

Generation and reactions of thiocarbonyl *S*-(2,2,2-trifluoroethanides). Synthesis of trifluoromethylated 1,3-dithiolanes, thiiranes and alkenes



Marcin K. Kowalski^{a,*}, Emilia Objalska^{a,*}, Grzegorz Mlostoń^a, Heinz Heimgartner^b

^a University of Łódź, Faculty of Chemistry, Department of Organic and Applied Chemistry, Tamka 12, PL-91-403 Łódź, Poland

^b University of Zurich, Department of Chemistry, Winterthurerstrasse 190, CH-8057 Zurich, Switzerland

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ABSTRACT

The 'in situ' generated 1,1,1-trifluorodiazaoethane reacts with thioketones as C=S dipolarophiles in a two-phase system (DCM/H₂O) at room temperature to yield trifluoromethylated 2,5-dihydro-1,3,4-thiadiazoles. Whereas stable crystalline products were obtained with cyclobutanethiones, the reaction with aromatic and heteroaromatic thioketones occurred with spontaneous elimination of nitrogen. The formation of sterically crowded 4,4,5,5-tetrahetaryl-1,3-dithiolanes indicates that thiocarbonyl *S*-methanides are formed immediately and entered formal [3+2]-cycloaddition as diradical species with the starting thioketone. A protocol for the preparation of 3,3,3-trifluoropropene derivatives starting from corresponding thioketones and 1,1,1-trifluorodiazaoethane is also presented.

1. Introduction

Thiocarbonyl *S*-methanides **4** belong to the class of so-called sulfur-centered allyl-type [1,3]-dipoles, which can be easily generated by thermal cycloreversion of the corresponding 2,5-dihydro-1,3,4-thiadiazoles **3** [1]. The precursors **3** are available via [3 + 2]-cycloaddition reactions of diazo compounds **1** with thioketones **2**, and diverse thioketones were shown to be superior reaction partners. Typically, the reactions with diazomethane occur already at low temperature yielding the required cycloadducts in a regioselective manner and almost quantitative yields (Scheme 1). Different mechanisms of [3 + 2]-cycloadditions with application of thiocarbonyl *S*-methanides **4** as the 'in situ' generated reactive [1,3]-dipoles are considered, i.e. concerted [2] [2a], stepwise reactions via zwitterionic [2b,c] or diradical [2] [2d] intermediates.

The stability of 1,3,4-thiadiazoles of type **3** depends strongly on the type of the substituents R¹–R⁴. For example, in the case of diazomethane **1** (R¹ = R² = H), cycloadducts **3** obtained with aryl thioketones **2** (R³ = R⁴ = Ar) decompose at –40 °C, whereas cycloaliphatic thioketones **2a** and **2b** gave the corresponding products **3** as fairly stable compounds, which release nitrogen only upon heating to ca. 45 °C.

The generation of thiocarbonyl *S*-methanides **4** in the presence of suitable dipolarophiles leads to the [3 + 2]-cycloadducts, and thioketones were found to react as 'superdipolarophilic' reagents to give 1,3-dithiolanes with variable regioselectivity. On the other hand, in the absence of a trapping agent, they undergo [1,3]-dipolar

electrocyclization leading to thiiranes or dimerize to yield, in most cases, the sterically more crowded 1,4-dithianes [3].

