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Novel Platinum-Catalyzed Tandem Reaction: An Efficient Approach to Construct Naphtho[1,2-*b*]furan

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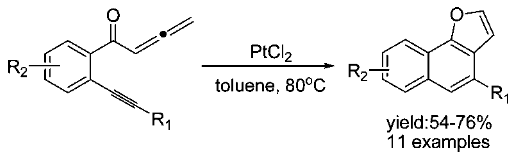
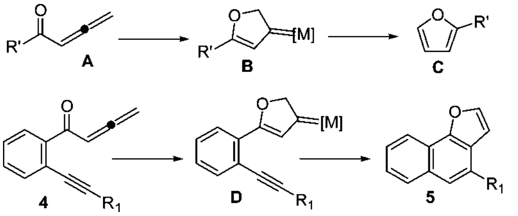


An efficient approach to synthesize naphtho[1,2-*b*]furan has been developed via platinum-catalyzed tandem reaction. This new tandem catalysis induces a cycloisomerization of allenyl ketone, followed by a 6π-electrocyclization-type reaction of carbene intermediate. The metal carbene proved to be an effective intermediate in the 6π-electrocyclization-type reaction.

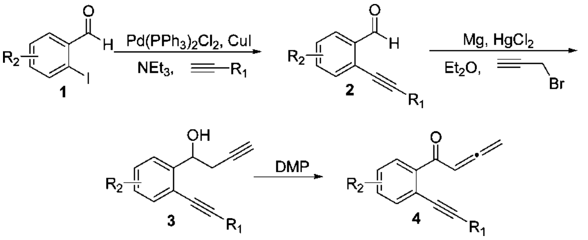
Modern synthetic research has been directed toward the development of new methodologies that provide synthetic efficiency and atom economy.[1] One of the ways to fulfill this goal is to develop and use tandem reactions. Tandem reactions serve as a powerful tool for the rapid and efficient assembly of complex structures from simple starting materials with minimal production of waste.[2] Development of catalytic tandem reactions has proven to be a challenging task. There has been tremendous development in gold and platinum catalysis, which has led to new synthetic methods as well as versatile applications in the total synthesis of natural products. Both gold and platinum catalysts are superior reagents in activating alkynes, allenes, and alkene functionalities under mild conditions and at low catalyst loading. They offer an attractive alternative means for highly efficient tandem reactions.[3]

Recently, Hashimi reported that the cycloisomerization of allenyl ketones was catalyzed by cationic $AuCl_3$ (Scheme 1).[4a] Ag-, Cu-, and Pt-catalyzed cycloisomerizations of allenyl ketones have also been reported by Gevorgyan.[4b] The carbonyl oxygen atom served as an intramolecular nucleophile and the carbene intermediate **B** finally delivered the product **C**. We envisioned that the 1,3-dien-5-yne intermediate **D** with an alkynyl group at the ortho-position would undergo a 6π-electrocyclization-type reaction to afford naphtho[1,2-*b*]furan.[5] Naphtho[1,2-*b*]furan is widely identified as a key structural subunit in numerous natural products. Although a number of synthetic methods have appeared for the preparation of this class of heterocycle, further development of novel expeditious methods is still desired.[6]

SCHEME 1. Proposed Tandem Reaction



SCHEME 2. Synthesis of Precursors



The starting materials were prepared in three steps as shown in Scheme 2. Aldehyde **2** was obtained by a Sonogashira cross-coupling of 2-iodobenzaldehyde **1** with a terminal alkyne.[7] Treatment of **2** with propargyl magnesium bromide in the presence of a catalytic amount of $HgCl_2$ in Et_2O gave the alcohol **3**.[8] This was then oxidized to **4** by using the Dess–Martin reagent.[9] This step included a subsequent isomerization of the propargyl function to the allenyl ketone during the workup.[10]

Initially, we started our investigation by using the substrate **4a** (Table 1). The desired transformation was examined by using

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[†] Lanzhou University.

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(1) Trost, B. M. *Science* **1991**, *254*, 1471.

