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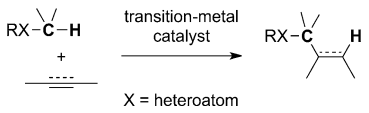
C–H Activation

Iridium-Catalyzed Intramolecular Methoxy C–H Addition to Carbon–Carbon Triple Bonds: Direct Synthesis of 3-Substituted Benzofurans from *o*-Methoxyphenylalkynes

Takeru Torigoe, Toshimichi Ohmura,* and Michinori Suginome*[a]

Abstract: Catalytic hydroalkylation of an alkyne with methyl ether was accomplished. Intramolecular addition of the C–H bond of a methoxy group in 1-methoxy-2-(arylethynyl)benzenes across a carbon–carbon triple bond took place efficiently either in toluene at 110 °C or in *p*-xylene at 135 °C in the presence of an iridium catalyst. The initial 5-exo cyclization products underwent double-bond migration during the reaction to give 3-(arylmethyl)benzofurans in high yields.

Transition-metal-catalyzed hydroalkylation, that is, addition of a C(sp^3)–H bond to a carbon–carbon unsaturated bond, is an atom- and step-economical bond-forming reaction. Hydroalkylation at the C–H bond α to a heteroatom such as oxygen, nitrogen, and sulfur is particularly attractive because it allows chemoselective functionalization of heteroatom-containing organic compounds (Scheme 1).[1] Indeed, catalytic addition of



Scheme 1. Transition-metal-catalyzed hydroalkylation of alkynes and alkenes by cleavage of the C(sp^3)–H bond α to heteroatoms.

a C–H bond α to nitrogen atoms in alkylamines and their derivatives to carbon–carbon unsaturated bonds has been demonstrated by using various transition-metal catalysts (Scheme 1, X = N).[2,3] The protocol has been extended to intramolecular variants, which lead to the formation of nitrogen-containing heterocyclic compounds.[3d,e,g] In contrast, utilization of an oxygen-bound C–H bond in hydroalkylation remains limited (Scheme 1, X = O).[3d,e,4–6] Lewis acid mediated reactions involving a 1,5-hydride shift and variants using platinum and gold catalysts are known for benzylic and cyclic ethers.[4] In addition, transition-metal-catalyzed hydroalkylation with alcohols and THF, which may involve a radical process[5] or a redox-triggered C–C coupling mechanism[6] instead of direct activation and insertion of α-C–H into C–C unsaturated bonds, has also been reported. However, to our knowledge, hydroalkylation with methyl ethers ($ROCH_3$) has not been achieved.[7] Given that the methyl ether functionality is ubiquitous in organic compounds, it is synthetically valuable to establish hydroalkylation at the α-C–H bond of methoxy groups by using transition-metal catalysts. In the course of our study on the catalytic activation of C(sp^3)–H bonds of the methyl group on a silicon atom,[8] we became interested in the activation of methyl groups bound to an oxygen atom. We herein report the intramolecular addition of a C–H bond of the methoxy group across the carbon–carbon triple bond of *o*-methoxyphenylalkynes. The initial 5-*exo* cyclization products underwent double-bond migration during the reaction to afford 3-substituted benzofurans selectively.

