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Tributylammonium fluorochromate(TriBAFC): An efficient and mild oxidant for coupling of thiols to disulfides

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ABSTRACT

Various kinds of aliphatic and aromatic thiols are converted into the corresponding disulfides by tributylammonium fluorochromate in excellent yields. 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. © 2007 Trade Science Inc. -INDIA

KEYWORDS

Thiol;
Oxidation;
Disulfide;
Tributylammonium
fluorochromate;
Solution;
Microwave.

INTRODUCTION

Disulfides are one of the most important organic sulfur compounds possessing an exclusive chemistry both in biochemistry^[1,2], 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], tetrabutyl ammonium ceric(IV) nitrate^[16], sodium perborate^[17], silver trifluoromethane sulphonate^[18], and permanganate^[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 tributylammonium fluorochromate (TriBAFC) able to oxidize thiols to their disulfides efficiently under different reaction conditions.

EXPERIMENTAL

Material and instruments

CrO₃ (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, ¹³C, ¹⁹F 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; ¹H and ¹³C NMR spectra were referenced to external SiMe₄ and ¹⁹F NMR spectra to external CFC₃. Chromium was estimated iodometrically. In the case of the reduced product of the oxidant, chromium was determined after oxidizing with acidic peroxodisulfate (K₂S₂O₈) 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 and are uncorrected. We used a Microsynth Milstone laboratory microwave oven.

Preparation of tributylammonium fluorochromate (TriBAFC)

Chromium(VI) oxide (10.0g, 0.1mol) was dissolved in water in a polyethylene beaker and 40 % hydrofluoric acid (9ml, 0.2mol) was added with stirring at 0°C. To the resultant clear orange solution, tributylamine (23.5ml, 0.1mol) was added dropwise with stirring to this solution over a period of 0.5h and stirring was continued for 0.5h at 0°C. The precipitated orange solid was isolated by filtration, washed with petroleum ether (3 × 60ml) and dried in vacuum for 2 h at room temperature. Yield: 25.62g (84%); m.p. 134°C; Anal. Calcd. For C₁₂H₂₈CrFNO₃: C, 47.20, H 9.24, N 4.58%; found: C 46.92, H 9.64, N 5.2%. I.R. (KBr) ν_{\max} /cm⁻¹: 914 cm⁻¹ (A₁) or ν (CrO₃), 634 cm⁻¹ ν_2 (A₁) or ν (Cr-F), 950 cm⁻¹ ν_4 (E) or ν (CrO₃) cm⁻¹. Electronic absorption at 22026 cm⁻¹, corresponded to ¹A₂ → ¹E (ε = 145 M⁻¹

cm⁻¹); 28985 cm⁻¹ to ¹E → ¹E (ε = 577 M⁻¹ cm⁻¹) and 43103 cm⁻¹ to ¹A₂ → ¹A₁ (ε = 1081 M⁻¹ cm⁻¹). ¹H-NMR (500 MHz, CD₃CN): δ = 1.2 (t, 3H, -CH₃), δ = 1.6 (m, 4H, -CH₂-CH₂-), δ = 2.7 (t, 2H, -CH₂-), δ = 7.5 ppm (s, 1H, -NH). UV/Visible, ¹³C NMR, and ¹H 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 (1 M = 1 mol lit.⁻¹) of TriBAFC in water was 124 Ω⁻¹ cm² mol⁻¹. The pH of 0.01 M solution of TriBAFC in water was 3.15.

General procedure for oxidative coupling of thiols in acetonitrile

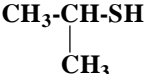
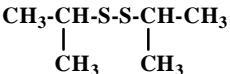
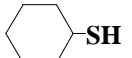
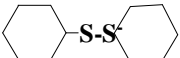
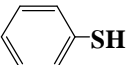
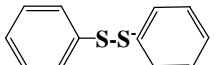

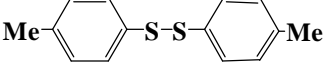
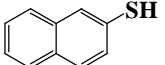
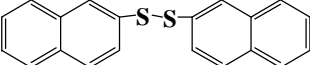
To a stirred solution of 4-methylthiophenol (0.248g, 2mmol) in acetonitrile, (5ml) TriBAFC (0.305g, 1mmol) was added, and the mixture was stirred at room temperature for 68 min. A solid was formed and was treated with a 1:1 mixture of ether and water (2 ml). The reaction mixture was extracted with ether (3 × 10ml). The organic layers were combined together and dried over anhydrous MgSO₄. Evaporation of the solvent followed by recrystallization or chromatography on silica gel afforded the pure disulfides in 84% (0.207g) yield, which characterized from its NMR and IR spectrum mp 45°C (Lit. [20] mp 45-46°C) TABLE 1.

General procedure for oxidative coupling of thiols under microwave radiations

To a stirred suspension of tributylammonium fluorochromate (1mmol) in acetonitrile (generally 5ml), 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 1 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 348nm. A very small magnetic stir-

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TABLE 1 : Oxidative coupling of thiols with TriBAFC in solution and microwave conditions

Substrate	Solution		Solution under microwave		
	Time(min)	Product	Yield(%)	Time(min)	Yield(%)
1 	64		73	8	85
2 $n\text{-C}_5\text{H}_{11}\text{-SH}$	67	$\text{C}_5\text{H}_{11}\text{-S-S-C}_5\text{H}_{11}$	82	8	88
3 $n\text{-C}_8\text{H}_{17}\text{-SH}$	72	$\text{C}_8\text{H}_{17}\text{-S-S-C}_8\text{H}_{17}$	78	8	90
4 	60		70	10	82
5 $\text{HOOC-CH}_2\text{-SH}$	65	$\text{HOOC-CH}_2\text{-S-S-H}_2\text{COOH}$	72	7	92
6 	62		68	10	90
7 	68		70	10	84
8 	72		65	15	81

rer was designed at the cell(10mm 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.

