Journal of Fluorine Chemistry 203 (2017) 75–80

Contents lists available at ScienceDirect

Journal of Fluorine Chemistry

journal homepage: www.elsevier.com/locate/fluor

Unusual reactivity of trifluoromethyl groups in *meso*-tetrakis (trifluoromethyl)porphyrin

Anikó Nemes[a], Egmont Mérész[a], István Jalsovszky[a], Dénes Szabó[a], Zsolt Böcskei[b], József Rábai[a,*]

[a] Institute of Chemistry, Eötvös Loránd University, Pázmány Péter sétány 1/A, 1117 Budapest, Hungary
[b] Sanofi R & D Chilly Mazarin, France

ARTICLE INFO

This article is dedicated to Professor Dr. Antonio Togni on the occasion of his 2017 ACS Award for Creative Work in Fluorine Chemistry.

Keywords:
Porphyrin
Trifluoromethyl group
Ester formation
Solvolysis
X-ray structure

ABSTRACT

Based on the unusual reactivity of trifluoromethyl groups in nitrogen containing heterocycles, we synthesized the appropriate porphyrin mono-, di-, tri- or tetra-carboxylic ester derivatives by treatment of the precursor *meso*-tetrakis(trifluoromethyl)porphyrin with an excess of sodium- or potassium alkoxide in the respective alcohol. This method offers an efficient route for the synthesis of lower symmetry *meso*-substituted porphyrins compared to usual preparations utilizing stepwise condensation reactions. The structure of tetrakis(butyloxycarbonyl)porphyrin **5** was determined by X-ray analysis.

1. Introduction

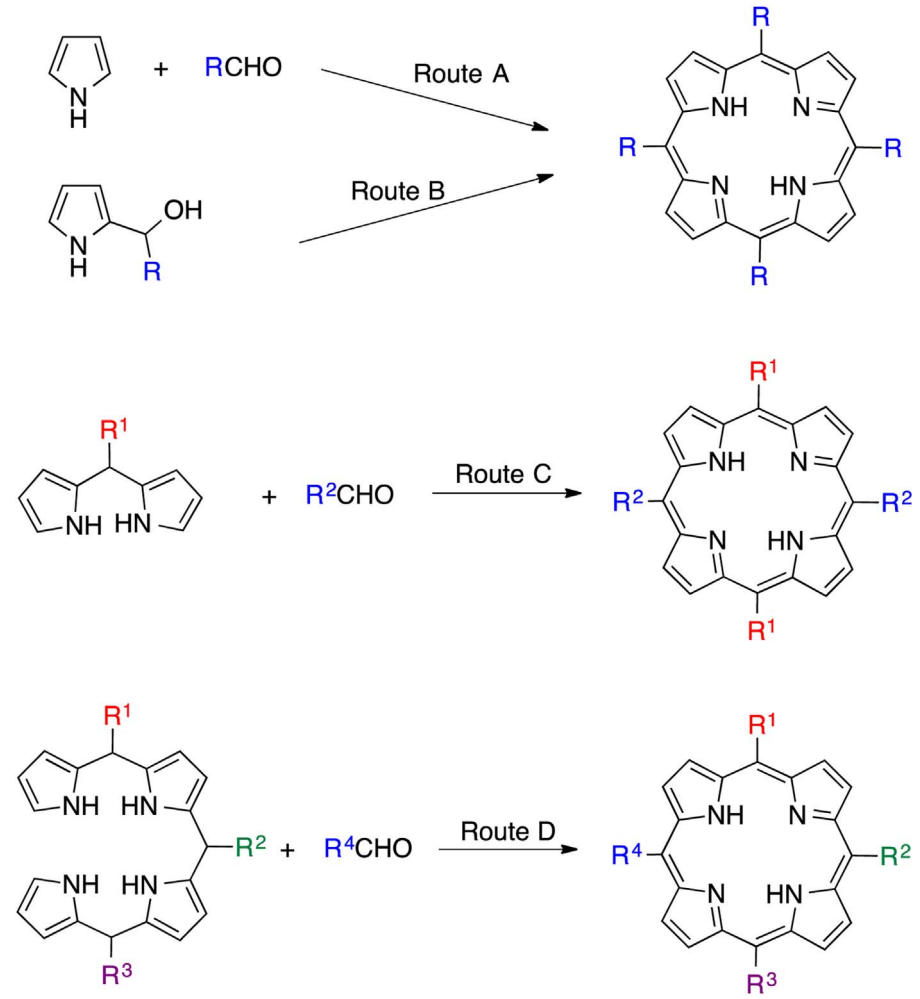
Porphyrin derivatives play important role both in nature and chemical research [1]. In chemistry they are used as biomimetic catalysts in oxidation reactions [2] and in chemical sensors [3]. In pharmaceutical chemistry *meso*-substituted porphyrins are used for development of Gd-free contrast agents [4], treatment of neurodegenerative diseases (e.g. Parkinson disease) [5] and the attenuation of oxidative stress induced liver perfusion injury [6]. In materials science porphyrin derivatives are found in liquid crystals, nanoparticles and nanocomposites [7]. These applications utilize the aptitude of porphyrins to self-assembly by hydrogen bonding [8]. As photoactive materials they are used as photosenitizers in solar cells [9], photodynamic therapy and bioimaging [10]. For the latter applications usually carboxylic acid derivatives of porphyrins serve as building blocks. These compounds typically bear different substituents in their *meso* positions. This type of lower symmetry porphyrins are difficult to synthesize.

