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# A SIMPLE METHOD OF DETHIOACETALIZATION

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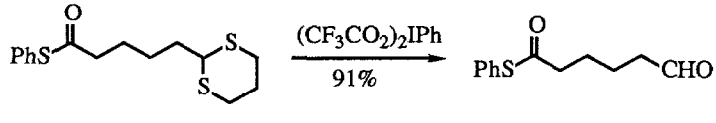
*Summary: Thioacetals and thioketals can be cleaved to carbonyl compounds in high yields by treatment with bis (trifluoroacetoxy)iodobenzene*

The potential of thioacetals and ketals as protecting groups for carbonyl compounds is limited by the not infrequent difficulty of regenerating the carbonyl function [1]. We now report a method which can be used for the selective deprotection of either thioketals or thioacetals and which is compatible with a variety of other functional groups. The new method involves treatment with bis(trifluoroacetoxy)iodobenzene at room temperature for a short time. An example is shown in Scheme 1. It is quite reasonable that cleavage is initiated by nucleophilic attack of sulfur on the hypervalent iodine center, followed at some later stage by addition of a hydroxyl (from water or an alcohol) , but we have no concrete evidence to support this possibility.

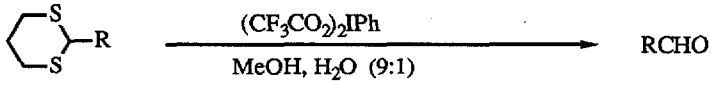



Scheme I

Aldehydes are obtained by treating thioacetals with bis(trifluoroacetoxy)-iodobenzene[2] in aqueous acetonitrile (table I). A mixture of methanol and water can also be used in the case of thioketals (table 2). In contrast to earlier methods involving metal-ion, alkylative, or oxidative hydrolysis[3], these conditions are sufficiently mild that various

functional groups such as esters, nitriles, secondary amides[4], alcohols, halides, alkenes and alkynes are unaffected. Even thioesters and amines[4] survive; the latter, presumably, because they are protected by the trifluoroacetic acid formed in the reaction.

Table 1: Dethioacetalization[5]



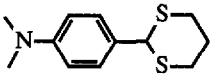
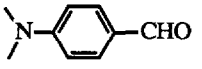
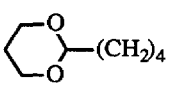
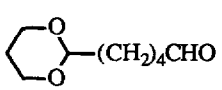
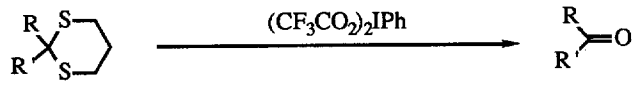
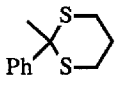
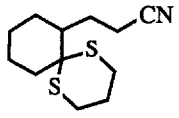
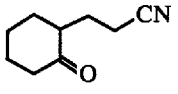
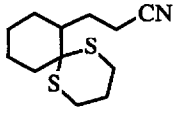
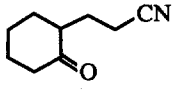

| R | RCHO | Time (min.) | Yield[a] |
|---|---|---|---|
|  |  | 10 | 99% |
| $MeO_2C(CH_2)_4$ | $MeO_2C(CH_2)_4CHO$ | 5 | 91% |
| $HO(CH_2)_5$ | $HO(CH_2)_5CHO$ | 2 | 97% |
| $AcO(CH_2)_5$ | $AcO(CH_2)_5CHO$ | 2 | 85% |
| $TsO(CH_2)_5$ | $TsO(CH_2)_5CHO$ | 1 | 92% |
| $Br(CH_2)_2O_2C(CH_2)_4$ | $Br(CH_2)_2O_2C(CH_2)_4CHO$ | 1 | 91% |
| $PhSOC(CH_2)_4$ | $PhSOC(CH_2)_4CHO$ | 1 | 91% |
| $CH_2$=$CHCH_2NHOC(CH_2)_4$ | $CH_2$=$CHCH_2NHOC(CH_2)_4CHO$ | 1 | 91% |
| $CH{\equiv}CCH_2O_2C(CH_2)_4$ | $CH{\equiv}CCH_2O_2C(CH_2)_4CHO$ | 2 | 84% |
|  |  | 1 | 85% |

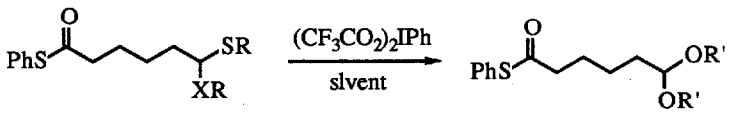
Table 2: Dithioketalization




| Thioketal | Product | solvents | Time | Yield |
|---|---|---|---|---|
|  |  | MeOH:H2O (9:1) | 5 min. | 85% |
|  |  | MeOH:H2O (9:1) | 5 min. | 86% |
|  |  | MeCN:H2O (9:1) | 5 min. | 90% |

a) Isolated yields.

Table 3: Dithioacetalization in alcohols




| R | X | R' | Solvent | Time (minutes) | Yield[a] |
|---|---|---|---|---|---|
| Et | S | Me | MeOH | 5 | 97% |
| Ph | S | $CH_2CH_2$ | $HOCH_2CH_2OH$ | 5 | 91% |
| $(CH_2)_3$ | S | Me | MeOH | 5 | 86% |
| $(CH_2)_2$ | S | | Me | MeOH | 5 93% |
| $(CH_2)_2$ | O | Me | MeOH | 360 | 90% |

a) Isolated yields.

The cleavages can also be run in alcohol or ethylene glycol to form the corresponding acetals directly from the thioacetals (Table 3).

General procedure: Bis(trifluoroacetoxy)iodobenzene (15mmol) was added at room temperature to a stirred solution of thioacetal or thioketal (10mmol) in the solvents indicated in the tables (10ml). After the reaction was completed, as judged by TLC (usually <10 min.), the solution was poured into saturated aqueous sodium bicarbonate (20ml) and extracted with diethyl ether (20mlx3). Drying ($MgSO_4$) and removal of solvents gave a residue which was purified by flash chromatography on silica gel (petroleum ether/EtOAc). The identify of the purified compounds was confirmed by comparison with authentic samples.

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References and notes

1. E. Vedejs and P. L. Fuchs, J. Org. Chem., 36, 366 (1971).
2. R. H. Boutin and G. M. Loudon, J. Org. Chem., 49, 4277 (1984).
3. M. Balogh, A. Cornelis and P. Laszlo, Tetrahedron Lett., 31, 3313 1984); I.Degani, R. Fochi and V. Regondi, Synthesis, 51 (1981), and references therein.
4. Primary amides are rearranged to amines under these conditions: see reference 2.
5. The starting thioacetals were prepared and purified by known procedures[6]. The was made from the ester[7], the thioester from the acid[8].
6. R. K. Olsen and J. O. Currie, in "The Chemistry of the Thiol Group", S. Patai, ed., John Wiley and Sons, New York, 1974, part 2, p. 5197.
7. S. M. Weinreb, Synthetic Commun., 989 (1982).
8. B. Neises and W. Steglich, Angew Chem. Int. Ed. Engl., 522 (1978).

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