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Rhodium-catalyzed Intramolecular Dehydrogenative Aryl–Aryl Coupling Using Air as Terminal Oxidant

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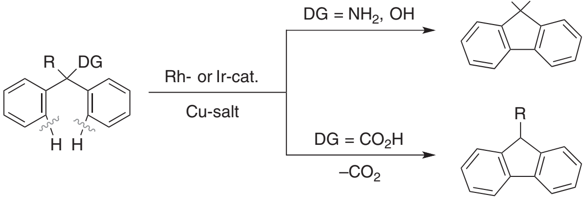
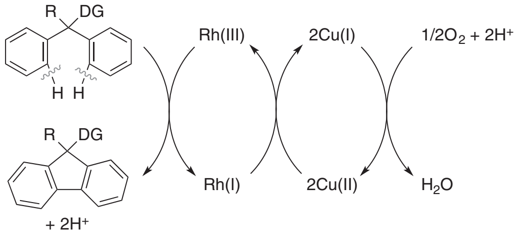
Intramolecular dehydrogenative cyclization involving twofold Csp^2–H bond cleavages directed by the amino- or carboxy group proceeds smoothly when using a rhodium–copper catalyst system under air as the terminal oxidant. A variety of fluorene derivatives can be prepared by the environmentally benign procedure.

Chelation-assisted catalytic C–H bond transformation reactions utilizing directing groups (DGs) are now recognized as powerful tools in the precise synthesis of functional organic molecules.[1] In particular, dehydrogenative C–H arylation and alkenylation at specified positions of substituted arenes are highly useful for constructing π-conjugated molecules in an atom- and step-economical manner. In the course of our continuous study on rhodium- and iridium-catalyzed dehydrogenative coupling reactions,[2,3] we found that di- and triphenylmethylamines undergo intramolecular dehydrogenative aryl–aryl coupling through amino-directed C–H bond cleavage (Scheme 1, $DG = NH_2$).[4] Similar cyclizations directed by carboxy ($DG = CO_2H$) and hydroxy groups ($DG = OH$) also proceeded efficiently when using a rhodium- or an iridium catalyst.[4,5] In the former case ($DG = CO_2H$), the cyclization was accompanied by decarboxylation. These reactions provide straightforward routes to fluorene frameworks, which are important structural units in the field of organic materials.[6] However, a stoichiometric amount of copper salt is usually needed as the oxidant to carry out these reactions smoothly.

To perform the above-mentioned reactions in a more environmentally benign manner, it is highly desirable to use molecular oxygen as the terminal oxidant (Scheme 2).[3h,7] Consequently, we have explored a new catalyst system and succeeded in conducting the coupling under air in the presence of a rhodium complex, a copper salt, and a carboxylic acid as the catalyst, cocatalyst, and promoter, respectively. The results obtained with this second-generation catalytic system are described herein.



Scheme 1.



Scheme 2.

As reported in our previous paper,[4] treatment of tritylamine (**1a**) (0.5 mmol) in the presence of $[RhCl(cod)]_2$ (0.005 mmol, cod: 1,5-cyclooctadiene) and $Cu(OAc)_2 \cdot H_2O$ (1 mmol) in *o*-xylene at 130 °C for 2 h under N_2 gave a dehydrogenative cyclization product, 9-phenylfluoren-9-amine (**2a**), in 98% yield (Entry 1 in Table 1). When **1a** (0.25 mmol) was treated with a reduced amount of $Cu(OAc)_2 \cdot H_2O$ (0.05 mmol) under air, the yield of **2a** decreased to 22% (Entry 2). In diglyme, a higher **2a** yield of 45% was obtained (Entry 7) as compared to those in other solvents such as PhCl, DMF, DMAc, and NMP (Entries 3–6). Interestingly, addition of a carboxylic acid (0.25 mmol) was found to improve the yield of **2a** (Entries 8–12). In particular, pivalic acid (PivOH) and 2,6-difluorobenzoic acid were the most effective among the acids examined. Increasing the amounts of reagents relative to that of the rhodium catalyst significantly reduced the yield (Entry 13). However, even with a lower loading of rhodium catalyst, a high **2a** yield (90%) was obtained by increasing the reaction temperature to 150 °C (Entry 14). Note that the reaction with a catalytic amount of $Cu(OAc)_2 \cdot H_2O$ could be readily scaled up to a gram scale. Thus, from **1a** (5 mmol), **2a** was obtained in 95% yield (1.23 g, Entry 15).

