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We showed for the first time, the fundamental role of CH$_3$CN associated to TMSCl/NaI combination to deprotect S,S-ethylene- and S,S-propylene-ketals into ketones. Indeed, if the TMSCl/NaI association leads to the reduction of dithioketals in CH$_2$Cl$_2$, we have demonstrated that this association can be used to deprotect a large variety of various dithioketals into ketones in CH$_3$CN. Otherwise, under mild experimental conditions, O,O-acetals as well as O,S-oxathianes were cleanly deprotected with high yields. It is also possible to easily regenerate the carbonyl function of various hydrazones and imines using this novel protocol. We believe that this metal-free process is a good alternative to other known methodologies used to deprotect dithioketals into ketones.

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Mild Deprotection of Dithioacetals by TMSCl / NaI Association in CH₃CN

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Abstract. A mild process using a combination of TMSCl and NaI in acetonitrile is used to regenerate carbonyl compounds from a variety of dithiane and dithiolane derivatives. This easy to handle and inexpensive protocol is also efficient to deprotect oxygenated and mixed acetals as 1,3-dioxanes, 1,3-dioxolanes and 1,3-oxathianes quantitatively. As a possible extension of this method, it was also showed that nitrogenated-substrates as hydrazones, N-tosylhydrazones and ketimines reacted well under these conditions to give the expected ketones in high yields. The methodology proposed herein is a good alternative to the existing methods since it does not use metals, oxidants, reducing agents, acidic or basic media, and keto-products were obtained in high to excellent yields.

Keywords: dithioacetal; deprotection; trimethylsilylchloride; sodium iodide; ketone

Introduction

Dithianes are commonly used in organic chemistry to mask the electrophilic nature of carbonyl groups[5] in elaborated molecules but also serve as acyl anions in syntheses according to the Umpolung concept.[6] The main advantages of dithianes are their easy access from a carbonyl compound by using propane-1,3-dithiol and a Lewis acid and their stabilities in alkaline and acid conditions notably permitting their purification on silica columns. In counterparts to this stability, many procedures have been developed for their deprotection but generally require drastic conditions.[3] Most of the time, toxic metal salts as Hg(II),[11] Ag(I),[5] Zn(II),[6] Ga(III),[7] Cu(II),[8] Ti(V)[9] and others are used in excess in harsh conditions with some success. The use of hypervalent-iodine reagents for the removal of dithianes has been also reported as an efficient process using periodic acid,[10] diacetoxiyiodobenzene, [11] bis(trifluoroacetoxy)iodobenzene (BTI),[12] Duss-Martin periodinane[13] and N-halosuccinimides.[14] However, a large variety of the aforementioned methods require the use of toxic metals, the need of oxidizing species in large amounts sometimes accompanied with co-oxidants mainly in harsh reaction conditions. In this context, we believe that an alternative milder process is still needed using for example inexpensive and soft reagents to achieve this transformation at room temperature in the presence of various functional groups.

Recently, we reported the interesting reducing properties of the TMSCl/NaI association in CH₂Cl₂ towards various functional groups as unsymmetrical α-diketones,[15] α-ketoesters,[16] and hydrazones[16] derivatives. Under similar reaction conditions, we next demonstrated that a variety of dithialacetals were cleanly desulfurized at room temperature[17] in CH₂Cl₂ using this metal-free process in a Mozingo-type reaction.[18]

By replacing CH₂Cl₂ by CH₃CN as the reaction solvent, we surprisingly observed that dithianes derivatives were not reduced into methylene substrates but were totally and cleanly deprotected into ketones. It seemed interesting to study in detail this method for the deprotection of thioacetals which does not use metal salts, nor oxidants, nor toxic or expensive reagents (Figure 1). Herein, we wish to report the mild deprotection conditions of a range of dithianes, dithiolanes and oxygenated derivatives using the TMSCl/NaI association in CH₃CN.

Figure 1. Properties of the TMSCl / NaI combination towards dithioacetals in CH₂Cl₂ and CH₃CN.

Results and Discussion

First, we have selected 2-methyl-2-(naphthalen-2-yl)-1,3-dithiane 1a which was totally reduced into 2- ethynaphtalene by TMSCl/NaI combination in CH₃CN.