1-Methoxy-2-(phenylethynyl)benzene (**1a**) was reacted in toluene at 110 °C in the presence of $[IrCl(C_2H_4)_2]_2$ (2 mol%) as a catalyst precursor and DTBM-SEGPHOS (**L1**, 4 mol%) as a ligand (Table 1, entry 1).[9] The reaction gave 3-benzylbenzofuran (**2a**) and (*E*)-3-benzylidene-2,3-dihydrobenzofuran ((*E*)-**3a**) in 36 and 20% yield, respectively, after 12 h (entry 1). When the reaction was carried out with an extended reaction time (24 h), **2a** and (*E*)-**3a** were formed in 91 and 2% yield, respectively (entry 2). These results and deuterium-labeling experiments, which are described later, indicate that intramolecular addition of a C–H bond of the methoxy group of **1a** took place across the C–C triple bond in a *syn* fashion to give (*E*)-**3a**, which underwent double-bond migration to afford **2a**. The reaction proceeded efficiently at 110 °C, whereas conducting the reaction at 80 °C resulted in low conversion (entry 3). $[IrCl(C_2H_4)_2]_2$ was the most suitable catalyst precursor, whereas the use of $[IrCl(cod)]_2$ or $[Ir(OMe)(cod)]_2$ (cod = 1,5-cyclooctadiene) resulted in slower or no reaction (entries 4 and 5). Ligands **L1** and DTBM-MeOBIPHEP (**L4**) were optimal for both hydroalkylation and double-bond migration (entries 2 and 9); an inefficient catalyst was formed with DM-SEGPHOS (**L2**, entry 7), and the iridium complex bearing DTBM-BINAP (**L3**) demonstrated moderate catalyst activity (entry 8). These results indicate that the 3,5-*tert*-butyl-4-methoxyphenyl (DTBM) group on the phosphorus atoms and the 6,6′-dialkoxy-1,1′-biphenyl backbone are key ligand structures that are required to accomplish high catalyst efficiency. Iridium and ligand were both es-

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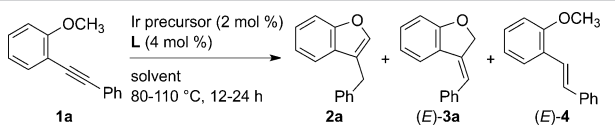
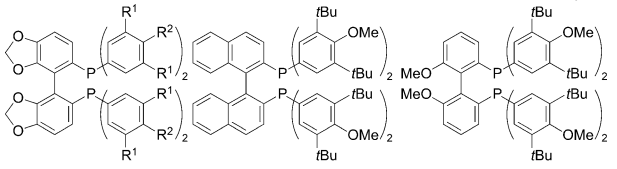
Table 1. Reaction conditions.[a]



1a 2a (*E*)-3a (*E*)-4

Entry	Ir precursor	L	Solvent	*T* [°C], *t* [h]	Yield [%] 2a[b]	3a[b]	4[b]
1	$[IrCl(C_2H_4)_2]_2$	**L1**	toluene	110, 12	36	20	0
2	$[IrCl(C_2H_4)_2]_2$	**L1**	toluene	110, 24	91	2	0
3	$[IrCl(C_2H_4)_2]_2$	**L1**	toluene	80, 24	1	6	0
4	$[IrCl(cod)]_2$	**L1**	toluene	110, 24	57	18	2
5	$[Ir(OMe)(cod)]_2$	**L1**	toluene	110, 24	0	0	0
6	–	**L1**	toluene	110, 24	0	0	0
7	$[IrCl(C_2H_4)_2]_2$	**L2**	toluene	110, 24	6	3	0
8	$[IrCl(C_2H_4)_2]_2$	**L3**	toluene	110, 24	36	16	0
9	$[IrCl(C_2H_4)_2]_2$	**L4**	toluene	110, 24	89	2	0
10	$[IrCl(C_2H_4)_2]_2$	-	toluene	110, 24	0	0	0
11	$[IrCl(C_2H_4)_2]_2$	**L1**	THF	110, 24	0	4	40
12	$[IrCl(C_2H_4)_2]_2$	**L1**	octane	110, 24	11	10	40

[a] **1a** (0.10 mmol), an Ir precursor (0.0020 mmol), and **L** (0.0040 mmol) were stirred in solvent (0.2 mL) at 80–110 °C for 12–24 h. [b] ^{1}H NMR yield.



