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Functionalized *S*-perfluorinated sulfoximines: Preparation and evaluation in catalytic processes

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ABSTRACT

N-substituted *S*-perfluoroalkylated sulfoximines were synthesized from the NH sulfoximines either by a copper coupling reaction with aryl halides or by a reaction with electrophilic substrates. The procedure allowed the preparation of N,N′-bridged bis sulfoximines and of thioureas. The potential of these new sulfoximines was evaluated in different catalytic processes.

1. Introduction

The growing interest for the sulfoximines is explained by both the wide structural variation offered by this original structure and by their numerous applications in chemistry. They indeed demonstrated promising potential activities for medicinal chemistry [1] or in crop sciences [2]. Sulfoximines were also plentifully employed as ligands in catalytic reactions or in enantioselective metal catalysis [3], but surprisingly much more rarely for organocatalytic transformations.[4] The *S*-perfluoroalkylated sulfoximines have recently grown in importance and revealed very particular properties. They were described as building blocks for liquid crystals [5], as very powerful electron-withdrawing substituents and especially as nucleophilic and electrophilic perfluoroalkylating reagents [6]. This panel of applications clearly emphasized the need of new and reliable methods for the preparation of sulfoximines. In this paper, we herein disclose the synthesis of original per-, polyfluoroalkyl substituted sulfoximines and present some seminal evaluations of these compounds in catalytic and organocatalytic processes.

2. Results and discussion

We have previously developed a three-step methodology for the preparation of *NH S*-perfluoroalkylated sulfoximines **1** (Scheme 1) [7]. Compared to the previous procedures [7c,8,9], our method revealed advantages especially concerning the opportunity to be extended to various per-, polyfluorinated chains.

Practically, we were able to finely-tune the aryl and the perfluorinated substituents attached to the sulfur atom to give rise to a wide range of free *NH*-sulfur (VI) derivatives **1a**–**e**. This enabled thus the further post-functionalization on this iminosulfane group (HN=S). As part as our program [10,11] devoted to the comprehensive studies of the reactivity of this specific nitrogen atom, we report now recent developments of this chemistry.

2.1. N-*Functionalization by copper catalysis*

The copper based catalytic system, initially developed by Bolm et al. [12] was previously adapted by us to *S*-perfluoroalkylated

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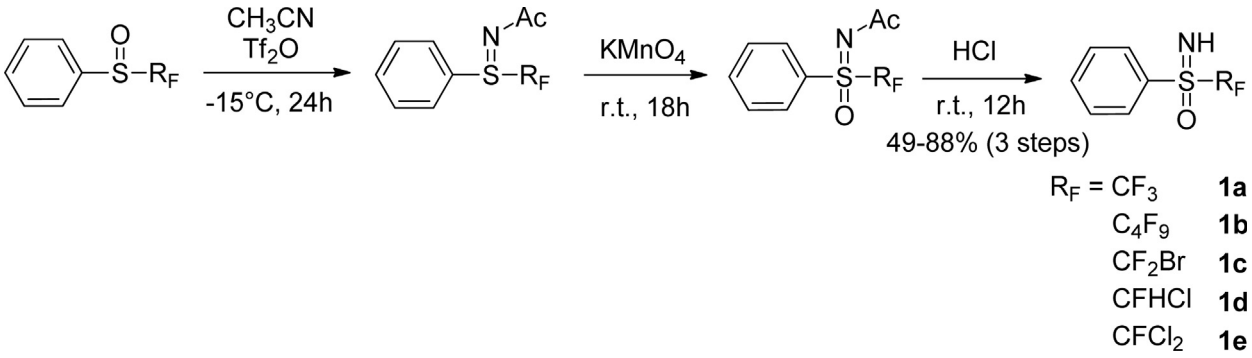