Table 1. Optimization of reaction conditions a)

| Entry | Conditions | Yield % |
|-------|------------|---------|
| 1     | TMSCl/NaI (10 eq), EtOH, rt | 0%     |
| 2     | TMSCl/NaI (10 eq), TFE, rt | <10%   |
| 3     | TMSCl/NaI (10 eq), tBuOH, rt | 0%     |
| 4     | TMSCl/NaI (10 eq), Et₂O, rt | 24%    |
products, with a poor yield of 10%.

Comparison. After only 3 h of reaction, we observed the presence of TMSI (10 eq) at rt (entry 19) for the deprotection reaction at 60 °C in the presence of 20 eq of TMSCl/NaI combination. Longer reaction times or higher temperatures will probably be needed to complete this transformation in these solvents. In CH$_2$CN, in which the nitrogen atom is linked to the silicon atom of TMSCl, we were pleased to isolate 2a with a promising yield of 52% (entry 7) with no trace of the reduced 2-ethynaphthalene obtained in CH$_2$Cl$_2$.[17] Under the same reaction conditions but without NaI, 1a was found unchanged thus showing the essential role of NaI (entry 8). Addition of water, NaOH$_{aq}$ or HCl$_{aq}$ had a deleterious effect on the reaction since a large part of 1a was recovered after 24 h of reaction (entries 9-12). The amount of TMSCl/NaI and the temperature of the reaction were next examined (entries 13-17) and the best result was obtained by achieving the deprotection reaction at 60 °C in the presence of 20 eq of TMSCl/NaI leading to ketone 2a in an excellent yield of 92% (entry 17). To examine the influence of solvents (deprotection vs reduction), 1a was reacted with TMSCl/NaI in CH$_2$CN/CH$_2$Cl$_2$ (1/1) for 24 h at 60 °C (entry 18). In this mixture of solvents, we have isolated only ketone 2a (85%) with no trace of the 2-ethynaphthalene (reduced compound) showing the predominant role of CH$_2$CN when linked to TMSCl[20] (see plausible mechanism in Scheme 4). Last, the reaction was also run in CH$_2$CN in the presence of TMSI (10 eq) at rt (entry 19) for comparison. After only 3 h of reaction, we observed by TLC the total disappearance of 1a but 2a was isolated, beside a large number of unidentified by-products, with a poor yield of 10%[21] thus showing the superiority of the TMSCl/NaI association compared to TMSI for carrying out these deprotection reactions in CH$_2$CN.

Next, we were interested to evaluate this mild protocol with 1,3-dioxolane 3, 1,3-dioxane 4, and with 1,3-oxathiane 5.

**Scheme 1. Deprotection of cyclic ketals 3,4 and oxathiane 5 by TMSCl/NaI in MeCN**

As it could be seen in Scheme 1, by using TMSCl/NaI in CH$_2$CN under conditions A (see in entry 7 of Table 1), we observed a clean and complete deprotection of ketals 3 and 4 as well as 1,3-oxathiane 5 into ketones (93 to 97%). For comparison, Jung reported that TMSI in CHCl$_3$ deprotected ethylene ketals into ketones but with very low yields (20%) and that TMSI did not react with thioacetals after 24 h of mixing at 75 °C.[22]

Encouraged by these results and by the simplicity of this process, the deprotection of a variety of thioacetals 1 was carried out with the TMSCl/NaI association in CH$_2$CN for 24 h. Table 2 summarizes the results of this study achieved using 10 eq of TMSCl/NaI at rt (conditions A) or 20 eq of TMSCl/NaI at 60 °C (conditions B) for less cooperative substrates.

**Table 2. Deprotection of 1a-u by TMSCl/NaI in MeCN**

| Substrate | TMSCl/NaI(eq) | T °C | Product | Yield (%) |
|-----------|---------------|------|---------|-----------|
| 1a        | 20            | 60   | 2a      | 92        |
| 1b        | 10            | rt   | 2c      | 89        |
| 1c        | 10            | rt   | 2d      | 94        |
| 1d        | 20            | 60   | 2d      | 83        |
| 1e        | 10            | rt   | 2e      | 86        |

As it could be seen in Scheme 1, by using TMSCl/NaI in CH$_2$CN under conditions A (see in entry 7 of Table 1), we observed a clean and complete deprotection of ketals 3 and 4 as well as 1,3-oxathiane 5 into ketones (93 to 97%). For comparison, Jung reported that TMSI in CHCl$_3$ deprotected ethylene ketals into ketones but with very low yields (20%) and that TMSI did not react with thioacetals after 24 h of mixing at 75 °C.[22]
Dithioacetals were prepared from the corresponding ketones with dithiols in the presence of BF$_3$-Et$_2$O. All purified ketones had H and $^3$C NMR data identical to those of authentic samples. 1-Benzyl-4-methoxybenzene (40%) resulting from the dithioketal redation was also isolated. NaBr replaced NaI.