DTBM-SEGPHOS, **L1** (R^1 = *t*Bu, R^2 = OMe) DM-SEGPHOS, **L2** (R^1 = Me, R^2 = H)

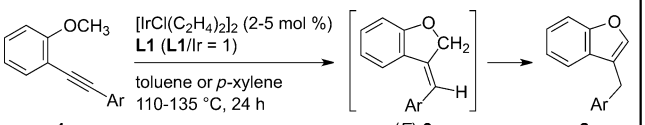
DTBM-BINAP, **L3**

DTBM-MeOBIPHEP, **L4**

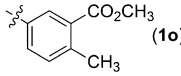
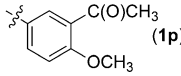
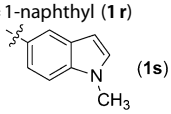
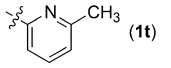
sential; no reaction took place in the absence of either of these components (entries 6 and 10). A possible side reaction was hydrogenation of the C–C triple bond to give 1,2-diarylethane (*E*)-**4**, which can occur through iridium-catalyzed hydrogen transfer from solvent.[10,11] Indeed, the reaction of **1a** in either THF or octane gave predominantly (*E*)-**4**, rather than **2** and (*E*)-**3a** (entries 11 and 12). This undesirable reaction was completely suppressed when the reaction was conducted in toluene (entry 2).[12]

A range of 1-methoxy-2-(arylethynyl)benzene derivatives were subjected to the iridium-catalyzed intramolecular hydroalkylation double-bond migration (Table 2).[13] Substrate **1b**, bearing a 4-tolyl group at the terminus of the ethynyl group, reacted smoothly under the standard conditions to give **2b** in high yield (Table 2, entry 2). Higher catalyst loading (8 mol%) was required for full conversion in the reaction of trifluoromethylphenyl-substituted substrate **1c** (entry 3). The relative reactivity decreased in the order **1b** > **1a** > **1c**,[14] indicating that the presence of an electron-rich aryl group increases the reactivity. Substrates **1d**–**h** bearing methoxy, benzyloxy, siloxy, phenoxy, and trifluoromethyloxy groups, respectively, were all tolerated in the reaction (entries 4–8). Methoxy- and benzyloxy-substituted compounds **1d** and **1e** showed lower reactivity than **1f**–**h** and the reaction required both elevated temperature and higher catalyst loading (entries 4 and 5), indicating that coordination of the ether functionality may reduce the activity of the catalyst.

Table 2. Iridium-catalyzed intramolecular hydroalkylation double-bond migration of **1** to give benzofuranes.[a]



1 (*E*)-3 2

Entry	Substrate	*T* [°C], $[IrCl(C_2H_4)_2]_2$ [mol%]	Yield [%][b]
1	R = H (**1a**)	110, 2	85 (**2a**)
2	R = CH_3 (**1b**)	110, 2	82 (**2b**)
3	R = CF_3 (**1c**)	110, 4	83 (**2c**)
4	R = OCH_3 (**1d**)	135, 4	74 (**2d**)
5	R = OCH_2Ph (**1e**)	135, 4	74 (**2e**)
6	R = OTBS (**1f**)	110, 4	77 (**2f**)
7	R = OPh (**1g**)	110, 3	80 (**2g**)
8	R = OCF_3 (**1h**)	110, 3	84 (**2h**)
9	R = B(pin) (**1i**)	135, 3	78 (**2i**)
10	R = $C(O)CH_3$ (**1j**)	135, 5[c]	46 (**2j**)
11	R = $C(O)CF_3$ (**1k**)	135, 5[c]	66 (**2k**)
12	R = CH_3 (**1l**)	110, 3	81 (**2l**)
13	R = OCH_3 (**1m**)	135, 2	80 (**2m**)
14	R = Br (**1n**)	135, 5	76 (**2n**)
15	Ar =  (**1o**)	135, 5[c]	40 (**2o**)
16	Ar =  (**1p**)	135, 5[c]	70 (**2p**)
17	Ar = 2-naphthyl (**1q**)	110, 2	77 (**2q**)
18	Ar = 1-naphthyl (**1r**)	135, 3	85 (**2r**)
19	Ar =  (**1s**)	110, 2	81 (**2s**)
20	Ar =  (**1t**)	135, 5[c]	33 (**2t**)

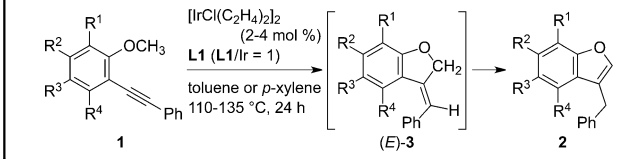
[a] **1** (0.20 mmol), $[IrCl(C_2H_4)_2]_2$ (0.0040–0.010 mmol), and **L1** (**L1**/Ir = 1) were stirred for 24 h either in toluene (0.2 mL) at 110 °C or in *p*-xylene (0.2 mL) at 135 °C unless otherwise noted. [b] Isolated yield. [c] **L4** was used as a ligand.

