Journal of Sulfur Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713926081

Developments in the deprotection of thioacetals

T. E. Burghardt[a]
[a] Johns Manville, Littleton, CO, USA

To cite this Article Burghardt, T. E.(2005) 'Developments in the deprotection of thioacetals', Journal of Sulfur Chemistry, 26: 4, 411 — 427
To link to this Article: DOI: 10.1080/17415990500195198
URL: http://dx.doi.org/10.1080/17415990500195198

Journal of Sulfur Chemistry
Vol. 26, No. 4–5, August–October 2005, 411–427

Taylor & Francis
Taylor & Francis Group

Developments in the deprotection of thioacetals

T. E. BURGHARDT*

Johns Manville, Littleton, CO 80127, USA

(Received 26 April 2005; in final form 23 May 2005)

Dithioacetals are very important and commonly used protecting groups for carbonyl compounds. Among the advantages of their use are the ease of formation, stability under both acidic and basic conditions, and *umpolung* reactivity. Unfortunately, their deprotection into the corresponding carbonyls is quite often difficult and requires special conditions. Hence, numerous protocols for the dithiane deprotection have been devised. In this review, various methodologies that were developed for the hydrolysis of thioacetal protecting groups are summarised and the detailed reaction conditions are presented.

Keywords: Dithiane; Thioacetal; Dithiolane; Deprotection; Hydrolysis

1. Introduction

Protection of carbonyl compounds as thioacetals is a common procedure in organic chemistry, particularly in multi-step syntheses [1–8]. Use of thioacetals as carbonyl masking groups is very convenient due to their ease of formation and stability under both basic and acidic conditions. Additionally, they are highly valuable in syntheses due to their *umpolung* reactivity [1–8]. Dithianes can be perceived as equivalents of acyl anions, which allow for selective carbon–carbon couplings of complex building blocks. Moreover, the resulting materials have the resulting carbonyl group protected. Furthermore, careful choice of the electrophilic components allow for the control of stereochemistry [1–8].

The most commonly used dithioacetals are cyclic 6-membered 1,3-dithianes, followed by 5-membered 1,3-dithiolanes. The open *S*,*S*-acetals are typically disfavoured due to their obnoxious odour; consequently, they are seldom utilized.

Unfortunately, the ease of formation of dithioacetals is not matched by the convenience of their deprotection into the parent carbonyl compounds, as clearly evidenced by the number of deprotection methods (*vide infra*). Three general thioacetal hydrolysis methods have been devised and are commonly used: (1) metal coordination, (2) oxidation, and (3) alkylation. In addition to the above, there are numerous underdeveloped methods for the hydrolysis of thioacetals, such as the protocols based on single-electron transfer (SET) or electro-oxidation.

*Email: Burghardt@JM.Com

Journal of Sulfur Chemistry
ISSN 1741-5993 print/ISSN 1741-6000 online © 2005 Taylor & Francis
http://www.tandf.co.uk/journals
DOI: 10.1080/17415990500195198

Coordination with mercury is historically the first and still the prevalent deprotection method in academic organic laboratories, in spite of serious health and environmental concerns [9–11]. Oxidations with compounds such as *N*-bromosuccinimide or bis(trifluoroacetoxy)iodobenzene as well as alkylation are much safer alternatives and they are slowly phasing out the procedures involving the use of heavy metals.

In spite of a plethora of the reported procedures, there is still one to be found that would be safe, inexpensive, and suitable for all kinds of sensitive substrates. The disadvantages of the reported protocols include toxicity of the reagents, long reaction times, harsh conditions, unavailability or high cost of materials, cumbersome work-up procedures, and quite often low yields and undesired side reactions. Among the numerous procedures presented herein, only a few are commonly used: mercury salts, *N*-halogenosuccinimides, hypervalent iodine, and iodomethane remain the reagents of choice for the synthetic organic chemists. However, there is an abundance of less known protocols for dithiane hydrolysis, including several procedures providing interesting chemospecificities that are mentioned in this review and should be of interest to chemists.

2. Mechanism

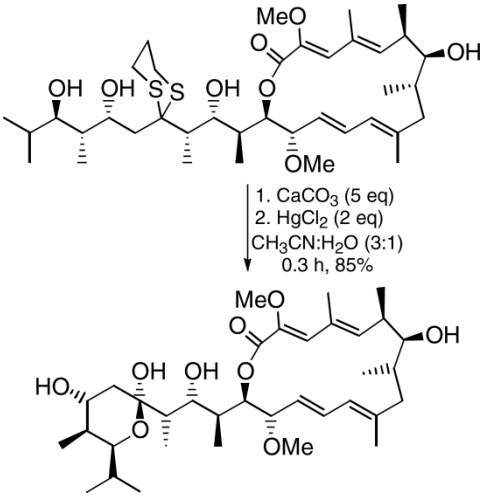
The vast majority of dithioacetal hydrolyses proceed *via* a similar mechanism. In the metal-mediated reactions, the first step is the coordination of sulfur atom to the metal to form a thiometallic intermediate, followed by the addition of water or another source of oxygen. As the dithio by-product is eliminated, the free carbonyl compound is liberated. For the metal-mediated hydrolyses, two or more equivalents of metal are required for efficient deprotection. The mechanism for the oxidative or alkylative hydrolysis of thioacetals to carbonyls involves conversion of sulfur into much more labile sulfoxides or sulfonium salts, respectively. Several other mechanisms have been proposed for the deprotection of thioacetals to carbonyls, depending on the used reagents. Detailed discussion regarding the mechanistic and kinetic considerations can be found in the literature and in several references cited herein [12–15].

3. Metal coordination

3.1 *Mercury*

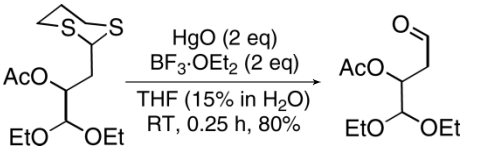
The first deprotection of a dithioacetal into a carbonyl was reported in 1894 by Fisher during his work on glucose [16]. The hydrolyses in the presence of 2 eq of $HgCl_2$, with a few modern modifications, remains the most common method to this day, partially due to the low cost and versatility of the reagent [17]. Deprotection with mercury salts requires exactly 1.0 eq of Hg per sulfur atom, as any excess could lead to undesired solvomercuriation reactions, and a lesser amount would not allow for a complete reaction. Typically, to avoid acidic conditions, the reactions are run in the presence of an excess of a mild base such as $CaCO_3$ or $CdCO_3$. The most commonly used medium for dithiane deprotection using $HgCl_2$ is a solution of acetonitrile or THF in water. The reactions are usually complete within 1 h at RT. This deprotection method is efficient for the removal of dithiane in the presence of a variety other sensitive groups, including macrolactones, as recently reported by Hanessian and co-workers during

the synthesis of bafilomycin (equation 1) [18].



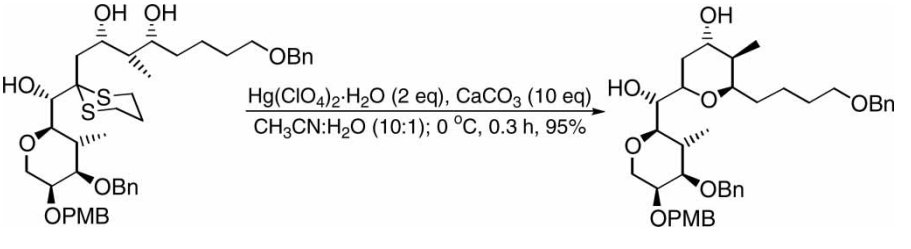
(1)

A modification of mercury deprotection by using HgO in the presence of 2 eq. of boron trifluoride diethyl etherate was developed by Vedejs and Fuchs [19]. This development was necessary as hydrolysis of β-substituted dithiane (equation 2) to an aldehyde failed when $HgCl_2$ or *N*-bromosuccinimide was used. This protocol, however, is not general since enolisable ketones could not be deprotected successfully. An adjustment of this procedure, where aqueous tetrafluoroboric acid was used instead of $BF_3 \cdot OEt_2$, was also reported [20]. The main advantages of using this modification were shorter reaction times and insensitivity to air.



