DOI: 10.1002/adsc.201500186

Practical Solvent-Free Ruthenium Trichloride-Mediated Benzannulation Approach to Fused Functionalized Arenes

Jeremy Jacquet,[a] Anne-Laure Auvinet,[a] Anil Kumar Mandadapu,[a] Mansour Haddad,[a] Virginie Ratovelomanana-Vidal,[a,*] and Véronique Michelet[a,*]

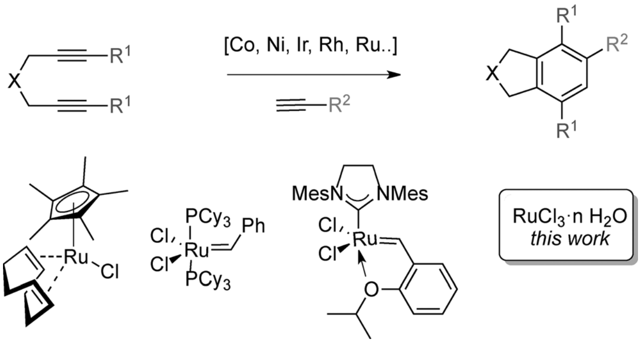
[a] PSL Research University, Chimie ParisTech – CNRS, Institut de Recherche de Chimie Paris, 11 rue P. et M. Curie, 75005 Paris, France
Fax: (+33)-1-4407-1062; phone: (+33)-1-4427-6742; e-mail: virginie.vidal@chimie-paristech.fr or veronique.michelet@chimie-paristech.fr

Received: February 23, 2015; Revised: March 30, 2015; Published online: April 29, 2015

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201500186.

Abstract: The solvent- and ligand-free [2+2+2] ruthenium-promoted cycloaddition of α,ω-diynes and alkynes provides a facile and efficient strategy for the synthesis of substituted benzene-derived systems. The search for the optimal reaction conditions revealed the unprecedented catalytic activity of ruthenium trichloride for benzannulation reactions and this atom-economical process allowed the synthesis of fused arenes including dihydrobenzofurans, isoindolines, indanes in good to high yields. This practical protocol also gave rise to the preparation of pentasubstituted aromatic derivatives and was applied to the one-gram scale synthesis of a functionalized heterocycle.

Keywords: alkynes; benzannulation; cycloaddition; α,ω-diynes; ruthenium; solvent-free conditions

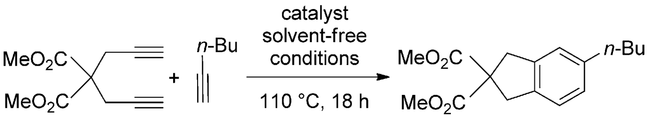


Scheme 1. Selected [Ru] catalysts for [2+2+2] cycloaddition reactions of α,ω-diynes.

Benzannulation is an atom-economical and a straightforward approach to access complex structures starting from relatively simple materials. Transition metal-catalyzed [2+2+2] cycloadditions have proven to be a powerful tool in the construction of highly substituted arenes. Indeed, the [2+2+2] cycloaddition has been widely reported with several metals, the most common being cobalt, nickel, iridium, rhodium and ruthenium.[1] Ruthenium-catalyzed [2+2+2] cycloadditions[2–5] have been reported using mainly elaborated and expensive Ru complexes such as Cp*Ru(cod)Cl, $[RuCp(MeCN)_3]PF_6$, $[RuCl_2(p\text{-cymene})]_2$, $[Cp^*RuCl_2]_2$, Grubbs (I and II), Hoveyda–Grubbs catalysts (Grubbs III), or $Ru(ethene)(CO)_4$, $Ru_3(CO)_{12}$ (Scheme 1) combined with organic solvents, additional ligands, supported systems or microwave assistance. Due to environmental concerns to make chemical processes greener, the development of atom-economical synthetic procedures involving, for instance, solvent-free conditions has become crucial.[6]

