CHEMISTRY LETTERS, pp. 1177-1178, 1978. Published by the Chemical Society of Japan

REDUCTION OF INACTIVATED CARBONYL COMPOUNDS BY 1,5-DIHYDRO-PYRIMIDO[4,5-b]QUINOLINE-2,4(3H,10H)-DIONE (1,5-DIHYDRO-5-DEAZAFLAVIN)

Fumio YONEDA* and Yoshiharu SAKUMA
Faculty of Pharmaceutical Sciences, Kumamoto University, Kumamoto 862
Yoshihiro NITTA
Shizuoka College of Pharmacy, Shizuoka 422

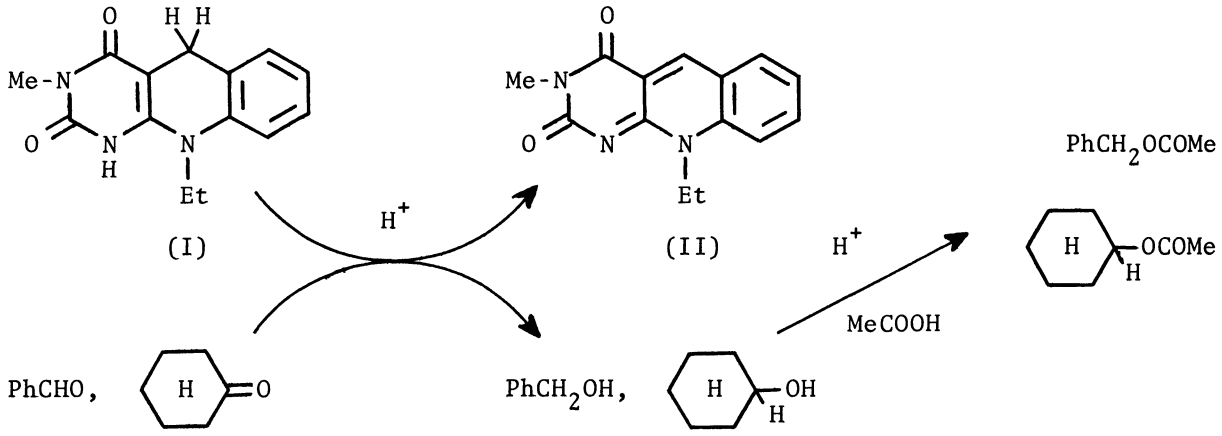
1,5-Dihydropyrimido[4,5-b]quinoline-2,4(3H,10H)-dione (1,5-dihydro-5-deazaflavin) reduced inactivated carbonyl compounds in acetic acid in the presence of hydrochloric acid to yield the corresponding alcohols which were identified as their acetates, while 1,5-dihydro-5-deazaflavin itself was oxidized to 5-deazaflavin.

Model studies have hitherto revealed that 1,4-dihydropyridine derivatives can reduce nonenzymically the carbonyl compounds which are highly activated by the introduction of electron-deficient and ortho-phenolic hydroxy groups, or by the presence of Zn(II) and Mg(II) catalysts.[1,2] Furthermore it was demonstrated that such model NADH reduction of carbonyl compounds is facilitated by the presence of general acid catalyst such as acetic acid and hydrochlorides of tertiary amines.[3] Also, 1,5-dihydro-5-deazaflavin, which is a model of 1,5-dihydroflavin nucleotide as well as NADH, reduced ortho-hydroxy substituted aromatic aldehydes to the corresponding alcohols.[4] Recently, it was reported that in the presence of hydrochloric acid N-benzyl-3-carbamoyl-1,4-dihydroquinoline reduced p-nitrobenzaldehyde to p-nitrobenzyl alcohol albeit in 10% yield.[5] We now report the first example of the reduction of inactivated simple carbonyl substrates to the corresponding alcohols by 1,5-dihydro-5-deazaflavin.

A mixture of 10-ethyl-3-methyl-1,5-dihydro-5-deazaflavin (I)[6,7] (300 mg, 1.17 mmol) and benzaldehyde (300 mg, 2.83 mmol) in acetic acid (3 ml) in the presence of concentrated hydrochloric acid (0.2 ml) was gently refluxed for 2 hr under nitrogen (under aerobic conditions also) in the dark. The reaction mixture was analyzed by

gas chromatography and the product was identified to be benzyl acetate (68%, not optimum). From the reaction mixture, 10-ethyl-3-methyl-5-deazaflavin hydrochloride precipitated, which was filtered off and treated with aqueous potassium carbonate to give 10-ethyl-3-methyl-5-deazaflavin (II)[8] in almost quantitative yield. The similar reaction as above in the absence of concentrated hydrochloric acid led to complete recovery of starting materials. Therefore, strong proton sources were required for this reaction.

The reduction of cyclohexanone in acetic acid in the presence of hydrochloric acid under the same conditions afforded cyclohexyl acetate (65%, not optimum), while I was oxidized to II.



We thank Prof. S. Shinkai for discussions and Ministry of Education of Japan for Grant-in-aid for Scientific Research.

REFERENCES

1) T. C. Bruice and S. Benkovic, "Bioorganic Mechanisms," Vol. II, 1966, Benjamin Inc., New York, pp 343-346.

2) S. Shinkai, S. Shiraishi, and T. Kunitake, Bull. Chem. Soc. Japan, 46, 3656 (1976), and references cited therein.

3) S. Shinkai and T. Kunitake, Chem. Lett., 1977, 297.

4) S. Shinkai and T. C. Bruice, J. Am. Chem. Soc , 95, 7526 (1973).

5) S. Shinkai, H. Hamada, T. Ide, and O. Manase, Chem. Lett., 1978, 685.

6) F. Yoneda, Y. Sakuma, and P. Hemmerich, J. C. S. Chem. Comm., 1977, 825.

7) F. Yoneda, Y. Sakuma, and Y. Matsushita, J. C. S. Chem. Comm., 1978, 398.

8) F. Yoneda, Y. Sakuma, S. Mizumoto, and T. Ito, J. C. S. Perkin I, 1976, 1805.

(Received August 1, 1978)