As observed 1,3-dithianes and 1,2-dithiolanes of acetophenones 1a-g were deprotected into their parent ketones with good yields ranging from 54 to 94%. It is of note that, 1,3-dithianes 1b,c, and 1f,g were more cooperative substrates than our model substrate 1a since the deprotection reaction required half quantity of TMSCl/NaI and was achieved at rt under conditions A. Examination of these results also shows that 1,3-dithianes seem easier to deprotect using TMSCl/NaI in CH$_2$CN than their 1,2-dithiolane counterparts (compare 1c and 1d) and that electron-donating groups on the aromatic nucleus allowed more efficient deprotection reactions (compare 1c and 1g). As expected, 1,3-dithianes prepared from aliphatic aryl (cyclic or not) ketones 1h-l reacted well with the TMSCl/NaI combination and furnished ketones 2h-l in good to excellent isolated yields (64 to 91%). The case of dialkyldithianes derivatives was next examined with compounds 1m-p and showed that these compounds were also cooperative substrates as they were rapidly and cleanly deprotected to give the desired ketones 2m-p with satisfactory yields (76 to 95%). When α-bromo dithiane 1q was reacted with TMSCl/NaI, acetophenone 2q was obtained indicating that, besides the expected deprotection reaction, a α-debromination reaction occurred too in agreement with a previous report of Olah.[24] Then, the case of diaryldithianes was examined. Under A classical conditions (TMSCl/NaI 10 equiv, rt, 24 h), we observed that 1,3-dithiane 1r having no Hα reacted with TMSCl/NaI to give a mixture composed in almost equal parts of the expected ketone 2r (43%) accompanied by the reduction[17] product 1-benzyl-4-methoxybenzene (40%). To avoid the formation of the reduction by-product, we successfully replaced NaI by NaBr, increased the quantity of TMSCl/NaBr and heated the solution at 60 °C for a prolonged time (TLC monitoring). By using these conditions, diarylketones 2r and 2s were then obtained with acceptable yields and without any traces of the reduced diarylmethane by-products. Next, 1,3-dithianes of aldehydes were also studied with compounds 1t and 1u. It is of note that these 1,3-dithianes reacted rapidly under A mild conditions to give the corresponding aldehydes in variable yields. For the deprotection of dithioketals of aldehydes, it is very important to examine carefully the course of the deprotection reaction by TLC monitoring because prolonged reaction times resulted in a severe decrease in yields. Indeed, it has been reported that, at rt, aldehydes reacted rapidly with TMSI to give iodosilyl ethers and diiodoethers.[25] This suggests that, as soon as aldehydes are formed after thioacetal deprotection, they add nucleophilic iodides which may arise from TMSI very slowly generated in the media according to an exchange Finkelstein reaction.[26] To show the interest of this process with respect to other previously reported methods using for examples HgO associated with BF$_3$-Et$_2$O,[27] 2,6-dicarboxy pyridinium chlorochromate (DCPCC)[28] or SbCl$_5$[29] we have deprotected dithiolanes 1v and 1w by TMSCl/NaI in CH$_2$CN (Scheme 2). The comparison of the yields obtained using the TMSCl/NaI mild
association in CH$_3$CN vs toxic oxidizing agent as HgO (86 % vs 65%), DCPCC (93% vs 70%) or SbCl$_5$ (93% vs 77%) supports well that this novel metal-free process is welcome since the yields in desired ketones are significantly higher and the reagents used for the deprotection are inexpensive, not toxic and very easy to handle.

Scheme 2. Deprotection of dithianes 1v and 1w by TMSCl/NaI in CH$_3$CN.

Next, as dithioacetals, the regeneration of carbonyl compounds from nitrogen-derivatives as hydrazones, N-tosylhydrazones, ketimines and oximes required most of the time harsh reaction conditions including oxidative or reducing process, acidic or alkaline media, expensive reagents or hazardous experimental protocols.$^{[30]}$ In order to find a milder process, we next examined if the TMSCl/NaI combination in CH$_3$CN process could be applied successfully to these robust nitrogen substrates.

