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Reagents for the preparation and cleavage of 1,3-dithiolanes

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Abstract. Data on procedures for protection of the carbonyl group by its conversion into the 1,3-dithiolane moiety and on cleavage of the latter under the action of different reagents are surveyed. The preparation of 1,3-dithiolanes from carbonyl compounds followed by deprotection can be used in syntheses of various organic compounds. The bibliography includes 54 references.

I. Introduction

Syntheses of organic compounds, including natural products, often generate a need to use protective groups. Thus if it is necessary that the reaction proceed selectively at one of several reaction centres of a polyfunctional compound, all other centres should be temporarily blocked. A good protective group must be removed selectively and quantitatively under the action of readily accessible reagents which do not react with functional groups to be regenerated. Various protective groups have already been developed and these investigations are being continued. Analysis of the published data demonstrated that the introduction and removal of a protective group is often a complex multistep process.

In the synthesis of particular carbonyl-containing products, it is sometimes necessary to prevent the reaction of the carbonyl group with reducing agents of acidic or alkaline nature, catalytic reducing agents and hydrides, some oxidising agents, strong and moderate nucleophiles, organometallic compounds, *etc*. In the reactions of polyfunctional organic compounds, it is very convenient to protect the carbonyl group by converting it into the 1,3-dithiolane moiety because sulfur-containing functional groups are inert with respect to many reagents. Various reagents, which are stable under conventional reaction conditions, have been developed for the synthesis of 1,3-dithiolanes.[1,2] Generally, 1,3-dithiolanes are prepared by condensation of carbonyl compounds with 1,2-dithiols catalysed by protic or Lewis acids.[3,4]

In the present review, the data on the reagents for the synthesis and cleavage of 1,3-dithiolanes developed in the last decade are surveyed. The mechanisms of formation and cleavage of 1,3-dithiolanes are beyond the scope of this review.

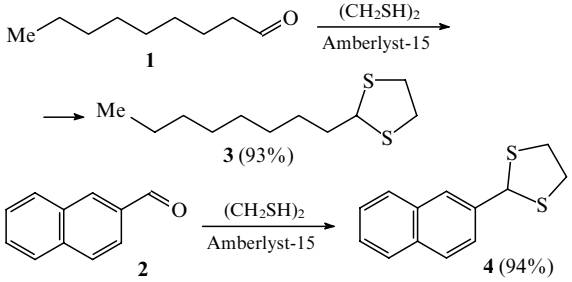
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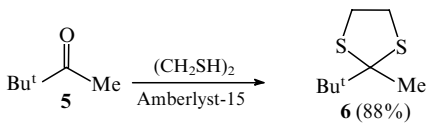
II. Reagents for the synthesis of 1,3-dithiolanes based on 1,2-ethanedithiol

1. Catalysis by Amberlyst-15

Amberlyst-15 is an efficient catalyst of the synthesis of 1,3-dithiolanes from some aldehydes,[5] for example, from **1** or **2**, under the action of 1,2-ethanedithiol $(CH_2SH)_2$.



The reactions proceed at room temperature to form derivatives **3** or **4** in high yields. If the reaction mixtures contain ketones along with aldehydes, the former do not react with $(CH_2SH)_2$ under these conditions. However, this procedure can also be used for protection of ketones (even sterically hindered ketones), if the reaction is carried out with boiling. Under these conditions, 1,3-dithiane **6** is formed from pinacolone **5**.

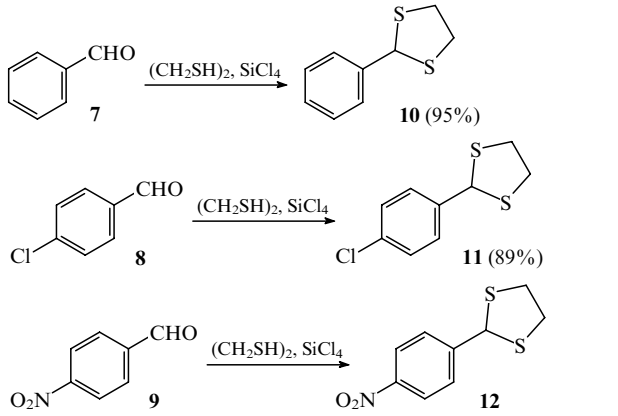


In this case, the workup procedure is substantially simpler than those used in the synthesis of 1,3-dithiolanes catalysed by other reagents, in particular, by thionyl chloride and impregnated silica gel,[6] or in the synthesis of 1,3-dithianes from 2,2-dimethyl-1,3,2-dithiasilane in the presence of boron trifluoride etherate as a catalyst.[7] Ketones of the type **5** react with $(CH_2SH)_2$ in the presence of Amberlyst-15 to form dithiolane **6**. An important characteristic feature of this system is the fact that the reactions with ketones proceed at a slow rate because of which this procedure can be used for separation of aldehydes and ketones.

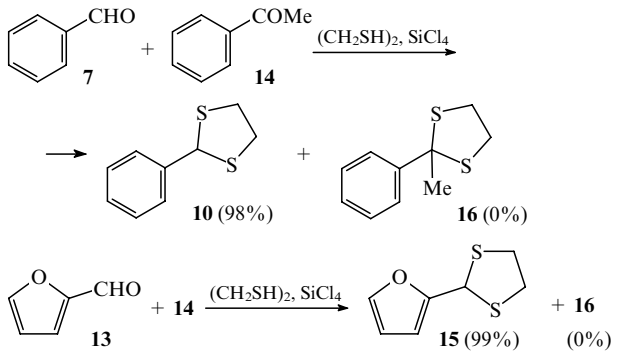
2. Catalysis by tetrachlorosilane

It is known[8] that tetrachlorosilane (Lewis acid) is a soft and efficient catalyst of the synthesis of 1,3-dithiolanes. This compound catalyses the formation of dithiolanes from aromatic aldehydes containing both electron-donating and electron-with-

drawing substituents. Thus the reactions of aldehydes **7**–**9** with $(CH_2SH)_2$ in the presence of $SiCl_4$ afforded dithiolanes **10**–**12**, respectively.



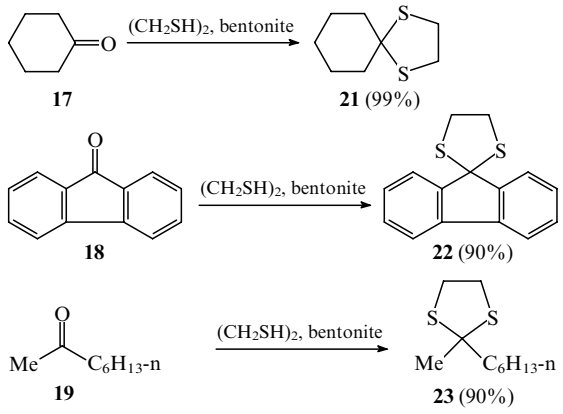
The $SiCl_4$-catalysed reactions of aromatic aldehydes (for example, **7** and **13**) with $(CH_2SH)_2$ in the presence of acetophenone (**14**) proceed absolutely chemoselectively to form the 1,3-dithiolanes **10** and **15**, respectively. Methyl-substituted dithiolane **16** is not formed in this reaction. Good selectivity is observed also in the case of aliphatic aldehydes.

