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ARTICLE

ELECTRON-CATALYZED RADICAL PERFLUOROALKYLATION OF ORGANIC SULFIDES. THE SERENDIPITOUS USE OF TMEDA/I_2 COMPLEX AS RADICAL INITIATOR

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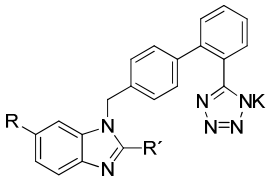
Radical initiation for the perfluoroalkylation reaction of sulfides has been performed using the complex [(TMEDA) I.I_3] and visible light. This methodology bypasses the use of metal(organo)catalysts where the complex [(TMEDA) I.I_3] acts as a good electron donor / reductant radical initiating agent. Biologically-relevant sulfides are easily substituted with R_F moieties employing a mild and environmentally benign radical strategy starting from readily-available R_FI.

Introduction

Perfluoroalkyl sulfides have found wide applications, such as in liquid crystal displays[1],[2], for oleophobic surface coatings[3], as well as in the synthesis and development of potential hypotensive agents for clinical use containing SR_F moieties such as Losartan derivatives (Dup 753) in Figure 1.[4]

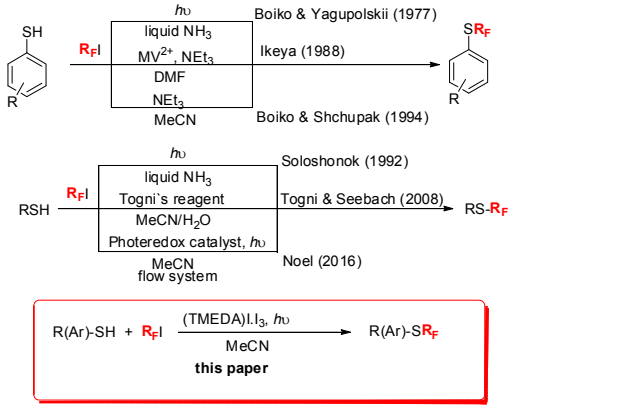


R = SCF_3, SC_2F_5, SC_3F_7,
R = SC_2F_5, SC_3F_7, SC_4F_9

Figure 1. Losartan analogs containing S-R_F

In order to avoid the use of gaseous CF_3I for the trifluoromethylation of sulfides RS-H, several trifluoromethylthiolating reagents have appeared in the literature in order to effect late-stage SCF_3 substitutions; however, fewer direct perfluoroalkylthiolating reagents are known to date.[5] To that effect, the direct perfluoroalkylation of sulfides still remains a simple and viable strategy towards the synthesis of perfluoroalkylsulfides.

Electrophilic perfluoroalkyl radicals R_F derived from R_F-I have recently been informed to functionalize sulfide RSH residues very efficiently[6], when the reactions are initiated by visible light and a metal-photocatalyst in the presence of *N,N,N´,N´*-tetramethylethylene diamine, TMEDA, in MeCN as solvent. In the past, the perfluoroalkylation of sulfides has been accomplished by different methods under diverse reaction conditions,[4],[7],[8],[9],[10],[11],[12] such as those indicated in Scheme 1.



Scheme 1. Methods for radical perfluoroalkylation of thiols by R_FI

Inspired by the results of Noel and collaborators[6] for the perfluoroalkylation of cysteine derivatives employing TMEDA, R_F-I and a transition metal photoorganocatalyst, we replaced our reported strategy for the radical perfluoroalkylation reactions using Cs_2CO_3[13] for TMEDA and used a commercial fluorescent light CFL in the absence of an organophotocatalyst (POC). In this work, we will show the serendipitous discovery of a radical initiation event from visible light irradiation of a complex between TMEDA and I_2 (i.e. :[(TMEDA) I.I_3]) which

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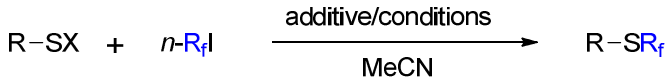
triggers an electron-catalyzed process towards the synthesis of perfluoroalkyl sulfides in improved substitution yields.

Results and discussion

Table 1. Optimization of reaction conditions for the perfluoroalkylation of organic thiols R-SX (0.2 mmol), with a perfluoroalkyl iodide R_FI (1.5 equiv.), an additive (1.5 equiv.), under diverse reaction conditions (2 h reaction, 25 °C, Ar-deoxygenated)



Entry	R	X	Additive	R_FI	Conditions	% RS-C_4F_9
1	Ph	H	Cs_2CO_3	*n*-C_4F_9I	*hν*[a,b]	80
2	Ph	H	Cs_2CO_3	*n*-C_4F_9I	[c]	63
3	Ph	H	TMEDA	*n*-C_4F_9I	*hν*[a]	80
4	Ph	H	TMEDA	*n*-C_4F_9I [d]	*hν*[a]	11
5	Ph	H	TMEDA	*n*-C_4F_9I	[c]	30
6	Ph	H	-	*n*-C_4F_9I	*hν*[a]	-
7	Ph	H	TMEDA *n*Bu_4NI[e]	*n*-C_4F_9I [d]	[c]	< 5
8	$HOCH_2CH_2$-	H	TMEDA	*n*-C_4F_9I	*hν*[a]	75
9	$HOCH_2CH_2$-	H	TMEDA	*n*-C_4F_9I [d]	*hν*[a]	42
10	$HOCH_2CH_2$-	H	TMEDA	*n*-C_4F_9I	[c]	< 5
11	$HOCH_2CH_2$-	Na	TMEDA	*n*-C_4F_9I	*hν*[a]	< 5
12	$HOCH_2CH_2$-	Na	-	*n*-C_4F_9I	*hν*[a]	< 5

a.- irradiation with a commercial fluorescent lamp CFL, 60 Watt; **b**.-Rose Bengal as photocatalyst, 0.1 equiv.; **c**.-dark reaction conditions; **d**.-dissolved iodine was excluded from the neat reagent *n*-C_4F_9I by passing through a neutral alumina column; **e**.- [*n*-Bu_4NI] = 0.2 equiv

The visible light-Rose Bengal (RB)-photocatalyzed reaction of benzene thiol in the presence of Cs_2CO_3 and *n*-C_4F_9I affords 80 % yield of PhS-C_4F_9 **1** (entry 1, Table 1). Under dark reaction conditions, a 63 % yield of product **1** (entry 2, Table 1) is obtained.[14] These results are very encouraging in terms of initiation efficiency and chain propagation by the Cs_2CO_3 salt.[14] Replacing Cs_2CO_3 for the less expensive TMEDA affords 80% yield of product **1** under visible light irradiation (entry 3, Table 1) in the absence of POC.

We suspected that, in the absence of POC (i.e. Rose Bengal) and presence of TMEDA, the residual absorption of benzene thiolate[15],[4] at the irradiation wavelengths of the commercial fluorescent lamp CFL, could start the reaction through the well-known photoinduced electron transfer initiation process from thiolates to R_FI.[16],[4]

The UV-vis spectrum of a solution mixture of commercial *n*-C_4F_9I to be irradiated at the working concentrations shows an absorption band with λ_{max} = 458 nm, corresponding to the absorption of iodine in MeCN (Figure S1, Supporting Information), with enough optical density to initiate the radical reaction through the production of iodine atoms.[17],[18] Concerned about this absorption, we excluded dissolved iodine from the neat reagent *n*-C_4F_9I, passing the neat liquid through a neutral alumina column, and subjected the mixture of RSH, iodine-free *n*-C_4F_9I, and TMEDA to the photoreaction under visible-light (CFL) in MeCN as solvent. Under these latter conditions, we obtained only 11 % yield of product **1** (entry 4, Table 1), indicating that the residual absorption of benzene thiolate at the irradiation wavelengths with a CFL is not sufficient for maintaining the radical chain and that the presence of I_2 is intervening in the initiation process.

