Oxidative Coupling of Carbonyl Compounds by Using Pentavalent Biphenyl-2,2′-ylenebismuth Reagents

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p-Tolylbiphenyl-2,2′-ylenebismuth bis(trifluoromethanesulfonate) reacted with lithium enolates derived from ketones, carboxylic esters, and thioesters to afford the corresponding oxidative coupling products in good to high yields.

Because of the unique chemical behaviors of organobismuth compounds, a number of interesting reports on oxidation, phenylation, and other organic reactions are being published.[1] Generally, bismuth compounds are known to exist exclusively in two oxidation states, namely, (III) and (V), and most of their reactions were carried out by utilizing the oxidation properties of bismuth(V) compounds that were converted to organobismuth(III). It was reported from our laboratory that both functionalized and simple tertialy alcohols smoothly underwent O-phenylation to afford sterically hindered tertialy-alkyl aryl ether by using powerful oxidation properties of bismuth(V) compounds such as fluorotetraphenylbismuth.[2] In the present communication, the synthesis of *p*-tolylbiphenyl-2,2′-ylenebismuth bis(trifluoromethanesulfonate) and its application to the oxidative coupling of carbonyl compounds are described.

The synthesis of 1,4-dicarbonyl compounds has attracted interests of many chemists because these compounds are utilized as useful intermediates for the synthesis of thienyl, pyrrol, or furyl heterocycles.[3] The method for the synthesis of 1,4-dicarbonyl compounds is generally classified into the following three categories: 1) addition reaction of lithium, magnesium and stannyl enolates to the α-halogenated carbonyl compounds,[4] 2) direct oxidation of silyl enolates,[5] 3) oxidative coupling of copper, silver, iron, and manganese(III) enolates.[6] The oxidative coupling reactions are conveniently used because no preparation of silyl enolates or α-halogenated carbonyl compounds in advance is needed. Although there are synthesis of (2-oxoalkyl)-triarylbismuthonium salts and their addition reactions with alcohols and amines reported by Suzuki et al., there have been no reports on the oxidative coupling of carbonyl compounds that promoted by bismuth reagents.[7]

The coupling product and organobismuth(III) are thought to be obtained by a reductive elimination of bismuth(V) after ligand exchanges of the bismuth(V) reagents with lithium enolates (Figure 1). If two oxoalkyl groups of intermediate **1** that is prepared from triarylbismuth dichloride and lithium enolates occupied two axial positions, an approach of the two oxoalkyl groups would be prevented. The bismuth(V) reagent having a trigonal bipyramidal structure such as triphenylbismuth dichloride would not show high reactivity toward oxidative coupling because the phenyl groups located in equatrial positions and the chlorine occupied axial positions.[8] In the case of the cyclic biphenylyl derivative, on the other hands, Fedorov and Finet suggested that one phenyl group of the biphenylyl group formed an equatorial bond to bismuth and another one lay in the apical position.[9] Therefore, it was assumed that one of the oxoalkyl groups was blocked at the unfavorable axial positions when the cyclic biphenylyl bismuth derivatives were used, and the coupling reaction of oxioalkyl groups would proceed smoothly.

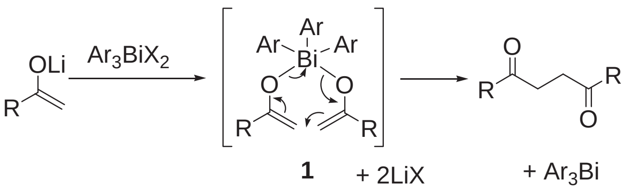
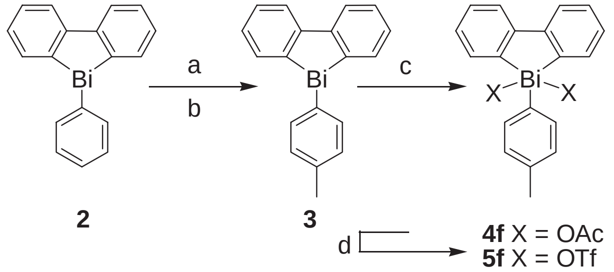


Figure 1. A plausible reaction pathways.