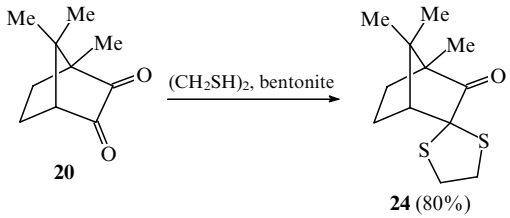


Ku and Oh [8] believed that the bulkiness and branching of the carbonyl compound are the major factors governing the chemoselectivity of formation of 1,3-dithiolanes.

3. Catalysis by bentonite

Miranda *et al.*[9] developed an excellent procedure for the synthesis of 1,3-dithiolanes. This procedure involves condensation of ketones with $(CH_2SH)_2$ in the presence of bentonite, which has also been used for the oxirane ring-opening [10] and conversion of oximes into ketones.[11, 12] Dithiolanes **21**–**24** were prepared in high yields from ketones **17**–**20**, respectively. The reactions were performed in anhydrous toluene in the presence of bentonite as a catalyst.





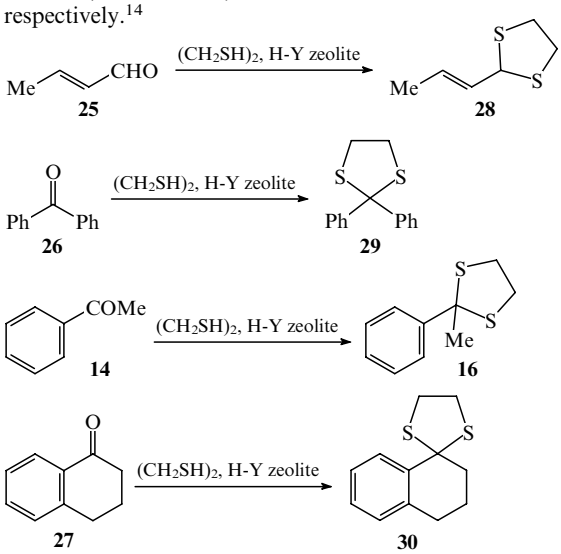
This procedure is very simple and bentonite is inexpensive. It should be noted that the amount of the catalyst required in this case is seven times smaller than the amount of montmorillonite KSF in analogous reactions and the crude reaction mixture gives only one spot on a thin-layer chromatogram.

4. Catalysis by anhydrous $LaCl_3$

Anhydrous $LaCl_3$ proved to be a convenient and efficient catalyst [13] of conversions of the carbonyl compounds **7**, **9**, **13** and **17** under the action of $(CH_2SH)_2$ into the dithiolanes **10**, **12**, **15** and **21**, respectively. The reactions proceeded smoothly giving the products in very high yields. Owing to mild conditions and the simplicity, this procedure is suitable for multistep syntheses of complex organic compounds. Hydrated rare-earth metal chlorides were ineffective for the preparation of 1,3-dithiolanes from some carbonyl compounds. Apparently, anhydrous salts adsorb water much more actively than the hydrates, which facilitates substitution in the intermediate hemithioacetal with elimination of a water molecule and coordination of the lanthanum ion at the oxygen atom of the carbonyl group resulting in an increase in the electrophilicity of the carbon atom.

5. Catalysis by H-Y zeolite

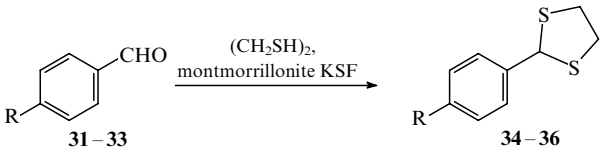
The reactions of crotonaldehyde (**25**) and aromatic and sterically hindered ketones **26**, **14** and **27** with $(CH_2SH)_2$ in the presence of H-Y zeolite (Si : Al = 2.43) afforded 1,3-dithiolanes **28**, **29**, **16** and **30**, respectively.[14]



The use of H-ZSM-5 zeolite (Si : Al = 45) and H-mordenite has met with only limited success. The advantages of H-Y zeolite are the simplicity of separation, high yields of the products and the possibility of regeneration of the catalyst.

6. Catalysis by montmorillonite KSF

Montmorillonite KSF was used [15] for conversions of some aldehydes, for example, of **7**, **9** and **31**–**33**, in the absence of solvents at room temperature to form 1,3-dithiolanes **10**, **12** and **34**–**36**, respectively.



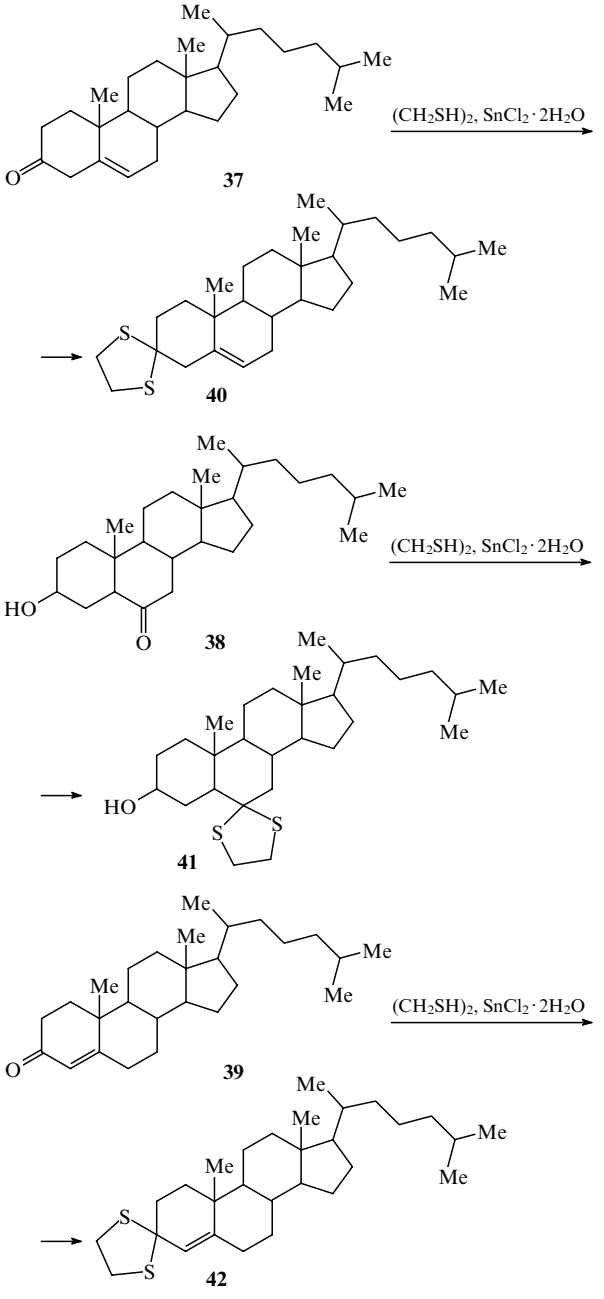
31 – 33 **34 – 36**

R = C(O)Me (**31**, **34**), OMe (**32**, **35**), NMe_2 (**33**, **36**).