To the best of our knowledge, solventless metal-catalyzed [2+2+2] cycloadditions of diynes have been scarcely described although the search for environmentally friendly protocols is essential.[7] To complete our recent interest in [2+2+2] cycloaddition reactions,[8] we were wondering if a more practical strategy could be envisaged to access fused arenes in the absence of solvent and in the absence of additional ligand by using the commercially available, cheap and easy to handle $RuCl_3 \cdot nH_2O$. Noteworthy, Mitsudo and Tanaka reported the inefficiency of $RuCl_3$ and the $RuCl_3$/amine system toward [2+2+2] cycloadditions of terminal alkynes with dimethyl acetylenedicarboxylate and cyclotrimerization of ethyl phenylpropiolate.[9] We and others previously demonstrated the efficiency of $RuCl_3 \cdot nH_2O$ in C−H, C−C, C−N and C−O bond forming processes.[10,11] In this context, we report here the first efficient $RuCl_3$-catalyzed [2+2+2] cycloaddition reactions of α,ω-diynes and alkynes under solvent-free conditions.

Table 1. Optimization of the reaction conditions.[a]



1 **2**

Entry	Catalyst [mol%]	Conv.[b] [%]	Yield[c] [%]
1	$FeCl_3$ (8)	–	–
2	$Fe(acac)_3$ (8)	–	–
3	$FeSO_4{\cdot}7\,H_2O$ (8)	–	–
4	$AuCl_3$ (8)	–	–
5	AuCl (8)	–	–
6	$HAuCl_4$ (8)	–	–
7	$PPh_3AuCl/AgOTf$ (8)	–	–
8	AgOTf (8)	–	–
9	$AgSbF_6$ (8)	–	–
10	$InBr_3$ (8)	–	–
11	$In(OTf)_3$ (8)	–	–
12	InCl (8)	–	–
13	$Cu(OTf)_2$ (8)	–	–
14	CuI (8)	–	–
15	$CuSO_4{\cdot}5\,H_2O$ (8)	–	–
16	[Ir][d] (4)	100	80
17	$IrCl_3$ (8)	80	65
18	$PdCl_2$ (8)	–	–
19	$PtCl_2$ (8)	20	15
20	$RuCl_3{\cdot}n\,H_2O$ (8)	100	85
21[e]	**$RuCl_3{\cdot}n\,H_2O$ (2)**	**100**	79

[a] *Reaction conditions:* 0.4 mmol of diyne **1** and 10 equivalents of *n*-hexyne, screw-capped tube.

[b] Determined by ^1H NMR.

[c] Isolated yields.

[d] [Ir] = [{Ir(H)[*rac*-binap]}$_2$(μ-I)$_3$]I.

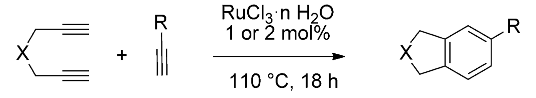
[e] 6 equivalents of *n*-hexyne

The first set of experiments was carried out using several transition metal complexes. The optimization showed that $RuCl_3{\cdot}n\,H_2O$ was the best catalytic system to access indane **2** (Table 1).

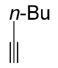
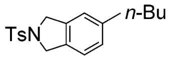
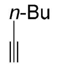
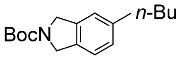
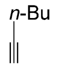
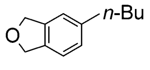
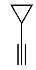
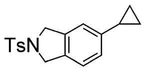
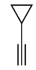
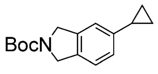
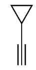
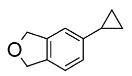
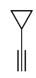
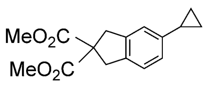
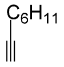
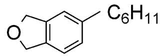
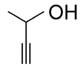
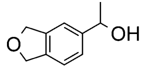
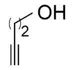
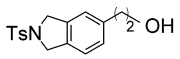
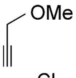
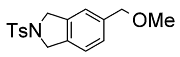
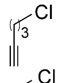
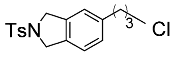
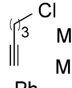
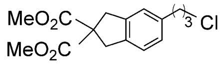
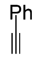
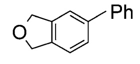
Indeed, iron (Table 1, entries 1–3), gold(I) and gold(III) (Table 1, entries 4–7), silver (Table 1, entries 8 and 9), indium (Table 1, entries 10–12), and copper complexes (Table 1, entries 13–15) were totally ineffective toward cycloaddition. In our previous report, we showed the efficiency of an Ir(III) complex in *i*-PrOH.[8] Employing 4 mol% of the Ir(III) complex[12] allowed the same transformation to provide indane derivative **2** in 80% yield (Table 1, entry 16). The use of the $IrCl_3$ complex afforded the corresponding indane **2**, in a lower 65% yield (Table 1, entry 17). The catalytic activity of other transition metal complexes such as $PdCl_2$ and $PtCl_2$ was evaluated (Table 1, entries 18 and 19), only the latter allowed the isolation of a small amount of **2**. The same reaction was carried out with 8 mol% of $RuCl_3{\cdot}n\,H_2O$ and furnished **2** in 85% yield (Table 1, entry 20). Pleasingly, indane **2** was obtained with a similar yield of 79% when the catalyst loading was decreased to 2 mol% and the quantity of *n*-hexyne to 6 equivalents (Table 1, entry 21).[13]