(2) For recent review of tandem reactions, see: (a) Guo, H.-C.; Ma, J.-A. *Angew. Chem., Int. Ed.* **2006**, *45*, 354. (b) Nicolaou, K. C.; Edmonds, D. J.; Bulger, P. G. *Angew. Chem., Int. Ed.* **2006**, *45*, 7134. (c) Pellissier, H. *Tetrahedron* **2006**, *62*, 2143. (d) Tietze, L. F.; Rackelmann, N. *Pure Appl. Chem.* **2004**, *76*, 1967. (e) Nicolaou, K. C.; Montagnon, T.; Snyder, S. A. *Chem. Commun.* **2003**, 551.

(3) (a) Früstner, A.; Davies, P. W. *Angew. Chem., Int. Ed.* **2007**, *46*, 3410. (b) Bongers, N.; Krause, N. *Angew. Chem., Int. Ed.* **2008**, *47*, 2178. (c) Gorin, D. J.; Toste, F. D. *Nature* **2007**, *446*, 395. (d) Jiménez, N. E.; Echavarren, A. M. *Chem. Commun.* **2007**, 333. (e) Hashmi, A. S. K.; Hutchings, G. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 7896.

(4) (a) Hashimi, A. S. K.; Schwarz, L.; Choi, J.-H.; Frost, T. M. *Angew. Chem., Int. Ed.* **2000**, *39*, 2285. (b) Schwier, T.; Gevorgyan, V. *J. Am. Chem. Soc.* **2007**, *129*, 9868.

(5) (a) Tantillo, D. J. *Annu. Rep. Prog. Chem., Sect. B: Org. Chem.* **2006**, *102*, 269. (b) Beaudry, C. M.; Malerich, J. P.; Trauner, D. *Chem. Rev.* **2005**, *105*, 4757.

(6) See e.g.: (a) van Otterlo, W. A. L.; Morgans, G. L.; Madeley, L. G.; Kuzvidza, S.; Moleele, S. S.; Thornton, N.; de Koning, C. B. *Tetrahedron* **2005**, *61*, 7746. (b) Maertens, F.; Toppet, S.; Compernolle, F.; Hoornaert, G. J. *Eur. J. Org. Chem.* **2004**, *12*, 2707. (c) Martín-Matute, B.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *J. Am. Chem. Soc.* **2003**, *125*, 5757. (d) Arrault, A.; Merour, J.-Y.; Leger, J.-M.; Jarry, C.; Guillaumet, G. *Helv. Chim. Acta* **2001**, *84*, 2198. (e) Duperrouzel, P.; Lee-Ruff, E. *Can. J. Chem.* **1980**, *58*, 51.

(7) Hamze, A.; Provot, O.; Alami, M.; Brion, J.-D. *Org. Lett.* **2005**, *7*, 5625.

(8) Albert, P.; August, R.; Mahrokh, T.; Tadamichi, F. *J. Am. Chem. Soc.* **1983**, *105*, 933.

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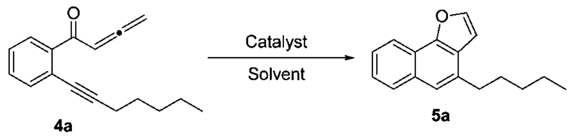
TABLE 1. Optimization of Reaction Conditions[a]