Symmetrical *meso*-substituted porphyrins are commonly synthesized by the condensation reactions of a pyrrole and an aldehyde. However, this well known method is not efficient for the synthesis of porphyrins with more than one type of substituent in the *meso* position. For *trans*-ABAB type porphyrins (e.g. Route C) one must carry out condensation reactions between dipyrromethanes and aldehydes [11] while the synthesis of lower symmetry molecules (e.g. *cis*-AABB) calls for the use of linear tetrapyrroles. These synthetic routes are far less developed and more costly than the pyrrole – aldehyde condensation reaction (Scheme 1). On the other hand *cis*-AABB type molecules usually are synthesized either by sequential condensation reactions [12] or by modification of other porphyrins [13].

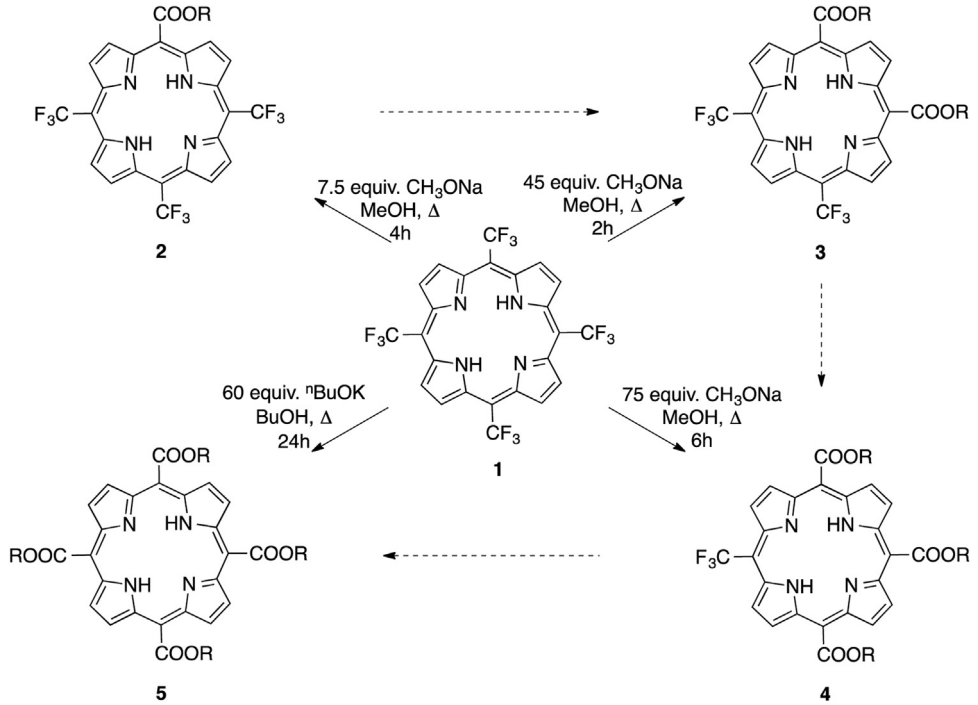
Some aromatic trifluoromethyl compounds show enhanced reactivity towards nucleophilic reagents. Trifluoromethyl groups attached to aromatic core can be hydrolysed in strong acidic media [14], but under basic conditions activation is needed [15]. The alcoholysis of the trifluoromethyl group in nitrogen containing heterocycles such as 2-(trifluoromethyl)quinolines, 2-(trifluoromethyl)indoles and 2-(trifluoromethyl)pyrroles have been reported in several journals [16]. We supposed, that in the case of *meso*-tetrakis(trifluoromethyl)porphyrin **1** the inner nitrogens' lone electron pairs could also assist the cleavage of the C-F bond *via* electron movement (mesomer effect). This unusual reactivity of the trifluoromethyl group offers a synthetic pathway to 5,10,15-$(CF_3)_3$-20-(COOR)-, 5,15-$(CF_3)_2$-10,20-$(COOR)_2$-, 5,10,15-$(COOR)_3$-20-(CF_3)- and 5,10,15,20-$(COOR)_4$-type porphyrins starting from 5,10,15,20-tetrakis(trifluoromethyl)-21H,23H-porphyrin **1** [17]. These derivatives (**2-5**) could be used for the synthesis of novel porphyrins and biologically active molecules (Scheme 2). Previously we also developed an efficient synthetic method that afforded **1** in good yield and high purity without using chromatography [18].

* Corresponding author.
E-mail address: rabai@elte.hu (J. Rábai).

http://dx.doi.org/10.1016/j.jfluchem.2017.05.009
Received 11 April 2017; Received in revised form 17 May 2017; Accepted 19 May 2017
Available online 22 May 2017



Scheme 1. Synthetic strategies of porphyrins with different *meso*-substitution patterns.



Scheme 2. *meso*-Tetrakis(trifluoromethyl)porphyrin **1** as precursor for the synthesis of esters **2**-**5** (R = CH_3 for **2**, **3**, and **4**; R = *n*-Bu for **5**).