Under the conditions using $[RhCl(cod)]_2$–$Cu(OAc)_2 \cdot H_2O$ as the catalyst in air, 1,1-diphenylethan-1-amine (**1b**) underwent the cyclization to produce 9-methylfluoren-9-amine (**2b**) (Entry 1 in Table 2). The cyclization of other 1-amino-1,1-diarylalkanes **1c**–**1e** also proceeded efficiently to afford the corresponding fluorenamine derivatives (Entries 2–4). In the reaction of 1,1-di(2-naphthyl)ethan-1-amine (**1e**), a mixture of isomers **2e** and **2e′** was obtained (Entry 4). In this case, cyclization at a sterically less hindered position took place preferably. 1,1,1-Tris(4-substituted phenyl)methylamines **1f**–**1h** underwent the reaction smoothly to give **2f**–**2h** in 67–89% yields (Entries 5–7). Treatment of unsymmetrically substituted triarylmethylamines **1i** and **1j** gave the corresponding mixtures of fluorene isomers (Entries 8 and 9).

This cyclization seems to proceed through a similar pathway to that proposed in our previous work,[4] involving coordination of

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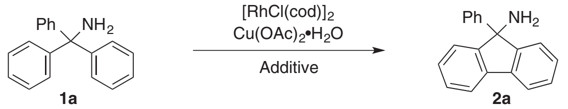
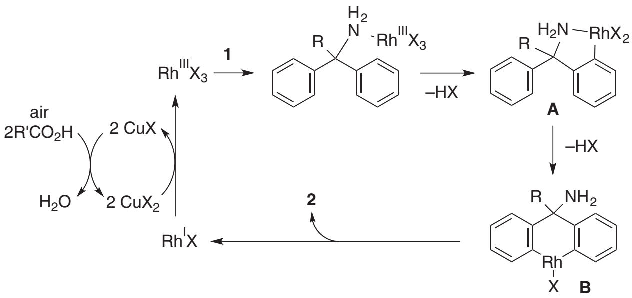
Table 1. Cyclization of tritylamine (**1a**)[a]



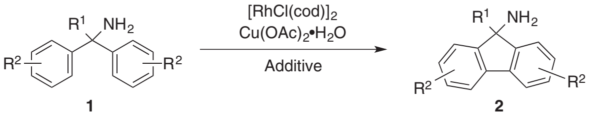
Entry	Additive	Solvent	Time/h	Yield of **2a**[b] /%
1[c]	—	*o*-xylene	2	(98)
2	—	*o*-xylene	2	22
3	—	PhCl	6	21
4	—	DMF	3	36
5	—	DMAc	3	20
6	—	NMP	6	27
7	—	diglyme	3	45
8	AcOH	diglyme	3	67
9	1-AdCO$_2$H	diglyme	6	76
10	PivOH	diglyme	4	83
11	2,6-Me$_2$C$_6$H$_3$CO$_2$H	diglyme	3	69
12	2,6-F$_2$C$_6$H$_3$CO$_2$H	diglyme	4	83
13[d]	PivOH	diglyme	6	27
14[d,e]	PivOH	diglyme	3	90 (83)
15[e,f]	PivOH	diglyme	5	(95)

