단   신

SbI₃/PhSiH₃을 이용한 카보닐 화합물로부터의 대칭 에테르 합성

백지연 · 이석중 · 한병회*

충남대학교 자연과학대학 화학과

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Direct Synthesis of Symmetric Ethers from Carbonyl Compounds Using SbI₃/PhSiH₃

Ji Yoen Baek, Suk Joong Lee, and Byung Hee Han*

Department of Chemistry, College of Natural Sciences, Chungnam National University, Taejon, 305-764, Korea

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INTRODUCTION

The formation of carbon-oxygen single bond is one of the oldest and most widely used functional group transformation in organic synthesis. The Williamson ether synthesis,[1] with its modification, still a most widely used method, predates Wurtz's report by 6 years.[2] Other methods are ZnCl₂,[3] Ni/silica,[4] Pd/C,[5] Wilkinson catalyst,[6] trialkylsilane/liquid acids (CF₃COOH,[7] BF₃-OEt₂,[8] CF₃SO₃H[9]), Al-Mont.,[10] Fe-Mont.[11] CF₃SO₃Si(CH₃)₃/Et₃SiH,[12] BiX₃ (Cl, Br)/Et₃SiH,[13] trityl perchlorate,[14] hydrosilane on solid acid and base,[15] electolytic process,[16] have been known as reagents for the ether syntheses from carbonyl compounds. We recently described the preparation of organosilane by hydrosilylation of olefin with alkylsilane such as phenylsilane, methylphenylsilane and methyloctylsilane.[17]

During the development of new hydrosilylation catalyst for the reaction of an alkylsilane with carbonyl compounds using various metal halides as a catalytic system, we observed that dialkyl ether was formed from the corresponding carbonyls instead of silyl ether using antimony (III) iodide. In this communication, we now report the direct synthesis of symmetric ethers from carbonyl compounds using antimony (III) iodide/phenylsilane.

RESULTS AND DISCUSSION

The results of dialkyl ether formation from aldehydes and ketones using antimony (III) iodide/phenylsilane are summarized in *Table* 1. Moderate yields with mild reaction condition are observed in most cases. In a general procedure, aldehyde (1 mmol), antimony (III) iodide (1 mmol) and phenylsilane (1.1 mmol) were added in dry tetrahydrofuran (5 ml). The reaction mixture was stirred under a nitrogen atmosphere for 1 hr. The work-up procedure was very simple. After the reaction, the solvent was evaporated. The residue was chromatographed on a short column of silicagel to give the corresponding dialkyl ethers (*Table* 1). Our yields are based on quantities obtained after this step. Each product was characterized by comparison of their IR, NMR and Mass spectra with those of authentic samples. Aldehydes, such as pentanal, nonanal and benzaldehyde gave the corresponding di-*n*-hexyl ether, di-*n*-nonyl ether and diphenyl ether in 34, 56 and 67% isolated yields respectively (entry

Table 1. A PhSiH₃ / SbI₃ promoted reduction of aldehydes and ketones to symmetric ether[a]

Entry	Carbonyl Compounds	Symmetric ethers	Isolation Yield (%)
1	$CH_3(CH_2)_4CH$ (O)	$CH_3(CH_2)_5O(CH)_5CH_3$	34
2	$CH_3(CH_2)_8CH$ (O)	$CH_3(CH_2)_9O(CH)_9CH_3$	56
3	ph—C(O)—H	Ph⌒O⌒Ph	67
4	ph⌒C(O)—H	Ph⌒⌒O⌒⌒Ph	92
5	cyclopentanone (O)	(cyclopentyl)–O–(cyclopentyl)	96
6	cyclohexanone (O)	(cyclohexyl)·O·(cyclohexyl)	97
7	cycloheptanone (O)	(cycloheptyl)–O–(cycloheptyl)	72
8	4-tert-butylcyclohexanone (O), $C(CH_3)_3$	$(H_3C)_3C$–(cyclohexyl)–O–(cyclohexyl)–$C(CH_3)_3$	58

[a]Reactions were run 1 mmol of carbonyl compound, 1 mmol of SbI₃, 1.1 mmol of PhSiH₃ in 5 ml of THF for 1 hr under the nitrogen gas

