Heterocycle Synthesis

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Rhodium(III)-Catalyzed [3+2] Annulation of 5-Aryl-2,3-dihydro-1*H*-pyrroles with Internal Alkynes through C(sp^2)–H/Alkene Functionalization**

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Abstract: *This study describes a new rhodium(III)-catalyzed [3+2] annulation of 5-aryl-2,3-dihydro-1H-pyrroles with internal alkynes using a $Cu(OAc)_2$ oxidant for building a spirocyclic ring system, which includes the functionalization of an aryl C(sp^2)–H bond and addition/protonolysis of an alkene C=C bond. This method is applicable to a wide range of 5-aryl-2,3-dihydro-1H-pyrroles and internal alkynes, and results in the assembly of the spiro[indene-1,2′-pyrrolidine] architectures in good yields with excellent regioselectivities.*

The 1-azaspiro[4.4]nonanes, including spiro[indene-1,2′-pyrrolidines], are used in many bioactive natural products, pharmaceuticals, and pesticides, as they have important pharmacological and pesticidal properties,[1] including inhibition of the hepatitis C virus (HCV),[1a] inhibition of β-secretase (BACE-1),[1b] agonism of the nicotinic acetylcholine receptors (mAChR),[1c–d] as well as herbicidal activity[1e] and anticancer activity[1f–k] (Figure 1). The routes most commonly used to build the 1-azaspiro[4.4]nonane ring system are the formation of a cyclopentane ring onto a pre-existing pyrrolidine ring and the formation of a pyrrolidine ring onto a pre-existing cyclopentane ring.[2,3] However, these transformations often require multiple synthetic steps, thus limiting the functional group choice. Therefore, a new strategy for the facile one-pot assembly and derivatization of the 1-azaspiro-[4.4]nonane ring system is highly desirable.

Transition-metal-catalyzed cycloaddition reactions have emerged as powerful and step-economic methodologies for the construction of complex cyclic compounds in organic synthesis.[4–8] The transition-metal-catalyzed cycloadditon of aromatic compounds with 2π components (e.g., alkenes, allenes, and alkynes) involving the functionalization of the C(sp^2)–H bonds is promising, as it exhibits a high efficiency and provides opportunities to discover new reactions.[5–7] However, annulation methods[6,7] using this C(sp^2)–H functionalization strategy for the construction of five-membered carbocycles, particularly the annulation methods in the presence of oxidants,[6] are uncommon. These transformations are focused on aryl carbonyl compounds and their derivatives, including benzadehydes, arylketones, benzamides, and aryl imines, and their reaction with alkynes (Scheme 1a).[6,7] However, approaches involving the cleavage of the C–C π bond of alkenes for the annulation of 2π components remain an unexploited area.[8] We report a new, highly selective rhodium(III)-catalyzed [3+2] annulation of 5-aryl-2,3-dihydro-1*H*-pyrroles with internal alkynes for the selective synthesis of spiro[indene-1,2′-pyrrolidines] (Scheme 1b). This method achieves C(sp^2)–H functionalization, the insertion of an alkyne, the addition of a C–C double bond, and a protonolysis.

We began our investigations by optimizing the reaction conditions for the annulation of 3,5-diphenyl-1-tosyl-2,3-dihydro-1*H*-pyrrole (**1a**) with 1,2-diphenylethyne (**2a**) (Table 1). Extensive screening of various reaction parameters revealed that 5 mol% [{Cp*$RhCl_2$}$_2$], 20 mol% $AgSbF_6$,

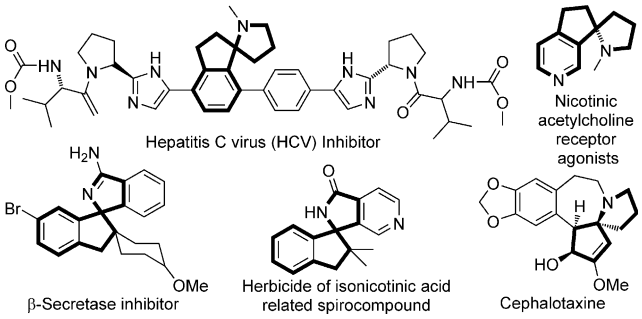

Figure 1. Examples of important 1-azaspiro[4.4]nonanes.

