TRIETHYLAMMONIUM HALOCHROMATES/SILICA GEL: AN EFFICIENT REAGENT FOR OXIDATIVE COUPLING OF THIOLS TO DISULFIDES

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Triethylammonium halochromates, \((\text{C}_2\text{H}_5)_3\text{NCrO}_3\text{X}\), TEAXC (X = Cl, F) are easily synthesized by the reaction of triethylamine with a solution of chromium(VI) oxide in 6M hydrochloric acid, or a solution of chromium(VI) oxide in 40% hydrofluoric acid. These reagents are easily supported on common silica gel and can be used as heterogeneous oxidants. Triethylammonium halochromate(VI) is a versatile reagent for the effective and selective oxidation of organic substrates. Various aliphatic (cyclic and acyclic) and aromatic thiols are converted into the corresponding disulfides by treatment with triethylammonium fluorochromate(VI), (TEACC) or triethylammonium chlorochromate(VI), (TEAFC) supported on silica gel, in excellent yields and under mild reaction conditions.

Key words: triethylammonium fluorochromate(VI); triethylammonium chlorochromate(VI); heterogeneous oxidants; silica gel; oxidation; thiol; disulfides

INTRODUCTION

Disulfides are one of the most important organo-sulfur compounds possessing an exclusive chemistry both in biochemistry and in synthetic area [1]. Disulfides are also key intermediates in a wide variety of organic synthetic routes. The importance of sweetening of catalyst poisons thiols to low volatile disulfides in petroleum industries, and the industrial applications of disulfides in vulcanization of rubbers and elastomers, led us to investigate the introduction and applications of a new member of this category of reagents in oxidation of thiols to the corresponding disulfides [2].
The main type of these reactions is the oxidation of thiols in the presence of molecular oxygen [3], DMSO [4], using borohydride exchange resin [5], DMSO/alumina reagent [6], CBr4/18-crown-6/benzene [7] and NaIO3/alumina [8].

However, some of the reported reagents suffer from disadvantages such as instability, hygroscopicity, low selectivity, long reaction time, difficulty of preparation and need for a large excess of the reagent. Thus a milder, more selective and inexpensive reagent is still in demand. The need for overcoming these problems, lead to the development of a good number of other oxidants, such as: pyridinium chlorochromate (PCC) by Corey and Boger [9], pyridinium fluorochromate by Bhattacharjee and co-workers [10], quinolinium dichromate by Chaubey [11], 2,2'-bipyridinium chlorochromate by Guziec and Luzzio [12], quinolinium chlorochromate, by Jayanthi [13] and isoquinolinium fluorochromate by Srinivasan and co-workers [14]. We have prepared tetramethylammonium fluorochromate [15] and cetyltrimethylammonium bromochromate [16], with the belief that these reagents may have oxidative properties and could be used for oxidation of organic substrates, particularly thiols.

This manuscript introduces triethylammonium fluorochromate(VI) (TEAFC) and triethylammonium chlorochromate(VI) (TEACC) absorbed on silica gel as new reagents with improved work-up efficiency and durability, for the oxidation of thiols to disulfides.

**EXPERIMENTAL SECTION**

**Material and instruments**

Chromium(VI) oxide (p.a.) was obtained from Merck, and silica gel (–150 mesh) was obtained from Aldrich. These reagents were used without further purification. The TLC plates were obtained from Merck.

Solvents were purified by standard methods. Infrared spectra were recorded as KBr disks on a Shimadzu model 420 spectrophotometer. The UV/Vis measurements were made on an Uvicon model 922 spectrophotometer. 1H, 13C, 19F-NMR were carried out on a Bruker AVANCE DRX 500 spectrometer at 500, 125, 470.66 MHz, respectively. All the chemical shifts are quoted in ppm using the high-frequency positive convention; the 1H and 13C-NMR spectra were referenced to external SiMe4 and the 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 percent composition of carbon, hydrogen and nitrogen were obtained from the Microanalytical Laboratories of the Department of Chemistry, OIRC, Tehran.