(2)

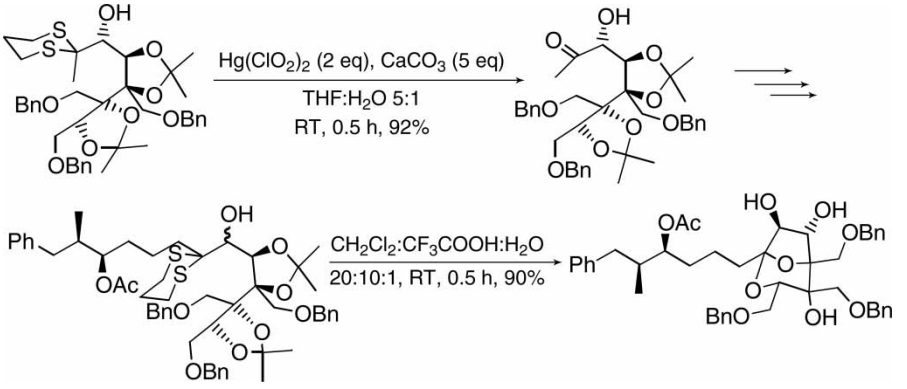
A significant development in the mercury-based deprotection came from Fujita's group in 1978 as a result of extensive studies involving 'soft-soft affinity' between sulfur and heavy metals [21]. Within the past few years, the use of 2 eq. of mercury(II) perchlorate in the presence of a significant excess of a mild base in aqueous acetonitrile for the hydrolysis of the 1,3-dithiane moiety appeared to be the most commonly used protocol. The extensive use of this costly [22] procedure is mostly due to the tolerance of a wider array of sensitive substrates than is observed with $HgCl_2$. Fujita's method was very recently used by Smith and co-workers in their total synthesis of spongistatin (equation 3) [23].



(3)

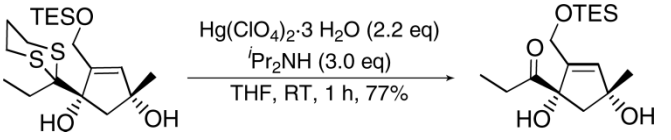
During the recent synthesis of zaragozic acid in Armstrong's group, $Hg(ClO_4)_2$ was successfully used in one step of the synthesis. Interestingly, in subsequent transformations, the

1,3-dithiane moiety was removed simultaneously with acetonide protection upon treatment of the compound with aqueous trifluoroacetic acid (equation 4) [24].



(4)

The use of 3 eq. of diisopropylamine to neutralise the reaction conditions allowed for the use of 2.2 eq. of $Hg(ClO_4)_2 \cdot 3H_2O$ to successfully hydrolyse a 1,3-dithiane in the presence of an α-hydroxy group as reported by Smith and co-workers (equation 5) [25].

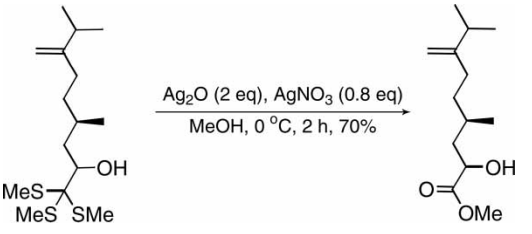


(5)

Among another methods involving mercury, the use mercury(II) trifluoroacetate on polymer support (polystyrene) was reported to both significantly improve the work-up and suppress side reactions observed with different mercury-mediated methods [26]. The use of $Hg(OAc)_2$ was reported as well [27, 28]. The newest modification in the use of Hg^{+2} for the hydrolysis of thioacetals is the use of $Hg(NO_3)_2 \cdot 3H_2O$ [29]. In comparison with other mercury-based methods, this one was reported to afford significantly reduced reaction times and to proceed under solvent-free conditions.

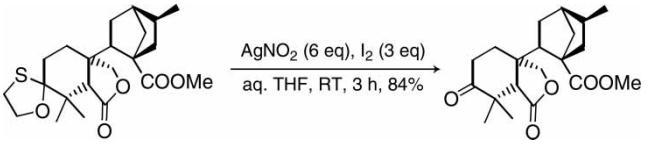
3.2 *Silver*

Silver compounds are significantly less harmful than ones containing mercury; however, they are more expensive [30]. This may be one of the reasons why the procedures involving silver salts are not widely adopted by synthetic organic chemists. The hydrolysis of dithiane with 2 eq. of $AgNO_3$ was first used to improve yield and work-up of the synthesised natural products, where the use of $HgCl_2$ did not furnish satisfactory results, albeit the yields were only moderate [31]. Sutherland and co-workers successfully used Ag_2O [32], in combination with $AgNO_3$, to convert a tris(methylthio) group into an ester (equation 6) [33]. The kinetic effects of the silver-mediated dithiane deprotection were studied by Satchell and co-workers [34].



(6)

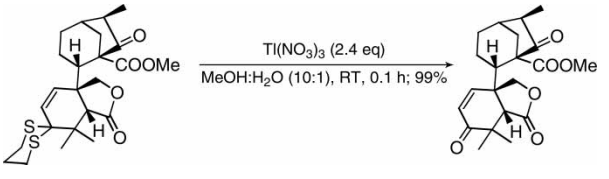
A mixture of 3 eq. of $AgNO_3$ and 6 eq. of iodine was reported to efficiently deprotect 1,3-dithianes, as well as 1,3-dithiolanes and 1,3-oxathianes [35]. This method was sufficiently mild to provide the carbonyl compound in high yield in the presence of a lactone moiety (equation 7). The use of $AgClO_4$ in place of $AgNO_3$ has been investigated as well. It was reported that the reactions were highly facile, but due to the suspected possibility of explosion, this reagent was not recommended [35].



(7)

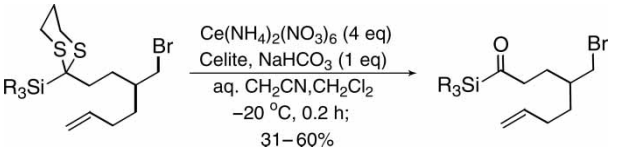
3.3 *Other metals*

Several other thioacetal hydrolysis protocols utilise the coordination with heavy metals. Among them, the procedures based on Tl^{+3} and Ce^{+4} are the most common. The use of 2 eq. of $Tl(NO_3)_3$ as dithiane-deprotecting reagent was first reported and later developed by Fujita and coworkers [21, 36–38]. This reagent was found to be highly effective for a facile hydrolysis of open and closed *S*,*S*-acetals and safe for numerous sensitive moieties, such as lactone, alkene, ester, or a bicyclic moiety prone to rearrangement (equation 8). However, it also was reported that phenolic substrates failed to react [36]. The use of thallium(III) nitrate was also reported to remove 1,3-dithiolane from a sensitive compound containing a terminal alkyne [39].



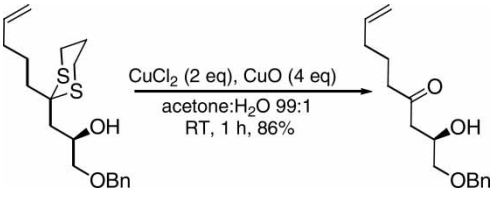
(8)

The use of 4 eq. of cerium(IV) ammonium nitrate (CAN) was first reported by Ho and co-workers to facilitate removal of thioacetal protection [40]. Subsequent studies shown that 4 eq. of CAN are indeed necessary for the deprotection, since the reaction most probably proceeds *via* an oxidative mechanism [41]. Recently, CAN was used on clay support in Tsai's group to deprotect a number of different α-silyl dithianes, albeit the yields were only moderate (equation 9) [42].



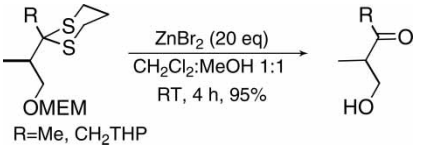
(9)

A protocol involving the use of 2 eq. of copper(II) chloride was also devised [43]. It was recently used by Uemura and co-workers, in conjunction with an excess of CuO, to deprotect 1,3-dithiane moiety during the synthesis of attenols (equation 10) [44, 45].



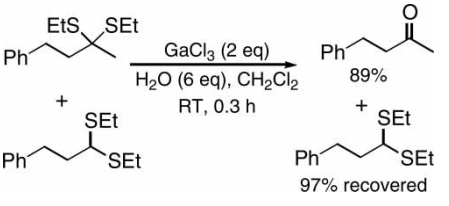
(10)

Chelation and proximity factors play a role in simultaneous deprotection of dithiane and 2-(methoxy)ethoxymethyl (MEM) groups using an excess of $ZnBr_2$ as reported by Hoffmann and co-workers (equation 11) [46]. Similar double deprotection was observed using the less coordinating 2-(trimethylsilyl)ethoxymethyl (SEM) group.



(11)

Among other metal-mediated thioacetal hydrolyses, the deprotection using 2 eq. of gallium(III) chloride was reported to exhibit an interesting specificity. The reagent does not remove terminal or cyclic thioacetals, while efficiently deprotecting open *S*,*S*-thioacetals (equation 12) [47]. Among other developments, iron(III) chloride was recently used by Kamal and co-workers for the removal of an open *S*,*S*-acetal in a synthesis of the benzodiazepine ring [48].