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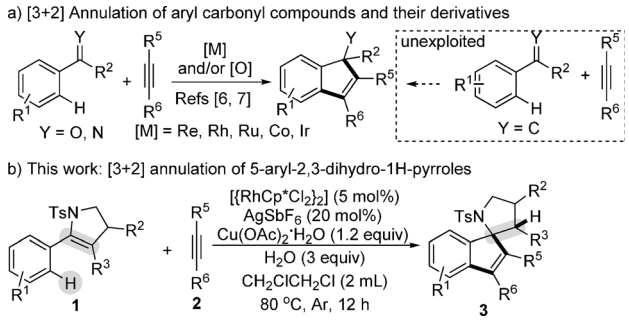
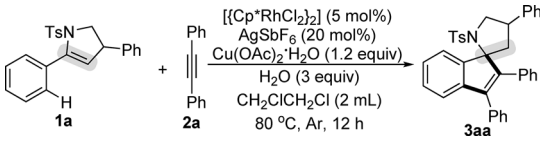


Scheme 1. [3+2] annulation routes to carbocycles. Cp* = C_5Me_5, Ts = 4-toluenesulfonyl.

Table 1: Screening for optimal reaction conditions.[a]



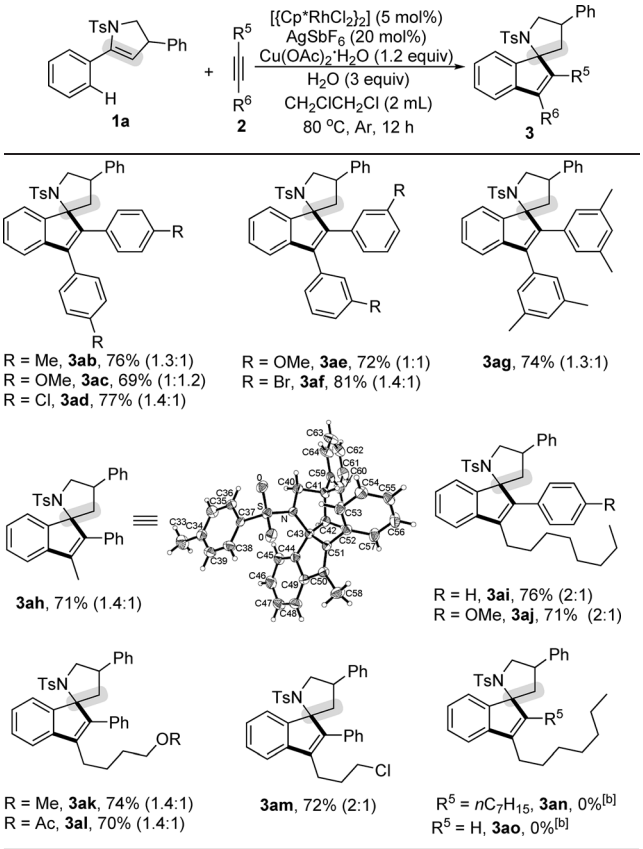
Entry	Variation from the standard conditions	Yield [%]
1	none	82
2	at 60 °C	70
3	at 100 °C	67
4	$[\{Cp^*RhCl_2\}_2]$ (2 mol %)	71
5	$[\{Cp^*RhCl_2\}_2]$ (10 mol %)	81
6	without $[\{RhCpCl_2\}_2]$	0
7	$AgSbF_6$ (30 mol %)	80
8	$AgSbF_6$ (10 mol %)	52
9	without $AgSbF_6$	0
10	AgOAc, Ag_2CO_3, or AgOTf instead of $AgSbF_6$	trace
11	$Cu(OAc)_2{\cdot}H_2O$ (2 equiv)	82
12	$Cu(OAc)_2{\cdot}H_2O$ (0.6 equiv)	66
13	without $Cu(OAc)_2{\cdot}H_2O$	16
14	MeOH instead of $CH_2ClCH_2Cl_2$	trace
15	*t*AmOH instead of $CH_2ClCH_2Cl_2$	36
16	H_2O (6 equiv)	75
17	without H_2O for 24 h	78
18[b]	none	80

