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# Palladium Complex-Catalyzed Cross-Coupling Reaction of Organobismuth Dialkoxides with Triflates

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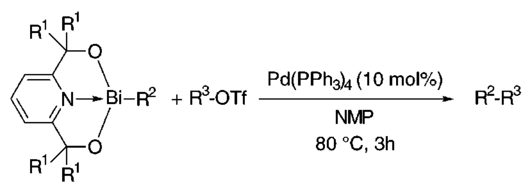
**ABSTRACT**




**Pd(PPh$_3$)$_4$ catalyzes cross-coupling reaction between organobismuth alkoxides and aryl and vinyl triflates.**

Use of heteroatom compounds in organic synthesis is a rapidly growing area of research. Our successful development of transition metal-catalyzed reactions of heteroatom compounds[1] has led us to scrutinize organobismuth compounds, since bismuth is one of the least used elements in organic synthesis. Although the unique performance of bismuth salts as Lewis acid catalysts or reagents is becoming evident,[2] the application of organobismuth reagents in organic synthesis is still very limited.[3,4] Organobismuth compounds are normally nontoxic and potentially meet the recent requirement for the reagent, process, and product of little or no risk to humans and environment, which is a major contemporary concern in the chemistry community.[5] It is in this respect that we became interested in the opportunity for use of bismuth reagents in organic synthesis. Recently we prepared new organobismuth dialkoxides, **1a−1d**.[6] We report herein

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(2) Recent examples: Komatsu, N.; Uda, M.; Suzuki, H. *Chem. Lett.* **1997**, 1229. Wada, M.; Takahashi, T.; Domae, T.; Fukuma, T.; Miyoshi, N.; Smith, K. *Tetrahedron: Asymmetry* **1997**, *8*, 3939. Shen, Z.; Zhang, J. Q.; Zou, H. X.; Yang, M. M. *Tetrahedron Lett*. **1997**, *38*, 2733. Le Boisselier, V.; Postel, M.; Duñach, E. *Tetrahedron Lett.* **1997**, *38*, 2981. Komatsu, N.; Uda, M.; Suzuki, H.; Takahashi, T.; Domae, T.; Wada, M. *Tetrahedron Lett.* **1997**, *38*, 7215. Komatsu, N.; Ishida, J.; Suzuki, H. *Tetrahedron Lett.* **1997**, *38*, 7219. Wada, M.; Fukuma, T.; Miyoshi, N. *Tetrahedron Lett.* **1997**, *38*, 8045. Desmurs, J. R.; Labrouillere, M.; Le Roux, C.; Gaspard, H.; Laporterie, A.; Dubac, J. *Tetrahedron Lett*. **1997**, *38*, 8871. Ren, P. D.; Shao, D.; Dong, T. W. *Synth. Commun.* **1997**, *27*, 2569. Wada, M.; Honna, M.; Miyoshi, N. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 2265. Boruah, A.; Baruah, B.; Prajapati, D.; Sandhu, J. S. *Synlett* **1997**, 1251. Montero, J. L.; Winum, J. Y.; Leydet, A.; Kamal, M.; Pavia, A. A.; Rogue, J. P. *Carbohydr. Res*. **1997**, *297*, 175. Kallal, K.; Coin, C.; Duñach, E.; Postel, M. *New J. Chem*. **1997**, *21*, 495. Le Boisselier, V.; Postel, M.; Duñach, E. *Chem. Commun.* **1997**, 95. Robert, H.; Garrigues, B.; Dubac, J. *Tetrahedron Lett.* **1998**, *39*, 1161. Repichet, S.; Le Roux, C.; Dubac, J.; Desmurs, J. R. *Eur. J. Org. Chem*. **1998**, 2743. Winum, J. Y.; Kamal, M.; Barragan, V.; Leydet, A.; Montero, J. L. *Synth. Commun.* **1998**, *28*, 603. Boyer, B.; Keramane, E. M.; Montero, J. L.; Roque, J. P. *Synth. Commun.* **1998**, *28*, 1737.

(3) Recent review: Suzuki, H.; Ikegami, T.; Matano, Y. *Synthesis* **1997**, 249.

(4) Examples of Pd complex-mediated or -catalyzed reaction of organobismuth compounds: Asano, R.; Moritani, I.; Fujiwara, Y.; Teranishi, S. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 2910. Kawamura, T.; Kikukawa, K.; Takagi, M.; Matsuda, T. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 2021. Barton, D. H. R.; Ozbalik, N.; Ramesh, M. *Tetrahedron* **1988**, *44*, 5661. Suzuki, H.; Murafuji, T.; Azuma, N. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1593. Cho, C. S.; Yoshimori, Y.; Uemura, S. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 950.

