IAU-ARAK

J. Iran. Chem. Res. 3 (2010) 155-160

Journal of the Iranian Chemical Research

www.iau-jicr.com

Microwave assisted oxidation coupling of thiols to symmetrical disulfides with tripropylammonium fluorochromate (VI) (TPAFC)

Neda Hasanzadeh [a], Shahriare Ghammamy [b], Mohammad Kazem Mohammadi [a,*]

[a] *Islamic Azad University, Ahvaz Branch , Faculty of Science, Ahvaz , Iran*
[b] *Department of Chemistry, Faculty of Science, Imam Khomeini International University, Qazvin, Iran*

Received 2 August 2010; received in revised form 28 August 2010; accepted 2 September 2010

Abstract

Tripropylammonium fluorochromate(VI) (TPAFC), is an efficient and new reagent, which is prepared easily and oxidizes thiols to the corresponding disulfides, quickly. The reactions are performed cleanly and are controlled to stop at the disulfide stage, without over-oxidation and side products. Coupling of thiols to their corresponding disulfides, are 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; Coupling; Disulfide; Tripropylammonium fluorochromate; Microwave irradiation.

1. Introduction

Many oxidative reagents are 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] are developed for this transformation. These reagents suffered 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 had 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. Microwave

* Corresponding author. Tel. & fax: +98 611 3348363.
E-mail address: mohammadi@iauahvaz.ac.ir (M.K. Mohammadi)

synthesis is a new technique for conducting chemical reactions. Acceleration of organic reactions by microwaves is largely proved elsewhere, and in many cases, microwave techniques were became more effective than conventionally conducted reactions [20].

Moreover, in a number of applications, reactions under microwave conditions could provided pure products in high yield [21]. In this respect, we wish to report that tripropylammonium fluorochromate (TPAFC) able to oxidize thiols to their disulfides efficiently under different reaction conditions.

2. Experimental

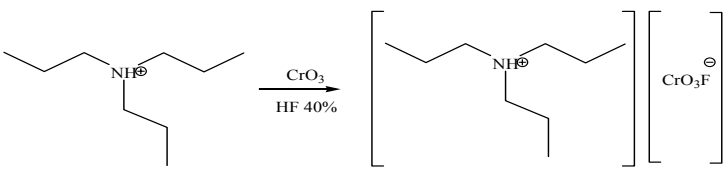
2.1. Material and methods

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.^{1}H and ^{13}C, are carried out on a BRUKER AVANCE DRX 500 spectrometer at 300 MHz. All the chemical shifts were quoted in ppm using the high-frequency positive convention. ^{1}H and ^{13}C NMR spectra were referenced to external $SiMe_4$. Chrommium, 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 micro analytical laboratories, department of Chemistry, OIRC, Tehran. Melting points are measured on an Electrothermal 9100 melting point apparatus. We used a Microsynth Millstone laboratory microwave oven. Experiments were carried out in closed vessel multi mode Microsynth Milstone laboratory microwave oven using a 400 Watts Westpointe microwave operating at 3.67 GHz. All experiments had good reproducibility by repeat the experiments in same conditions.

2.2. Preparation of tripropylammonium fluprochromate (TPAFC)

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 were cooled to ca. 1-2 °C and (28.3 mL), (150 mmol) of distilled tripropylamine, were 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, and 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, 41.19; H, 8.43; N, 5.43. IR. (KBr): 904 cm^{-1} $\nu_1(A_1)$ or $\nu(CrO_3)$ that shown as ν(Cr-O), 647 cm^{-1} $\nu_2(A_1)$ or ν(Cr-F), 949 cm^{-1} $\nu_4(E)$ or $\nu(CrO_3)$ that shown as ν(Cr-O). Electronic absorption at 248 nm, corresponding to $1a_2 \rightarrow 9e$ (ε = 140 M^{-1} cm^{-1}); 348 nm to $8e \rightarrow 9e$ (ε = 667 M^{-1} cm^{-1}); and 278 nm to $12a_1 \rightarrow 9e$ (ε = 1287 M^{-1} cm^{-1}).

^{1}H-NMR (500 MHz, CD_3CN): δ = 0.91 (*t*, 3H -CH_3), δ= 1.97 (*m*, 2H, -CH_2 -), δ = 3.23 (*t*, 2H, -CH_2-). ^{13}C-NMR (124.44 MHZ, CD_3CN): δ 11.45, 20.25, 55.26. HRMS Calcd 263.1035 for $C_9H_{22}CrFNO_3$ .found 260.1038 (Scheme 1).



