ORGANOMETALLICS

Direct Access to Fluorene by Successive C–O/C–H Bond Activations of 2-Phenylbenzyl Ester

Masafumi Hirano,* Sosuke Kawazu, and Nobuyuki Komine

Department of Applied Chemistry, Graduate School of Engineering, Tokyo University of Agriculture and Technology, 2-24-16 Nakacho, Koganei, Tokyo 184-8588, Japan

Supporting Information

ABSTRACT: Catalytic formation of fluorene has been achieved from 2-phenylbenzyl trifluoroacetate via successive C-O and C-H bond cleavage reactions by $Pd(OAc)_2/PPh_3$ in 97% yield. This reaction involves the oxidative addition of ester to give (carboxylato)(2-phenylbenzyl)palladium(II) species and deprotonation from the 2-phenylbenzyl group by the cleaved carboxylato group via an internal electrophilic substitution mechanism.



D irect C-H functionalization is one of the major current topics in organometallic chemistry.¹ In many cases, hydrogen is believed to be abstracted as a proton by an associated basic ligand such as carboxylato at a transition-metal center. This process is now widely accepted as the internal electrophilic substitution (IES)² mechanism, although other names such as concerted metalation-deprotonation (CMD)³ and ambiphilic metal-ligand activation (AMLA)⁴ have been also used. This process normally involves (i) an oxidative addition of carbon-halogen bond, (ii) anion exchange from halido to carboxylato in a polar solvent, and then (iii) abstraction of hydrogen in a substrate as a proton by the coordinating carboxylato group (Scheme 1).

Scheme 1



If we can directly access the key intermediate **A** from esters, a straightforward transformation would be achieved without using organic halides, carboxylato anion, and a polar solvent that is generally difficult to remove. One of the major difficulties may arise from the C–O bond oxidative addition of esters that generally gives the undesired (acyl)(alkoxo)metal species **B** rather than **A** (Scheme 2).⁵

However, when benzyl, allyl, and alkenyl esters are employed, the (carboxylato)(organo)metal species **A** is formed.^{5,6} In addition, naphthyl and some aryl esters are recently found to give **A** by Ni(0) as an intermediate in the C–H functionalization.⁷ For benzyl esters, although Kuwano and Scheme 2



co-workers have documented extensive Tsuji–Trost type transformations,⁸ no direct C–H functionalization using benzyl carboxylates has been reported.⁹ We describe here the first catalytic formation of fluorene by successive C–O/C–H bond activation of 2-phenylbenzyl esters.

Because electron-deficient carboxylates would lead to facile C–O bond oxidative addition¹⁰ and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) is a potentially effective base for trapping of evolved carboxylic acid,¹¹ we started the screening using 2phenylbenzyl trifluoroacetate in the presence of DBU and Pd(OAc)₂ as the catalyst precursor (Table 1).

Upon screening of a broad range of ligands (entries 1-6), the PPh₃ system showed a promising performance to give fluorene, which is currently attractive for OLEDs and solar cells.¹² Note that there was almost no catalytic activity (0-2%) in the presence of non-phosphorus ligands such as NHC/Ag₂O and 2,2'-bipyridine or in the absence of ligand. Nonpolar solvents such as benzene gave the best result (entries, 1 and 7– 9). This reaction requires addition of base (entry 12), and Proton Sponge was not effective for this reaction (entry 13). The optimized amount of DBU is 1 equiv with respect to substrate (entries 1, 10, and 11). Because DBU having an

Received: February 21, 2014 Published: April 15, 2014 Table 1. Effect of Solvent, Base, and Ligand on the C–O/C–H Bond Activation a



^{*a*}Conditions: Pd(OAc)₂, 10 mol %; L, 20 mol % (10 mol % for DPPP and BINAP). ^{*b*}DBU, 2 equiv. ^{*c*}DBU, 0.5 equiv. ^{*d*}No addition of base. ^{*e*}Temperature 100 °C.

amidine framework was a promising base, we thought that the similar superbase 7-methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene (MTBD) was worth trying. In fact, MTBD gave the best result among these trials and the yield of fluorene improved to 97%.

