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Redox chemistry of trifluoromethyl sulfonium salts as CF_3 radical sources[☆]

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ABSTRACT

The electrochemical behaviour of Umemoto reagent **5** and the sulfonium-based Shibata reagents **7**, **8**, **12** and **13** was investigated in anhydrous acetonitrile, *N*,*N*-dimethylformamide and methanol using cyclic voltammetry. In MeCN, all reagents are reduced in two distinct steps with the first reduction occurring at low cathodic potentials between −0.49 and −0.72 V on a glassy carbon electrode. This event probably corresponds to the cleavage of the S–CF_3 bond with formation of the trifluoromethyl radical. In contrast to the Umemoto reagent **5**, the Shibata reagents **7**, **8**, **12** and **13** were found to be unstable in *N*,*N*-dimethylformamide (in the absence of electrochemical or photochemical activation), giving either the ring-opened alkyne **14** for Shibata reagent **7** or the corresponding 2-substituted benzothiophene derivatives **15**–**18** for reagents **8**, **12** and **13**. In MeOH, the Umemoto reagent **5** and Shibata reagent **7** underwent irreversible reductions at more cathodic potentials than observed in MeCN and DMF; the Shibata reagent **7** was unstable in this solvent. The electrochemical data obtained in this study should be of general interest for those interested in the development of trifluoromethylation processes carried out under photoredox and electrochemical conditions.

1. Introduction

Radical and nucleophilic trifluoromethylation remains one of the most direct approaches to introduce a trifluoromethyl moiety into arenes and heteroarenes of medicinal interest, for the development of trifluoromethyl agrochemicals, and to access novel non aromatic trifluoromethylated synthetic intermediates [1]. New metal mediated or catalysed trifluoromethylation reactions have appeared [2] and known processes optimised; such advances were possible in part due to the development of novel CF_3 reagents [3]. In recent years, photoredox catalysis [4] has received great attention with a number of synthetic useful trifluoromethylations disclosed by different groups including our own contributions [5]. The choice of CF_3 reagent is driven not only by availability, cost and solubility but also its redox properties as these should allow for efficient reduction through single electron transfer (S.E.T) in the presence of a suitable photoredox catalyst (ruthenium, iridium or copper complex). Reagents **1**–**6** (Chart 1) have served as trifluoromethyl radical sources for these photoredox transformations. CF_3I [6] and CF_3SO_2Cl [7] have been known for some years to generate the trifluoromethyl radical in a series of transformations. More recently, it was found that the Togni reagents **3** and **4** [2b,c,8], the Umemoto reagent **5** [5b,9] and the Yagupolskii–Schreeve reagent **6** [10] are also suitable sources of trifluoromethyl radical using either photoredox or alternative classical initiators. To the best of our knowledge, the *S*-(trifluoromethyl)thiophenium salts **7**–**8** [11,12] and the sulfoximinium reagent **9** (fluorinated Johnson's type reagent) [13] developed by Shibata and co-workers have not been used in radical mediated trifluoromethylation processes.

We recently reported that, under photoredox catalysis, allylsilanes [5a] and unactivated alkenes [5b] underwent in methanol allylic trifluoromethylation and hydrotrifluoromethylation, respectively. The choice of trifluoromethyl radical source and solvent had a critical impact on the outcome of the reactions, both in terms of yields and selectivity. The trifluoromethylation of

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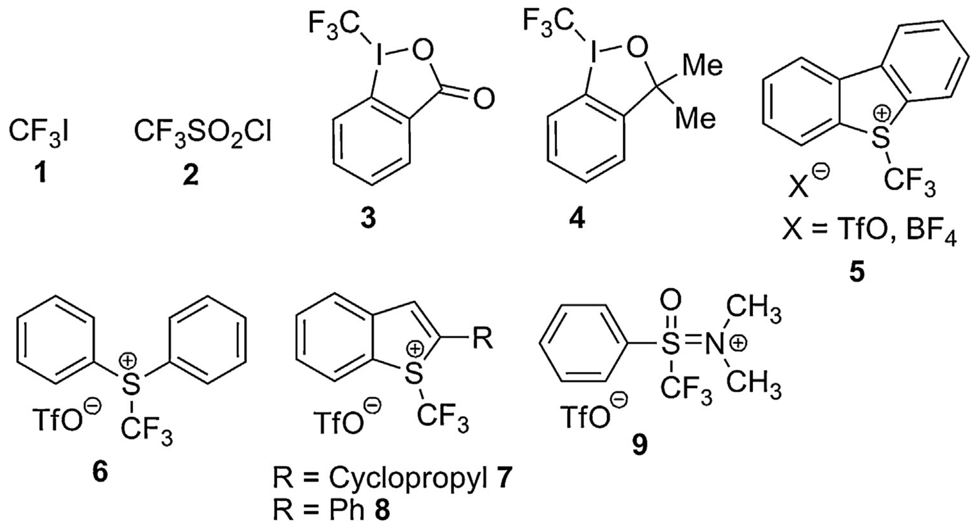


