Platinum- and Palladium-Catalyzed Sequential Reactions: Regioselective Synthesis of 9-Fluorenylidenes from 9-Ethynylfluoren-9-yl Carboxylates and Furans

Koji Miki, Yoshinori Senda, Toshiyuki Kowada, Kouichi Ohe*

Department of Energy and Hydrocarbon Chemistry, Graduate School of Engineering, Kyoto University, Nishikyo-ku, Kyoto 615-8510, Japan
Fax +81(75)3832495; E-mail: ohe@scl.kyoto-u.ac.jp

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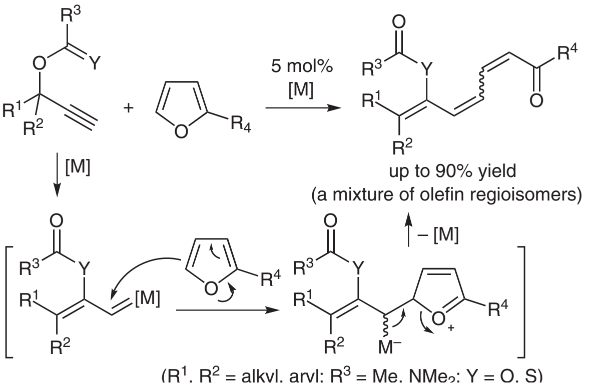
Abstract: The transformation of 9-acyloxy-9-ethynylfluorene and furans with platinum and palladium co-catalysts gave 9-fluorenylidenes in excellent yields with high regioselectivity in a one-pot manner.

Key words: carbene, ring opening, fluorene, platinum, palladium

Fluorene is the core structure of potent molecules such as the blue-light emitting materials,[1] interferon inducers,[2] antitumor compounds,[3] and inhibitor of microsomal triglyceride-transfer protein.[4] 9-Fluorenylidene structure has also been attracted and applied to a molecular motor for reorganization of cholesteric molecules,[5] organic field-effect transistor devices,[6] and pH sensors.[7] Although many reports to construct fluorenylidene skeleton have been reported,[8] simple and highly atom-economical catalytic transformations from fluorene derivatives are still limited.

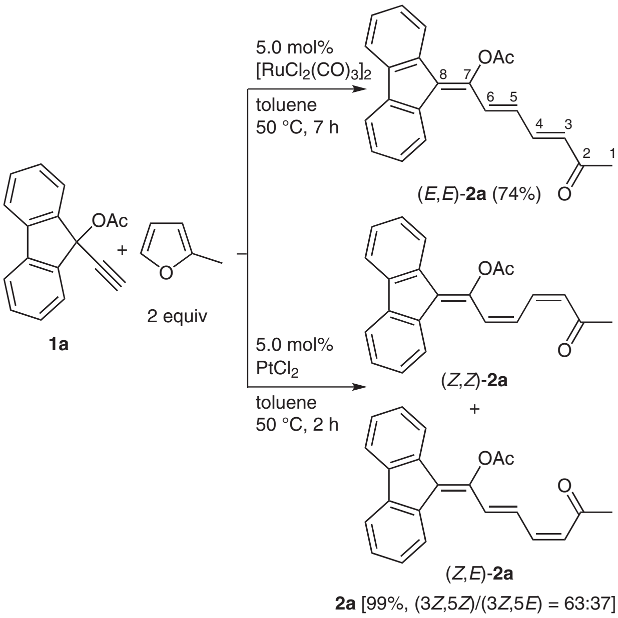
Recently, we reported the ruthenium- and platinum-catalyzed ring-opening reactions of furans with propargyl carboxylates, carbamates, and thiocarbamates to give trienones (Scheme 1).[9]



Scheme 1 Transition-metal-catalyzed ring-opening reaction of furans

Although 5 mol% of ruthenium or platinum catalyst is necessary, π-conjugated compounds are efficiently produced but as a mixture of olefin regioisomers. To construct highly π-conjugated and planer fluorenylidene skeleton, we preliminarily tried to apply our method to the synthesis of fluorenylidenes from 9-ethynylfluoren-9-yl carboxylates under transition-metal catalysis. In the course of our continuous investigation, we found the platinum-catalyzed ring-opening reactions of furans with 9-ethynylfluoren-9-yl carboxylates and sequential palladium-catalyzed isomerization of trienones to give completely *trans*-isomer in a one-pot manner.