The reactivity of triarylbismuth dichloride was examined by taking the coupling reactions of lithium enolates as a model. The reaction of triphenylbismuth dichloride with lithium enolates generated from acetophenone and LHMDS afforded the coupling products in only 12% yield in THF at 0 °C. By comparison, the coupling products were obtained in 33% yield in the same solvent at −45 °C when the cyclic bismuth **5b** was used.

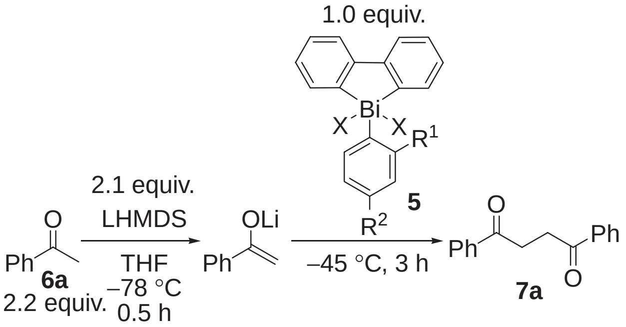
Next, a series of new cyclic biphenylyl derivatives was prepared, and the preparation of *p*-tolylbiphenyl-2,2′-ylenebismuth bis(trifluoromethanesulfonate) (**5f**) was shown in Scheme 1 as a typical example. According to the same procedure, other cyclic bismuth compounds were similarly synthesized just by changing the substituents on the Grignard reagents. Then, effects of counter ions on the bismuth reagents as well as those of electron-donating and electron-withdrawing groups on the aryl derivatives were investigated (Table 1).

The coupling reactions were promoted more effectively when the cyclic bismuth reagents having more labile counter ions were used (Entries 1–4). In contrast, aryl substituents having trifluoromethyl, methoxy and 2-methyl groups were not effective (Entries 5, 7, and 8). It is noted then, that the desired



Scheme 1. (a) I_2, THF, rt, 1 h; (b) *p*-$CH_3C_6H_4$-MgBr, THF, rt, 12 h, 68%; (c) CH_3CO_3H, CH_3CO_2H, THF, CH_2Cl_2, 0 °C, 0.5 h, 89%; (d) TfOH, CH_2Cl_2, −78 °C, 3 h, 84%.

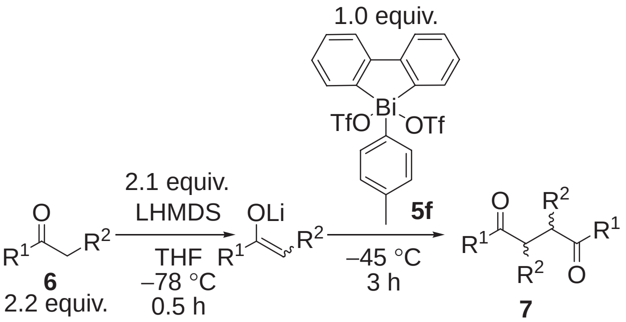
Table 1. Dimerization of lithium enolates of acetophenone by using bismuth(V) compounds

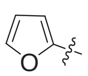
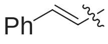


Entry		R^1	R^2	X	Yield/%[a]
1	**5a**	H	H	OAc	21
2	**5b**	H	H	Cl	33
3	**5c**	H	H	OTs	55
4	**5d**	H	H	OTf	78
5	**5e**	H	CF_3	OTf	63
6	**5f**	**H**	**CH_3**	**OTf**	**88**
7	**5g**	CH_3	H	OTf	73
8	**5h**	H	OMe	OTf	68

[a]Based on the bismuth(V) compounds.