With these promising results, we decided to investigate the scope of the solvent-free $RuCl_3{\cdot}n\,H_2O$-promoted [2+2+2] cycloaddition of α,ω-diynes and alkynes (Table 2). Thus, the next step was the screening of different class of diynes **3–5** with *n*-hexyne. To our delight, the reaction proceeded with *N*-tethered **3** and **4** (Table 2, entries 1 and 2) and *O*-tethered **5** diynes

Table 2. [Ru]-catalyzed cycloaddition reactions of carbon-, nitrogen- and oxygen-tethered diynes.[a]



X = C(CO$_2$Me)$_2$ **1**, NTs **3**, NBoc **4**, O **5** **6–19**

Entry	Diyne	Alkyne	Product		Yield[b] [%]
1	**3**			**6**	75
2	**4**			**7**	66
3	**5**			**8**	58
4	**3**			**9**	80
5	**4**			**10**	73
6	**5**			**11**	65
7	**1**			**12**	78
8	**5**			**13**	59
9	**5**			**14**	61
10	**3**			**15**	71
11	**3**			**16**	71
12	**3**			**17**	72
13	**1**			**18**	77
14	**5**			**19**	77

[a] *Conditions:* 1 or 2 mol% [Ru], 1 equivalent of diyne and 5 or 6 equivalents of alkyne (see the Supporting Information for details).

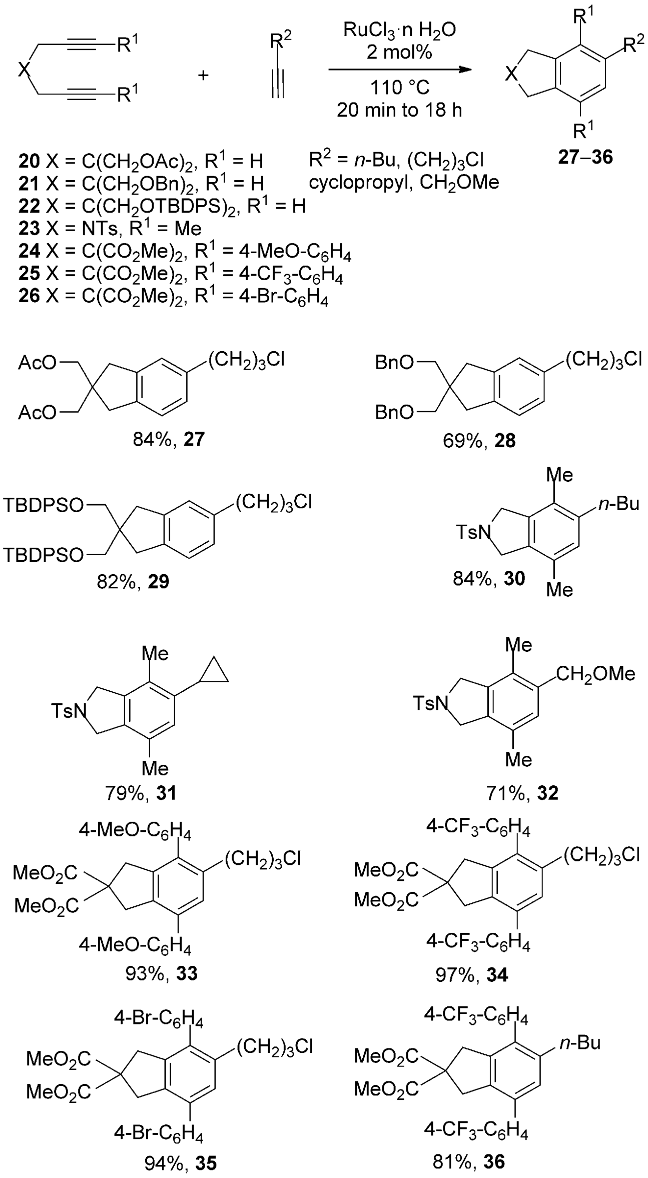
[b] Isolated yields.