(12)

4. Oxidation

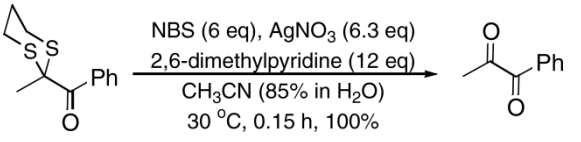
Oxidative methods utilise the fact that sulfoxides are significantly better leaving groups than thioacetals and break out upon the treatment with a base. Although the protocols utilising the oxidation of sulfur are the most abundant, only a few are commonly used. The oxidation protocol was initially developed during the work on steroids, which were protected as open or closed thioacetals and were resistant to mercury-mediated hydrolysis. Before other methods were developed, the procedure involved the conversion of thioacetals into mono- or bis-sulfoxides in the presence of monoperoxyphthalic acid, followed by the treatment with sodium ethoxide [49]. Later, 1-chlorobenzotriazole was used as the oxidating reagent at −95 °C and the sulfoxide elimination occurred in the presence of sodium hydroxide [50]. Currently, *N*-halogenosuccinimides or hypervalent iodine are the preferred oxidative reagents.

Oxidation with bromine was the first alternative to mercury in the deprotection of dithianes. The procedure was developed by Weygand and co-workers [51] and was used by Zinner during his work on sugars [52]. A bromine-releasing reagent, pyridinium bromide perbromide, was used to remove dithianes and dithiolanes under phase-transfer catalysis conditions or in aqueous acetonitrile [53]. Dithiane deprotection with 2 eq. of *tert*-butyl hypochlorite, as a source of Cl^+, in aqueous CCl_4 has been reported, too [54]. Similarly, an alcoholic mixture of concentrated HCl and H_2O_2 provides Cl^+, which can be used to deprotect thioacetals [55].

4.1 *N-Halogenosuccinimides*

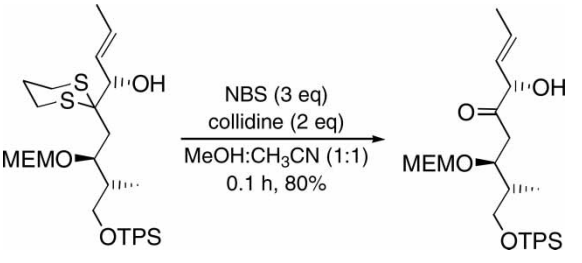
Readily available *N*-bromosuccinimide (NBS) was studied extensively by Corey and co-workers and was found to be an effective reagent for the removal of thioacetals from complex

substrates, on which the use of $HgCl_2$ or HgO did not provide optimal results [27]. This method is one of the most commonly used as it is quite reliable, compatible with sensitive substrates, and less toxic than the heavy metal-mediated processes. Unfortunately, the need to use 6 eq. of NBS, along with an excess (in relation to NBS) of $AgNO_3$ to scavenge the released free bromine, makes this protocol quite costly [56]. In the original report, 12 eq. of 2,6-dimethylpyridine (or 2,4,6-trimethylpyridine) was used to maintain neutral reaction conditions (equation 13).



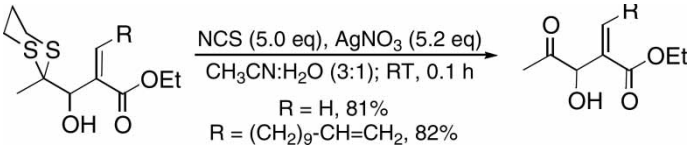
(13)

Williams and co-workers reported that the treatment of a sensitive dithiane-containing substrate with α-hydroxy-β, γ-unsaturation with 3 eq. of NBS in the presence of 2 eq. of 2,3,5-trimethylpyridine allowed for efficient deprotection to the parent carbonyl, even in the absence of $AgNO_3$ (equation 14) [57].



(14)

In addition to NBS, Corey and co-workers studied the use of *N*-chlorosuccinimide (NCS) [27]. It was found superior to NBS for the hydrolysis of dithianes containing an alkene moiety. Again, the excess of $AgNO_3$ (relative to NCS) is required to scavenge the released free chlorine. This method was successfully utilised to remove dithiane from Baylis-Hillman and vinylalumination adducts, on which metal-mediated deprotection did not work well (equation 15) [58].

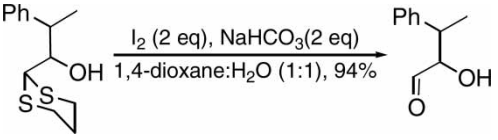


(15)

4.2 *Iodine*

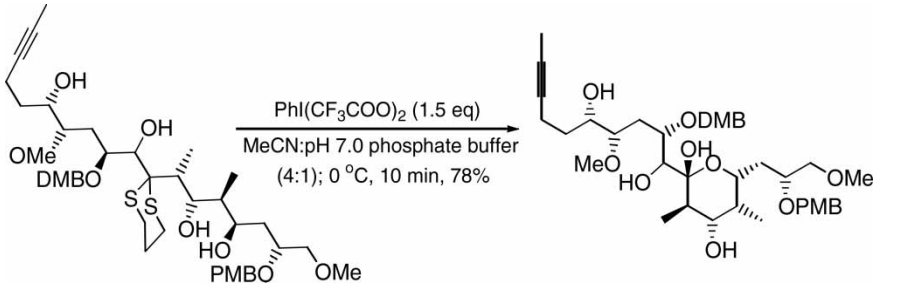
Deprotection of thioacetals with iodine was first used during studies of α-hydroxymercaptals (equation 16) [59]. Treatment of this type of substrates with $HgCl_2$ made separation difficult and long reaction times were required; the use of Br_2 afforded only rearranged products. The presence of a mild base, such as $NaHCO_3$, was necessary to maintain neutral reaction conditions [59]. The use of 1 eq. of KI in the presence of 1 eq. of $FeCl_3$ was also shown to

deprotect a number of dithianes and dithiolanes [60].



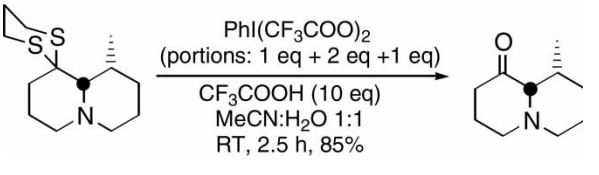
(16)

However, the most commonly used iodine-based compound for the hydrolysis of thioacetals is bis(trifluoroacetoxy)iodobenzene. This reagent was developed in 1989 in Stork's laboratory [61] and within the past few years it has emerged as one of those most commonly used to remove dithianes in spite of its prohibitive cost [62]. This mild deprotection technique proceeds *via* nucleophilic attack of sulfur on the hypervalent iodine. A parallel procedure, using di(acetoxy)iodobenzene, was also reported [63]. Among many uses of this reagent on sensitive substrates are the works by Burke and co-workers, where bis(trifluoroacetoxy)iodobenzene was successfully used on a chlorinated substrate [64]. Another example for the use of this reagent came in a recent synthesis of apoptolidin in Nicolaou's group (equation 17) [65].



(17)

The usefulness of $PhI(CF_3COO)_2$ as a reagent for thioacetal removal was recently underlined since it was found suitable for deprotection of dithiane from various alkaloid substrates (equation 18). Although 5 eq. of the reagent added in portions were required, the 1,3-dithiane group was successfully removed from compounds on which other attempted protocols afforded only low yields or resulted in decomposition of the material [66].

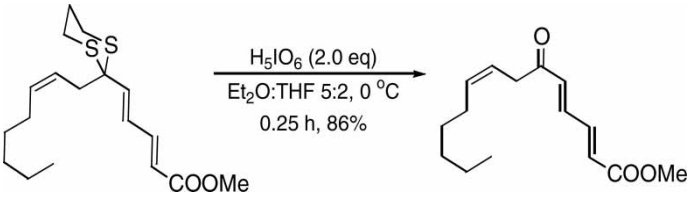


(18)

The discovery of periodinane as a mild oxidising reagent by Dess and Martin [67] in 1983 sparked the ongoing interest in hypervalent iodine chemistry. In the case of the dithiane deprotection using hypervalent iodine compounds, the oxygen incorporated in the resulting carbonyl compound is obtained from the reagent. The use of 2 eq. of Dess–Martin periodinane in aqueous dichloromethane–acetonitrile was recently reported to efficiently deprotect several dithianes [68].