Scheme 3. Reaction of 6-10 by TMSCl/NaI in MeCN

In Scheme 3 were presented the results of the regeneration of carbonyl functions of diphenylhydrazone 6, N-tosylhydrazone 7, N-benzylimine 8, ketimine 9 and diphenylmethanone oxime 10, using TMSCl/NaI in CH$_3$CN. We were pleased to observe that the TMSCl/NaI combination in CH$_3$CN was able to transform imines and hydrazones into ketones with good yields (90 to 100%) as well as N-tosylhydrazone 7 which required the use of stronger reaction conditions. On the contrary, imine 8 and ketimine 9 were easily transformed into their ketones with high yields using the TMSCl/NaI association in CH$_3$CN at rt. When diphenylmethanone oxime 10 was reacted with the TMSCl/NaI association (10 eq), we isolated, after 24 h of reaction achieved at rt, 4-methoxy-N-(4-methoxyphenyl)benzamide 11 in a good yield (84%) accompanied by only 4 % of the bis(4-methoxyphenyl)methanone 2r. The scope of this interesting Beckmann rearrangement, using the TMSCl/NaI combination, is currently under investigation in our lab with a range of oxime substrates.$^{[31]}$

Scheme 4. Plausible mechanism
MeCN: + Me₃S

A plausible reaction mechanism is indicated in (Scheme 4). First, CH₃CN activates the TMSCl/NaI association as mentioned previously by Olah[30] to promote intermediate I and II after halide exchange in the presence of NaI. Then, II reacts with a sulfur atom of dithiolane 1c to give a sultinum species of type III. Further assistance from the neighboring dithiane sulfur atom possibly leads to a fragmented sulfonium intermediate IV which added H₂O (from reagents, CH₃CN or during hydrolysis) to promote hemithioketal V which is then activated into a sulfonium intermediate VI (having or not Hα). With no Hα as in 1r or 1s, VI finally rearranges into the desired ketone 2d. For dithiolanes prepared from enolizable ketones as 1c, the same (a) pathway could be followed but it is also reasonable to consider an additional pathway (b) in which an iodide deprotonates intermediate VI to furnish an enol species which tautomerizes into ketone 2d. Since dithioacets having Hα can evolve according to two different pathways, this can explain that these entities are easier to deprotect than diaryldithiolates counterparts. It is of note that a similar mechanism has been previously proposed by Nicolaou for the deprotection of S,S-acetals and ketals using IBX.[31]

**Conclusion**

In this article we showed for the first time, the fundamental role of CH₃CN associated to TMSCl/NaI combination to deprotect S,S-ethylene- and S,S-propylene-ketals into ketones. Indeed, if the mild TMSCl/NaI association leads to the reduction of dithioacetals in CH₂Cl₂, we have demonstrated that this association can be used to deprotect a large variety of various dithioacetals into ketones in CH₃CN. Otherwise, under mild experimental conditions, O,O-acetals as well as O,S-oxathianes were cleanly deprotected with high yields. It is also possible to easily regenerate the carbonyl function of various hydrazones and imines using this novel protocol. We believe that this metal-free process is a good alternative to other known methodologies used to deprotect dithioacetals into ketones.

**Experimental Section**

A general experimental procedure is described as following: a mixture of thioletal (100 mg) and NaI (10 eq) was stirred in MeCN for 5 min. Then, 10 eq of TMSCl were added to the solution which was stirred for 24 h at rt. The reaction was then hydrolyzed for 5 min. with H₂O (5 mL) and extracted with CH₂Cl₂. Organic layers were dried over MgSO₄, and concentrated under reduced pressure to give a residue which was purified by chromatography on silica gel to give the expected carbonyl compound which have identical NMR spectra with starting ketones.