(Table 2, entry 3) with satisfactory yields up to 75%. Then, we turned our attention to cycloalkylalkynes. The reaction proved to be successful with cyclopropylacetylene (Table 2, entries 4–7, 65–80% yields) and cyclohexylacetylene (Table 2, entry 8). Rewardingly, the isolated yield of isoindoline **9** was significantly improved under solvent-free conditions using $RuCl_3{\cdot}nH_2O$ compared to that obtained in our previous report[8] using an Ir(III) complex (entry 4, 80% yield *vs.* 61% yield).

Alkynyl alcohols could also be involved in the cycloaddition with different functionalized diynes providing the desired fused arenes in respectable yields (Table 2, entries 9 and 10, up to 71% yield). Ether-linked (Table 2, entry 11) and halogen-containing alkynes (Table 2, entries 12 and 13, 72% and 77% yield) could be envisaged, the cycloaddition furnished the desired compounds **16**, **17** and **18** in good yields up to 77%. The reaction of phenylacetylene with oxygen-tethered diyne **5** was also successful as the corresponding adduct **19** was isolated in 77% yield (Table 2, entry 14).

We then decided to evaluate the activity of $RuCl_3{\cdot}nH_2O$ catalyst toward cycloaddition reactions of functionalized carbon-, nitrogen-tethered and disubstituted diynes (Scheme 2). We were pleased to find that the reaction conditions were compatible with such protective groups as the corresponding functionalized indanes **27**, **28** and **29** were respectively obtained in 84%, 69% and 82% yields (Scheme 2). The scope of the solvent-free reaction was further extended to the synthesis of challenging polysubstituted arenes.[1,2] The cycloadditions were conducted in the presence of 2 mol% of ruthenium catalyst.

The synthesis of various dimethylisoindolines **30–32** was successful in the presence of alkyl, ether or chloro functionalized alkynyl partners (71–84% yields). In the case of isoindoline **30**, a notable increase of the isolated yield was observed in the presence of $RuCl_3{\cdot}nH_2O$ compared to the previous Ir(III) complex[8] (84% *vs.* 43%). Diynes **24–26** bearing electron-withdrawing or electron-donating groups on the aryl moieties also reacted very nicely. Their cycloaddition reactions allowed an easy and effective access to pentasubstituted aromatic rings, regardless of the alkynyl partner. Indanes **33–36** were isolated in good to excellent yields (81–97%). The presence of a bromine atom such as in **35** was fully tolerated and gives opportunities for further cross-coupling reactions.[14]

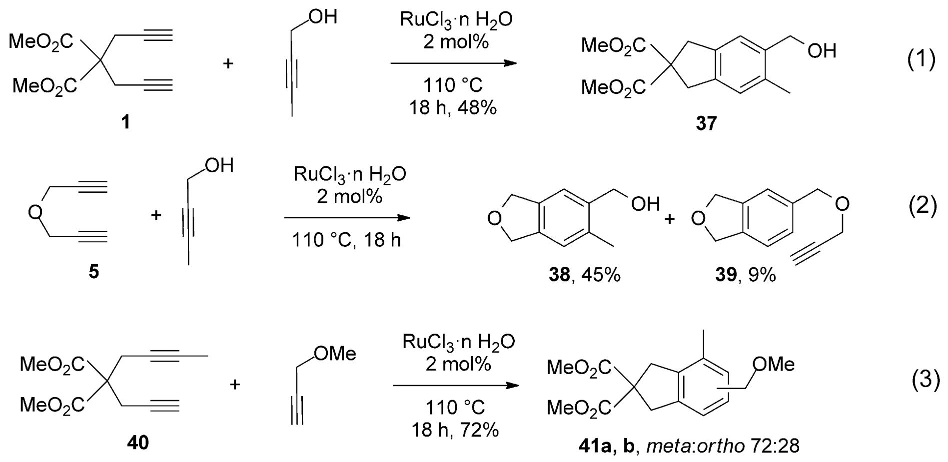


Scheme 2. [Ru]-catalyzed [2+2+2] cycloaddition reactions of functionalized diynes.