4a **5a**

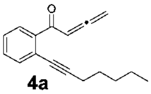
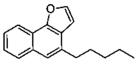
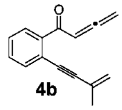
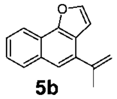
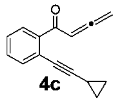
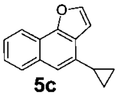
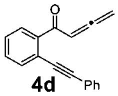
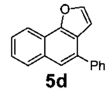
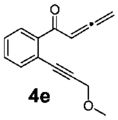
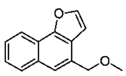
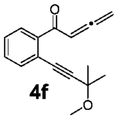
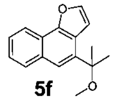
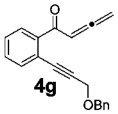
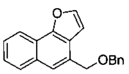
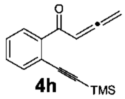
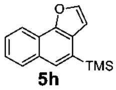
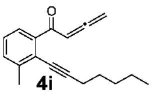
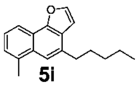
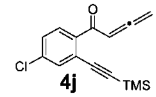
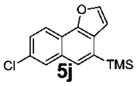
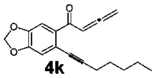
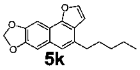
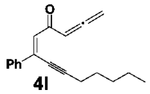
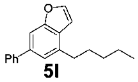
entry	catalyst (mol %)	solution	*t* (°C)	time (h)	yield
1	Au(PPh$_3$)Cl (5)	DCM	40	24	NR[b]
2	AuCl (5)	DCM	40	24	NR
3	AuCl$_3$ (5)	DCM	40	24	trace
4	AgBF$_4$ (5)	DCM	40	24	NR
5	AgOTf (5)	DCM	40	24	NR
6	PtCl$_2$ (10)	DCM	40	5	51%
7	PtCl$_2$ (10)	DCE	60	6	42%
8	PtCl$_2$ (10)	CH$_3$CN	60	6	14%
9	PtCl$_2$ (10)	toluene	60	5	69%
10	PtCl$_2$ (10)	toluene	80	5	72%
11	PtCl$_2$ (10)	toluene	rt	24	11%
12	PtCl$_2$ (10)	toluene	100	5	62%

[a] Reactions were conducted with 0.4 mmol of **4a** in 3 mL of solvent. [b] No reaction.

a variety of transition metal complexes in CH$_2$Cl$_2$ at 40 °C.[11] In the presence of Au(PPh$_3$)Cl and AuCl, the formation of naphtha[1,2-*b*]furan **5a** was not observed (Table 1, entries 1 and 2). Treatment of compound **4a** with 5 mol % of AuCl$_3$ only produced a small amount of **5a**, and the reaction did not proceed to completion even after 24 h (Table 1, entry 3). In the absence of transition metal salts, the reaction did not take place at all. With 5% of AgBF$_4$ or AgOTf as a catalyst, the starting material **4a** was rapidly consumed, but TLC monitoring did not indicate that any trace of **5a** was formed (Table 1, entries 4 and 5). Fortunately, naphtha[1,2-*b*]furan **5a** was obtained by using PtCl$_2$ (10 mol %) as a catalyst (Table 1, entry 6). On the other hand, the effect of the solvent was investigated and the use of toluene afforded comparable results. Employing 1,2-dichloroethane and MeCN resulted in diminished yields (Table 1, entries 7 and 8). Finally, upon increasing the temperature to 80 °C, a yield of 72% was obtained (Table 1, entry 10). Thus, the use of PtCl$_2$ (10 mol %) at 80 °C in toluene was found to be the most efficient conditions.

With the optimized reaction conditions in hand, we next explored the scope of this process by studying a wide variety of substrates (Table 2). Substrates **4b**, **4c**, and **4d**, which have alkenyl, cycloalkyl, and aryl substituents, afforded the desired products **5b**, **5c**, and **5d** in moderate to good yields. Substrates **4e**, **4f**, **4g**, and **4h**, which bear methyl and benzyl ethers or trimethylsilyl substituent, gave the corresponding naphtho[1,2-*b*]furans **5e**, **5f**, **5g**, and **5h** in good yields. The reactions of **4i**, **4j**, and **4k**, which have an electron-rich group or an electron-deficient group on the aromatic ring, also furnished the desired products **5i**, **5j**, and **5k** in good yields. However, the substrate **4*l*** did not provide desired benzofuran **5*l*** even with high catalyst loading (15 mol %) and a prolonged reaction time at an elevated temperature.