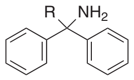
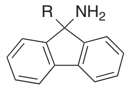
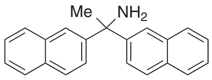
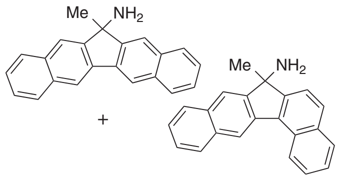
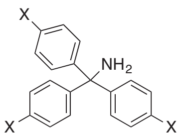
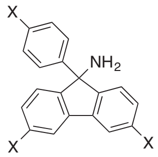
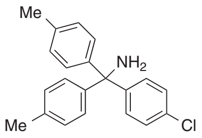
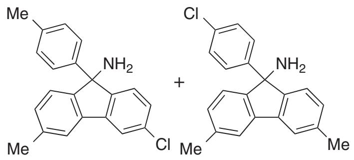
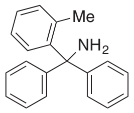
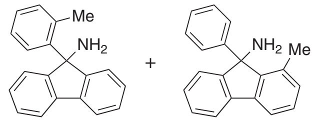
[a]Reaction conditions: **1a** (0.25 mmol), $[\mathrm{RhCl(cod)}]_2$ (0.005 mmol), $\mathrm{Cu(OAc)_2{\bullet}H_2O}$ (0.05 mmol), and additive (0.25 mmol) at 130 °C under air, unless otherwise noted. [b]GC yield based on the amount of **1a** used. Value in parentheses indicates yield after isolation. [c]The reaction was conducted using **1a** (0.5 mmol), $[\mathrm{RhCl(cod)}]_2$ (0.005 mmol), and $\mathrm{Cu(OAc)_2{\bullet}H_2O}$ (1 mmol) at 130 °C under N$_2$. [d]**1a** (0.5 mmol), $[\mathrm{RhCl(cod)}]_2$ (0.005 mmol), $\mathrm{Cu(OAc)_2{\bullet}H_2O}$ (0.1 mmol), and PivOH (0.5 mmol) were employed. [e]At 150 °C. [f]**1a** (5 mmol), $[\mathrm{RhCl(cod)}]_2$ (0.05 mmol), $\mathrm{Cu(OAc)_2{\bullet}H_2O}$ (1 mmol), and PivOH (5 mmol) were employed.



Scheme 3.

Table 2. Cyclization of di- or triarylmethylamines **1**[a]

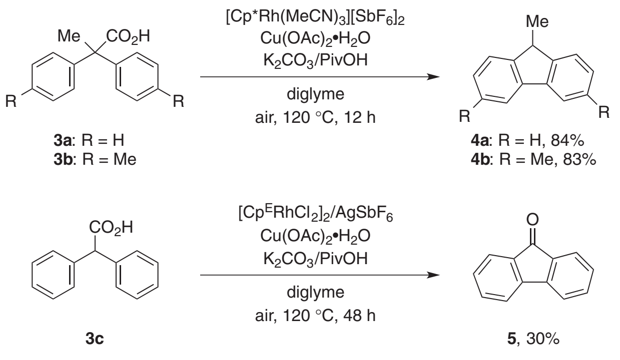


Entry	1	Time/h	Product(s), yield/%
			
1	**1b**: R = Me	2	**2b**: R = Me, 66
2	**1c**: R = Pr^n	1.5	**2c**: R = Pr^n, 74
3	**1d**: R = Pr^i	1	**2d**: R = Pr^i, 76
4	 **1e**	1.5	 **2e** + **2e'**, 54 (3:1)
			
5	**1f**: X = Me	1	**2f**: X = Me, 89
6	**1g**: X = F	1.5	**2g**: X = F, 83
7	**1h**: X = Cl	1.5	**2h**: X = Cl, 67
8	 **1i**	1	 **2i** + **2i'**, 71 (7.5:1)
9	 **1j**	1	 **2j** + **2j'**, 80 (1:1)

[a]Reaction conditions: **1** (0.5 mmol), $[\mathrm{RhCl(cod)}]_2$ (0.01 mmol), $\mathrm{Cu(OAc)_2{\bullet}H_2O}$ (0.1 mmol), and PivOH (0.5 mmol) at 150 °C under air.

the amino group of **1** to a rhodium(III) center, amino-directed cyclorhodation to form a five-membered rhodacycle intermediate **A**, a second cyclorhodation to form a six-membered intermediate **B**, and reductive elimination (Scheme 3). The rhodium(I) species yielded in the last step may be reoxidized by a copper(II) cocatalyst to regenerate the rhodium(III) active species along with copper(I). The latter may be reoxidized under air in the present reaction system.[8]

