

A NOVEL METHOD FOR THE PREPARATION OF SYMMETRICAL  
AND UNSYMMETRICAL ETHERS. TRITYL PERCHLORATE  
PROMOTED REDUCTION OF CARBONYL COMPOUNDS WITH TRIETHYLSILANE

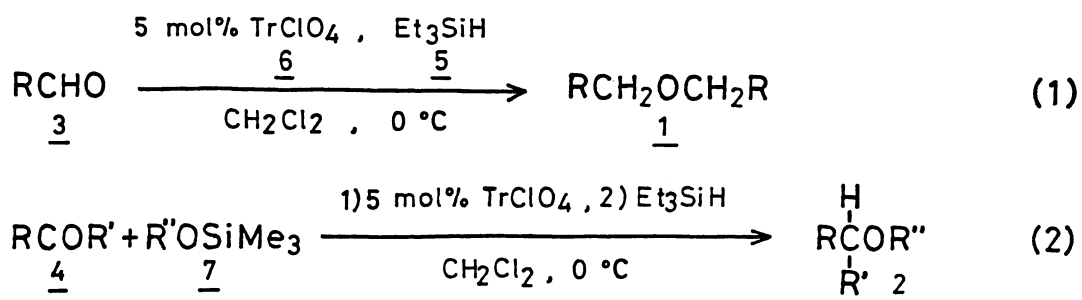
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In the presence of a catalytic amount of trityl perchlorate, symmetrical ethers are prepared from aldehydes and triethylsilane, and unsymmetrical ethers are also obtained from carbonyl compounds, alkoxytrimethylsilanes and triethylsilane, in good yields, respectively.

The preparation of ethers is generally accomplished by coupling alkyl halides and sodium alkoxides, however, olefin formation sometimes occurs under these basic conditions. Thus, it is desired to develop a useful method for the synthesis of symmetrical and unsymmetrical ethers under non-basic conditions.


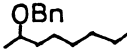
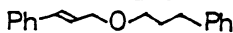
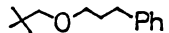

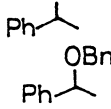
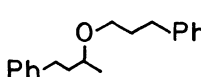
Now we wish to report a convenient method for the preparation of the ethers (1, 2) from free carbonyl compounds (3, 4) and triethylsilane (5) by the promotion of a catalytic amount of trityl perchlorate (6).<sup>1)</sup> According to the reaction shown in the Scheme 1, various ethers are synthesized in good yields under mild reaction conditions (See Table 1).



Scheme 1.

A typical procedure is described for the synthesis of benzyl 3-phenylpropyl ether: Under an argon atmosphere, a  $\text{CH}_2\text{Cl}_2$  (2 ml) solution of benzaldehyde (53 mg, 0.5 mmol) and 3-phenylpropyloxytrimethylsilane was added to a solid trityl

Table 1. The Synthesis of Ethers<sup>a)</sup>

Entry	Carbonyl compound <u>8</u>	Alkoxy silane	Product	Yield /% from <u>8</u>
1	PhCHO	—	BnOBn	84 b)
2	PhCH <sub>2</sub> CH <sub>2</sub> CHO	—	[Ph(CH <sub>2</sub> ) <sub>3</sub> ] <sub>2</sub> O	83 b)
3	n-C <sub>8</sub> H <sub>17</sub> CHO	—	(n-C <sub>9</sub> H <sub>19</sub> ) <sub>2</sub> O	88 b)
4	PhCHO	BnOSiMe <sub>3</sub>	BnOBn	72 c)
5	"			72 c)
6	"	Ph(CH <sub>2</sub> ) <sub>3</sub> OSiMe <sub>3</sub>	BnO(CH <sub>2</sub> ) <sub>3</sub> Ph	83 c)
7	(E)-PhCH=CHCHO	"		88 c)
8	t-BuCHO	"		65 c)
9	n-C <sub>8</sub> H <sub>17</sub> CHO	"	n-C <sub>9</sub> H <sub>19</sub> O(CH <sub>2</sub> ) <sub>3</sub> Ph	64 c)
10	PhCOMe	"		69 c)
11	"	BnOSiMe <sub>3</sub>		76 c)
12	PhCH <sub>2</sub> CH <sub>2</sub> COCH <sub>3</sub>	Ph(CH <sub>2</sub> ) <sub>3</sub> OSiMe <sub>3</sub>		68 c)

Bn=PhCH<sub>2</sub>

- a) All the products gave satisfactory <sup>1</sup>H-NMR and IR spectra.  
 b) Ethers were synthesized according to the reaction (1) in the Scheme 1.  
 c) Ethers were synthesized according to the reaction (2) in the Scheme 1.