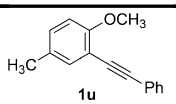
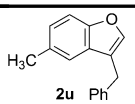
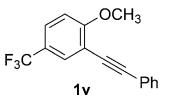
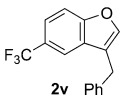
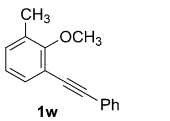
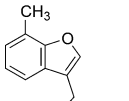
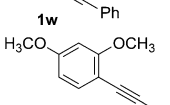
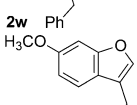
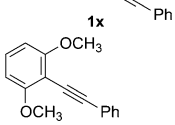
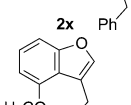
The reaction was applicable to a boronic ester **1i**, giving the synthetically attractive compound **2i** in good yield (Table 2, entry 9). In the reaction of methyl- and trifluoromethyl ketone derivatives **1j** and **1k**, ligand **L4** was more suitable than **L1**; by using **L4**, the corresponding benzofurans **2j** and **2k** were obtained in moderate yields (entries 10 and 11). The reaction of **1l**–**n**, bearing *ortho*-substituted phenyl groups, proceeded effi-

ciently either by increasing the catalyst amount or upon heating the system to 135 °C (entries 12–14). The 2-bromophenyl group of **1n** was tolerated (entry 14), whereas the reaction was completely inhibited by the 4-bromophenyl group of **1z** (Scheme 2). Similar effects of neighboring substituents were observed in the reaction of carbonyl-substituted substrates: only low conversion was observed in the reaction of methyl ester **1aa** (Scheme 2), whereas the *o*-methyl-substituted compound **1o** gave **2o** in moderate yield (entry 15). Ketone **1p**, bearing a methoxy group *ortho* to the carbonyl group, gave a higher yield than that obtained for **1j** (entries 10 and 16). The higher catalyst efficiency with these substrates than with **1aa** is probably due to steric shielding of the carbonyl group from interaction with the iridium catalyst. In addition to naphthalene derivatives **1q** and **1r** (entries 17 and 18), the hydroalkylation double-bond migration was applicable to **1s** and **1t**, which bear 5-indolyl and 2-pyridyl groups, respectively (entries 19 and 20).

1-Methoxy-2-(phenylethynyl)benzene derivatives **1u–y**, which bear substituents R^1–R^4 on the tethering benzene ring, were then subjected to the hydroalkylation double-bond migration (Table 3).[13] Compound **1u** ($R^3 = CH_3$) was slightly more reactive than **1a**, and **2u** was formed efficiently under the standard conditions (entry 1). In contrast, the reaction of **1v** ($R^3 = CF_3$) was slower than that of **1a** and **1u** (entry 2), indicating that an electron-withdrawing group at the R^3-position decreases the reactivity. The reaction of **1w** ($R^1 = CH_3$) was slower than that of **1u**, probably for steric reasons (entry 3). Slower reaction was also observed for **1x** ($R^2 = OCH_3$), which required 135 °C for full conversion (entry 4). In contrast, **1y** ($R^4 = OCH_3$) reacted smoothly under the standard conditions to give **2y** in good yield (entry 5).