[a] Reaction conditions: **1a** (0.15 mmol), **2a** (0.18 mmol), $[\{Cp^*RhCl_2\}_2]$ (5 mol %), $AgSbF_6$ (20 mol %), $Cu(OAc)_2{\cdot}H_2O$ (1.2 equiv), H_2O (3 equiv), and CH_2ClCH_2Cl (2 mL) at 80 °C under Ar for 12 h. The d.r. value is 1.1:1 as determined by ^1H NMR analysis. [b] **1a** (1 g) for 48 h.

1.2 equivalents $Cu(OAc)_2$, and 3 equivalents H_2O in CH_2ClCH_2Cl at 80 °C for 12 hours was the best set of conditions for the annulation of **1a** with **2a**, thus providing the desired spiro[indene-1,2′-pyrrolidine] **3aa** in 82 % yield (entry 1). The reaction temperatures were found to affect the reaction, as the yield of **3aa** decreased from 82 % at 80 °C to 70 % at 60 °C (entry 2) and to 67 % at 100 °C (entry 3). For the amounts of $[\{Cp^*RhCl_2\}_2]$ and $AgSbF_6$ used, we found that 5 mol % $[\{Cp^*RhCl_2\}_2]$ and 20 mol % $AgSbF_6$ were preferred for the annulation reaction (entry 1 versus entries 4, 5, 7, and 8). Notably, a rhodium catalyst was necessary for successful annulation, as its absence resulted in no detectable amount of **3aa** (entry 6). In addition, the reaction did not proceed without silver salts (entry 9) because the formation of an active cationic rhodium species requires a silver salt to trap the Cl anions from the rhodium catalyst.[6] The use of other silver salts, including AgOAc, Ag_2CO_3, and AgOTf, showed relatively lower reactivity (entry 10). Subsequently, the amount of $Cu(OAc)_2$ was examined (entries 11–13). The reaction yield when using 2 equivalents $Cu(OAc)_2$ was identical to that of 1.2 equivalents $Cu(OAc)_2$, whereas the yield decreased from 82 to 52 % when using 0.6 equivalents $Cu(OAc)_2$ (entry 1 versus entries 11 and 12). It should be noted that the reaction can take place without $Cu(OAc)_2$, albeit with a lower yield (entry 13). The screening of solvents revealed that MeOH and *t*AmOH, two reported efficient solvents for the rhodium-catalyzed annulation,[5–7] were less efficient than CH_2ClCH_2Cl for the annulation of **1a** (entries 14 and 15). Notably, the presence of H_2O accelerated the reaction (entries 1, 16, and 17). In the presence of additional H_2O **1a** was consumed completely within 12 hours (entries 1 and 16). However, without additional H_2O a longer reaction time was required (approximately 24 h) to complete the reaction (entry 17). Gratifyingly, a reaction on a one gram scale of **1a** was successfully performed in good yield (entry 18).

After determining the optimal reaction conditions, the scope of this rhodium(III)-catalyzed annulation protocol with respect to the 5-aryl-1-tosyl-2,3-dihydro-1*H*-pyrroles **1** and alkynes **2** was investigated (Table 2 and Table 3).[9] As shown in Table 2, we first applied these optimal reaction conditions

Table 2: Variation of internal alkynes (**2**).[a]



[a] Reaction conditions: **1a** (0.15 mmol), **2** (0.18 mmol), $[\{Cp^*RhCl_2\}_2]$ (5 mol %), $AgSbF_6$ (20 mol %), $Cu(OAc)_2{\cdot}H_2O$ (1.2 equiv), H_2O (3 equiv,) and CH_2ClCH_2Cl (2 mL) at 80 °C under Ar 12 h. The d.r. value is given within parentheses. [b] 4-Methyl-*N*-(4-oxo-2,4-diphenylbutyl)benzenesulfonamide (**4a**), a ring-opening product from **1a** and H_2O, was isolated in about 60 % yield.[9]