Next, carboxy-directed cyclization using air as the terminal oxidant was examined. After optimizing the conditions (see Supporting Information), it was found that the cyclization of 2,2-diphenylpropionic acid (**3a**) (0.5 mmol) proceeds efficiently, accompanied by decarboxylation,[9] in the presence of $[\mathrm{Cp^{*}Rh(MeCN)_3}][\mathrm{SbF_6}]_2$ (0.02 mmol), $\mathrm{Cu(OAc)_2{\bullet}H_2O}$ (0.02 mmol), $\mathrm{K_2CO_3}$ (0.25 mmol), and PivOH (0.5 mmol) in diglyme at 120 °C under air to produce 9-methylfluorene (**4a**) in 84% yield (Scheme 4). It should be noted that this yield is higher than that in the reaction using a stoichiometric amount of $\mathrm{Cu(OAc)_2{\bullet}H_2O}$ as the oxidant (63%).[4,5] Under the same conditions, treatment of 2,2-bis(4-methylphenyl)propionic acid (**3b**) gave fluorene **4b** in 83% yield. In contrast, the reaction of 2,2-diphenylacetic acid (**3c**) proceeded through cyclization, decarboxylation, and successive oxygenation to give fluoren-9-one (**5**) as a single major product.[10] In the latter reaction, the use of $[\mathrm{Cp^ERhCl_2}]_2$ (0.01 mmol), $\mathrm{AgSbF_6}$



Scheme 4.

(0.04 mmol), and Cu(OAc)$_2$•H$_2$O (0.02 mmol) as the catalyst system gave a better result than [Cp*Rh(MeCN)$_3$][SbF$_6$]$_2$/Cu(OAc)$_2$•H$_2$O (Cp^E: 1,3-bis(ethoxycarbonyl)-2,4,5-trimethylcyclopentadienyl).[11]

In summary, we demonstrated that fluorene frameworks can be readily constructed through rhodium–copper-catalyzed intramolecular dehydrogenative aryl–aryl coupling using air as the terminal oxidant. Addition of a carboxylic acid such as pivalic acid effectively enhanced the reaction. This seems to provide environmentally benign catalytic routes with low emission toward various π-conjugated molecules.

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Supporting Information is available electronically on J-STAGE.

References and Notes

1 Selected reviews for transition-metal-catalyzed C–H functionalization: a) D. A. Colby, A. S. Tsai, R. G. Bergman, J. A. Ellman, *Acc. Chem. Res.* **2012**, *45*, 814. b) K. M. Engle, T.-S. Mei, M. Wasa, J.-Q. Yu, *Acc. Chem. Res.* **2012**, *45*, 788. c) E. A. Mitchell, A. Peschiulli, N. Lefevre, L. Meerpoel, B. U. W. Maes, *Chem.—Eur. J.* **2012**, *18*, 10092. d) G. Song, F. Wang, X. Li, *Chem. Soc. Rev.* **2012**, *41*, 3651. e) F. W. Patureau, J. Wencel-Delord, F. Glorius, *Aldrichimica Acta* **2012**, *45*, 31. f) S. H. Cho, J. Y. Kim, J. Kwak, S. Chang, *Chem. Soc. Rev.* **2011**, *40*, 5068. g) J. Wencel-Delord, T. Dröge, F. Liu, F. Glorius, *Chem. Soc. Rev.* **2011**, *40*, 4740. h) Y. Kuninobu, K. Takai, *Chem. Rev.* **2011**, *111*, 1938. i) C. Liu, H. Zhang, W. Shi, A. Lei, *Chem. Rev.* **2011**, *111*, 1780. j) L. Ackermann, *Chem. Rev.* **2011**, *111*, 1315. k) J. Le Bras, J. Muzart, *Chem. Rev.* **2011**, *111*, 1170. l) T. W. Lyons, M. S. Sanford, *Chem. Rev.* **2010**, *110*, 1147. m) D. A. Colby, R. G. Bergman, J. A. Ellman, *Chem. Rev.* **2010**, *110*, 624. n) C.-L. Sun, B.-J. Li, Z.-J. Shi, *Chem. Commun.* **2010**, *46*, 677. o) T. Satoh, M. Miura, *Chem.—Eur. J.* **2010**, *16*, 11212. p) D. Lapointe, K. Fagnou, *Chem. Lett.* **2010**, *39*, 1118. q) B. Karimi, H. Behzadnia, D. Elhamifar, P. F. Akhavan, F. K. Esfahani, A. Zamani, *Synthesis* **2010**, 1399. r) X. Chen, K. M. Engle, D.-H. Wang, J.-Q. Yu, *Angew. Chem., Int. Ed.* **2009**, *48*, 5094. s) O. Daugulis, H.-Q. Do, D. Shabashov, *Acc. Chem. Res.* **2009**, *42*, 1074. t) C.-J. Li, *Acc. Chem. Res.* **2009**, *42*, 335. u) F. Kakiuchi, T. Kochi, *Synthesis* **2008**, 3013. v) Y. J. Park, J.-W. Park, C.-H. Jun, *Acc. Chem. Res.* **2008**, *41*, 222. w) I. V. Seregin, V. Gevorgyan, *Chem. Soc. Rev.* **2007**, *36*, 1173. x) E. M. Beccalli, G. Broggini, M. Martinelli, S. Sottocornola, *Chem. Rev.* **2007**, *107*, 5318. y) D. Alberico, M. E. Scott, M. Lautens, *Chem. Rev.* **2007**, *107*, 174. z) K. Godula, D. Sames, *Science* **2006**, *312*, 67.

