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meso-Tetra(*tert*-butyl)porphyrin as a precursor of porphine

Saburo Neya* and Noriaki Funasaki

Department of Physical Chemisrty, Kyoto Pharmaceutical University, Yamashina, Kyoto 607-8414, Japan

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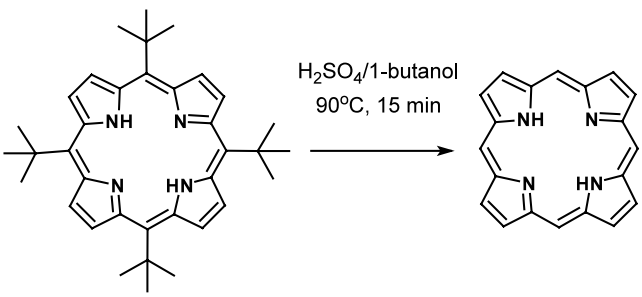
Abstract—Treatment of *meso*-tetra(*tert*-butyl)porphyrin with sulfuric acid/1-butanol at 90°C over 15 min afforded porphine in an isolated yield of 74%. De-*tert*-butylation of the substituted porphyrin provides a rational access to porphine.

Many kinds of oligomeric porphyrins[1] and porphyrin isomers[2] have appeared as a result of recent advances in porphyrin synthesis. However, porphine (**1**), the parent nucleus of every natural and synthetic porphyrin, is still difficult to prepare in any amount. It is consequently quite expensive.[3] Continuing effort has been exerted to improve the porphine synthesis.[4,5] Adding 2 ml of 2-hydroxymethyl-pyrrole over 2 weeks to 3 l of ethylbenzene at 100°C, Longo et al.[6] obtained **1** in an 8–10% yield. Neya et al.[7] prepared porphine from formalin and pyrrole. Although their yield is as low as 0.9%, the synthesis is readily carried out on a large scale to afford more than 100 mg of **1** at one time. In 1999, Taniguchi et al.[8] reported an elegant porphine synthesis through coupling of tripyrrane and 2,5-bis(hydroxymethyl)-pyrrole. The yield of 31% is indeed the highest, but the pyrrolic precursors tend to be available only by proficient preparative hands.



(**2**) (**1**)

Scheme 1. Conversion of *meso*-tetra(*tert*-butyl)porphyrin (**2**) into porphine (**1**).

Porphine **1**, owing to the fundamental importance in porphyrin chemistry, has been the subject of continuing theoretical[9] and experimental[10] investigations. Sato et al.[11] employed iron porphine as the prosthetic group of myoglobin to perturb the heme-globin interaction in the protein pocket. Neya et al.[12] resolved the crystallographic structure of the myoglobin reconstituted with iron porphine. Sugiura[13] examined the X-ray structure of various metallo porphines and explained the peculiar packing modes in crystalline lattice in terms of the CH-π interactions. In view of the extreme preparative difficulty as well as increasing chemical and biological applications for **1**, the simple porphine synthesis is to be developed.

According to the textbook of organic chemistry,[14] *tert*-butyl group can be cleaved from the aromatic ring while the primary and secondary alkyl substituents do not. Removal of *tert*-butyl group or de-*tert*-butylation is effected with proton and Lewis acid. Acid-labile *tert*-butyl group has been frequently employed as a protecting or blocking group in organic synthesis.[15] It is hence expected that a porphyrin bearing *tert*-butyl substituents will be used as an intermediary compound for the synthesis of porphine. The expected porphyrin with *tert*-butyl substituents is fortunately present. Smith et al. first reported in 1994 the synthesis of *meso*-tetra(*tert*-butyl)porphyrin (**2**).[16,17] This porphyrin was originally prepared to analyze characteristic spectroscopic profiles in terms of nonplanar macrocyclic conformation induced by the flanking bulky substituents.

We attempted the de-*tert*-butylation of **2** with several acids such as sulfuric acid, *p*-toluenesulfonic acid and

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* Corresponding author. Tel.: +81-75-595-4664; fax: +81-75-595-4762; e-mail: sneya@mb.kyoto-phu.ac.jp

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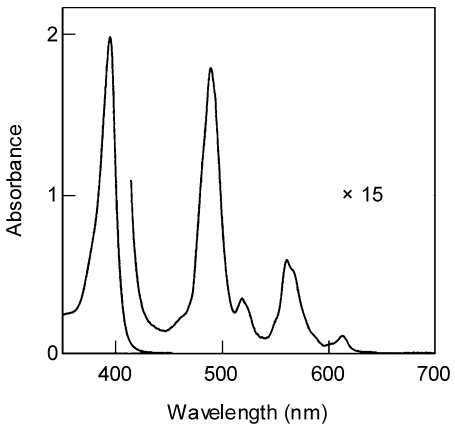

Figure 1. Visible absorption of porphine in dichloromethane.

aluminum chloride. Sulfuric acid diluted with 1-butanol was found to be the most effective catalyst; an equal volume mixture of sulfuric acid and 1-butanol smoothly dealkylated **2** to afford **1** (Scheme 1) in an isolated yield of 74%.[18] The reaction, without protection against air, was completed within 15 min at 90°C. The Soret peak sizably blue-shifted from 447 to 394 nm, and the visible absorption changed from etio- to phyllo-types (Fig. 1). Since a direct correlation between Soret red-shift and non-planarity of porphyrin ring is known,[16] the remarkable Soret blue-shift on the acid treatment suggests release of porphyrin distortion and hence removal of the bulky substituents. Analytical results[18] of the product were consistent with the expected structure.

Pivalaldehyde and pyrrole for **2** are inexpensive reagents. Senge et al.[17] optimized the synthesis of **2** to afford multi grams of the product in 15% yield. In addition, the de-*tert*-butylation of **2** and subsequent workup are easy to perform. These observations taken together allow us to prepare **1** in large amounts. It is now turned out that compound **2** is a useful precursor for the synthesis of porphine. More importantly, the de-*tert*-butylation referred to porphine preparation will be generally applicable to the synthesis of asymmetrically substituted porphyrin derivatives.

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18. *meso*-Tetra(*tert*-butyl)porphyrin **2** (200 mg), dissolved in sulfuric acid (8 ml)/1-butanol (8ml) mixture, was heated with stirring in oil bath at 90°C for 15 min. The dark green solution turned into reddish purple during the incubation. Methanol (40 ml) and chloroform (200 ml) were added to the cooled solution before being washed with dilute aqueous sodium hydroxide and water until neutrality. The chloroform layer was evaporated to dryness. The residue, washed on a centrifuge with small portions of methanol until colorless, was purified by silica-gel column chromatography with chloroform. The fast-running red band containing **1** was collected and evaporated to dryness. Recrystallization from chloroform/methanol afforded 86 mg of copper-colored leaflets, **1** (74% yield). Anal calcd for $C_{20}H_{14}N_4$: C, 77.40; H, 4.55; N, 18.05. Found: C, 77.38; H, 4.82; N, 17.80. MS: m/z, 310 (M^+). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 10.38 (s, 4H, *meso*-H), 9.54 (s, 8H, pyrrole-H), −3.95 (br s, 2H, NH). Visible (dichloromethane) λ_{max}, nm (ε): 394 (272000), 489 (16400), 519 (3200), 560 (5400), 568 (sh, 4800), 613 (1100).