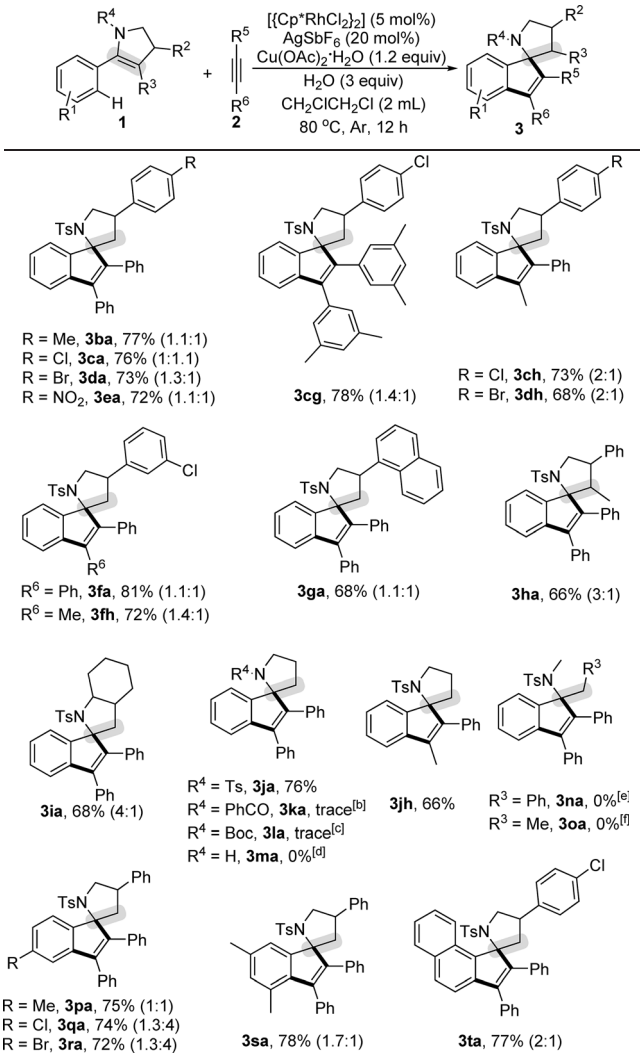
to the annulation of **1a** with a variety of symmetrical or unsymmetrical internal alkynes (**2b–m**), thus affording a broad array of spiro[indene-1,2′-pyrrolidines] (**3ab–am**) in good yield. In the presence of **1a**, $[\{Cp^*RhCl_2\}_2]$, $AgSbF_6$, $Cu(OAc)_2$, and H_2O, the 1,2-diarylethynes **2b–g**, bearing Me, MeO, Cl, and Br groups on the aromatic rings, afforded the products **3ab–ag** in 69–81 % yield. Importantly, halogen substituents were well-tolerated under the optimal reaction conditions, thereby making the [3+2] annulation protocol more useful in organic synthesis because of the potential to further modify at the halogenated positions (**3ad** and **3af**). The annulation of the unsymmetrical internal alkynes **2h–m**

also afforded **3ah**–**am** in good yields with excellent levels of regiocontrol. Several substituents, including OMe, OAc, and Cl, were compatible with the optimal reaction conditions. The reaction of 1-phenylpropyne (**2h**) with **1a** regiospecifically delivered **3ah** in 71% yield.[10] We were pleased to find that the alkynes **2k**–**m**, containing OMe, OAc, and Cl groups, respectively, on the alkyl moiety also had high reactivity and afforded **3ak**–**am** in 70–74% yield. However, the aliphatic internal alkyne **2n** and the aliphatic terminal alkyne **2o** were not viable substrates in the construction of the spiro[indene-1,2′-pyrrolidines] **3an** and **3ao**, respectively.