2 Selected our recent reports: a) K. Nobushige, K. Hirano, T. Satoh, M. Miura, *Org. Lett.* **2014**, *16*, 1188. b) T. Iitsuka, K. Hirano, T. Satoh, M. Miura, *Chem.—Eur. J.* **2014**, *20*, 385. c) M. Itoh, M. Shimizu, K. Hirano, T. Satoh, M. Miura, *J. Org. Chem.* **2013**, *78*, 11427. d) T. Iitsuka, P. Schaal, K. Hirano, T. Satoh, C. Bolm, M. Miura, *J. Org. Chem.* **2013**, *78*, 7216. e) Y. Unoh, Y. Hashimoto, D. Takeda, K. Hirano, T. Satoh, M. Miura, *Org. Lett.* **2013**, *15*, 3258. f) K. Morimoto, K. Hirano, T. Satoh, M. Miura, *Chem. Lett.* **2011**, *40*, 600.

3 Selected examples from other groups: a) M. E. Tauchert, C. D. Incarvito, A. L. Rheingold, R. G. Bergman, J. A. Ellman, *J. Am. Chem. Soc.* **2012**, *134*, 1482. b) P. Wang, H. Rao, R. Hua, C.-J. Li, *Org. Lett.* **2012**, *14*, 902. c) J. Jayakumar, K. Parthasarathy, C.-H. Cheng, *Angew. Chem., Int. Ed.* **2012**, *51*, 197. d) H. Li, Y. Li, X.-S. Zhang, K. Chen, X. Wang, Z.-J. Shi, *J. Am. Chem. Soc.* **2011**, *133*, 15244. e) X. Wei, M. Zhao, Z. Du, X. Li, *Org. Lett.* **2011**, *13*, 4636. f) T. K. Hyster, T. Rovis, *Chem. Sci.* **2011**, *2*, 1606. g) Y.-F. Wang, K. K. Toh, J.-Y. Lee, S. Chiba, *Angew. Chem., Int. Ed.* **2011**, *50*, 5927. h) S. H. Park, J. Y. Kim, S. Chang, *Org. Lett.* **2011**, *13*, 2372. i) N. Guimond, S. I. Gorelsky, K. Fagnou, *J. Am. Chem. Soc.* **2011**, *133*, 6449. j) F. W. Patureau, T. Besset, N. Kuhl, F. Glorius, *J. Am. Chem. Soc.* **2011**, *133*, 2154. k) D. R. Stuart, P. Alsabeh, M. Kuhn, K. Fagnou, *J. Am. Chem. Soc.* **2010**, *132*, 18326. l) L. Li, W. W. Brennessel, W. D. Jones, *J. Am. Chem. Soc.* **2008**, *130*, 12414.

4 K. Morimoto, M. Itoh, K. Hirano, T. Satoh, Y. Shibata, K. Tanaka, M. Miura, *Angew. Chem., Int. Ed.* **2012**, *51*, 5359.

5 M. Itoh, K. Hirano, T. Satoh, Y. Shibata, K. Tanaka, M. Miura, *J. Org. Chem.* **2013**, *78*, 1365.

6 Selected examples: a) J. L. Zafra, J. Casado, I. I. Perepichka, I. F. Perepichka, M. R. Bryce, F. J. Ramírez, J. T. L. Navarrete, *J. Chem. Phys.* **2011**, *134*, 044520. b) M. Zhu, T. Ye, C.-G. Li, X. Cao, C. Zhong, D. Ma, J. Qin, C. Yang, *J. Phys. Chem. C* **2011**, *115*, 17965. c) K.-Y. Pu, R. Zhan, B. Liu, *Chem. Commun.* **2010**, *46*, 1470. d) S. M. Aly, C.-L. Ho, W.-Y. Wong, D. Fortin, P. D. Harvey, *Macromolecules* **2009**, *42*, 6902. e) H.-C. Yeh, C.-H. Chien, P.-I. Shih, M.-C. Yuan, C.-F. Shu, *Macromolecules* **2008**, *41*, 3801. f) Y. Mo, X. Jiang, D. Cao, *Org. Lett.* **2007**, *9*, 4371.

