## Cleavage of the 1,3-Dithiane Protective Group

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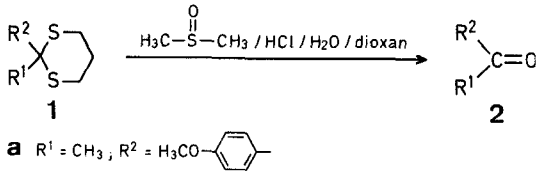
Protection of the carbonyl function by formation of the 1,3-dithiane group has been widely used, e.g., as a starting point for the synthetically important "umpolung" procedure. The most relevant drawback, however, is the removal of the protecting group: several methods have been proposed but none of them is of sufficiently general applicability[1,2].

In connection with our work on the stability of $\alpha$-sulfur-substituted carbenium ions[3], we have now developed two new procedures which, although applied so far only to model compounds, appear to be simpler than the ones currently used. In our previous work on the chemistry of sulfoxides in hydrogen halide acid solutions[4], we have shown the intermediacy of halosulfonium ions

which are responsible for the reduction to sulfides (when X = J) and for racemization (when X = Cl, Br). Thus, in aqueous hydrochloric acid dimethyl sulfoxide is in equilibrium with small (undetectable) amounts of chlorodimethylsulfonium ion, a positive halogen donor which may be used as a mild chlorinating agent[5]. Chlorination of dithianes in aqueous media has been used to restore the carbonyl function[2]. On the basis of these facts, we have now elaborated two new procedures for the cleavage of 1,3-dithianes **(1)** to give the corresponding carbonyl compounds **(2)**. The dithiane **1** and a tenfold excess of dimethyl sulfoxide are dissolved in dioxan/hydrochloric acid (70/30); work-up affords the carbonyl compound **2** (Method A).



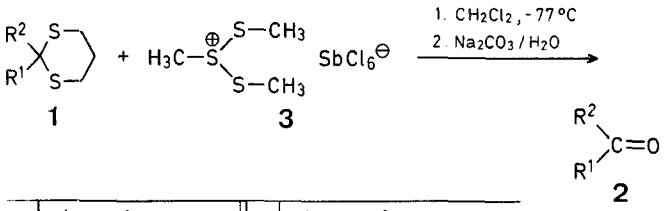

1 2

**a** $R^1 = CH_3$; $R^2 = H_3CO$–C6H4–

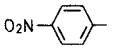
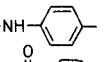
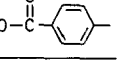
**b** $R^1 = CH_3$; $R^2 = n$-$C_6H_{13}$

Thus, in a reaction medium 1.8 molar in hydrochloric acid, 4-methoxyacetophenone **(2a)** is obtained from the dithiane **1a** in 96.5% yield (according to G.L.C. analysis of the reaction mixture) after a reaction time of 7.5 h; by increasing the acid concentration to 3.6 molar hydrochloric acid, the same yield of **2a** can be obtained after a 5 min reaction time. A comparable yield (90%) of 2-heptanone **(2b)** is achieved using a 1.8 molar acid concentration after a reaction time of 24 h.

The conditions of Method A may be too drastic for acid-sensitive compounds. In these cases, the cleavage may be performed under milder conditions using a positive sulfur donor such as methyl-bis[methylthio]-sulfonium hexachloroantimonate[6,7] **(3)** (Method B). The reaction is carried out in dichloromethane at −77 °C; it is applicable to 2-phenyl-1,3-dithianes **(1d–i)** having various heterofunctional groups on the phenyl ring, the yields of carbonyl compounds **(2)** being high.




1 3 2

| | $R^1$ | $R^2$ | | $R^1$ | $R^2$ |
|---|---|---|---|---|---|
| b | $CH_3$ | $n$-$C_6H_{13}$ | f | H |  |
| c | $CH_3$ | $t$-$C_4H_9$ | g | $CH_3$ |  |
| d | $CH_3$ |  | h | H |  |
| e | H |  | i | $CH_3$ |  |

Solvents and commercial reagents are purified by conventional methods before use. Methyl-bis[methylthio]-sulfonium hexachloroantimonate (**3**; also commercially available: FLUKA) is prepared from dimethyl disulfide and antimony(V) chloride as described[6,7] and recrystallized from dichloromethane/ether. The starting 1,3-dithianes **1** were prepared and purified according to known procedures[8,9].

