Tetrahedron Letters 58 (2017) 4803–4815

Contents lists available at ScienceDirect

Tetrahedron Letters

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

Digest paper

Recent advancements in the synthesis of pentafluorosulfanyl (SF_5)-containing heteroaromatic compounds

Prajwalita Das, Etsuko Tokunaga, Norio Shibata *

Department of Nanopharmaceutical Sciences, Nagoya Institute of Technology, Gokiso, Showa-ku, Nagoya 466-8555, Japan

ARTICLE INFO

Article history:
Received 16 October 2017
Revised 4 November 2017
Accepted 6 November 2017
Available online 7 November 2017

Keywords:
Pentafluorosulfanyl
Fluorine
Sulfur
Trifluoromethyl
Heteroaromatics

ABSTRACT

The unique features of the pentafluorosulfanyl (SF_5) group have made it renowned as a "super trifluoromethyl (CF_3)" group. Owing to the big success of CF_3-containing heteroaromatic compounds in medicinal chemistry, agro-chemistry and material sciences, SF_5-substituted heteroaromatic compounds have gained a lot of attention in very recent years as novel and potential candidates in these fields. However, the synthetic methodology for SF_5-substituted heteroaromatic compounds is still highly limited. This digest highlights the recent, rapid, and significant advances made in the synthesis of SF_5-heteroaromatics.

Contents

Introduction

Although the first report on the synthesis of pentafluorosulfanyl (SF_5) benzenes was made by Sheppard over five decades ago,[1] the true virtue of the SF_5 group has only been realized in the recent years.[2] The high values of lipophilicity (Hansch hydrophobicity constant: $\pi = 1.51$) and electronegativity (Hammett substituent constant: $\sigma_I = 0.55$), as well as its high chemical and thermal stability, has made the SF_5 group an ideal alternative to the trifluoromethyl (CF_3) group in the design of new drugs, agrochemicals and surface materials.[2] SF_5-substituted compounds are highly

* Corresponding author.
E-mail address: nozshiba@nitech.ac.jp (N. Shibata).

https://doi.org/10.1016/j.tetlet.2017.11.015
0040-4039/

sought after, and due to their increased popularity, new synthetic routes have been developed for their preparation. In recent years, we have witnessed many reports on the synthesis of SF_5-heteroaromatic compounds.[3] This progress is very crucial as it places additional importance to aromatic heterocycles in bioactive compounds, and provides access to various SF_5-heteroaromatic scaffolds that are necessary during drug exploration.

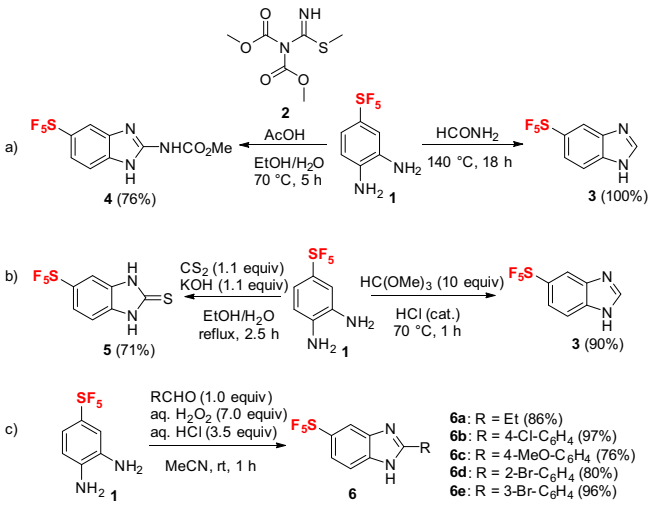
The only literature review which is dedicated to SF_5-heteroaromatic compounds is a book chapter by Kanishchev and Dolbier, published in 2016.[3] That chapter beautifully reviews the detailed synthesis and biological application of SF_5-substituted aromatic heterocycles, which were reported until the end of 2015. However, due to the increasing importance of the SF_5 group, considerable number of reports have been published in this field since 2016. Thus, this digest is a concise representation of that chapter, while also providing an update that summarizes the important advancements made in SF_5-heteroaromatics synthesis. The formation of any SF_5-heteroaromatic is primarily derived in three ways: (1) transformation of SF_5-substituted benzenes, (2) application of SF_5-substituted alkenes and alkynes as building blocks, and (3) oxidative fluorination of (hetero)aryl-sulfides. The various SF_5-aromatic heterocycles have been categorized according to the class of heterocycle and their modes of synthesis have also been illustrated.