At first, we examined the reactivity of 9-ethynylfluoren-9-yl acetate (**1a**)[10] with 2-methylfuran in the presence of ruthenium or platinum catalyst, which is an efficient catalyst for in situ generated carbene transfer reactions (Scheme 2).[11,12]



Scheme 2 Ru- and Pt-catalyzed ring-opening reaction of furans

In the case of the Ru-catalyzed ring-opening reaction, (*E*,*E*)-**2a** (3*E*,5*E*-isomer) was obtained regioselectively with unidentified byproducts.[13] On the other hand, platinum(II) chloride gave the corresponding π-conjugated products as a mixture of (*Z*,*Z*)-**2a** and (*Z*,*E*)-**2a** isomers in excellent yields. These results indicate that the platinum

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catalyst is superior to the ruthenium one in the catalytic activity for the ring-opening reaction, and the platinum catalyst is inferior to the ruthenium one in the regioselectivity for the isomerization of produced trienones. Among the reaction conditions we tried, we could not improve the chemoselectivity of the Ru-catalyzed reaction and the regioselectivity of the Pt-catalyzed reaction, therefore we next examined the isomerization reaction using other transition-metal compounds.

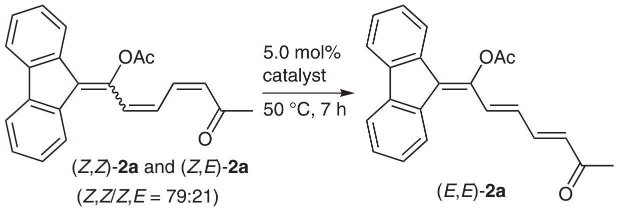
Then, we examined the isomerization of olefin moieties in **2a** to give one regioisomer with a catalytic amount of palladium compounds, which have been reported as good catalysts for olefin isomerization.[14] A mixture of regioisomers **2a** with a ratio of *Z*,*Z*/*Z*,*E* = 79:21 was employed in the isomerization reaction, and selected results are summarized in Table 1.[15]

After heating a mixture of (*Z*,*Z*)-**2a** and (*Z*,*E*)-**2a** at 50 °C with 5 mol% of $PtCl_2$, **2a** was recovered quantitatively with retaining an original ratio of regioisomers (*Z*,*Z*/*Z*,*E* = 77:23; entry 1). This indicates that $PtCl_2$ does not cause olefin isomerization, hence the regioisomeric ratio of (*Z*,*Z*)-**2a** and (*Z*,*E*)-**2a** obtained from the $PtCl_2$-catalyzed ring-opening reactions of 2-methylfuran with **1a** shown in Scheme 2 might be kinetically controlled. When the isomerization reaction of **2a** was carried out with a catalytic amount of $PdCl_2$ in toluene at 50 °C for 7 hours, a mixture of (*Z*,*Z*)-**2a** and (*Z*,*E*)-**2a** was converted to all *trans*-regioisomer (*E*,*E*)-**2a** in quantitative yield, although the diluted conditions were necessary (entries 2 and 3). The reaction with $PdCl_2(MeCN)_2$ also gave (*E*,*E*)-**2a** selectively (entry 4). The isomerization of a mixture of (*Z*,*Z*)-**2a** and (*Z*,*E*)-**2a** proceeded smoothly in THF solution, while CH_2Cl_2 gave **2a** as a mixture of three regioisomers (entries 5 and 6). Palladium(0) complex, such as $Pd(PPh_3)_4$, underwent isomerization of **2a** to some extent, but **2a** was converted into unidentified products with low recovery of **2a** (entry 7).

Since we found that $PdCl_2$ converts a mixture of regioisomers **2a** to (*E*,*E*)-**2a** with high selectivity, we next examined the ring-opening reaction of 2-methylfuran with **1a** in one-pot manner. When the reaction of **1a** with 1.1 equivalents of 2-methylfuran in the presence of 1 mol% of $PtCl_2$ and $PdCl_2$ was carried out in toluene at 50 °C for 7 hours, we succeeded to obtain only one isomer (*E*,*E*)-**2a** in 99% yield (Scheme 3).[16–19] We next applied this one-pot transformation reaction using $PtCl_2$ and $PdCl_2$ to various furans. These results are summarized in Table 2.