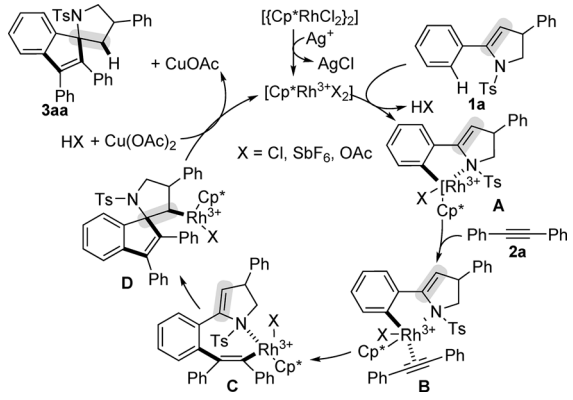
We next turned our attention to applying the optimal redaction conditions to the annulation of various 5-aryl-2,3-dihydro-1*H*-pyrroles (**1**) with either **2a**, **2g**, or **2h** (Table 3). The pyrroles **1b**–**g**, which contain several substituted aryl groups, including 4-MeC_6H_4, 4-ClC_6H_4, 4-BrC_6H_4, 4-$NO_2C_6H_4$, 3-ClC_6H_4, and naphthalen-1-yl, were compatible with the optimal reaction conditions, and gave **3ba**–**ga**, **3cg**, **3ch**, **3dh**, and **3fh** in good yields. Moreover, the electronic properties of the substituted aryl groups had no distinct effect on the reaction. While the 4-MeC_6H_4-substituted pyrrole **1b** delivered **3ba** in 77% yield, **1e**, containing an electron-withdrawing NO_2 group, afforded **3ea** in 72% yield. The chloro-substituted pyrroles **1c** and **1f** were also successfully reacted with the alkynes **2a**, **2g** or **2h**, providing **3cg**, **3ch**, **3fa** and **3fh** in good yields and excellent regioselectivities. The pyrrole **1h**, containing two substituents—a 3-phenyl group and a 4-methyl group—provided **3ha** in 66% yield.[9] 2-Phenyl-3*a*,4,5,6,7,7*a*-hexahydro-1*H*-indole (**1i**) was also a viable substrate, thus giving **3ia** in 68% yield. Several substituents on the pyrrole nitrogen atom (Ts, PhCO, Boc, and H) were examined (**3ja**–**ma** and **3jh**), and only the N-tosyl-substituted substrate **1j** smoothly delivered the spiro[indene-1,2′-pyrrolidine] ring system (**3ja** and **3jh**). The substrates **1n** and **1o** were unsuitable for the annulation reaction (**3na** and **3oa**). Notably, the optimal reaction conditions were applicable to the pyrroles **1p**–**s**, which bore a Me, Cl, or Br group on the aromatic ring of the 5-phenyl moiety (**3pa**–**sa**). When using **1p** to react with **2a**, $[\{Cp^*RhCl_2\}_2]$, $AgSbF_6$, $Cu(OAc)_2$, and H_2O, the reaction afforded **3pa** in 75% yield. Interestingly, the chloro- (**1q**) and bromo-substituted pyrroles (**1r**) were well-tolerated and provided the corresponding **3qa** and **3ra** in 74 and 72% yield, respectively. The more sterically hindered 3,5-dimethyl-substituted pyrrole **1s** was annulated with **2a** smoothly to deliver **3sa** in 78% yield. Notably, the annulation was applicable to the assembly of the polycyclic aromatic spirocyclic ring **3ta** in good yield using the naphthalen-1-yl-substituted pyrrole **1t**.

