Trimethylsilyl Triflate Mediated New Carbon–Carbon Bond Forming Reactions between Benzyl Diphenylphosphinates and Organosilicon Compounds

Yohei Kobashi,[†,††] Tomofumi Minowa,[†,††] and Teruaki Mukaiyama*[†,††]
[†]*Center for Basic Research, The Kitasato Institute (TCI), 6-15-5 Toshima, Kita-ku, Tokyo 114-0003*
[††]*Kitasato Institute for Life Sciences, Kitasato University, 5-9-1 Shirokane, Minato-ku, Tokyo 108-8641*

(Received February 24, 2005; CL-050234)

The trimethylsilyl triflate mediated reaction of benzyl diphenylphosphinate with allyltrimethylsilane or trimethylsilyl enolate afforded the corresponding cross-coupling products in good yields.

A carbon–carbon bond forming reaction by using Lewis acid promoters is one of the important tools for the syntheses of complex organic compounds and many examples have been reported;[1] for example, an allylation of an electrophile by using allyltrimethylsilane in the presence of a Lewis acid, the Sakurai–Hosomi reaction, gives the corresponding product in high yield.[1c,1d] On the other hand, allylations at sp^3-carbon by promotion of a Lewis acid is known to be quite difficult[2] and few examples have been reported with some limitations.[3]

Recently, etherification reactions between alkyl diphenylphosphinate and alkoxytrimethylsilanes in the presence of trimethylsilyl triflate (TMSOTf) was reported from our group.[4] This reaction proceeded efficiently because of the strong affinity of alkyl diphenylphosphinate toward TMSOTf and a highly electrophilic property of the phosphonium salt intermediate. Then, a carbon–carbon bond forming reaction between alkyl diphenylphosphinate and carbon nucleophiles was planned in order to extend this unique properties.

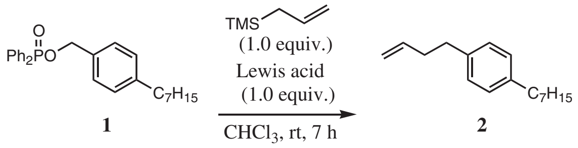
In this communication, we would like to report an efficient method for carbon–carbon bond forming reaction between benzyl diphenylphosphinate and various electrophiles in the presence of TMSOTf.

In the first place, allylations of 4-*n*-heptylbenzyl diphenylphosphinate[5] (**1**) with allyltrimethylsilane were tried in the presence of various Lewis acids in chloroform at room temperature (Table 1). When $TiCl_4$, $SnCl_4$, $AlCl_3$, or $MgBr_2OEt_2$ was used, the corresponding 4-*n*-heptylbenzyl halide was afforded in moderate to high yields (Table 1, Entry 1–4). No reaction took place when other Lewis acids including BF_3OEt_2, $LiClO_4$, $LiBF_4$, and various metal triflates were used (Table 1, Entries 5–17). On the other hand, the use of trialkylsilyl triflate effectively promoted the reaction and the desired **2** was afforded in moderate yields (Table 1, Entries 18–21). It is noted that a higher yield of **2** was attained effectively by increasing the amount of allyltrimethylsilane (Table 1, Entry 22)

Next, carbon–carbon bond forming reactions between benzyl diphenylphosphinates and organosilicon compounds were tried in the presence of TMSOTf. When allyltrimethylsilane (**7**) was used as an allylation reagent, 1,2-dimethoxyethane was found to be the most effective solvent and **2** was obtained in 77% yield (Table 2, Entry 2). Similarly, (2-methylallyl)trimethylsilane (**8**), (3,3-dimethylallyl)trimethylsilane (**9**), and (3-chloroallyl)trimethylsilane (**10**) reacted with **1** in chloroform to afford the corresponding cross-coupling products in 72–83% yields (Table 2, Entries 3–5).[6] 4-Phenylbenzyl diphenylphosphinate (**3**) also reacted with **9** at 0 °C in chloroform (Table 2, Entry 6). However, 4-methoxycarbonylbenzyl diphenylphosphinate (**4**) having an electron-withdrawing group at C-4 position reacted with **9** at the refluxing temperature to afford the cross-coupling products in good yields (Table 2, Entries 7–8). When chiral phosphinate **5** was used, the corresponding racemic product was obtained, and the result indicates that this reaction proceeded via S_N1 mechanism (Table 2, Entry 9). In the case when 3,3-diphenylpropyl diphenylphosphinate (**6**), a non-benzylic substrate, was used, the corresponding β-elimination product **14** was formed in 56% yield (Table 2, Entry 10). Trimethylsilyl enolates **11**–**13** also worked as useful nucleophiles of this reaction and the corresponding cross-coupling compounds were afforded in good yields (Table 2, Entries 11–13).