Periodic acid in aqueous alcoholic solution at $-30\,^{\circ}C \rightarrow$ RT was used by Corey and co-workers to remove dithiane protection during the synthesis of gingkolide [69]. Using periodic acid under non-aqueous conditions, Rokach and co-workers achieved deprotection on sensitive materials [70]. An interesting substrate selectivity was observed, since *O*,*S*-acetals were deprotected in the presence of 1.0 eq. of H_5IO_6, while 2.0 eq. of this reagent were required

for the complete removal of *S*,*S*-thioacetal protection. Under the reaction conditions, acid-sensitive moieties such as α, β-unsaturated aldehydes, *O*,*O*-acetals, or TBS groups remained unaffected. The protocol was sufficiently mild to remove protection from a very acid-sensitive dienyl ester (equation 19) [70].

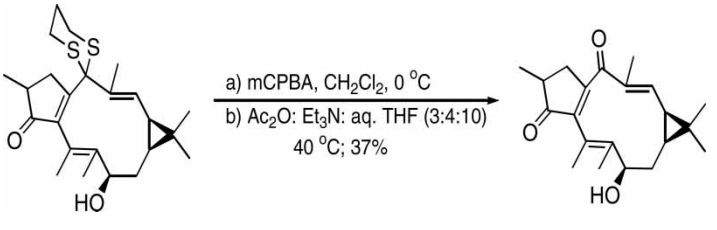


(19)

The use of another hypervalent iodine compound, *o*-iodoxybenzoic acid (IBX), as a reagent for the hydrolysis of thioacetals was recently studied by Nicolaou and co-workers. Upon the treatment of various benzylic or aliphatic dithianes with 2 eq. of IBX in aqueous DMSO, the parent carbonyl compounds were recovered in high yields in 0.1–6 h [71, 72]. Removal of benzylic and allylic *S*,*S*-acetals by treatment with 1.5 eq. of IBX in wet DMSO, with remarkable stability of unactivated acetals, was also reported [73]. This reagent was found to work well under supramolecular catalysis conditions using 0.1 eq. of β-cyclodextrin in water, too [74]. Additionally, numerous dithianes and dithiolanes were deprotected to the parent carbonyls under solvent-free conditions in the presence of 1.0 eq. of 1-benzyl-4-aza-1-azoniabicyclo[2,2,2]octane periodate in the presence of 0.3 eq. of $AlCl_3$ during their grinding in a mortar [75].

4.3 *Other oxidising reagents*

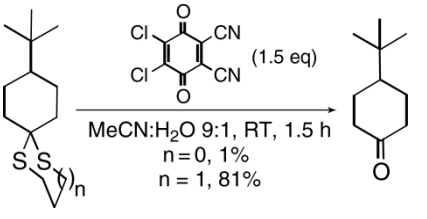
There are numerous other methods that utilise the oxidative reaction path for the removal of thioacetals. These protocols, in spite of being interesting alternatives, remain mostly undeveloped. Among them, the most interesting is the use of 3-chloroperoxybenzoic acid (mCPBA). This reagent, in the presence of CF_3COOH, was first reported by Cossy to effectively remove various open and cyclic dithioacetals [76]. It was successfully used for the removal of a dithiane protecting group by Smith and co-workers during the synthesis of bertyadionol (equation 20) [77]. Upon treatment with mCPBA, the 1,3-dithiane was oxidised to a monosulfoxide, which then underwent decomposition upon treatment with acetic anhydride *via* a Pummerer-like mechanism to provide the desired product, albeit in only 37% yield. It is quite interesting that this protocol was used due to failure of 23 other deprotection methods! [77].



(20)

Among other reagents, 5 eq. of Oxone®, a commercially available potassium hydrogen persulfate, on wet alumina support under chloroform reflux conditions, have been used to deprotect a variety of thioacetals [78]. Deprotection of 1,3-dithiolanes under these conditions required significantly longer reaction times than for removal of 1,3-dithianes. The use of 1 eq. of benzyltriphenylphosphonium tribromide was reported to efficiently deprotect

numerous thioacetals [79]. The hydrolysis of keto-protected aryl methyl ketones mediated by lithium diisopropylamide was reported as well [80]. Phenyl dichlorophosphate (1 eq.) in the presence of 4.5 eq. of NaI and 1.1 eq. of DMF was used to deprotect a number of *S*,*S*-acetals [81]. Yet another novel method for dithioacetal deprotection involves the treatment of 1,3-dithianes with 2.4 eq. of 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) (Selectfluor^{TM}) in aqueous acetonitrile for 5 minutes [82]. The reported reaction conditions were quite mild and the reagent was not only cleanly hydrolysing dithioacetals, but also *p*-methoxybenzylidene (PMB) and tetrahydropyranyl (THP) groups. Removal of open *S*,*S*-thioacetal protection from a variety of substrates using 1.5 eq. of DDQ was first reported to proceed under photochemical conditions and presumably with SET mechanism [83]. Later, it was reported that oxidative 1,3-dithiane deprotection using DDQ could be used to selectively deprotect a 1,3-dithiane moiety in the presence of a 1,3-dithiolane (equation 21) [84, 85]. Deprotection using DDQ has high synthetic potential due to the observed chemoselectivity and to the fact that DDQ is known to deprotect PMB groups.



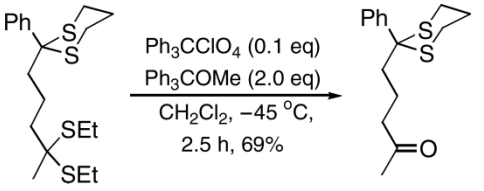
(21)

Trichloroisocyanauric acid is an inexpensive and safe compound that was demonstrated to remove dithiane protection from several compounds under solvent-free conditions while ground in a mortar with silica gel [86]. Benzyltriphenylphosphonium peroxymonosulfate in the presence of $AlCl_3$ was also reported to deprotect a variety of dithianes under solvent-free conditions [87]. Non-hydrolytic deprotection of open or closed non-enolisable benzylic thioacetals using $KMnO_4$, $BaMnO_4$, and MnO_2 in the presence of $AlCl_3$ was also reported [88].

The use of 5 eq. of SeO_2 in acetic acid as a solvent was reported to deprotect 1,3-dithiolanes from substrates containing ester and ether moieties [89]. Chloramine-T (sodium *N*-chloro-4-methylbenzenesulfonamide) was reported to react with 1,3-oxothiolanes and 1,3-dithiolanes under mild conditions to rapidly afford the parent carbonyl compounds in good yields [90, 91]. Zirconium sulfophenylphosphonate under heterogeneous catalytic conditions (in glyoxic acid monohydrate at 60 °C) deprotects dithioacetals from non-enolisable aldehydes and ketones in good yields [92]. Under these conditions, the 5-membered 1,3-dithiolanes require longer reaction times than do the 6-membered 1,3-dithianes. For a rapid (1 minute) hydrolysis of a dithiane moiety on sensitive substrates, 2 eq. of methyl bis(methylthio)sulfonium hexachloroantimonate in anhydrous CH_2Cl_2 at −77 °C could be used [93]. Likewise, a rapid deprotection was reported to proceed in the presence of 2 eq. of $ZnCr_2O_7 \cdot 3\,H_2O$ in dry acetonitrile [94]. Similarly, the use of 0.5 eq. of chromium(VI) oxide provided several carbonyl compounds from dithioacetals while grinding in a mortar with wet alumina [95]. The use of 1.5 eq. of lead(IV) oxide in the presence of 3 eq. of $BF_3 \cdot OEt_2$ in aqueous THF was reported as a good method to deprotect a γ-acetoxyaldehyde [96]. Compared with other oxidative and heavy metal-mediated thioacetal deprotection methods, this procedure showed a significantly improved yield on that substrate [96]. Oxidative deprotection of 1,3-dithiolanes using 1 eq. of tetramethylammonium superoxide (generated *in situ* from potassium superoxide and tetramethylammonium bromide in anhydrous DMF) was reported to require 3–7 h under anhydrous conditions; unfortunately, overoxidation of the obtained aldehydes to acids was observed [97].

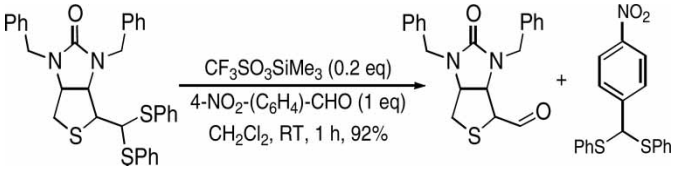
Deprotection of various 1,3-dithiolanes took place in the presence of 3 eq. of sulfuryl chloride fluoride in diethyl ether at RT [98]. The use of 1 eq. of 1-(phenylsulfinyl)piperidine in the presence of 1.1 eq. of trifluoromethanesulfonic anhydride at −60 °C under argon atmosphere was used to deprotected a number of thioacetals [99]. An oxidative hydrolysis of a 1,3-dithiane group using 10 eq. of $NaClO_2$ in the presence of 5 eq. of NaH_2PO_4 and 10 eq. of 2-methyl-2-butene in dilute aqueous 2-methyl-2-propanol (standard conditions for the oxidation of aldehydes to acids) was also reported [100].