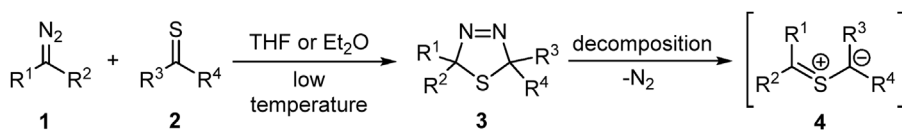
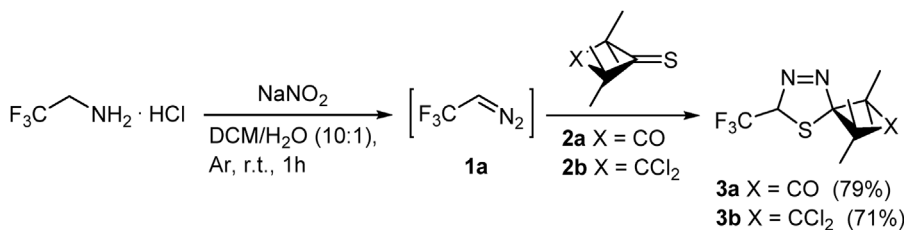
Thiocarbonyl *S*-methanides which contain fluorine atoms in their structure are scarcely reported in the literature. In our earlier publication however, reactions of diazomethane with fluorinated benzyl pentanedithioates leading to dimers of the intermediate thiocarbonyl ylides were described [4]. Furthermore, hexafluorothioacetone was reacted with diphenyldiazomethane, and after spontaneous elimination of nitrogen, 2,2-diphenyl-3,3-bis(trifluoromethyl)thiirane was obtained [5]. Finally, hexafluorothioacetone and 2-diazohexafluoropropane formed the stable 2,2,5,5-tetrakis(trifluoromethyl)-2,5-dihydro-1,3,4-thiadiazole [6].

1,1,1-Trifluorodiazaoethane (**1a**) is easily available via direct diazotization of commercially available 2,2,2-trifluoroethylamine hydrochloride and recently has extensively been explored as a versatile fluorine-containing organic building block. The [3 + 2]-cycloaddition reactions with **1a** and dipolarophiles such as metal acetylides [7], alkynes [8], alkenes [9], and the C≡P group [10] were reported in recent years. Cyclopropanations of alkenes were performed with **1a** via sequential cycloaddition/elimination reaction [11]. However, **1a** has not yet been used in cycloaddition reactions with thioketones (C=S dipolarophiles).

Due to our ongoing interest in the exploration of thioketones as useful building blocks in the synthesis of diverse fluoroalkylated *S*-heterocycles [12], we performed a study aimed at the examination of their reactions with 1,1,1-trifluorodiazaoethane (**1a**).

* Corresponding authors.

E-mail addresses: marcin.kowalski.chem@gmail.com (M.K. Kowalski), emilkaobjalska@gmail.com (E. Objalska).

Scheme 1. Generation of thiocarbonyl *S*-methanides.Scheme 2. Generation of 1,1,1-trifluorodiazethane (**1a**) and its [3 + 2]-cycloaddition with thioketones **2a,b**.

2. Results and discussion

Two thioketones, the cycloaliphatic 2,2,4,4-tetramethyl-3-thioxocyclobutanone (**2a**) and aromatic thiobenzophenone (**2c**) were selected for examination of the reactivity of **1a** towards C=S dipolarophiles.

The reactions with **2a** and **2c** were performed at room temperature with the ‘*in situ*’ generated **1a** (Scheme 2). The characteristic color of thioketones disappeared within *ca.* 1 h, and after typical aqueous workup, the crude products were analyzed by ¹H NMR spectroscopy. The solid product obtained from **2a** showed four signals for methyl groups and a characteristic quartet at 6.71 ppm (³J_{H,F} = 6.6 Hz). These data suggested that the expected 2,5-dihydro-1,3,4-thiadiazole **3a** was formed as the sole product. The ¹³C NMR spectrum confirmed this structure by the presence of two signals at 97.6 ppm (q, ²J_{C,F} = 28.9 Hz) and 117.2 ppm (s), which were attributed to C(7) and C(4), respectively. The molecular mass for C₁₀H₁₃F₃N₂OS was confirmed by ESI-MS and corresponded to the results of the elemental analysis. In analogy to the cycloadduct obtained from **2a** and diazoethane [13], **3a** was stable at room temperature.

In addition to **2a**, 3,3-dichloro-2,2,4,4-tetramethylcyclobutaneone (**2b**) was treated with **1a** under analogous conditions (two-phase system DCM/H₂O, Ar, room temperature, *ca.* 1 h) and the only observed product was the corresponding 2,5-dihydro-1,3,4-thiadiazole **3b** (Scheme 2). Also in that case, no decomposition was observed at room temperature.

