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Oxidation coupling of organic thiols to disulphides with Tetramethylammonium Fluorochromate(VI) (TMAFC)

Hosein Imanieh^a, Shahriar Ghamami^a, Mohammad kazem Mohammadi^{b*}

a-Department of Chemistry, Faculty of Science, Imam Khomeini International University
Qazvin, Iran.P.O.Box:288, Fax: 0098-281-3780040 .

b-Department of Chemistry; ;Cslamic Azad University of Firouzabad; Firouzabad, Iran; Postal Code : 74715 ; Fax
(+98) 712 – 6229702 .

Abstract : Tetramethylammonium Fluorochromate has been found to oxidize alcohols to corresponding aldehydes and ketones. Without polymerization of double bonds, over oxidation and other side reactions. This reagent has been found that effective for oxidation of thiols to disulphides.

Key words: Tetramethylammoniumfluorochromate(VI) – Thiols – Oxidation.

1. Introduction

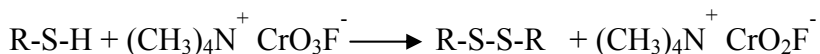
The oxidation of thiols to disulphides¹ or to sulphonic acid² in the absence and presence of catalysts has been the subject of several recent investigations. Attention has been focused primarily on the range of products which may be produced as a function of reaction conditions. in general the reaction seems to lead to the almost exclusive production of disulphides when oxidation occurs in aqueous solution, and to a variety of disulphides and sulphenic, sulphinic, and sulphonic acids when carried out in non aqueous solutions³ In both cases the reaction has been suggested⁴ to involve the initial production of disulphide, followed by hydrolysis of this compound to produce sulphur – containing acids. Over recent years, chromium based oxidizing agents have been extensively worked on leading to development of a good number of reagents. Some of which have become quite popular and performing well as oxidizing agents. Some of the important entries in the list of reagents are the collins reagent⁵, chromium trioxide -3, 5-dimethyl-pyrazole complex⁶, pyridinium chlorochromate (PCC)⁷, pyridinium fluorochromate (PFC)⁸ and quolinium bromochromate (QBC)⁹. As a part of our effort to develop¹⁰ new methodologies in economically viable and environmentally benign conditions we report herein a very simple oxidative protocol using TMAFC at room temperature in the acetonitrile as a solvent with novel findings and greater advantages over the conventional oxidation reagents in various organic solvents.

2. Results and discussion

At the outset, a number of aliphatic, aromatic and allylic thiols were subjected to oxidative transformation with TMAFC in solvent to give some new results. Quite interestingly, several constitutionally varied aliphatic primary thiols¹¹ gave the corresponding alkyl disulphide under mild conditions without a detectable (by 300 MHz 1H NMR) trace of the sulphones, whereas, allylic primary thiol, under the same oxidative condition produced the corresponding disulphides without further oxidation to the corresponding sulphones or sulphonic acid. (Table 1)

As is evident from Table 1, structurally varied saturated aliphatic acyclic, aryl alkyl), and allylic thiols underwent clean oxidation to the corresponding disulphides at ambient temperature within a reasonable period of time in the presence of acetonitrile as a solvent with TMAFC in good yield and high purity. This can be attributed mainly to the immobilization of the Cr-containing by-products in the solvent¹².

The oxidation of organic thiols by TMAFC resulted in the formation of the corresponding disulphides. The overall reaction may be represented as,



TMAFC undergoes a two electron change. This is accord to our earlier observation with other halochromates and TMAFC.

No over oxidation was noted even in using an excess of reagent. The reaction of aromatic thiols was essentially insensitive to substitution of the aromatic ring, but possibly depended on the solvent employed. The reaction conditions have the advantages of leaving unchanged a chiral amino acid group.

The notable feature of the said methodology is the elimination of several side-reactions which are often associated with various conventional oxidative methods using higher valent metals as oxidants¹³. 1,2-diols and α -hydroxyketones have been reported to undergo oxidative cleavage of the C-C bond with TMAFC in dichloromethane, but the said substrates under the present solvent-free conditions cleanly produce the desired oxidation products, namely, 1,2-diketones in appreciable yield without much formation of side-products. Allylic primary thiols smoothly underwent oxidation in the present condition to the corresponding di α,β -unsaturated disulphide in fairly good yield and purity without polymerization of the olefinic linkage. Another very important advantage of the said methodology is that the isolated double bonds remain unaffected under the present conditions). Even no isomerization of the isolated double bonds to the more stable conjugated ones in the oxidation products was observed.