Acetate, benzoate, and 4-nitrobenzoate did not give fluorene under these conditions (Table 2). On the basis of the

Table 2. Effect of Carboxylate on the C–O/C–H Bond Activation



pioneering report by Chang and co-workers, fluorene was also formed from 2-phenylbenzyl chloride by $Pd(OAc)_2/BINAP$ or $P(m-tol)_3$ in the presence of Cs_2CO_3 , and they noted that 2-phenylbenzyl acetate did not give fluorene at all.¹³

In order to understand the mechanism, we also tried stoichiometric reactions. When Pd(styrene)(dppe) (1) was treated with 2-phenylbenzyl trifluoroacetate in benzene, C–O bond oxidative addition to Pd(0) took place smoothly within 1 h at room temperature to give $Pd(OCOCF_3)(2-phenylbenzyl)$ -(dppe) (2) quantitatively in 42% isolated yield as analytically pure brown crystals from cold THF/Et₂O (eq 1). Note that a

similar C–O bond oxidative addition of a simple benzyl ester to Pd(0) was also reported by Yamamoto and co-workers.¹⁴



The molecular structure of **2** clearly shows the oxidative addition of the C–O bond to give (carboxylato)(2-phenylbenzyl)palladium(II), as shown in Figure 1.¹⁵ The C–



Figure 1. Molecular structure of $Pd(OCOCF_3)(2$ -phenylbenzyl)-(dppe) (2). All hydrogen atoms, incorporated Et_2O , and disordered CF_3 groups are omitted for clarity. Ellipsoids represent 50% probability.

O bond oxidative addition of a benzyl ester proceeds despite the existence of a bulky substituent at the ortho position. The ³¹P{¹H} NMR spectrum of **2** shows two doublets at δ 57.35 (d, 1P) and 39.96 (d, 1P), suggesting a cis configuration. In the ¹H NMR, the most characteristic benzylic methylene protons appear at δ 2.90 (dd, 2H). The trifluoromethyl group resonates at δ -73.77 (s). The IR spectrum of **2** shows intense ν (C=O) and ν (C-O) bands at 1688 and 1435 cm⁻¹, respectively, suggesting κ ¹O monodentate coordination to the Pd center.^{16,17}

In contrast to the case for trifluoroacetate, the C–O bond oxidative addition of 2-phenylbenzyl acetate did not proceed at all under the same conditions, and at 70 $^{\circ}$ C 1 resulted in decomposition and no C–O oxidative addition occurred. Thus, the C–O bond oxidative addition must be the key for the present reaction.

Treatment of **2** with MTBD at 70 °C for 8 h gave fluorene in 74% yield (Table 3, entry 1). When DBU was employed in this reaction, fluorene was also produced in 68% yield (entry 2). NEt₃ and Cs_2CO_3 were not suitable bases for this reaction (entries 3 and 4). The best result was obtained by the reaction in toluene with MTBD at 100 °C to give fluorene in quantitative yield (entry 5).

Table 3. Effect of Base on Stoichiometric Formation of Fluorene from Pd(OCOCF₃)(2-phenylbenzyl)(dppe)



These results, taken together, are consistent with the catalytic cycle shown in Scheme 3 for the catalytic successive C-O/C-



H bond activation. A key Pd(0) species, PdL_w is generated by the facile reduction of $Pd(OAc)_2$ with PPh_3 .¹⁷ The C–O bond oxidative addition of the ester to Pd(0) gives C, which has been isolated in the case of the dppe analogue **2**. Because the 2phenyl group is forced in proximity to the Pd(II) center, the internal C–H bond activation proceeds to give **E**. A similar cyclometalation has also been reported.¹⁸ Finally, reductive elimination from E releases fluorene.

