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Facile Synthesis of Silyl Enol Ethers by Mg-Promoted Coupling of Aliphatic Carbonyl Compounds with Trimethylsilyl Chloride

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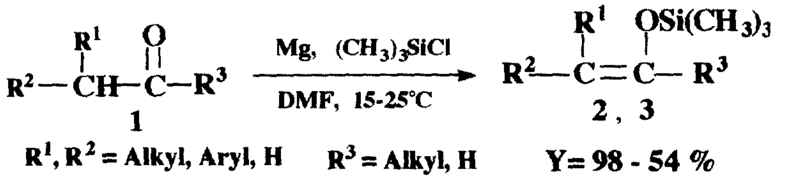
Abstract: Treatment of aliphatic carbonyl compounds with trimethylsilyl chloride with Mg turning for Grignard reaction without any pre-treatment in N,N-dimethylformamide at room temperature brought about highly facile, effective and stereoselective coupling to give the corresponding silyl enol ethers in good yields.

Key words: Carbonyl compounds; Enol ethers; Magnesium and compounds; Silicon halides

Synthetic utility and importance of silyl enol ethers have been well established [1-2]. The numerous methods for their preparation have been reported [3-14] although some difficulties have been encountered in the actual preparation, especially in the large-scale production, owing to requirement of troublesome procedure, low temperature such as -78°C, special equipment, carcinogenic solvent and/or expensive reagents.

In this study, we wish to present novel Mg-promoted coupling of aliphatic carbonyl compounds (**1a-t**) with trimethylsilyl chloride (TMSCl) at room temperature to give the corresponding silyl enol ethers (**2a-t** and **3j,p,q,s,t**) in excellent to good yields. This reaction may provide a highly convenient method for the stereoselective preparation of **2j-m** and **2p,q** in which the (Z)-isomers were formed predominantly.



$$R^2-\overset{R^1}{CH}-\overset{O}{\overset{\|}{C}}-R^3 \xrightarrow[\text{DMF, 15-25°C}]{\text{Mg, }(CH_3)_3SiCl} R^2-\overset{R^1}{C}=\overset{OSi(CH_3)_3}{C}-R^3$$

The reaction was usually carried out at room temperature in a N,N-dimethyl-formamide (DMF) solution (120 mL) containing TMSCl (240 mmol) and Mg-turning (120 mmol) for Grignard reaction without any pre-treatment. A DMF solution (10 mL) of aliphatic carbonyl compounds**1a-t** (20 mmol) was dropwise added into the above solution for 1 h with magnetically stirring at 15-25°C on cooling with a water bath, and then stirred overnight. After the usual work-up of the reaction mixture with aqueous $NaHCO_3$ solution, the

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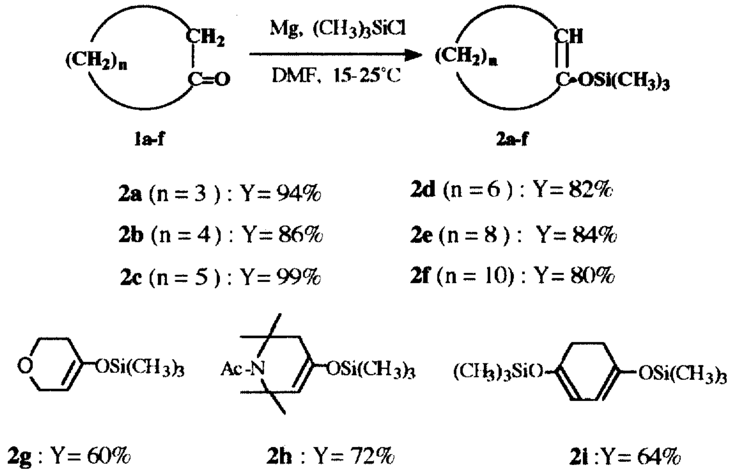
corresponding silyl enol ethers (**2a-t** and **3j,p,q,s,t**) were isolated in excellent to good yields through distillation by Kugel rohr and/or preparative thin layer chromatography.

It was found that this coupling was largely influenced by various conditions. For example, in the silyl enolization of **1j**, Mg showed the best results (a total yield of **2j** and **3j**: 94%) whereas use of other metals such as Zn, Al, Sn and Ca instead of Mg resulted in a little or no formation of the products (Total yields of **2j** and **3j** in the reaction using Zn, Al, Ca, and Sn, were 46, 0, 18, and 0%, respectively.). Furthermore, this coupling reaction was influenced by a relative ratio of Mg-metal, a starting carbonyl compounds **1j**, and TMSCl. The best result for formation of the products, **2j** and **3j** ,was obtained when the relative proportion of Mg : **1j** : TMSCl was **6 : 1 : 12**. Also DMF was found to be a much better solvent for this reaction than other aprotic polar solvents such as N,N-dimethylactamide (DMAC) or 1,3-dimethyl-2-imidazolidinone (DMI).