Based on the above results,[9] as well as previous studies,[5–8] the mechanism outlined in Scheme 2 is proposed. Initially, $[\{Cp^*RhCl_2\}_2]$ is easily converted into the active $[Cp^*Rh^{3+}X_2]$ species (X = Cl, SbF_6, OAc) by a Ag^+ species.[5,6] Subsequently, the C(sp^2)–H bond of **1a** is cleaved by the $[Cp^*Rh^{3+}X_2]$ species to form the rhodium intermediate **A**. The complexation of **A** with alkyne **2a** produces the intermediate **B**, and subsequent insertion of **2a** into the aryl C(sp^2)–Rh bond of **B** gives the intermediate **C**. Within intermediate **C**, the addition of the vinyl C(sp^2)–Rh bond to the C–C double bond of the pyrrole moiety leads to the

Table 3: Variation of 5-Aryl-2,3-dihydro-1*H*-pyrroles (**1**).[a]



[a] Reaction conditions: **1** (0.15 mmol), **2** (0.18 mmol), $[\{Cp^*RhCl_2\}_2]$ (5 mol%), $AgSbF_6$ (20 mol%), $Cu(OAc)_2\cdot H_2O$ (1.2 equiv), H_2O (3 equiv), and CH_2ClCH_2Cl (2 mL) at 80 °C under Ar for 12 h. The d.r. value is given within parentheses. [b] *N*-(4-Oxo-4-phenylbutyl)benzamide (**4k**) was isolated in 61% yield. [c] *tert*-Butyl 4-oxo-4-phenylbutylcarbamate (**4l**) was obtained in 66% yield. [d] 5-Phenyl-3,4-dihydro-2*H*-pyrrole (**5m**) was obtained in 72% yield. [e] 1,2-Diphenylethanone (**6n**; 43% yield) and benzil (**7n**; 22% yield) from **1n** were isolated. [f] Greater than 89% of **1o** was recovered. Boc = *tert*-butoxycarbonyl.



Scheme 2. Possible mechanism.

intermediate **D** (*cis* addition is major according the diastereoselectivity[10] as a result of the complex of the Rh species with the nitrogen atom). Finally, cleavage of the C–Rh bond of **D** through protonolysis produces **3aa** and regenerates the active $[Cp^*Rh^{3+}X_2]$ species with the aid of $Cu(OAc)_2$.

In summary, we have developed the first rhodium(III)-catalyzed [3+2] annulation of 5-aryl-2,3-dihydro-1*H*-pyrroles with internal alkynes through aryl C(sp^2)–H/alkene functionalization. This new method is general for the construction of the spiro[indene-1,2′-pyrrolidine] ring system with excellent functional-group tolerance and good control of selectivity. Moreover, DFT calculations were carried out to better understand the exclusive regioselectivity observed.[9] Studies on the detailed mechanism and applications of this annulation method are currently underway in our laboratory.

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[1] a) "Preparation of amino-acid-linked spiroring compounds as hepatitis C virus (HCV) inhibitors": Y. Zhang, J. Zhang, H. Xie, Q. Ren, X. Wu, H. Luo, C. Fu, B. Hu, S. Li, C. Tang, Y. Lei, Q. Yu, Q. Fang, C. Qang, PCT Int. Appl. WO 2014048072A1 20140403, **2014** [CAN 160:530540]; b) "Preparation of spiro-heterocyclic compounds as inhibitors of β-secretase": L. W. Dillard, J. Yuan, K. Leftheris, S. Venkatraman, G. Wu, L. Jia, Z. Xu, S. Cacatian, A. Morales-Ramos, S. Singh, Y. Zheng, PCT Int. Appl. WO 2011106414A1 20110901, **2011** [CAN 155:380365]; c) P. Jimonet, A. Boireau, M. Chevé, D. Damour, A. Genevois-Borella, A. Imperato, J. Pratt, J. C. R. Randle, Y. Ribeill, J.-M. Stutzmann, S. Mignani, *Bioorg. Med. Chem. Lett.* **1999**, *9*, 2921; d) T. Ullrich, S. Krich, D. Binder, K. Mereiter, D. J. Anderson, M. D. Meyer, M. Pyerin, *J. Med. Chem.* **2002**, *45*, 4047; e) "Isonicotinic acid derivatives and related spirocompounds with herbicidal action and their preparation and compositions containing them": H. R. Waespe, G. R. E. van Lommen, V. K. Sipido, PCT Int. Appl. WO 9209577A1 19920611, **1992** [CAN 117:191692]; f) W. W. Paudler, G. I. Kerley, J. McKay, *J. Org. Chem.* **1963**, *28*, 2194; g) H. M. Kantarjian, M. Talpaz, V. Santini, A. Murgo, B. Cheson, S. M. O'Brien, *Cancer* **2001**, *92*, 1591; h) S. Sacchi, H. M. Kantarjian, S. O'Brien, J. Cortes, M. B. Rios, F. J. Giles, M. Beran, C. A. Koller, M. J. Keating, M. Talpaz, *Cancer* **1999**, *86*, 2632; i) V. I. Shifrin, P. Anderson, *J. Biol. Chem.* **1999**, *274*, 13985; j) H. M. Kantarjian, M. Talpaz, V. Santini, A. Murgo, B. Cheson, S. M. O'Brien, *Cancer* **2001**, *6*, 1591; k) V. Lévy, S. Zohar, C. Bardin, A. Vekhoff, D. Chaoui, B. Rio, O. Legrand, S. Sentenac, P. Rousselot, E. Raffoux, F. Chast, S. Chevret, J. P. Marie, *Br. J. Cancer* **2006**, *95*, 253.