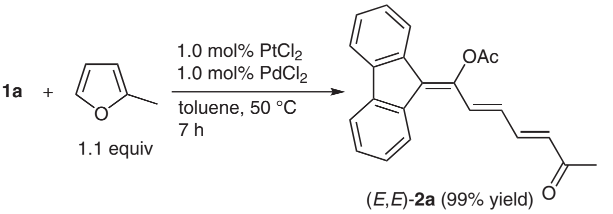
The reaction of 2-methoxyfuran gave the corresponding fluorenylidene (*E*,*E*)-**2b** in 85% yield, although furan gave (*E*,*E*)-**2c** in lower yield (entries 2 and 3). 2-Acetoxyfuran is not suitable for this transformation, giving a trace amount of the corresponding product (entry 4). 2-Arylfurans afforded high yields of fluorenylidene **2d**–**g** (entries 5–8). 2-Benzylfuran afforded the corresponding product (*E*,*E*)-**2h** in good yield (entry 9).

Table 1 Transition Metal-Catalyzed Isomerization of Olefin Moieties[a]

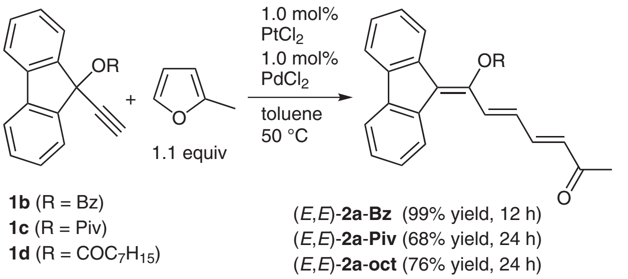


Entry	Catalyst	Solvent	Yield (%)[b]	*Z*,*Z*/*Z*,*E*/*E*,*E*[c]
1	$PtCl_2$	toluene	>99	77:23:0
2	$PdCl_2$	toluene	>99	3:13:84
3[d]	$PdCl_2$	toluene	>99	0:0:100
4	$PdCl_2(MeCN)_2$	toluene	>99	0:0:100
5	$PdCl_2$	THF	>99	0:0:100
6	$PdCl_2$	CH_2Cl_2	>99	48:20:32
7	$Pd(PPh_3)_4$	toluene	89	34:41:25

[a] Reaction conditions: **2a** (0.20 mmol, *Z*,*Z*/*Z*,*E* = 79:21) and catalyst (5 mol%) in solvent (2.0 mL) at 50 °C for 7 h.
[b] Isolated yield.
[c] Determined by ^1H NMR.
[d] Toluene (4.0 mL) was used.



Scheme 3

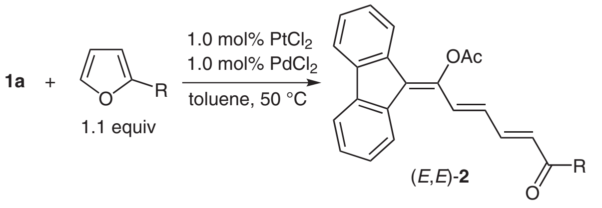


Scheme 4

Finally, we examined the transformation of benzoate **1b**, pivalate **1c**, and octanoate **1d** with 2-methylfuran (Scheme 4). As expected, the corresponding *E*,*E*-isomers were obtained in each case, but giving pivalate (*E*,*E*)-**2a-Piv** and octanoate (*E*,*E*)-**2a-oct** in a little lower yields, respectively.