A very interesting chemospecificity was observed during the hydrolysis of diethylthioacetals with 2 eq. of trityl methyl ether in the presence of catalytic trityl perchlorate. Under the reaction conditions, the 1,3-dithiane and *S*,*S*-diphenylacetals remained intact, while *S*,*S*-diethylacetals were smoothly hydrolysed (equation 22) [101].



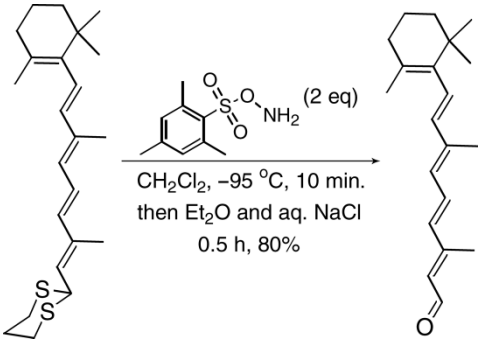
(22)

A catalytic method using $CF_3SO_3SiMe_3$ or $CF_3SO_3Si^tBuMe_2$ was developed to deprotect open dithioacetals during the synthesis of biotin, where other deprotection methods gave only low yields [102]. This procedure is transthioacetalisation, as the thioacetal moiety is transferred on a reactive aldehyde acceptor, with the best results being obtained with 4-nitrobenzaldehyde (equation 23). Catalytic amounts of $CF_3SO_3SiMe_3$ in conjunction with 4-nitrobenzaldehyde on a solid support were also reported as an efficient mix for removal of oxothioacetals [103].



(23)

An interesting alternative to oxidation is amination using 2 eq. of 2-[(aminooxy)sulfonyl]-1,3,5-trimethylbenzene at −95 °C [104]. This protocol was developed by Solladié and co-workers during the synthesis of retinal when dithiane hydrolysis using mercury, as well as various oxidative and alkylation methods, caused degradation of the sensitive all-*trans* substrate (equation 24).



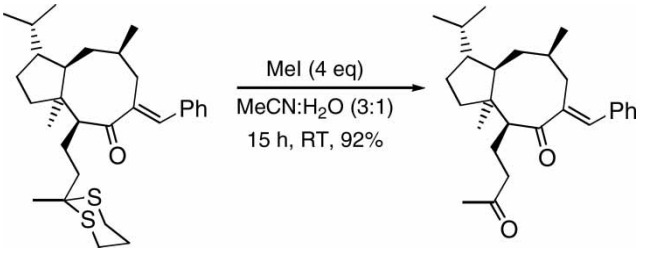
(24)

4.4 *Oxidation in the presence of DMSO*

Dimethyl sulfoxide (DMSO) can be used both as a reaction medium and as the reactive species in the oxidative dithioacetal hydrolysis. The protocols utilising DMSO remain obscure since in most cases the reaction conditions are rather harsh. Refluxing in DMSO caused hydrolysis of dithianes, dithiolanes, and open thioacetals to the parent carbonyl compounds [105]. Iodine in hot DMSO was reported to deprotect thioacetals and *S*-trithianes in good yields [106]. A large excess (35 eq.) of *tert*-butyl bromide or *tert*-butyl iodide in the presence of DMSO were reported to remove 1,3-dithiolanes from a variety of substrates. The reactive, generated *in situ* species, were identified as iododimethylsulfonium halides [107]. Similarly, efficient removal of 1,3-dithiolane protection during heating in at 80 °C for up to 24 h in the presence of iodotrimethylsilane and bromotrimethylsilane in DMSO was reported to proceed *via* the same intermediate [108]. DMSO in conjunction with aqueous hydrochloric acid in 1,4-dioxane gave the same results and was reported to proceed *via* similar mechanism as well [93]. Recently, Firouzabadi, Iranpoor and co-workers introduced silicon tetrachloride in the presence of DMSO as an effective reagent for the deprotection of thioacetals [109]. Additionally, several dithianes and dithiolanes were converted into the parent carbonyls by treatment with 0.5 eq. of 2,4,6-trichloro-1,3,5-triazine in 2.5 eq. of DMSO [110]. Moreover, several commonly used reagents for the thioacetal hydrolysis, such as bromine or NBS, as well as 2,4,4,6-tetrabromocyclohexa-2,5-dienone were used in 0.1–0.2 eq. in the presence of DMSO at RT to provide the desired carbonyl compounds from a variety of 1,3-dithianes. The reaction was reported to proceed *via* sulfenyl bromide intermediate with DMSO as the source of the carbonyl oxygen [111]. The removal of dithiane moiety in dry DMSO with 0.8 eq. of $MoCl_5$ was reported, too [112].

5. Alkylation

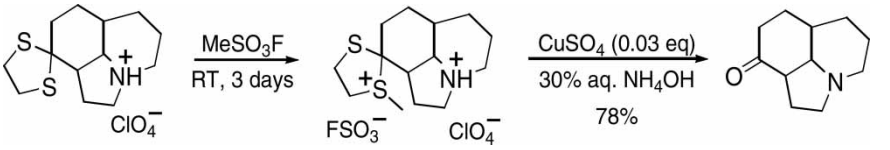
Similar to oxidation, the alkylation of thioacetals proceeds by generating much better leaving groups: isolable sulfonium salts. Iodomethane as a compound for dethioacetalisation was independently reported in 1972 by Fetizon and co-workers [113] and by Chang [114]. Alkylation using iodomethane appears to be one of the most commonly used methods for the hydrolysis of dithianes. Among the advantages are clean work-up procedures, the use of materials that are relatively benign for the humans and the environment, and low cost [115]. Drawbacks of the alkylation procedures, however, are incompatibility with substrates prone to alkylation, extended reaction times, and quite often elevated reaction temperatures. The alkylation using 4 eq. of MeI in aqueous acetonitrile for 15 h at RT cleanly removed dithiane protection from a substrate containing a sensitive macrocyclic ring (equation 25) [116].



(25)

Cleavage of 1,3-dithiolanes on a nitrogen-containing heterocycle was accomplished by Oishi and co-workers *via* alkylation using methyl fluorosulfonate [113] for 3 days followed

by treatment with catalytic $CuSO_4$ in the presence of NH_4OH (equation 26) [117]. Alkylation using 6 eq. of Meerwein's salt for 0.2 h was sufficient to remove more labile dithianes [118].



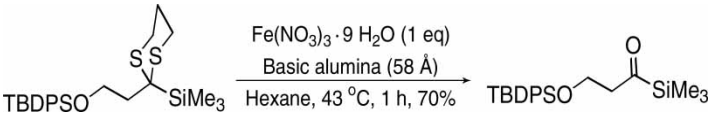
(26)

6. Other methods for the removal of thioacetals

6.1 *Deprotections with nitrosonium ion*

Among other protocols for the removal of dithioacetals, the use of reagents releasing NO^+ is the most developed and the results are quite promising. Although deprotections using nitronium or nitrosonium ions appear to be easy and convenient, they have yet to see extensive use in organic syntheses. This highly reactive species, in most cases generated from nitrites, reacts with sulfur to form thionitrites. In the first report of the deprotection of thioacetals using NO^+, Fujita and co-workers used 1 eq. of isoamyl nitrite to hydrolyse several open thioacetals [119]. This method showed an interesting chemospecificity, as the aldehyde protection could be removed in the presence of keto protection; nevertheless, it was not developed any further. The reaction of 5 eq. of $NaNO_2$ in aqueous 4 M HCl was reported to deprotect various thioacetals, albeit that certain substrates decomposed or failed to react [54]. Recently, deprotection of various 1,3-dithianes and 1,3-oxathioacetals using 1 eq. of $NaNO_2$ in the presence of 1 eq. of acetyl chloride in CH_2Cl_2 was reported to proceed rapidly at RT [120].

