EVIDENCE FOR THE ENEDIOL FORM OF SEPIAPTERIN

Yasuo Iwanami and Miki Akino

Department of Chemistry, Sasaki Institute, Kanda-Surugadai, Chiyoda-ku, Tokyo 101
and Department of Biology, Tokyo Metropolitan University, Fukazawa, Setagaya-ku, Tokyo 158
(Received January 10, 1975)

Sepiapterin is a structural isomer of biopterin whose reduced form is thought to play a role as cofactor in hydroxylation of aromatic amino acids and other compounds (1). Although biosyntheses of these unconjugated pterins have not been wholly elucidated, there might be a possibility of a biosynthetic route of the cofactor via sepiapterin in some organisms (2, 3). As a hypothetical intermediate, 7,8-dihydropterin with an enol (4) or enediol (2) side chain has been proposed. The latter corresponds with sepiapterin enediol.

Apart from these enzymic reactions, however, it has been claimed in a recent paper on the chemical synthesis of sepiapterin that the interconversion of sepiapterin into its enediol form is improbable (5). This conclusion is based on the observation that the structure of a by-product was determined to be an isomer of sepiapterin with another ketol construction in the side chain, 6-(1-hydroxy-2-oxopropyl)-7,8-dihydropterin, which would turn into sepiapterin if there was no barrier against the interconversion.

As part of our continuing studies on sepiapterin (6-10), we obtained NMR spectral evidence for the presence of the enediol form. The NMR spectrum in dimethyl sulfoxide (DMSO)-d₆ which represents an α-ketol form is shown in Fig. 1. We dissolved sepiapterin in 1 N NaOD and recorded the NMR spectra of the solution at a certain interval of time. After 4 min approximately half of the CH₃ signal, the whole of which would probably appear at 1.35 ppm in 3 values as a doublet at 0 time, had migrated to 2.22 ppm constituting a singlet. The appearance of the CH₃ singlet in the lower field is quite consistent with the conversion into the enediol form in which there is no hydrogen adjacent to the CH₃ group since it is attached to the newly formed double bond. With the conversion, the signal of the ring CH₃, originally appearing at 4.27 ppm, is shifted to a downfield position, 4.38 ppm. The changes in these signals were extended to a ratio of 1:3 at 8 min. Surprisingly, the conversion of sepiapterin into its enediol was almost completed at 13 min as seen in Fig. 1.

1 岩波泰夫，秋野美樹
Fig. 1. $^1$H-NMR spectrum (100 MHz) of sepiapterin in DMSO-$d_6$ using TMS as an external standard (left), and three $^1$H-NMR spectra (100 MHz) of sepiapterin in 1 N NaOD recorded at 4, 8, and 13 min after dissolving, respectively (right).

The presence in the enediol form, thus approved, may lend support to the above hypothesis in the intermediary metabolism of unconjugated pterins. Recently, L-threo, L-erythro, and D-erythro isomers of neopterin were successively found in several organisms (11–13). Since epimerization of sugars through an enediol form is well-known, a similar form of the intermediate could be involved in the formation of neopterin isomers, sepiapterin, or biopterin. It has been elucidated that these pterins are all biosynthesized from GTP, hence, the side
chain is derived from ribose portion of GTP probably being maintained its D-erythro form at least in the beginning step of the biosynthesis. Sepiapterin has a side chain of L-configuration, and biopterin possesses that of L-erythro form. In this respect, further studies on the enediol are necessary.

We are grateful to Dr. T. Kishikawa, Research Laboratories, Morishita Pharmaceutical Co., Ltd. for providing facilities to measure the NMR spectra. This investigation was supported in part by a Grant-in-Aid from the Ministry of Education.

REFERENCES