In these reactions, clay KSF acts as a Brønsted solid acid. The procedure for the synthesis is simple. Montmorillonite KSF is an inexpensive and selective catalyst, which does not exhibit corrosive action. The reactions of aromatic and aliphatic aldehydes with $(CH_2SH)_2$ in the presence of clay KSF are chemoselective, *viz*., only aromatic aldehydes are converted into dithiolanes. The reactions with aromatic ketones (for example, **14** and **18**) proceed more rapidly than those with aliphatic aldehydes.

7. Catalysis by $SnCl_2 \cdot 2H_2O$

A simple and efficient procedure for conversions of steroid ketones **37 – 39** into 1,3-dithiolanes **40 – 42**, respectively, involves their treatment with 1,2-ethanedithiol in the presence of soft Lewis acid, *viz*., $SnCl_2 \cdot 2H_2O$, in THF.[16]



The reactions can be performed in a neutral medium. This procedure is suitable for the synthesis of various aliphatic, aromatic and sterically hindered steroid ketones. Under the reaction conditions, the double bond at the 4,5 position of α,β-unsaturated ketone **39** remains intact. This procedure for the preparation of dithiolanes may also be of use in more general cases. Anhydrous $SnCl_2$ can be used as a catalyst as well.

8. Catalysis by bis(trimethylsilyl) sulfate adsorbed on silica gel

Bis(trimethylsilyl) sulfate adsorbed on silica gel is a soft and efficient catalyst of conversions of some carbonyl compounds (**7**, **9**, **14**, **17** and **18**) into dithiolanes (**10**, **12**, **16**, **21** and **22**, respectively) under the action of $(CH_2SH)_2$ in anhydrous dichloromethane at room temperature.[17] The reaction conditions and the synthetic procedure are simple and convenient.

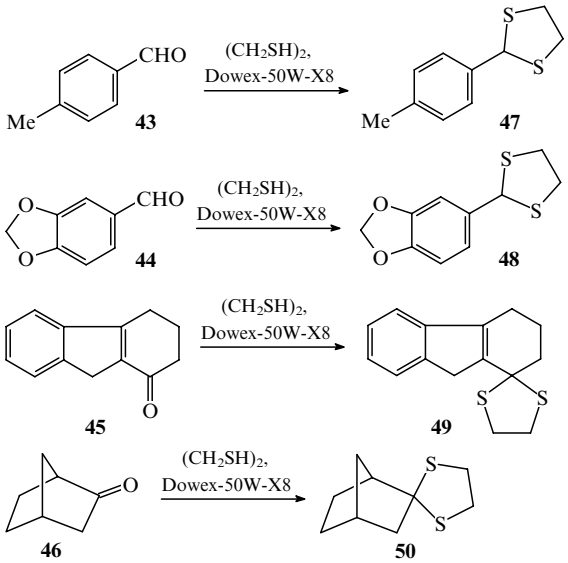
The high activity of this catalyst is supported by the fact that low-reactivity ketones, for example, benzophenone (**26**), acetophenone (**14**) and 9-fluorenone (**18**), are smoothly converted into the dithiolanes **29**, **16** and **22**, respectively. These compounds were also synthesised with the use of another catalyst. It was demonstrated that the reaction in the absence of silicon dioxide requires drastic conditions, *viz*., boiling in benzene with azeotropic distillation of water. Undoubtedly, this reagent will find wider use in organic synthesis.

9. Catalysis by MgI_2 in diethyl ether

Magnesium iodide in diethyl ether is an efficient catalyst of conversions of a series of carbonyl compounds, for example, of **7**, **18**, **38** and **39**, into the dithiolanes **10**, **22**, **41** and **42**, respectively, under the action of $(CH_2SH)_2$.[18] The reactions proceed at room temperature giving dithiolanes in very high yields. This procedure is chemoselective. Thus dithiolanes are not formed from aromatic ketones, for example, from benzophenone (**26**) and acetophenone (**14**), even upon prolonged storage of the reaction mixtures in the presence of this reagent at room temperature.

10. Catalysis by Dowex-50W-X8

Bhattacharyya and coworkers [19] proposed that cation exchange resin Dowex-50W-X8 be used for conversions of ketones **43 – 46** under mild conditions to form dithiolanes **47 – 50**, respectively, in high yields.

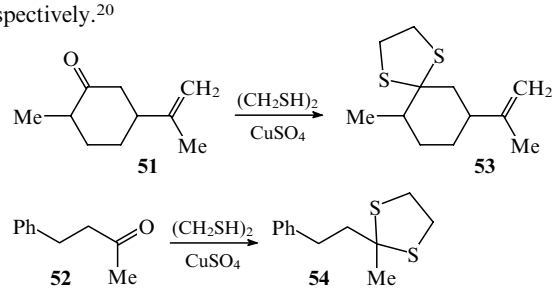


Apparently, resin Dowex-50W-X8 treated with HCl acts as an acidic catalyst and increases the electrophilicity of the carbon atom of the carbonyl group. In the presence of this catalyst, the sterically hindered aromatic ketones **14** and **26** are smoothly converted into the dithiolanes **16** and **29**, respectively. This

method can also be used in the case of compounds containing acid-sensitive groups. The reactions are completed in a short time.

11. Catalysis by $CuSO_4$

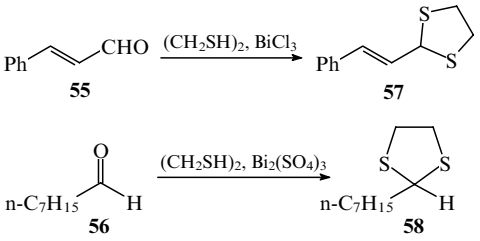
The reactions of some carbonyl compounds, for example, of α-tetralone (**27**), 5α-cholestan-3-one (**37**), dihydrocarvone (**51**), 4-phenylbutan-2-one (**52**), acetophenone (**14**) and benzophenone (**26**), with 1,2-ethanedithiol in dry THF in the presence of anhydrous copper sulfate, which is a gentle and inexpensive catalyst, afforded the thiolanes **30**, **40**, **53**, **54**, **16** and **29**, respectively.[20]



The reactions catalysed by $CuSO_4 \cdot 5H_2O$ afford dithiolanes in very low yields. The advantage of this method is the fact that it can be applied in the case of various aliphatic, aromatic and steroid ketones.

