discussed only on the samples prepared *in situ*.[3] Neither biological nor chemical synthesis of them has been succeeded because of their instabilities. Described herein are synthesis and some properties of the quinonoid dihydropterins 1 and 2.



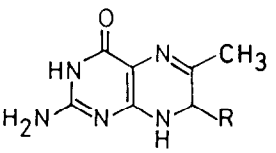
1



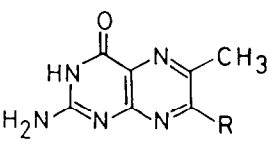
2



3,4



5,6



7,8

3,5,7: R = H 4,6,8: R = CH_3

To a solution of 6-methyl-5,6,7,8-tetrahydropterin (**3**) dihydrochloride (960 mg, 3.5 mmol) and KI (19 mg, 0.15 mmol) in H_2O (8 ml) was added 30% H_2O_2 (0.34 ml, 3.5 mmol) at 0 °C, and the mixture was stirred for 5 min. The pale yellow crystals (hydrochloride of **1**, 535 mg, 70% yield, mp. 230 °C (dec)) were obtained by filtration and washing with cold THF. Quinonoid 6,7-dimethyldihydropterin (**2**) was obtained as the hydrogen sulfate (10%) from 6,7-dimethyl-5,6,7,8-tetrahydropterin (**4**) dihydrochloride by a similar procedure: mp. 158—162 °C (dec).

The onium salts of **1** and **2**, thus obtained, could be stored in a refrigerator for a long period. The IR (KBr disk) absorptions at 1750 cm^{-1} (**1**) and 1740 cm^{-1} (**2**) were typical of the quinonoid dihydropterin structure. Once **1** or **2** were dissolved, a rapid decomposition started. The time-alternations of their UV spectra in pH 7.0 were consistent with the reported results.[3] The isomerization of **1** to the 7,8-dihydropterin **5** was the main process in pH 7.0 as described previously.[3] When the solution of **1** in pH 3.0 hydrochloric acid was examined by the HPLC (column: Partisil SCX, eluant: 30 mM ammonium phosphate buffer containing with 3 mM $NaHSO_3$ pH 3.2), unexpectedly, the disproportionation to **3** and **7** was observed as the major pathway (65%) together with the isomerization (35%).[4] Similar results, **2** ⟶ **4** + **8** in pH 3.5 and **2** ⟶ **6** in pH 7.0, were observed.[4] Fortunately, the decompositions were not so rapid for the measurement of ^1H NMR spectra,[5] which strongly supported the illustrated p-quinonoid structures of **1** and **2**.

The authors acknowledge to Chemical Instrument Center in Nagoya University for the kindly help to observe the NMR spectra. This research was supported by the grant-in-Aids for Scientific Research, No.58540332 from the Japanese Ministry of Education, Science and Culture.

References and Notes

1. Studies on the biologically active pteridines part IX. Part VIII is Matsuura, S.; Sugimoto, T.; Nagatsu, I.; Nagatsu, T. Biogenic Amines **1984**, 1, 259—266.
2. Kaufman, S. Adv. Enzymol. **1971**, 35, 245—319.
3. (a) Lazarus, R. A.; DeBrosse, C. W.; Benhovic, S. J. J. Am. Chem. Soc. **1982**, 104, 6871—6872; (b) Kaufman, S. J. Biol. Chem. **1964**, 239, 332—338; (c) Nielsen, K. H.; Simonsen, V.; Lind, K. E. Eur. J. Biochem. **1969**, 9, 497—502; (d) Archer, M. C.; Scrimgeour, K. G. Can. J. Biochem. **1970**, 48, 278—287.
4. Retention volumes of pterins were as follows: **1**, 3.96 ml; **2**, 4.24 ml; **3**, 13.28 ml; **4**, 17.32 ml; **5**, 15.52 ml; **6**, 23.58 ml; **7**, 9.36 ml; **8**, 15.32 ml.
5. 500 MHz ^1H NMR (D_2O): **1**, 1.43 (d, J = 6.0 Hz, CH_3), 3.42 (dd, J = 15.5 and 10.0 Hz, $C(7)H_{ax}$), 3.74 (dd, J = 15.5 and 3.0 Hz, $C(7)H_{eq}$), and 4.34 (m, C(6)H); **2**, 4.00 (C(7)H) and 4.44 (C(6)H).

(Received in Japan 21 May 1985)