DFT calculations were performed on the model reaction using *cis*-Pd(OCOCF₃- $\kappa^1 O$)(2-phenylbenzyl)(PH₃)₂ (**2-PH₃**). Because the monophosphine compound Pd(OCOCF₃- $\kappa^2 O, O'$)(2-phenylbenzyl)(PH₃) (INT1) is 8.1 kcal mol⁻¹ more stable than the bis-phosphine species *cis*-Pd(OCOCF₃- $\kappa^1 O$)(2-phenylbenzyl)(PH₃)₂, the reaction initiates from INT1 (Figure 2). Then haptotropic change of the carboxylato group occurs to give INT2 and the C–H bond is cleaved by the carboxylato group to form the six-membered transition state



Figure 2. Computed reaction profile for key steps in the catalysis. All hydrogen atoms are omitted for clarity.

TS1. A significant polarization in the calculated natural atomic charges for the species at **TS1** occurs at the activating C–H bond, the negative charge at C increasing by -0.526, while the H becomes more positive by +0.399, suggesting the IES mechanism. The overall mechanism is similar to aromatic C–H bond activation through the IES mechanism by Pd(II),^{19,20} but this is closer to the Wheland type species.²¹ The rate-determining step is the reductive elimination step involving **TS2** that gives a η^2 -coordinating fluorene complex of Pd(0), **INT4**.

In summary, we have a new example for successive C-O/C-H bond cleavage reaction of a benzyl ester by Pd(0) catalyst. The key for the present reaction seems to be facile oxidative addition of the C-O bond, and trifluoroacetate is one of the best candidates. This fundamental finding should open up direct C-H functionalization using benzyl esters on the basis of the IES mechanism.

ASSOCIATED CONTENT

S Supporting Information

Text, figures, tables, and a CIF file giving synthetic details and full characterization data for all compounds prepared in this paper, crystallographic data for **2**, and computational details. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

*M.H.: e-mail, hrc@cc.tuat.ac.jp; tel and fax, +81 423 887 044. Notes

The authors declare no competing financial interest.

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REFERENCES

Recent reviews: (a) Ackermann, L. Chem. Rev. 2011, 111, 1315.
 Ackermann, L.; Vicente, R.; Kapdi, A. R. Angew. Chem., Int. Ed. 2009, 48, 9792.

(2) Oxgaard, J.; Tenn, W. J., III; Nielsen, R. J.; Periana, R. A.; Goddard, W. A., III Organometallics **200**7, *26*, 1565.

(3) (a) Lapointe, D.; Fagnou, K. Chem. Lett. 2010, 29, 1118.
(b) Winstein, S.; Traylor, T. G. J. Am. Chem. Soc. 1955, 77, 3747.

(4) (a) Boutadla, Y.; Davies, D. L.; Macgregor, S. A.; Poblador-Bahamonde, A. I. *Dalton Trans.* **2009**, 5820. (b) Boutadla, Y.; Davies, D. L.; Macgregor, S. A.; Poblador-Bahamonde, A. I. *Dalton Trans.* **2009**, 5887.

(5) Reviews for C-O bond cleavage of esters: (a) Komiya, S.; Hirano, M. In Fundamentals of Molecular Catalysis; Kurosawa, H., Yamamoto, A., Eds.; Elsevier: Amsterdam, 2003; p 115. (b) Ling, Y.-S.; Yamamoto, A. In Activation of Unreactive Bonds and Organic Synthesis; Murai, S., Ed.; Springer: Berlin, 1999; p 161. (c) Yamamoto, A. Adv. Organomet. Chem. 1992, 34, 111. (d) Vinyl ester by Pt(0): Manbeck, K. A.; Kundu, S.; Walsh, A. P.; Brennessel, W. W.; Jones, W. D. Organometallics 2012, 31, 5018.

(6) Recent direct C-H arylation using alkenyl acetate: Ogiwara, Y.; Tamura, M.; Kochi, T.; Matsuura, Y.; Chatani, N.; Kakiuchi, F. *Organometallics* **2014**, 33, 402.