In conclusion, we have investigated one-pot transformation of 9-acyloxy-9-ethynylfluorenes to 9-fluorenylidenes

Table 2 $PtCl_2$/$PdCl_2$-Catalyzed Ring-Opening Reaction of Furans and Sequential Isomerization[a]



Entry	R	Time (h)	Isolated yield (%)
1	Me	7	99 [(*E*,*E*)-**2a**]
2	OMe	7	85 [(*E*,*E*)-**2b**]
3	H	24	45 [(*E*,*E*)-**2c**]
4	OCOMe	24	trace
5	Ph	9	99 [(*E*,*E*)-**2d**]
6	4-$MeOC_6H_4$	9	99 [(*E*,*E*)-**2e**]
7	4-$F_3CC_6H_4$	15	92 [(*E*,*E*)-**2f**]
8	1-naphthyl	15	95 [(*E*,*E*)-**2g**]
9	Bn	15	92 [(*E*,*E*)-**2h**]

[a] Reaction conditions: **1a** (0.50 mmol), furan (0.55 mmol), and $PtCl_2$ (1.0 mol%) and $PdCl_2$ (1.0 mol%) in toluene (4 mL) at 50 °C.

under platinum/palladium co-catalyst system in excellent yields with high regioselectivity. Trienone skeleton in 9-fluorenylidenes is to be converted to more complex molecules and high π-conjugated materials. These transformations are under investigation in our laboratory.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synlett.

Acknowledgment

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References and Notes

(1) (a) Grimsdale, A. C.; Müllen, K. *Macromol. Rapid Commun.* **2007**, *28*, 1676. (b) Chen, P.; Yang, G.; Liu, T.; Li, T.; Wang, M.; Huang, W. *Polym. Int.* **2006**, *55*, 473. (c) Scherf, U.; List, E. J. W. *Adv. Mater.* **2002**, *14*, 477.

(2) Lyakhov, S. A.; Lyakhova, E. A.; Karpenko, A. S.; Mal'tsev, G. V.; Vel'cheva, I. V.; Litvinova, L. A.; Lebedyuk, M. N.; Khorokhorina, G. A.; Fedchuk, V. P. *Pharm. Chem. J.* **2004**, *38*, 128.

(3) (a) Pan, H.-L.; Fletcher, T. L. *J. Med. Chem.* **1965**, *8*, 491. (b) Morgan, L. R.; Thangaraj, K.; LeBlanc, B.; Rodgers, A.; Wolford, L. T.; Hooper, C. L.; Fan, D.; Jursic, B. S. *J. Med. Chem.* **2003**, *46*, 4552.

(4) Sulsky, R.; Robl, J. A.; Biller, S. A.; Harrity, T. W.; Wetterau, J.; Conolly, F.; Jolibois, K.; Kunselman, L. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 5067.

(5) (a) Feringa, B. L. *J. Org. Chem.* **2007**, *72*, 6635. (b) Eelkema, R.; Pollard, M. M.; Katsonis, N.; Vicario, J.; Broer, D. J.; Feringa, B. L. *J. Am. Chem. Soc.* **2006**, *128*, 14397. (c) Pijper, D.; Feringa, B. L. *Angew. Chem. Int. Ed.* **2007**, *46*, 3693.

(6) Heeney, M.; Bailey, C.; Giles, M.; Shkunov, M.; Sparrowe, D.; Tierney, S.; Zhang, W.; McCulloch, I. *Macromolecules* **2004**, *37*, 5250.

(7) (a) Zheng, G.; Wang, Z.; Tang, L.; Lu, P.; Weber, W. P. *Sens. Actuators, B* **2007**, *122*, 389. (b) Wang, Z.; Xing, Y.; Shao, H.; Lu, P.; Weber, W. P. *Org. Lett.* **2005**, *7*, 87. (c) Wang, Z.; Zheng, G.; Lu, P. *Org. Lett.* **2005**, *7*, 3669. (d) Wang, Z.; Li, W.; Lu, P. *Sens. Actuators, B* **2007**, *122*, 389.

(8) For selected examples, see: (a) Dahl, B. J.; Mills, N. S. *J. Am. Chem. Soc.* **2008**, *130*, 10179. (b) Johnson, A. W.; LaCount, R. B. *Tetrahedron* **1960**, *9*, 130.

(9) (a) Ikeda, Y.; Murai, M.; Abo, T.; Miki, K.; Ohe, K. *Tetrahedron Lett.* **2007**, *48*, 6651. (b) Miki, K.; Fujita, M.; Uemura, S.; Ohe, K. *Org. Lett.* **2006**, *8*, 1741.

(10) Hennion, G. F.; Fleck, B. R. *J. Am. Chem. Soc.* **1955**, *77*, 3253.

