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Research Article

Study of oxidation coupling of thiols to disulfides with Tripropylammonium fluorochromate (VI) (TriPAFC) in convenient and microwave conditions

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ABSTRACT

Tripropylammonium fluorochromate is an efficient and new reagent, which prepares easily and oxidizes thiols to the corresponding disulfides quickly. The reactions perform cleanly and controlled to stop at the disulfide stage without over-oxidation side products. Coupling of thiols to their corresponding disulfides studied in solution at room temperature and in solution under microwave radiation. The easy procedure, simple work-up, short reaction times, and excellent yields are another advantages of this reagent.

Keywords: Thiol, Oxidation, Disulfide, Tripropylammonium fluorochromate, Solution, Microwave Irradiation.

1. Introduction

Many oxidative reagents have been developed in recent years with some success. [1] Disulfides are one of the most important organic sulfur compounds possessing an exclusive chemistry both in biochemistry [2] and in synthetic area. [3] Disulfides are also key intermediates in a wide variety of organic synthetic routes. [4–6] Sweetening of catalyst poisons thiols to low volatile disulfides in oil industries [7–8] and also industrial applications of disulfides in vulcanization of rubbers and elastomers led us to investigate the introduction and applications of new member of this category of reagents in oxidation of thiols to the corresponding disulfides.

Many stoichiometric reagents like manganese dioxide, [9] dichromates, [10] halosilane-chromium trioxide, [11] diethyl azodicarboxylate, [12] nickel peroxide, [13] chromium peroxide, [14] diaryl telluroxide, [15] tetrabutylammonium ceric(IV) nitrate, [16] sodium perborate, [17] silver trifluoromethane sulphonate [18] and permangenate [19] have been developed for this transformation. These reagents suffer from either one or more of the following disadvantages such as availability of the reagent, cumbersome work-up procedure, high cost of the reagent, over oxidation or oxidation of other functional groups in the presence of thiol group. As a result, there is still a need for the development of general, efficient, and new reagents to synthesize disulfides from the corresponding thiols under mild reaction conditions. These reactions are not only interest from ecological viewpoint, but also in many cases offer considerable synthetic advantages in terms of the yield, selectivity and simplicity of the reaction procedure. In this respect, we wish to report that tripropylammonium fluorochromate (TriPAFC) able to oxidize thiols to their disulfides efficiently under different reaction conditions.

2. Experimental

2.1. Materials and method

CrO_3 (Merck, P.A.) was used without further purification. Solvents were purified by standard methods. Infrared spectra were recorded as KBr disks on a Shimadzu model 420 spectrophotometer. The UV/Visible measurements were made on an Uvicon model 922 spectrometer. Proton, ^{13}C, ^{19}F NMR were carried out on a Bruker AVANCE DRX 500 spectrometer at 500, 125, 470.66 MHz. All the chemical shifts are quoted in ppm using the high-frequency positive convention; ^{1}H and ^{13}C NMR spectra were referenced to external $SiMe_4$ and ^{19}F NMR spectra to external $CFCl_3$. Chromium was estimated iodometrically. In the case of the reduced product of the oxidant, chromium was determined after oxidizing with acidic peroxodisulfate ($K_2S_2O_8$) solution. The percent composition of carbon, hydrogen and nitrogen were obtained from the Microanalytical laboratories, Department of Chemistry, OIRC, Tehran. Melting points were measured on an Electrothermal 9100 melting point apparatus. We used a Microsynth Milstone laboratory microwave oven.

2.2. Preparation of Tripropylammonium fluorochromate (TriPAFC)

A 15 g (150 mmol) sample of chromium (VI) oxide, CrO_3, and 11.3 ml (225 mmol) of 40% hydrofluoric acid were added to 20 ml of water in a 100 ml polyethylene beaker with stirring. After 5-7 min the homogeneous solution was cooled to ca. 1-2 °C and 28.3 ml (150 mmol) of distilled tripropylamine, was added in small portions, to this solution with stirring over a period of 0.5 h and stirring was continued for 0.5 h at 0 °C. The precipitated orange solid was isolated by filtration on a polyethylene funnel, washed with petroleum ether (3 × 60 ml) and dried in vacuum for 2 h at room temperature. Yield: 37.5 g (95%); mp 142 °C. $C_9H_{22}CrFNO_3$: Calc. C, 41.05; H, 8.35; N, 5.31 Found: C, 41.22; H, 8.46; N, 5.02. I.R. (KBr): 904 cm^{-1} $\nu_1(A_1)$ or $\nu(CrO_3)$, 647 cm^{-1} $\nu_2(A_1)$ or $\nu(Cr\text{-}F)$, 949 cm^{-1} $\nu_4(E)$ or $\nu(CrO_3)$ cm^{-1}. UV/Visible, ^{13}C NMR, ^{1}H NMR and ^{19}F NMR were all consistent with the TriPAFC structure. The above procedure can be scaled up to larger quantities, if desired. Molar conductance (Λ_M, 25 °C) of 0.001 M solutions (1M=1 mol lit.$^{-1}$) of TriPAFC in water was 125 Ω^{-1}cm^{2} mol^{-1}. The pH of 0.01 M solution of TriPAFC in water was 3.3.