Scheme 1

IR, UV, ^{13}C NMR, and ^{1}H NMR were all consistent with the TPAFC structure. The above procedure could 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 TPAFC in water was 125 $\Omega^{-1}cm^2$ mol^{-1}. The pH of 0.01 M solution of TPAFC in water was 3.3.

2.3. General procedure for oxidative coupling of thiols in solution

To a stirred solution of 4-methylthiophenol 1 g (0.248 g, 2 mmol) in dichloromethane (5 mL) TPAFC (0.263 g, 1 mmol) were added, and the mixture was stirred at room temperature for 67 min. A solid were formed and 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 disulfide **2g** in 77 % (0.207 g) yield, which characterized from its NMR and IR spectrum. mp 45°C (Lit. [22] mp 45-46 °C)

4,4-di–methyl disulfanyl-benzene **(2g)** or bis(4-methylphenyl)disulfide: IR (KBr) cm^{-1} 3200-2100 C-H(Ar . strech) , 3000-2900 C-H(aliph . strech) 1480-1400 C-H (Ar.bend) ,1200- 1100 C-S (strech) .

^{1}H NMR (300MHz , $CDCl_3$) δ 7.5 (d , 4 H) , 7.2(d, 4H) , 2.5(s, 6H) . ^{13}C NMR (300 MHz , $CDCl_3$) δ 126 .21(S) , 130 .42(d) , 127 .3 (d) , 124.85 (s) , 21 .17 (q) .
HRMS Calcd 246.05423 for $C_{14}H_{14}S_2$ .found 246.05425.

2- isopropyldisulfanyl-propane **(2a)**. IR (KBr) cm^{-1} 3000-2900 C-H(aliph . strech), 1400-1350 C-H (aliph .bend) , 1200- 1100 C-S (strech) . ^{1}H NMR (300 MHz , $CDCl_3$) δ 2.7 (m, 2H) ,1.5 (d, 12H) . ^{13}C NMR (300 MHz , $CDCl_3$) δ 38.5 (d) , 24.65(q). HRMS Calcd 150.0571 for $C_6H_{14}S_2$ .found 150.0569.

1-pentyldisulfanyl – pentane **(2b)**. IR (KBr) cm^{-1} 3000-2900 C-H(aliph . strech) 1200- 1100 C-S (strech) . ^{1}H NMR (300 MHz , $CDCl_3$) δ 2.5 (t , 4 H) ,1.6 (m, 4H) , 1.25(m, 4H) 1.3 (m , 4H) , .85 (t , 6H) . ^{13}C NMR (300 MHz , $CDCl_3$) δ 36.53 , 33.78 , 31.13, 23.55 , 14.5. HRMS Calcd 206.1281 for $C_{10}H_{22}S_2$ .found 206.1283 .

1-octyldisulfanyl-octane **(2c)**. IR (KBr) cm^{-1} 3000-2900 C-H(aliph . strech) 1200- 1100 C-S (strech) . ^{1}H NMR (300 MHz , $CDCl_3$) δ 2.6 (t , 4 H) ,1.5 (m, 4H) , 1.2(m, 18H) .9 (t, 6H) . ^{13}C NMR (300 MHz , $CDCl_3$) δ 33.66, 32.5, 31.43, 31.35, 31.22, 27.03 , 23.5, 15.02. HRMS Calcd 290.2142 for $C_{16}H_{34}S_2$ .found 290.2146 .

disulfanyl-cyclohexane **(2d)** . IR (KBr) cm^{-1} 3000-2900 C-H(aliph . strech) , 1200- 1100 C-S (strech) . ^{1}H NMR (300 MHz , $CDCl_3$) δ 2.5 (m , 2 H) ,1.65 (dt, 8H) , 1.4 (m, 12H) . ^{13}C NMR (300 MHz, $CDCl_3$) δ 52.56, 34.52, 26.59, 25.38. HRMS Calcd 230.1235 for $C_{12}H_{22}S_2$ .found 230.1232 .