At this point, the evidence showed that in the absence of POC [13] (RB) and presence of TMEDA, product formation seemed to improve substantially upon illumination (entries 3, 8, Table 1) when traces of I_2 were present in commercial *n*-C_4F_9I.

The photoreaction of benzenethiol in the absence of TMEDA (entry 6, Table 1), does not afford any product. The dark reaction in the presence of *n*-Bu_4NI, a known thermal radical initiator,[19] affords < 5% yield of product **1** (entry 7, Table 1). The photoreaction of β-mercaptoethanol[9] in the presence of *n*-C_4F_9I and TMEDA, affords 75% yield of $HOCH_2CH_2S$-C_4F_9 **2**[9] (entry 8, Table 1). Excluding the presence of dissolved iodine, reduces the yield of **2** to 42% (entry 9, Table 1). Under dark conditions, a low yield of product **2** is obtained (< 5%, entry 10, Table 1). The photoreactions of the sodium salt of β-mercaptoethanol, either in the presence or absence of TMEDA, do not afford appreciable quantities of product (entries 11, 12, Table 1), emphasizing the role of the organic covalent salt $RS^-TMEDAH^+$.

A complex between TMEDA and I_2 (i.e.: [(TMEDA) $I.I_3$] has been reported by Adam and colleagues[20], with λ_{max} = 360 nm in

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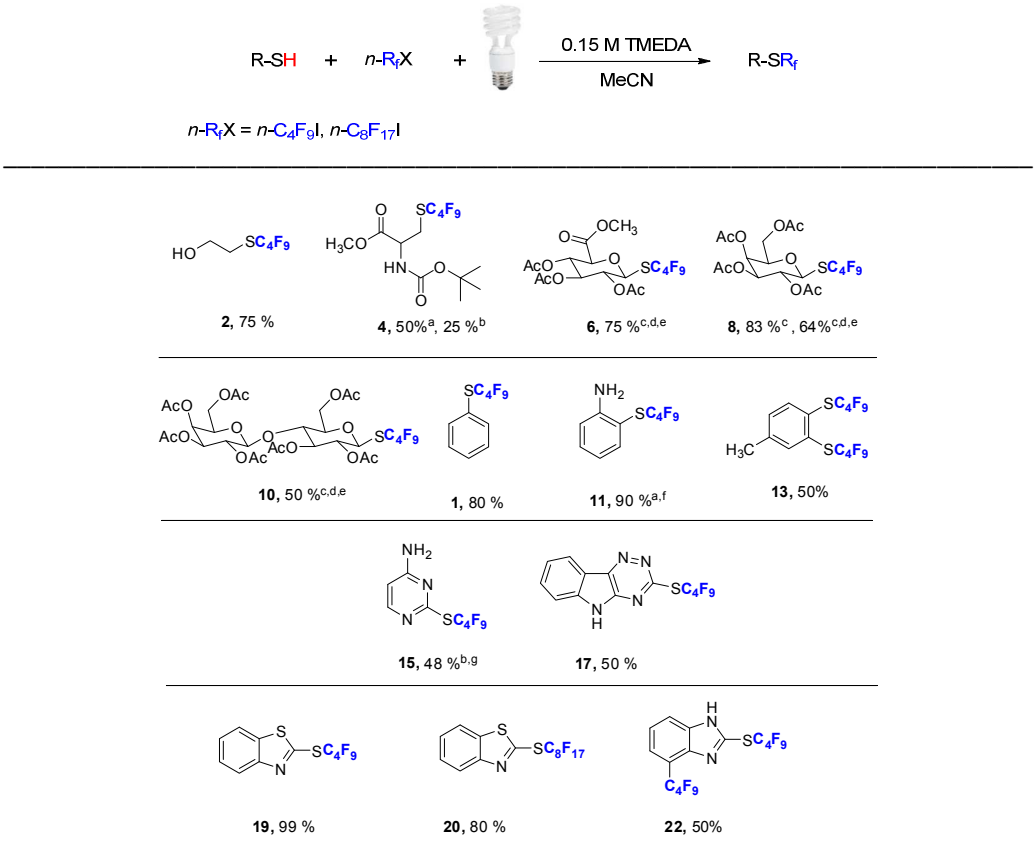
MeCN, (ε = 4x10^4 M^{-1}cm^{-1}, a complex formation constant ca. 4.7 x 10^7 M^{-1} and E_{CT} = 4.35 eV). Due to the traces of I_2 present in the neat starting *n*-C_4F_9I, we consider convenient to inspect whether complexation of these trace amounts of I_2 present in *n*-C_4F_9I with TMEDA could be responsible for the radical initiation process. Figures S2-S3, show the UV-vis spectra of mixtures of TMEDA and I_2, confirming the remarkable increase in the absorptivity at 360 nm (ε = 4x10^4 M^{-1}cm^{-1} in MeCN), responsible for the absorption of light.

Table 2: % Yields of perfluoroalkylation of organic sulfides RS-H (0.2 mmol) with RFI (1.5 equiv.) in the presence of TMEDA (1.5 equiv.) in MeCN as solvent and visible light in de-oxygenated (Ar) atmosphere.



a.-%NMR yield; b.- isolated yield; c.-24-h reaction; d.- in the presence of RB and Cs_2CO_3; e.-with excess of *n*-C_4F_9I; f.- 20 h reaction; g.- in DMSO: DMF 1 :2-

UV-vis spectra of mixtures of iodine-free *n*-C_4F_9I and TMEDA do not show a distinct change in absorption or extinction coefficients. The TMEDA•2-CF_3I complex has been reported before[21], based on calculations, X-Ray crystallographic analysis, and spectroscopic data (^{1}H, ^{19}F, ^{13} C NMR). The same trends for the formation of a complex TMEDA•2C_4F_9I[22] based on NMR data (^{19}F NMR) is presented in Table S1, showing spectral changes going from free reagents to the complexed mixtures.

The ^{19}F NMR upfield shifts observed in the I-**CF_2**-C_3F_7 are indicative of a debilitated I-C bond in *n*-C_4F_9I when TMEDA is present, being the largest shift when a stoichiometry of the complex TMEDA: 2C_4F_9I is reached (Table S1). Also, from Table S1, there seems to be the presence of complexes between perfluoroalkyl iodides and thiols[23], the existence of which result in chemical shift changes of the signal from I-**CF_2**-R_F in the ^{19}F NMR spectra when *n*-C_4F_9I is in the presence of the RSH as compared with the innate chemical shift value of I**CF_2**-R_F signal, interpreted as halogen bonding to the sulfur atom of the substrate.[24] We have observed the same trends in the ^{19}F NMR spectra of mixtures of TMEDA / R_FI / amino(hetero)aromatic compounds.[22]

In a previous report[22] we have shown the efficient visible light-initiated reaction of 2-mercaptoaniline with *n*-C_4F_9I at the sulfur atom (product **11**, Table 2) in the absence of organophotocatalyst and presence of TMEDA. Encouraged by

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this result, and that from Noel and collaborators on the perfluorobutylation of cysteine derivatives in the presence of TMEDA and a transition-metal photoorganocatalysts,[6] we attempted the perfluoroalkylation of organic sulfides, as shown in Table 2, in the presence of [(TMEDA)I.I_3] complex, a CFL and absence of photoorganocatalyst. The concentration of the complex between I_2-contaminated *n*-C_4F_9I and TMEDA was ca. 0.25 mM.

