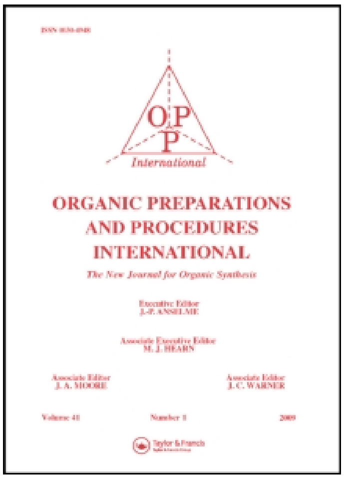

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# DETHIOACETALIZATION OF DITHIOLANES WITH FERRIC NITRATE AND SILICA GEL IN HEXANE

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8. Compound **11** was prepared in two steps by reduction of 2,3-dimethoxybenzaldehyde with sodium borohydride in methanol (88%) followed by treatment of the alcohol for 6 h with triphenylphosphine in refluxing carbon tetrachloride (85%).

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# DETHIOACETALIZATION OF DITHIOLANES WITH FERRIC NITRATE AND SILICA GEL IN HEXANE

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(12/09/97)

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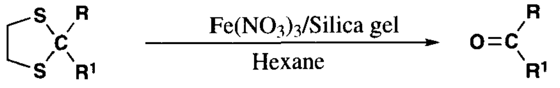
The importance of protection/deprotection processes for certain functionalities in the synthesis of organic compounds has led to the development of a large numbers of protective groups and of methods for their removal.[1] Of the typical deprotective procedures (*e.g.* chemically, photolytically and electrolytically), chemical deprotection is the most convenient and widely applicable; however, it often involves the use of heavy metal reagents[2] such as $Hg^{2+}$, $Ag^{+}$, $Tl^{3+}$, $Cd^{2+}$, $Se^{4+}$ which are inherently toxic and/or expensive to use. It occurred to us that these problems might be overcome by simple use of a nontoxic and inexpensive metal salt such as ferric nitrate **1**, for example. We have recently reported simple oxidations of alcohols[3a] and sulfides[3b] with *in situ* generated supported $Fe(NO_3)_3$ reagents. This success[3] together with our recent involvement in the chemistry of sulfur compounds[4] has prompted us to investigate deprotection reaction of dithioacetals and ketals since these are useful protecting groups for carbonyl compounds.[5,6] In addition, scant attention has been paid to the utility of supported reagents for this purpose,[7,8] although supported reagent chemistry is of recent and rapidly growing interest[7-9] and constitutes a new *cleaner* synthetic methods.[10] We report here a convenient deprotection of 1,3-dithiolanes by **1** and chromatographic silica gel under neutral and anhydrous conditions.

The current deprotection procedure is very simple, being carried out simply by efficient stirring of a heterogeneous mixture of hexane, silica gel, **1**, and a dithiolane in a flask. The reaction was clean and the work-up was straightforward. In the absence of silica gel, however, the reaction is sluggish; more importantly, ferric nitrate formed an intractable solid mass during the reaction, which makes the stirring and product isolation considerably more difficult. The reaction conditions given in the Table were optimized. Thus the combination of ferric nitrate and silica gel worked efficiently and proved to be generally applicable to aliphatic, alicyclic, aromatic, and unsaturated substrates— the parent ketones **3a-f** and aldehydes **3g-s** (Scheme) being regenerated in excellent yields. In the cases of aromatic substrates, the electronic property of the substituents and their positions on the benzene ring did not affect the rate nor the product selectivity (Entries 6-17), even though certain deprotection procedures suffer from strong electronic effects as such the oxidative dethioacetalization of dithianes with DDQ in wet acetonitrile.[6c]

In summary, we have demonstrated that the *in situ* generated silica gel supported $Fe(NO_3)_3$ reagent can be successfully used for dethioacetalization of various 1,3-dithiolanes. The method can be favorably compared to the previous methods. Thus, reaction times were much shorter than those using



**2** **3**

a) $R = Me, R^1 = n\text{-}C_7H_{15}$
b) $R, R^1 = -(CH_2)_5-$
c) $R, R^1 = -(CH_2)_{11}-$
d) $R = Me, R^1 = Ph$
e) $R = Et, R^1 = Ph$
f) $R = Ph, R^1 = Ph$
g) $R = H, R^1 = n\text{-}C_7H_{15}$
h) $R = H, R^1 = Ph$
i) $R = H, R^1 = p\text{-}MeOC_6H_4$
j) $R = H, R^1 = o\text{-}MeC_6H_4$
k) $R = H, R^1 = m\text{-}MeC_6H_4$
l) $R = H, R^1 = p\text{-}MeC_6H_4$
m) $R = H, R^1 = p\text{-}ClC_6H_4$
n) $R = H, R^1 = o\text{-}BrC_6H_4$
o) $R = H, R^1 = m\text{-}BrC_6H_4$
p) $R = H, R^1 = p\text{-}BrC_6H_4$
q) $R = H, R^1 = p\text{-}O_2NC_6H_4$
r) $R = H, R^1 = C_6H_4CH{=}CH$ (*trans*)
s) R = H, R¹ = 1-Naphtyl

