Tetrahedron Letters No. 48, pp 4175 - 4178, 1977. Pergamon Press. Printed in Great Britain.

# NON-AQUEOUS CONVERSION OF KETALS TO KETONES VIA TREATMENT WITH TRIMETHYLSILYL IODIDE[1]

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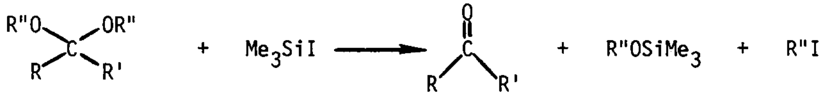
(Received in USA 22 July 1977; received in UK for publication 11 October 1977)

The conversion of ketals to ketones is often a useful and necessary organic transformation. This is normally accomplished by acid-catalyzed aqueous hydrolysis. We now wish to report a simple and efficient method for the transformation of ketals into ketones under non-aqueous conditions[4] via treatment with the interesting electrophilic reagent, trimethylsilyl iodide.[5-9]

We have recently reported the use of trimethylsilyl iodide in several important synthetic transformations, namely, the efficient conversion of alkyl carboxylates into trimethylsilyl carboxylates and thence acids;[6] the transformation of dialkyl and aryl alkyl ethers into the corresponding alkyl and aryl trimethylsilyl ethers and thence alcohols and phenols;[7] and the conversion of alcohols into iodides either directly or via the trimethylsilyl ethers.[8] Others have also reported on the usefulness of this silyl iodide in dealkylations.[9]

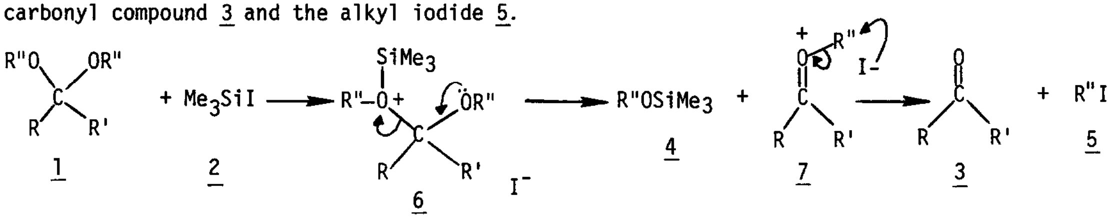
When a dialkyl ketal or acetal 1 in a solution in dichloromethane or chloroform is treated with trimethylsilyl iodide 2 at 25°C for 15 minutes a rapid reaction occurs which results in the complete formation of the corresponding ketone or aldehyde 3, the trimethylsilyl ether 4, and the iodide 5. Aqueous workup followed by chromatography on silica gel and a final distillation affords excellent yields of the carbonyl compounds.[10] The results obtained with a series of ketals and acetals are shown in the Table.



1 2 3 4 5

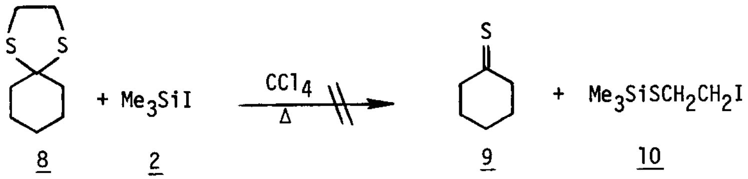
The solvent of choice for the reaction is chloroform which has been saturated with propene gas. The olefin is used in order to eliminate traces of hydrogen iodide which are always present in the trimethylsilyl iodide due to hydrolysis by atmospheric moisture. The hydrogen iodide reacts with propene in an irreversible reaction to form isopropyl iodide which does not affect the desired reaction and is volatile enough to be removed by evaporation at reduced pressure. In most cases if propene is not used the yield of desired product is decreased due to the formation of products from acid-catalyzed aldol condensations.

We propose the following mechanism for the ketal to ketone transformation. Initial attack of the oxygen lone pair on the silyl iodide should afford the intermediate 6. The lone pair on the other oxygen should assist in the ejection of the silyl ether 4 from 6 with the formation of the second intermediate 7. Attack of the iodide ion on the alkyl group of 7 should then produce the carbonyl compound 3 and the alkyl iodide 5.



Whereas dimethyl and diethyl ketals are cleanly converted into the corresponding ketones, ethylene ketals are not. The treatment of an ethylene ketal, e.g. 1h, with trimethylsilyl iodide 2 leads to a complex mixture of products containing at most only 20 percent of the desired ketone, e.g. 3h. The reasons for this difference in behavior are not known at present.

The interesting possibility of forming thiones by this reaction was also investigated. However, thioketals are totally stable to this reaction. For example, a solution of the ethylene thioketal of cyclohexanone 8 and trimethylsilyl iodide in carbon tetrachloride was refluxed for 24 hr



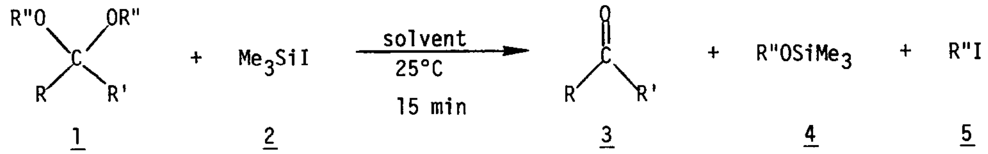
without any reaction taking place. This is not unexpected since the silicon-sulfur bond is known to be much weaker than the silicon-oxygen bond and thus there should be much less thermodynamic driving force for the formation of the thione 9 and the silyl sulfide 10.