The reaction of 2-mercaptoethanol under conditions of Table 2, affords 75% yield of product **2**. Noncanonical aminoacids have proven to be efficient tools to advantageously modulate the biophysical and biochemical properties of peptides and proteins. Moreover, owing to its nearly total absence in biological media, fluorine is an outstanding bioorthogonal atom useful as a probe for NMR spectroscopy to explore conformational changes in peptides and proteins and their interactions with other biological molecules.[25] We therefore embarked on exploring the perfluoroalkylation of cysteine derivative **3**, which affords product **4** in 50 % yield (Table 2, purified yield 25%).

Pefluoroalkylated thiosugar derivatives have been paid much attention in the last decades due to their useful liquid–crystalline properties[1] and relevance as surfactants and emulsifiers for "water-in-fluorocarbon" emulsions.[26a] On the other hand, the sulfur atoms in thiosugars make the interglycosidic bonding stable to glycosidases.[26b-d] The incorporation of a hydrophobic chain as aglycone, such as a perfluorinated residue, could have a high impact in protein–carbohydrate recognition events which take place between sugars and glycosidases, glycosyltransferases and also lectins. For these reasons, fluorinated thiosugars have a great potential as tools in the field of Glycobiology. To that effect, we proceeded to studying the S-perfluoroalkylation of thiocarbohydrates. The reactions of the sugar thioaldoses[26] 2,3,4-tri-*O*-acetyl-1-thio-β-D-glucuronic acid methyl ester[27] **5** and 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranose[26] **7** under our standard reaction conditions, afford 75 and 83 % yields of SC_4F_9 -substituted products **6** and **8** respectively (Table 2). The disaccharide 2´,3´,4´,6´,2,3,6-hepta-*O*-acetyl-1-thio-β-D-cellobiose **9** affords product **10** in 50 % yield as indicated in Table 2. However, the reaction of galactoside-disulfide (1,1´-bis-(2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranose)) did not afford any S-C_4F_9 substitution product.

Benzene thiol affords **1** in 75-80% yield, whereas 2-mercaptoaniline gives product **11** in 90% yield. When the dithiol 4-methylbenzene-1,2-dithiol **12** is treated under reaction conditions from Table 2, 50 % yield of **13** is obtained.

When 2-mercapto-4-amino-pyrimidine **14** is subjected to the same reaction conditions, a 48% yield of product **15** is observed.

When 5*H*-[1,2,4]triazino[5,6-b]indole-3-thiol **16,** a dihydrofolate reductase (DHFR) inhibitor,[28] which has successfully been used as a drug target in the area of parasitic diseases is subjected to reaction conditions of Table 2, a 50% yield of product **27** is found.

2-Mercaptobenzothiazol[29] **18** gives product **19** in 99% yield. When *n*-$C_8F_{17}I$ is used instead of *n*-C_4F_9I, product **20** is isolated in 80% yield.

1*H*-Benzo[d]imidazole-2-thiol **21**, affords 50% yield of di-substituted compound **22** (Table 2), i.e.: 4-(perfluorobutyl)-2-((perfluorobutyl)thio)-1*H*-benzo[d]imidazole**.**

For the reaction of sulfides, an ET mechanism between visible light-excited sulfides and R_FI has been accepted as initiation process, where the radical anion of the substitution product is the chain carrier.[4] The reaction, depending on the substrate, has a thermal spontaneous component (see entries 5, 9, Table 1) that contributes to some product formation. Notwithstanding, the reaction is always accelerated after irradiation under the conditions illustrated in Table 2. When the reactions of sulfides were carried out in the absence of [(TMEDA) I.I_3] complex (i.e.: I_2 excluded or absence of TMEDA), under visible light irradiation, low yields of substitution products were obtained (entries 4, 6, Table 1). The dark reactions in the presence of the complex [(TMEDA) I.I_3] afford lower yields of substitution products (entries 5, 10, Table 1). Taking into account the presence of dissolved iodine in commercial R_FI, the use of TMEDA can aid in the initiation process through the [(TMEDA) I.I_3] complex formation. This is likely the case in many studies[6],[30],[31a] where a combination of R_FI, TMEDA, and visible light is employed. In fact, a very recent report on the trifluoromethylation of alkynes in the presence of TMEDA and that of heteroaromatics and alkenes in the presence of DBU with CF_3I shows that the reactions proceed in good-to-excellent yields when irradiated with white light and absence of photocatalyst. However, no explanation is supplied.[31b]

The reactions in the presence of TEMPO ((2,2,6,6-Tetramethyl-piperidin-1-yl)oxyl, a well-known radical scavenger) as well as in the presence of 1,4-dinitrobenzene afford little or no substitution products, indicating the presence of radicals.

For the visible light irradiation of amino-(hetero)aromatic compounds in the presence of R_FI and TMEDA we have previously proposed[22] a reaction mechanism, where the visible light-excited complex [(TMEDA) I.I_3] produces iodine atoms[32],[33],[34] capable of abstracting I from *n*-C_4F_9I producing *n*-C_4F_9 radicals that commence the radical reaction. However, the visible light irradiation of the complex [(TMEDA) I.I_3] in the presence of oleic acid methyl ester (see Supporting Information) does not produce the corresponding *trans*-fatty acid methyl ester, indicating that iodine atoms, if produced, do not induce the isomerization process with efficiency.[17],[18],[35],[33],[32],[34],[36] We have[22] also found that TMEDA is not acting as a sacrificial donor in the perfluoroalkylation of amino(hetero)aromatic compounds under visible light-irradiation, as very little decomposition of TMEDA into a carbonyl compound was detected, as in eq. 1 (see Supporting Information). Therefore, the complex [(TMEDA) I.I_3] does not undergo significant ET to *n*-C_4F_9I to produce the radical cation of TMEDA according to eq. 1. [37]

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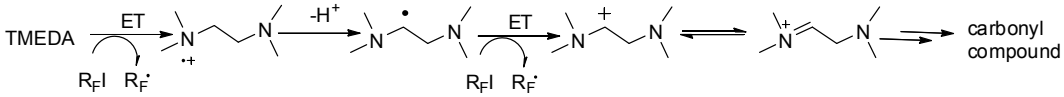
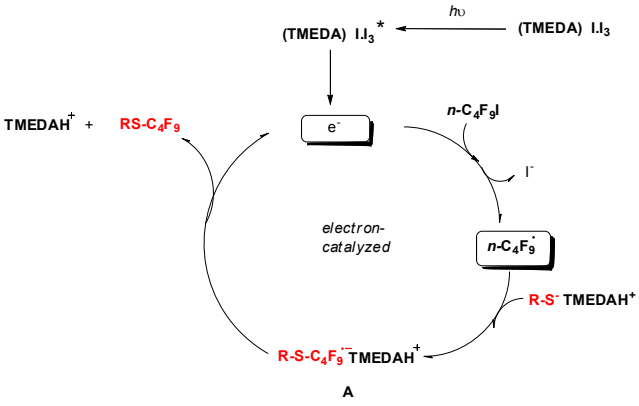


(1)

Another possibility should be considered: that of the complex [(TMEDA) $I.I_3$] acting as a radical initiator. Organic iodides such as n-Bu_4NI, and inorganic iodide salts XIn (where X = Na, K, Li, Cu (with n=1), Fe (n = 2), Ni (n = 2)) are known to act as radical initiators under thermal conditions.[38] In the proposed mechanism (Scheme 2), electrons from excited (under illumination conditions) or ground state (under dark thermal conditions) complex [(TMEDA) $I.I_3$] reduce R_FI, forming the radical of R_F• and iodide anion. This process is facilitated in view of the debilitated RF-I bond in the TMEDA•$2C_4F_9I$ complex (Table S1); reaction with RS- (or the TMEDA salt) would ensue, leading to the formation of the radical anion of the substitution product RSC_4F_9 •-, which by further ET to R_FI (or the complex TMEDA•$2C_4F_9I$) yields thermoneutral RSC_4F_9 and further electrons to maintain the chain. This possibility does not entail the formation of the radical cation of TMEDA. In this respect, TMEDA is acting as a complexing agent to iodine, and a Brønsted base to deprotonate RS-H.