1-3). We have examined this catalytic activity to cyclic ketones. As expected, using SbI₃/PhSiH₃, the corresponding symmetric ethers were formed in moderate yields under the same reaction conditions (entry 5-8). However, in case of *trans*-cinnamaldehyde, hydrogenated diphenethyl ether was formed (entry 4). This result is rather not surprising, because phenylsilane has been known as a hydrogen source for hydrogenation reaction.[18]

Unfortunately, ketones such as acetone or acetophenone did not give the corresponding dialkyl ethers. For example, when acetophenone (1 mmol) was treated with a mixture of antimony iodide (1 mmol) and phenylsilane (1.1 mmol) in dry tetrahydrofuran (5 mL) and stirred under nitrogen for 1 hr, acetophenone was recovered. But, phenylsilane was disappeared completely and some unidentified polymeric materials were appeared probably by the polymerization of phenylsilane (by GLC).

We have also examined the catalytic activities of other metal halides with phenylsilane for the formation of dibenzyl ether from benzaldehyde. We found that using metal halides (such as NiI₂, NiCl₂, NiBr₂, TiI₄, MnCl₂, or MnI₂) and PhSiH₃ under the same reaction condition, dibenzyl ether was formed only 5-40% (40% - NiI₂; 35% - NiBr₂; 18% - NiCl₂; 18-5%; TiI₄, MnCl₂, or MnI₂) along with unidentified by product by GLC. Heat to reflux or longer reaction time did not improve the yields. Phenylsilane was the best choice of silane as a hydrogen source for this investigation. For example, when benzaldehyde (1 mmol) was treated with antimony iodide (1 mmol) and methylphenylsilane (2 mmol) in dry tetrahydrofuran (5 mL) and stirred under nitrogen for 1 hr, only 20% of dibenzyl ether was formed and most of benzaldehyde was recovered even when methylphenylsilane was disappeared completely.

But some unidentified polymeric materials appeared presumably from the polymerized methylphenylsilane (by GLC).[19]

For the sake of mechanistic study, a reaction mixture of benzaldehyde (1 mmol), antimony iodide (1

mmol) and phenylsilane (1.1 mmol) in THF (5 mL) was monitored using gas chromatography to measure the disappearance of benzaldehyde and the appearance of dibenzyl ether along with others. We assumed that the corresponding alcohol could be formed as a transient intermediate.

Small aliquots of the reaction mixture were removed at appropriate time intervals (20 minutes), quenched in water, and extracted with methylenechloride, the organic solution was analyzed.

We found that benzyl alcohol was detected (> 5-10%) through the reactions. The results of such studies show that the dibenzyl ether could be formed via benzyl alcohol.

The concentration of dibenzyl ether increases gradually from the initial period as the benzyl alcohol concentration increases. The concentration of benzaldehyde is dropped to zero after 1hr when the concentration of dibenzyl ether reaches its maximum. In particular, benzyl alcohol appears in a small quantity (>5-10%) which suggests that dibenzyl ether may arise from the benzyl alcohol. Phenylsilane was disappeared completely.

Some unidentified polymeric materials (possibly from phenylsilane) were detected. We examined the possible formation of dibenzyl ether from the corresponding benzyl alcohol formation. Surprisingly, using SbI$_3$/PhSiH$_3$ under the same reaction condition, benzyl alcohol it self did not give the dibenzyl ether and neither the benzyloxyphenylsilane at all.[20] We also examined the formation of dibenzyl ether from the benzyl alcohol and benzaldehyde using SbI$_3$/PhSiH$_3$ under the same reaction condition. However, yields were dropped to 30% along with unreacted starting materials (by GLC).

We also attempted the preparation of asymmetric ether by the reaction of benzaldehyde and cyclohexanone using SbI$_3$/PhSiH$_3$ under the same reaction condition. However, the desired asymmetric ether such as benzyl cyclohexylether was only formed in minor product (less than 5%) and also yields of the corresponding symmetric ethers dropped to about 20% (dibenzyl ether : 15% and dicyclohexyl ether : 5%). The rest of starting material was remained by GLC analysis.