**Acknowledgements**

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To a solution of ketone or aldehyde (1 mmol) in 20 mL of DCM was added the thiol derivative (1,2-ethanediethiol or 1,3-propanediethiol; 5 mmol), followed by 1 mL of BF$_3$-Et$_2$O. The solution was stirred at rt until disappearance of starting material (judged by TLC). Then, H$_2$O (20 mL) and DCM (30 mL) were added to the solution. The organic layer was separated, washed with H$_2$O (2 x 10 mL) and saturated NaCl solution (2 x 10 mL), dried over MgSO$_4$, and concentrated under reduced pressure to give a dithioacetal which was purified by chromatography on silica gel.
Mild Deprotection of Dithioacetals by TMSCl / NaI Association in CH$_3$CN

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Abstract. A mild process using a combination of TMSCl and NaI in acetonitrile is used to regenerate carbonyl compounds from a variety of dithiane and dihiole derivatives. This easy to handle and inexpensive protocol is also efficient to deprotect oxygenated and mixed acetals as 1,3-dioxanes, 1,3-dioxolanes and 1,3-oxathianes quantitatively. As a possible extension of this method, it was also showed that nitrogenated-substrates as hydrazones, N-tosylhydrazones and keties reacted well under these conditions to give the expected ketones in high yields. The methodology proposed herein is a good alternative to the existing methods since it does not use metals, oxidants, reducing agents, acidic or basic media, and keto-products were obtained in high to excellent yields.

Keywords: dithioacetal; deprotection; trimethylsilylchloride; sodium iodide; ketone

Introduction

Dithianes are commonly used in organic chemistry to mask the electrophilic nature of carbonyl groups in elaborated molecules but also serve as acyl anions in syntheses according to the Umpolung concept. The main advantages of dithianes are their easy access from a carbonyl compound by using propane-1,3-dithiol and a Lewis acid and their stabilities in alkaline and acid conditions notably permitting their purification on silica columns. In counterparts to this stability, many procedures have been developed for their depreduction but generally require drastic conditions. Most of the time, toxic metal salts as Hg(II), Ag(I), Zn(II), Ga(III), Cu(II), and others are used in excess in harsh conditions with some success. The use of hypervalent-iodine reagents for the removal of dithianes has been also reported as an efficient process using periodic acid, diacetoxyiodobenzene, bis(trifluoracetoxy)iodo-benzene (BTI), Dess-Martin periodinane and N-halosuccinimides. However, a large variety of the aforementioned methods require the use of toxic metals, the need of oxidizing species in large amounts sometimes accompanied with co-oxidants mainly in harsh reaction conditions. In this context, we believe that an alternative milder process is still needed using for example inexpensive and soft reagents to achieve this transformation at room temperature in the presence of various functional groups.

Recently, we reported the interesting reducing properties of the TMSCl/NaI association in CH$_3$Cl towards various functional groups as unsymmetrical $\alpha$-diketones, $\alpha$-ketoesters, and hydrazones. Under similar reaction conditions, we next demonstrated that a variety of dithioacetals were cleanly desulfurized at room temperature in CH$_3$Cl using this metal-free process in a Mozingo-type reaction.

By replacing CH$_2$Cl$_2$ by CH$_3$CN as the reaction solvent, we surprisingly observed that dithianes derivatives were not reduced into methylene substrates but were totally and cleanly deprotected into ketones. It seemed interesting to study in detail this method for the deprotection of thioacetals which does not use metal salts, nor oxidants, nor toxic or expensive reagents (Figure 1). Herein, we wish to report the mild deprotection conditions of a range of dithianes, dithianes and oxygenated derivatives using the TMSCl/NaI association in CH$_3$CN.

Results and Discussion

First, we have selected 2-methyl-2-(naphthalen-2-yl)-1,3-dithiane 1a which was totally reduced into 2-ethynaphthalene by TMSCl/NaI combination in

| Entry | Conditions | Yield % |
|-------|------------|---------|
| 1     | TMSCl/NaI (10 eq), EtOH, rt | 0%     |
| 2     | TMSCl/NaI (10 eq), TFE, rt | <10%   |
| 3     | TMSCl/NaI (10 eq), tBuOH, rt | 0%     |
| 4     | TMSCl/NaI (10 eq), EtO, rt | 24%    |