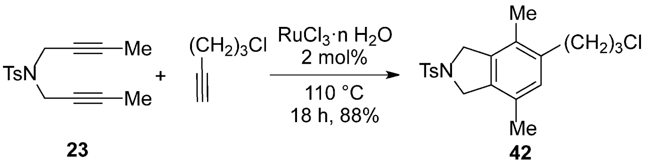
Preliminary results were obtained in the presence of internal alkynes such as but-2-yn-1-ol [Scheme 3, Eq. (1) and Eq. (2)]. The reaction of diynes **1** and **5** afforded the desired alcohols **37** and **38** in moderate yields (48% and 45%, respectively). In the case of diyne **5**, dimer **39** was also isolated in 9% yield. The reactivity of unsymmetrical diyne **40** was attempted and gave rise, as anticipated,[3d] to a mixture of *meta*- and *ortho*-substituted indanes **41** (72:28 ratio) in 72% yield [Scheme 3, Eq. (3)]. The reaction of 1,7-diynes was also tested and led to either no conversion or degradation of diynes. No desired products were observed in all cases (see the Supporting Information).

We finally performed a one gram-scale [2+2+2] cycloaddition under the optimized conditions in the presence of 2 mol% of ruthenium catalyst (Scheme 4). The catalytic activity of the complex was still excellent and the corresponding isoindoline **42** was isolated in 88% yield.

While the mechanism of the metal-catalyzed [2+2+2] cycloaddition has been thoroughly studied,[1,2] it is not so clear how the active ruthenium(II) species is generated in the case of some ruthenium cata-



Scheme 3. Reactivity of internal alkynes and unsymmetrical diynes.



Scheme 4. One gram-scale synthesis of **42**.

lysts.[15,16] According to the recent report by Pérez-Castells and co-workers,[4f] we may anticipate that the $RuCl_3 \cdot nH_2O$ catalyst has a similar behavior under thermal conditions as the Grubbs II catalyst. The *in situ* generation of an active Ru(II) species may also occur *via* the reduction of Ru(III) by the alkyne.[10b,e] Further studies are currently under investigation to characterize organometallic intermediates and therefore shed the light on the mechanism.

In conclusion, we have demonstrated that fused arenes bearing a range of substitution patterns can be efficiently accessed *via* $RuCl_3$-promoted [2+2+2] cycloaddition of diynes and α,ω-alkynes. This unprecedented protocol is more cost effective than conventional methods using elaborated ruthenium complexes. No additional ligands are used for the transformation. Moreover, $RuCl_3 \cdot nH_2O$ is cheap, easy to handle and not sensitive to water or air. The reaction proceeds efficiently with low catalyst loading under solvent-free conditions. This practicality renders this process an attractive approach to access challenging pentasubstituted aromatic compounds.

Experimental Section

General Procedure for [2+2+2] Cycloaddition Reactions

To a sealed tube was added $RuCl_3 \cdot nH_2O$ (1 or 2 mol%), followed by addition of the diyne (1 equiv.) and the alkyne (5–8 equiv.). The tube was sealed and the reaction mixture was stirred at 110 °C from 20 min to 18 h. The crude reaction mixture was purified by flash chromatography over silica gel. Experimental details are provided in the Supporting Information.

Acknowledgements

This work was supported by the Ministère de l'Education et de la Recherche and the Centre National de la Recherche Scientifique (CNRS), A.-L. A. and A. K. M. are grateful to the Fondation Pierre-Gilles de Gennes pour la Recherche for grants. Johnson Matthey Inc. is acknowledged for generous loans of $HAuCl_4$*,* $PdCl_2$ *and* $PtCl_2$*.*