disulfanyl –acetic acid **(2e)** . IR (KBr) cm^{-1} 3500-3200 COOH(strech) , 3000-2900 C-H(aliph . strech) ,1200- 1100 C-S (strech) . ^{1}H NMR (300 MHz , $CDCl_3$) δ 2.27 (s , 4H) ,11.5 (s, 2H) . ^{13}C NMR (300 MHz , $CDCl_3$) δ 35.81 (t) , 179.91 (s) . HRMS Calcd 181.9714 for $C_4H_6S_2$ .found 181.9717 .

disulfanyl-benzene **(2f)** . IR (KBr) cm^{-1} 3200-3100 C-H(Ar . strech) , 1200- 1150 C-S (strech) . ^{1}H NMR (300 MHz , $CDCl_3$) δ 7.65 (d , 4 H) ,7.25 (m, 6H). ^{13}C NMR (300 MHz , $CDCl_3$) δ 133.21, 131.48, 130.25, 129.53. HRMS Calcd182.0224 for $C_{12}H_{10}S_2$ .found 182.0226.

β-disulfanyl – naphthalene **(2h)** . IR (KBr) cm^{-1} 3200-3100 C-H(Ar . strech) , 1200- 1150 C-S (strech) . ^{1}H NMR (300 MHz , $CDCl_3$) δ 8.1 (s , 2 H) ,7.7 (d, 2H), 7.5 (d,6H) 7.32(d,4H) . ^{13}C NMR (300 MHz, $CDCl_3$) δ 137.76, 137.11, 135.26, 134.52, 131.57, 128.92, 127.08, 126.16, 125.02, 124.87. HRMS Calcd 318.0512 for $C_{20}H_{14}S_2$ .found 318.0509 .

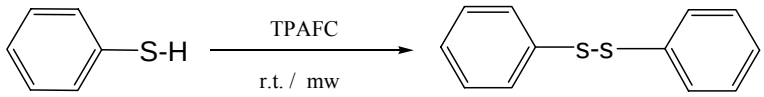
2.4. General procedure for oxidative coupling of thiols under microwave irradiation

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 drop wise. The molar ratio of substrate to the oxidant being 1:1 .The mixture was irradiated for the time indicated in the table by microwave radiation. The completion of the reaction was followed by UV 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 were also monitored and checked by UV 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.

3. Results and discussion

TPAFC is an easily prepared reagent, which was used for oxidation of alcohols recently. [22] The oxidative coupling of thiols with this reagent are 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 are reacted with 1 molar equivalent of the reagent to afford the corresponding disulfides in excellent yields. This oxidation is also performed under microwave conditions with 1 molar equivalent of the reagent. The results show that under microwave condition, the reaction times were shorter.

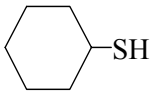
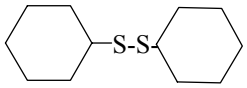
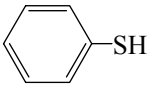
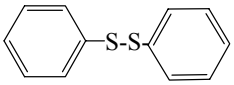
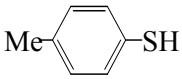
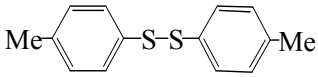
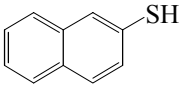
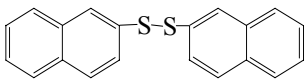
TPAFC is used for the oxidation of some organic thiols under microwave irradiation in CH_2Cl_2 as solvent. This method offers some advantages in term of simplicity of performance, simple operation condition, no side product formation, very low reaction time and a wide range of substrates could be converted to their corresponding disulfides. In addition, the reduced reagent $(C_3H_7)_3\ N^+CrO_2F^-$ could also be recycled after oxidation. TPAFC is very well reagent for the oxidant based on quaternary ammonium halochromates. In our research on oxidation processes. TPAFC as an oxidant is a very well suited reagent for microwave synthesis, because as an ionic and magnetically retrievable material, it carries a benefit of efficient conversion of electromagnetic energy into heat according to the dielectric heating mechanism (Table 1 and Scheme 2).



Scheme 2

In conclusion, the TPAFC act 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 would 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 had not been observed, even when the reactions were carried out in different conditions. In this paper, we reported a procedure where the oxidation are performed in microwave irradiation, in order to improve the conditions and to prevent problems connected with conventional conditions (cost, handling, safety, pollution, and decreases in reactivity by dilution of the reactants).

Table 1
Oxidation coupling of thiols (1a- h) with TPAFC in solution and microwave irradiation.