Scheme 2. Alternative proposed mechanism where the excited complex [(TMEDA) $I.I_3$] undergoes outer-sphere ET with *n*-C_4F_9I

Experimental

A. GENERAL CONSIDERATIONS

All reactions were carried out in an argon atmosphere under anhydrous conditions or otherwise noted.

Reaction solvents such as acetonitrile, were chromatography quality and were not further purified. Chromatography and extraction solvents dichloromethane, chloroform, *iso*-octane, *n*-hexane, *n*-heptane, ethyl acetate, acetone, and, ethanol were purchased from commercial suppliers.

N,N,N´,N´-tetramethylethylene diamine TMEDA was 99% pure and used as received from the supplier. Fluorinated reagents 1,1,1,2,2,3,3,4,4-nonafluoro-4-iodobutane (perfluorobutyl iodide), 1,1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8-heptadecafluoro-8-iodooctane were used as received from the supplier without further purification, except when traces of iodine had to be removed, in which case, the neat liquid was passed through a neutral alumina column. Sulfides were commercially available and purified by column chromatography or vacuum-distilled; the synthesis of sugar thioaldoses 2,3,4-tri-*O*-acetyl-1-thio-β-D-glucuronic acid methyl ester **5** and 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranose **7** and disaccharide 2´,3´,4´,6´,2,3,6-hepta-*O*-acetyl-1-thio-β-D-cellobiose **9** have been accomplished by standard techniques and are given in section **D**. 2,2,6,6-Tetramethyl-1-piperidinyloxy (TEMPO) and 1,4-dinitrobenzene were Ultra-pure grade. Dye Rose Bengal (4,5,6,7-Tetrachloro-3',6'-dihydroxy-2',4',5',7'-tetraiodo-3*H*-spiro[isobenzofuran-1,9'-xanthen]-3-one), was 99.9% pure and used as received from the supplier. Yields were referred to as isolated yields of analytically pure material unless otherwise noted, as the case of yields calculated from ^{19}F NMR and ^{1}H NMR spectral integration.

Reactions were magnetically stirred and monitored by thin-layer chromatography (TLC) using Silica gel 60 F254 pre-coated plates (0.25 mm, Merk), and revealed by UV-light or CAN solution. Purification of the reaction products was carried out by flash column chromatography using Ultra Pure Silica Gel (230–400 mesh) or standard silica-gel for column chromatography (60 mesh).

The light source was a commercially available household 60-watt fluorescent light bulb or a 50 Watt black light (λ_{max} = 370 nm).

^{1}H NMR spectra were recorded on a Bruker Avance 600 (600 MHz) spectrometers, and are reported in ppm using the solvent residual peak resonance as the internal standard (dimethylsulfoxide-*d6* at 2.54 ppm, $CDCl_3$ at 7.26 ppm). ^{1}H NMR data are reported as follows: chemical shift; multiplicity; number of hydrogens, coupling constants (Hz); H assignment when necessary.

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Multiplicity is abbreviated as follows: s = singlet, d = doublet, t = triplet, dd = double doublet, m = multiplet, br = broad. Proton-decoupled ^{13}C NMR spectra were recorded on a Bruker Avance 500 (at 125.758 MHz), or on a Bruker Avance 600 (at 150.903 MHz) spectrometers and are reported in ppm using the C resonance signal from the solvent as the internal standard (acetone-*d6* at 29.8 ppm, $CDCl_3$ at 77.00 ppm). ^{19}F NMR spectra were recorded on a Bruker Avance 500 (at 470.592 MHz), or a Bruker Avance 600 (at 564.686 MHz) spectrometers and are reported in ppm using the internal standard signal from the spectrometer. High-resolution mass spectra (HRMS) were obtained using JEOL-DX 700 mass spectrometer.

B. EXPERIMENTAL PROCEDURES AND CHARACTERIZATION DATA

B.1.-PREPARATION OF PRECURSORS AND SUSBTRATES

Sugar thioaldoses 2,3,4-tri-*O*-acetyl-1-thio-β-D-glucuronic acid methyl ester **5** and 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranose were prepared by standard techniques. The disaccharide 2´,3´,4´,6´,2,3,6-hepta-*O*-acetyl-1-thio-β-D-cellobiose was also prepared by conventional techniques (see characterization, for preparation procedures).

B2.-GENERAL PROCEDURE FOR THE (TMEDA.I).I_3)-INITIATED REACTIONS

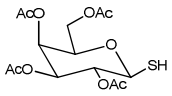
In a 4 mL screw-cap vial provided with a micro stir bar, (TMEDA) $I.I_3$ complex, ca. 0.25 mM, substrate (0.2 mmol thiol), photocatalyst Rose Bengal where needed (0.05 equiv) and 3 mL of acetonitrile were introduced. The mixture was de-oxygenated with a stream of Ar for 15 min. C_4F_9I or other R_FI (3 equiv) was introduced by microliter syringe, and the vial sealed. The closed reaction vessel was placed in front of a 60 Watt household fluorescent light bulb (or 20 Watt fluorescent black light, λ_{max} = 370 nm) and illuminated, under constant vigorous stirring, for 24 hrs or otherwise noted. After the reaction time was completed, the mixture was extracted thrice with CH_2Cl_2 / water / brine. The organic layers were gathered and dried over anhydrous Na_2SO_4, filtered and evaporated under vacuo. The crude reaction mixture was purified by silica-gel (60 mesh) column chromatography, with the eluants indicated in the TLC conditions (*vide infra*, spectral data). The polarity of the dye did not introduce any particular difficulty in the separation and purification protocol, as the several CH_2Cl_2 extractions eliminated the PC. The eluants employed are referred to in the TLC conditions of each compound.

C.-TRIAL EXPERIMENT FOR THE CIS/TRANS ISOMERIZATION OF OLEIC ACID METHYL ESTER

Experiment 1:
Methyl oleate (0.5 mmol) was added to degassed MeCN (3 mL) along with TMEDA (1 equiv) and I_2 (2 equiv) in a 3 mL glass vial capped with a screw-cap provided with septum and a stirring bar. The set-up was placed on a stir plate, and vigorously stirred throughout the irradiation with a 60 Watt CFL bulb (commercial fluorescent light bulb). Aliquots were taken at 30 min. intervals, added an internal standard (palmitic acid methyl ester), and analyzed through capillary GC/MS with an appropriate capillary column (DB-5, 30 m). There was no conversion of oleic acid methyl ester into elaidic acid methyl ester. This experiment rules out the production of I atoms through irradiation of the complex [(TMEDA) $I.I_3$], or else are produced in sufficiently low quantities to enable the cis/trans isomerization. Conducting the irradiation with a black fluorescent light bulb (20 Watt), λ_{max} = 370 nm from a black fluorescent light bulb), the same results were obtained.
Experiment 2:
Methyl oleate (0.5 mmol) was added to degassed MeCN (3 mL) along with TMEDA (1 equiv) and I_2-unfiltered C_4F_9I (3 equiv) in a 3 mL glass vial equipped with a screw-cap provided with a septum containing a stirring bar. The set-up was placed on a stir plate, sealed, and vigorously stirred throughout the irradiation with a 60 Watt CFL bulb. Aliquots were taken at 30 min. intervals, added a standard, and analyzed through capillary GC/MS with a DB-5 capillary column and an internal standard (palmitic acid methyl ester). There was no conversion of oleic acid methyl ester into elaidic acid methyl ester noticed through irradiation time. This experiment rules out that I_2 present in neat C_4F_9I, or else I_2 produced through photolytic cleavage of C_4F_9I complexes efficiently with TMEDA but do not produce I atoms on irradiation capable of the cis/trans isomerization of oleic acid methyl ester.