**Triethylammonium fluorochromate (TEAFC),**

\[ (C_2H_5)_3NH^+ [CrO_3F]^- \]

Chromium(VI) oxide (1.0 g, 0.01 mol) and 40% hydrofluoric acid (0.9 ml, 0.02 mol) were added to 20 ml of water in a 100 ml polyethylene beaker with stirring. After 5 min the homogeneous solution was cooled to ca. 0–2 °C. To the resultant clear orange solution, triethylamine (1.400 ml, 0.010 mol) was added drop-wise with stirring over a period of 0.5 hours and stirring was continued for additional 0.5 hours at −4 °C. The precipitated yellowish-orange solid was isolated by filtration on a polyethylene funnel, washed with petroleum ether (3 × 60 ml) and dried in vacuum for 2 hours at room temperature. Yield: (88%); mp 132 °C; C6H16CrFNO3: Calc. C 32.57%, H 7.23%, N 6.33%. Found: C 32.08%, H 7.64%, N 6.44%. 13C NMR (125 MHz, CDCl3): δ 45.9 (CH2), δ 8.7 (CH3). 1H NMR (500 MHz, CDCl3): δ 7.1 (s, 1 H), δ 3.32 (q, 2 H), δ 1.58 (t, 3 H). IR (KBr): 904 cm–1 ν1(A1) or ν(CrO3), 648 cm –1 ν2(A1) or ν(Cr–F), 948 cm–1 ν4(E) or ν(CrO3). UV-Vis: Electronic absorption at 2232 cm–1, corresponded to 1A2→1E (ε = 270 M–1 cm–1); 28735 m–1 to 1E→3E (ε = 845 M–1 cm–1) and 36231 cm–1 to 1A2→1E (ε = 1233 M–1 cm–1). The UV/Visible, 13C NMR and 1H NMR data was consistent with the TEAFC structure. The above procedure can be scaled up to larger quantities, if desired. The pH of 0.01 M solution of TEAFC in water was 3.45.

**Triethylammonium chlorochromate (TEACC),**

\[ (C_2H_5)_3NH^+ [CrO_3Cl]^- \]

Chromium(VI) oxide (1.0 g 0.01 mol) was dissolved in water and 6 M hydrochloric acid (0.251 ml, 0.015 mol) was added with stirring at 0 °C. To the resulting orange solution, triethylamine
(0.101 ml, 0.01 mol) was added drop-wise with stirring over a period of 30 minutes and the stirring was continued for 30 minutes at –4 °C. The precipitated orange solid was isolated by filtration, washed with petroleum ether (3×60 ml) and dried under vacuum for 2 h at room temperature. Yield: (54 %); mp 120 °C; calcd. for C16H34S2: C 31.35, 31.22, 27.03, 23.5, 15.02. HRMS calcd. for C16H34S2: M+, 290.1213. Found: M+, 290.3564 amu (average).

Electronic absorption at 22075 cm⁻¹, corresponded to λ→ε (e = 316 M⁻¹ cm⁻¹); 28169 cm⁻¹ to ε→ε (ε = 803 M⁻¹ cm⁻¹) and 41152 cm⁻¹ to λ→ε (e = 1327 M⁻¹ cm⁻¹). The UV/Visible, 13C NMR and ¹H NMR data was consistent with the TEACC structure. The pH of 0.01 M solution of TEACC in water was 2.4.

General procedure for preparation of silica gel supported reagents

A 500 ml suction flask equipped with a constant-pressure dropping funnel was used. The cold solution of TEAFC or TEACC, prepared by dissolving TEAXC (X = F: 0.2 mol, 44.2 g; X = Cl: 0.2 mol, 47.4 g) in CH₂Cl₂ (10 ml), was stirred under low-pressure vacuum for 30 min, yielding an orange-red slurry of triethylammonium halochromates/silica gel. The slurry was completely dried on the surface of highly dried day plate in the air to give 140 g of the desired reagent.

Typical procedure for oxidation coupling of benzenethiol with Triethylammonium halochromates / Silica gel

A suspension of benzenethiol (1f) (0.110 g, 0.001 mol), TEAFC (0.221 g, 0.001 mol) and wet silica gel (50% (w/w), 0.2 g) in CH₂Cl₂ (10 ml) was magnetically stirred at room temperature for 114 minutes. The completion of the reaction was followed by TLC using ether/petroleum ether (6:4) as eluant. The mixture was diluted with ether (1:1 v/v) and filtered through a short column of silica gel to give a clear solution. The solution was evaporated and the residual product was purified by distillation, recrystallization or column chromatography to give 1,2 diphenyldisulfane (2f) in 87 % yield. m.p 57–58 °C; lit.[17] m.p 58–60 °C. For other thiols (1a–e, 1g–h), the procedures were the same as above (see Table 1). The same procedure was applied for coupling of benzenethiol to 1,2–diphenyldisulfane with TEACC and above procedure could be achieved for larger scales, without any difficulties.