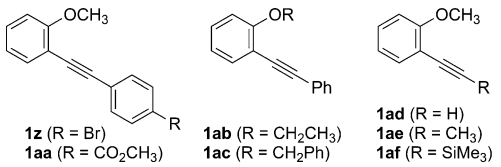
Table 3. Effect of substituents on the tethering benzene ring.[a]



Entry	Substrate	Conditions[b]	Product	Yield [%][c]
1	 **1u**	110 °C, 2 mol%	 **2u**	80
2	 **1v**	110 °C, 4 mol%	 **2v**	78
3	 **1w**	135 °C, 2 mol%	 **2w**	81
4	 **1x**	135 °C, 4 mol%	 **2x**	75
5	 **1y**	110 °C, 2 mol%	 **2y**	76

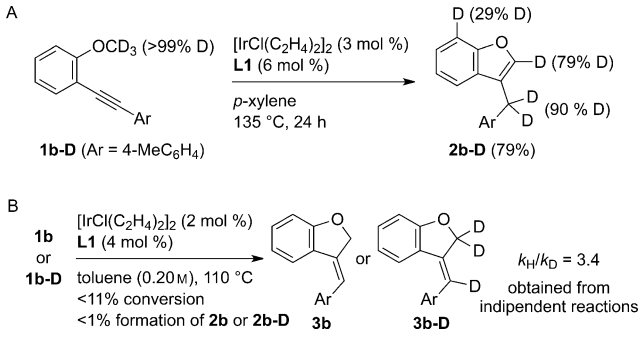
[a] **1** (0.20 mmol), $[IrCl(C_2H_4)_2]_2$ (0.0040–0.0080 mmol), and **L1** (**L1**/Ir = 1) were stirred for 24 h either in toluene (0.2 mL) at 110 °C or in *p*-xylene (0.2 mL) at 135 °C. [b] Mol% of $[IrCl(C_2H_4)_2]_2$ is given. [c] Isolated yield.

Substrates that were not suitable for the reaction under the present conditions are summarized in Scheme 2. In addition to the reaction of **1z** and **1aa** described above, no desired cyclization occurred in the reaction of either **1ab** or **1ac**, bearing ethoxy or benzyloxy groups, respectively, instead of a methoxy group. Submitting terminal alkyne **1ad** to the reaction conditions resulted in the formation of a complex mixture, whereas no reaction took place with trimethylsilylethyne **1af**. Compound **1ae** did not give the desired product, although its conversion was observed at 135 °C.

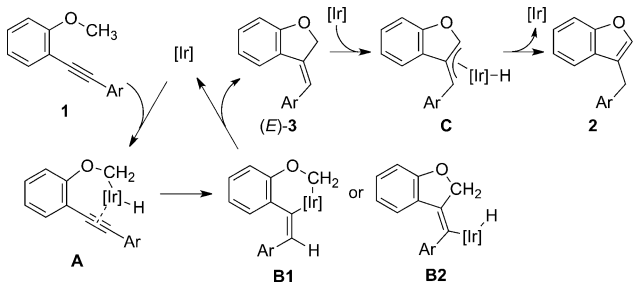


Scheme 2. Unsuitable substrates.

To obtain insight into the mechanism, the reaction of **1b-D** was carried out (Scheme 3A). Given that the reaction of **1b-D** at 110 °C was rather slow compared with that of **1b**, the reaction temperature was set to 135 °C. A benzofuran **2b-D** was obtained in 79% yield with reasonably high deuterium incorporation at both C2 and the benzylic carbon atoms (79 and 90% D, respectively). The observed decrease in the deuterium content is attributed to partial delivery of the deuterium to the C–H bond at C7 of the benzofuran ring.[15] A large kinetic isotope effect ($k_H/k_D = 3.4$) was observed in the independent reactions of **1b** and **1b-D** (Scheme 3B). Based on these results, we propose a possible mechanism for the hydroalkylation double-bond migration (Scheme 4). Coordination of the C–C triple bond of **1** and oxidative addition of the C–H bond of the methoxy group to Ir^I give complex **A**. Insertion of the C–C triple bond into either the Ir–H or Ir–C bond proceeds in an intramolecular *syn* fashion to afford alkenyliridium **B1** or **B2**. Subse-



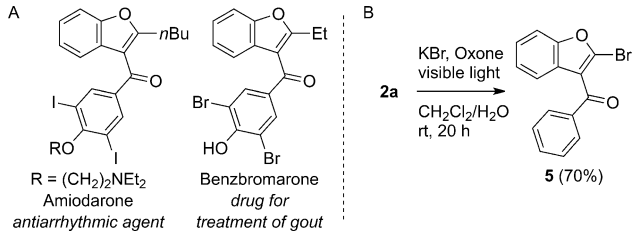
Scheme 3. D-Labeling experiments.



