

A FACILE PREPARATION OF METHYL ENOL ETHERS FROM ACETALS  
 AND KETALS USING TRIMETHYLSILYL IODIDE

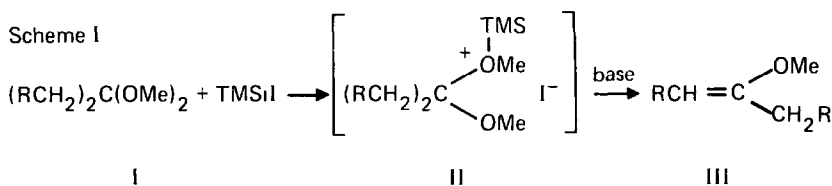
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**Summary** Acetals and ketals are converted in high yields to the corresponding methyl vinyl ethers by treatment with trimethylsilyl iodide in the presence of hexamethyldisilazane at room temperature or below

Alkyl vinyl ethers are reagents of considerable synthetic utility <sup>1</sup> Unfortunately, the most useful preparative technique involves the pyrolytic cracking of acetals and ketals usually in the presence of acid catalysts <sup>2</sup> These vigorous reaction conditions often limit the generality of the procedure, particularly when other sensitive functionality is present

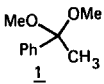




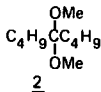
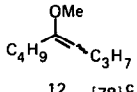
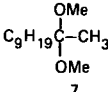
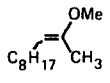

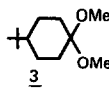
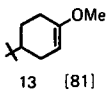
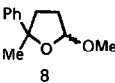



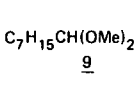




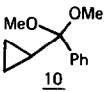

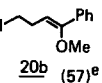
In connection with another program, we needed a mild, selective procedure for the preparation of methyl vinyl ethers which did not require either elevated temperatures or strong acid catalysis In this respect, it seemed that the utilization of the strong affinity for oxygen of electrophilic silicon derivatives might provide the mild technique needed In this regard, trimethylsilyl iodide is such a highly electrophilic reagent which is finding considerable recent synthetic usage <sup>3</sup>

Since we have shown that the treatment of certain oxygenated functionality with TMSiI in the presence of selected sterically hindered amines (e g , 2,6-di-t-butyl-4-methylpyridine and hexamethyldisilazane (HMDS)) led to rapid deprotonation, <sup>4</sup> the application of this procedure to acetals and ketals <sup>5</sup> should result in a mild, selective technique for the formation of methyl vinyl ethers under neutral or weakly basic conditions (Scheme I) We describe here the successful utilization of this procedure for this purpose



Examination of Table I shows the scope and utility of this process <sup>6</sup> In most cases, the product yields are high and the isolation procedure is simple The reaction progress is easily monitored by NMR or glpc and the products are isolated in high purity virtually uncontaminated by the corresponding carbonyl compounds <sup>7</sup> Unsymmetrical ketals result in regioisomers which appear significantly equilibrated Consistently when the mixture of 16a and 16b isolated by distillation was treated with a catalytic quantity of p-toluenesulfonic acid for 8 days (25°C), the ratio of the reisolated enol ethers remained relatively constant (63/37 after equilibration versus 67/33 initially) <sup>8</sup>

Table I

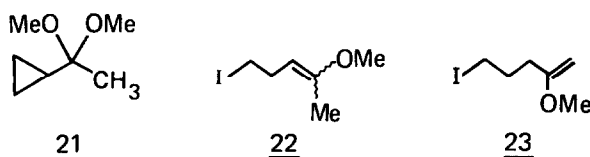
Starting Material	Reaction <sup>a</sup> Conditions	Products	Starting Material	Reaction Conditions	Products
	CHCl <sub>3</sub> , 1.5 hr, 0° 2.0 hr, 25°	 <b>11</b> [81] <sup>b</sup>		CHCl <sub>3</sub> , 1.0 hr, 0° 1.5 hr, 25°	 <b>16a</b> (67) <sup>d</sup>  <b>16b</b> (33) [83]
	CH <sub>2</sub> Cl <sub>2</sub> , 0.5 hr, 0° 1.0 hr, 25°	 <b>12</b> [78] <sup>c</sup>		CH <sub>2</sub> Cl <sub>2</sub> , 15 hr, 0°	 <b>17a</b> (60) <sup>c</sup>  <b>17b</b> (40) [85]
	CH <sub>2</sub> Cl <sub>2</sub> , 2.0 hr, 0° 2.0 hr, 25°	 <b>13</b> [81]		CCl <sub>4</sub> , 47 hr, 25°	 <b>18</b> [85]
	CHCl <sub>3</sub> , 1.5 hr, 0°	 <b>14</b> [86]		CCl <sub>4</sub> , 3.0 hr, 0° 3.0 hr, 25°	 <b>19a</b> (72) <sup>e</sup>  <b>19b</b> (28) <sup>e</sup> [45]
	CH <sub>2</sub> Cl <sub>2</sub> , 2.0 hr, 0° 2.0 hr, 25°	 <b>15</b> [89]		CHCl <sub>3</sub> , 0.5 hr, 0° 3.0 hr, 25°	 <b>20a</b> (43) <sup>e</sup>  <b>20b</b> (57) <sup>e</sup> [65]