**Carbonyl Compounds (2) from 1,3-Dithianes (1); General Procedures:**

Method A; General Analytical Procedure: Dimethyl sulfoxide (1.08 g, 13.8 mmol) is added at room temperature to a stirred solution of the 1,3-dithiane (**1**; 1.38 mmol) and a hydrocarbon (hexadecane or tridecane, 0.08 g, to be used as internal standard) in dioxan /70 ml)/conc. hydrochloric acid (30 ml). Aliquots withdrawn at intervals are poured into ether and neutralized with aqueous sodium carbonate. For analytical runs, the ether layer is analyzed by G.L.C. (UCW 982, 2 m, column temperature 135–270 °C).

Method A; Typical Preparative Procedure:

*Cleavage of 2-methyl-2-(4-methoxyphenyl)-1,3-dithiane* **(1a)**: Dimethyl sulfoxide (6.66 g, 85.4 mmol) is added at room temperature to a stirred solution of 1,3-dithiane **1a** (2.0 g, 8.3 mmol) in dioxan/aqueous 3.6 molar hydrochloric acid (70/30; 145 ml). After 5 min, the solution is poured into saturated aqueous sodium carbonate (200 ml) and extracted with ethyl ether (3 × 100 ml). The ether is washed with water (100 ml) and dried with sodium sulfate. The solvent is removed at reduced pressure and the residual product column chromatographed on silica gel (220 g) using ethyl acetate/petroleum ether (1/9) as eluent to give *4-methoxy-acetophenone* **(2a)**; yield: 1.20 g (96%); m.p. and mixture m.p. 37–38 °C (Ref.[10], m.p. 38.5–39.5 °C.

Method B; General Analytical Procedure: A solution of methyl-bis[methylthio]-sulfonium hexachloroantimonate (**3**; 0.761 g, 1.6 mmol) in anhydrous dichloromethane (15 ml) is added dropwise to a stirred solution of the 1,3-dithiane (**1**; 0.8 mmol) and a hydrocarbon (decane or hexadecane, 0.035 g, to be used as internal standard) in anhydrous dichloromethane (25 ml) at −77 °C. Aliquots withdrawn at intervals are poured into aqueous sodium carbonate and this mixture is extracted with ether. The ether extract is analyzed by G.L.C. (UCW 982, 2 m, column temperature 135–270 °C).

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**Table.** 2-Substituted 1,3-Dithianes **(1)** and their Cleavage to Carbonyl Compounds **(2)**