7 Selected examples for Rh-catalyzed oxidative coupling using molecular oxygen as oxidant: a) M. Fukui, Y. Hoshino, T. Satoh, M. Miura, K. Tanaka, *Adv. Synth. Catal.* **2014**, *356*, 1638. b) Y. Hoshino, Y. Shibata, K. Tanaka, *Adv. Synth. Catal.* **2014**, *356*, 1577. c) L. Yang, G. Zhang, H. Huang, *Adv. Synth. Catal.* **2014**, *356*, 1509. d) G. Zhang, H. Yu, G. Qin, H. Huang, *Chem. Commun.* **2014**, *50*, 4331. e) W. Dong, L. Wang, K. Parthasarathy, F. Pan, C. Bolm, *Angew. Chem., Int. Ed.* **2013**, *52*, 11573. f) G. Zhang, L. Yang, Y. Wang, Y. Xie, H. Huang, *J. Am. Chem. Soc.* **2013**, *135*, 8850. g) K. Ueura, T. Satoh, M. Miura, *J. Org. Chem.* **2007**, *72*, 5362. h) K. Ueura, T. Satoh, M. Miura, *Org. Lett.* **2007**, *9*, 1407. See also reviews: i) Z. Shi, C. Zhang, C. Tang, N. Jiao, *Chem. Soc. Rev.* **2012**, *41*, 3381. j) A. N. Campbell, S. S. Stahl, *Acc. Chem. Res.* **2012**, *45*, 851. k) K. M. Gligorich, M. S. Sigman, *Chem. Commun.* **2009**, 3854.

8 One of possible roles of added PivOH is to enhance the oxidative ability of molecular oxygen (for example, see ref 7c). Alternatively, it was reported that carboxylic acids promote C–H bond activation steps: a) E. F. Flegeau, C. Bruneau, P. H. Dixneuf, A. Jutand, *J. Am. Chem. Soc.* **2011**, *133*, 10161, and references therein. See also: b) Y. Boutadla, D. L. Davies, S. A. Macgregor, A. I. Poblador-Bahamonde, *Dalton Trans.* **2009**, 5820. c) D. L. Davies, O. Al-Duaij, J. Fawcett, M. Giardiello, S. T. Hilton, D. R. Russell, *Dalton Trans.* **2003**, 4132.

9 Selected reviews concerning transition-metal-catalyzed decarboxylative coupling: a) J. Cornella, I. Larrosa, *Synthesis* **2012**, 653. b) N. Rodríguez, L. J. Goossen, *Chem. Soc. Rev.* **2011**, *40*, 5030. c) J. D. Weaver, A. Recio, III, A. J. Grenning, J. A. Tunge, *Chem. Rev.* **2011**, *111*, 1846. d) T. Satoh, M. Miura, *Synthesis* **2010**, 3395. e) L. J. Goоßen, N. Rodríguez, K. Goоßen, *Angew. Chem., Int. Ed.* **2008**, *47*, 3100. f) O. Baudoin, *Angew. Chem., Int. Ed.* **2007**, *46*, 1373. For reviews concerning coupling via C–C bond cleavage, see: g) M. Murakami, T. Matsuda, *Chem. Commun.* **2011**, *47*, 1100. h) H. Yorimitsu, K. Oshima, *Bull. Chem. Soc. Jpn.* **2009**, *82*, 778.

10 Recently, Wang and co-workers reported a Pd-catalyzed version of similar fluorene synthesis: L. Liu, F. Wang, Z. Li, J. Wang, *Asian J. Org. Chem.* **2014**, *3*, 695.

11 Y. Shibata, K. Tanaka, *Angew. Chem., Int. Ed.* **2011**, *50*, 10917.

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