CHEMISTRY LETTERS, pp. 1331-1334, 1987.

A Novel Method for the Preparation of Ethers from Carbonyl Compounds with Benzenetellurol Catalyzed by ZnI$_2$1)

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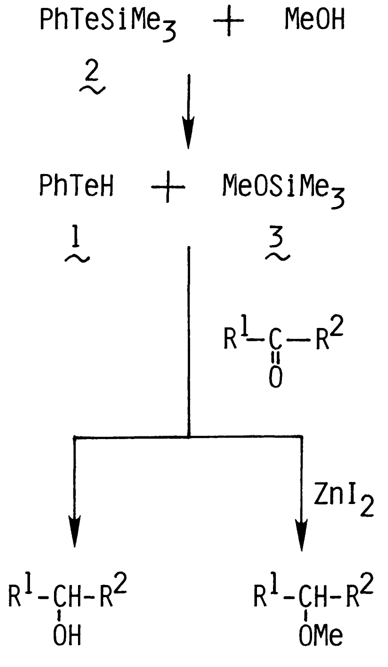
Benzenetellurol is shown to behave as an effective reagent for the reductive conversion of carbonyl compounds into unsymmetrical ethers under the catalytic influence of ZnI$_2$.

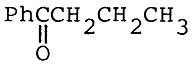
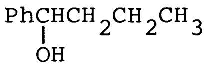
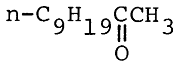
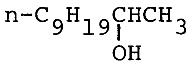
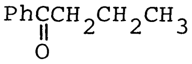
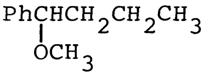
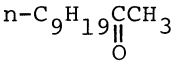
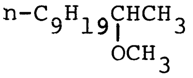
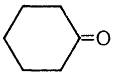
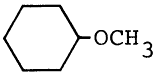
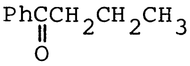
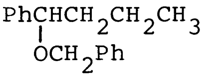
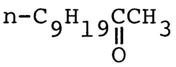
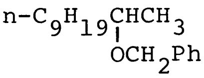
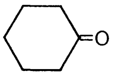
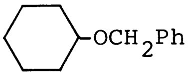
In recent years, several methods for in situ generation of benzenetellurol (1) were reported,2) and the reagent has been recognized as an effective reducing agent due to the weak H-Te bond, in contrast to highly nucleophilic nature of benzenetellurolate. However, its reactivity fairly depends on the generating method. In a previous paper,3) we have demonstrated that benzenetellurol (1) could be more conveniently generated by the methanolysis of phenyltellurotrimethylsilane (2),4) and that several chemoselective reductions of nitro, carbonyl, olefinic, acetylenic, and tellurium compounds with 1 were efficiently carried out in nonpolar solvents such as benzene or chloroform. Moreover, acetals could be reduced to the corresponding ethers under the catalytic influence of ZnI$_2$. The application of similar conditions to reduction of carbonyl compounds has led us to the discovery of the useful direct conversion of those into ethers.5)



Scheme 1.

As shown in the previous paper,3) aliphatic ketones were hardly reactive toward benzenetellurol (1) in benzene at room temperature. When to this reaction mixture was added ZnI$_2$ as a catalyst, those were not reduced to secondary alcohols, but reductively converted into the corresponding sec-alkyl methyl ethers in high yields. Aldehydes and aromatic ketones similarly afforded the methyl ethers in the presence of 50 mol% ZnI$_2$, in spite of the easy formation of alcohols under the normal conditions (Scheme 1). Some results of reduction of carbonyl compounds are shown in Table 1. It is apparent that methyl trimethylsilyl ether (3) serves as a methylating agent in these reactions, so the corresponding alkyl ethers can be obtained by using

Table 1. Reactions of carbonyl compounds with benzenetellurol in benzene at room temperature[a)]

