Gold Catalysis

DOI: 10.1002/anie.201310146

Synthesis of Highly Substituted 3-Formylfurans by a Gold(I)-Catalyzed Oxidation/1,2-Alkynyl Migration/Cyclization Cascade**

*Tao Wang, Shuai Shi, Max M. Hansmann, Eva Rettenmeier, Matthias Rudolph, and A. Stephen K. Hashmi**

Abstract: *3-Formylfuran derivatives are core structures of a variety of bioactive natural products. However, procedures for their preparation are still rare and generally inefficient in terms of atom economy: These methods require multiple steps or harsh reaction conditions and show selectivity problems. An efficient gold(I)-catalyzed cascade reaction that leads to 3-formylfurans from easily accessible starting materials is now described. A wide variety of 3-formylfurans were obtained from the corresponding symmetric and unsymmetric 1,4-diyn-3-ols in the presence of an N-oxide in good to excellent yields. Isotope-labeling experiments as well as DFT calculations support a mechanism in which, after an initial oxygen transfer, a 1,2-alkynyl migration is favored over a hydride shift; a cyclization ensues to afford the desired functionalized furan core.*

Polysubstituted furans are not only common motifs in natural products and pharmaceuticals, but also useful building blocks for the construction of highly complex target structures.[1] As important members of the furan family, 3-formylfuran derivatives are core structures of some bioactive natural products, such as lophotoxin and its derivatives pukalide and lophodiol A (Figure 1). Lophotoxin, which can be isolated from pacific gorgonians of the genus *Lophogorgia*, is a potent neurotoxin that leads to paralysis and asphyxiation.[2] The importance of furan motives initiated substantial efforts directed towards the development of efficient synthetic strategies for this heteroarene. However, methods for the preparation of 3-formylated furans are still rare, and their development can be considered as one of the great remaining challenges of furan chemistry. Commonly used methods are based either on the direct formylation of furans[3] or on the reduction of other functional groups, such as carboxylic acids or carboxylic esters, at the 3-position.[4] Because of the high intrinsic selectivity for the 2-position of the furan ring, the direct formylation of the 3-position is only possible if the 2- and 5-positions are occupied, and harsh conditions are often required. For the latter method, the use of other functional groups is limited to those that tolerate the required reducing agents. Furthermore, both methods start from pre-synthesized furan systems. Cascade reactions for the synthesis of 3-formylfurans have also been reported;[5] however, these reactions were usually carried out at high temperatures, and several steps were required for the preparation of the starting materials. Therefore, the development of an efficient and simple method for the synthesis of 3-formylfurans from readily available starting materials is still highly desired. As part of our efforts on the synthesis of polysubstituted furans,[6] we herein report a highly efficient gold(I)-catalyzed cascade reaction for the preparation of 3-formylfurans from easily accessible starting materials.

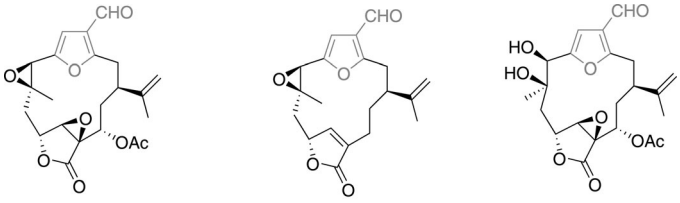


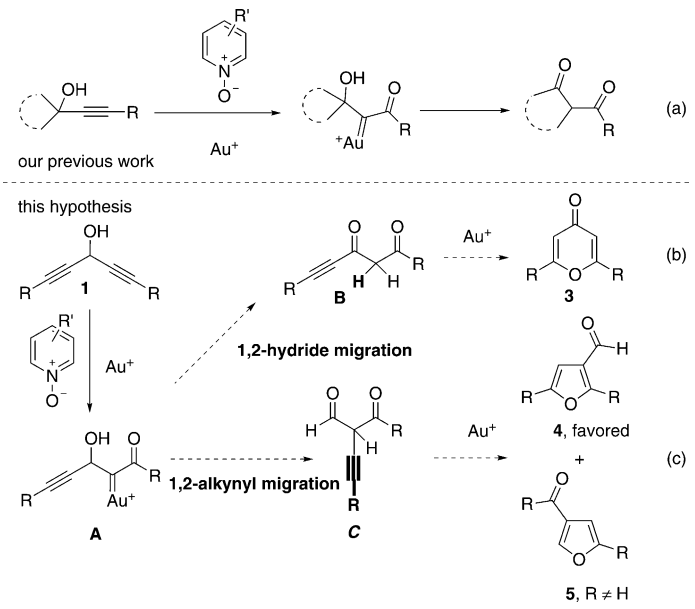
Figure 1. Selected examples of natural products with the 3-formylfuran motif.