<sup>a</sup>1.3 equivalents HMDS, 1.2 equivalents TMSiI <sup>b</sup>Absolute Yields <sup>c</sup>Single isomer of unknown stereochemistry <sup>d</sup>Relative Yields <sup>e</sup>Stereochemistry tentatively assigned on the basis of NMR chemical shifts, H O House, L J Czuba, M Gall and H D Olmstead, *J Org Chem*, **34**, 2324 (1969)

Interestingly, the rate of disappearance of the starting material was quite sensitive to the solvent. The reaction was rapid in methylene chloride or chloroform while the rate in pentane and carbon tetrachloride was much slower. This solvent effect was exploited in the conversion of the acetals **8** and **9**. In each case, the disappearance of the starting material was rapid in either methylene chloride or in chloroform, but the enol ethers were apparently unstable in the reaction media. The use of carbon tetrachloride, on the other hand, resulted in lower rates but allowed the isolation of the respective vinyl ethers **18** and **19** in reasonable yields. Interestingly, when **9** was treated with TMSiI-HMDS in carbon tetrachloride at 0°C (3h) and a sample worked up in the usual fashion, gpc analysis indicated that the major product (unreacted ketal was present) was capryl aldehyde. Infrared analysis of the reaction mixture at this point showed little aldehyde carbonyl. However, when the mixture was allowed to further warm to 25°C for three additional hours and was reanalyzed, the respective enol ethers **16a** and **16b** were the major products and capryl aldehyde comprised <5% of the mixture. It is significant that the respective trimethylsilyl enol ethers of capryl aldehyde were not detected in the reaction mixture even though they are produced in good yield when the aldehyde itself was treated with TMSiI-HMDS. On the basis of these observations, it seems reasonable to propose that in carbon tetrachloride at 0°C an intermediate is produced

which hydrolytically reverts to the aldehyde upon aqueous work up. Alternatively, at higher temperatures, elimination is competitive and the respective vinyl ethers are produced. The corresponding  $\alpha$ -iodooctyl methyl ether should be considered as a possible candidate for the base labile intermediate. In this regard, we note that NMR examination of the crude reaction mixture after 2h at  $-10^{\circ}\text{C}$  showed the appearance of a new single proton triplet ( $J=5$  Hz) at  $\delta$  6.0<sup>9</sup>. At this point, starting material was still in evidence, but the product enol ethers, 19a and 19b were absent. Warming to  $25^{\circ}\text{C}$  led to the disappearance of the low field triplet and to the appearance of the characteristic vinyl ether signals of 19a and 19b at  $\delta$  6.25 and 5.75.

Cyclopropylcarbinyl ketals (e.g., 10) also react rapidly under the reaction conditions but with ring opening to yield the corresponding iodo enol ethers. In a similar fashion, the aliphatic ketal 21 rapidly ring opens to produce initially the enol ether 22. Continuous monitoring of the reaction by NMR indicated that while 22 was the major (>90%) product generated initially, after workup and upon standing, some of the terminal isomer 23 was detected (singlet at 3.86 $\delta$ , olefinic protons)<sup>9</sup>. The equilibration which apparently takes place upon standing may be caused by traces of  $\text{I}_2$  present which is known to be a very efficient catalyst for enol ether equilibration<sup>8</sup>.



#### General Procedure for Preparation of Methyl Enol Ethers

345 mg (2 mmole) of cyclooctanone dimethyl ketal was dissolved in 4 ml of methylene chloride under  $\text{N}_2$ . After cooling to  $-10^{\circ}\text{C}$ , 2.5 mmole (527  $\mu\text{l}$ ) of hexamethyldisilazane and 2.3 mmole (327  $\mu\text{l}$ ) of TMSiI were added. The reaction was stirred 2h at  $0^{\circ}\text{C}$  and allowed to warm to  $25^{\circ}\text{C}$  (2h). The mixture was diluted with 25 ml of pentane, washed with cold saturated sodium bicarbonate and dried over  $\text{K}_2\text{CO}_3$ . The pentane was removed and the residue distilled from  $\text{K}_2\text{CO}_3$  using a Kugelrohr apparatus ( $85^{\circ}\text{C}$ , 15 mm) to yield 250 mg (89%) of the vinyl ether 15. Glpc analysis (10% SE-30) indicated that the product was >97% pure.

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- 6 Consistent spectroscopic data has been obtained for all compounds The yields reported are for isolated  
material with no attempt at optimization Regioisomers were separated by glpc (10% SE-30 on  
Chromosorb W)
- 7 The apparent stability of the methyl enol ethers under the stated reaction conditions is interesting, in light of  
the report by Cohen and coworkers that such ethers are rapidly cleaved by a mixture of trimethylsilyl  
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 $\alpha$ -iodooctyl methyl ether and is quite similar in position to that recently reported for a number of related  
aldehyde trimethylsilylhydrodrins<sup>10</sup>
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- 11 The structures of 22 and 23 were assured by the displacement of iodide using lithium thiophenoxide (THF,  
25°C) to produce the corresponding thiophenyl methyl enol ether which could be purified by glpc In a  
similar fashion, the dimethyl ketal of  $\gamma$ -thiophenyl-2-pentanone was treated with TMSiI-HMDS to yield the  
same mixture of enol ethers for spectral and glpc comparison

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