Table 2. Dimerization of lithium enolates of carbonyl compounds using cyclic bismuth **5f**



Entry		R^1	R^2	Product	Yield/%[a]
1	**6b**	4-MeO–C_6H_4	H	**7b**	84
2	**6c**	4-Cl–C_6H_4	H	**7c**	81
3	**6d**		H	**7d**	90
4	**6e**		H	**7e**	88
5[b]	**6f**	Ph	Me	**7f**	67
6[b]	**6g**	OBn	H	**7g**	68
7	**6h**	SPh	H	**7h**	87

[a]Based on the cyclic bismuth **5f**. [b]3.0 equivalent of starting carbonyl compounds and LHMDS was used.

1,4-diketone was obtained in high yield when biphenylyl bismuth containing 4-methyl group on the aryl substituent was used (Entry 6).

The results of a dimerization of lithium enolates derived from ketones and carboxylic esters with cyclic biphenylyl bismuth **5f** were summarized in Table 2. The oxidative coupling of thioesters also proceeded smoothly under the same conditions, and the corresponding coupling product was obtained in high yield (Entry 7). Thus, a direct oxidative coupling of lithium enolates generated from thioester was accomplished.

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References

1 H. Suzuki, T. Ogawa, N. Komatsu, Y. Matano, T. Murafuji, T. Ikegami, in *Organobismuth Chemistry*, ed. by H. Suzuki, Y. Matano, Elsevier, Amsterdam, **2001**.
2 a) K. Ikegai, K. Fukumoto, T. Mukaiyama, *Chem. Lett.* **2006**, *35*, 612. b) T. Mukaiyama, N. Sakurai, K. Ikegai, *Chem. Lett.* **2006**, *35*, 1140. c) N. Sakurai, K. Ikegai, T. Mukaiyama, *ARKIVOC* **2007**, *7*, 254.
3 a) E. Baltazzi, L. I. Krimen, *Chem. Rev.* **1963**, *63*, 511. b) P. Bosshard, C. H. Eugster, *Adv. Heterocycl. Chem.* **1966**, *7*, 384. c) W. C. Christopfel, L. Miller, *J. Org. Chem.* **1986**, *51*, 4169. d) R. A. Ellison, *Synthesis* **1973**, 397. e) K. Oshima, H. Yamamoto, H. Nozaki, *J. Am. Chem. Soc.* **1973**, *95*, 4446.
4 a) M. Yasuda, S. Tsuji, Y. Shigeyoshi, A. Baba, *J. Am. Chem. Soc.* **2002**, *124*, 7440. b) B. C. Ranu, P. Dutta, A. Sarkar, *Tetrahedron Lett.* **1998**, *39*, 9557.
5 a) R. M. Moriarty, R. Penmasta, I. Prakash, *Tetrahedron Lett.* **1987**, *28*, 873. b) R. Moriarty, O. Prakash, M. Duncan, *J. Chem. Soc., Perkin Trans. 1* **1987**, 559.
6 a) Y. Ito, T. Konoike, T. Harada, T. Saegusa, *J. Am. Chem. Soc.* **1977**, *99*, 1487. b) Y. Ito, T. Konoike, T. Saegusa, *J. Am. Chem. Soc.* **1975**, *97*, 649. c) R. H. Frazier, Jr., R. L. Harlow, *J. Org. Chem.* **1980**, *45*, 5408. d) R. M. Dessau, E. I. Heiba, *J. Org. Chem.* **1974**, *39*, 3457.
7 Y. Matano, N. Azuma, H. Suzuki, *J. Chem. Soc., Perkin Trans. 1* **1994**, 1739.
8 R. A. Shaw, B. C. Smith, C. P. Thakur, *Chem. Commun.* **1966**, 228.
9 A. Y. Fedorov, J. P. Finet, *J. Chem. Soc., Perkin Trans. 1* **2000**, 3775.