Recently, gold-catalyzed oxygen transfer from sulfoxides[7] and nitrogen oxides[8] to alkynes has become an efficient strategy for the generation of α-oxo gold carbenoids, which can undergo a variety of valuable transformations. Very recently, our group developed an efficient approach for the synthesis of 1,3-diketones from propargyl alcohols and pyridine *N*-oxides by gold catalysis (Scheme 1 a).[9] 1,2-Aryl and 1,2-hydride migrations were key steps of the outlined reaction mechanism. In this specific case, 1,2-aryl migration was favored over 1,2-hydride migration. We envisioned that a gold catalyst should activate 1,4-diyn-3-ol **1** in the presence

[*] M. Sc. T. Wang, M. Sc. S. Shi, M. Sc. M. M. Hansmann, Dipl.-Chem. E. Rettenmeier, Dr. M. Rudolph, Prof. Dr. A. S. K. Hashmi
Organisch-Chemisches Institut
Ruprecht-Karls-Universität Heidelberg
Im Neuenheimer Feld 270, 69120 Heidelberg (Germany)
E-mail: hashmi@hashmi.de
Homepage: http://www.hashmi.de
Prof. Dr. A. S. K. Hashmi
Chemistry Department, Faculty of Science
King Abdulaziz University
Jeddah 21589 (Saudi Arabia)

[**] T.W. and S.S. are grateful for fellowships from the China Scholarship Council (CSC). M.M.H. is grateful to the Fonds der chemischen Industrie for a Chemiefonds scholarship and the Studienstiftung des deutschen Volkes. E.R. is grateful for a scholarship of the state of Baden-Württemberg via the Graduate Academy of Heidelberg University. We thank Umicore AG & Co. KG for the generous donation of gold salts. The computational studies were supported by bwGRiD, member of the German D-Grid initiative, funded by the Ministry for Education and Research and the Ministry for Science, Research and Arts Baden-Württemberg.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201310146.



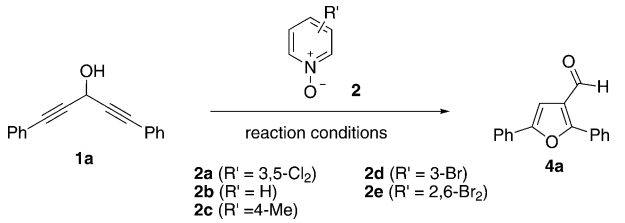
Scheme 1. Previous work and our hypothesis.

of pyridine *N*-oxide to form an α-oxo gold carbenoid intermediate **A**, which could undergo a 1,2-hydride migration to provide 1,3-diketone **B**. Upon cyclization, this intermediate should generate 4-pyranone **3** (Scheme 1b). Alternatively, α-oxo gold carbenoid **A** could also form intermediate **C** through a 1,2-alkynyl migration, but no report of such a 1,2-alkynyl migration onto a gold carbenoid species can be found in the literature. Cyclization of intermediate **C** would afford 3-formylfuran **4** or 4-acylfuran **5** (Scheme 1c). Considering the greater nucleophilicity of the ketone, the formation of 3-formylfuran **4** should be the favoured pathway.