Scheme 4. Possible mechanism.

quent reductive elimination gives (*E*)-**3** with regeneration of Ir^{I}. Compound (*E*)-**3** then undergoes migration of the double bond through a 1,3-H shift via π-allyl iridium **C**, which is formed through oxidative addition of the allylic C–H to Ir^{I}. The observed large kinetic isotope effect indicates that cleavage of the C–H bond to form **A** should be the rate-determining step in the intramolecular hydroalkylation.

2-Alkyl-3-aroylbenzofurans constitute an important structural motif in certain bioactive compounds such as amiodaron[16] and benzbromarone.[17] (Scheme 5 A). The hydroalkylation double-bond migration of **1** provides a new route to such compounds through conversions of **2**. Direct conversion of **2a** into 2-bromo-3-benzoylbenzofuran (**5**) was accomplished by treatment with KBr/Oxone under visible-light irradiation (Scheme 5 B).[18] It has been reported that the bromo group in **5** can be converted by Negishi coupling into an alkyl group with retention of the carbonyl group.[19]



Scheme 5. 2-Substituted 3-aroylbenzofurans as a core structure of biologically active molecules (A), and synthesis of 3-benzoyl-2-bromobenzofuran from the hydroalkylation product (B).

In conclusion, we have established the first catalytic hydroalkylation of C–C multiple bonds with methyl ethers in the iridium-catalyzed conversion of *o*-methoxyphenylalkynes. 3-Substituted benzofurans are formed through intramolecular addition of a C–H bond of a methoxy group across a C–C triple bond and subsequent migration of the double bond. The insights obtained in this study are expected to lead to further catalytic functionalization of $C(sp^3)$–H bonds, the development of which still lags behind that of $C(sp^2)$–H bonds. Further exploration of catalytic addition reactions utilizing $C(sp^3)$–H bonds is being undertaken in this laboratory.

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Keywords: C–C bond formation · C–H activation · hydroalkylation · iridium · oxygen heterocycles

[1] For selected reviews, see: a) S.-Y. Zhang, F.-M. Zhang, Y.-Q. Tu, *Chem. Soc. Rev.* **2011**, *40*, 1937; b) S. Pan, T. Shibata, *ACS Catal.* **2013**, *3*, 704; c) Y. Qin, J. Lv, S. Luo, *Tetrahedron Lett.* **2014**, *55*, 551; d) E. Chong, P. Garcia, L. L. Schafer, *Synthesis* **2014**, *46*, 2884; for reviews on catalytic $C(sp^3)$–H functionalization, see: e) R. Jazzar, J. Hitce, A. Renaudat, J. Sofack-Kreutzer, O. Baudoin, *Chem. Eur. J.* **2010**, *16*, 2654; f) G. Rouquet, N. Chatani, *Angew. Chem. Int. Ed.* **2013**, *52*, 11726; *Angew. Chem.* **2013**, *125*, 11942.

[2] For examples of hydroalkylation with alkylamines catalyzed by Ti, Zr, Nb, Ta, and W, see: a) M. G. Clerici, F. Maspero, *Synthesis* **1980**, 305; b) W. A. Nugent, D. W. Ovenall, S. J. Holmes, *Organometallics* **1983**, *2*, 161; c) S. B. Herzon, J. F. Hartwig, *J. Am. Chem. Soc.* **2007**, *129*, 6690; d) S. B. Herzon, J. F. Hartwig, *J. Am. Chem. Soc.* **2008**, *130*, 14940. For a review, see ref. 1d.