The use of 1.1 eq. of $Fe(NO_3)_3$ or 2 eq. of $Cu(NO_3)_2$ on Montmorillonite K10 clay support ('Clayfen' and 'Claycop', respectively) were developed by Laszlo and co-workers as a protocol for the deprotection of various thioacetals in high yield [121–123]. In spite of their oxidising properties, the clay-supported compounds were totally unreactive toward aldehydes. The chief, but not only, advantage of using a solid support is the ease of purification as simple filtration is sufficient in most cases [121–123]. Similarly, the use of $Cu(NO_3)_2$ on silica gel support in CCl_4 solvent has been reported as a fast and efficient deprotecting compound for 1,3-dithianes and 1,3-dithiolanes, as well as for oximes and tosylhydrazones [124]. Also, iron(III) nitrate on silica gel support was found to mediate the hydrolysis of several dithioacetals [125]. A modification of this procedure, where basic alumina support was used, was recently utilised by Wipf and co-workers to deprotect an α-silyldithiane (equation 27), where deprotection with other reagents did not furnish satisfactory results [126].



(27)

A novel, rapid method for deprotection is use of the 5 eq. of clay-supported ammonium nitrate ('Clayan') as a source of NO^+ under microwave conditions [127]. This method failed to selectively deprotect thioketals in the presence of acetonides, but removed the dithiane from a number of substrates. Irradiation in a microwave for 2–3 minutes in the presence of wet natural kaolinic clay was sufficient to remove certain dithiane and dithiolane protections [128].

The deprotection of dithianes with catalytic $Bi(NO_3)_3$ under open-air conditions [129] has recently been extended to hydrolysis of *O*,*O*-, *O*,*S*-, and *S*,*S*-acetals [130]. The principal

advantage of this method is the need for only 0.1 eq. of relatively non-toxic and inexpensive bismuth(III) nitrate pentahydrate [131]. Addition of 0.05 eq. of $BiCl_3$ accelerated some sluggish reactions [129]. The TBS and THP groups remained intact under the reaction conditions. According to the mechanism proposed by Komatsu and co-workers, the nitronium ion reacts with one sulfur atom while the other sulfur is coordinating to the bismuth metal; the presence of thionitrite intermediate was identified by its pink colour [130]. 'Oxides of nitrogen' was used to remove thioacetal protection from a polycyclic compound, on which other methods were ineffective [132]. This procedure has significant limitations, as certain thioacetals were removed only in modest yields. Additionally, preparation of the 'oxides of nitrogen' involves the use of highly toxic As_2O_3. Hydrolysis of a dithiane moiety using 1 eq. of dinitrogen tetraoxide complexes of Fe^{+3} or Cu^{+2} in CH_2Cl_2 (or neat) was reported. Under the reaction conditions, not only *S*,*S*-acetals, but also silyl and THP ethers, as well as *O*,*O*-acetals, were removed [133].

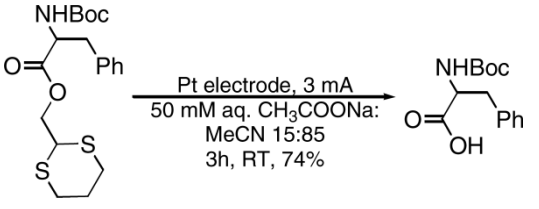
6.2 *Single-electron transfer (SET)*

There are several methods for the hydrolysis of thioacetals where an SET mechanism is proposed. These protocols, although available since the early 1990s, remain obscure. The first reported SET method for dithiane deprotection required the use of 1.5 eq. of $SbCl_5$ [134]. It afforded moderate to good yields and short reaction times. The use of 2.5 eq. of trisphenanthroline iron(III) hexafluorophosphate as an outer-sphere one-electron oxidant allowed for recovery of certain benzylic carbonyls from dithianes in moderate yields [135]. Although this method was found to be superior to the metal-mediated procedures for a variety of tested substrates, it was not general, as some materials decomposed. The SET reactions under visible or ultraviolet light require sensitisers. The first reported successful deprotection of a thioacetal under UV light required catalytic amounts of Methylene Green and proceeded in the presence of $MgClO_4$ [136]. Later, it was found that 2,4,6-triphenylpyrylium perchlorate was a good sensitiser in a deprotection of 1,3-dithianes and 1,3-dithiolanes; still, the yields were only moderate [137]. Subsequent study of sensitizers [138] showed 2,4,6-tris(4-chlorophenyl)pyrylium perchlorate [139] to be better than 9,10-dicyanoanthracene, Methylene Green, or *meso*-tetraphenylporphine in the reactions involving hydrolysis of the dithiane or dithiolane groups [140]. A conjunction of electrolysis with a stable cation radical source was reported to remove various dithianes and dithiolanes from several compounds [141]. In that case, *para*-substituted triphenylammonium pentachloroantimonate salts were the preferred source of radicals, which were generated *in situ via* an electrochemical process. That allowed for the use of catalytic amounts of the ammonium salts [142]. A photochemical dithiane hydrolysis process using 4 eq. of H_2O_2 under UV irradiation was reported as well [142].

6.3 *Electrochemical protocols*

Electrochemical hydrolysis of thioacetals remains unexplored: To date, there are only three reports presenting dethioacetalisation using only electrical current. In the first report, the yields were quite low [143] and the second publication dealt only with sugars, which were deprotected in moderate yields [144]. Most recently, the results of electrooxidation of dithioacetals using Pt electrode (1.5 V, 0.3 A cm^{-3}) for 6 h in aqueous acetonitrile were improved, but not superior to the obtained by traditional methods [145]. As an interesting note, efficient hydrolysis of 2-hydroxymethyl-1,3-dithiane ester to carboxylic acid, using a mild electrochemical method,

was recently reported by Kutateladze and co-workers (equation 28) [146].



(28)

7. Conclusions

Among the methods presented above for the hydrolysis of dithioacetals, the most commonly employed are the reagents containing mercury: Compounds such as $HgCl_2$ or $Hg(ClO_4)_2$ are being widely used in spite of their toxicity and the pressures toward conservation of the environment [147]. The methods involving less toxic reagents, such as iodomethane or bis(trifluoroacetoxy)iodobenzene, are slowly gaining popularity in the laboratories. Novel protocols, including the use of a plethora of different reagents, including catalytic methods, are constantly being developed and introduced. The multitude of the known procedures and the difficulties reported by various researchers prove that the removal of thioacetal protection is not always a straightforward task and that the deprotection of *S*,*S*-acetals into their parent carbonyl compounds remains a challenge for organic chemists.

Acknowledgements

The author wishes to express his sincere thanks to Professors P.V. Ramachandran and John B. Grutzner.

References

[1] B.-T. Gröbel, D. Seebach. *Synthesis*, 357 (1977).
[2] P.C.B. Page, M.B. van Niel, J.C. Prodger. *Tetrahedron*, **45**, 7643 (1989).
[3] M. Schelhaas, H. Waldmann. *Angew. Chem.*, **108**, 2192 (1996); *Angew. Chem., Int. Ed.*, **35**, 2056 (1996).
[4] A.K. Banerjee, M.S. Laya. *Russ. Chem. Rev.*, **69**, 947 (2000).
[5] M. Yus, C. Nájera, F. Foubelo. *Tetrahedron*, **59**, 6147 (2003).
[6] A.R. Hajipour, S. Khoee, A.E. Ruoho. *Org. Prep. Proc. Int.*, **35**, 527 (2003).
[7] A.B. Smith, C.M. Adams. *Acc. Chem. Res.*, **37**, 365 (2004).
[8] P.J. Kocieński. *Protecting groups*, 3rd ed., pp. 77–92, Georg Thieme, Stuttgart (2004).
[9] S. Deflora, C. Bennicelli, M. Bagnasco. *Mutat. Res.*, **317**, 57 (1994).
[10] K. Schumann, B. Elsenhans. *J. Trace Elem. Med. Biol.*, **16**, 139 (2002).
[11] C.G. Daughton. *Environ. Health Persp.*, **111**, 775 (2003).
[12] T.H. Fife, E. Anderson. *J. Am. Chem. Soc.*, **92**, 5464 (1970).
[13] C. Moreau, J. Lecomte, S. Mseddi, N. Zmimita. *J. Mol. Cat. A*, **125**, 143 (1997).
[14] D.P.N. Satchell, R.S. Satchell. *Chem. Soc. Rev.*, 55 (1990).
[15] M. Ali, D.P.N. Satchell. *J. Chem. Soc., Chem. Commun.*, 866 (1991).
[16] E. Fisher. *Ber. Dtsch. Chem. Ges.*, **27**, 673 (1894).
[17] $13 for deprotection of 100 mmol of dithiane [2005 Aldrich U.S. prices].
[18] S. Hanessian, J. Ma, W. Wang. *J. Am. Chem. Soc.*, **123**, 10200 (2001).
[19] E. Vedejs, P.L. Fuchs. *J. Org. Chem.*, **36**, 366 (1971).
[20] I. Degani, R. Fochi, V. Regondi. *Synthesis*, 51 (1981).
[21] E. Fujita, Y. Nagao, K. Kaneko. *Chem. Pharm. Bull.*, **26**, 3743 (1978).
[22] $90 for deprotection of 100 mmol of dithiane [2005 Aldrich U.S. prices]
[23] A.B. Smith, W. Zhu, S. Shirakami, C. Sfoggatakis, V.A. Doughty, C.S. Bennett, Y. Sakamoto. *Org. Lett.*, **5**, 761 (2003).
[24] A. Armstrong, P.A. Barsanti, L.H. Jones, G. Ahmed. *J. Org. Chem.*, **65**, 7020 (2000).
[25] A.B. Smith, A.T. Lupo, M. Ohba, K. Chen. *J. Am. Chem. Soc.*, **111**, 6648 (1989).