Diynol **1a** was prepared according to a simple one-step procedure by treating phenylacetylene with *n*-butyllithium, which was followed by the one-pot addition of ethyl formate. **1a** was then treated with 3,5-dichloropyridine *N*-oxide (1.5 equiv) in the presence of [IPrAuCl]/$AgNTf_2$ (IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene, Tf = trifluoromethylsulfonyl). Pleasingly, a clean reaction took place at room temperature. To our surprise, 3-formyl furan **4a** was formed within ten minutes as the exclusive product (Table 1, entry 1). This indicates that an unprecedented 1,2-alkynyl migration seems to be involved in the reaction cascade. Encouraged by this result, we started to optimize the reaction conditions (Table 1). First, a variety of pyridine *N*-oxides were tested, but no improvement was achieved. Using relatively electron-rich pyridine *N*-oxide (**2b**) or 4-picoline *N*-oxide (**2c**) resulted in an incomplete conversion of **1a** (entries 2 and 3), whereas 3-bromopyridine *N*-oxide (**2d**) and 2,6-dibromopyridine *N*-oxide (**2e**) afforded **4a** in a slightly lower yield (entries 4 and 5). A further screen revealed that both $AuCl_3$ and AuCl can catalyze the reaction, but **4a** was only obtained in moderate yield even after prolonged reaction times (entries 7 and 8). With $AgNTf_2$ as the catalyst, product **4a** was not observed (entry 9). Replacing $AgNTf_2$ with different silver salts, such as AgOTf, $AgClO_4$, and $AgSbF_6$, as the activator for [IPrAuCl] did not have a substantial effect on the yield (entries 10–12). Among the tested silver salts, AgOTf in combination with [IPrAuCl] gave the best result. A solvent screen (entries 13–15) revealed that toluene was the most suitable solvent for this transformation (entry 15). Decreasing the catalyst loading to 3 mol% was possible without a drop in yield (entry 16). Reducing the amount of pyridine *N*-oxide to 1.2 equivalents led to a slightly lower yield (entry 18).

Under the optimized reaction conditions, a wide variety of 1,4-diyn-3-ols **1** were examined, and the results are summarized in Table 2. Substrates with substituents at the *para* position of the phenyl group reacted smoothly to afford 3-formylfurans **4** in good to excellent yields under standard conditions. Substrates with electron-donating groups usually gave the corresponding products with slightly higher yields (entries 2–4) than those with electron-withdrawing groups (entries 6 and 7). Phenyl substrates with a substituent in *meta* position also worked well to give the corresponding furans **4** in good yields (entries 9 and 10). The furans **4e**, **4h**, and **4k** were obtained in good yields by using 1.2 equivalents of pyridine *N*-oxide (**2a**; entries 5, 8, and 11). The reduced amount of *N*-oxide for these substrates was necessary because of the low solubility of the products; crystallization was the preferred purification method, and larger amounts of the *N*-oxide led to impure products. A heteroaromatic

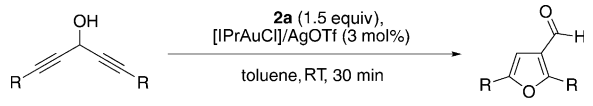
Table 1: Optimization of the reaction conditions.[a]



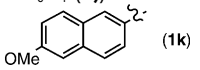
Entry	Catalyst	*N*-oxide	Solvent	*t*	Yield[b] [%]
1	[IPrAuCl]/$AgNTf_2$	**2a**	$(CH_2Cl)_2$	10 min	85
2	[IPrAuCl]/$AgNTf_2$	**2b**	$(CH_2Cl)_2$	2 h	66 (30)
3	[IPrAuCl]/$AgNTf_2$	**2c**	$(CH_2Cl)_2$	2 h	59 (33)
4	[IPrAuCl]/$AgNTf_2$	**2d**	$(CH_2Cl)_2$	2 h	83
5	[IPrAuCl]/$AgNTf_2$	**2e**	$(CH_2Cl)_2$	1 h	80
6	[Ph_3PAuCl]/$AgNTf_2$	**2a**	$(CH_2Cl)_2$	10 min	30[c]
7	$AuCl_3$	**2a**	$(CH_2Cl)_2$	24 h	75
8	AuCl	**2a**	$(CH_2Cl)_2$	24 h	71
9	$AgNTf_2$	**2a**	$(CH_2Cl)_2$	24 h	–[d]
10	[IPrAuCl]/AgOTf	**2a**	$(CH_2Cl)_2$	10 min	88
11	[IPrAuCl]/$AgClO_4$	**2a**	$(CH_2Cl)_2$	10 min	85
12	[IPrAuCl]/$AgSbF_6$	**2a**	$(CH_2Cl)_2$	10 min	83
13	[IPrAuCl]/AgOTf	**2a**	CH_3CN	5 h	50 (45)
14	[IPrAuCl]/AgOTf	**2a**	CH_2Cl_2	10 min	85
15	[IPrAuCl]/AgOTf	**2a**	toluene	10 min	91
16	[IPrAuCl]/AgOTf[e]	**2a**	toluene	30 min	90
17	[IPrAuCl]/AgOTf[f]	**2a**	toluene	2 h	78 (20)
18	[IPrAuCl]/AgOTf[e]	**2a**[g]	toluene	30 min	85