(11) **General Procedure of Ring-Opening Reaction of 2-Methylfuran**
In a flame-dried Schlenk tube, $PtCl_2$ (6.5 mg, 0.025 mmol, 5 mol%) was dispersed in toluene (2.0 mL). To the solution were added **1a** (124 mg, 0.50 mmol) and 2-methylfuran (90 μL, 1.0 mmol) at r.t. The mixture was stirred at 50 °C for 7 h. The yellow suspension was cooled and the solvent was removed under reduced pressure to give **2a**. To remove the platinum catalyst, the crude **2a** was dissolved in THF (30 mL) and the solution was passed through a short Florisil column. The THF solution was evaporated under reduced pressure to give **2a** (99%, *Z*,*Z*/*Z*,*E* = 63:37). In the case of $[RuCl_2(CO)_3]_2$, the THF solution obtained after a Florisil column was evaporated in vacuo, and the residue was purified by centrifuge with hexane and a small amount of THF to give a first crop of (*E*,*E*)-**2a** (ca. 65% yield). The hexane and THF solution containing a small amount of (*E*,*E*)-**2a** was evaporated in vacuo, and the residue was purified by column chromatography on SiO_2 with hexane–EtOAc (v/v = 4:1) to give a second crop of (*E*,*E*)-**2a** (ca. 10% yield). The yield in Scheme 2 was obtained by combining first and second crops of (*E*,*E*)-**2a**.

(12) **Analytical Data of (*E*,*E*)-2a, (*Z*,*Z*)-2a and (*Z*,*E*)-2a**
Compound (*E*,*E*)-**2a**: yield 74%; a yellow solid; mp 203.7–204.1 °C. IR (KBr): 3054, 1752 (C=O), 1654, 1198, 1176, 728 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.34 (s, 3 H), 2.51 (s, 3 H), 6.32 (d, *J* = 15.2 Hz, 1 H), 6.63 (dd, *J* = 11.2, 14.6 Hz, 1 H), 7.25–7.34 (m, 5 H), 7.63 (d, *J* = 14.6 Hz, 1 H), 7.68 (d, *J* = 8.0 Hz, 1 H), 7.70 (d, *J* = 8.0 Hz, 1 H), 7.77 (d, *J* = 8.0 Hz, 1 H), 7.79 (d, *J* = 8.0 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.1, 27.6, 119.9, 120.2, 125.2, 125.3, 127.3, 127.7, 128.8, 129.2, 130.8, 131.1, 132.3, 132.7, 135.6, 136.7, 140.3, 140.9, 141.6, 144.8, 168.2, 198.0. Anal. Calcd for $C_{22}H_{18}O_3$: C, 79.98, H, 5.49. Found: C, 79.87; H, 5.66.
Compounds (*Z*,*Z*)-**2a** and (*Z*,*E*)-**2a**: yield 99%; a yellow solid. ^1H NMR (400 MHz, $CDCl_3$): δ [(*Z*,*Z*)-**2a**] = 2.27 (s, 3 H), 2.38 (s, 3 H), 6.14 (d, *J* = 11.7 Hz, 1 H), 7.04 (dd, *J* = 11.2, 11.7 Hz, 1 H), 7.04 (d, *J* = 11.7 Hz, 1 H), 7.22–7.37 (m, 4 H), 7.64–7.70 (m, 4 H), 7.77-7.80 (m, 1 H); δ [(*Z*,*E*)-**2a**] = 2.27 (s, 3 H), 2.56 (s, 3 H), 6.17 (d, *J* = 11.2 Hz, 1 H), 6.68 (dd, *J* = 11.2, 11.2 Hz, 1 H), 7.22–7.37 (m, 4 H), 7.49 (d, *J* = 15.1 Hz, 1 H), 7.64–7.70 (m, 2 H), 7.81 (d, *J* = 8.0 Hz, 2 H), 7.97 (dd, *J* = 11.7, 15.1 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.1, 21.2, 31.9, 31.9, 119.8, 119.8,

120.0, 125.0, 125.1, 125.1, 125.4, 126.6, 127.1, 127.1, 127.4, 127.6, 127.7, 128.4, 128.5, 128.7, 128.9, 129.0, 130.2, 130.5, 130.8, 132.9, 135.7, 135.7, 136.4, 136.5, 136.8, 140.0, 140.1, 140.3, 140.7, 140.8, 144.0, 145.6, 167.7, 168.4, 198.5, 198.6 (two carbon peaks could not be distinguished with other aromatic carbons).