12. Catalysis by bismuth halides and sulfate

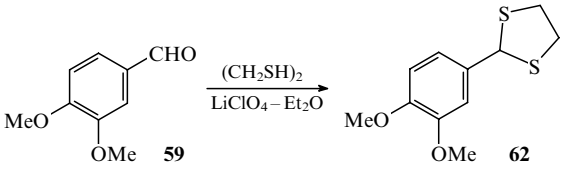
Bismuth halides BiX_3 (X = Cl, Br or I) and bismuth sulfate $Bi_2(SO_4)_3$ in acetone are powerful catalysts[21] of conversions of carbonyl compounds, for example, of **8**, **14**, **55** and **56**, under the action of $(CH_2SH)_2$ at room temperature giving rise to the dithiolanes **11**, **16**, **57** and **58**, respectively.

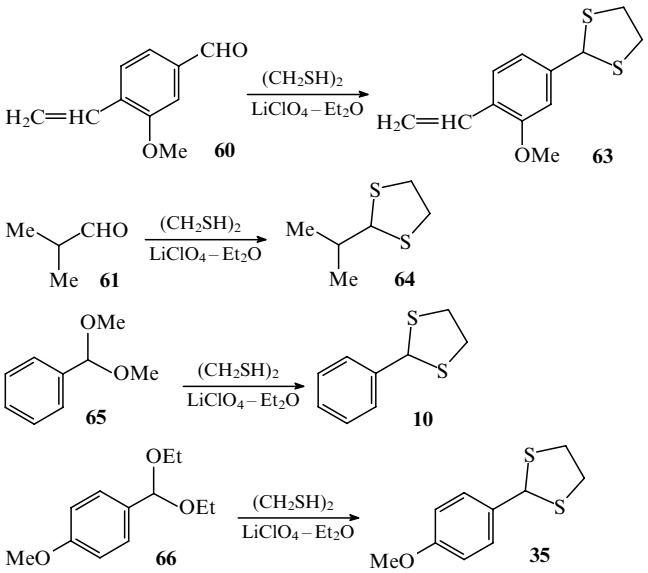


These bismuth salts offer the following advantages over various Lewis and Brønsted acids: (1) minimum amounts of these salts are required; (2) the salts exhibit catalytic activities under mild conditions; (3) the synthetic procedure is simple; (4) the products are prepared in high yields; (5) the reactions are chemoselective; (6) the catalyst is inexpensive and nontoxic; (7) it is possible to recognise the type of the carbonyl functional group. The high activity of this catalyst is retained in the presence of a small amount of water. An acid-sensitive substrate, such as furfurol (**13**), is readily converted into dithiolane without self-condensation and ring opening.

13. Catalysis by lithium perchlorate in diethyl ether

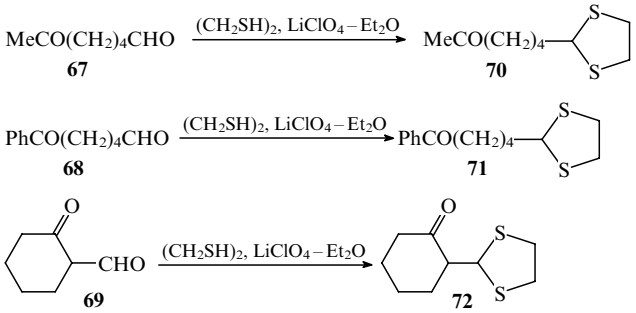
The reactions of aldehydes **59**–**61** with $(CH_2SH)_2$ yielding dithiolanes **62**–**64**, respectively, are catalysed by lithium perchlorate in diethyl ether.[22] Analogously, acetals **65** and **66** are converted into the dithiolanes **10** and **35**, respectively.





These reactions proceed at room temperature to form 1,3-dithiolanes in high yields.† It appeared that ketones and their acetals react much more slowly than aldehydes and their acetals.

Yet another advantage of the above-mentioned system is its ability to perform chemoselective thioacetalisation of oxoaldehydes **31** and **67**–**69** in the synthesis of dithiolanes **34** and **70**–**72**, respectively.



In this case, the aldehyde carbonyl group is selectively protected, while the keto group remains intact. The selectivity is absent in the reactions performed with the use of such Lewis acids as BF_3 or $AlCl_3$.

14. Catalysis by ammonium cerium nitrate

Some aldehydes, for example, **7**, **25**, **59** and **61**, were converted into dithiolanes **10**, **28**, **62** and **64**, respectively, under the action of $(CH_2SH)_2$ catalysed by $(NH_4)_2Ce(NO_3)_6$.[24] These dithiolanes were prepared in high yields at room temperature. In the presence of ketones, only aldehydes enter into the reactions. The reaction conditions and the synthetic procedure are very simple and convenient. This procedure can be extended to ketones. For example, cyclohexanone (**17**) gave the dithiolane **21** upon refluxing in chloroform for 10 h. It should be noted that aromatic ketones, γ-lactones and acyclic ketones do not react under the above-mentioned conditions, and hence, this catalyst is convenient for chemoselective thioacetalisation. Ammonium cerium nitrate is comparable in efficiency with the above-described solution of lithium perchlorate in diethyl ether.[22]

† It should be noted that the reaction of dimethyl acetal **65** with 1,2-ethanedithiol in the presence of $TeCl_4$ in dichloromethane affords the dithiolane **10** in 99% yield.[23]

15. Catalysis by zirconium(IV) chloride adsorbed on silica gel

The dithiolanes **10**, **16**, **21**, **22**, **29** and **57** are formed in high yields by the reactions of the carbonyl compounds **7**, **14**, **17**, **18**, **26** and **55**, respectively, with 1,2-ethanedithiol in the presence of $ZrCl_4$ adsorbed on silica gel.[25] This method has the following advantages: (1) the procedure is simple and convenient; (2) the reactions proceed smoothly; (3) the reactions are rapid and the system can be used in the case of low-reactivity ketones, such as **26** and **14**. Thioacetalisation of α,β-unsaturated aldehydes, for example, of cinnamaldehyde (**55**), can be performed with excellent yield, but attempts to prepare dithiolanes from α,β-unsaturated ketones in good yields were unsuccessful.