Table 1. Optimization of reaction conditions
CH₂Cl₂ as our model substrate to herein examine the dithiane deprotection reaction by the same reagents under a variety of reaction conditions (Table 1). In view of using EtOH as a green solvent,[19] we firstly tried to deprotect 1,3-dithiane 1a in EtOH in the presence of 10 equiv. of TMSCl/NaI combination. However, EtOH and other alcohols of different nucleophilicity as trifluoroethanol (TFE) or tBuOH were found to be ineffective as 1a was mainly found unchanged after 24 h of reaction at rt (entries 1-3). When the deprotection-reactions were done in Et₂O, THF or acetone (entries 4-6), a better trend was noticed since 2b was isolated in low yields accompanied by a large part of unreacted 1a. Longer reaction times or higher temperatures will probably be needed to complete this transformation in these solvents. In CH₂CN, in which the nitrogen atom is linked to the silicon atom of TMSCl, we were pleased to isolate 2a with a promising yield of 52 % (entry 7) with no trace of the reduced 2-ethynaphthalene obtained in CH₂Cl₂. Under same reaction conditions but without NaI, 1a was found unchanged thus showing the essential role of NaI (entry 8). Addition of water, NaOHaq or HClaq had a deleterious effect on the reaction since a large part of 1a was recovered after 24 h of reaction (entries 9-12). The amount of TMSCl/NaI and the temperature of the reaction were next examined (entries 13-17) and the best result was obtained by achieving the deprotection reaction at 60 °C in the presence of 20 eq of TMSCl/NaI leading to ketone 2a in an excellent yield of 92% (entry 17). To examine the influence of solvents (deprotection vs reduction), 1a was reacted with TMSCl/NaI in CH₂CN/CH₂Cl₂ (1/1) for 24 h at 60 °C (entry 18). In this mixture of solvents, we have isolated only ketone 2a (85 %) with no trace of the 2-ethynaphthalene (reduced compound) showing the predominant role of CH₂CN when linked to TMSCl[20] (see plausible mechanism in Scheme 4). Last, the reaction was also run in CH₂CN in the presence of TMSi (10 eq) at rt (entry 19) for comparison. After only 3 h of reaction, we observed by TLC the total disappearance of 1a but 2a was isolated, beside a large number of unidentified by-products, with a poor yield of 10%[21] thus showing the superiority of the TMSCl/NaI association compared to TMSi for carrying out these deprotection reactions in CH₂CN.

Next, we were interested to evaluate this mild protocol with 1,3-dioxolane 3, 1,3-dioxane 4, and with 1,3-oxathiane 5.

### Scheme 1. Deprotection of cyclic ketals 3, 4, and oxathiane 5 by TMSCl/NaI in MeCN

As it could be seen in Scheme 1, by using TMSCl/NaI in CH₂CN under conditions A (see in entry 7 of Table 1), we observed a clean and complete deprotection of ketals 3 and 4 as well as 1,3-oxathiane 5 into ketones (93 to 97%). For comparison, Jung reported that TMSI in CHCl₃ deprotected ethylene ketals into ketones but with very low yields (20%) and that TMSI did not react with thioketals after 24 h of mixing at 75 °C.[22]

Encouraged by these results and by the simplicity of this process, the deprotection of a variety of thiacetals 1 was carried out with the TMSCl/NaI association in CH₂CN for 24 h. Table 2 summarizes the results of this study achieved using 10 eq of TMSCl/NaI at rt (conditions A) or 20 eq of TMSCl/NaI at 60 °C (conditions B) for less cooperative substrates.