D. CHARACTERIZATION OF COMPOUNDS

All compounds are unknown chemicals, unless otherwise noted, and are reported as % yields obtained by weight or NMR integration (from ^1H and ^{19}F NMR integration) of the crude reaction mixtures. Isolated purified masses of compounds are expressed in Gram units. Characterizations employ ^1H, ^{13}C, ^{19}F 1D-NMR techniques, and 2D NMR spectroscopic techniques (HSQC, HMBC, COSY experiments)
2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranose 7



2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranose was obtained as previously described[39] and showed the same properties as reported. Briefly, the thioaldose was obtained by hydrolysis of the corresponding isothiouronium salt promoted by sodium carbonate. The isothiouronium salt was in turn obtained by reaction of acetobromogalactose with thiourea in boiling acetone.

^1H NMR (200 MHz, Cl_3CD) δ = 5.45 (dd, 1H, $J_{3,4}$ = 3.4, H-4), 5.20 (t, 1H, $J_{2,3} = J_{1,2}$ = 10.0 Hz, H-2), 5.00 (dd, $J_{3,4}$ = 3.4, $J_{2,3}$ = 10.0Hz, H-3), 4.55 (t, 1H, $J_{1,2} = J_{1,SH}$ = 10.0 Hz, H-1), 4.20 (m, 2H, H-6a, H-6b), 3.95 (t, 1H, $J_{5,6a} = J_{5,6b,}$ H-5), 2,40 (bs, 1H, SH), 2.09, 2.02, 1.97, 1.91 (4s, 12H, 4 CH_3CO). **^{13}C NMR** (50.3 MHz, Cl_3CD) δ = 170.3, 170.1, 169.9, 169.7 (4 *C*OCH_3), 79.2 (C-1), 74.9, 71.6, 70.8, 67.2 (C-5, C-3, C-2, C-4), 61.5 (C-6), 20.8, 20.7 (2×), 20.6 (4 CO*C*H_3).

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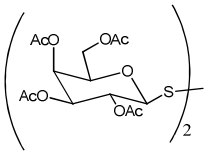
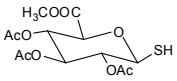
Bis(2,3,4,6-tetra-*O*-acetyl-1-deoxy-1-thio-β-D-galactopyranosyl) 1,1'-disulfide **7S**



The disulfide was obtained by oxidation of the corresponding 1-thio-β-D-galactopyranose.[40]

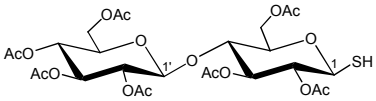
^{1}H NMR (200 MHz, Cl_3CD) δ = 5.43 (d, 1H, $J_{3,4}$ = 2.8 Hz, H-4), 5.35 (t, 1H, $J_{2,3}$ = $J_{1,2}$ = 9.9 Hz, H-2), 5.07 (dd, $J_{2,3}$ = 9.9, $J_{3,4}$ = 3.4 Hz, H-3), 4.56 (d, 1H, $J_{1,2}$ = 9.9 Hz, H-1), 4.27-3.96 (m, 3H, H-5, H-6a, H-6b), 2.17, 2.09, 2.04, 1.98 (4s, 12H, 4 CH_3CO). **^{13}C NMR** (50.3 MHz, Cl_3CD) δ = 170.7, 170.3, 70.2, 170.0 (4 *C*OCH$_3$), 88.7 (C-1), 74.9, 72.0, 67.8, 67.2 (C-5, C-3, C-2, C-4), 61.0 (C-6), 20.8, 20.7, 20.6, 20.5 (4 CO*C*H$_3$).

Methyl 2,3,4-tri-*O*-acetyl-1-thio-β-D-glucopyranosyluronate, **5**



Methyl 2,3,4-tri-*O*-acetyl-1-thio-β-D-glucopyranosyluronate was obtained as previously described[41] and showed the same properties as reported. Briefly, methyl (2,3,4-tri-O-acetyl-D-glucopyranosyl) uronate bromide was first reacted with potassium thioacetate in acetone to yield the 1-thioacetyl derivative which upon treatment with sodium methoxide, at −45 °C, provided the corresponding glucuronyl 1-thiol.
^{1}H-NMR (200 MHz, Cl_3CD) δ = 5.28-5.16 (m, 2H, H-3, H-4), 4.98 (t, 1H, $J_{2,3}$ = $J_{1,2}$ = 9.6 Hz, H-2), 4.57 (t, 1H, $J_{1,2}$ = $J_{1,SH}$ = 9.9 Hz, H-1), 4.04 (d, 1H, $J_{4,5}$ = 9.8 Hz, H-5), 3.75 (s, 3H, OCH_3), 2.38 (d, 1H, $J_{1,SH}$ = 9.9 Hz, *SH*), 2.07, 2.01 (2×) (3s, 9H, 3 CH_3CO). **^{13}C NMR** (50.3 MHz, Cl_3CD) δ = 169.7, 169.5, 169.3 (3 *C*OCH$_3$), 166.7 (*C*OOCH$_3$), 79.0 (C-1), 76.6, 73.3, 72.7, 69.3 (C-5, C-3, C-2, C-4), 53.0 (O*C*H$_3$), 20.7, 20.6, 20.5 (3 CO*C*H$_3$).

2,2',3,3',4',6,6'-hepta-*O*-acetyl-1-thio-β-D-cellobiose **9**



^{1}H-NMR (500 MHz, Cl_3CD) δ = 5.15 (t, 1H, $J_{2,3}$ = $J_{3,4}$ = 9.3 Hz, H-3), 5.13 (t, 1H, $J_{2',3'}$ = $J_{3',4'}$ = 9.4 Hz, H-3'), 5.05 (dd, 1H, $J_{3',4'}$ = 9.4, $J_{4',5'}$ = 9.9 Hz, H-4'), 4.91 (dd, 1H, $J_{1',2'}$ = 8.1, $J_{2',3'}$ = 9.4 Hz, H-2'), 4.88 (dd, 1H, $J_{2,3}$ = 9.3, $J_{1,2}$ = 9.9 Hz, H-2), 4.51 (d, 1H, $J_{1,2}$ = 9.9 Hz, H-1), 4.49 (d, 1H, $J_{1',2'}$ = 8.1 Hz, H-1'), 4.47 (dd, 1H, $J_{5,6a}$ = 2.0, $J_{6a,6b}$ = 12.1 Hz, H-6a), 4.36 (dd, 1H, $J_{5,6a'}$ = 4.4, $J_{6a',6b'}$ = 12.5 Hz, H-6a'), 4.08 (dd, 1H, $J_{5,6b}$ = 5.3, $J_{6a,6b}$ = 12.1 Hz, H-6b), 4.03 (dd, 1H, $J_{5,6b'}$ = 2.2, $J_{6a',6b'}$ = 12.5 Hz, H-6b'), 3.77 (dd, 1H, $J_{3,4}$ = 9.3, $J_{4,5}$ = 9.9 Hz, H-4), 3.66-3.60 (m, 2H, H-5, H-5'), 2.13, 2.08, 2. 06, 2.02, 2.01, 2.00, 1.97 (7s, 21H, 7 CH_3CO). **^{13}C NMR** (125 MHz, Cl_3CD) δ = 170.6, 170.4, 170.3, 170.0, 169.8, 169.4, 169.2 (7 *C*OCH$_3$), 100.9 (C-1'), 78.6 (C-1), 77.3 (C-5), 76.4 (C-4), 73.9 (C-2), 73.3 (C-3), 73.0 (C-3'), 72.1 (C-5'), 71.7 (C-2'), 67.9 (C-4'), 62.2 (C-6), 61.7 (C-6'), 21.0, 20.9, 20.8, 20.7 (4×) (7 CO*C*H$_3$).