[a] All reactions were carried out on a 0.4 mmol scale in 2 mL of solvent with the catalyst (5 mol%) and the *N*-oxide (1.5 equiv) at room temperature. [b] Yields of isolated products; the number in parentheses represents the amount of **1a** that was recovered after column chromatography. [c] Decomposition of **1a** was observed. [d] No reaction was observed. [e] 3 mol%. [f] 1 mol%. [g] 1.2 equiv.

Table 2: Scope of the reaction for symmetric starting materials.

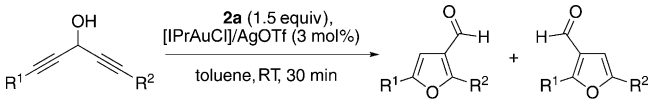


1 4

Entry	1	4	Yield[a] [%]
1	R = Ph (**1a**)	**4a**	90
2	R = 4-$CH_3C_6H_4$ (**1b**)	**4b**	88
3	R = 4-$MeOC_6H_4$ (**1c**)	**4c**	95
4	R = 4-$Me_2NC_6H_4$ (**1d**)	**4d**	90
5[b]	R = 3,4,5-$(MeO)_3C_6H_2$ (**1e**)	**4e**	85
6	R = 4-ClC_6H_4 (**1f**)	**4f**	86
7	R = 4-FC_6H_4 (**1g**)	**4g**	85
8[b]	R = 4-PhC_6H_4 (**1h**)	**4h**	85
9	R = 3-MeC_6H_4 (**1i**)	**4i**	86
10	R = 3-FC_6H_4 (**1j**)	**4j**	82
11[b]	R=  (**1k**)	**4k**	80
12	R=  (**1l**)	**4l**	86
13	R = *n*Bu (**1m**)	**4m**	63
14	R = H (**1n**)	**4n**	–[c]

[a] Yields of isolated products. [b] **2a** (1.2 equiv) was used. [c] The expected product was not obtained.

Table 3: Scope of the reaction for unsymmetric starting materials.



1 4 4'

	R^1	R^2	**4**, Yield[a] [%]	**4'**, Yield[a] [%]
1[b]	4-ClC_6H_4	Ph (**1o**)	**4o**, 50	**4o'**, 29
2	4-$MeOC_6H_4$	Ph (**1p**)	**4p**, 8	**4p'**, 78
3	4-$CF_3C_6H_4$	4-$OMeC_6H_4$ (**1q**)	**4q**, 85	–
4	2,4,6-$(CH_3)_3C_6H_2$	Ph (**1r**)	**4r**, 83	–
5		Ph (**1s**)	**4s**, 14	**4s'**, 71
6	TMS	Ph (**1t**)	**4t**, 60	–
7	TIPS	Ph (**1u**)	**4u**, 62	–
8	*t*Bu	Ph (**1v**)	**4v**, 90	–
9	Cy	Ph (**1w**)	**4w**, 75	**4w'**, 12
10[b]	*n*Bu	Ph (**1x**)	**4x**, 63	**4x'**, 20
11		Ph (**1y**)	**4y**, 13	**4y'**, 69
12	H	Ph (**1z**)	–	**4z'**, 50
13	*t*Bu	*n*Bu (**1α**)	**4α**, 78	–
14	2,4,6-$(CH_3)_3C_6H_2$		**4β**, 83	–

[a] Yields of isolated products. [b] **2e** (1.5 equiv) was used instead of **2a** as the oxygen donor.