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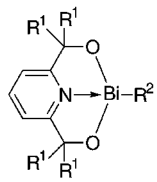
that the cross-coupling reaction of **1a−1d** with aryl and vinyl triflates does proceed smoothly in the presence of palladium complex catalysts (Figure 1).



**1a** : $R^1$ = Me, $R^2$ = Ph
**1b** : $R^1$ = Et, $R^2$ = Ph
**1c** : $R^1$ = $^i$Pr, $R^2$ = Ph
**1d** : $R^1$ = $R^2$ = Me

**Figure 1.**

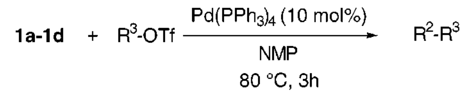
Organobismuth dialkoxides **1a−1d** can be easily prepared by the ligand exchange reaction of $R^2Bi(OEt)_2$ and 2,6-pyridinedimethanols.[5] The cross-coupling reaction with triflates is best catalyzed by $Pd(PPh_3)_4$. Thus, the reaction of **1b** with 1-naphthyl triflate over 16 h in toluene at 60 °C using 10 mol % of $Pd(PPh_3)_4$ gave the cross-coupling product, 1-phenylnaphthalene, in 55% yield along with 10% of biphenyl. Other palladium complexes such as $Pd(dba)_2$/2L [L = $PPh_3$ (39%), $PCy_3$ (15%), $P(p\text{-Tol})_3$ (37%), $P(o\text{-Tol})_3$ (0%), $P(C_6F_5)_3$ (0%), $AsPh_3$ (3%); 2L = 1,2-bis(diphenylphosphino)ethane (0%)] and $PdCl_2$(dpaf) (dpaf = 1,1′-bis(diphenylarsino)ferrocene) (32%) were less effective. $Ni(cod)_2/2PPh_3$ and $Pt_2(dba)_3/4PPh_3$ were not effective either, giving 1-phenylnaphthalene in only 2% and 4% yields, respectively. $RhCl(PPh_3)_3$ formed only biphenyl in 33% yield.

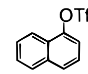
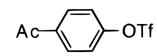
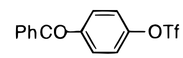
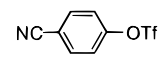
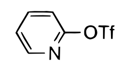
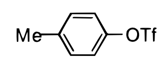
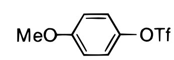
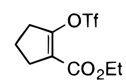
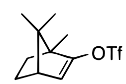
This reaction is highly affected by the solvent. The performance of various solvents (yield of 1-phenylnaphthalene) in the same reaction under identical conditions decreased as follows ($Pd(PPh_3)_4$ (10 mol %), 60 °C, 18 h): NMP and DMF (77−78%) > 1,3-dimethyltetrahydropyrimidin-2-one, toluene, THF, *N*,*N*-dimethylacetamide, dioxane, ethyl acetate (48−62%) > pyridine, 1,2-dichloroethane, acetonitrile (16−17%). Reduction of the catalyst quantity to 5 and 1 mol % (NMP, 60 °C, 16 h) only slightly decreased the yield to respectively give 70% and 54% of the cross-coupling product. The yield was not dramatically improved by extension of the reaction time.

Table 1 provides a preliminary summary of the scope and limitation of the new cross-coupling reaction.[7,8] The substituents $R^1$ in the alkoxide ligands bound to bismuth affect the reactivity of **1** to some extent, and the use of **1b** results in the highest yield (entries 1−3). Aryl and vinyl triflates with electron-withdrawing substituents afford excellent yields of products (entries 4, 6, 8, and 13). On the other hand, aryl triflates with electron-donating substituents are almost unreactive (entries 11−12). Methylation of triflates with methylbismuth compound **1d** also proceeds albeit less efficiently than the phenylation with **1b** (entries 5, 7, and 9).

Commercially available $Ph_3Bi$ proved to be much less reactive than **1a−c**. Its reaction with 1-naphthyl triflate under similar conditions (NMP, 60 °C, 12 h, 10 mol % of $Pd(PPh_3)_4$) resulted in much lower yields (18% yield of 1-phenylnaphthalene when $Ph_3Bi$:triflate = 1:3 and 37% yield when $Ph_3Bi$:triflate = 1:1). On the other hand, organic halides appear to be less reactive in the present recipe than triflates. Thus, the reaction of **1b** with 1-naphthyl bromide (NMP, 60 °C, 12 h, 10 mol % of $Pd(PPh_3)_4$) gave 1-phenylnaphthalene in only 15% yield along with 13% of biphenyl.