16. Catalysis by natural kaolin

Recently, it has been demonstrated[26] that kaolin efficiently catalyses conversions of the carbonyl group into the dithiolane moiety, for example, in the reactions of the compounds **7**, **13**, **26** and **55** with $(CH_2SH)_2$ giving rise to the 1,3-dithiolanes **10**, **15**, **29** and **57**, respectively. It was also noted that the reaction of a mixture of benzaldehyde (**7**) and acetophenone (**14**) with 1,2-ethanedithiol in the presence of 10% of kaolin afforded only the dithiolane **10**, while acetophenone remained unconsumed.

Owing to high chemoselectivity, the reactions catalysed by kaolin may be advantageous in the selective protection of aldehydes in the presence of other carbonyl compounds.

17. Catalysis by LiBr

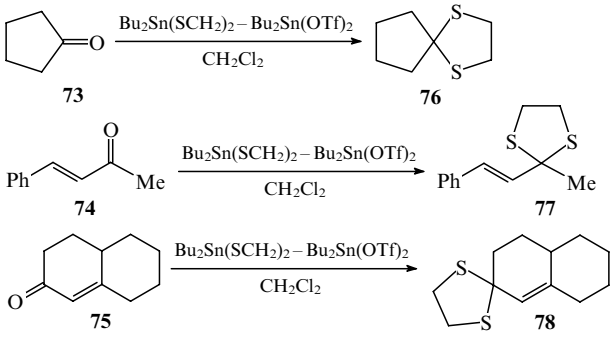
Aldehydes, for example, **7** and **55**, are converted into the dithiolanes **10** and **57**, respectively, in high yields under the action of $(CH_2SH)_2$ without a solvent in the presence of catalytic amounts of lithium bromide.[27] Under similar conditions, the aromatic and aliphatic ketones **14** and **61** do not react even over several hours. This procedure is unsuitable for the preparation of dithiolanes in such solvents as THF and dichloromethane. In the latter solvents, aldehydes remain unconsumed. Due to the neutrality of the reaction medium, the procedure under consideration is very useful in the case of substrates highly sensitive to acids. The excellent selectivity and simplicity allow one to use this method successfully for selective conversions of aromatic and α,β-unsaturated aldehydes containing other carbonyl groups into 1,3-dithiolanes under very mild conditions.

18. Catalysis by copper(II) trifluoromethanesulfonate adsorbed on silica gel

A large number of aldehydes and ketones, for example, **7**, **8**, **14**, **26**, **32** and **43**, were converted into 1,3-dithiolanes by reactions with $(CH_2SH)_2$ in the absence of a solvent and in the presence of catalytic amounts of copper(II) trifluoromethanesulfonate $Cu(OTf)_2$ adsorbed on silica gel.[28] Analogous conversions are catalysed by $Cu(OTf)_2$ in dichloromethane. Aldehydes react more rapidly than ketones. The reactions with aldehydes and ketones proceed chemoselectively, *viz*., primarily aldehydes are involved in the reactions. In most cases, the reactions proceed smoothly. Such a sterically hindered and low-reactivity ketone as benzophenone (**26**) is inert with respect to the system under consideration without a solvent at room temperature, but the reaction proceeds in toluene on heating to 80 °C. Conversions of some aldehydes and ketones into 1,3-dithiolanes without a solvent were also observed in the presence of catalytic amounts of copper chloride adsorbed on silica gel, but the reactions proceeded slowly with low yields. The procedure for thioacetalisation of carbonyl compounds without a solvent may find wide use in organic synthesis in the future.

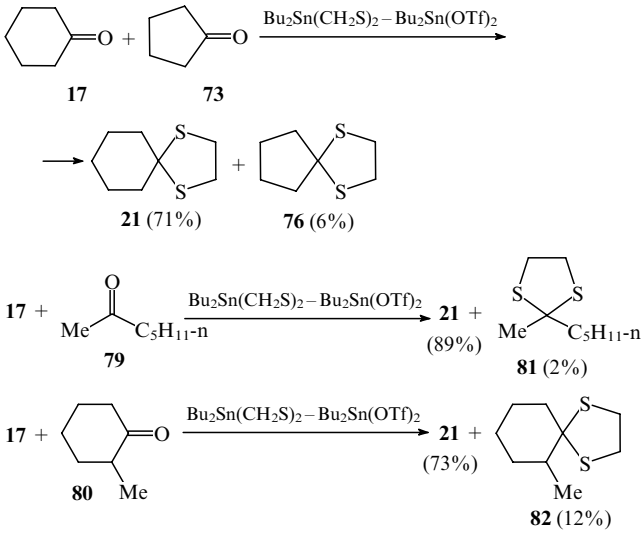
19. Catalysis by dibutyl(ethylenedithio)stannane in the presence of $Bu_2Sn(OTf)_2$

Sato *et al*.[29] reported the conversions of the ketones **17** and **73**–**75** into the dithiolanes **21** and **76**–**78**, respectively, upon treatment with dibutyl(ethylenedithio)stannane $Bu_2Sn(SCH_2)_2$ in the presence of $Bu_2Sn(OTf)_2$ in dichloromethane.



This procedure for the synthesis of dithiolanes is to some extent comparable with that proposed by Evans *et al*.[30] The latter procedure involves thiosilanes and has been used only for carbonyl compounds. An important advantage of the procedure under consideration is the simplicity of the synthesis of thiostannane from various organotin compounds. In addition, thiostannane is air- and moisture-stable and can be stored in air. The procedure with the use of thiostannane and organotin triflate may be useful in preparing dithiolanes not only from ketones but also from their ketals.

Organotin triflates can be used for separation of ketones (or their ketals). If the reaction mixtures contain cyclopentanone (**73**), heptan-2-one (**79**) or 2-methylcyclohexanone (**80**) along with cyclohexanone (**17**), the reactions proceed primarily with cyclohexanone. The yield of the dithiolane **21** is very high compared to the yields of the compounds **76**, **81** and **82**.



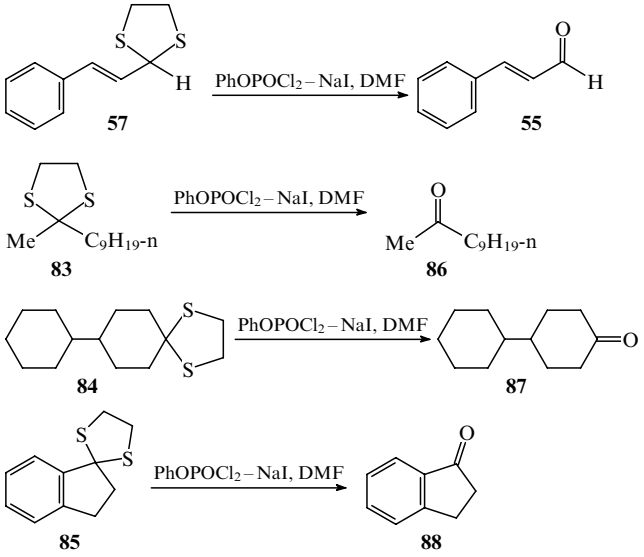
This high selectivity cannot be achieved by conventional methods, for example, with the use of $(CH_2SH)_2$ and $BF_3 \cdot OEt_2$. This possibility of separation is of great importance in the chemistry of steroids.