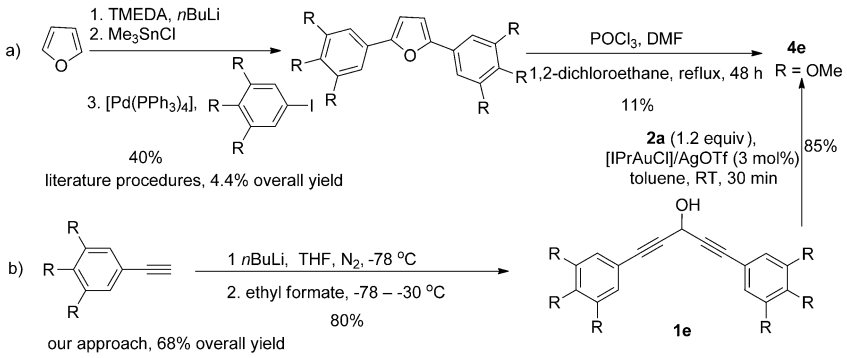
substrate was also examined and led to the corresponding 3-formylfuran in good yield (entry 12). An aliphatic diyne starting material such as **1m** afforded the corresponding 2,5-dibutylfuran-3-carbaldehyde (**4m**) under standard conditions (entry 13). A substrate with two terminal alkynes did not give the desired product (entry 14).

Next, we evaluated unsymmetric starting materials (Table 3). **4o** and **4o'** were obtained with poor selectivity and in 50% and 29% yield, respectively (entry 1). This result may be explained in terms of the competing electronic effects of the halogen substituent at the *para* position. A significantly higher selectivity was observed with compounds **4p** and **4p'**, which were obtained in a 1:10 ratio (entry 2). It was found that the electron-rich phenyl group ends up at the 2-position of the 3-formylfuran. This regioselectivity can be explained by the preference of the cationic gold fragment to coordinate to the more electron-rich alkyne system (based on the donating ability of the methoxy group at the *para* position), which facilitates the nucleophilic attack by pyridine *N*-oxide to the activated alkyne. **4q** was obtained as a single regioisomer, which further supports this hypothesis (entry 3). Substrate **1r**, which contains a sterically hindered aromatic group, was also tested and afforded **4r** as the sole product (entry 4). The unsymmetric combination of a phenyl and a thiophenyl group led to **4s** and **4s'** in a 1:5 ratio (entry 5). As for entry 4, 1,4-diyn-3-ols that comprise bulky groups, such as TMS (trimethylsilyl), TIPS (triisopropylsilyl), or *t*Bu (*tert*-butyl) substituents, all afforded single regioisomers (entries 6–8). The regioselectivity substantially decreased when the sterically hindered group (*t*Bu; 100% selectivity) was replaced for a less bulky group, such as a cyclohexyl (6:1) or an *n*-butyl (3:1) moiety (entries 8–10). Vinyl groups were also tolerated in this reaction (entry 11). Furthermore, a terminal alkyne generated 4-formylfuran **4z'** in moderate yield (entry 12). Substrates with two different aliphatic groups (*n*Bu and *t*Bu) led to a single regioisomer with the formyl group positioned next to the less bulky group (entry 13). An ether group was also tolerated in this furan synthesis (entry 14).

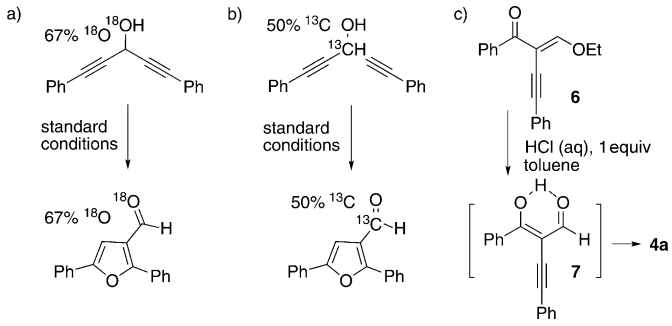
Product **4e** displays anti-proliferation effects against two cancer cell lines, including a solid tumor (UACC-62, melanoma) and a human lymphoma (JURKAT) line.[10a] However, based on literature precedents, this compound could only be obtained in very low yield under harsh reaction conditions; for example, the procedures involve a Stille coupling with toxic tin compounds and a Vilsmeier–Haack formylation reaction that requires high temperatures (Scheme 2a).[10] In contrast to the literature procedures (4.4% overall yield), our simple approach delivered this useful product in good overall efficiency (68% overall yield; Scheme 2b).