Thus, the said oxidative method under mild conditions has set out to minimize the dispersion of offensive materials in the environment and maximize the use of renewable resources. From this standpoint this method can be considered as a relatively green technology having more advantages and wider applicability compared to the conventional oxidation reagents.

The yields of the products are, in general, good. In some cases lower yields were obtained as the loss of the products could not be avoided during the isolation process due to highly volatile nature of the products. Sometimes the products were contaminated (as detected by ¹H NMR) with starting materials after initial isolation, which were further purified by filtration chromatography over a short plug of silica gel or neutral silica using hexane as eluent. Some unidentified by-products were formed (to the extent of nearly 10% by ¹H NMR) in a few cases which were removed by column chromatography.

3. Conclusion

The present procedure using Tetramethylammonium fluorochromate (TMAFC) in solvent conditions has been found to oxidize selectively primary aliphatic, aromatic and allylic thiols to corresponding disulphides without isomerization and polymerization of double bonds, over oxidation and other side-reactions keeping intact the acid sensitive functionalities. The important advantages of this procedure include (a) operational simplicity (ease of set up and work-up), (b) good yield of the oxidized products, with high purity (by immobilization of the chromium by-products on the surface of silica), (c) mild reaction conditions, (d) good selectivity and (e) general applicability accommodating a variety of substitution patterns.

4. Experimental

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 CFCl₃. 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 relative concentrations 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. The substrates are commercially available. Most of the products are also reported and the references have been provided whenever necessary. The thiols were either commercial products or prepared by known methods¹⁴ and were purified by distillation under reduced pressure or crystallization. Their purity was checked by comparing their boiling or melting points with the literature values.

4.1. Preparation of Tetramethylammonium fluorochromate (TMAFC):

This reagent, (CH₃)₄N⁺ CrO₃F⁻ (TMAFC), can be easily prepared in excellent yield from the reaction of CrO₃ with tetramethylammonium fluoride in acetonitrile in a molar ratio of 1:1. The entire procedure had been subscribed in paper that published with us¹⁵.

4.2. General procedure for the oxidation of thiol

RS-H or PhS-H (.1mmole) and TMAFC (.1mmole) was dissolved in CH₃CN (30ml) and the mixture of the reaction was shaken by mechanical stirrer and progress of reaction was monitored by UV/Vis(at 350nm) and TLC using ether / petroleum ether (60/40) as eluent. The mixture was allowed for about 20hr. most of the solvent was removed under reduced pressure. the residue was diluted with water and extracted with chloroform (3×50ml).the chloroform layer was dried over anhydrous magnesium sulphate ,the solvent was removed by evaporation and the residue was analyzed by IR and ¹H NMR spectroscopy .the spectra were identical with those of the corresponding disulphide . Peak characteristic of sulphide and sulphone could not be detected. In IR spectra, the product showed a strong and broad absorption at 1200cm⁻¹. No bond either at 1330 or 1135cm⁻¹, characteristic of sulphone was seen. In NMR spectroscopy, studied in the case of CH₃(CH₂)₇-S-H, the peak due to methylene attacked to sulphur atom, shifted from 57δ in the thiol, to 37 δ in the product. In all cases, the products were the corresponding disulphides .the oxidation state of chromium in completely reduced reaction mixtures, determined by the iodometric method.

4.2.1. Typical Reaction Procedure.

TMAFC (3.86g, 20mmoles) is made in to a solution with acetonitrile (30ml) in a two necked round bottom flask of 100ml capacity fitted with a reflux condenser and a mechanical stirrer. A solution of octan thiol (20 mmoles) in acetonitrile (3ml) was added to the solution and the mixture was stirred vigorously at room temperature. The course of

the reaction was followed by GC analysis after every one hour. After the completion of the reaction mixture was stirred for a further of 30 minutes, diluted with dry diethyl ether (40ml) and filtered through a short column of silicagel (2cm). The combined filtrate on evaporation gave the crude product which was distilled through a short vigereux column. Yield of di octyl sulphide (b.p. 178-180 30mmHg) was (79 %).