**Table 1.** Reaction of Organobismuth Dialkoxides **1a−1d** with Triflates[a]




| entry | 1a-1d | triflate | yield / %[b] |
|---|---|---|---|
| 1 | 1a |  | 66 |
| 2 | 1b | | 80 |
| 3 | 1c | | 67 |
| 4 | 1b |  | 99 |
| 5 | 1d | | 72 |
| 6 | 1b |  | 95 |
| 7 | 1d | | 52 |
| 8 | 1b |  | 99 |
| 9 | 1d | | 61 |
| 10 | 1b |  | 78 |
| 11 | 1b |  | 3 |
| 12 | 1b |  | 0 |
| 13 | 1b |  | 99 (96)[c] |
| 14 | 1b |  | 33 |

[a] **1a−1d**: triflate = 1.2:1. [b] Yields were determind by GLC analysis of the crude reaction mixture by using *n*-hexadecane as an internal standard. [c] In the parentheses is shown the isolated yield.

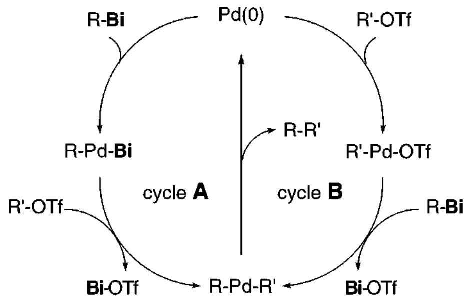
(6) Shimada, S.; Rao, M. L. N.; Tanaka, M. Submitted for publication.

(7) **Representative Experimental Procedures:** An NMP solution (3 mL) of **1b** (161 mg, 0.300 mmol), ethyl 2-(trifluoromethanesulfonyloxy)-1-cyclopentene-1-carboxylate (53.3 mg, 0.250 mmol), and $Pd(PPh_3)_4$ (28.8 mg, 0.0250 mmol) was stirred at 80 °C for 3 h under nitrogen. After cooling, the mixture was analyzed by GLC with *n*-hexadecane as an internal standard to determine the yield of the product (ethyl 2-phenyl-1-cyclopentene-1-carboxylate, 99%). The crude mixture was dissolved in EtOAc (90 mL) and washed with water (10 mL), 10% aqueous HCl (10 mL), water (10 mL), and brine (10 mL). The organic layer was dried over $Na_2SO_4$, filtered, and concentrated in vacuo. The residue was purified by preparative TLC to give 52 mg (96%) of ethyl 2-phenyl-1-cyclopentene-1-carboxylate.

(8) Bismuth-containing products of this reaction have not been characterized at the moment. The initial products (probably dialkoxybismuth triflates) are highly air-sensitive and hydrolyzed by aqueous workup to give the free ligands, 2,6-pyridinedimethanols, and bismuth-containing compounds which are insoluble in organic solvents.

Although the mechanistic aspects remain to be clarified, one can consider two possibilities. One is cycle A in Scheme 1. This catalytic cycle is triggered by oxidative addition of the R−Bi bond to generate an organopalladium intermediate, which somehow undergoes metathesis with a triflate molecule. The Bi−C bond is very weak[9] and envisioned to readily add to Pd(0) species. Indeed, we have found that oxidative addition of the Bi−C bond of **1a**−**1d** to a Pt(0) complex does take place.[10] The formation of biphenyl as byproduct in the catalytic reactions substantiates this mechanism. The other mechanistic possibility is the same as those generally accepted for the cross-coupling reactions of organotin and organoboron compounds; oxidative addition of triflate to Pd(0) species, a transmetalation step to form diorganopalladium species, and a subsequent reductive elimination step to form the cross-coupling product and regenerate the Pd(0) species (Scheme 1, cycle B).[11] At the moment we do not have unequivocal evidence to exclude either of these possibilities. However, in view of (1) the higher reactivity of the Ph−Bi bond of **1c** as compared with 4-acetylphenyl triflate in oxidative addition with Pt(0)[8] and (2) the unusually large difference in reactivity between electron-withdrawing and -donating triflates in the catalysis, cycle A appears to be more likely.

**Scheme 1.** Possible Catalytic Cycles




In summary, we have demonstrated the high reactivity of organobismuth compounds in the cross-coupling reaction with aryl and vinyl triflates catalyzed by a palladium complex. Further studies are underway to elucidate the reaction mechanism and to broaden the applicability of organobismuth compounds in organic synthesis.

**Acknowledgment.** We are grateful to the Japan Science and Technology Corporation (JST) for financial support through the CREST (Core Research for Evolutional Science and Technology) program and for a postdoctoral fellowship to M.L.N.R.

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(9) Mean bond-dissociation energy of Bi−Ph bond of $Ph_3Bi$ was estimated to be 193.9 ± 10.8 kJ $mol^{-1}$: Steele, W. V. *J. Chem. Thermodyn.* **1979**, *11*, 187.

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(11) Suzuki, A. In *Metal-catalyzed Cross-coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, 1998; p 49. Mitchell, T. N.. In *Metal-catalyzed Cross-coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, 1998; p 167.