The typical experimental procedure is described for the reaction of **1**[7] and **9** (Table 1, Entry 3): to a stirred mixture of **1** (81.3 mg, 0.20 mmol) and **9** (42.7 mg, 0.30 mmol) in chloroform (1 mL) was added trimethylsilyl triflate (36.1 µL, 0.20 mmol) at 0 °C. The mixture was stirred for 1 h at 0 °C and then quenched with sat. $NaHCO_3$. After the resulting mixture was extracted

Table 1. Reactions of 4-*n*-heptylbenzyl diphenylphosphinate (**1**) and allyltrimethylsilane in the presence of various Lewis acids



Entry	Lewis acid	Yield/%	Entry	Lewis acid	Yield/%
1	$TiCl_4$	N.D.[a]	12	$Yb(OTf)_3$	N.D.
2	$SnCl_4$	N.D.[a]	13	$Cu(OTf)_2$	N.D.
3	$AlCl_3$	N.D.[a]	14	$Zn(OTf)_2$	N.D.
4	$MgBr_2OEt_2$	N.D.[b]	15	$Hf(OTf)_4$	N.D.
5	BF_3OEt_2	N.R.	16	$La(OTf)_3$	N.D.
6	$LiClO_4$	N.R.	17	$Gd(OTf)_3$	N.D.
7	$LiBF_4$	N.R.	18[c]	TESOTf	35
8	$Sn(OTf)_2$	N.D.	19[c]	TBDMSOTf	31
9	AgOTf	N.D.	20[c]	TIPSOTf	29
10[b]	$Mg(OTf)_2$	N.D.	21[c]	TMSOTf	36
11	$Sc(OTf)_3$	N.D.	22[c,d]	TMSOTf	59

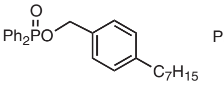
[a] 4-*n*-Heptylbenzyl chloride was obtained in moderate to high yields (Entry 1: 87%, Entry 2: 57%, Entry 3: 44%). [b] 4-*n*-Heptylbenzyl bromide was obtained in 88% yield. [c] The reaction was performed at 0 °C for 1 h. [d] 3.0 equiv. of allyltrimethylsilane was used.

Table 2. Reaction of alkyl diphenylphosphinate and organosilicon compounds in the presence of TMSOTf

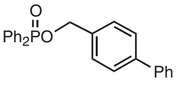
$$\underset{\text{(1.0 equiv.)}}{\mathbf{Ph_2P(=O)OR}} + \underset{\text{(3.0 equiv.)}}{\mathbf{R'TMS}} \xrightarrow[\text{CHCl}_3]{\text{TMSOTf (1.0 equiv.)}} \mathbf{R{-}R'}$$

Entry	$Ph_2P(=O)OR$	R′TMS	Temp	Time	Yield/%
1	**1**	**7**	0 °C	1 h	59
2[a]	**1**	**7**	0 °C	1 h	77
3	**1**	**8**	0 °C	1 h	76
4	**1**	**9**[c]	0 °C	1 h	83
5	**1**	**10**	0 °C	1 h	72
6	**3**	**9**[c]	0 °C	1 h	79
7	**4**	**7**	reflux	7 h	87
8	**4**	**9**[c]	40 °C	9 h	79
9	**5**	**7**	reflux	9 h	72
10[b]	**6**	**9**	reflux	11 h	N.D.[d]
11	**1**	**11**	0 °C	1 h	88
12	**1**	**12**	0 °C	1 h	91
13	**1**	**13**	0 °C	1 h	84

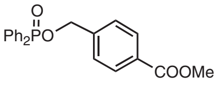
[a] The reaction was carried out in DME. [b] The reaction was carried out in 1,2-dichloropropane. [c] 1.5 equiv. of **R′TMS** was used. [d] 1,1-Diphenyl-2-propene (**14**) was obtained in 56% yield.