To investigate the mechanism of this transformation, ^{18}O- and ^{13}C-labeled starting materials were prepared and subjected to the standard conditions of this gold-catalyzed process. Both of the ^{18}O and ^{13}C labels were transferred from the former propargylic position to the formyl group (Scheme 3a, b). Compound **6** was independently prepared and treated with HCl (aq) to generate the assumed intermediate 1,3-diketone **7**. However, **6** was rapidly converted into **4a** in the presence of HCl. **7** exists in the enol form, which was observed by in situ ^1H NMR spectroscopy of a quickly prepared sample.

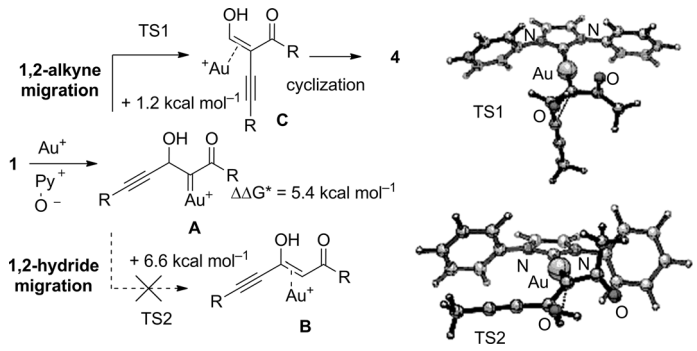
Based on the labeling experiments in combination with literature reports,[8,9] a plausible mechanism that accounts for the novel furan synthesis is depicted in Scheme 4. In an established process, an α-oxo gold carbenoid is generated from **1** and pyridine *N*-oxide. As we propose an unprece-



Scheme 2. A comparison of synthetic approaches to the bioactive product **4e**. TMEDA = *N*,*N*,*N*′,*N*′-tetramethylethylenediamine.



Scheme 3. Mechanistic investigations. The ^{18}O content was determined by mass spectrometry; the ^{13}C content was determined by mass spectrometry and NMR analysis.



Scheme 4. Plausible reaction mechanism that supports a 1,2-alkyne migration. The calculated transition states (B3LYP/cc-pVDZ/cc-pVTZ(Au)) for the two conceivable shift reactions and the activation barriers are shown; the calculations were carried out for the gaseous phase.

dented 1,2-alkyne shift onto the gold carbenoid to form intermediate **C** in the following step, we performed DFT calculations to test this hypothesis. We located the optimized starting and product geometries as well as the transition states for the alkyne and hydride shift processes at the B3LYP/cc-pVDZ and cc-pVTZ(Au) level of theory by employing an NHC ligand with a methyl or a phenyl substituent on the nitrogen atom (see the Supporting Information). In both cases, the shift processes are highly exergonic (40–50 kcal mol^{-1}), which indicates an irreversible and kinetically controlled reaction. In accordance with the outlined mechanism, the transition state for the 1,2-alkyne shift ($+1.2$ kcal mol^{-1}) is lower in free energy than that for the corresponding 1,2-hydride shift process ($+6.6$ kcal mol^{-1}) by $\Delta\Delta G^{*} = 5.4$ kcal mol^{-1} (Scheme 4). After the 1,2-alkyne shift, intermediate **C** undergoes cyclization with the ketone oxygen atom to afford the observed 3-formylfurans **4**.[11]