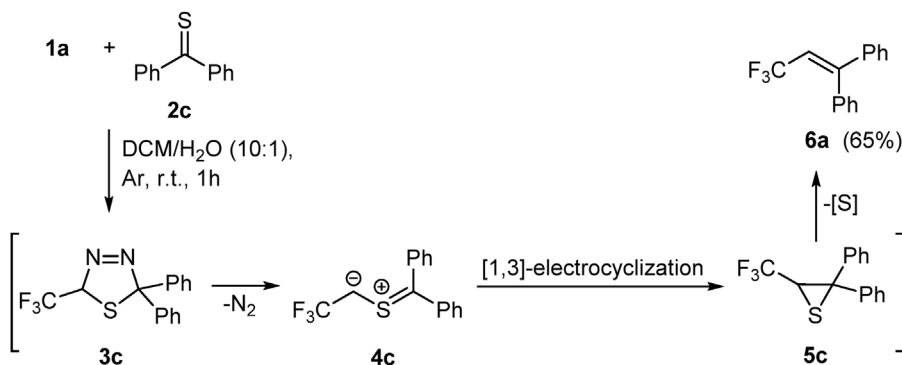
The experiment with **2c** led to an oily product, which in the ¹H NMR spectrum along with signals of the phenyl groups displayed a single quartet at 6.17 ppm (³J_{H,F} = 8.3 Hz). In the ¹³C NMR spectrum, two signals located at 115.5 ppm (q, ²J_{C,F} = 33.8 Hz) and 152.5 ppm (q, ³J_{C,F} = 5.6 Hz), together with the typical quartet for the trifluoromethyl group (CF₃) at 123.1 ppm (q, ¹J_{C,F} = 270.6 Hz),

suggested the structure of the alkene **6a** [14] (Scheme 3). This assumption was also confirmed by MS measurement. The observed instability of the initially formed cycloadduct **3c** is in line with the reported behavior of the analogous product obtained with diazomethane [15]. Apparently, the presence of the electron-withdrawing trifluoromethyl group accelerates the extrusion of the sulfur atom.

The isolated cycloadducts **3a** and **3b** were used as precursors of fluorinated thiocarbonyl *S*-methanides **4a,b** (Scheme 4). In the first series of experiments, their solutions in dichloromethane were stirred at room temperature overnight. The isolated products showed similar sets of signals in the ¹H NMR spectra with four singlets for Me groups and a quartet attributed to a CH–CF₃ group. The ¹³C NMR spectra revealed signals at 64.0 and 65.3 ppm, respectively. The comparison with structurally similar spirothiiranes [13] allowed to attribute them the structures of thiirane derivatives **5a** and **5b**. In both cases, the molecular masses were confirmed by mass spectrometry.

The thermal decomposition of the isolated 2,5-dihydro-1,3,4-thiadiazoles **3a,b** in toluene at 100 °C in the presence of equimolar amounts of aromatic thioketones, *i.e.* thiobenzophenone (**2c**), di(thiophen-2-yl) thioketone (**2e**) and di(selenophen-2-yl) thioketone (**2f**), was aimed at trapping of the initially formed fluorinated thiocarbonyl ylides **4** with C=S dipolarophiles. In a typical experiment with **3a** and **2c**, the reaction was complete after 24 h, and subsequent chromatographic workup led to a single crystalline product, which was identified as the expected 1,3-dithiolane **7a** (Scheme 4). The structure of this regioisomer was elucidated on the basis of its ¹³C NMR spectrum. Two quartets at 125.0 and 61.2 ppm are characteristic for the CF₃–CH unit. The chemical shift of the high-field signal corresponds with the range of values reported for analogous, sterically less crowded regioisomers [3]. Finally, the structure **7a** was unambiguously proved by the X-ray structure investigation [16] (Fig. 1).

An analogous result was obtained in the reaction of **3b** with

Scheme 3. Formation of alkene **6a** in the reaction of **1a** with thiobenzophenone (**2c**).

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