We also attempted to prepare the asymmetric dialkyl ether using butanal and hexanal under the same reaction conditions. But the asymmetric butylhexyl ether was formed 30% together with symmetric ether (29% of dibutyl ether and 20% of dihexylether)..

We found that symmetric dibenzyl ether was formed selectively in 72% isolated yield from a mixture of acetophenone and benzaldehyde under the same reaction condition. In this experiment, acetophenone was recovered quantitatively without formation the corresponding asymmetric ether. Similar result was obtained from the reaction of a mixture of 3-pentanone and cyclopentanone. Symmetric dicyclopentyl ether was formed in 90% isolated yield without forming the corresponding asymmetric ether and 3-pentanone was recovered.

We are presently investigating the reduction of nitro group along with hydrogenation of olefins with SbI$_3$/PhSiH$_3$. The origin of the variation in scope and limitation of reactivity of the antimony (III)iodide/phenylsilane catalytic system to other organic functional group transformation as well as a mechanistic study will be discussed in more details in a subsequent paper.

Experimental Section

Materials. SbI$_3$ and phenylsilane were prepared by the standard method. Carbonyl compounds was purchased from Aldrich and used without further purification. Tetrahydrofuran (THF) was distilled under nitrogen from sodium/benzophenone ketyl just prior to use. Phenylsilane was prepared by the reduction of the trichlorophenylsilane with lithium aluminum hydride in dry diethylether.

General Methods. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian Inova 400 spectrometer at 400 and 100MHz. respectively. Chemical shifts were reported in ppm downfield from tetramethylsilane, and chloroform-d was used as the solvent. Two-dimensional NMR: HETCOR (^{1}H-^{13}C) and NOESY (^{1}H-^{1}H) spectra were obtained using an Inova 400 spectrometer. Mass spectra (70 eV electron impact) were taken on a Finnigan 4510 instrument equipped with a Finnigan-incos data

system. IR spectra were recorded on a Jasco Report-100 spectrophotometer.

Analytical gas chromatography (GLC) were carried out on a Varian 3300 Model equipped with a FID detector and stainless steel column packed with 10% OV-101, Chromosob W HP 80/100 (2m × 1/8 in). Column chromatography was performed on Merck silica gel 60(70-230 mesh). Thin layer chromatography was carried out on silica gel plate (E. Merck, 60, No. 5539). Melting point was determined with an Electrothermal apparatus and was uncorrected.

General procedure for the ether formation from carbonyl compounds using antimony (III) iodide/ phenylsilane.

To a dry reaction vessel equipped with a magnetic stirring bar was charged with SbI$_3$ 1mmol (0.502 g), carbonyl compounds (1 mmol) and freshly distilled THF (5 ml). Phenylsilane (1.1 mmol) were added dropwise. The reaction mixture was stirred for one hour under the nitrogen atmosphere. The progress of the reaction was monitored by GLC. After the reaction was completed, tetrahydrofuran was evaporated and a mixture of solvent (dichloromethane: hexane, v/v, 1:1) were added. The solution was filtered to remove the catalyst through a pad of silica gel column (1cm diameter x 6cm packed) using n-hexane:dichloromethane (1:1, v/v) as an eluent. The products were isolated by column chromatography using either hexane/ethylacetate (30:1, v/v) or hexane/chloroform (1:1, v/v) as an eluent. All products were identified by GC/MS, IR and NMR analysis.

Dihexyl ether
Yields (%): 34%
^{1}H-NMR (CDCl$_3$): δ 3.3 (t, 4H, OCH$_2$), 1.6 (m, 14H, (CH$_2$)$_4$), 0.9 (t, 6H, CH$_3$)
GC/MS (m/e): No parent M+, 186 (M+-4, 11), 100 (64), 82 (40), 55 (100), 41 (70)
FT-IR (NaCl, cm^{-1}): 1109 (C-O)

Didecyl ether
Yields (%): 56%
^{1}H-NMR(CDCl$_3$): δ 3.3 (t, 4H, OCH$_2$), 1.2(s,

14H, (CH$_2$)$_8$), 0.9 (t, 6H, CH$_3$)
GC/MS (m/e): 298 (M+, 1.8), 140 (9.4), 71 (58), 43 (100)
FT-IR (NaCl, cm^{-1}): 1112 (C-O)