In conclusion, we have developed an efficient and mild gold(I)-catalyzed cascade reaction that leads to 3-formylfurans from simple starting materials. This approach represents a significant improvement compared to literature procedures. ^{18}O- and ^{13}C-labeled starting materials were prepared to investigate the reaction mechanism. According to isotope-labeling experiments and in agreement with DFT calculations, a 1,2-alkynyl migration pathway was proposed as the key step for the transformation of an α-oxo gold carbenoid intermediate into the final product **4**. To the best of our knowledge, this is the first example of a 1,2-alkynyl migration onto a gold carbenoid intermediate.[12]

Received: November 22, 2013
Published online: February 24, 2014

Keywords: alkynyl migration · cyclization · furans · gold · *N*-oxides

[1] a) B. H. Lipshutz, *Chem. Rev.* **1986**, *86*, 795–819; b) X. L. Hou, Z. Yang, H. N. C. Wong, *Progress in Heterocyclic Chemistry*, *Vol. 15* (Eds.: G. W. Gribble, T. L. Gilchrist), Pergamon, Oxford, **2003**, pp. 167–205.

[2] a) W. Fenical, R. K. Okuda, M. M. Bandurraga, P. Culver, R. S. Jacobs, *Science* **1981**, *212*, 1512–1514; b) S. N. Abramson, J. A. Trischman, D. M. Tapiolas, E. E. Harold, W. Fenical, P. Taylor, *J. Med. Chem.* **1991**, *34*, 1798–1804.

[3] a) V. P. Baillargeon, J. K. Stille, *J. Am. Chem. Soc.* **1986**, *108*, 452–461; b) B. A. Keay, *Chem. Soc. Rev.* **1999**, *28*, 209–215.

[4] a) T. D. Hubert, D. P. Eyman, D. F. Wiemer, *J. Org. Chem.* **1984**, *49*, 2279–2281; b) D.-T. Hsu, C.-H. Lin, *J. Org. Chem.* **2009**, *74*, 9180–9187.

[5] a) J. Yang, C. Wang, X. Xie, H. Li, E. Li, Y. Li, *Org. Biomol. Chem.* **2011**, *9*, 1342–1346; b) G. Raffa, G. Balme, N. Monteiro, *Eur. J. Org. Chem.* **2013**, 105–110.

[6] a) A. S. K. Hashmi, L. Schwarz, *Chem. Ber./Recl.* **1997**, *130*, 1449–1456; b) A. S. K. Hashmi, P. Sinha, *Adv. Synth. Catal.* **2004**, *346*, 432–438; c) A. S. K. Hashmi, T. Häffner, M. Rudolph, F. Rominger, *Eur. J. Org. Chem.* **2011**, 667–671; d) T. Wang, S. Shi, M. H. Vilhelmsen, T. Zhang, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Chem. Eur. J.* **2013**, *19*, 12512–12516.

[7] a) N. D. Shapiro, F. D. Toste, *J. Am. Chem. Soc.* **2007**, *129*, 4160–4161; b) G. Li, L. Zhang, *Angew. Chem.* **2007**, *119*, 5248–5251; *Angew. Chem. Int. Ed.* **2007**, *46*, 5156–5159; c) N. Marion, S. P. Nolan, *Chem. Soc. Rev.* **2008**, *37*, 1776–1782; d) P. W. Davies, S. J.-C. Albrecht, *Angew. Chem.* **2009**, *121*, 8522–8525; *Angew. Chem. Int. Ed.* **2009**, *48*, 8372–8375; e) A. B. Cuenca, S. Montserrai, K. M. Hossain, G. Mancha, A. Lledós, M. Medio-

Simón, G. Ujaque, G. Asensio, *Org. Lett.* **2009**, *11*, 4906 – 4909; f) C.-W. Li, K. Pati, G.-Y. Lin, S. M. Abu Sohel, H.-H. Hung, R.-S. Liu, *Angew. Chem.* **2010**, *122*, 10087 – 10090; *Angew. Chem. Int. Ed.* **2010**, *49*, 9891 – 9894; g) C.-F. Xu, M. Xu, Y.-X. Jia, C.-Y. Li, *Org. Lett.* **2011**, *13*, 1556 – 1559; h) J. Xiao, X. Li, *Angew. Chem.* **2011**, *123*, 7364 – 7375; *Angew. Chem. Int. Ed.* **2011**, *50*, 7226 – 7236.