Run	Substrate	Alcohol[b)]	Catalyst[c)]	Time/h	Product	Yield/%[d)]
1	PhCHO	CH_3OH	None	0.5	$PhCH_2OH$	94
2	$n\text{-}C_{11}H_{23}CHO$	CH_3OH	None	2	$n\text{-}C_{12}H_{25}OH$	73
3	 $Ph\underset{\overset{\Vert}{O}}{C}CH_2CH_2CH_3$	CH_3OH	None	3	 $Ph\underset{\overset{\vert}{OH}}{C}HCH_2CH_2CH_3$	95
4	 $n\text{-}C_9H_{19}\underset{\overset{\Vert}{O}}{C}CH_3$	CH_3OH	None	3	 $n\text{-}C_9H_{19}\underset{\overset{\vert}{OH}}{C}HCH_3$	23[e)]
5	PhCHO	CH_3OH	ZnI_2(50 mol%)	3	$PhCH_2OCH_3$	89[f)]
6	$n\text{-}C_{11}H_{23}CHO$	CH_3OH	ZnI_2(5 mol%)	3	$n\text{-}C_{12}H_{25}OCH_3$	77
7	 $Ph\underset{\overset{\Vert}{O}}{C}CH_2CH_2CH_3$	CH_3OH	ZnI_2(50 mol%)	3	 $Ph\underset{\overset{\vert}{OCH_3}}{C}HCH_2CH_2CH_3$	81[g)]
8	 $n\text{-}C_9H_{19}\underset{\overset{\Vert}{O}}{C}CH_3$	CH_3OH	ZnI_2(5 mol%)	3	 $n\text{-}C_9H_{19}\underset{\overset{\vert}{OCH_3}}{C}HCH_3$	88
9		CH_3OH	ZnI_2(5 mol%)	3		91
10	PhCHO	$PhCH_2OH$	ZnI_2(50 mol%)	3	$PhCH_2OCH_2Ph$	96
11	$n\text{-}C_{11}H_{23}CHO$	$PhCH_2OH$	ZnI_2(5 mol%)	3	$n\text{-}C_{12}H_{25}OCH_2Ph$	96
12	 $Ph\underset{\overset{\Vert}{O}}{C}CH_2CH_2CH_3$	$PhCH_2OH$	ZnI_2(50 mol%)	3	 $Ph\underset{\overset{\vert}{OCH_2Ph}}{C}HCH_2CH_2CH_3$	76
13	 $n\text{-}C_9H_{19}\underset{\overset{\Vert}{O}}{C}CH_3$	$PhCH_2OH$	ZnI_2(5 mol%)	3	 $n\text{-}C_9H_{19}\underset{\overset{\vert}{OCH_2Ph}}{C}HCH_3$	84
14		$PhCH_2OH$	ZnI_2(5 mol%)	3		83

a) The molar ratio of substrate : **2** : alcohol = 1 : 2.2 : 2.2.

b) The alcoholysis reagent for **2**.

c) The quantity of catalyst was shown in parenthesis.

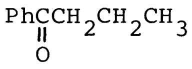
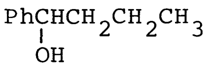
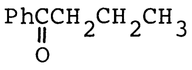
d) Isolated yield, unless otherwise stated.

e) The substrate was recovered in 74% yield.

f) Determined by GLC analysis.

g) Determined by ^1H NMR analysis.

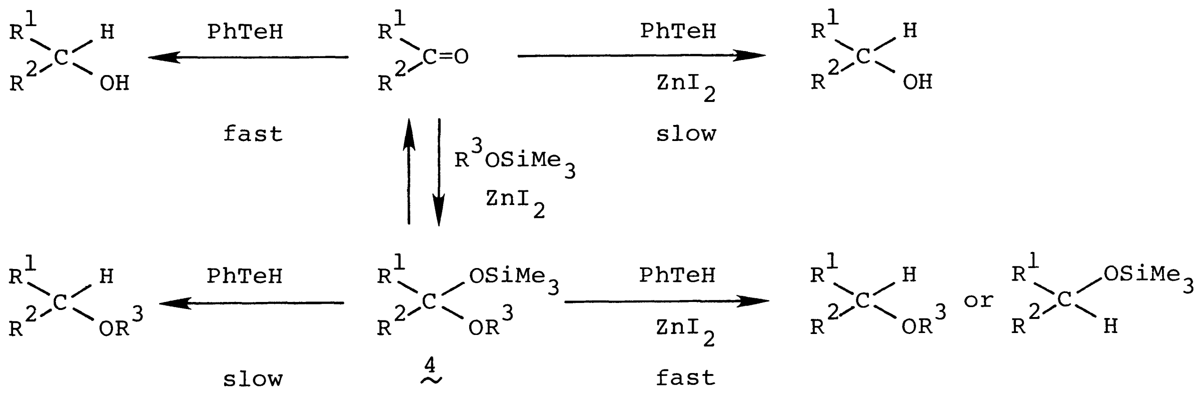
Table 2. Effects of trimethylsilyl ether and ZnI_2 on reduction of carbonyl compounds[a)]

Run	Substrate	Silyl ether	Catalyst	Product	Yield/%
1	 $\mathrm{Ph}\underset{\mathrm{O}}{\underset{\|}{\mathrm{C}}}\mathrm{CH_2CH_2CH_3}$	None	None	 $\mathrm{Ph}\underset{\mathrm{OH}}{\underset{\mid}{\mathrm{C}}}\mathrm{HCH_2CH_2CH_3}$	75
2	 $\mathrm{Ph}\underset{\mathrm{O}}{\underset{\|}{\mathrm{C}}}\mathrm{CH_2CH_2CH_3}$	None	ZnI_2	Recovery	87
3	PhCHO	$PhOSiMe_3$	ZnI_2	$PhCH_2OSiMe_3$	39

a) The reaction was carried out in benzene at room temperature for 3 h.