Dibenzyl ether
Yields (%): 67%
^{1}H-NMR (CDCl$_3$): δ 7.3 (s, 10H, C$_6$H$_5$), 4.5 (s, 4H ,OCH$_2$)
GC/MS (m/e): No parent M+, 187 (M+-11), 85 (57), 56 (56), 43 (100)
FT-IR (NaCl, cm^{-1}): 1090 (C-O)

Bis (3-phenyl-1-propyl) ether
Yields (%) : 92%
^{1}H-NMR (CDCl$_3$): δ 7.18 (s, 10H, C$_6$H$_5$), 3.3 (t, 4H, OCH$_2$), 2.05-1.78 (m, 4H, CH$_2$)
GC/MS (m/e): 254 (M+, 2), 118 (100), 91 (83), 65 (17)
FT-IR (NaCl, cm^{-1}): 1115 (C-O)

Dicyclopentyl ether
Yields (%): 96%
^{1}H-NMR (CDCl$_3$) : δ 3.94 (m, 1H, OCH), 3.4-3.1 (dt, 1H, OCH), 1.9-0.9(m, 16H, (CH$_2$)$_4$)
GC/MS (m/e): 154 (M+, 75), 85 (47), 41 (100)
FT-IR (NaCl, cm^{-1}): 1098 (C-O)

Dicyclohexyl ether
Yields (%): 97%
^{1}H-NMR (CDCl$_3$): δ 3.32 (br, 2H, OCH), 1.9-0.9 (m, 20H, (CH$_2$)$_5$)
GC/MS (m/e): 182 (M+, 11), 100 (62), 55 (100), 41 (70)
FT-IR (NaCl, cm^{-1}): 1090 (C-O)

Dicycloheptyl ether
Yields (%): 72%
^{1}H-NMR (CDCl$_3$): δ 3.32 (m, 2H, OCH), 1.9-0.9 (m, 24H, (CH$_2$)$_6$)
GC/MS (m/e): 210 (M+, 2), 114 (19), 55 (100), 41 (40)
FT-IR (NaCl, cm^{-1}): 1074 (C-O)

Bis (4-t-butylcyclohexyl) ether

Yields (%): 58%

(*a,a*)-Bis (4-t-butylcyclohexyl)ether (49%) and (*a,e*)-Bis (4-t-butylcyclohexyl) ether (51%) (*a,a*)-Bis (4-t-butylcyclohexyl) ether

^{1}H-NMR (CDCl$_3$): δ 3.5 (m, 2H, OC$\underline{H}$), 1.8 (m 8H, C$\underline{H}_2$), 0.8 (m, 9H, C(C$\underline{H}_3$)$_3$)

GC/MS (*m/e*): 294 (M+, 4), 237 (2), 138 (21), 57 (100)

FT-IR (NaCl, cm^{-1}): 1109 (C-O).

REFERENCES

1. (a) Williamson, A. W. *J. Chem. Soc.*, 4. **1851**, *106*, 229; 7. **1854**, *109*, 122 and typical methods, see: Duffy, I. *J. Chem. Soc.*, **1960**, *545*, 853; Barnett, O. *J. Chem. Soc., Chem. Commun.* **1972**, 525; Barnett, O. *J. Chem. Soc., Perkin Trans.* **1972**, *2*, 2378.

2. (a) Wurtz, A. *Ann Chem.* **1856**, *46*, 222. (b) March, J. *Advanced Organic Chemistry, Reactions, Mechanisms and Structure*, 2nd ed.: McGraw-Hill Book Company: NY. **1978**; pp 357-358 and references therein.

3. Kim, S.G., Chung, K.N., Yang, S.B. *J. Org. Chem.*, **1987**, *52*, 3917.

4. Kraus, L.S. *Diss. Abstr. Int. B.* **1990**, *50*, 3596.

5. Bethmont, V.; Fache, F.; Lemaire M.,*Tetrahedron Lett.*, **1995**, *36*, 4235.

6. (a) Review: Weber W. P. *Silicon Reagents for Organic Synthesis* Springer-Verlag, Berlin **1983**, Chap. 18. 288-297; (b) Ojima I.; Nihonyanagi M.; Nagai M. *J. Chem. Soc., Chem., Commun.*, **1972**, 938.