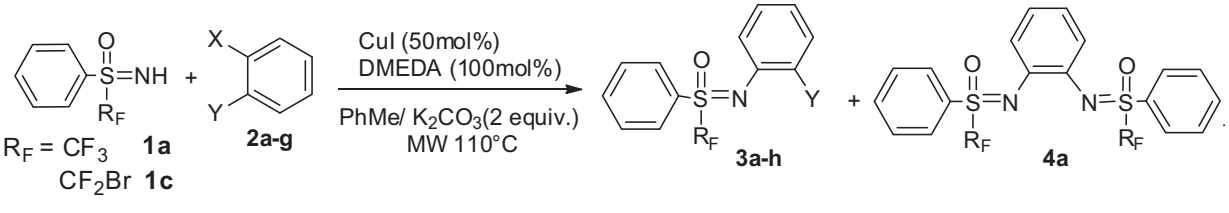
Scheme 1. Straightforward synthesis of *NH S*-perfluoroalkylated sulfoximines **1**.

compounds to provide various N-arylated sulfoximines [11]. To perform this transformation, a substoichiometric amount of copper salt (50%) was necessary. A reappraisal of this slightly modified system by the use of microwaves activation allowed a significant reduction of the reaction time (Table 1). As a typical example, the coupling between the iodobenzene **2a** and the sulfoximine **1a** was finished in 15 min instead of 3 hours without any erosion of the yield (entry 1). This result stimulated us to gain into increased molecular diversity. Ortho iodobenzenes **2b–d** reacted smoothly providing an augmentation of the reaction time (entries 2–4). This transformation was then tolerant to nitro, fluoro or amino group. The variation of the fluorinated moiety was quite surprising. Under previous conditions, the reaction with the *S*-dibromofluoromethyl sulfoximine **1a** was accompanied with the loss of the bromine atom and compound **3e** was isolated (entry 5). Fortunately, a slight decrease of the temperature, counter-balanced by a longer reaction time, gave rise to the desired sulfoximine **3f** (entry 6). As a next part of this study and inspired by the seminal work of Bolm et al., we turned our attention toward the preparation of bis-sulfoximines [13] starting from dibromo- or diiodobenzene. With stoichiometric amounts of each reagent, the monosulfoximines **3g** and **3h** were rationally isolated in good yields whereas a small amount of the bis-sulfoximine **4a** was nevertheless detected (entries 7–8). A reasonable increase of the equivalent the sulfoximine as well as the reaction time was necessary for the isolation of the compound **4a** in 71% yield (entries 9–12).

In order to circumvent the use of an excess of the sulfoximine for the synthesis of the target molecule **4a**, a two-step procedure was envisioned. Starting from **3g** or **3h**, we were pleased to perform a second coupling step (Scheme 2). The desired compound **4a** was isolated with the same yield with both substrates **3g** or **3h**. Beyond the good isolated yield without excess of sulfoximines, another advantage of this two-step sequence was the opportunity of the preparation of non-symmetrical bridged sulfoximines. This transformation was also effective when $R_F = C_4F_9$, delivering another original molecule **4b**.

For each of the products **4a** or **4b**, we succeeded in the separation of the two diastereoisomers with the help of the preparative plate chromatography. In the particular case of **4a**, the two couples were identified by X-ray analysis after crystallization (Fig. 1).

Table 1
Synthesis of mono and bis adducts (**3** and **4**) by copper coupling reaction between fluoroalkylated sulfoximines **1a**, **1c** and aryl halides **2a–g**.



Entry	R_F	X	Y	*n*	Time (min)	Yield (%)[a]	
						(**3a–h**)	**4a**
1	CF_3	I	H	1	15	91 (**3a**)	–
2	CF_3	Br	NO_2	1	45	81 (**3b**)	–
3	CF_3	I	F	1	60	90 (**3c**)	–
4	CF_3	I	NH_2	1	60	86 (**3d**)	–
5	CF_2Br	I	H	1	60	77 (**3e**)[b]	–
6	CF_2Br	I	H	1	240	76 (**3f**)[c]	–
7	CF_3	Br	Br	1	90	92 (**3g**)	5
8	CF_3	I	I	1	90	90 (**3h**)	6
9	CF_3	I	I	2	90	82 (**3h**)	13
10	CF_3	I	I	5	90	56 (**3h**)	27
11[d]	CF_3	I	I	5	150	5 (**3h**)	71
12[d]	CF_3	Br	Br	5	150	6 (**3g**)	68

[a] Isolated yield.
[b] CF_2Br reduced to CF_2H in **3e**, with 21% of **3f** (CF_2Br).
[c] MW activation at 100 °C, with 18% of **3e.**
[d] MW activation at 125 °C.