Spectral data for disulfides

1,2-Diisopropyldisulfane (2a), oil [17]. IR (KBr, cm⁻¹): 3000–2900 C–H (aliph. stretch), 1400–1350 C–H (aliph. bend), 1200–1100 C–S (stretch). ¹H NMR (500 MHz, CDCl₃): δ 3.1 (t, 4 H), 1.3 (m, 12 H), 1.1 (m, 4 H). ¹³C NMR (125 MHz, CDCl₃): δ 36.5, 30.32, 26.59, 24.46. HRMS calcd. for C₁₀H₂₂S₂: M⁺, 206.8542 amu. Found: M⁺, 206.1654 amu (average).

1,2-Dipentyldisulfane (2b), oil [17]. IR (KBr, cm⁻¹): 3000–2900 C–H (aliph. stretch), 1200–1100 C–S (stretch). ¹H NMR (500 MHz, CDCl₃): δ 2.5 (t, 4 H), 1.6 (m, 4 H), 1.25 (m, 4 H) 1.3 (m, 4 H), 0.85 (t, 6 H). ¹³C NMR (125 MHz, CDCl₃): δ 36, 33, 31, 23.5, 14.5. HRMS calcd. for C₁₀H₂₂S₂: M⁺, 206.8542 amu. Found: M⁺, 206.1654 amu (average).

1,2-Dicyclohexyl disulfane (2c), oil [17]. IR (KBr, cm⁻¹): 3000–2900 C–H (aliph. stretch), 1200–1100 C–S (stretch). ¹H NMR (500 MHz, CDCl₃): δ 2.5 (t, 4 H), 1.5 (m, 4 H), 1.2 (m, 18 H). ¹³C NMR (125 MHz, CDCl₃): δ 35.13, 31.35, 31.32, 27.03, 23.5, 15.02. HRMS calcd. for C₁₂H₂₄S₂: M⁺, 220.1213. Found: m/z 220.1213 (average).

1,2-Dicyclohexyl disulfane (2d), oil [17]. IR (KBr, cm⁻¹): 3000–2900 C–H (aliph. stretch), 1200–1100 C–S (stretch). ¹H NMR (500 MHz, CDCl₃): δ 2.5 (m, 2 H), 1.65 (dt, 8 H), 1.4 (m, 12 H). ¹³C NMR (125 MHz, CDCl₃): δ 35.13, 31.35, 31.32, 27.03, 23.5, 15.02. HRMS calcd. for C₁₂H₂₄S₂: M⁺, 230.2135. Found: m/z 230.2120 (average).

Disulfanylacetic acid (2e), oil [17]. IR (KBr, cm⁻¹): 3500–3200 OH (stretch), 3000–2900 C–H (aliph. stretch), 1200–1100 C–S (stretch). ¹H NMR (500 MHz, CDCl₃) δ 2.27 (s, 4 H), 11.5 (s, 2 H). ¹³C NMR (125 MHz, CDCl₃): δ 35 (CH₂), 179 (C=O). HRMS calcd. for C₁₀H₆O₂S₂: M⁺, 182.1478. Found: m/z 182.342 (average).
**1,2-diphenyldisulfane (2f)**, m.p 57–58 °C, lit. [17] 58–60 °C. IR (KBr, cm⁻¹): 3200–3100 C–H (aromatic stretch), 1200–1150 C–S (stretch). \(^1\)H NMR (500 MHz, CDCl₃): \(\delta\) 7.65 (d, 4 H), 7.25 (m, 6 H). \(^{13}\)C NMR (125MHz, CDCl₃): \(\delta\) 133.0, 131.4, 130.2, 129.53. C₁₂H₁₀S₂: Calc. C 66.1%, H 4.71%, S 29.37%. Found: C 66.22%, H 4.65%, S 29.2%.

**Bis(4-methylphenyl)disulfide (2g)**, m.p 42–44 °C, lit.[18] 43–44 °C. IR (KBr, cm –1): 3200–2100 C–H (aromatic stretch), 3000–2900 C–H (aliph. stretch), 1480–1400 C–H (aromatic bend), 1200–1100 C–S (stretch ). \(^1\)H NMR (300 MHz, CDCl₃): \(\delta\) 8.1 (s , 2 H), 7.7 (d, 2 H), 7.5 (d, 6 H), 7.32 (d, 4 H). \(^{13}\)C NMR (300 MHz, CDCl₃): \(\delta\) 137.76, 137.11, 135.26, 134.52, 131.57, 128.92, 127.08, 126.16, 125.02, 124.87. C₁₄H₁₄S₂: Calc. C 75.47%, H 4.40%, S 20.12%. Found: C 75.36%, H 4.32, S 20.89%.