[26] V. Janout, S.L. Regen. *J. Org. Chem.*, **47**, 2212 (1982).
[27] E.J. Corey, B.W. Erickson. *J. Org. Chem.*, **36**, 3553 (1971).
[28] H. Kotosuki, T. Kosumi, M. Inoue, Y. Ushio, M. Ochi. *Tetrahedron Lett.*, **32**, 4159 (1991).
[29] M.H. Habibi, S. Tangestaninejad, M. Montazerozohori, I. Mohamadpoor-Baltork. *Molecules*, **8**, 663 (2003).
[30] $36 for deprotection of 100 mmol of dithioacetal using $AgNO_3$ and $61 using Ag_2O [2005 Aldrich U.S. prices].
[31] C.A. Reece, J.O. Rodin, R.G. Brownlee, W.G. Duncan, R.M. Silverstein. *Tetrahedron*, **24**, 4249 (1968).
[32] D. Gravel, C. Vaziri, S. Rahal. *J. Chem. Soc., Chem. Commun.*, 1323 (1972).
[33] A.J. Sutherland, J.K. Sutherland, P.J. Crowley. *J. Chem. Soc., Perkin Trans. 1*, 349 (1996).
[34] D. Penn, Z. Saidi, D.P.N. Satchell, R.S. Satchell. *J. Chem. Res. (S)*, 200 (1987).
[35] K. Nishide, K. Yokota, D. Nakamura, T. Sumiya, M. Node, M. Ueda, K. Fuji. *Tetrahedron Lett.*, **34**, 3425 (1993).
[36] Y. Nagao, K. Kaneko, M. Ochiai, E. Fujita. *J. Chem. Soc., Chem. Commun.*, 202 (1976).
[37] E. Fujita, Y. Nagao, K. Kaneko. *Chem. Pharm. Bull.*, **24**, 1115 (1976).
[38] Y. Nagao, K. Seno, E. Fujita. *Tetrahedron Lett.*, **20**, 3167 (1979).
[39] T. Harayama, H. Cho, Y. Inubushi. *Tetrahedron Lett.*, **18**, 3167 (1977).
[40] T.-S. Ho, H.-C. Ho, C.M. Wong. *J. Chem. Soc., Chem. Commun.*, 791 (1972).
[41] H.-J. Cristeau, B. Chabaud, R. Labaudinière, H. Christol. *Synth. Commun.*, **11**, 423 (1981).
[42] W.-T. Jiaang, H.-C. Lin, K.-H. Tang, L.-B. Chang, Y.-M. Tsai. *J. Org. Chem.*, **64**, 618 (1999).
[43] T. Mukaiyama, K. Narasaka, M. Furusato. *J. Am. Chem. Soc.*, **94**, 8642 (1972).
[44] K. Suenaga, K. Araki, T. Sengoku, D. Uemura. *Org. Lett.*, **3**, 527 (2001).
[45] K. Araki, K. Suenaga, T. Sengoku, D. Uemura. *Tetrahedron*, **58**, 1983 (2002).
[46] A. Vakalopoulos, H.M.R. Hoffmann. *Org. Lett.*, **3**, 2185 (2001).
[47] K. Saigo, Y. Hashimoto, N. Kihara, H. Umehara, M. Hasegawa. *Chem. Lett.*, 831 (1990).
[48] A. Kamal, E. Laxman, P.S.M.M. Reddy. *Synlett*, 1476 (2000).
[49] S.J. Daum, R.L. Clarke. *Tetrahedron Lett.*, **8**, 165 (1967).
[50] P.R. Heaton, J.M. Midgley, W.B. Whalley. *J. Chem. Soc., Chem. Commun.*, 750 (1971).
[51] F. Weygand, H.J. Bestmann, H. Ziemann. *Chem. Ber.*, **91**, 1040 (1958).
[52] H. Zinner, H. Brandhoff, H. Schmandke, H. Kristen, R. Haun. *Chem. Ber.*, **92**, 3151 (1959).
[53] G.S. Bates, J. O'Doherty. *J. Org. Chem.*, **46**, 1745 (1981).
[54] M.T.M. El-Wassimy, K.A. Jørgensen, S.O. Lawesson. *J. Chem. Soc., Perkin Trans. 1*, 2201 (1983).
[55] G.A. Olah, S.C. Narang, G.F. Salem. *Synthesis*, 657 (1980).
[56] $9 for NBS and $118 for $AgNO_3$ needed to deprotect 100 mmol of dithiane [2005 Aldrich U.S. prices].
[57] D.R. Williams, P.A. Jass, H.-L.A. Tse, R.D. Gaston. *J. Am. Chem. Soc.*, **112**, 4552 (1990).
[58] P.V. Ramachandran, M.T. Rudd, T.E. Burghardt, M.V.R. Reddy. *J. Org. Chem.*, **68**, 9310 (2003).
[59] G.A. Russel, L.A. Ochrymowicz. *J. Org. Chem.*, **34**, 3618 (1969).
[60] S.P. Chavan, P.B. Soni, R.R. Kale, K. Pasupathy. *Synth. Commun.*, **33**, 879 (2003).
[61] G. Stork, K. Zhao. *Tetrahedron Lett.*, **30**, 287 (1989).
[62] $178 for deprotection of 100 mmol of dithiane [2005 Aldrich U.S. prices].
[63] X.-X. Shi, Q.-Q. Wu. *Synth. Commun.*, **30**, 4081 (2000).
[64] V.A. Keller, J.R. Martinelli, S.R. Strieter, S.D. Burke. *Org. Lett.*, **4**, 467 (2002).
[65] K.C. Nicolaou, Y. Li, K. Sugita, H. Monenschein, P. Guntupalli, H.J. Mitchell, K.C. Fylaktakidou, D. Vourloumis, P. Giannakakou, A. O'Brate. *J. Am. Chem. Soc.*, **125**, 15443 (2003).
[66] F.F. Fleming, L. Funk, R. Altundas, Y. Tu. *J. Org. Chem.*, **66**, 6502 (2001).
[67] D.B. Dess, J.C. Martin. *J. Org. Chem.*, **48**, 4155 (1983).
[68] N.F. Langille, L.A. Dakin, J.S. Panek. *Org. Lett.*, **5**, 575 (2003).
[69] E.J. Corey, M.-C. Kang, M.C. Desai, A.K. Ghosh, I.N. Houpis. *J. Am. Chem. Soc.*, **110**, 649 (1988).
[70] X.-X. Shi, S.P. Khanapure, J. Rokach. *Tetrahedron Lett.*, **37**, 4331 (1996).
[71] K.C. Nicolaou, C.J.N. Mathison, T. Montagnon. *Angew. Chem., Int. Ed.*, **42**, 4077 (2003).
[72] K.C. Nicolaou, C.J.N. Mathison, T. Montagnon. *J. Am. Chem. Soc.*, **126**, 5192 (2004).
[73] Y. Wu, X. Shen, J.-H. Huang, C.-J. Tang, H.-H. Liu, Q. Hu. *Tetrahedron Lett.*, **43**, 6443 (2002).
[74] N.S. Krishnaveni, K. Surendra, Y.V.D. Ageswar, K.R. Rao. *Synthesis*, 2295 (2003).
[75] R.A. Hajipour, A.E. Ruoho. *Sulfur Lett.*, **26**, 181 (2003).
[76] J. Cossy. *Synthesis*, 1113 (1987).
[77] A.B. Smith, B.D. Dorsey, M. Visnick, T. Maeda, M.S. Malamas. *J. Am. Chem. Soc.*, **108**, 3110 (1986).
[78] P. Ceccherelli, M. Curini, M.C. Marcotullio, F. Epifano, O. Rosati. *Synlett*, 767 (1996).
[79] A.R. Hajipour, S.A. Pourmousavi, A.E. Ruoho. *J. Sulfur Chem.*, **25**, 401 (2004).
[80] H. Ikehira, S. Tanimoto, T. Oida, M. Okano. *Synthesis (Stuttgart)*, 1087 (1982).
[81] H.-J. Liu, V. Wiszniewski. *Tetrahedron Lett.*, **29**, 5471 (1988).
[82] J. Liu, C.-H. Wong. *Tetrahedron Lett.*, **43**, 4037 (2002).
[83] L. Matthew, S. Sankararaman. *J. Org. Chem.*, **58**, 7576 (1993).
[84] K. Tanemura, H. Doha, M. Imamura, T. Suzuki, T. Horaguchi. *Chem. Lett.*, 965 (1994).
[85] K. Tanemura, H. Doha, M. Imamura, T. Suzuki, T. Horaguchi. *J. Chem. Soc., Perkin Trans. 1*, 453 (1996).
[86] H. Firouzabadi, N. Iranpoor, H. Hazarkhani. *Phosphorus*, *Sulfur*, *Silicon*, **177**, 2571 (2002).