III. Reagents for the cleavage of 1,3-dithiolanes

A large number of procedures were developed for conversions of dithiolanes into the initial carbonyl compounds.[1,31] Some of them require drastic conditions or the use of toxic compounds, for example, mercury salts. In some cases, dithiolanes are decomposed under mild conditions in several steps. In this connection, a demand arose for the development of new procedures for deprotection of dithiolanes and construction of new reagents which do not affect other functional groups.

1. The phenyl phosphorodichloridate – sodium iodide system in DMF

Liu and Wiszniewski [32] used phenyl phosphorodichloridate in combination with sodium iodide in DMF for conversions of dithiolanes, for example, of **57** and **83 – 85**, into the corresponding carbonyl compounds **55** and **86 – 88**.

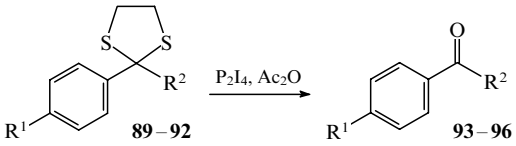


Ketones are formed in high yields. The reactions can be performed at room temperature. In the reactions with the use of acetonitrile instead of DMF, dithiolanes are recovered. The reactions carried out with boiling afford mixtures of products.

This procedure [32] is applicable to aliphatic, aromatic and allylic dithiolanes. In all cases, the reactions proceed smoothly yielding the only desired product, which was confirmed by TLC data.

2. Phosphorus tetraiodide in acetic anhydride

Shigemesa *et al.*[33] developed a procedure for decomposition of 1,3-dithiolanes, for example, of **89 – 92**, under the action of P_2I_4 in acetic anhydride, chloroform or CCl_4 giving rise to ketones **93 – 96**, respectively, in high yields.

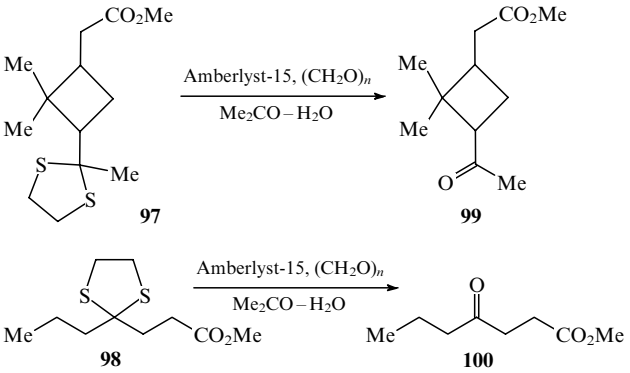


Dithiolane	Ketone	R^1	R^2
89	**93**	MeO	Ph
90	**94**	Me	Ph
91	**95**	Cl	Ph
92	**96**	MeO	Bu^n

The reactions of these 1,3-dithiolanes with P_2I_4 in dichloromethane result primarily in reductive desulfurisation and partial deprotection. In all cases, the amount of the reduced product is substantially higher than the amount of the ketone formed.

3. Amberlyst-15 – paraformaldehyde in wet acetone

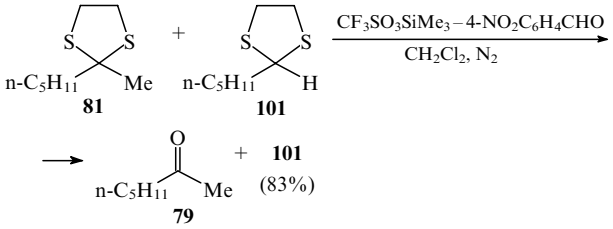
The dithiolanes **10**, **22**, **35**, **97** and **98** were converted into the ketones **7**, **18**, **33**, **99** and **100**, respectively, under the action of Amberlyst-15 and paraformaldehyde.[34]



The dithiolanes were dissolved in aqueous acetone. Then paraformaldehyde and Amberlyst-15 were added and the reaction mixture was heated at 80 °C for 15 – 20 h. In these reactions, acid-sensitive ethers and esters remain intact.

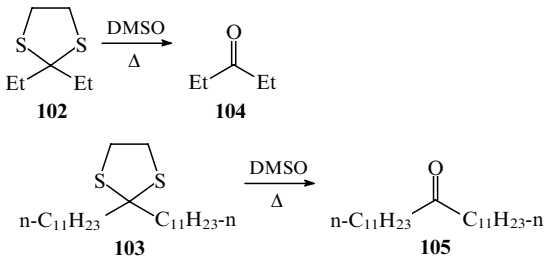
4. Trimethylsilyl trifluromethanesulfonate – 4-nitrobenzaldehyde in CH_2Cl_2

A new procedure for the cleavage of dithiolanes [35] involves the addition of $CF_3SO_3SiMe_3$ to a mixture of dithiolane and 4-nitrobenzaldehyde in dichloromethane at room temperature. This procedure was used for conversions of the dithiolanes **16**, **30**, **35** and **57** into the ketones and aldehydes **14**, **27**, **32** and **55**, respectively. The reactions can be performed with the use of $CF_3SO_3SiBu^tMe_2$ instead of $CF_3SO_3SiMe_3$. Of the four aldehydes tested in the study,[35] 4-nitrobenzaldehyde was chosen because this reagent made it possible to accelerate the reaction and to improve the efficiency of migration of the sulfur. This method can also be used for selective deprotection of dithiolanes prepared from ketones in the presence of dithiolanes obtained from aldehydes. Thus 1,3-dithiolane **81** was hydrolysed to give ketone **79** in the presence of compound **101**. This is the first example of catalytic transthioacetalisation with simultaneous migration of oxygen and alkanethiol proceeding irreversibly in an anhydrous medium.



5. Dimethyl sulfoxide, 140 – 160 °C

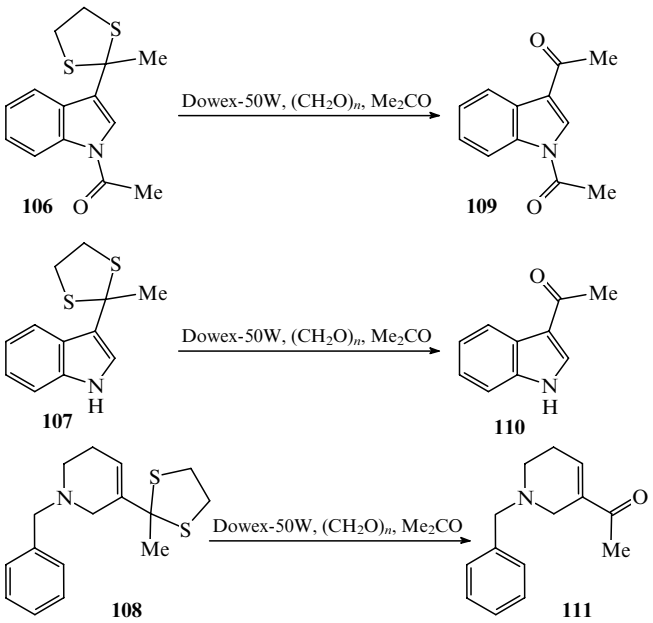
In the absence of other reagents, DMSO catalyses [36] cleavage of some dithiolanes, for example, of **30**, **57**, **102** and **103**, at high temperature giving rise to the corresponding carbonyl compounds **27**, **55**, **104** and **105** in high yields.