[2] For selected reviews, see: a) L. Huang in *The Alkaloids*, *Vol. 23* (Ed.: A. Brossi), Academic Press, New York, **1984**, p. 157; b) M. A. Jalil Miah, T. Hudlicky, J. W. Reed in *The Alkaloids*, *Vol. 51* (Ed.: A. Brossi), Academic Press, New York, **1998**, p. 199; c) S. A. A. El Bialy, H. Braun, L. F. Tietze, *Synthesis* **2004**, 2249.

[3] Selected recent papers: a) L. Planas, J. Pérard-Viret, J. Royer, *J. Org. Chem.* **2004**, *69*, 3087; b) Q. Liu, E. M. Ferreira, B. M. Stoltz, *J. Org. Chem.* **2007**, *72*, 7352; c) R. Sommerville, H. E. Rosenberg, P. A. Crooks, *J. Pharm. Sci.* **1985**, *74*, 553; d) M. Li, F.-M. Gong, L.-R. Wen, Z.-R. Li, *Eur. J. Org. Chem.* **2011**, 3482; e) A. R. Suresh Babu, D. Gavaskar, R. Raghunathan, *J. Organomet. Chem.* **2013**, *745 – 746*, 409; f) N. Sirisha, R. Raghunathan, *J. Chem. Pharm. Res.* **2013**, *5*, 382; g) R. Moreno-Fuquen, D. M. Soto, L. M. Jaramillo-Gómez, J. Ellena, J. C. Tenorio, *Acta Crystallogr. Sect. E* **2013**, *69*, o1192; h) R. Ćwiek, P. Niedziejko, Z. Kałuża, *J. Org. Chem.* **2014**, *79*, 1222.

[4] For selected reviews, see: a) *Advances in Cycloaddition*, *Vols. 1 – 6*, JAI, Greenwich, CT, **1988 – 1999**; b) W. Carruthers, *Cycloaddition Reactions in Organic Synthesis*, Tetrahedron Organic Chemistry Series, Pergamon, Elmsford, NY, **1990**; c) M. Lautens, W. Klute, W. Tam, *Chem. Rev.* **1996**, *96*, 49; d) L. Yet, *Chem. Rev.* **2000**, *100*, 2963; e) *Cycloaddition Reactions in Organic Synthesis* (Eds.: S. Kobayashi, K. A. Jørgensen), Wiley-VCH, Weinheim, **2002**; f) F. López, J. L. Mascareñas, *Beilstein J. Org. Chem.* **2011**, *7*, 1075; g) K. E. O. Ylijoki, J. M. Stryker, *Chem. Rev.* **2013**, *113*, 2244.

