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A Novel Approach toward Bacteriochlorophylls-*e* and *f*

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Abstract: Methyl bacteriopheophorbide-*f* was prepared from methyl bacteriopheophorbide-*d* with retention of the 3^1-chirality. The transformation of the methyl to the formyl group at the 7-position of the chlorin moiety will provide an alternative route for the synthesis of bacteriochlorophylls-*e* and *f*.

Bacteriochlorophyll(=BChl)-*e* is a major extramembraneous antenna pigment in anoxygenic photosynthetic brown-colored bacteria, e.g., *Chlorobium phaeovibriodes* and *phaeobacteriodes*.[1] BChl-*e* is a magnesium complex of 7-formyl chlorin and is differentiated by the 7-substituent from BChl-*c* which possesses the 7-methyl group and is a pigment in the light-harvesting antenna of green-colored bacteria (see Fig. 1). The same relationship is seen in natural pigments of higher plants between chlorophyll(=Chl)-*b* (7-CHO) and Chl-*a* (7-CH_3). Moreover, the name BChl-*f* is reserved for the compound in which the 7-methyl group of naturally occurring BChl-*d* is substituted by a 7-formyl group: BChl-*f* has not yet been found in any photosynthetic bacteria. Methyl bacteriopheophorbide-*f* (**1**) is a derivative of BChl-*f* (demetallation and transesterification) and has been prepared from methyl pyropheophoribide-*b* by hydration of the 3-vinyl group.[2] Here, we report the alternative synthesis of **1** from methyl bacteriopheophorbide-*d* (**2**) by transformation of the 7-methyl to the 7-formyl group.

Addition of **2** with OsO_4 in the presence of pyridine and cleavage of the resulting cyclic ester by H_2S[3] gave 7,8-*cis*-diol **3** (49%) which was *ca.* a 1:1 diastereomeric mixture at the 7,8-positions (see Scheme 1). The 7,8-double bond is the most reactive in the chlorin π-chromophore because of its relatively low conjugation, but the 3^1-hydroxyl group of the adduct was also oxidized under the above conditions to afford undesired 3-acetyl-7,8-diol in 7% yield. To suppress the over-reaction, the process of the oxidation was checked by TLC and the reaction was quenched by H_2S when the third quarter of **2** was consumed. Mild dehydration[4] of **3** by acidic treatment gave *ca.* a 1:8 isomeric mixture of primary alcohol **4** (7^1-OH) and more stable secondary alcohol **5** (8^1-OH). Flash column chromatography over silica gel with 1% MeOH and CH_2Cl_2 successfully separated the regio-isomers and pure **4** was isolated in 10% yield. Selective oxidation of the 7-hydroxymethyl group in **4** by PDC (see legend Scheme 1)

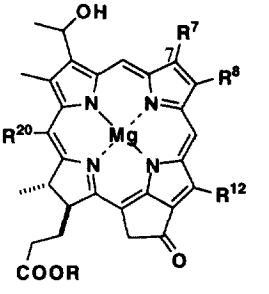

Figure 1. Photosynthetic antenna pigments.

BChl-*c*: $R^7=R^{20}=CH_3$
BChl-*d*: $R^7=CH_3$, $R^{20}=H$
BChl-*e*: $R^7=CHO$, $R^{20}=CH_3$
BChl-*f*: $R^7=CHO$, $R^{20}=H$

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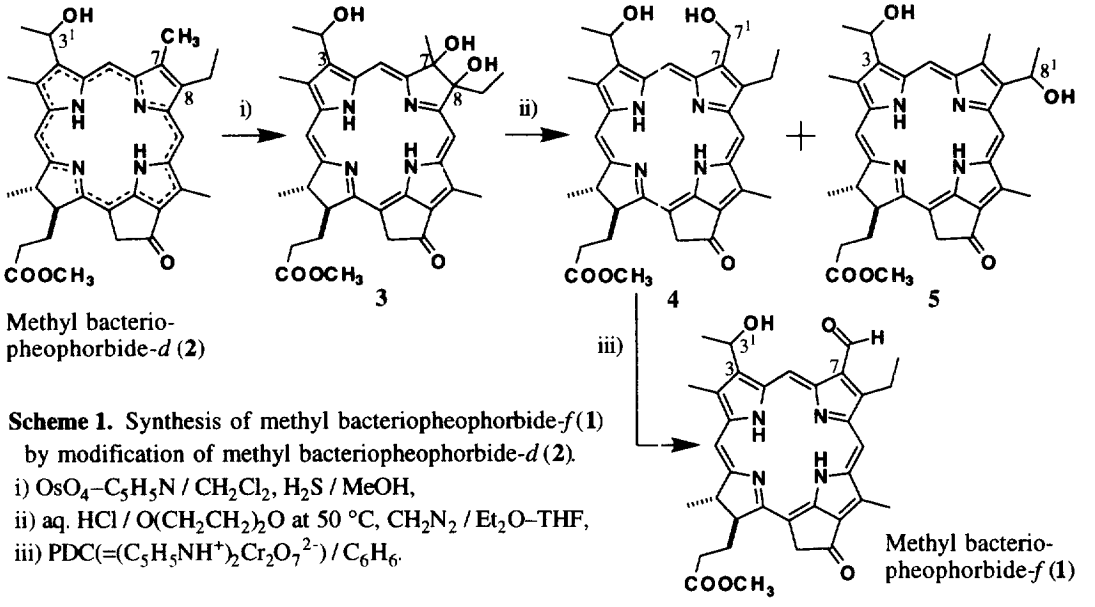

Scheme 1. Synthesis of methyl bacteriopheophorbide-*f* (**1**) by modification of methyl bacteriopheophorbide-*d* (**2**).
i) OsO_4–C_5H_5N / CH_2Cl_2, H_2S / MeOH,
ii) aq. HCl / $O(CH_2CH_2)_2O$ at 50 °C, CH_2N_2 / Et_2O–THF,
iii) PDC(=$(C_5H_5NH^+)_2Cr_2O_7^{2-}$) / C_6H_6.

yielded **1** (79%). When a (3^1S)-enriched sample of **2** (R/S=1/9)[5] was used as the starting material, the diastereomeric ratio of **1** produced was determined to be 1:9 from the HPLC analysis, indicating that no epimerization at the 3^1-position occurred during the transformation of the methyl to the formyl group at the 7-position. Transesterification from methyl group in **1** to a long chain (e.g., farnesyl group) followed by magnesium insertion would lead to BChl-*f* (R^8=Et, R^{12}=Me).

Molecular structures (including the stereochemistry) of various BChls-*c* and *d* separated from photosynthetic green bacteria have already been determined,[1] but many BChls-*e* have still not been confirmed in the R^8, R^{12} and R substituents as well as the 3^1-stereochemistry. Moreover, BChl-*f* has not been observed in any antenna pigment. The present transformation of 7-CH_3 to 7-CHO with retention of the 3^1-chirality will be useful for structural assignments of BChls-*e* and *f*. The structurally determined BChls-*f* and their derivatives will be helpful for elucidation of the mechanism in biosynthesis of BChl-*e* (BChlide-*d* (R=H in Fig. 1) → BChlide-*c* → BChlide-*e* or BChlide-*d* → BChlide-*f* → BChlide-*e*)[6] as well as for the first detection in chlorophyllous pigments extracted from photosynthetic bacteria.

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