5H-[1,2,4]triazino[5,6-b]indole-3-thiol **16** was prepared according to literature procedures[42] and the spectroscopic data match well with the reported values.

Perfluorobutyl)(phenyl)sulfane **1**[14]: Yield: 80 %. Isolated and purified mass obtained: 10 mg. TLC (Hexane): R_f = 0.75.

^{1}H-NMR (600 MHz, Cl_3CD) δ : 7.66 (d, 2H, J = 7.4 Hz), 7.51 (t, 1H, J = 7.5 Hz), 7.43 (t, 2H, J = 7.5 Hz). **^{13}C NMR** (150 MHz, Cl_3CD) δ : 137.6, 131.2, 129.6, 122.9. **^{19}F NMR** (564.603 MHz, Cl_3CD) δ : -81.0 (t, 3F), -87.1 (m, 2F), -120.1 (m, 2F), -125.5 (m, 2F)

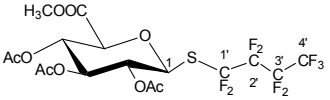
2-((perfluorobutyl)thio)etanol **2**[9]: Yield: 75 %. Isolated and purified mass obtained: 12 mg. TLC (AcOEt: Hexane 1:1 v/v): R_f = 0.7.

^{1}H-NMR (600 MHz, Cl_3CD) δ : 3.89 (t, 2H, J = 6.1 Hz), 3.14 (t, 2H, J = 6.1 Hz), 1.97 (bs, 1H). **^{13}C NMR** (150 MHz, Cl_3CD) δ : 61.6, 31.7. **^{19}F NMR** (564.603 MHz, Cl_3CD) δ : -81.0 (t, 3F), -87.0 (m, 2F), -120.7 (m, 2F), -125.5 (m, 2F).

Methyl 2-((*tert*-butoxycarbonyl)amino)-3-((perfluorobutyl)thio)propanoate,[6] 4: Yield: 25 %. Isolated and purified mass obtained: 10 mg. TLC (AcOEt: Hexane 4:6 v/v): R_f = 0.8.

^{1}H-NMR (500 MHz, Cl_3CD) δ : 5.37 (d, 1H, J =6.2 Hz), 4.63 (d, 1H, J = 5.5 Hz), 3.79 (bs, 3H), 3.53 (dd, 1H, J = 13.6 Hz, 4 Hz), 3.36 (dd, 1H, J = 13.7 Hz, 4.5 Hz), 1.44 (bs, 9H). **^{13}C NMR** (150 MHz, Cl_3CD) δ : 170.2, 164.4, 155.0, 131.4, 80.8, 53.2, 53.1, 31.1, 28.3. **^{19}F NMR** (564.603 MHz, Cl_3CD) δ : -81.0 (t, 3F), -86.7 (m, 2F), -120.5 (m, 2F), -125.5 (m, 2F).

Perfluorobutyl 2,3,4-tri-*O*-acetyl-1-thio-β-D-methylglucopyranosyluronate, **6**



Yield: 75 %. Isolated and purified mass obtained: 21 mg. **TLC** (AcOEt: Hexane 4:6 v/v): R_f = 0.7.

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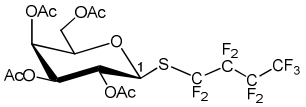
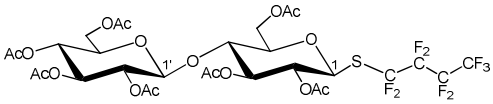
^{1}H-NMR (600 MHz, Cl_3CD) δ = 5.33, 5.22 (2dd, 2H, *J* = 9.9, *J* = 8.9 Hz, H-3, H-4), 5.08 (dd, 1H, $J_{2,3}$ = 9.9, $J_{1,2}$ = 10.2 Hz, H-2), 5.04 (d, 1H, $J_{1,2}$ = 10.2 Hz, H-1), 4.09 (d, 1H, $J_{4,5}$ = 9.9 Hz, H-5), 3.77 (s, 3H, OCH_3), 2.06, 2.03 (2×) (3s, 9H, 3 CH_3CO). **^{13}C NMR** (150.9 MHz, Cl_3CD) δ = 170.0, 169.4, 169.3 (3 $COCH_3$), 166.4 ($COOCH_3$), 80.8 (C-1), 76.4, 72.7, 69.1, 69.0 (C-5, C-3, C-2, C-4), 53.2 (OCH_3), 20.7, 20.6, 20.5 (3 $COCH_3$). **^{19}F NMR** δ = 470.592 Cl_3CD) δ = -80.9 (t, *J* = 9.4 Hz, 3H, CF_3), -85.6, -88.2 (2 brd, 2F, *J* = 240.0 Hz, $C^{1'}F_2$), -120.4, -121.0 (2 dt, 2F, *J* = 8.1, *J* = 294.4 Hz, $C^{2'}F_2$), -125.5 (t, 2F, *J* = 12.8 Hz, $C^{3'}F_2$). HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{17}H_{17}F_9NaO_9S$: 591.03418, found: 591.03342.

Perfluorobutyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranoside, **8**

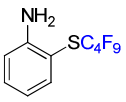


Yield: 83 %. Isolated and purified mass obtained: 30 mg. **TLC** (AcOEt: Hexane 1:1 v/v): R_f = 0.6
^{1}H NMR (600 MHz, Cl_3CD) δ = 5.44 (d, 1H, $J_{3,4}$ = 2.8Hz, H-4), 5.25 (t, 1H, $J_{2,3}$ = $J_{1,2}$ = 10.0 Hz, H-2), 5.10 (dd, $J_{3,4}$ = 3.3, $J_{2,3}$ = 10.0 Hz, H-3), 4.99 (d, 1H, $J_{1,2}$ = 10.0 Hz, H-1), 4.16 (dd, 1H, $J_{5,6a}$ = 7.2, $J_{6a,6b}$ = 11.4 Hz, H-6a), 4.10 (dd, 1H, $J_{5,6b}$ = 5.9, $J_{6a,6b}$ = 11.4 Hz, H-6b), 4.00 (dd, 1H, $J_{5,6a}$ = 7.2, $J_{5,6b}$ = 5.9 Hz, H-5), 2.16, 2.07, 2.03, 1.99 (4s, 12H, 4 CH_3CO). **^{13}C NMR** (150.9 MHz, Cl_3CD) δ = 170.5, 170.2, 169.9, 169.6 (4 $COCH_3$), 81.3 (C-1), 75.2, 71.7, 67.0, 66.5 (C-5, C-3, C-2, C-4), 61.4 (C-6), 20.7, 20.6 (3×) (4 $COCH_3$). **^{19}F NMR** (470.592 MHz, Cl_3CD) δ = -81.0 (t, *J* = 9.5 Hz, 3H, CF_3), -85.8, -88.9 (2 brd, 2F, *J* = 241.0 Hz, $C^{1'}F_2$), -120.3, -121.2 (2 dt, 2F, *J* = 8.4, *J* = 294.3 Hz, $C^{2'}F_2$), -125.5 (t, 2F, *J* = 13.2 Hz, $C^{3'}F_2$). HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{18}H_{19}F_9NaO_9S$: 605.04983, found: 605.04978.