(7) (a) Muto, K.; Yamaguchi, J.; Lei, A.; Itami, K. J. Am. Chem. Soc.
2013, 135, 16384. (b) Guan, B.-T.; Wang, Y.; Li, B.-J.; Yu, D.-G.; Shi,
Z.-J. J. Am. Chem. Soc. 2008, 130, 14468. (c) Quasdorf, K. W.; Tian, X.;
Garg, N. K. J. Am. Chem. Soc. 2008, 130, 14422.

(8) Kuwano, R.; Kondo, Y. Org. Lett. 2004, 6, 3545.

(9) Recent C-O/C-H activations of benzyl phosphates: Ackermann, L.; Barfüsser, S.; Pospech, J. Org. Lett. **2010**, *12*, 724.

(10) (a) Komiya, S.; Kabasawa, T.; Yamashita, K.; Hirano, M.; Fukuoka, A. J. Organomet. Chem. **1994**, 471, C6. (b) Planas, J. G.; Marumo, T.; Ichikawa, Y.; Hirano, M.; Komiya, S. J. Mol. Catal. A **1999**, 147, 137.

(11) Hirano, M.; Fujimoto, R.; Hatagami, K.; Komine, N.; Komiya, S. *ChemCatChem* **2013**, *5*, 1101.

(12) Recent reviews: (a) Li, Y. Acc. Chem. Res. 2012, 45, 723.
(b) Zotti, G.; Berlin, B. V. Acc. Chem. Res. 2008, 41, 1098.

(13) Hwang, S. J.; Kim, H. J.; Chang, S. Org. Lett. 2009, 11, 4588.

(14) Nagayama, K.; Shimizu, I.; Yamamoto, A. Bull. Chem. Soc. Jpn. 1999, 72, 799.

(15) Crystal data for 2•0.5Et₂O: formula $C_{43}H_{40}F_3O_{2.5}P_2Pd$, formula weight 822.13, monoclinic, $P2_1/n$, a = 13.5362(7) Å, b = 15.1262(6) Å, c = 18.9707(9) Å, $\beta = 93.720(3)^\circ$, V = 3876.1(4) Å³, Z = 4, temperature 200 K, crystal size (mm) 0.396 × 0.145 × 0.106, F(000) = 1684.00, $\mu = 0.613$ mm⁻¹, Mo K α radiation ($\lambda = 0.71075$ Å), 8857 reflections (total), 451 parameters, GOF = 1.054, $R(R_w) = 0.0738$ (0.2091). CCDC No. 986963 contains supplementary crystallographic data for **2**. These data can be obtained free of charge via http://www. ccdc.cam.ac.uk/data request/cif.

(16) Nakamoto, K. Infrared and Raman Spectra of Inorganic and Coordination Compounds, 5th ed.; Wiley: New York, 1997; Part B, p 59.

(17) Mandai, T.; Matsumoto, T.; Tsuji, J.; Saito, S. Tetrahedron Lett. 1993, 34, 2531.

(18) Kozhushkov, S. I.; Potukuchi, H. K.; Ackermann, L. Catal. Sci. Technol. 2013, 3, 526.

(19) (a) Biswas, B.; Sugimoto, M.; Sakaki, S. Organometallics 2000, 19, 3895. (b) Davies, L. D.; Donald, S. M. A.; Macgregor, S. A. J. Am. Chem. Soc. 2005, 127, 13754. (c) Gorelsky, S. I. Organometallics 2012, 31, 4631.

(20) (a) Tan, Y.; Barrios-Landeros, F.; Hartwig, J. F. *J. Am. Chem. Soc.* **2012**, *134*, 3683. (b) Wakioka, M.; Nakamura, Y.; Wang, Q.; Ozawa, F. Organometallics **2012**, *31*, 4810.

(21) Raybov, A. D. Chem. Rev. 1990, 90, 403.