It is known that DMSO can decompose dithiolanes in the presence of iodine [37] or *tert*-butyl chloride.[38]

6. Dowex-50W – paraformaldehyde in acetone

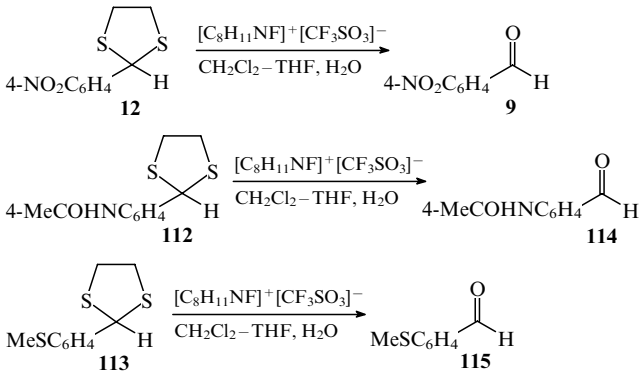
Giri and Sankar [39] used a mixture of the acidic catalyst Dowex-50W and paraformaldehyde in acetone for the cleavage of dithiolanes of nitrogen-containing heterocyclic compounds **106 – 108** to yield ketones **109 – 111**, respectively.



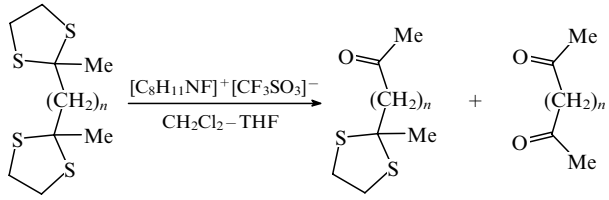
Although the cleavage of such dithiolanes is generally performed with the use of mercury salts, the latter sometimes form insoluble complexes. This difficulty was overcome [40] by protection of the nitrogen atom before hydrolysis of dithiolanes with triethyloxonium tetrafluoroborate. Taking into account the simplicity of the procedure and the good yield of the product, we believe that this procedure [39] is superior in efficiency to all other available procedures for dethioacetalisation of nitrogen-containing heterocycles.

7. *N*-Fluoro-2,4,6-trimethylpyridinium triflate in a 1 : 1 CH_2Cl_2 – THF mixture and H_2O

Dithiolanes **12**, **112** and **113** were decomposed to aldehydes **9**, **114** and **115**, respectively, with the use of *N*-fluoro-2,4,6-trimethylpyridinium triflate $[C_8H_{11}NF]^+[CF_3SO_3]^-$ in a 1 : 1 CH_2Cl_2 – THF mixture and 5 equiv. of H_2O.[41] High yields of compounds **9**, **114** and **115** were achieved by performing the reactions under an inert atmosphere (Ar or N_2). The reactions performed in the presence of oxygen or nitrobenzene give rise to a number of unidentified by-products. The reactions in pure dichloromethane, ether, hexane or acetonitrile as the solvent afford aldehydes in low yields. In DMF, dithiolanes do not decompose.

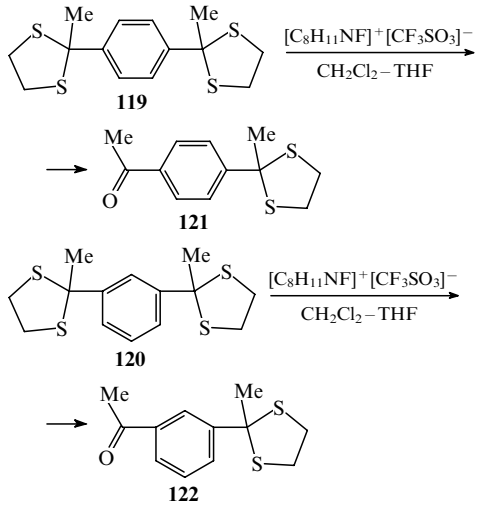


In the reactions of the title reagent with dithiolanes **116a – c**, the latter decompose to form mono- and diketones. The ratio between the monoketones **117a – c** and the diketones **118a – c** prepared from the thioacetals **116a – c** decreases as the length of the carbon chain separating two dithiolane groups increases.



Compound	*n*	Yield (%)	
116 – 118		**117**	**118**
a	0	74	5
b	1	57	15
c	2	52	21

The cleavage of dithiolanes of aromatic derivatives **119** and **120** with *N*-fluoro-2,4,6-trimethylpyridinium triflate in the presence of water also afforded predominantly monoketones. The higher selectivity of the formation of *para*-substituted **121** ketone compared to the *meta*-isomer **122** is indicative of the important role of electronic effects and agrees with the cationic nature of intermediates.



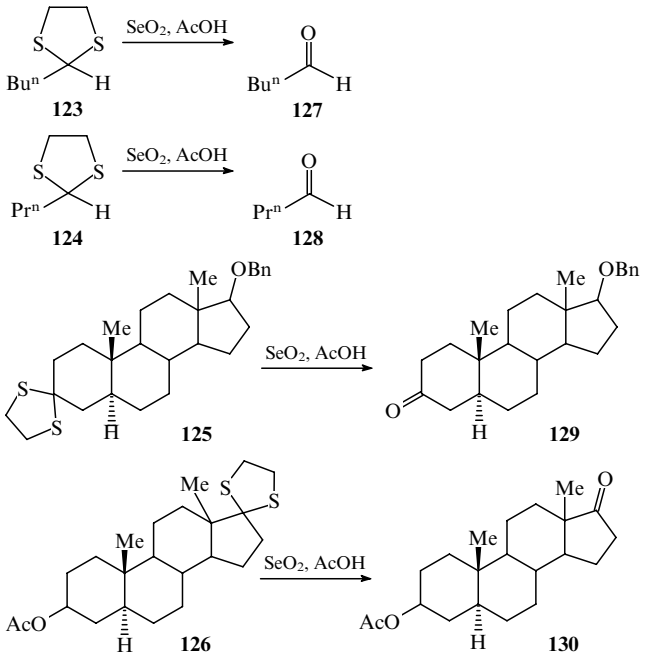
Finally, it should be noted that hydrolysis of dithiolanes with a mixture of *N*-fluoro-2,4,6-trimethylpyridinium triflate and water was not accompanied by migration of the electrophilic fluorine atom. This fact is in contradiction with the mechanism of fluorination of organic substrates with *N*-fluoro-2,4,6-trimethylpyridinium triflate or other *N*-fluoropyridinium cations proposed previously.[42]