Chart 1.

allylsilane (*E*)-**10a** [5a] was re-examined in various solvents (DMF, MeCN, CH_2Cl_2, MeOH and EtOH) using the CF_3 radical sources **1**–**5** and **7** (Table 1); the optimum solvent was MeOH for the Togni reagent **3** (entry 2) and EtOH for the Umemoto reagent **5** (entry 13). A higher isolated yield was obtained with Togni **3** but significantly better stereoselectivity (*E*/*Z* ratio) was observed with Umemoto **5**. The same trend applied for other allylsilanes [5a]. Unexpectedly, no conversion was observed in MeOH (entry 17) or in DMF (entry 19) in the presence of the Shibata reagent **7**. Complete conversion of the starting material **7** was observed in MeCN but the desired product **11a** was detectable in trace amount only (entry 18).

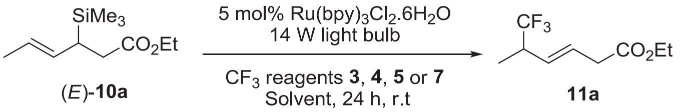
These results prompted us to initiate a comprehensive study to delineate the electrochemical behaviour of trifluoromethyl radical sources in various solvents. Such data could facilitate the understanding of our experimental observation, the reactivity trends for transformations reported in the literature and the development of novel trifluoromethylation processes.

2. Results and discussion

The cyclic voltammetry of reagents **3**–**5** and **7**–**8** was investigated in anhydrous MeCN, DMF and MeOH containing *n*-Bu_4NPF_6 (0.1 M) as supporting electrolyte. In addition to the

Table 1

Optimisation for the photocatalyzed trifluoromethylation of (*E*)-ethyl 3-(trimethylsilyl)hex-4-enoate **10a**.



Entry	“CF_3”[a]	Conditions	Solvent	Time (h)	Conv. (%)[b]	Yield (%)[b] (*E*:*Z*)
1	**3** (1.2)		MeOH	24	45	27 (2.5:1)
2	**3** (1.8)		MeOH	*48*	90	55 (1.7:1)
3	**3** (1.2)	*i*Pr_2NEt (2.0 equiv.)	MeOH	24	30	ND
4	**3** (1.2)		EtOH	24	55	30 (2.0:1)
5	**3** (1.2)		MeCN	24	18	17 (2.2:1)
6	**3** (1.2)		CH_2Cl_2	24	42	22 (1.7:1)
7	**3** (1.2)		DMF	24	89	37 (1.8:1)
8	**4** (1.2)		MeOH	24	<5	3(3.8:1)
9	**4** (1.2)		MeCN	24	<5	NR
10	**4** (1.2)		DMF	24	<5	NR
11	**5** (1.2)		MeOH	24	82[d]	30[c,d](5.3:1)
12	**5** (1.2)	*i*Pr_2NEt (2.0 equiv.)	MeOH	24	<5	NR
13	**5** (1.2)		EtOH	24	53	34[c] (4.3:1)
14	**5** (1.2)		MeCN	24	>99	7 (8.0:1)
15	**5** (1.2)		DMF	24	76	33 (5.4:1)
16	**5** (1.8)		EtOH	*48*	4	38[c] (3.4:1)
17	**7** (1.2)		MeOH	24	<5	trace
18	**7** (1.2)		MeCN	24	>99	<5
19	**7** (1.2)		DMF	24	<5	NR

[a] **10a** (0.15 mmol, 1.0 equiv.), **3** (0.18 mmol, 1.2 equiv.), $Ru(bpy)_3Cl_2·6H_2O$ (0.0075 mmol, 5 mol%), in MeOH (0.3 mL) at r.t for 24 h.

[b] Determined by ^{19}F NMR spectroscopy using fluorobenzene as an internal standard.

[c] Isolated yield.

[d] Transesterification of **10a** and **11a**.