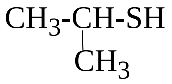
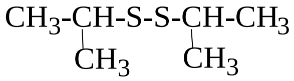
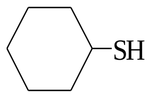
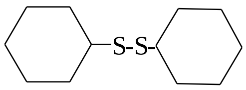
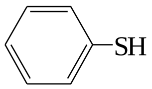
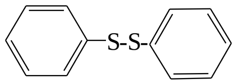
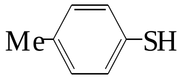
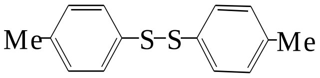
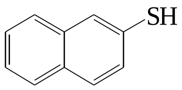
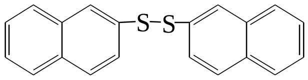
2.3. General procedure for oxidative coupling of thiols in dichloromethane

To a stirred solution of 4-methylthiophenol (0.248 g, 2 mmol) in dichloromethane (5 ml) TriPAFC (0.263 g, 1 mmol) was added, and the mixture was stirred at room temperature for 67 min. A solid was formed and was treated with a 1:1 mixture of ether and water (2 ml). The reaction mixture was extracted with ether (3 × 10 ml). The organic layers were combined together and dried over anhydrous $MgSO_4$. Evaporation of the solvent followed by recrystallization or chromatography on silica gel afforded the pure disulfides in 84 % (0.207 g) yield, which characterized from its NMR and IR spectrum mp 45°C (Lit. [20,21] mp 45-46 °C).

2.4. General procedure for oxidative coupling of thiols under microwave radiations

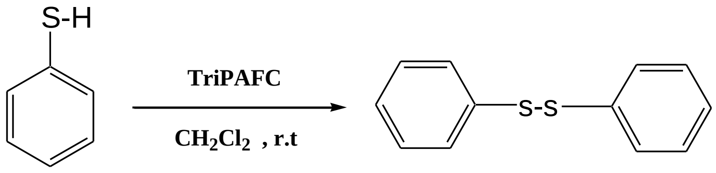
To a stirred suspension of tripropylammonium fluorochromate (1mmol) in dichloromethane (generally 5 ml), a solution of the substrate in the minimum amount of dichloromethane was added dropwise, the molar ratio of substrate to the oxidant being 1:2 .The mixture was irradiated for the time indicated in the table by microwave radiation. [The completion of the reaction is followed by UV/Visible and TLC using ether/petroleum ether (60/40) as eluant]. The mixture was diluted with ether (1:1 vol/vol) and filtered through a short column of silica gel to give a clear solution. The solution was evaporated and the residual product purified by distillation, recrystallization or column chromatography. The progress of the reactions was also monitored and checked by UV/Visible spectrophotometry. The amount of the oxidant during the reaction was measured spectrophotometrically at 350 nm. A very small magnetic stirrer was designed at the cell (10 mm quartz cell) compartment just in the bottom of sample cell in the spectrophotometer to stir up the solution under study in cell. The reaction mixtures remained homogenous in the solvent system used.

Table 1 . *Oxidative coupling of thiols under solution and microwave radiations*

	Substrate	Solution			Solution under Microwave	
		Time (min)	Product	Yield (%)	Time (min)	Yield (%)
1	 $CH_3\text{-}\underset{CH_3}{CH}\text{-}SH$	55	 $CH_3\text{-}\underset{CH_3}{CH}\text{-}S\text{-}S\text{-}\underset{CH_3}{CH}\text{-}CH_3$	78	6	78
2	$n\text{-}C_5H_{11}\text{-}SH$	54	$C_5H_{11}\text{-}S\text{-}S\text{-}C_5H_{11}$	86	6	86
3	$n\text{-}C_8H_{17}\text{-}SH$	60	$C_8H_{17}\text{-}S\text{-}S\text{-}C_8H_{17}$	90	6	90
4		50		35	6	35
5	$HOOC\text{-}CH_2\text{-}SH$	56	$HOOC\text{-}CH_2\text{-}S\text{-}S\text{-}H_2COOH$	80	5	80
6		67		87	8	87
7		67		84	6	84
8		70		81	8	81

3. Results and Discussions

TriPAFC is an easily prepared reagent, which was used for oxidation of alcohols recently.[20] The oxidative coupling of thiols with this reagent was investigated in dichloromethane at room temperature and in dichloromethane solution under microwave radiation. As shown in Table 1.A series of aliphatic and aromatic thiols were reacted with 0.5 molar equivalent of the reagent to afford the corresponding disulfides in excellent yields. This oxidation was also performed under microwave conditions with 0.5 molar equivalent of the reagent. The results show that under microwave condition, the reaction times are shorter. This advantage makes this procedure as a valuable method of preparation of disulfides. (Scheme 1.)



scheme 1

Scheme 1. Sematic of disulfide formation with TriPAFC

n conclusion, the TriPAFC acts as a simple, efficient, and fast oxidizing reagent for coupling thiols. The easy procedure, simple work-up, the easy preparation of the reagent, short reaction times, and excellent yields of the products will make this reagent a useful addition to available oxidant. It also should be emphasized that the reactions could be performed cleanly and controlled to stop at the disulfide stage. Over-oxidation has not been observed, even when the reactions were carried out in different conditions.

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