Perfluorobutyl 2,2',3,3',4',6,6'-hepta-*O*-acetyl-1-thio-β-D-cellobioside, **10**

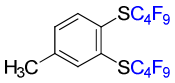


Yield: 50 %. Isolated and purified mass obtained: 20 mg. **TLC** (AcOEt: Hexane 1:1 v/v): R_f = 0.6
^{1}H NMR (600 MHz, Cl_3CD) δ = 5.23 (t, 1H, $J_{2,3}$ = $J_{3,4}$ = 9.0 Hz, H-3), 5.14 (t, 1H, $J_{2',3'}$ = $J_{3',4'}$ = 9.4 Hz, H-3'), 5.05 (dd, 1H, $J_{3',4'}$ = 9.4 Hz, $J_{4',5'}$ = 10.0 Hz, H-4'), 4.98 (dd, 1H, $J_{2,3}$ = 9.0, $J_{1,2}$ = 10.0 Hz, H-2), 4.95 (d, 1H, $J_{1,2}$ = 10.0 Hz, H-1), 4.92 (dd, 1H, $J_{2',3'}$ = 9.4 Hz, $J_{1',2'}$ = 8.0 Hz, H-2'), 4.49 (d, 1H,$J_{1',2'}$ = 8.0 Hz, H-1'), 4.46 (dd, 1H, $J_{5,6a}$ = 2.0 Hz, $J_{6a,6b}$ = 12.0 Hz, H-6a), 4.35 (dd, 1H, $J_{5',6a'}$ = 4.5 Hz, $J_{6a',6b'}$ = 12.4 Hz, H-6a'), 4.12 (dd, 1H, $J_{5,6b}$ = 6.1 Hz, $J_{6a,6b}$ = 12.0 Hz, H-6b), 4.03 (dd, 1H,$J_{5',6b'}$ = 2.0 Hz, $J_{6a',6b'}$ = 12.4 Hz, H-6b'), 3.76 (dd, 1H, $J_{3,4}$ = 9.0 Hz, $J_{4,5}$ = 10.0 Hz, H-4), 3.70-3.65 (m, 2H, H-5, H-5'), 2.10, 2.08, 2. 06, 2.03, 2.02, 2.01, 1.98 (7s, 21H, 7 CH_3CO). **^{13}C NMR** (150.9 MHz, Cl_3CD) δ = 170.5, 170.3, 170.2, 169.7, 169.6, 169.4, 169.2 (7 $COCH_3$), 100.9 (C-1'), 80.7 (C-1), 77.3 (C-5), 76.2 (C-4), 73.2 (C-3), 73.0 (C-3'), 72.2 (C-5'), 71.7 (C-2'), 69.6 (C-2), 67.9 (C-4'), 62.0 (C-6), 61.7 (C-6'), 20.8, 20.7, 20.6 (7 $COCH_3$). **^{19}F NMR** 470.592 Cl_3CD) δ = -80.9 (t, *J* = 9.7 Hz, 3H, CF_3), -85.8, -88.8 (2 brd, 2F, *J* = 242.0 Hz, $C^{1'}F_2$), -120.0, -121.2 (2 dt, 2F, *J*= 8.5, *J* = 294.6 Hz, $C^{2'}F_2$), -125.5 (t, 2F, *J* = 13.0 Hz, $C^{3'}F_2$). HRMS (ESI) : *m/z* $[M+H]^+$ calcd for $C_{30}H_{36}F_9O_{17}S$: 871.1451, found: 871.1456.



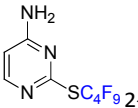
2-((perfluorobutyl)thio)aniline **11**[22]: Yield: 90 %. Isolated and purified mass obtained: 15 mg. TLC (CH_2Cl_2: iso-octane 1:1 v/v): R_f = 0.6

^{1}H-NMR (600 MHz, Cl_3CD) δ : 7.47 (d, 1H, *J* = 8.6 Hz), 7.28 (t, 1H, *J* = 8.2 Hz), 6.78 (d, 1H, *J* =8.1 Hz), 6.74 (t, 1H, *J* = 7.8 Hz), 4.45 (s, 2H). **^{13}C NMR** (150 MHz, Cl_3CD) δ : 151.1, 140.0, 133.4, 118.8, 115.8, 104.5. **^{19}F NMR** (564.603 MHz, Cl_3CD) δ : -81.1 (t, 3F), -87.1 (t, 2F), -120.4 (m, 2F), -125.5 (m, 2F).



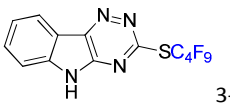
(4-methyl-1,2-phenylene)bis((perfluorobutyl)sulfane) **13**: Yield: 50 %. Isolated and purified mass obtained: 8 mg. TLC (Hexane): R_f = 0.6

^{1}H-NMR (500 MHz, Cl_3CD) δ : 7.78 (d, 1H, *J* = 8.0 Hz), 7.72 (bs, 1H), 7.37 (cplx d, 1H, J_o = 8 Hz, J_m = 2Hz, $J_{H\text{-}F5}$ = 0.7 Hz), 2.44 (s, 3H). **^{13}C NMR** (125.721 MHz, Cl_3CD) δ : 143.2, 140.3, 139.6, 133.0, 130.8, 127.3, 21.3. **^{19}F NMR** (470.585 MHz, Cl_3CD) δ : -81.0 (c, 6F), -86.3 (dt, 4F), -120.4 (m, 4F), -125.6 (m, 4F). HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{15}H_7F_{18}S_2$: 592.9623, found: 592.9641.



2-((perfluorobutyl)thio)pyrimidin-4-amine, **15**: Yield: 48 %. Isolated and purified mass obtained: 38 mg. TLC (AcOEt: MeOH + I Acetic Acid 9:1 v/v): R_f = 0.8

^{1}H-NMR (600 MHz, Cl_3CD) δ : 8.00 (d, 1H, *J* = 5.9 Hz), 7.34 (bs, 2H), 6.37 (d, 1H, *J* = 5.9 Hz). **^{13}C NMR** (150 MHz, Cl_3CD) δ : 163.7, 161.8, 155.6, 104.4. **^{19}F NMR** (564.603 MHz, Cl_3CD) δ : -80.7 (t, 3F), -87.6 (t, 2F), -120.1 (m, 2F), -125.3 (m, 2F). HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_8H_5F_9N_3S$: 345.9982, found: 345.9896.



3-((perfluorobutyl)thio)-5H-[1,2,4]triazino[5,6-b]indole **17**: Yield: 50 %. Isolated and purified mass obtained: 10 mg. TLC (AcOEt: Hexane 1:1 v/v): R_f = 0.8

^{1}H-NMR (600 MHz, Cl_3CD) δ : 8.42 (d, 1H, *J* = 7.8 Hz), 7.80 (t, 1H, *J* = 8.3 Hz), 7.66 (d, 1H, *J* = 8.2 Hz), 7.52 (t, 1H, *J* = 7.9 Hz). **^{13}C NMR** (150 MHz, Cl_3CD) δ : 158.2, 146.5, 143.1, 141.4,

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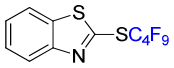
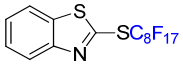
132.3, 123.1, 122.4, 116.9, 113.1. **^{19}F NMR** (564.603 MHz, Cl_3CD) δ : -80.4 (t, 3F), -86.3 (m, 2F), -119.8 (m, 2F), -125.1 (m, 2F). HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{13}H_6F_9N_4S$: 421.0091, found: 421.0045.