**RESULTS AND DISCUSSION**

Different thiols were subjected to oxidations with triethylammonium fluorochromate(VI) (TEAFC) and triethylammonium chlorochromate(VI) (TEACC), absorbed on silica gel, in dichloromethane (Scheme 1).

![Scheme 1](image)

These oxidations take place under mild and completely heterogeneous conditions giving excellent yields (Table 1).

### Table 1

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Product</th>
<th>TEAFC</th>
<th>TEACC</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH₃-CH-SH</td>
<td>CH₃-CH-S-S-CH₃</td>
<td>92</td>
<td>145</td>
</tr>
<tr>
<td>1a</td>
<td>2a</td>
<td>78</td>
<td>85</td>
</tr>
<tr>
<td>n-C₅H₁₁-SH</td>
<td>C₅H₁₁-S-S-C₅H₁₁</td>
<td>90</td>
<td>108</td>
</tr>
<tr>
<td>1b</td>
<td>2b</td>
<td>86</td>
<td>90</td>
</tr>
<tr>
<td>n-C₈H₁₇-SH</td>
<td>C₈H₁₇-S-S-C₈H₁₇</td>
<td>94</td>
<td>97</td>
</tr>
<tr>
<td>1c</td>
<td>2c</td>
<td>90</td>
<td>85</td>
</tr>
<tr>
<td>HOOC-CH₂-SH</td>
<td>HOOC-CH₂-S-S-CH₂-COOH</td>
<td>85</td>
<td>35</td>
</tr>
<tr>
<td>1d</td>
<td>2d</td>
<td>35</td>
<td>75</td>
</tr>
<tr>
<td>1e</td>
<td>2e</td>
<td>80</td>
<td>215</td>
</tr>
<tr>
<td>1f</td>
<td>2f</td>
<td>87</td>
<td>95</td>
</tr>
<tr>
<td>Me-C-SH</td>
<td>Me-C-S-S-C-Me</td>
<td>114</td>
<td>85</td>
</tr>
<tr>
<td>1g</td>
<td>2g</td>
<td>84</td>
<td>85</td>
</tr>
<tr>
<td>1h</td>
<td>2h</td>
<td>81</td>
<td>85</td>
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</table>

Oxidations may also occur using only TEAFC and TEACC, in the absence of silica gel, but considerable improvements are observed in the presence of the absorbent. This implies that the silica gel may act as a reaction medium, providing an effective heterogeneous surface area for the oxidation and at the same time making the procedure much more convenient. The nature of the solvent does not appear to be particularly critical. Hydrocarbons, benzene, ethers and chlorinated hydrocarbons are equally effective, the practical choice being mandated by the solubility of the products and the desired reaction temperature. The chromium(VI) contents were easily determined iodometrically. It seemed from the Table 1 that TEAFC were more effective than TEACC for saturated organic thiols (1a – 1d) in terms of yields and reaction times. Overoxidation to sulfones and/or sulfones was not observed in the above-mentioned reactions. The IR spectra of TEAFC and TEACC are similar to that of other fluoro and chlorochromates [19]. TEAFC and TEACC are soluble in water, dimethylformamide, acetonitrile, acetone and dichloromethane; they are only sparingly soluble in benzene, carbon tetrachloride, chloroform and hexane.

CONCLUSION

New reagents triethylammonium fluorochromate(VI), (TEAFC) and triethylammonium chlorochromate(VI), (TEACC) absorbed on silica gel were easily synthesized. They are inexpensive, readily available oxidizing reagents for a variety of aromatic and non-aromatic thiols. Their advantages include higher yields, shorter reaction times, lower thiol/oxidant molar ratios, and ease of separation of products. Moreover, during the reaction, the color of the oxidants change from orange to brown, thus providing a visual means for ascertaining the progress of the oxidation. These reactions are easily scaled up without any problems. We did not perform regeneration of the reagents, but this could probably be achieved via flow in a reaction vessel. Because of phase transfer properties, availability, versatility and high adsorbance on silica gel by the quaternary ammonium cation, these reagents were suitable for oxidative coupling of thiols to disulfides. The mechanism of oxidation is probably similar to those by other quaternary ammonium reagents described by Walters and coworkers [20] and by Patel and Mishra [21]. Many functional groups are inert towards these oxidizing agents, including, sulfides and phenols, enhancing the usefulness of the oxidants and the oxidation conditions for the synthesis of highly functionalized molecules.

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REFERENCES