A variety of trimethylsilylated adducts, **2** and **3**, were efficiently obtained in excellent to good yields as shown in Scheme 1 for cyclic ketones and Table for acyclic carbonyl compounds.[1] As shown in the entries 7 and 8 of the Table , the present silyl enolization proceeded for the carbonyl compounds possessing a cyano group or a chlorine atom, which would give some disturbances in conventional methods using a strong base. It may be also noteworthy that 1,4-diketones (**1i** in Scheme 1 and **1r** in the entry 9 of the Table) could be smoothly transformed into the corresponding conjugated 1,4-bis(trimethylsiloxy)-1,3-dienes, **2i** and **2r**, in satisfactory yields which may be useful as intermediates in organic synthesis.

It may be interesting that the present Mg-promoted coupling brought about preferential formation of the thermodynamically stable regioisomers of the silyl enol ethers, as shown in the reaction of 2-methylcyclohexanone (**1s**) and 2-methylcyclopentanone (**1t**) (Scheme 2).

Scheme 1 Mg-Promoted Silyl Enolization of Cyclic Ketones



2a (n = 3) : Y = 94%
2b (n = 4) : Y = 86%
2c (n = 5) : Y = 99%
2d (n = 6) : Y = 82%
2e (n = 8) : Y = 84%
2f (n = 10) : Y = 80%

2g : Y = 60%
2h : Y = 72%
2i : Y = 64%

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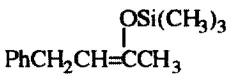
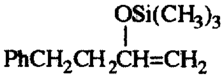
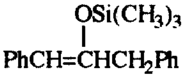
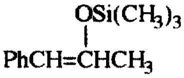
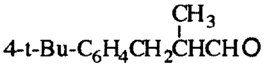
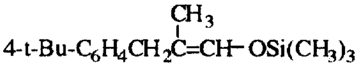
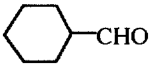
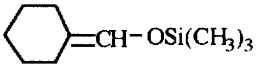
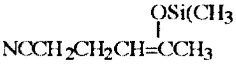
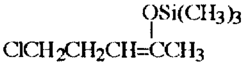
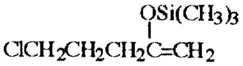
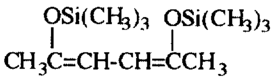
[1] All of the products, **2** and **3**, were identified by comparison of their gas chromatographic and spectroscopic behaviors with those of the authentic samples, and/or by spectroscopic and elemental analyses.

Table Mg-Promoted Silyl Enolization of Acyclic Carbonyl Compounds[a]

Entry	Substrate **1a - i**		Products **2a - l** and **3j, p, q** **(Yield (%), E / Z)**[b]	
1	$PhCH_2CH_2COCH_3$	**1j**	 $PhCH_2CH{=}\overset{OSi(CH_3)_3}{C}CH_3$ **2j(63, 1 / 8)**	 $PhCH_2CH_2\overset{OSi(CH_3)_3}{C}H{=}CH_2$ **3j(31)**
2	$PhCH_2COCH_2Ph$	**1k**	 $PhCH{=}\overset{OSi(CH_3)_3}{C}HCH_2Ph$	**2k(100, 3/93)**
3	$PhCH_2COCH_3$	**1l**	 $PhCH{=}\overset{OSi(CH_3)_3}{C}HCH_3$	**2l(98, 2/98)**
4	$PhCH_2CH_2CHO$	**1m**	$PhCH_2CH{=}CH\text{-}OSi(CH_3)_3$	**2m(70, 2/7)**
5	 $4\text{-}t\text{-}Bu\text{-}C_6H_4CH_2\overset{CH_3}{C}HCHO$	**1n**	 $4\text{-}t\text{-}Bu\text{-}C_6H_4CH_2\overset{CH_3}{C}{=}CH\text{-}OSi(CH_3)_3$	**2n(94, 3/2)**
6		**1o**		**2o(77, -)**
7	$NCCH_2CH_2CH_2COCH_3$	**1p**	 $NCCH_2CH_2CH{=}\overset{OSi(CH_3)_3}{C}CH_3$ **2p(43, 1/5)**	 $NCCH_2CH_2CH_2\overset{OSi(CH_3)_3}{C}{=}CH_2$ **3p(15)**
8	$ClCH_2CH_2CH_2COCH_3$	**1q**	 $ClCH_2CH_2CH{=}\overset{OSi(CH_3)_3}{C}CH_3$ **2q(66, 1/8)**	 $ClCH_2CH_2CH_2\overset{OSi(CH_3)_3}{C}{=}CH_2$ **3q(28)**
9	$CH_3COCH_2CH_2COCH_3$	**1r**	 $CH_3\overset{OSi(CH_3)_3}{C}{=}CH\text{-}CH{=}\overset{OSi(CH_3)_3}{C}CH_3$	**2r (54)**