[87] R.A. Hajipour, S.E. Mallakpour, I. Mohammadpoor-Baltork, H. Adibi. *Molecules*, **7**, 674 (2002).
[88] H. Firouzabadi, H. Hazarkhani, B. Karimi, U. Niroumand, S. Ghassamipour. *Proc. Electr. Conf. Synth. Org. Chem. (ECSOC-4*, www.mdpi.org*)*, A0044 (2000).
[89] S.A. Haroutounian. *Synthesis*, 39 (1995).
[90] W.F.J. Huurdeman, H. Wynberg, D.W. Emerson. *Tetrahedron Lett.*, **12**, 3445 (1971).
[91] D.W. Emerson, H. Wynberg. *Tetraherdon Lett.*, **12**, 3449 (1971).
[92] M. Curini, M.C. Marcotullio, E. Pisani, O. Rosati, U. Costantino. *Synlett*, 769 (1997).
[93] M. Prato, U. Quintily, G. Scorrano, A. Sturaro. *Synthesis*, 679 (1982).
[94] H. Firouzabadi, N. Iranpoor, H. Hassani, S. Sobhani. *Synth. Commun.*, **34**, 1967 (2004).
[95] A.R. Hajipour, A.E. Ruoho. *Sulfur Lett.*, **25**, 151 (2002).
[96] D. Ghiringhelli. *Synthesis*, 580 (1982).
[97] A.K. Shukla, M. Verma, K.N. Singh. *Indian J. Chem.*, *Sect. B*, **43**, 1748 (2004).
[98] G.A. Olah, S.C. Narang, A. Garcia-Luna, G.F. Salem. *Synthesis*, 146 (1981).
[99] D. Crich, J. Picione. *Synlett*, 1257 (2003).
[100] T. Ichige, A. Miyake, N. Kanoh, M. Nakata. *Synlett*, 1686 (2004).
[101] M. Ohshima, M. Mukarami, T. Mukaiyama. *Chem. Lett.*, 1593 (1996).
[102] T. Ravindranathan, S.P. Chavan, R.B. Tejwani, J.P. Varghese. *J. Chem. Soc.*, *Chem. Commun.*, 1750 (1991).
[103] T. Ravindranathan, S.P. Chavan, M.M. Awachat. *Tetrahedron Lett.*, **35**, 8835 (1994).
[104] G. Solladié, V. Berl. *Bull. Soc. Chim. Fr.*, **130**, 568 (1993).
[105] C.S. Rao, M. Chandrasekharma, H. Ila, H. Junjappa. *Tetrahedron Lett.*, **33**, 8163 (1992).
[106] J.B. Chattopadhyaya, A.V.R. Rao. *Tetrahedron Lett.*, **14**, 3735 (1973).
[107] G.A. Olah, A.K. Mahrotra, S.C. Narang. *Synthesis*, 151 (1982).
[108] G.A. Olah, S.C. Narang, A.K. Mahrotra. *Synthesis*, 965 (1982).
[109] H. Firouzabadi, N. Iranpoor, H. Hazarkhani, B. Karimi. *J. Org. Chem.*, **67**, 2572 (2002).
[110] B. Karimi, H. Hazarkhani. *Synthesis*, 2547 (2003).
[111] N. Iranpoor, H. Firouzabadi, H.R. Shaterian. *Tetrahedron Lett.*, **44**, 4769 (2003).
[112] H. Firouzabadi, B. Karimi. *Phosphorus*, *Sulfur*, *Silicon*, **175**, 207 (2001).
[113] M. Fetizon, M. Jurion. *J. Chem. Soc.*, *Chem. Commun.*, 382 (1972).
[114] H.-L.W. Chang. *Tetrahedron Lett.*, **13**, 1989 (1972).
[115] $8 for hydrolysis of 100 mmol of dithiane [2005 Aldrich U.S. prices].
[116] A.G. Myers, C.R. Condroski. *J. Am. Chem. Soc.*, **115**, 7926 (1993).
[117] T. Oishi, H. Takechi, K. Kamemoto, Y. Ban. *Tetrahedron Lett.*, **15**, 11 (1974).
[118] I. Stahl. *Synthesis*, 135 (1981).
[119] K. Fuji, K. Ichikawa, E. Fujita. *Tetrahedron Lett.*, **19**, 3561 (1978).
[120] A.T. Khan, E. Mondal, P.R. Sahu. *Synlett*, 377 (2003).
[121] M. Balogh, A. Cornélis, P. Laszlo. *Tetrahedron Lett.*, **25**, 3313 (1984).
[122] A. Cornélis, P. Laszlo. *Synthesis*, 909 (1985).
[123] P. Laszlo, A. Cornélis. *Aldrichimica Acta*, **21**, 97 (1988).
[124] J.G. Lee, J.P. Hwang. *Chem. Lett.*, 507 (1995).
[125] M. Hirano, K. Ukawa, S. Yakabe, T. Morimoto. *Synth. Commun.*, **27**, 1527 (1997).
[126] P. Wipf, M.J. Soth. *Org. Lett.*, **4**, 1787 (2002).
[127] H.M. Meshram, G.S. Reddy, G. Sumitra, J.S. Yadav. *Synth. Commun.*, **29**, 1113 (1999).
[128] B.P. Bandgar, S.P. Kasture. *Green Chem.*, **2**, 156 (2000).
[129] N. Komatsu, A. Taniguchi, M. Uda, H. Suzuki. *Chem. Commun.*, 1847 (1996).
[130] N. Komatsu, A. Taniguchi, S. Wada, H. Suzuki. *Adv. Synth. Catal.*, **343**, 473 (2001).
[131] $4 for deprotection of 100 mmol of dithiane [2005 Aldrich U.S. prices].
[132] G. Mehta, R. Uma. *Tetrahedron Lett.*, **37**, 1897 (1996).
[133] H. Firouzabadi, N. Iranpoor, M.A. Zolfigo. *Bull. Chem. Soc. Jpn.*, **71**, 2169 (1998).
[134] M. Kamata, S. Otogawa, E. Hesegawa. *Tetrahedron Lett.*, **32**, 7421 (1991).
[135] M. Schmittel, M. Levis. *Synlett*, 315 (1996).
[136] G.A. Epling, Q. Wang. *Tetrahedron Lett.*, **33**, 5909 (1992).
[137] M. Kamata, Y. Kato, E. Hasegawa. *Tetrahedron Lett.*, **32**, 4349 (1991).
[138] E. Fasani, M. Freccero, M. Mella, A. Albini. *Tetrahedron*, **53**, 2219 (1997).
[139] M. Kamata, Y. Murakami, Y. Tamagawa, M. Kato, E. Hasegawa. *Tetrahedron*, **50**, 12821 (1994).
[140] M. Kamata, M. Sato, E. Hasegawa. *Tetrahedron Lett.*, **33**, 5085 (1992).
[141] M. Platen, E. Steckhan. *Chem. Ber.*, **117**, 1679 (1984).
[142] M.H. Habibi, S. Tangestaninejad, I. Mohammadpoor-Baltork, M. Montazeroezohori. *Phosphorus*, *Sulfur*, *Silicon*, **179**, 597 (2004).
[143] Q.N. Porter, J.H.P. Utley. *J. Chem. Soc.*, *Chem. Commun.*, 255 (1978).
[144] A. Lebous, J. Simonet, J. Gelas, A. Dehbi. *Synthesis*, 320 (1987).
[145] M. Kimura, H. Kawai, Y. Sawaki. *Electrochemica Acta*, **42**, 497 (1997).
[146] L.A. Barnhurst, Y. Wan, A.G. Kutateladze. *Org. Lett.*, **2**, 799 (2000).
[147] I.T. Horváth. *Chem. Rev.*, **95**, 1 (1995).