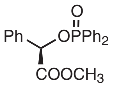
1



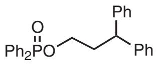
3



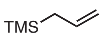
4



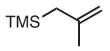
5



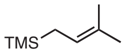
6



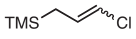
7



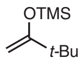
8



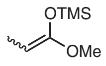
9



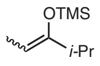
10



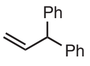
11



12



13



14

with dichloromethane, dried over $MgSO_4$ filtered and evaporated, it was purified by preparative TLC (silica gel, *n*-hexane) and the desired 1-(2,2-dimethylbut-3-enyl)-4-heptylbenzene (43.1 mg, 83%) was obtained as colorless oil.

Thus, carbon–carbon bond forming reactions between benzyl diphenylphosphinates and allyltrimethylsilanes or trimethylsilyl enolates successfully proceeded and the cross-coupling products were afforded in good yields. This method is the first successful result of allylation of a variety of primary benzylic compounds by the promotion of an acid. It is also noted that this method is quite practical one because benzyl diphenylphosphinates are prepared easily from the corresponding alcohols and diphenylchlorophosphinate often as white crystals in the presence of triethylamine. Further, diphenylphosphinic acid trimethylsilyl ester, a co-product, is easily separatd just by washing the reaction mixture with saturated $NaHCO_3$ solution.

This study was supported in part by the Grant of the 21st Century COE Program, Ministry of Education, Culture, Sports, Science and Technology (MEXT), Japan.

References and Notes

1. Reviews: a) H. Yamamoto, “Lewis Acids in Organic Synthesis,” WILEY-VCH, Weinheim (2000). b) A. D. Dilman and S. L. Ioffe, *Chem. Rev.*, **103**, 733 (2003). c) H. Sakurai, *Pure Appl. Chem.*, **54**, 1 (1982). d) A. Hosomi, *Acc. Chem. Res.*, **21**, 200 (1988).
2. A. Hosomi, T. Imai, M. Endo, and H. Sakurai, *J. Organomet. Chem.*, **285**, 95 (1985).
3. a) J. A. Cella, *J. Org. Chem.*, **47**, 2125 (1982). b) T. Yokozawa, K. Furuhashi, and H. Natsume, *Tetrahedron Lett.*, **36**, 5243 (1995). c) G. Kaur, M. Kaushik, and S. Trehan, *Tetrahedron Lett.*, **38**, 2521 (1997). d) M. Murakami, T. Kato, and T. Mukaiyama, *Chem. Lett.*, **1987**, 1167. e) K. Chiba, R. Uchiyama, S. Kim, Y. Kitano, and M. Tada, *Org. Lett.*, **3**, 1245 (2001).
4. Y. Kobashi, T. Minowa, and T. Mukaiyama, *Chem. Lett.*, **33**, 1326 (2004).
5. It is difficult to use benzyl diphenylphosphinate, a simpler benzyl derivative, because the products are often volatile.
6. Allyltrimethylsilane derivatives react with benzyl diphenylphosphinates at its γ-position because thus formed carbocation intermediate is stabilized by hyperconjugation of β-silicon atom.
7. Benzyl diphenylphosphinate was prepared according to the reported procedure and purified by silica gel chromatography. K. Goda, R. Okazaki, K. Akiba, and N. Inamoto, *Bull. Chem. Soc. Jpn.*, **51**, 260 (1978).

Published on the web (Advance View) April 30, 2005; DOI 10.1246/cl.2005.756