Benzimidazoles and benzotriazoles

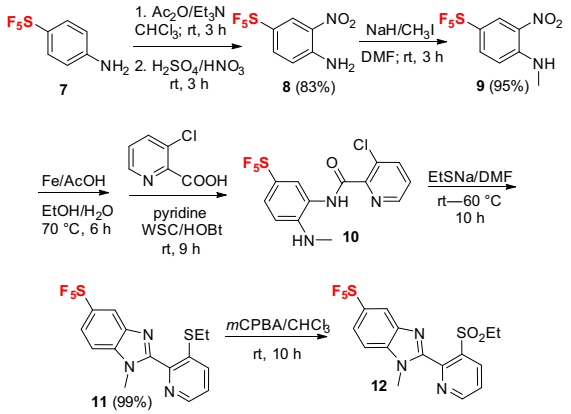
The synthesis of SF_5-benzimidazoles is reported to take place chiefly by using 4-SF_5-benzene-1,2-diamine **1** as the precursor.[4a,b] In the attempt to synthesize SF_5-benzimidazoles, different routes have been designed to avail the same benzene-diamine scaffold. In the first recorded synthesis of SF_5-benzimidazoles, as reported in the patent by Asahi Glass Co. Ltd.,[4a] the diamine **1** was condensed with formamide or *N,N*-(bis)methoxycarbonyl-*S*-methylisothiourea **2** to provide 5-SF_5-benzimidazole **3** in quantitative yield or 5-SF_5-substituted methyl (2-benzimidazolyl)carbamate **4** in good yield (Scheme 1a). Later in 2013, Beier et al. used a similar protocol by applying **1** as the precursor for SF_5-benzimidazoles, and to achieve this, they designed two new ways to obtain diamine **1**.[4b] After the formation of **1**, it was subjected to condensation reactions and 5-SF_5-benzimidazole **3** was successfully obtained, but in this case, excess trimethyl orthoformate and a catalytic amount of hydrochloric acid was used. They also synthesized 5-SF_5-1,3-dihydrobenzimidazole-2-thione **5**[4b] by condensation of diamine **1** with carbon disulfide under basic conditions (Scheme 1b). 2-Substituted SF_5-containing benzimidazoles **6a–e** were also prepared by condensation of **1** with aldehydes in the presence of an aqueous H_2O_2/HCl system in acetonitrile (Scheme 1c).

Another protocol was devised by Sumitomo chemists[4c] who began by using 4-SF_5-aniline **7** and converted it to SF_5-nitroaniline **8** in two steps. Nitroaniline **8** was then *N*-methylated to form *N*-methyl nitroaniline **9**. The nitro group in **9** was subsequently reduced to amino, and when coupled with 3-chloropyridine-2-carboxylic acid in the presence of *N*-(3-dimethylaminopropyl)-*N*'-ethylcarbodiimide and hydroxybenzotriazole (WSC/HOBt), this gave amide **10**. Nucleophilic substitution of the chlorine in **10** with sodium ethanethiolate, followed by condensation produced 2-substituted 5-SF_5-benzimidazole **11**. Oxidation of the sulfur function to sulfone by employing 3-chloroperoxybenzoic acid (*m*CPBA) provided product **12** (the yield is not mentioned in the original patent), which was used as an insecticide (Scheme 2).

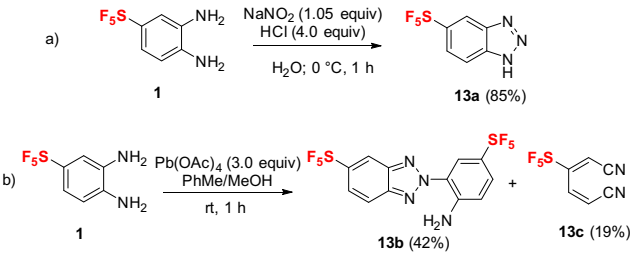
The diamine **1** was also used by Beier et al. for the synthesis of benzotriazole[4b] **13a** *via* the reaction of **1** with nitrous acid at 0 °C to obtain product **13a** in 85% yield (Scheme 3a). Another publication[5]



Scheme 1. Condensation of diamine **1** to obtain SF_5-benzimidazoles.



Scheme 2. Synthesis SF_5-benzimidazole.



Scheme 3. Synthesis of SF_5-benzotriazoles.

reported that oxidation of diamine **1** with $Pb(OAc)_4$ formed *N*2-substituted 5-SF_5-benztriazole **13b** as the main reaction product and a byproduct **13c** (Scheme 3b).

Benzisoxazoles and benzothiazole

The synthesis of benzisoxazoles was reported by Beier and Pastyrikova,[6] by allowing 3- and 4-nitro-SF_5-benzenes **14** and **15** to undergo the Davis reaction with arylacetonitriles to produce 6- and 5-SF_5-3-aryl-benzisoxazoles **16** and **17**, respectively (Scheme 4). The limitation of this procedure is that only an