Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron Letters 48 (2007) 7825–7828
Tetrahedron Letters

Retro-Diels–Alder reaction using bicyclo[2.2.2]octatriene-fused pyrrole during porphyrin synthesis

Hidemitsu Uno,* Yuri Sahara and Takahiro Takiue

Division of Synthesis and Analysis, Department of Molecular Science, Integrated Center for Sciences (INCS), Ehime University, Matsuyama 790-8577, Japan
CREST, Japan Science and Technology Agency (JST), Japan

Received 20 August 2007; accepted 3 September 2007
Available online 6 September 2007

Abstract—Porphyrin synthesis using 4,7-etheno-4,7-dihydro-2*H*-isoindole and tripyrranedicarbaldehyde gave a porphyrin derivative bearing no bicyclo[2.2.2]octatriene moiety as well as the targeted bicyclo[2.2.2]octatriene-fused porphyrin.

1. Introduction

Many excellent and reliable methods have been reported for the preparation of porphyrins and their analogues involving the naturally occurring porphyrinoids. Lindsey, MacDonald, and their related methods are commonly used in the preparations of a wide variety of porphyrins required for material chemistry due to their versatility, efficiency, and applicability.[1] In all these preparation methods of porphyrins, two chemical steps are involved: The first step is the construction of the macrocyclic ring skeletons by a cyclotetramerization or condensation reaction, and then the intermediary macrocyclic compounds are converted to the targeted porphyrin derivatives by treatment with oxidizing reagents such as quinones and oxygen. Among the macrocyclic intermediates, porphyrinogen (Fig. 1) is the most important intermediate with the lowest oxidation state, and has been synthesized and investigated by many groups from both synthetic and mechanistic points of view.[2] Other possible intermediates with higher oxidation states such as porphomethene, porphodimethene, phlorin, and isophlorin (Fig. 1) are also recognized, and were prepared in certain cases that they could resist the oxidation to porphyrins.[3] During our investigation for creation of new porphyrinoids, we found the intramolecular hydrogen transfer from the macrocyclic ring to the acetylenic *meso*-substituents affording *meso*-alkenyl-substituted porphyrins,[4] and became aware of an important role of the intermediates. In this Letter, we will reveal another example showing the importance of these intermediates in the porphyrin synthesis: In the preparation of bicyclo[2.2.2]octatriene-fused porphyrins, unusual porphyrin compounds bearing no

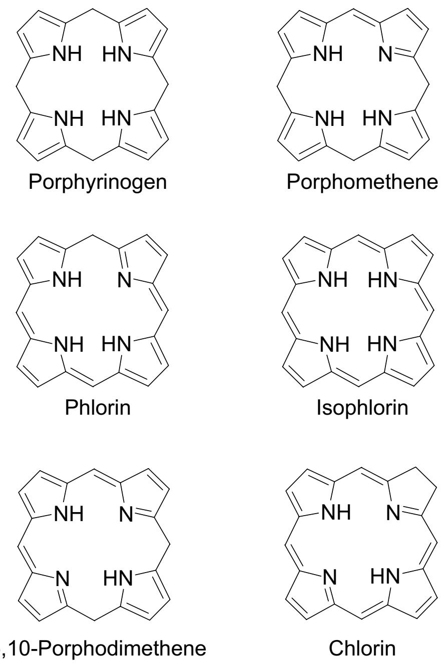


Figure 1. Intermediary compounds during porphyrin synthesis.

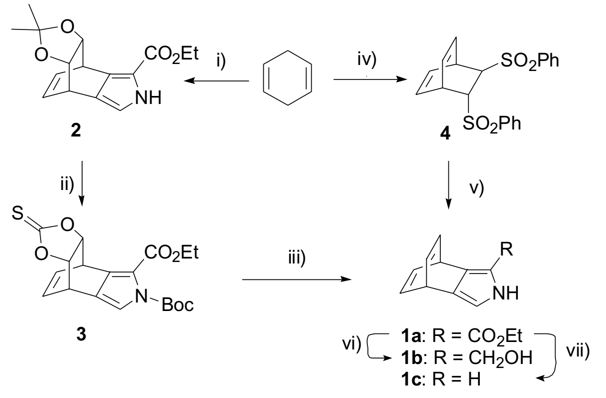
Keywords: Porphyrin synthesis; Retro-Diels–Alder reaction; Bicyclo[2.2.2]octatriene.

* Corresponding author. Tel.: +81 89 927 9660; fax: +81 89 927 9670; e-mail: uno@dpc.ehime-u.ac.jp

0040-4039/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2007.09.004

bicyclo[2.2.2]octatriene moiety were formed by the retro-Diels–Alder reaction.