[8] a) L. Cui, Y. Peng, L. Zhang, *J. Am. Chem. Soc.* **2009**, *131*, 8394 – 8395; b) L. Ye, L. Cui, G. Zhang, L. Zhang, *J. Am. Chem. Soc.* **2010**, *132*, 3258 – 3259; c) B. Lu, C. Li, L. Zhang, *J. Am. Chem. Soc.* **2010**, *132*, 14070 – 14072; d) D. Vasu, H.-H. Hung, S. Bhunia, S. A. Gawade, A. Das, R.-S. Liu, *Angew. Chem.* **2011**, *123*, 7043 – 7046; *Angew. Chem. Int. Ed.* **2011**, *50*, 6911 – 6914; e) A. Mukherjee, R. B. Dateer, R. Chaudhuri, S. Bhunia, S. N. Karad, R.-S. Liu, *J. Am. Chem. Soc.* **2011**, *133*, 15372 – 15375; f) H.-S. Yeom, J.-E. Lee, S. Shin, *Angew. Chem.* **2008**, *120*, 7148 – 7151; *Angew. Chem. Int. Ed.* **2008**, *47*, 7040 – 7043; g) G. Henrion, T. E. J. Chavas, X. L. Goff, F. Gagosz, *Angew. Chem.* **2013**, *125*, 6397 – 6402; *Angew. Chem. Int. Ed.* **2013**, *52*, 6277 – 6282; h) J. Fu, H. Shang, Z. Wang, L. Chang, W. Shao, Z. Yang, Y. Tang, *Angew. Chem.* **2013**, *125*, 4292 – 4296; *Angew. Chem. Int. Ed.* **2013**, *52*, 4198 – 4202; i) S. Kramer, T. Skrydstrup, *Angew. Chem.* **2012**, *124*, 4759 – 4762; *Angew. Chem. Int. Ed.* **2012**, *51*, 4681 – 4684; j) D. Qian, J. Zhang, *Chem. Commun.* **2012**, *48*, 7082 – 7084; k) D. Garayalde, C. Nevado, *ACS Catal.* **2012**, *2*, 1462 – 1479; l) S. Ghorpade, M.-D. Su, R.-S. Liu, *Angew. Chem.* **2013**, *125*, 4323 – 4328; *Angew. Chem. Int. Ed.* **2013**, *52*, 4229 – 4234.

[9] A. S. K. Hashmi, T. Wang, S. Shi, M. Rudolph, *J. Org. Chem.* **2012**, *77*, 7761 – 7767.

[10] a) G. A. Soares, R. B. de Oliveira, S. F. de Andrade, R. J. Alves, C. L. Zani, E. M. de Souza-Fagundes, *Molecules* **2010**, *15*, 12 – 26; b) R. B. Oliveira, A. B. M. Vaz, R. O. Alves, D. B. Liarte, C. L. Donnici, A. J. Romanha, C. L. Zani, *Mem. Inst. Oswaldo Cruz* **2006**, *101*, 169 – 173.

[11] A. Arcadi, M. Alfonsi, M. Chiarini, F. Marinelli, *J. Organomet. Chem.* **2009**, *694*, 576 – 582.

[12] For 1,2-alkynyl shifts in Wagner–Meerwein rearrangements, see: a) T. Nagasawa, K. Taya, M. Kitamura, K. Suzuki, *J. Am. Chem. Soc.* **1996**, *118*, 8949 – 8950; b) T. Saito, T. Suzuki, M. Morimoto, C. Akiyama, T. Ochiai, K. Takeuchi, T. Matsumoto, K. Suzuki, *J. Am. Chem. Soc.* **1998**, *120*, 11633 – 11644; c) K. Suzuki, H. Takikawa, Y. Hachisu, J. W. Bode, *Angew. Chem.* **2007**, *119*, 3316 – 3318; *Angew. Chem. Int. Ed.* **2007**, *46*, 3252 – 3254; d) C. M. Marson, A. J. Walker, J. Pickering, A. D. Hobson, *J. Org. Chem.* **1993**, *58*, 5944 – 5951.

