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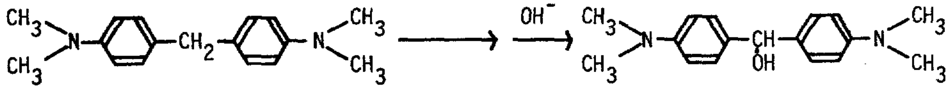
# 4,4'-TETRAMETHYLDIAMINODIPHENYLMETHANOL FROM TETRABASE WITH HEMIN IN ACETIC ACID

Atsushi Ohkoshi, Katsunobu Takahashi, Ayako Matsushima,
Kazuya Abe and Yuji Inada*

Department of Materials Science and Technology, Toin University
of Yokohama, Kurogane-cho 1614, Midori-ku, Yokohama 227, Japan

SUMMARY: 4,4'-Tetramethyldiaminodiphenylmethanol was formed in 90 % yield by oxidizing Tetrabase with hemin and hydrogen peroxide at 4 °C in acetic acid (80 %).

4,4'-Tetramethyldiaminodiphenylmethanol (Michler's Hydrol) has been widely used as an intermediate of dye stuffs, and heat- and pressure-sensitizing dyes. This compound is industrially synthesized by oxidation of 4,4'-tetramethyldiaminodiphenylmethane (Tetrabase) with lead dioxide (1) although lead dioxide has strong toxicity and a side reaction took place to form N,N'-tetramethylbenzidine (TMB) (2).



Tetrabase Michler's Hydrol

To exclude disadvantage mentioned above, the present paper deals with preparation of Michler's Hydrol from Tetrabase using hemin in the presence of hydrogen peroxide. This study is based on the application of peroxidase reaction induced by hemin (3).

To 1.25 ml of acetic acid solution containing 20 % water was added 80.5 nmoles of hemin, 6.3 $\mu$moles of Tetrabase, 11.9 $\mu$moles of hydrogen peroxide. After the reaction was started at 4 °C by the addition of hydrogen peroxide, an aliquot was taken out at a given time and was subjected to analyses of Michler's Hydrol, Tetrabase and TMB. Michler's Hydrol in acidic form was directly determined with a double beam spectrophotometer Model U-3400 (Hitachi Co., LTD., Japan) using its molar extinction coefficient of $1.47 \times 10^5\ M^{-1}\ cm^{-1}$ at 610 nm (4). Michler's hydrol in alkaline form, Tetrabase and TMB were determined with a high-performance liquid chromatography equipped with UV detector Model 490 (Waters Co., U.S.A.) at 254 nm (column; $C_8$ reverse phase, mobile phase; 50 % aqueous tetrahydrofuran containing 1 % acetonitrile).

Formation of Michler's Hydrol is the first to be successfully made by the application of peroxidase action of hemin in acetic acid. Fig. 1 represents the time course of Michler's Hydrol formation in acetic acid solution containing 20 % water in the presence of hemin and hydrogen peroxide at 4 °C. Tetrabase was markedly reduced with time and almost

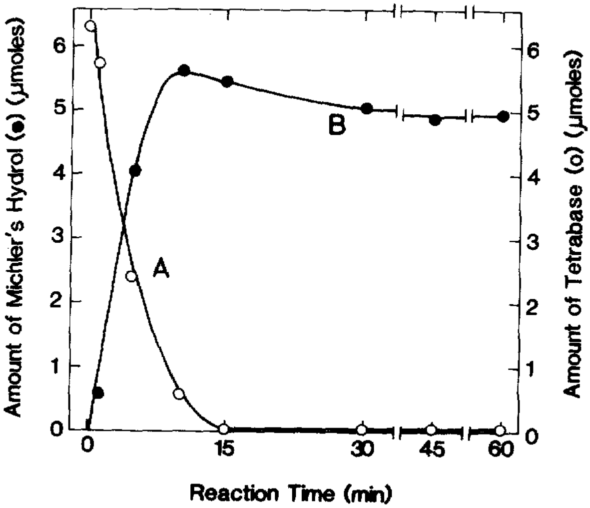


Fig. 1. Formation of Michler's hydrol in acetic acid with hemin at 4 °C. Curves A and B;Amounts of Tetrabase and Michler's hydrol, respectively.

completely lost in 15 min (curve A). On the other hand, Michler's Hydrol was increased with time and reached a maximum value (5.5 μmoles) at 10 min (curve B). The value corresponded to 90 % of Tetrabase without formation of TMB as a by-product. Michler's Hydrol was not formed without hemin. At reaction temperature higher than 4 °C, appreciable amount of TMB was formed by the oxidation of Tetrabase. In fact, approximately 40 % of Tetrabase was converted to TMB at 30 °C. The yield of Michler's Hydrol was also markedly influenced by acetic acid concentration and the maximum yield (90 %) was obtained in 80 % of acetic acid solution at 10 min-reaction.

It was demonstrated by Tohjo *et al*. that hematin-acetate complex is formed by chelation and exhibits high peroxidase activity (3). Baker *et al*. reported that Michler's Hydrol is quite stable in acetic acid solution (4). Therefore, it may be concluded that a high yield of Michler's Hydrol synthesis in the present study is accomplished by a peroxidase-like reaction of hemin-acetate complex and by stabilization of the product in acetic acid. This finding may lead to mass production of Michler's Hydrol as a materials of chromogen, since the reaction can be proceeded without using toxic oxidizing agent and without forming by-product.

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