The key starting pyrrole **1** was prepared from 1,4-cyclohexadiene as shown in Scheme 1. First, we planned to utilize Corey–Winter olefination[5] for the introduction of a double bond by conversion of the known isopropylidenedioxy-substituted ethanoisoindole **2** to the target pyrrole **1**. According to the literature, ethanoisoindole **2** was prepared in good yield.[6] The conversion of isopropylidenedioxy to thiocarbonate groups and then Boc protection of pyrrolic NH gave **3** in 87% yield. The olefination of **3** with 1,3-dimethyl-2-phenyl-1,3,2-diazaphospholidine[7] followed by deprotection gave the targeted pyrrole **1a** in 62% yield. From thermogravimetric analysis of pyrrole **1a**, no decomposition was observed under 200 °C and sublimation with decomposition occurred above 215 °C.

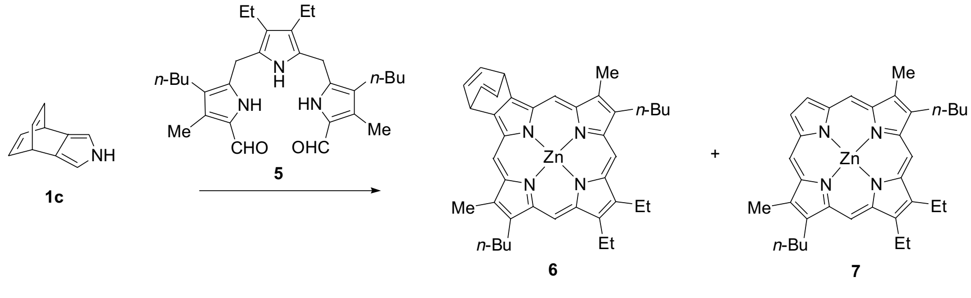


Scheme 1. Reagents, conditions, and yields: (i) Ref. 6; (ii) 1 M aq HCl, THF, 65 °C; thocarbonyldiimidazole, THF, 80 °C; $(Boc)_2O$, NaH, DMF, 80 °C; 87%; (iii) 1,3-dimethyl-2-phenyl-1,3,2-diazaphospholidine, toluene 125 °C; 62%; (iv) Ref. 8; (v) ethyl isocyanoacetate, *t*-BuOK, THF, 77%; (vi) $LiAlH_4$, THF, 0 °C, 89%; (vii) KOH, ethylene glycol, 200 °C.

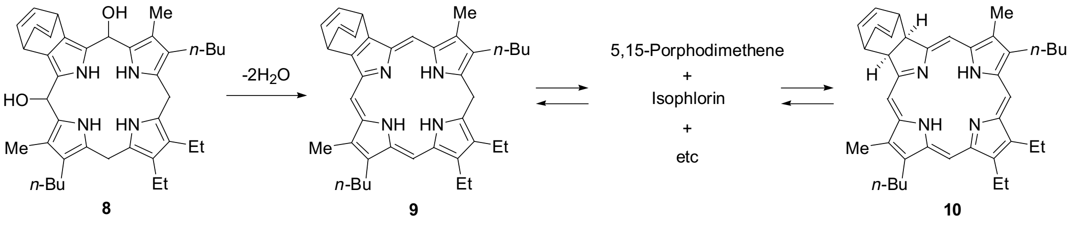
The shorter and more efficient synthesis of **1a** was achieved via the known bicyclo[2.2.2]octadiene **4**, which was prepared from 1,4-cyclohexadiene in very good overall yield according to the literature.[8] The modified Barton–Zard reaction of **4** with ethyl isocyanoacetate gave **1a** in 77% yield. The ester moiety of **1a** was converted to a hydroxymethyl group to give **1b** in 89% yield. Removal of the ester group in **1a** was quantitatively achieved by treatment with KOH in ethylene glycol at 200 °C to give **1c**.

First, we aimed at the preparation of porphyrins with one bicyclo[2.2.2]octatriene moiety in order to utilize the double bonds for porphyrin-ring construction.[9] Thus, the reaction of **1c** with tripyrranedicarbaldehyde **5** (3 mM concentration) was conducted in a 0.23 M solution of TFA in $CHCl_3$ at room temperature for 2 h under an inert atmosphere. After neutralization with triethylamine, oxidation with chloranil followed by complexation with $Zn(OAc)_2$ afforded two porphyrinic products, which were obtained as a mixture by silica-gel column chromatography. The products were successfully separated by preparative GPC, and the targeted porphyrin **6** and simple porphyrin **7** were obtained in 40% and 7% yields, respectively. A similar result was obtained by changing the oxidizing reagent from chloranil to DDQ (Scheme 2).

Formation of porphyrin **7** could be rationalized by the retro-Diels–Alder reaction of intermediary chlorin derivative **10**, which had the same oxidation state as 5,10-porphodimethene **9**, phlorin, and isophlorin. These intermediary compounds could be formed by acid-promoted dehydration and isomerization of the initial condensation product **8** (Scheme 3). In fact, a chlorin zinc



Scheme 2. Inverse [3+1] porphyrin synthesis of bicyclo[2.2.2]octatriene-fused pyrrole **1c** with tripyrranedicarbaldehyde **5**.



Scheme 3. Possible intermediates giving porphyrin **7**.