Finally, treatment of ortho esters with trimethylsilyl iodide results in the rapid formation of the carboxylic ester. For example, addition of trimethylsilyl iodide 2 to a solution of tri-

$$\underset{11}{HC(OMe)_3} + \underset{2}{Me_3SiI} \xrightarrow[25°C]{CHCl_3} \underset{12}{HCO_2Me} + MeOSiMe_3 + MeI$$

## TABLE

## CONVERSION OF KETALS INTO KETONES WITH $Me_3SiI$



| | KETALS | | | | YIELD (%) | |
|---|---|---|---|---|---|---|
| COMPOUND | R | R' | R" | Solvent | NMR | Isolated |
| a | $CH_3$ | $CH_3$ | $CH_3$ | $CCl_4$ | >95 | --- |
| b | $-(CH_2)_4$ | - | $CH_3$ | $CHCl_3$/propene | >95 | 87 |
| c | $-(CH_2)_5$ | - | $CH_3$ | $CHCl_3$/propene | >95 | 90 |
| d | $C_6H_{13}$ | $CH_3$ | $CH_3$ | $CH_2Cl_2$ | >95 | 87 |
| e | $C_5H_{11}$ | H | $CH_3$ | $CHCl_3$/propene | >95 | 85 |
| f | Ph | Ph | $CH_3$ | $CHCl_3$/propene | >95 | 98 |
| g | $-(CH_2)_5$ | - | $CH_2CH_3$ | $CHCl_3$/propene | >95 | 84 |
| h | $-(CH_2)_5$ | - | $-CH_2CH_2-$ | $CH_2Cl_2$ | ~20 | -- |

methyl orthoformate 11 in chloroform rapidly affords methyl formate 12 and the by-products methyl trimethylsilyl ether and methyl iodide.

The following is a typical experimental procedure. Propene was bubbled through 10 ml of chloroform in a 25 ml round bottom flask equipped with a serum cap and magnetic stirrer under a nitrogen atmosphere. Trimethylsilyl iodide 2 (950 mg, 4.75 mmol, 0.65 ml) was added via syringe and the solution stirred for 10 min. Benzophenone dimethyl ketal 1f (905 mg, 3.97 mmol) was added via syringe and the solution stirred for 15 min. Excess trimethylsilyl iodide was then destroyed by the addition of 5% aqueous $NaHCO_3$ and the iodine color discharged by shaking the organic solution with 10% aqueous $Na_2S_2O_5$. The chloroform layer was separated, the aqueous layer saturated with NaCl and extracted twice with chloroform. The combined chloroform layers were dried ($Na_2SO_4$), filtered, and concentrated under reduced pressure. The mixture was chromatographed on 34 g of silica gel (Baker). After passing 150 ml of $CCl_4$ through the column, the product was eluted with 300 ml of $CH_2Cl_2$. The solvent was evaporated under reduced pressure and the residue distilled (Büchi kugelrohr, 0.001 mm) to afford 710 mg (98%) of benzophenone 3f.

Since certain functionalities which are unstable in aqueous acid are stable to trimethylsilyl iodide - e.g., trimethylsilyl enol ethers, enol acetates, alkyl enol ethers - this non-aqueous formation of ketones from ketals should be useful in molecules with differentially protected ketones. In addition one would expect that a large variety of functional groups would survive these reaction conditions, including most ethers[7] and esters,[6] amines, amides, ketones, olefins, acetylenes, and halides.[6,7] However those functional groups which react very rapidly with trimethylsilyl iodide - e.g., alcohols;[8] trityl, *t*-butyl, and benzyl ethers[7] and esters;[6] and epoxides - would not survive these conditions. Other useful reactions of trimethylsilyl iodide with oxygen-containing substrates are underway in our laboratories.

## References and Notes

1. The research was presented in part at the 173rd National Meeting of the American Chemical Society, New Orleans, Louisiana, March 1977, Abstract ORGN89.
2. Undergraduate Research Participant, Summer 1976.
3. National Science Foundation Undergraduate Research Participant, Summer 1976.
4. Very few instances of non-aqueous "hydrolyses" of ketals have been reported. For an example in the steroid field see: A. Bowers, L. C. Ibanez and H. J. Ringold, *Tetrahedron*, **7**, 138 (1959).
5. Trimethylsilyl iodide is easily prepared in two steps from the chloride via hexamethyldisiloxane, M. E. Jung and M. A. Lyster, *Organic Syntheses*, submitted for publication. See also references 6 and 7.
6. M. E. Jung and M. A. Lyster, *J. Am. Chem. Soc.*, **99**, 968 (1977).
7. M. E. Jung and M. A. Lyster, *J. Org. Chem.*, in press.
8. M. E. Jung and P. L. Ornstein, *Tetrahedron Lett.*, 2659 (1977).
9. a) H. Schmidbauer and R. Seeber, *Chem. Ber.*, **107**, 1731 (1974); b) M. G. Voronkov, V. E. Puzanova, S. F. Pavlov, and E. I. Dubinskaya, *Izvestia Akad. Nauk SSSR*, 448 (1975); c) M. G. Voronkov, S. F. Pavlov, and E. I. Dubinskaya, *ibid.*, 657 (1975); *Dokl. Akad. Nauk SSSR*, **227**, 607 (1976); d) M. G. Voronkov, E. I. Dubinskaya, V. G. Komarov, and S. F. Pavlov, *Zh. Obshch. Khim.*, **46**, 1908 (1976); e) T.-L. Ho and G. A. Olah, *Angew. Chem.*, **88**, 847 (1976); *Synthesis*, 417 (1977).
10. Spectral data (NMR, IR) of the crude reaction mixture indicates that the carbonyl compounds are present before water is added. An aqueous workup is performed since direct distillation of the crude reaction mixture gives somewhat (10-20%) lower yields.