Substrate	Solution			Solution under Microwave	
	Time (min)	Product	Yield (%)	Time (min)	Yield (%)
CH_3-CH(-CH_3)-SH 1 a	55	CH_3-CH(-CH_3)-S-S-CH(-CH_3)-CH_3 2a	75	6	85
n-C_5H_{11}-SH 1b	54	C_5H_{11}-S-S-C_5H_{11} 2b	78	7	85
n-C_8H_{17}-SH 1 c	60	C_8H_{17}-S-S-C_8H_{17} 2c	72	10	83
 1d	50	 2d	65	6	89
HOOC-CH_2-SH 1e	56	HOOC-CH_2-S-S-H_2COOH 2e	72	5	80
 1f	73	 2f	80	8	92
 1g	67	 2g	77	6	84
 1h	84	 2h	68	14	81

Acknowledgment

The authors are grateful to the Research Council of Islamic Azad University, Ahvaz Branch for Valuable Help and Supports.

References

[1] L.F. Fieser, M. Fieser, Reagents for Organic Synthesis, Wiley, New York, 1967.
[2] D.C .Jocelyn, Biochemistry of the Thiol Group, Academic Press, New York, 1992.
[3] G. Capozzi, G. Modena, S. Patai, The Chemistry of the Thiol Group, Wiley, New York, 1974.
[4] J. Lam, H. Bildose, L.P. Christensen, T. Thomsen, Acta Chem. Scand. Ser B 43 (1989) 799-803.
[5] V. Srivastav, R. Gupta, R.R. Guptam, Ind. J. Chem. 39B (2000) 223-227.

[6] P. Metzner, Synthesis (1978) 669-674.
[7] D.L. Holbrook, Handbook of Petroleum Refining Processes, R.A. Meyers (Edi,) McGraw Hill, 1996.
[8] A. Leitao, C. Costa, A. Rodrigues, Chem. Eng. Sci. 42 (1987) 2291-2298.
[9] E.P. Papadopoulos, A. Jarrar, C. H.Issidoides, J. Org. Chem. 31 (1966) 615-620.
[10] C. Lopez, F. Conzales, P. Cossio, C. Palomo, Synth. Commun. 15 (1985) 1197-1206.
[11] J.M. Aizpurua, M. Juaristu, B. Lecea, C. Palomo, Tetrahedron 41 (1985) 2903-2908.
[12] F. Yoneda, K. Suzuki, Y. Nitta, J. Org. Chem. 32 (1967) 727-735.
[13] K. Nakagawa, S. Shiba, M. Horikawa, K. Sato, H. Nakamura, N. Harada, F. Harada, Synth. Commun. 10 (1980) 305-311.
[14] H. Firouzabadi, N. Iranpoor, F. Kiaeezadeh, J. Toofan, Tetrahedron 42 (1986) 719-726.
[15] S.V. Ley, A. Meerholz, D.H.R. Barton, Tetrahedron 37 (1982) 231-239.
[16] H.A. Muathen, Ind. J. Chem. 30B (1991) 522-530.
[17] A. Mckillop, D. Koyuncu, A. Krief, W. Dumont, P. Renier, M. Trabelsc, Tetrahedron Lett. 31 (1990) 5007-5011.
[18] H. Tamamura, A. Otaka, J. Nakamura, K. Okubo, T. Koide, K. Ikeda, N. Fujii, Tetrahedron Lett. 34 (1993) 4931-4936.
[19] N.A. Noureldin, M. Coldwell, J. Hendry, D.G. Lee, Synthesis (1998) 1587-1595.
[20] (a) R.A. Abramovitch, Org. Prep. Proc. Int. 23 (1991) 683-689, (b) G. Majetich, R.J. Elec, Energy 30 (1995) 27-38, (c) S. Caddick, Tetrahedron 51 (1995) 10403-10409, (d) C.R. Strauss, R.W. Trainor, Aust. J. Chem. 48 (1995) 1665-1672.
[21] (a) D. Bogdal, M. Warzala, Tetrahedron 56 (2000) 8769-8775, (b) D. Bogdal, J. Chem. Res. (1998) 468-472, (c) D. Bogdal, J. Pielichowski, K. Jaskot, Org. Prep. Proc. 30 (1998) 427-434.
[22] N. Iranpoor, B. Zeynizadeh, Synthesis (1999) 49-56.