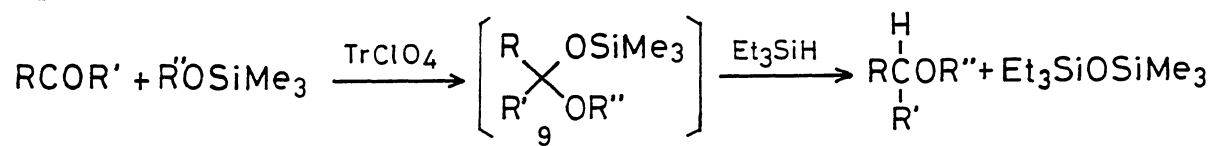
perchlorate (9 mg, 0.026 mmol) and the solution was stirred for 5 min at 0 °C, and a CH<sub>2</sub>Cl<sub>2</sub> (1 ml) solution of triethylsilane (59 mg, 0.5 mmol) was added, and the stirring was continued for another 5 min. Then the phosphate buffer was added and the organic materials were extracted with diethyl ether and dried over MgSO<sub>4</sub>. After the removal of the solvents under reduced pressure, benzyl 3-phenylpropyl ether (94 mg, 83%) was isolated by thin layer chromatography on silica gel. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ 1.5-2.1 (2H, m), 2.4-2.8 (2H, m), 3.30 (2H, t, J=6 Hz), 4.30 (2H, s), 7.00 (5H, s), 7.10 (5H, s), IR(NaCl) 1100 cm<sup>-1</sup>.

Several methods have been reported for the preparation of ethers by the triethylsilane reduction of carbonyl compounds or acetals by the promotion of protic acid or Lewis acids, such as trifluoroacetic acid,<sup>2)</sup> boron trifluoride etherate,<sup>3)</sup> and trimethylsilyl triflate.<sup>4)</sup> These reactions have some limitations; for example, the protic acid as trifluoroacetic acid is necessary, 4 times the molar quantity of aldehydes. When boron trifluoride etherate is used, a mixture

of ethers and alcohols is often produced under these conditions. By the use of a catalytic amount of trimethylsilyl triflate, symmetrical ethers are obtained in reasonable yields, however, it is necessary to transform aldehydes to acetals to obtain unsymmetrical ethers.

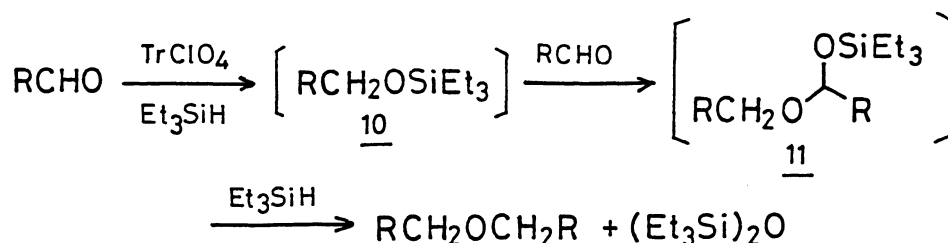
On the other hand, the following items indicate several synthetic utilities of the present reaction: 1) Equimolar quantities of carbonyl compounds (aldehydes and ketones), and alkoxytrimethylsilanes yield the reasonable quantities of ethers by the promotion of a catalytic amount of trityl perchlorate under mild reaction conditions.<sup>5,6)</sup> 2) This is a convenient method for the preparation of various alcohols protected by synthetic useful protecting group. a) By the use of benzyl-oxytrimethylsilane, carbonyl compounds are reductively converted to the alcohols protected by benzyl group (entries 4,11). b) When benzaldehyde is employed as the carbonyl component, silylated alcohols are directly transformed to the alcohols protected by benzyl group (entries 4,5,6).

The mechanism is considered in the following way as shown in Scheme 2 and 3. Hemiacetal-type compounds (9) initially generated by an addition of alkoxytrimethylsilane to carbonyl compounds are readily reduced with triethylsilane to form unsymmetrical ethers.



Scheme 2.

While, in case when aldehyde was employed alone, the initially produced alkoxytrimethylsilane (10) reacts with aldehyde faster than the triethylsilane to give hemiacetal-type compound (11), and the reduction of this compound with triethylsilane yields symmetrical ether.



Scheme 3.

When aldehyde was employed as a carbonyl component, the reaction was instantly completed, however, in case of acetophenone, the color of trityl cation

disappeared soon, and the reaction seems to proceed subsequently by keeping the reaction mixture overnight. This indicates that the reaction may proceed by the promotion of triethylsilyl perchlorate generated by the reduction of trityl perchlorate with triethylsilane.<sup>6)</sup>

Thus, by the promotion of a catalytic amount of trityl perchlorate, hemiacetal-type intermediates (9) are reductively converted to unsymmetrical ethers, and intermediates (11) are also converted to symmetrical ethers, in good yields, respectively.

#### References

- 1) Our recent reports on the new synthetic reactions by using trityl perchlorate are: T. Mukaiyama, S. Kobayashi, and S. Shoda, *Chem. Lett.*, 1984, 907, 1529; T. Mukaiyama, S. Kobayashi, and M. Murakami, *ibid.*, 1984, 1759.
- 2) D. N. Kursanov, Z. N. Parnes, and N. M. Loim, *Synthesis*, 1974, 633.
- 3) M. P. Doyle, C. T. West, S. J. Donnelly, and C. C. Mcosker, *J. Organomet. Chem.*, 117, 129 (1976).
- 4) R. Noyori, S. Murata, and M. Suzuki, *Tetrahedron*, 37, 3899 (1981).
- 5) In entry 11 alone, benzyloxytrimethylsilane was used 2 times molar quantity of acetophenone.
- 6) See: T. J. Barton, A. K. Hovland, and C. R. Tully, *J. Am. Chem. Soc.*, 98, 5695 (1976).

(Received March 19, 1985)