### Table 2. Deprotection of 1a-u by TMSCl/NaI in MeCN

| Substrate | TMSCl/NaI(eq) | T (°C) | t (h) | Product | Yield (%) |
|-----------|---------------|--------|-------|---------|-----------|
| 1a        | 20            | 60     | 24    | 2a      | 92        |
| 1b        | 10            | rt     | 24    | 2c      | 89        |
| 1c        | 10            | rt     | 24    | 2d      | 94        |
| 1d        | 20            | 60     | 24    | 2e      | 86        |
| 1e        | 10            | rt     | 24    | 2f      | 76        |
As observed, 1,3-dithianes and 1,2-dithiolanes of acetophenones 1a–g were deprotected into their parent ketones with good yields ranging from 54 to 94%. It is of note that, 1,3-dithianes 1b,c, and 1f,g were more cooperative substrates than our model substrate 1a since the deprotection reaction required half quantity of TMSCl/NaI and was achieved at rt under conditions A. Examination of these results also shows that 1,3-dithianes seem easier to deprotect using TMSCl/NaI in CH3CN than their 1,2-dithiolane counterparts (compare 1c and 1d) and that electron-donating groups on the aromatic nucleus allowed more efficient deprotection reactions (compare 1c and 1g). As expected, 1,3-dithianes prepared from aliphatic aryl (cyclic or not) ketones 1h–l reacted well with the TMSCl/NaI combination and furnished ketones 2h–l in good to excellent isolated yields (64 to 91%). The case of dialkyldithiane derivatives was next examined with compounds 1m–p and showed that these compounds were also cooperative substrates as they were rapidly and cleanly deprotected to give the desired ketones 2m–p with satisfactory yields (76 to 95%). When α-bromo dithiane 1q was reacted with TMSCl/NaI, acetophenone 2q was obtained indicating that, besides the expected deprotection reaction, a α-debromination reaction occurred too in agreement with a previous report of Olah[24]. Then, the case of diaryldithianes was examined. Under A classical conditions (TMSCl/NaI 10 equiv, rt, 24 h), we observed that 1,3-dithiane 1r having no Hα, reacted with TMSCl/NaI to give a mixture composed in almost equal parts of the expected ketone 2r (43%) accompanied by the reduction product 1-benzyl-4-methoxybenzene (40%). To avoid the formation of the reduction by-product, we successfully replaced NaI by NaBr, increased the quantity of TMSCl/NaBr and heated the solution at 60 °C for a prolonged time (TLC monitoring). By using these conditions, diarylketones 2r and 2s were then obtained with acceptable yields and without any traces of the reduced diarylmethylene by-products. Next, 1,3-dithianes of aldehydes were also studied with compounds 1t and 1u. It is of note that these 1,3-dithianes reacted rapidly under A mild conditions to give the corresponding aldehydes in variable yields. For the deprotection of dithioketals of aldehydes, it is very important to examine carefully the course of the deprotection reaction by TLC monitoring because prolonged reaction times resulted in a severe decrease in yields. Indeed, it has been reported that, at rt, aldehydes reacted rapidly with TMSI to give iodosilyl ethers and diiodoethers.[25] This suggests that, as soon as aldehydes are formed after thioacetal deprotection, they add nucleophilic iodides which may arise from TMSI very slowly generated in the media according to an exchange Finkelstein reaction.[26] To show the interest of this process with respect to other previously reported methods using for examples HgO associated with BF3-Et2O,[27] 2,6-dicarboxy pyridinium chlorochromate (DCPCC)[28] or SbCl5[29] we have deprotected dithioketals 1v and 1w by TMSCl/NaI in CH3CN (Scheme 2). The comparison of the yields obtained using the TMSCl/NaI mild association in CH3CN vs toxic oxidizing agent as HgO (86 % vs 65%), DCPCC (93 % vs 70%) or SbCl5 (93 % vs 77%) supports well that this novel metal-free process is welcome since the yields in desired ketones are significantly higher and the reagents used for the deprotection are inexpensive, not toxic and very easy to handle.

![Table of results](image)

*a* Dithioacetals were prepared from the corresponding ketones with dithiols in the presence of BF3-Et2O. All purified ketones had 1H and 13C NMR data identical to those of authentic samples. 1-Benzyl-4-methoxybenzene (40%) resulting from the dithioketal reduction was also isolated. NaNBr replaced NaI.
Scheme 2. Deprotection of dithianes 1v and 1w by TMSCl/NaI in CH$_3$CN.

\[ \text{Scheme 2. Deprotection of dithianes 1v and 1w by TMSCl/NaI in CH}_3\text{CN.} \]

A : TMSCl/NaI 10 eq, CH$_3$CN, 24 h, rt. B : TMSCl/NaI 20 eq, CH$_3$CN, 24 h, 60 °C.

Next, as dithioacetals, the regeneration of carbonyl compounds from nitrogen-derivatives as hydrazones, N-tosylhydrazones, ketimines and oximes required most of the time harsh reaction conditions including oxidative or reducing process, acidic or alkaline media, expensive reagents or hazardous experimental protocols.\[30\] In order to find a milder process, we next examined if the TMSCl/NaI combination in CH$_3$CN process could be applied successfully to these robust nitrogen substrates.

Scheme 3. Reaction of 6-10 by TMSCl/NaI in MeCN

A : TMSCl/NaI 10 eq, CH$_3$CN, 24 h, rt. B : TMSCl/NaI 20 eq, CH$_3$CN, 24 h, 60 °C.