**TABLE**. Deprotection of 1,3-Dithiolanes with Ferric Nitrate[a]

| Entry No. | Substrate | Time (min) | **3** (%)[b] | bp. (°C) or (found) | mp. (°C/torr) (reported)[d] |
|---|---|---|---|---|---|
| 1 | **2a** | 10 | 99 | 74-76/12 | 75-77/12 |
| 2 | **2b** | 5 | 93 | 62-64/12 | 67/15 |
| 3 | **2c** | 10 | 85 | 60-61 | 61 |
| 4[c] | **2d** | 30 | 85 | 65-67/5 | 67/5 |
| 5 | **2e** | 10 | 94 | 89-90/12 | 84-85/8 |
| 6 | **2f** | 10 | 97 | 48-50 | 48.5-49 |
| 7 | **2g** | 10 | 96 | 70-72/20 | 72/20 |
| 8 | **2h** | 10 | 95 | 65-68/12 | 62/10 |
| 9 | **2i** | 10 | quant. | 133-135/12 | 134-135/12 |
| 10 | **2j** | 10 | 97 | 69-71/6 | 68-72/6 |
| 11 | **2k** | 10 | 98 | 89-90/15 | 93-94/17 |
| 12 | **2l** | 10 | quant. | 113-115/12 | 106/10 |
| 13 | **2m** | 15 | 93 | 46-48 | 47 |
| 14 | **2n** | 10 | quant. | 117-118/12 | 118-119/12 |
| 15 | **2o** | 10 | 94 | 66-68/2 | 66-68/2 |
| 16 | **2p** | 15 | 94 | 58-60 | 59-60 |
| 17 | **2q** | 15 | quant. | 104-106 | 106 |
| 18 | **2r** | 10 | 95 | 120-122/12 | 130/20 |
| 19 | **2s** | 10 | quant. | 160-161/12 | 150/9 |

a) At 50°, under argon; 1,3-dithiolane (1 mmol), $Fe(NO_3)_3$ (1 mmol), silica gel (1 g), hexane (10 mL). b) Yield based on **2**. c) At 40°. d) Ref. 12.

Montmorillonite K10 supported $Fe(NO_3)_3$ (*Clayfen*) and $Cu(NO_3)_2$ reagent (*Claycop*) [2-6 h],[7b] and shorter or comparable to those with silica gel supported $Cu(NO_3)_2$ reagent [15-60 min],[7d] This clearly indicates that independent preparation of a supported reagent is unnecessary for the efficient performance of ferric nitrate. The present system, therefore, provides a simple and practical procedure for high yielding deprotection of 1,3-dithiolanes, applicable to a wide range of substrates, and constitutes an economically and environmentally acceptable alternative to the currently available methodologies.

## EXPERIMENTAL SECTION

The $^1H$ NMR spectra were recorded with a JEOL PMX-60 (60 MHz) spectrometer for solutions in deuteriochloroform with TMS as an internal standard. The IR spectra were measured on a JASCO A-100 spectrophotometer as thin films (neat) or KBr disks. Analytical gas chromatography was performed on a Shimadzu GC-4CM or a Shimadzu GC-14B instrument equipped with a flame ionization detector through a 2 m x 5 mmØ glass column packed with 3% Silicone OV-17 on Uniport HP or 5% PEG-20M on Chromosorb WAW-DMCS, respectively, with temperature programming. Melting points were determined on a Yanagimoto MP-S3 melting point apparatus and were uncorrected.

Merck Silica Gel 60 (70-230 mesh) was used for both the deprotection reaction and column chromatography. Commercial $Fe(NO_3)_3$ was used as received. 1,3-Dithiolanes were synthesized from 1,2-ethanedithiol and the corresponding carbonyl compounds in chloroform in the presence of $ZnCl_2$, according to the standard method.[11] Hexane was dried and distilled prior to use.

**Deprotection Procedure**.- Dethioacetalization of the dithiolane **2f** derived from benzophenone **3f** (Entry 6) is representative. A 30 mL two-necked round-bottom flask, equipped with a Teflon-coated stir bar, a 25 cm long reflux condenser and a glass tubing connected to an argon-filled balloon, was arranged for conducting the reaction under inert atmosphere by connecting the top of the condenser to a liquid paraffin trap. The flask was charged with hexane (10 ml), silica gel (1 g), finely ground ferric nitrate nonahydrate (1 mmol; 0.404 g), and **2f** (1 mmol; 0.258 g) in that order, and the resultant mixture was magnetically stirred at 50° for 10 min. The cooled mixture was filtered through a sintered glass funnel and the residue was washed thoroughly with portions of dry ether. The combined clear solution was evaporated on a rotary evaporator *in vacuo*. Analysis of the crude material on GC-4CM apparatus using p-chlorobenzophenone as an internal standard showed that **3f** was regenerated quantitatively. Chromatography on silica gel (hexane/ethyl acetate) afforded pure ($^1$H NMR, GC, and TLC) **3f** (0.177 g, 97%: mp 48-50°, lit.[12] mp 48.5-49°).

Dethioacetalization of the other dithiolanes were carried out as above. Specific reaction conditions (reaction time and temperature) for each dithiolane were determined in terms of the reactivity of the substrate and yield of the carbonyl compound. Isolated carbonyl compounds were identified by comparing their spectral ($^1$H NMR and IR) and/or physical data with commercial authentic samples.

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