References

[1] For seminal examples, see: a) S. Saito, Y. Yamamoto, *Chem. Rev.* **2000**, *100*, 2901; b) M. Rubin, A. W. Sromek, V. Gevorgyan, *Synlett* **2003**, 2265; c) D. M. D'Souza, T. J. J. Müller, *Chem. Soc. Rev.* **2007**, *36*, 1095; d) S. Kotha, E. Brahmachary, K. Lahiri, *Eur. J. Org. Chem.* **2005**, 4741; e) Y. Yamamoto, *Curr. Org. Chem.* **2005**, *9*, 503; f) V. Gandon, C. Aubert, M. Malacria, *Chem. Commun.* **2006**, *21*, 2209; g) V. Gandon, C. Aubert, M. Malacria, *Curr. Org. Chem.* **2005**, *9*, 1699; h) P. R. Chopade, J. Louie, *Adv. Synth. Catal.* **2006**, *348*, 2307; i) D. Leboeuf, V. Gandon, M. Malacria, in: *Handbook of Cyclization Reactions*, Vol. 1, (Ed.: S. Ma), Wiley-VCH, Weinheim, **2009**, pp 367; j) L. Haughton, J. M. J. Williams, *J. Chem. Soc. Perkin Trans.* **1999**, 2645; k) N. Weding, M. Hapke, *Chem. Soc. Rev.* **2011**,

40, 4525; l) P. A. Inglesby, P. A. Evans, *Chem. Soc. Rev.* **2010**, *39*, 2791; m) G. Domingez, J. Pérez-Castells, *Chem. Soc. Rev.* **2011**, *40*, 3430; n) Y. Shibata, K. Tanaka, *Synthesis* **2012**, *44*, 323; o) F. R. Truscott, G. Maestri, R. Rodriguez, M. Malacria, in: *Modern Alkyne Chemistry*, (Eds.: B. M. Trost, C.-J. Li), Wiley-VCH, Weinheim, **2014**, pp 143; p) G. Domingez, J. Pérez-Castells, in: *Comprehensive Organic Synthesis*, 2nd edn., (Eds.: P. Knochel,G. A, Molander), Elsevier, Amsterdam, **2014**, Vol. 5, p 1537.

[2] For recent reviews on applications of [CpRu]-type catalysts and carbohydrate chemistry, see: a) Y. Yamamoto, *Heterocycles* **2013**, *87*, 2459; b) R. Roy, S. K. Das, *Chem. Commun.* **2000**, *36*, 519.

[3] For selected references: a) Y. Yamamoto, H. Kitahara, R. Ogawa, K. Itoh, *J. Org. Chem.* **1998**, *63*, 9610; b) Y. Yamamoto, H. Kitahara, R. Hattori, K. Itoh, *Organometallics* **1998**, *17*, 1910; c) Y. Yamamoto, H. Kitahara, R. Ogawa, H.; Kawaguchi, K. Tatsumi, K. Itoh, *J. Am. Chem. Soc.* **2000**, *122*, 4310; d) Y. R. Yamamoto, R. Ogawa, K. Itoh, *Chem. Commun.* **2000**, *36*, 549; e) Y. Yamamoto, R. Ogawa, K. Itoh, *J. Am. Chem. Soc.* **2001**, *123*, 6189; f) Y. Yamamoto, H. Takagishi, K. Itoh, *Org. Lett.* **2001**, *3*, 2117; g) Y. Yamamoto, S. Okuda, K. Itoh, *Chem. Commun.* **2001**, *37*, 1102; h) Y. Yamamoto, H. Takagishi, K. Itoh, *J. Am. Chem. Soc.* **2002**, *124*, 28; i) Y. Yamamoto, T. Arakawa, R. Ogawa, K. Itoh, *J. Am. Chem. Soc.* **2003**, *125*, 12143; j) Y. Yamamoto, K. Hata, T. Arakawa, K. Itoh, *Chem. Commun.* **2003**, *39*, 1290; k) E. Rüba, R. Schmid, K. Kirchner, M. J. Calhorda, *J. Organomet. Chem.* **2003**, *682*, 204; l) Y. Yamamoto, K. Kinpara, T. Saigoku, H. Nishiyama, K. Itoh, *Org. Biomol. Chem.* **2004**, *2*, 1287; m) Y. Yamamoto, J.-I. Ishii, H. Nishiyama, K. Itoh, *J. Am. Chem. Soc.* **2004**, *126*, 3712; n) Y. Yamamoto, K. Kinpara, T. Saigoku, H. Takagishi, S. Okuda, H. Nishiyama, K. Itoh, *J. Am. Chem. Soc.* **2005**, *127*, 605; o) Y. Yamamoto, J.-I. Ishii, H. Nishiyama, K. Itoh, *J. Am. Chem. Soc.* **2005**, *127*, 9625; p) D. D. Young, R. S. Senaiar, A. Deiters, *Chem. Eur. J.* **2006**, *12*, 5563; q) Y. Yamamoto, K. Kinpara, R. Ogawa, H. Nishiyama, K. Itoh, *Chem. Eur. J.* **2006**, *12*, 5618; r) R. S. Senaiar, J. A. Teske, D. D. Young, A. Deiters, *J. Org. Chem.* **2007**, *72*, 7801; s) D. D. Young, L. Sripada, A. Deiters, *J. Comb. Chem.* **2007**, *9*, 735; t) S. Garcia-Rubin, J. A. Varela, L. Castedo, C. Saa, *Chem. Eur. J.* **2008**, *14*, 9772; u) L. Iannazzo, N. Kotera, M. Malacria, C. Aubert, V. Gandon, *J. Organomet. Chem.* **2011**, *696*, 3906; v) B. O. Oztürk, S. Karabulut, Y. Imamoglu, *Appl. Catal. A: General* **2012**, *433–434*, 214; w) N. Saito, T. Ichimaru, Y. Sato, *Org. Lett.* **2012**, *14*, 1914; x) F. Xu, C. Wang, X. Li, B. Wan, *ChemSusChem* **2012**, *5*, 854.