[5] For special reviews on the cycloaddition reaction involving the C–H functionalization, see: a) P. Thansandote, M. Lautens, *Chem. Eur. J.* **2009**, *15*, 5874; b) T. Satoh, M. Miura, *Synthesis* **2010**, 3395; c) D. A. Colby, R. G. Bergman, J. A. Ellman, *Chem. Rev.* **2010**, *110*, 624; d) T. Satoh, M. Miura, *Chem. Eur. J.* **2010**, *16*, 11212; e) D. A. Colby, A. S. Tsai, R. G. Bergman, J. A. Ellman, *Acc. Chem. Res.* **2012**, *45*, 814; f) P. B. Arockiam, C. Bruneau, P. H. Dixneuf, *Chem. Rev.* **2012**, *112*, 5879; g) E. M. Simmons, J. F. Hartwig, *Angew. Chem. Int. Ed.* **2012**, *51*, 3066; *Angew. Chem.* **2012**, *124*, 3120; h) F. W. Patureau, J. Wencel-Delord, F. Glorius, *Aldrichimica Acta* **2012**, *45*, 31; i) G. Song, F. Wang, X. Li, *Chem. Soc. Rev.* **2012**, *41*, 3651; j) L. Ackermann, *Acc. Chem. Res.* **2014**, *47*, 281; k) S. De Sarkar, W. Liu, S. I. Kozhushkov, L. Ackermann, *Adv. Synth. Catal.* **2014**, *356*, 1461.

[6] For papers on rhodium-catalyzed [3+2] annulation with alkynes in the presence of oxidants: a) T. Fukutani, N. Umeda, K. Hirano, T. Satoh, M. Miura, *Chem. Commun.* **2009**, 5141; b) F. W. Patureau, T. Besset, N. Kuhl, F. Glorius, *J. Am. Chem. Soc.* **2011**, *133*, 2154; c) K. Muralirajan, K. Parthasarathy, C.-H. Cheng, *Angew. Chem. Int. Ed.* **2011**, *50*, 4169; *Angew. Chem.* **2011**, *123*, 4255.

[7] For papers on the [3+2] annulation of aryl carbonyl compounds and their derivatives with alkynes without oxidants using rhenium: a) Y. Kuninobu, A. Kawata, K. Takai, *J. Am. Chem. Soc.* **2005**, *127*, 13498; copper: b) E. J. Park, S. H. Kim, S. Chang, *J. Am. Chem. Soc.* **2008**, *130*, 17268; rhodium(I): c) Z.-M. Sun, S.-P. Chen, P. Zhao, *Chem. Eur. J.* **2010**, *16*, 2619; d) D. N. Tran, N. Cramer, *Angew. Chem. Int. Ed.* **2011**, *50*, 11098; *Angew. Chem.* **2011**, *123*, 11294; rhodium(III): e) Y. Chen, F. Wang, W. Zhen, X. Li, *Adv. Synth. Catal.* **2013**, *355*, 353; Ru^{II}: f) J. Zhang, A. Ugrinov, P. Zhao, *Angew. Chem. Int. Ed.* **2013**, *52*, 6681; *Angew. Chem.* **2013**, *125*, 6813; iridium-catalyzed [3+2] annulation of ketimines with alkynes toward indenamine-based spirocycles: g) M. Nagamoto, T. Nishimura, *Chem. Commun.* **2014**, *50*, 6274.

[8] Within the annulation of alkenes with alkynes, the vinyl C–H functionalization generally takes place rather than the addition of the carbon–carbon π bonds: a) K. Morimoto, K. Hirano, T. Satoh, M. Miura, *J. Org. Chem.* **2011**, *76*, 9548; b) A. Seoane, N. Casanova, N. Quiñones, J. L. Mascareñas, M. Gulías, *J. Am. Chem. Soc.* **2014**, *136*, 834; c) A. Seoane, N. Casanova, N. Quiñones, J. L. Mascareñas, M. Gulías, *J. Am. Chem. Soc.* **2014**, *136*, 7607.

[9] Detailed data, including the deuterium-labelling experiments and an intermolecular kinetic isotope effect experiment (see Scheme S1 in the Supporting Information), the DFT calculations, the crystallographic data of **3ah**, 2D NMR spectra of the two isomers of **3ah**, and 2D NMR spectra of **3ha**, are summarized in the Supporting Information.

[10] CCDC 971156 (**3ah**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