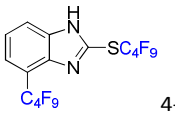
2-((perfluorobutyl)thio)benzo[d]thiazole **19**[29]: Yield: 99 %. Isolated and purified mass obtained: 23 mg. TLC ($CHCl_3$: iso-octane: MeOH 0.8:1: 0.2 v/v): R_f = 0.85

^{1}H-NMR (500 MHz, Cl_3CD) δ : 8.17 (cplx d, 1H, *J* = 8.2 Hz, 0.7 Hz), 7.92 (cplx d, 1H, *J* = 8.1 Hz, 0.7 Hz), 7.58 (m, 1H, *J* = 8.3 Hz, 1.2 Hz), 7.52 (m, 1H, *J* = 7.2 Hz, 1.3 Hz). **^{13}C NMR** (125.721 MHz, Cl_3CD) δ : 153.4, 150.0, 138.7, 127.2, 127.1, 124.6, 121.5. **^{19}F NMR** (470.585 MHz, Cl_3CD) δ : -80.9 (t, 3F), -85.2 (t, 2F), -119.8 (m, 2F), -125.5 (m, 2F). HRMS (ESI):*m/z* $[M+H]^+$ calcd for $C_{11}H_5F_9NS_2$: 385.9641, found: 385.9625.



2-((perfluorooctyl)thio)benzo[d]thiazole **20**: Yield: 50 %. Isolated and purified mass obtained: 10 mg. TLC ($CHCl_3$: iso-octane: MeOH 0.8:1: 0.2 v/v): R_f = 0.75

^{1}H-NMR (600 MHz, Cl_3CD) δ : 8.18 (d, 1H, *J* = 8.2 Hz), 7.92 (d, 1H, *J* = 8.0 Hz), 7.58 (t, 1H, *J* = 7.2 Hz), 7.52 (t, 1H, *J* = 8.01 Hz). **^{13}C NMR** (150 MHz, Cl_3CD) δ : 157.7, 153.4, 138.7, 127.2, 127.1, 124.6, 121.5. **^{19}F NMR** (564.603 MHz, Cl_3CD) δ :-80.7 (t, 3F), -84.9 (t, 2F), -118.8 (m , 2F), -121.1 (m, 2F), -121.7 (m, 2F), -121.9 (m, 2F), -122.7 (m, 2F), -126.1 (m, 2F). HRMS (ESI):*m/z* $[M+H]^+$calcd for $C_{15}H_5F_{17}NS_2$: 585.9514, found: 585.9515.



4-(perfluorobutyl)-2-((perfluorobutyl)thio)-1H-benzo[d]imidazole **22**: Yield: 50 %. Isolated and purified mass obtained: 15 mg. TLC (CHCl3: hexane 7:3 v/v): R_f = 0.5

^{1}H-NMR (600 MHz, Cl_3CD) δ : 9.87 (bs, 1H), 8.08 (d, 1H, *J* = 8.1 Hz,, 7.61 (d, 1H, *J* = 7.7 Hz), 7.49 (t, 1H, *J* = 8.0 Hz). **^{13}C NMR** (150 MHz, Cl_3CD) δ : 145.3, 137.3, 132.6, 125.5, 125.1, 123.6, 122.9. **^{19}F NMR** (564.603 MHz, Cl_3CD) δ : -81.0 (m, 6F), -84.7 (t, 2F), -109.9 (t, 2F), -120.0 (m, 2F), -123.1 (m, 2F), -125.6 (m, 4F). HRMS (ESI):*m/z* $[M+H]^+$calcd for $C_{15}H_4F_{18}N_2S$: 586.9808, found: 586.9815.

Conclusions

A simple and metal-/ photoorganocatalyst-free strategy has been presented for the perfluoroalkylation of sulfides employing a complex [(TMEDA) $I.I_3$] that upon visible light illumination acts as a good initiator for the electron-catalyzed reduction of R_FI, to generate R_F• radicals from R_F-I sources. These R_F• radicals are capable of substituting biologically-relevant targets such as cysteine derivatives, thioaldoses, heteroaromatic sulfides, etc. This convenient, high-yielding and metal-photoorganocatalyst-free strategy outperforms traditional near-UV photocatalytic methods while operating under visible light and in the presence of only an additive (TMEDA).

We must remark that caution has to be exercised when employing R_FI and TMEDA, since traces of iodine in the reagents (i.e.: R_FI) can form a stable complex with TMEDA which could be responsible for the radical initiation process upon visible light irradiation.

In summary, we came up, serendipitously, with a convenient radical initiator made up of TMEDA / and *in-situ* iodine present in R_FI, which is capable of triggering the perfluoroalkylation of organic thiols.

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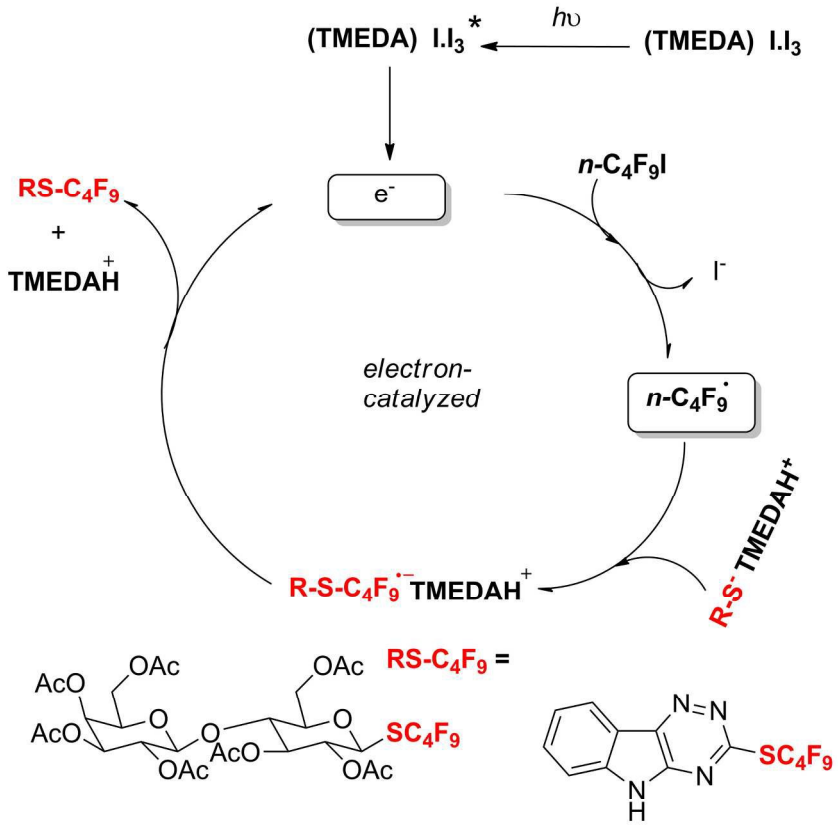

(TMEDA) $I.I_3$ complex as new radical initiator for the perflurooalkylation of RSH

100x90mm (600 x 600 DPI)