7. (a) Doyle, M.P.; Debruyn, D.J.; Donnelly, S.J.; Koistra, D.A.; Odubela, A.A.; West, C.T.; Zonnebelt, S.M. *J. Org. Chem.*, **1974**, *39*, 2740; (b) Doyle, M.P. *J. Org. Chem.*, **1975**, *40*, 3821. (c) Kursanov, D.N.; Parnes, Z.N.; Loim, N.M. *Synthesis*, **1974**, 633.

8. Doyle, M.P.; Doyle, M.P.; Donelly, S.J.; Mcosker, C.C., *J. Oganomet. Chem.*, **1976**, *117*, 129.

9. (a) Tomihiro, N.; Hideaki, K.; Hideki, M.; Kouhei, W. Canadian J. Chem. **1999**, *77*(2), 258. (b) Olah, G.A.; Arvanaghi, M.; Ohannesian, L. *Synthesis*, **1986**, 770.

10. (a) Kawai, M.; Onaka, M.; Izumi, Y. *Chem Lett.*, **1986**, 381. (b) Onaka, M.; Ohno, R.; Kawai, M.; Izumi, Y. *Bull. Chem. Soc. Jpn.*, **1987**, *60*, 2689. (c) Kawai, M.; Onaka, M.; Izumi, Y. *Bull. Chem. Soc. Jpn.*, **1988**, *61*, 1237. (d) Kawai, M.; Onaka, M.; Izumi, Y. *Bull. Chem. Soc. Jpn.*, **1988**, *61*, 2157.

11. (a) Kawai, M.; Onaka, M.; Izumi, Y. *Tetrahedron lett.*, **1989**, *30*, 6341. (b) Onaka, M.; Ohno, R.; Izumi, Y. *Synlett*, **1993**, 141.

12. (a) Sassaman, M.B.; Kotian, K.D.; Prakash, G.K.S.; Olah, G.A. *J. Org.Chem.* **1987**, *52*, 4314. (b) Noyori, R.; Murata, S.; Suzuki, M. *Tetrahedron.* **1981**, *37*, 3899.

13. (a) Makoto, W.; Sonoe, N.; Kaori, M.; Ryoichi, H.; Norikazu, M. *Chemistry Lett.* **2002**, *2*, 248. (b) Komatsu, N.; Ishida, J. Y.; Suzuki, H. *Tetrahedron Lett.* **1997**, *38*(41), 7219.

14. Kato, J.I.; Iwasawa, N.; Kukaiyama, T. *Chemistry Lett.* **1985**, *6*, 743.

15. Makoto, O.; Katsumi, H.; Hiroyuki, N.; Yusuke, I. *Bull. Chem. Soc. Jpn.* **1993**, *66*(9), 2638.

16. Shigeru, T.; Tsutomu, I.; Sadato, T.; Minoru, K. Jpn Kokai Tokkyo 1988, 5. Coden: JKXXAF JP 63047387 A2 19880229. Showa, Patent Application: JP 86-191284 19860814. CAN 109:118232.

17. (a) Lee, S.J.; Park, M.K.; Han, B.H. *Silicon Chemistry*, **2002**, *1*, 41. (b) Lee, S.J.; Han, B.H.*Main Group Metal Chemistry*, **1998**, *21*(6), 315.

18. Boudjouk, P.; Choi, S.B.; Hauck, B.J.; Rajkumar, A.B. *Tetrahedron Lett.* **1988**, *39*(23), 3951.

19. Park, M.J.; Lee, S.J.; Park, M.K.; Han, B.H. *Bull. Kor. Chem. Soc.*, **2000**, *21*(3), 336.

20. *Alkoxysilane from carbonyls with alkylsilanes see*: (a) Sakurai, H.; Miyoshi, K.; Nakadaira, Y. *Tetrahedron Lett.* **1977**, *31*, 2671. (b) Ojima, I.; Donovan, R.J. Clos. N. *Organometallics*, **1991**, *10*, 2606.