[3] For examples of hydroalkylation with alkylamines and their derivatives catalyzed by Ru, Rh, and Ir, see: a) C. H. Jun, D.-C. Hwang, S.-J. Na, *Chem. Commun.* **1998**, 1405; b) N. Chatani, T. Asaumi, S. Yorimitsu, T. Ikeda, F. Kakiuchi, S. Murai, *J. Am. Chem. Soc.* **2001**, *123*, 10935; c) K. Tsuchikama, M. Kasagawa, K. Endo, T. Shibata, *Org. Lett.* **2009**, *11*, 1821; d) Q. Li, Z.-X. Yu, *J. Am. Chem. Soc.* **2010**, *132*, 4542; e) Q. Li, Z.-X. Yu, *Angew. Chem. Int. Ed.* **2011**, *50*, 2144; *Angew. Chem.* **2011**, *123*, 2192; f) S. Pan, K. Endo, T. Shibata, *Org. Lett.* **2011**, *13*, 4692; g) T. Shibata, H. Hirashima, M. Kasagawa, K. Tsuchikama, K. Endo, *Synlett* **2011**, 2171; h) S. Pan, Y. Matsuo, K. Endo, T. Shibata, *Tetrahedron* **2012**, *68*, 9009; i) D. C. Schmitt, J. Lee, A.-M. R. Dechert-Schmitt, E. Yamaguchi, M. J. Krische, *Chem. Commun.* **2013**, *49*, 6096; j) G. Lahm, T. Opatz, *Org. Lett.* **2014**, *16*, 4201; k) Y. Tahara, M. Michino, M. Ito, K. S. Kanyiva, T. Shibata, *Chem. Commun.* **2015**, *51*, 16660.

[4] For hydroalkylation with benzylic and cyclic ethers catalyzed by Sc, Pt and Au, see: a) S. J. Pastine, K. M. McQuaid, D. Sames, *J. Am. Chem. Soc.* **2005**, *127*, 12180; b) P. A. Vadola, D. Sames, *J. Am. Chem. Soc.* **2009**, *131*, 16525; c) I. D. Jurberg, Y. Odabachian, F. Gagosz, *J. Am. Chem. Soc.* **2010**, *132*, 3543; d) B. Bolte, F. Gagosz, *J. Am. Chem. Soc.* **2011**, *133*, 7696.

[5] For hydroalkylation with alcohols and cyclic ethers catalyzed by Fe, Co, Rh, and Cu, see: a) L. Shi, Y.-Q. Tu, M. Wang, F.-M. Zhang, C.-A. Fan, Y.-M. Zhao, W.-J. Xia, *J. Am. Chem. Soc.* **2005**, *127*, 10836; b) S.-Y. Zhang, Y.-Q. Tu, C.-A. Fan, F.-M. Zhang, L. Shi, *Angew. Chem. Int. Ed.* **2009**, *48*, 8761; *Angew. Chem.* **2009**, *121*, 8917; c) L. Huang, K. Cheng, B. Yao, J. Zhao, Y. Zhang, *Synthesis* **2009**, 3504; d) L. Chen, J. Yang, L. Li, Z. Weng, Q. Kang, *Tetrahedron Lett.* **2014**, *55*, 6096.

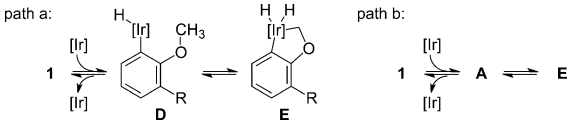
[6] For examples of hydroalkylation with alcohols catalyzed by Ru and Ir, see: a) J. F. Bower, E. Skucas, R. L. Patman, M. J. Krische, *J. Am. Chem. Soc.* **2007**, *129*, 15134; b) F. Shibahara, J. F. Bower, M. J. Krische, *J. Am. Chem. Soc.* **2008**, *130*, 6338; c) R. L. Patman, M. R. Chaulagain, V. M. Williams, M. J. Krische, *J. Am. Chem. Soc.* **2009**, *131*, 2066; d) Y. Obora, S. Hatanaka, Y. Ishii, *Org. Lett.* **2009**, *11*, 3510; e) J. Moran, A. Preetz, R. A. Mesch, M. J. Krische, *Nat. Chem.* **2011**, *3*, 287. For a review, see: J. M. Ketcham, I. Shin, T. P. Montgomery, M. J. Krische, *Angew. Chem. Int. Ed.* **2014**, *53*, 9142; *Angew. Chem.* **2014**, *126*, 9294.