[4] For selected references: a) J. Peters, S. Blechert, *Chem. Commun.* **1997**, *33*, 1983; b) B. Witulski, T. Stengel, J. M. Fernandez-Hernandez, *Chem. Commun.* **2000**, *36*, 1965; c) G. B. Hoven, J. Efskind, C. Romming, K. Undheim, *J. Org. Chem.* **2002**, *67*, 2459; d) A. Mallagaray, S. Medina, G. Domínguez, J. Perez-Castells, *Synlett* **2010**, 2114; e) B. O. Oztürk, S. Karabulut, Y. Imamoglu, *Inorg. Chim. Acta* **2011**, *378*, 257; f) A. Mallagaray, K. Mohammadiannejad-Abbasabadi, S. Medina, G. Domínguez, J. Perez-Castells, *Org. Biomol. Chem.* **2012**, *10*, 6665; g) S. Medina, G. Dominguez, J. Perez-Castells, *Org. Lett.* **2012**, *14*, 4982; h) S. Alvarez, S. Medina, G. Domínguez, J. Perez-Castells, *J. Org. Chem.* **2013**, *78*, 9995.

[5] a) E. Lindner, R.-M. Jansen, H. A. Mayer, W. Hiller, R. Fawzi, *Organometallics* **1989**, *8*, 2355; b) M. Kawatsura, M. Yamamoto, J. Namioka, K. Kajita, T. Hirakawa, T. Itoh, *Org. Lett.* **2011**, *13*, 1001.

[6] a) H. M. Marvaniya, K. N. Modi, D. J. Sen, *Int. J. Drug Dev. Res.* **2011**, *3*, 34; b) P. T. Anastas, J. C. Warner, *Green Chemistry: Theory and Practice*, Oxford University Press, New York, **1998**, p 30.

[7] a) T. Konno, K. Moriyasu, R. Kinugawa, T. Ishihara, *Org. Biomol. Chem.* **2010**, *8*, 1718; b) E. R. Bonfield, C. J. Li, *Adv. Synth. Catal.* **2008**, *350*, 370; c) A.-L. Auvinet, V. Michelet, V. Ratovelomanana-Vidal, *Synthesis* **2013**, *45*, 2003.

[8] a) A.-L. Auvinet, M. Ez-Zoubir, M. R. Vitale, J. A. Brown, V. Michelet, V. Ratovelomanana-Vidal, *ChemSusChem* **2012**, *5*, 1888; b) A.-L. Auvinet, M. Ez-zoubir, S. Bompard, M. R. Vitale, J. A. Brown, V. Michelet, V. Ratovelomanana-Vidal, *ChemCatChem* **2013**, *5*, 2389; c) ref.[7c]

[9] a) Y. Ura, Y. Sato, M. Shiotsuki, T. Kondo, T.-A. Mitsudo, *J. Mol. Cat. A: Chemical* **2004**, *209*, 35; b) K. Yoshida, I. Morimoto, K. Mitsudo, H. Tanaka, *Tetrahedron* **2008**, *64*, 5800; c) K. Yoshida, I. Morimoto, K. Mitsudo, H. Tanaka, *Tetrahedron Lett.* **2008**, *49*, 2363; d) K. Yoshida, I. Morimoto, K. Mitsudo, H. Tanaka, *Chem. Lett.* **2007**, *36*, 998.