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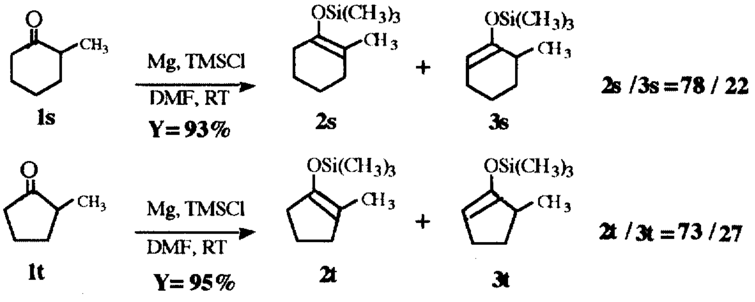
[a] reaction conditions: carbonyl compounds(20 mmol), trimethylsilyl chloride(240 mmol), Mg turning (120 mmol), anhydrous DMF(130 mL), under N_2 atmosphere, at 15-25°C. [b] isolated yield

Scheme 2 Silyl Enolization of 2-Methylcycloalkanones



Another feature of this Mg-promoted coupling may be predominant formation of the (Z)-isomers of the silyl enol ethers such as **2j-m** and **2p,q**. Thus, in the typical conventional silyl enolization of benzyl methyl ketone (**1l**) the (E) / (Z) ratio was 40-15 / 60-85 [11,13,14], and highly stereoselective formation (more than 95%) of the (Z)-silyl enol ether[2] has generally required use of carcinogenic HMPA as a solvent or a co-solvent through complexing in equilibration of the generated enolate [7-9,11,12]. Therefore, it may be quite noteworthy that high stereoselectivity (98%) was observed in this reaction even in the absence of HMPA although a clear-cut explanation is not available at the present stage.[3]

The electron-transfer mechanism [15] may be proposed for this silyl enolization. One-electron transfer may take place from Mg-metal to an oxonium intermediate generated by coordination of an electrophilic silicon atom of TMSCl with the oxygen atom of the enol form of a carbonyl compound to eliminate a hydrogen radical and the silyl enol ether. This hypothesis was partially supported by evolution of hydrogen gas and efficient O-silylation (86%) of cyclohexanol under the reaction conditions, whereas the absence of Mg-metal resulted in only a little formation (17%) of 1-cyclohexyl trimethylsilyl ether.

Further detailed study on mechanism and stereoselectivity of this Mg-promoted coupling is on progress.

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References

[1] Brownbridge P., *Synthesis*, **1983**, 1 and 85.

[2] Reets von M.T., *Angew. Chem.*, **94**, 97 (1982).

[3] Colvin E.W., *Silicon in Organic Synthesis*, Butterworths, London, 1981.

[4] Pawkinko S., *Organo Silicon Chemistry*, Walter de Gruyter, Berlin, 1986.

[5] Weber W.P., *Silicon Reagents for Organic Synthesis*, Spring-Verlag, Berlin, 1983.

[6] Negishi E., *Organometallics in Organic Synthesis*, John Wiley & Sons, New York, Vol.1, Chap. 6, 1980.

[7] Bonafoux D., Bordeau M., Biran C., Cazeau P., and Dunogues J. , *J. Org. Chem.*, **61**, 5532 (1996).

[8] Bonafoux D., Bordeau M., Biran C., and Dunogues J., *J. Organomet. Chem.*, **493**, 27 (1995).

[9] Davis F.A., Sheppard A.C, Chen B.C., and Haque M., *J. Am. Chem. Soc.*, **112**, 6679 (1990).

[10] Takai K., Kataoka Y., Okazoe T.,and Utimoto K., *Tetrahedron Lett.*, **29**, 1065 (1988).

[11] Davis F.A., Lal G.S., and Wei J., *Tertahedron Lett.*, **29**, 4269 (1988).

[12] Dedier J., Gerval P., and Frainnet E., *J. Organomet. Chem.*, **185**, 183 (1980).

[13] House H.O., Czuba L.J., Gall M.,and Olmstead H.D., *J. Org. Chem.*, **34**, 2324 (1969).

[14] Cazeau P., Duboudin F., Moulines F., Babot O., Dunogues J., *Tetrahedron.*, **43**, 2075 (1987).

[15] Ishino Y., Maekawa H. , Takeuchi H., Sukata K., and Nishiguchi I., *Chem. Lett.*, **1995**, 829.

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2. Dunogues et al reported that silyl enolization in the presence of NaI and Et_3N in CH_3CN gave 100% (Z)-selectivity for some aliphatic methyl ketones, but 85-63% (Z)-selectivity for other aliphatic ketones and aldehydes[14].

3. Recently high (Z)-selectivity in the silyl enolization was observed by the addition of tetramethylethylene diamine or tris(3,6-dioxaheptyl)amine as a complexing agent instead of HMPA in the electrolysis using magnesium as the anode in a mixed solvent of dimethoxyethane and N-methylpyrrolidone [8]. Therefore, complexing of Mg^{2+} ion and/or DMF under the acidic conditions with the intermediates may be responsible to high (Z)-stereoselectivity in the present silyl enolization.