TABLE 2. Platium-Catalyzed Synthesis of Naphtho[1,2-*b*]furan[a]

entry	substrate	product	t	yield
1	 **4a**	 **5a**	5h	72%
2	 **4b**	 **5b**	6h	60%
3	 **4c**	 **5c**	5h	67%
4	 **4d**	 **5d**	5h	54%
5	 **4e**	 **5e**	7h	72%
6	 **4f**	 **5f**	4h	76%
7	 **4g**	 **5g**	5h	74%
8	 **4h**	 **5h**	4h	68%
9	 **4i**	 **5i**	5h	70%
10	 **4j**	 **5j**	7h	63%
11	 **4k**	 **5k**	5h	71%
12	 **4l**	 **5l**	12h	NR[b]

[a] All reactions were carried out with **4** (0.4 mmol) with 10 mol % of PtCl$_2$ in toluene (3 mL) at 80 °C. [b] No reaction.

Two mechanistic pathways for this reaction are proposed in Scheme 3. The intermediate **6**, generated from compound **4** with PtCl$_2$, is converted into α,β-unsaturated carbene complex **8** through intramolecular nucleophilic attack of the oxygen atom on the PtCl$_2$-π-complexed allenic double bond.[12] In path a, platinum carbene **8** converts into **9** through a 6π-electrocyclization-type reaction, and the intermediate **9** then undergoes a 1,3-hydrogen shift and loss of the proton to give the intermediate

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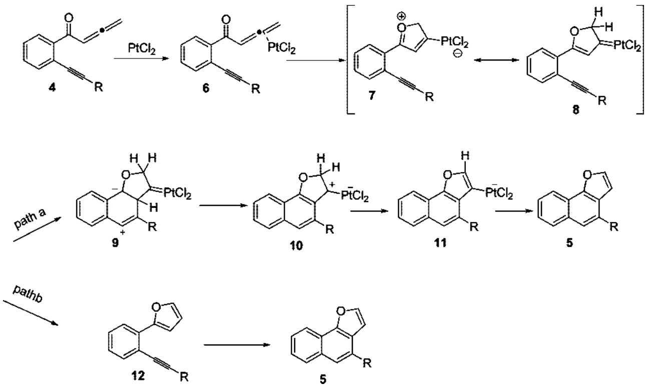
(9) (a) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4156. (b) Frigerio, M.; Santagostino, M.; Sputore, S. *J. Org. Chem.* **1999**, *64*, 4537. (c) Ireland, R. E.; Liu, L. *J. Org. Chem.* **1993**, *58*, 2899. (d) Meyer, S. D.; Schreiber, S. L. *J. Org. Chem.* **1994**, *59*, 7549.

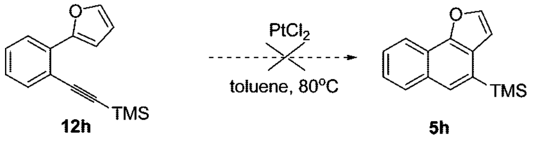
(10) Hashmi, A. S. K.; Bats, J. W.; Choi, J.-H.; Schwarz, L. *Tetrahedron Lett.* **1998**, *39*, 7491.

(11) For recent examples on transition metal catalysis, including reactions of allenes, see e.g.: (a) Chianese, A. R.; Lee, S. J.; Gagné, M. R. *Angew. Chem.* **2007**, *119*, 4118; *Angew. Chem., Int. Ed.* **2007**, *46*, 4042. (b) Marion, N.; Nolan, S. P. *Angew. Chem.* **2007**, *119*, 2806; *Angew. Chem., Int. Ed.* **2007**, *46*, 2750. (c) Hashmi, A. S. K. *Chem. Rev.* **2007**, *107*, 3180. (d) Widenhoefer, R. A.; Han, X. *Eur. J. Org. Chem.* **2006**, *20*, 4555. (e) Zhang, L.; Sun, J.; Kozmin, S. A. *Adv. Synth. Catal.* **2006**, *348*, 2271. (f) Hoffmann-Röder, A.; Krause, N. *Org. Biomol. Chem.* **2005**, *3*, 387.