4.3. General experimental procedure for the oxidation of thiols

The thiol (5 mmol) was added dropwise to the TMAFC in acetonitrile [prepared by adding the TMAFC (5mmole, .96 gr) to a solution of acetonitrile (10ml) followed by evaporation of solvent to get a white easy flowing powder] in ice-cold conditions (0–58 C⁰) with stirring and then kept at room temperature till the reaction was complete (as monitored by TLC).

The product was isolated almost in pure form by filtration chromatography of the solid reaction mixture on a short plug of neutral silica using diethyl ether as eluent followed by evaporation of the solvent under reduced pressure. It was further purified, if required, by column chromatography over silica gel or neutral silica to yield the corresponding products as mentioned in Tables 1. For solid thiols, ethereal solution was added followed by immediate evaporation of the solvent and then the process was followed as mentioned above.

Most of the products are known compounds as substantiated by appropriate references and they were easily identified by their spectral (IR and ¹H NMR) data.

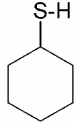
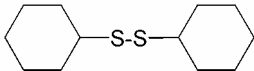
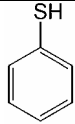
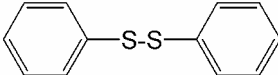
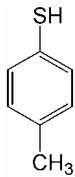
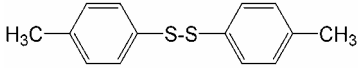
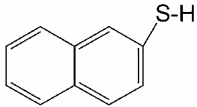
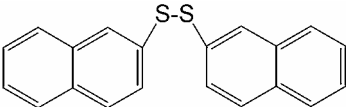
References

1. Hollenberg, D. H.; Klein, R. S.; Fox, J. J. *Carbohydr Res* .1978, 67, 491.
2. Shabani, A.; Lee, D. G. *Tetrahedron Lett.* 2001, 42, 5833.
3. Vyas, S.; Sharma, P K. *Proc. Indian Acad. Sci.(Chem. Sci.)*, 2002, 114, 137-148.
4. Fraile, J. M.; Garcia, J. I.; Lazaro, B.; Mayoral, J. A. *Chem. Commun.* 1998, 1807.
- 5). J. C. Callins, W. W. Hess and F. J. Frank, *Tetrahedron Lett.* 1968, 3363.
- 6). Bora, U.; Chaudhuri, M.; Dey, D.; Kalita, D.; *Kharmawphlang,W.;* Mandal G. C. *Tetrahedron*, 2001,57, 2445.
- 7). Piancatelli, A.; A. Scettri, M. D'Auria, *Synthesis*, 1982, 245.
- 8). M. N. Bhattacharjee, M. K. Chaudhuri, H. S. Dastagupta, N. Roy, *Synthesis*, 1982, 588.
- 9). S. Saraswat, V. Sharma and K. K.Banerji, *Indian Acad. Soc*, 2003, 115, 75-82.
10. Bhar, S.; Panja, C. *Green Chem.* 1999, 1, 253–255.
- 11). Vyas, Shashi. Sharma.;P K .*Proc.Indian Acad.Sci.(Chem.Sci.)*. 2002, 114,137-148.
12. Verma, R. S.; Saini, R. K. *Tetrahedron Lett.* 1998, 39, 1481–1482.
13. Fatiadi, A. J. In *Organic Synthesis by Oxidation with Metal Compounds*; Mijs, W. J., de Jonge, C. R. H. I., Eds.; Plenum: New York, 1986; pp 119–260.

14. Aldrich Handbook of Fine Chemicals and Laboratory Equipment; Aldrich Chemical Co: Milwaukee, 2000–2001.

15).A. R. Mahjoub, Sh. Ghammami, A. R. Abbasi, A. Hosseinian, Indian J. Chem. 2000, 39 , 434.

Table 1: oxidation coupling of organic thiols to disulphides with TMAFC

SUBSTRAT	OXIDANT /SUBSTRATE RATIO	TIME (Min)	PRODUCT	YIELD %
HS-CH ₂ -CO ₂ H	1/1	105	H ₂ OC-CH ₂ -S-S-CH ₂ -CO ₂ H	82
HS-(CH ₂) ₇ -CH ₃	1/1	160	CH ₃ -(CH ₂) ₇ -S-S-(CH ₂) ₇ -CH ₃	82
CH ₂ =CH-CH ₂ -SH	1/1	75	CH ₂ =CH-CH ₂ -S-S-CH ₂ -CH=CH ₂	
	1/1	240		80
	1/1	120		80
	1/1	85		80
	2/1	450		78