[7] An iridium-catalyzed dehydrogenative coupling of methyl ethers with 3,3-dimethyl-1-butene has been reported. Y. Lin, D. Ma, X. Lu, *Tetrahedron Lett.* **1987**, *28*, 3249.

[8] a) T. Ohmura, T. Torigoe, M. Suginome, *J. Am. Chem. Soc.* **2012**, *134*, 17416; b) T. Ohmura, T. Torigoe, M. Suginome, *Organometallics* **2013**, *32*, 6170; c) T. Ohmura, T. Torigoe, M. Suginome, *Chem. Commun.* **2014**, *50*, 6333.

[9] Ir–**L1** has been reported as an effective catalyst for the hydroarylation of alkenes. C. S. Sevov, J. F. Hartwig, *J. Am. Chem. Soc.* **2013**, *135*, 2116.

[10] J. Choi, A. H. R. MacArthur, M. Brookhart, A. S. Goldman, *Chem. Rev.* **2011**, *111*, 1761.
[11] Probably the reaction took place in a *syn* fashion to give (*Z*)-**4**, which underwent subsequent iridium-catalyzed isomerization to form (*E*)-**4**. The *Z* to *E* isomerization was confirmed by an independent reaction of (*Z*)-**4** (see the Supporting Information).
[12] Formation of a small amount of **4** in entry 4 (Table 1) is probably due to hydrogen transfer from cod.
[13] A protocol to find the suitable reaction conditions is as follows: i) The standard conditions (110 °C/24 h with 4 mol% of Ir–**L1**) were applied; ii) for the substrates that reacted moderately but did not reach full conversion, the reaction was re-examined with higher catalyst loading (6–8 mol%); iii) For the substrates that resulted in low conversion or no reaction, the reaction was retried at 135 °C.
[14] Conversions after 12 h at 110 °C in the presence of Ir–**L1** (4 mol%): **1a** (56%), **1b** (76%), and **1c** (35%).
[15] There are two possible pathways for partial H/D exchange at C7. One is reversible formation of iridacycle **E** from **1** triggered by activation of *ortho* C(sp^2)–H (path a). The other is an alternative formation of **E** via **A** (path b).



[16] J. Wolff, *Pharmacol. Rev.* **1998**, *50*, 89.
[17] R. C. Heel, R. N. Brogden, T. M. Speight, G. S. Avery, *Drugs* **1977**, *14*, 349.
[18] K. Moriyama, M. Takemura, H. Togo, *Org. Lett.* **2012**, *14*, 2414.
[19] J. H. Chaplin, G. S. Gill, D. W. Grobeiny, B. L. Flynn, G. Kremmidiotis, PCT Int. Appl. 2007087684, 2007.

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COMMUNICATION

C–H Activation

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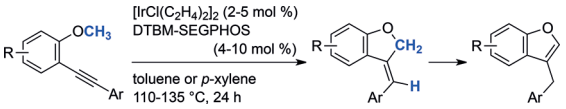
Iridium-Catalyzed Intramolecular Methoxy C–H Addition to Carbon–Carbon Triple Bonds: Direct Synthesis of 3-Substituted Benzofurans from *o*-Methoxyphenylalkynes



Make it active: Intramolecular addition of the C–H bond of a methoxy group in 1-methoxy-2-(arylethynyl)benzenes across a carbon–carbon triple bond took place efficiently in the presence of an iridium catalyst. The initial 5-*exo*-cyclized products underwent double-bond migration during the reaction to give 3-(arylmethyl)benzofurans in high yields (see scheme).