The spectral data for all disulfides are followed :

2-Isopropyldisulfanyl-propane(2a)

IR(KBr) cm^{-1} 3000-2900C-H(aliph.strech), 1400-1350C-H(aliph .bend), 1200-1100C-S(strech). ^1H NMR(300MHz, CDCl_3) δ 2.7(m, 2H), 1.5(d, 12H). ^{13}C NMR(300MHz, CDCl_3) δ 38.5(d), 24(q). HRMS Calcd for $\text{C}_6\text{H}_{14}\text{S}_2$: M^+ , 150.4125. Found : m/z 150.4117.

1-Pentyldisulfanyl-pentane(2b)

IR(KBr) cm^{-1} 3000-2900 C-H(aliph . stretch) 1200-1100 C-S(strech). ^1H NMR(300 MHz, CDCl_3) δ 2.5(t, 4 H), 1.6(m, 4H), 1.25(m, 4H) 1.3(m, 4H), 0.85(t, 6H). ^{13}C NMR(300MHz, CDCl_3) δ 36(t), 30(t), 21(t), 14.5(q). HRMS Calcd for $\text{C}_{10}\text{H}_{22}\text{S}_2$: M^+ , 206.8542. Found : m/z 206.8538 .

1-Octyldisulfanyl-octane

IR(KBr) cm^{-1} 3000-2900 C-H(aliph. stretch) 1200-1100 C-S(strech). ^1H NMR(300MHz, CDCl_3) δ 2.6(t, 4 H), 1.5(m, 4H), 1.2(m, 18H). 9(t, 6H). ^{13}C NMR(300MHz, CDCl_3) δ 38(t), 30(t), 23(t), 14.5(q). HRMS Calcd for $\text{C}_{16}\text{H}_{34}\text{S}_2$: M^+ , 291.1213. Found : m/z 291.1221.

Disulfanyl-cyclohexane

IR(KBr) cm^{-1} 3000-2900 C-H(aliph . stretch), 1200-1100 C-S(strech). ^1H NMR(300MHz, CDCl_3) δ 2.5(m, 2 H), 1.65(dt, 8H), 1.4(m, 12H). ^{13}C NMR(300MHz, CDCl_3) δ 43(d), 31(t), 23(t). HRMS Calcd for $\text{C}_{12}\text{H}_{22}\text{S}_2$: M^+ , 230.2135. Found: m/z 230.2120.

Disulfanyl-acetic acid(2e)

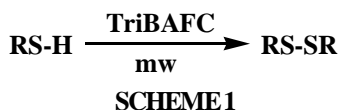
IR(KBr) cm^{-1} 3500-3200 COOH(strech), 3000-2900 C-H(aliph.strech), 1200-1100 C-S(strech). ^1H NMR(300MHz, CDCl_3) δ 2.27(s, 4H), 11.5(s, 2H). ^{13}C NMR(300MHz, CDCl_3) δ 35(t), 179(s). HRMS Calcd for $\text{C}_4\text{H}_6\text{O}_4\text{S}_2$: M^+ , 182.1478. Found: m/z 182.1461.

Disulfanyl-benzene

IR(KBr) cm^{-1} 3200-3100 C-H(Ar.strech), 1200-1150 C-S(strech). ^1H NMR(300MHz, CDCl_3) δ 7.65(d, 4 H), 7.25(m, 6H). ^{13}C NMR(300MHz, CDCl_3) δ 135(s), 130(d), 127(d). HRMS Calcd for $\text{C}_{12}\text{H}_{10}\text{S}_2$: M^+ , 219.3674. Found: m/z 219.3412.

4,4-di-methyl disulfanyl-benzene(2g)

IR(KBr) cm^{-1} 3200-2100 C-H(Ar.strech), 3000-2900 C-H(aliph.strech) 1480-1400 C-H(Ar.bend), 1200-1100C-S(strech). ^1H NMR(300 MHz, CDCl_3) δ 7.5(d, 4 H), 7.2(d, 4H), 2.5(s, 6H). ^{13}C NMR(300MHz, CDCl_3) δ 26(S), 130(d), 127(d), 124(s), 21(q). HRMS Calcd for $\text{C}_{14}\text{H}_{14}\text{S}_2$: M^+ , 247.2008. Found : m/z 247.1759.



β -Disulfanyl-naphthalene(2h)

IR(KBr)cm⁻¹ 3200-3100 C-H(Ar.strech), 1200-1150 C-S(strech). ¹H NMR(300MHz, CDCl₃) δ 8.1(s, 2H), 7.7(d, 2H), 7.5(d, 6H) 7.32(d, 4H). ¹³C NMR(300 MHz, CDCl₃) δ 130(s), 128(d), 125(d). HRMS Calcd for C₂₀H₁₄S₂: M⁺, 319.4689. Found: m/z 319.4358.

RESULTS AND DISCUSSION

Among several methods of preparing disulfides, most methods involve oxidation of thiols. Oxidation of thiols to disulfides without over oxidation is an important process in organic chemistry and biochemistry, which has been extensively investigated over the years. TriBAFC is an easily prepared reagent, which no examples of its applications in organic synthesis seem to have been recorded. 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.

CONCLUSION

The TriBAFC 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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