(13) We reported that the Ru-catalyzed reaction of 3-methylbut-1-yn-3-yl acetate with 2-methylfuran gave the corresponding *Z,E*-isomer regioselectively.[9b] Although we cannot explain the difference at present, we presume that the reaction of **1a** using the ruthenium catalyst would proceed via a completely different pathway.

(14) (a) Yu, J.; Gaunt, M. J.; Spencer, J. B. *J. Org. Chem.* **2002**, *67*, 4627. (b) Kim, I. S.; Dong, G. R.; Jung, Y. H. *J. Org. Chem.* **2007**, *72*, 5424; and references therein.

(15) **General Procedure of Isomerization Reaction**
In a flame-dried Schlenk tube, a mixture of (*Z*,*Z*)-**2a** and (*Z*,*E*)-**2a** (66 mg, 0.20 mmol, *Z*,*Z*/*Z*,*E* = 79:21) and a transition-metal compound (0.010 mmol) were dispersed in toluene (2.0 mL). The mixture was stirred at 50 °C for 7 h. The yellow suspension was cooled, and the solvent was removed under reduced pressure. The purification step using column chromatography on SiO_2 was necessary for $Pd(PPh_3)_4$-catalyzed reaction. $PdCl_2$ was purchased from Wako Pure Chemicals Inc. (Japan) and used without further purification.

(16) Without $PtCl_2$, no (*E*,*E*)-**2a** was detected, and **1a** was recovered in 70% yield.

(17) Although THF is one of the suitable solvents for the isomerization reaction of **2a**, the reaction of **1a** and 2-methylfuran with $PtCl_2/PdCl_2$ in THF gave (*E*,*E*)-**2a** selectively but in a lower yield than that in toluene because of unidentified byproduct formation.

(18) Since the reaction using $[RuCl_2 (CO)_3]_2$ gave (*E*,*E*)-**2a** regioselectively, as shown in Scheme 2, we also examined co-catalytic system using $[RuCl_2 (CO)_3]_2$ and $PtCl_2$. When the reaction of **1a** with 2-methylfuran (2 equiv) in 5 mol% of $PtCl_2$ and 5 mol% of $[RuCl_2(CO)_3]_2$ was carried out at 50 °C, we obtained **2a** with a mixture of three regioisomers (*Z*,*Z*/*Z*,*E*/*E*,*E* = 27:28:45) in 93% yield. This indicates that the ruthenium complex has comparatively lower catalytic activity for isomerization reaction than palladium compounds shown in Table 1.

(19) **General Procedure of Ring-Opening Reaction and Sequential Isomerization Reaction**
In a flame-dried Schlenk tube, $PtCl_2$ (1.3 mg, 0.0050 mmol) and $PdCl_2$ (0.9 mg, 0.0050 mmol) were dispersed in toluene (4.0 mL). To this solution were added **1a** (124 mg, 0.50 mmol) and 2-methylfuran (50 μL, 0.55 mmol) at r.t. The mixture was stirred at 50 °C for 7 h. The yellow suspension was cooled, and the solvent was removed under reduced pressure to give **2a**. To remove the transition-metal catalysts, the crude **2a** was dissolved in THF (30 mL), and the solution was passed through a short Florisil column. The THF solution was evaporated under reduced pressure to give (*E*,*E*)-**2a** in 99% yield. For reactions using other furans, the THF solution obtained after a Florisil column was evaporated in vacuo, and the residue was purified by centrifuge with hexane and a small amount of THF to give a first crop of (*E*,*E*)-**2**. The hexane and THF solution containing a small amount of (*E*,*E*)-**2** was evaporated in vacuo, and the residue was purified by column chromatography on SiO_2 with hexane–EtOAc (v/v = 4:1) to give a second crop of (*E*,*E*)-**2**. The yield in Table 2 was obtained by combining first and second crops of (*E*,*E*)-**2**. The analytical data of (*E*,*E*)-**2** are summarized in the Supporting Information.