In Scheme 3 were presented the results of the regeneration of carbonyl functions of diphenylhydrazone 6, N-tosylhydrazone 7, N-benzylimine 8, ketimine 9 and diphenylmethane oxide 10, using TMSCl/NaI in CH$_3$CN. We were pleased to observe that the TMSCl/NaI combination in CH$_3$CN was able to transform imines and hydrazones into ketones with good yields (90 to 100%) as well as N-tosylhydrazone 7 which required the use of stronger reaction conditions. On the contrary, imine 8 and ketimine 9 were easily transformed in their ketones with high yields using the TMSCl/NaI association in CH$_3$CN at rt. When diphenylmethane oxime 10 was reacted with the TMSCl/NaI association (10 eq), we isolated, after 24 h of reaction achieved at rt, 4-methoxy-N-(4-methoxyphenyl)benzamide 11 in a good yield (84%) accompanied by only 4% of the bis(4-methoxyphenyl)methane 2r. The scope of this interesting Beckmann rearrangement, using the TMSCl/NaI combination, is currently under investigation in our lab with a range of oxime substrates.\[31\]

Scheme 4. Plausible mechanism

A plausible reaction mechanism is indicated in (Scheme 4). First, CH$_3$CN activates the TMSCl/NaI association as mentioned previously by Olah\[Error! Bookmark not defined.\] to promote intermediate I and II after halide exchange in the presence of NaI. Then, II reacts with a sulfur atom of dithiolane 1c to give a sulfonium species of type III. Further assistance from the neighboring dithiane sulfur atom possibly leads to a fragmented sulfonium intermediate IV which added H$_2$O (from reagents, CH$_3$CN or during hydrolysis) to promote hemithioketal V which is then activated into a sulfonium intermediate VI (having or not H$_2$O). With no H$_2$O as in 1r or 1s, VI finally rearranges into the desired ketone 2d.\[32\] For dithiolanes prepared from enolizable ketones as 1c, the same (a) pathway could be followed but it is also reasonable to consider an additional pathway (b) in which an iodide deprotonates intermediate VI to furnish an enol species which tautomers into ketone 2d. Since dithioacetals having H$_2$O can evolve according to two different pathways, this can explain that these entities are easier to deprotect than diarylthioketals counterparts. It is of note that a similar mechanism has been previously proposed by Nicolaou for the protection of S,S-acetals and ketals using IBX.\[33\]
Conclusion

In this article we showed for the first time, the fundamental role of CH₂CN associated to TMSCl/NaI combination to deprotect S,S-ethylene- and S,S-propylene-ketals into ketones. Indeed, if the mild TMSCl/NaI association leads to the reduction of dithioketals in CH₂Cl₂, we have demonstrated that this association can be used to deprotect a large variety of various dithioketals into ketones in CH₂CN. Otherwise, under mild experimental conditions, O,O-acetals as well as O,S-oxathianes were cleanly deprotected with high yields. It is also possible to easily regenerate the carbonyl function of various hydrazones and imines using this novel protocol. We believe that this metal-free process is a good alternative to other known methodologies used to deprotect dithioketals into ketones.

Experimental Section

A general experimental procedure is described as following: a mixture of thioëtal (100 mg) and NaI (10 eq) was stirred in MeCN for 5 min. Then, 10 eq of TMSCl were added to the solution which was stirred for 24 h at rt. The reaction was then hydrolyzed for 5 min, with H₂O (5 mL) and extracted with CH₂Cl₂. Organic layers were dried over MgSO₄ and concentrated under reduced pressure to give a residue which was purified by chromatography on silica gel to give the expected carbonyl compound which have identical NMR spectra with starting ketones.

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To our knowledge, only one paper reported the use of TMSCl in CH$_3$CN to achieve at a high temperature of 100 °C, the Beckmann rearrangement of the cyclododecanone oxime into $\omega$-laurolactam (a single example having no functional groups was described in this letter; no isolated yield is mentioned), see: S. Sato, S.Hoshino, T.; Sugimoto, K. Kashiwagi, Chem. Lett. 2010, 39, 1319-1320.

With a dithioketal having no H$\alpha$ as 1t, an iodine may attack intermediate IV to give a mixed unstable S,I-ketal which evolves into the reduction product 1-benzyl-4-methoxybenzene (footnote c); Table 2). For a possible mechanism explaining the reduction process, see ref. [17].

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