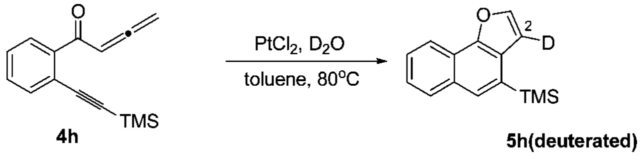
SCHEME 3. **Proposed Mechanism**



SCHEME 4. **Proof of the Proposed Mechanism**



SCHEME 5. **Deuterium Labeling Experiment**



11, which ultimately leads to the observed product **5**. Alternatively, platinum carbene **8** undergoes a 1,2-hydrogen shift first to give the intermediate **12**. Then, 6-endocyclization of **12** leads to the product **5** (path b).

To uncover the reaction mechanism, we investigated the reaction of compound **12h** (R = TMS) in the presence of 10 mol % of $PtCl_2$ in toluene at 80 °C (Scheme 4). The reaction did not occur to give the product **5h**[6c] and we concluded that the reaction could not occur through path b. Furthermore, we carried out the deuterium-labeling experiment (Scheme 5). When D_2O (1.5 equiv) was added to the reaction mixture, the product **5h** with the deuterium-labeling at the C-2 position (56% D incorporation) was obtained in 66% yield. The result was consistent with the mechanism of path a.

In conclusion, we have developed an efficient method for constructing various substituted naphtho[1,2-*b*]furan via the Pt-catalyzed tandem cycloisomerization and 6π-electrocycliztion-type reaction. The deuterium-labeling experiment shows the metal carbene intermediate generated from cycloisomerization of allenyl ketones may be an effective functionality in the 6π-electrocyclization-type reaction.

Experimental Section

General Procedure for Substituted Naphtha[1,2-*b*]furan 5 from the Tandem Reaction of Compound 4. To a solution of substrate **4** (0.40 mmol) in toluene (3.0 mL) was added 10.0 mg (0.04 mmol, 10 mol %) of $PtCl_2$ under air at 80 °C. When the reaction was complete as determined by TLC analysis, the reaction mixture was diluted with diethyl ether (40 mL). The mixture was washed with water and brine. The organic layer was separated, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel to afford the corresponding naphtho[1,2-*b*]furan **5**.

Trimethyl(naphtho[1,2-*b*]furan-4-yl)silane (5h). 5b was prepared according to the above procedure in 68% yield as an oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87−7.85 (d, *J* = 8.0 Hz, 1 H), 7.58−7.55 (dd, *J* = 1.6, 8.8 Hz, 1 H), 7.50 (s, 1H), 7.44−7.43 (d, *J* = 3.6 Hz, 1 H), 7.40−7.36 (m, 1 H), 7.22−7.18 (td, *J* = 1.2, 8.0 Hz, 1 H), 6.54−6.52 (q, *J* = 1.6 Hz, 1 H), 0.32 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.9, 141.8, 134.2, 132.0, 128.8, 126.5, 125.3, 118.0, 111.5, 109.7, 105.2, 99.5, 0.19. IR (KBr, cm^{-1}) 2958, 2154, 1479, 1250, 862, 759; HRMS (EI) (calcd for $C_{15}H_{15}OSi$) 240.0965, found 240.0960 [M^+].

Acknowledgment. We are grateful for the financial support of the National Natural Science Foundation of China (NSFC, 20772051) and the Program for program "111" and NCET-05-0880 from the Chinese Ministry of Education of the People's Republic of China.

Supporting Information Available: Experimental details and characterization data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(12) For platinum−carbene intermediates, see, e.g.: (a) Chatani, N.; Furukawa, N.; Sakurai, H.; Murai, S. *Organometallic* **1996**, *15*, 901. (b) Mamane, V.; Gress, T.; Krause, H.; Fürstner, A. *J. Am. Chem. Soc.* **2004**, *126*, 8654. (c) Funami, H.; Kusama, H.; Iwasawa, N. *Angew. Chem., Int. Ed.* **2007**, *46*, 909. (d) Früstner, A.; Szillat, H. *J. Am. Chem. Soc.* **1998**, *120*, 8305. (e) Früstner, A.; Stelzer, F.; Szillat, H. *J. Am. Chem. Soc.* **2001**, *123*, 12863.