| 1, 2 | 1,3-Dithiane **(1)** | | | Carbonyl Compound **(2)** | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | b.p./torr or m.p. [°C] (ethanol) | Molecular Formula[a] or Lit. m.p. [°C] | $^1$H-N.M.R. ($CDCl_3$/$TMS_{int}$) $\delta$ [ppm] | Method | Reaction time [min] | Yield [%] Isolated | Yield [%] G.L.C. | m.p. or b.p./torr [°C] found | m.p. or b.p./torr [°C] reported |
| **a** | 37.5–38.5° | $C_{12}H_{16}OS_2$ (240.4) | 6.7–7.7 (m, 4H); 3.75 (s, 3H); 2.65 (t, 4H); 1.9 (m, 2H); 1.66 (s, 3H) | A (1.8 normal in HCl) | 420 | | 96.5 | | |
| | | | | A (3.6 normal in HCl) | 5 | 96 | 96.4 | 37–38° | 38.5–39.5°[10] |
| **b** | 122–123°/0.05 | $C_{11}H_{22}S_2$ (218.4) | 2.85 (t, 4H, S—$CH_2$); 0.95, 1.36, 1.95 (m, 15H, $H_3C$—$(CH_2)_5$ and $CH_2$—$CH_2$—S); 1.65 (3H) | A (1.8 normal in HCl) | 1400 | | 90 | | |
| | | | | B, $(H_3C)_3S_3^{\oplus}$ $SbCl_6^{\ominus}$ | 1 | | 97 | | |
| **c** | 42–43° | $C_9H_{18}S_2$ (190.4) | 2.75 (t, 4H); 1.8 (m, 2H); 1.8 (s, 3H); 1.15 (s, 9H) | B | 1 | | 100 | | |
| **d** | 125–126° | $C_{11}H_{13}NO_2S_2$ (255.4) | 8.2 (s, 4H); 2.6 (t, 4H); 1.95 (m, 2H); 1.7 (s, 3H) | B | 1 | 97 | 100 | 77–78° | 80–82°[10] |
| **e** | 74–75° | 74–75° | — | B | 5 | | 97 | | |
| **f** | 131–132° | 123–126° | — | B | 1 | | 100 | | |
| **g** | 124–126° | $C_{11}H_{15}NS_2$ (225.4) | 6.6–7.6 (m, 4H); 3.6 (s, br, 2H); 2.72 (t, 4H); 1.98 (m, 2H); 1.75 (s, 3H) | B | 1 | 97 | 100 | 104–105° | 106°[10] |
| **h** | 196–198° | $C_{12}H_{15}NOS_2$ (253.4) | 9.87 (s, 1H); 7.37 (q, 4H); 5.25 (s, 1H); 2.88 (m, 4H); 2.02 (s, 5H) | B | 1 | 95 | | 158–159° | 156°[10] |
| **i** | 79–80° | $C_{13}H_{16}O_2S_2$ (236.4) | 7.97 (s, 4H); 3.90 (s, 3H); 2.68 (t, 4H); 1.96 (m, 2H); 1.75 (s, 3H) | B | 1 | | 98.5 | | |

[a] The microanalyses for the new compounds were in satisfactory agreement with the calculated values: C, ±0.25; H, ±0.12; N, ±0.15; S, ±0.18.

Method B; Typical Preparative Procedure:

*Cleavage of 2-Methyl-2-(4-nitrophenyl)-1,3-dithiane* **(1d):** A solution of methyl-bis[methylthio]-sulfonium hexachloroantimonate (**3**; 8.6 g, 18.06 mmol) in anhydrous dichloromethane (125 ml) is added dropwise, within ~20 min, to a stirred solution of 1,3-dithiane **1d** (2.19 g, 8.58 mmol) in anhydrous dichloromethane (150 ml) at −77 °C. The resultant solution is then poured into saturated aqueous sodium carbonate (400 ml) in a beaker. The organic layer is isolated, washed with water (3 × 100 ml), and dried with sodium sulfate. The solvent is removed at reduced pressure and the residual product column-chromatographed on silica gel (250 g) using ether/petroleum ether (0/10→4/6) as eluent to give *4-nitroacetophenone* **(2d)** as the main product; yield: 1.38 g (97%); m.p. and mixture m.p. 77–78 °C. As a by-product, *2,3,7,8,12,13-hexathiatetradecane* is isolated; yield: 0.45 g; oil. In addition, minor amounts of unidentified material are obtained.

*2,3,7,8,12,13-Hexathiatetradecane:*

| | | | | |
|---|---|---|---|---|
| $C_8H_{18}S_6$ | calc. | C 31.34 | H 5.92 | S 62.74 |
| (306.61) | found | 31.44 | 5.88 | 62.62 |

$^1$H-N.M.R. ($CDCl_3$/$TMS_{int}$): $\delta$ = 2.15 (m, $CH_2$); 2.40 (s, S—$CH_3$); 2.80 ppm (t, $CH_2$—S).

In the case of products **2f** and **2g**, the reaction is quenched by pouring the mixture into 2 normal or 6 normal hydrochloric acid, respectively. In the case of **2g**, the aqueous phase is neutralized with sodium hydrogen carbonate and extracted with ether (3 × 150 ml); evaporation of the dried extract affords 4-aminoacetophenone; yield: 97%; m.p. 104–105 °C (Ref.[10], m.p. 106 °C); purity: >99% (according to G.L.C. analysis).

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