8. Copper(II) chloride – silica gel in CH_2Cl_2

The dithiolanes **16**, **40**, **53** and **54** were decomposed under the action of $CuCl_2 \cdot 2H_2O$ adsorbed on silica gel under mild conditions to form the corresponding carbonyl compounds **14**, **37**, **51** and **52**.[22] The yields of the products obtained with the use of dichloromethane are substantially higher than those obtained with the use of THF. The reagent under consideration can be successfully used for the cleavage of dithiolanes of various aliphatic, aromatic and sterically hindered steroid compounds. The reaction conditions are very simple and convenient.

9. Selenium dioxide in acetic acid

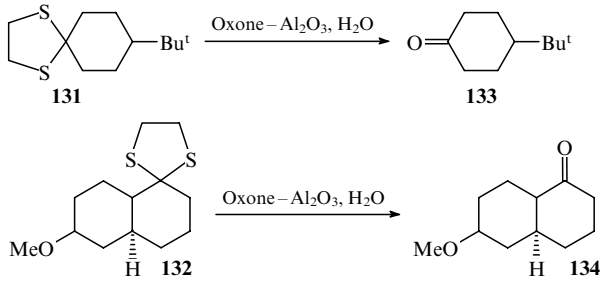
A solution of SeO_2 in acetic acid proved to be an efficient reagent for the deprotection of 1,3-dithiolanes **123 – 126** to yield the aldehydes and ketones **127 – 130**, respectively.[43]



The reactions proceed readily at room temperature giving rise to carbonyl compounds in very high yields. Widespread functional groups, such as ethers and esters, do not react with selenium dioxide. This procedure is very useful in the case of dithiolane derivatives of C(7)- and C(13)-steroid ketones whose cleavage generally requires drastic conditions. The presence of acetic acid is of importance because the reactions in aprotic solvents, for example, in THF, dichloromethane or toluene, proceed with very low yields. Hydrolysis in aqueous acetonitrile or acetone proceeds slowly (20–30 h) and affords cleavage products in low yields. Heating of the mixture accelerates the reaction, but the yield becomes even lower because a number of undesirable products are formed. The best results of the cleavage of dithiolanes and the highest yields of ketones regenerated are achieved with the 1,3-dithiolane to SeO_2 ratio of 1 : 5. On the whole, the procedure proposed for hydrolysis of 1,3-dithiolanes is rapid and convenient, characterised by high yields and is applicable to various compounds.

10. Oxone – wet Al_2O_3

Dithiolanes **30**, **131** and **132** were converted into ketones **27**, **133** and **134**, respectively, in high yields under mild conditions with the use of Oxone (potassium hydrogen persulfate, $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$) and wet alumina.[44]



The carbonyl compounds were obtained in high yields by refluxing 1,3-dithiolanes in chloroform in the presence of Oxone on Al_2O_3, the functional groups, such as ethers and esters, and double bonds remaining intact. The procedure is simple and convenient, which is an additional advantage of this reagent for dethioacetalisation. This procedure is comparable in efficiency with the above-described procedures for hydrolysis of dithiolanes or even superior to these methods.

11. Iron(III) nitrate – montmorillonite K10 – hexane

Hirano *et al.*[45] developed an efficient and simple procedure for oxidative cleavage of 1,3-dithiolanes with the use of iron(III) nitrate and montmorillonite K10 in hexane at 50 °C. This procedure was used for conversions of the 1,3-dithiolanes **12**, **57** and **89–92** into the carbonyl compounds **9**, **55** and **93–96**, respectively, in very high yields. In the absence of the clay, the reactions proceed slowly and afford ketones in lower yields. The advantages of this system over other supported reagents, such as iron(III) or copper(II) nitrates on montmorillonite K10 in the absence of hexane [46] or copper(II) nitrate on silica gel,[47] are the high reaction rate and the fact that there is no need for pretreatment of the reagent. Therefore, this procedure is an improved modification of the above-described methods. Hexane is a better solvent from economic and environmental standpoints compared to chlorinated hydrocarbons (CH_2Cl_2, $CHCl_3$ and CCl_4), which are often used in standard heterogeneous systems. On the whole, this procedure for the cleavage of 1,3-dithiolanes and regeneration of carbonyl compounds is simple and convenient and satisfies economic requirements.

12. Zirconium sulfophenylphosphonate

Mixed zirconium(IV) methylphosphonate sulfophenylphosphonate, $Zr(O_3PCH_3)_{1.2}(O_3PC_6H_4SO_3H)_{0.8}$, proved to be a very useful catalyst [48] for mild hydrolysis of 1,3-dithiolanes to form the corresponding carbonyl compounds. Dithiolanes are heated with a catalyst in the presence of glyoxylic acid monohydrate as an exchange reagent. This procedure was used for the preparation of the carbonyl compounds **7**, **14**, **37** and **133** from the dithiolanes **10**, **16**, **40** and **131**, respectively, in very high yields. Zirconium sulfophenylphosphonate is also a very efficient catalyst of the cleavage of cyclic dithioacetal, which is resistant to a number of other reagents.[49] It is noteworthy that zirconium sulfophenylphosphonate is comparable in activity with the above-described reagents or even superior to them. The essential advantages of this procedure are the absence of the solvent, mild conditions and the simplicity.

13. Miscellaneous procedures

The major reagents and catalysts used for the deprotection of 1,3-dithiolanes were considered in the previous sections. In addition, some dithiolanes were decomposed with the use of systems based on silver nitrate,[50] bis(trifluoroacetoxy)iodobenzene,[51] nitrogen oxides,[52] visible light [53] and tantalum chloride.[54] Since these procedures were rarely used, we do not consider them in detail in the present review.

IV. Conclusion

The problem of protection of the carbonyl groups in aldehydes and ketones, in particular, the protection giving rise to 1,3-dithiolanes, is of great importance in organic synthesis due to which an array of procedures for the introduction of this group were developed. The most frequently used methods were considered above. It should be noted that a large number of reagents for subsequent cleavage of 1,3-dithiolanes and regeneration of carbonyl-containing compounds have been proposed in recent years. Apparently, new reagents for introduction and removal of the dithiolane group will be developed in the future. In our opinion, the dithiolane moiety should be more extensively used as a protective group. We hope the present review will help to attract the attention of chemists engaged in organic chemistry to this problem.

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