[10] For selected references: a) J. Madec, X. Pfister, P. Phansavath, V. Ratovelomanana-Vidal, J.-P. Genêt, *Tetrahedron* **2001**, *57*, 2563; b) C.-J. Li, C. Wei, *Chem. Commun.* **2002**, *38*, 268; c) S. W. Youn, S. J. Pastine, D. Sames, *Org. Lett.* **2004**, *6*, 581; d) J.-J. Lian, C.-C. Lin, H.-K. Chang, P.-C. Chen, R.-S. Liu, *J. Am. Chem. Soc.* **2006**, *128*, 9661; e) E. R. Bonfield, C.-J. Li, *Org. Biomol. Chem.* **2007**, *5*, 435; f) O. Labeeuw, C. Roche, P. Phansavath, J.-P. Genêt, *Org. Lett.* **2007**, *9*, 105; g) K. Cheng, B. Yao, J. Zhao, Y. Zhang, *Org. Lett.* **2008**, *10*, 5309; h) L. J. Goossen, M. Arndt, M. Blanchot, F. Rudolphi, F. Menges, G. Niedner-Schatteburg, *Adv. Synth. Catal.* **2008**, *350*, 2701; i) S. Denmark, S. T. Nguyen, *Org. Lett.* **2009**, *11*, 781; j) G. E. Shou, J. Li, T. Guo, Z. Lin, G. Jia, *Organometallics* **2009**, *28*, 6847; k) M.-O. Simon, J.-P. Genêt, S. Darses, *Org. Lett.* **2010**, *12*, 3038; l) M.-O. Simon, G. Ung, S. Darses, *Adv. Synth. Catal.* **2011**, *353*, 1045; m) M. Kawatsura, K. Uchida, S. Terasaki, H. Tsuji, M. Minakawa, T. Itoh, *Org. Lett.* **2014**, *16*, 1470.

[11] For a seminal book and reviews on ruthenium in organic synthesis, see: a) *Ruthenium in Organic Synthesis*, (Ed.: S.-I. Murahashi), Wiley-VCH, Weinheim, **2004**; b) B. M. Trost, D. F. Toste, A. B. Pinkerton, *Chem. Rev.* **2001**, *101*, 2067; c) T. Naota, H. Takaya, S.-I. Murahashi, *Chem. Rev.* **1998**, *98*, 2599.

[12] T. Yamagata, H. Tadaoka, H. Nagata, T. Hirao, Y. Kataoka, V. Ratovelomanana-Vidal, J.-P. Genêt, K. Mashima, *Organometallics* **2006**, *25*, 2505.

[13] Noteworthy is that the use of a 1:1 ratio of diyne:alkyne gave rise to the formation of an unseparable mixture of products including starting material **1**, the de-

sired product **2** and by-products resulting from cycloaddition reactions of diyne **1** (see the Supporting Information).

[14] a) R. Chinchilla, C. Najera, *Chem. Rev.* **2007**, *107*, 874; b) H. Doucet, J.-C. Hierso, *Angew. Chem.* **2007**, *119*, 850; *Angew. Chem. Int. Ed.* **2007**, *46*, 834; c) C. C. C. Johansson Seechurn, M. O. Kitching, T. J. Colacot, V. Snieckus, *Angew. Chem.* **2012**, *124*, 5150; *Angew. Chem. Int. Ed.* **2012**, *51*, 5062; d) *Palladium-Catalyzed Coupling Reactions: Practical Aspects and Future Developments*, (Ed. A. Molnar), Wiley-VCH, Weinheim, **2013**.

[15] For the use of Ru(III) complex ($[Cp^*RuCl_2]_2$ and $Ru_3(CO)_{12}$) as catalyst for [2+2+2] cycloadditions, see refs.[3i,5b]

[16] For the use of Ru(IV) pre-catalyst in [2+2+2] reactions, see: V. Cadierno, S. E. Garcia-Garrido, J. Gimeno, *J. Am. Chem. Soc.* **2006**, *128*, 15094.