the other alcohols as an alcoholysis reagent for **2**. Hence ethers containing benzyl group, a versatile protecting group of alcohols, were easily prepared directly from carbonyl compounds (Runs 10-14).[6)]

These reactions seem to proceed via hemiacetal-type compounds (**4**), for under the same conditions dimethyl acetals were smoothly reduced to methyl ethers[3)] and no etherification of an alcohol was observed. Tables 1 and 2 show the influence of silyl ether and ZnI_2 on reduction of carbonyl compounds with **1**. In the coexistance of methyl trimethylsilyl ether (**3**) and ZnI_2, butyrophenone was converted effectively to methyl 1-phenylbutyl ether, but was reduced quantitatively to 1-phenylbutanol in the absence of the catalyst (Table 1, Runs 7 and 3). When **3** was removed by evaporation in vacuo after generation of **1** and then butyrophenone was mixed, 1-phenylbutanol was obtained in a yield of 75%, but the reduction was nearly completely depressed by the presence of 50 mol% ZnI_2 (Table 2, Runs 1 and 2). These results support a mechanism summarized in Scheme 2. Zinc iodide, evidently interacting with both substrate and the reagent as a Lewis acid, probably activates carbonyl group and **4** and deactivates benzenetellurol (**1**). Thus the reactivity of **1** in the presence of ZnI_2 would depend on a balance of these effects. The predominant production of ether is explained by a more prominent activating effect of ZnI_2 on hemiacetal (**4**) than on carbonyl compound because the former can form a more cationic complex with ZnI_2. Moreover,



Scheme 2.

when phenol was used as an alcoholysis reagent for **2**, the reduction product of benzaldehyde was not the phenyl ether but the trimethylsilyl ether (Table 2, Run 3). The structure of produced ethers seems to represent the ease of heterolytic cleavage of C-OR, C-OSi, and C-OAr bonds.7)

A typical procedure is illustrated for the synthesis of benzyl dodecyl ether: Under an atmosphere of nitrogen, **2** (610 mg; 2.2 mmol) was added into a dry benzene (10 ml) solution of benzyl alcohol (238 mg; 2.2 mmol), and the solution was stirred for 30 min at room temperature. To the solution, ZnI_2 (16 mg; 0.05 mmol) suspended in benzene (3 ml) followed by dodecanal (184 mg; 1.0 mmol) was added, and stirring was continued for additional 3 h. After water was added, the mixture was extracted with benzene. The benzene extract was dried over anhydrous magnesium sulfate. After the solvent was evaporated under reduced pressure, column chromatography of the residue on silica gel using benzene-hexane as eluent gave a colorless liquid of benzyl dodecyl ether; yield, 265 mg (96%).

References

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2) N. Ohira, Y. Aso, T. Otsubo, and F. Ogura, Chem. Lett., 1984, 853; M. Akiba and M. P. Cava, Synth. Commun., 14, 1119 (1984).
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5) Several methods have been reported for the preparation of ethers by the hydrosilane reduction of carbonyl compounds; M. P. Doyle, D. J. DeBruyn, and D. A. Kooistra, J. Am. Chem. Soc., 94, 3659 (1972); M. P. Doyle, D. J. DeBruyn, S. J. Donnelly, D. A. Kooistra, A. A. Odubela, C. T. West, and S. M. Zonnebelt, J. Org. Chem., 39, 2740 (1974); D. N. Kursanov, Z. N. Parnes, and N. M. Loim, Synthesis, 1974, 633; M. P. Doyle, C. T. West, S. J. Donnelly, and C. C. McOsker, J. Organomet. Chem., 117, 129 (1976); R. Noyori, S. Murata, and M. Suzuki, Tetrahedron, 37, 3899 (1981); J. Kato, N. Iwasawa, and T. Mukaiyama, Chem. Lett., 1985, 743; S. Torii, S. Takagishi, T. Inokuchi, and H. Okumoto, Bull. Chem. Soc. Jpn., 60, 775 (1987).
6) In the case of benzaldehyde and butyrophenone, more than 0.5 equiv. of ZnI_2 was necessary to depress the reduction to alcohols and yield ethers as a sole major product (Runs 5, 7, 10, and 12).
7) Since it has been known that triphenylsilanol is much more acidic than triphenylmethanol, being almost as acidic as phenol, the acidity is presumed to increase in the order of methanol, trimethylsilanol, and phenol; E. W. Colvin, "Silicon in Organic Synthesis," Butterworths, London (1981), p. 12.

(Received April 21, 1987)