

Hydrogenation

International Edition: DOI: 10.1002/anie.201912161

German Edition: DOI: 10.1002/ange.201912161

Mechanistic Divergence in the Hydrogenative Synthesis of Furans and Butenolides: Ruthenium Carbenes Formed by *gem*-Hydrogenation or through Carbophilic Activation of Alkynes

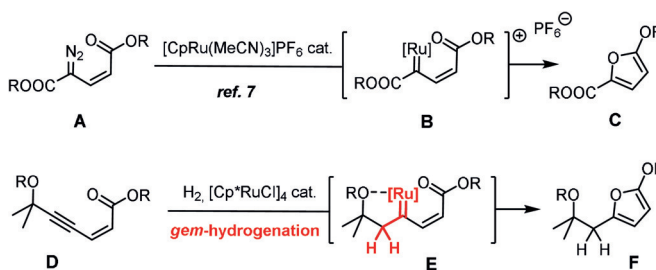
Sebastian Peil and Alois Fürstner*

Abstract: Enynes with a tethered carbonyl substituent are converted into substituted furan derivatives upon hydrogenation using $[\text{Cp}^*\text{RuCl}]_4$ as the catalyst. Paradoxically, this transformation can occur along two distinct pathways, each of which proceeds via discrete piano-stool ruthenium carbenes. In the first case, hydrogenation and carbene formation are synchronized (“*gem*-hydrogenation”), whereas the second pathway comprises carbene formation by carbophilic activation of the triple bond, followed by hydrogenative catalyst recycling. Representative carbene intermediates of either route were characterized by X-ray crystallography; the structural data prove that the attack of the carbonyl group on the electrophilic carbene center follows a Bürgi–Dunitz trajectory.

After a century of intense research by the scientific community on catalytic hydrogenation, our group has recently been able to identify an entirely new reactivity mode. Specifically, it was shown that alkynes can undergo *gem*-hydrogenation, a reaction in which both H-atoms of H_2 are delivered to one and the same acetylenic C-atom while the adjacent position is concomitantly transformed into a discrete metal carbene.^[1,2] At the current stage of development, $[\text{Cp}^*\text{RuCl}]_4$ is the precatalyst of choice; moreover, heteroatom substituents in vicinity of the triple bond are often necessary to render the reaction efficient. Detailed spectroscopic and computational data indicate that the resulting piano-stool ruthenium complexes basically exhibit a Fischer-carbene character with a certain overtone reminiscent of Grubbs-type catalysts.^[3] This view is corroborated by the fact that they participate in either intramolecular cyclopropanation or metathesis reactions, depending on the chosen substrate.^[4]

For their largely electrophilic nature, such complexes should be able to participate in various other catalytic transformations too. If this is the case, *gem*-hydrogenation might eventually evolve into an attractive alternative to diazoalkane decomposition, which is arguably the most

common gateway to highly reactive late-transition metal carbenes.^[5,6] The foray along these lines outlined below was inspired by a recent publication describing an innovative entry into highly substituted furan derivatives (Scheme 1).^[7]



Scheme 1. Conceived furan formation by alkyne *gem*-hydrogenation, emulating known diazo-decomposition chemistry; Cp = cyclopentadienyl; Cp* = pentamethylcyclopentadienyl.

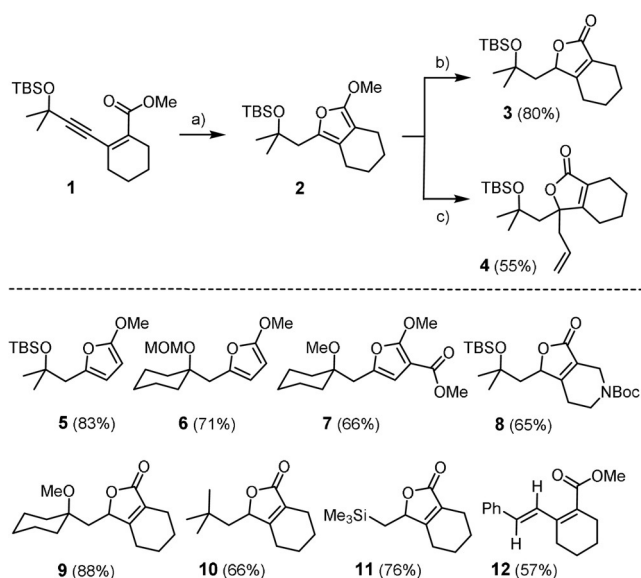
Specifically, diazo compounds **A** were shown to react with catalytic $[\text{CpRu}(\text{MeCN})_3]\text{PF}_6$ to generate transient cationic ruthenium carbenes **B**, which get trapped by the tethered ester group to give the corresponding heterocycle **C**. We reasoned that this type of transformation might be emulated by *gem*-hydrogenation of enyne **D**, in which the propargylic -OR substituent directs carbene formation to the distal acetylenic site.^[1,2] Akin to **B**, the resulting intermediate **E** might furnish furan **F**, even though **E** is a neutral rather than cationic entity.

In line with our expectations, product **2** was formed in almost quantitative yield ($\geq 95\%$) upon stirring of a solution of **1** and $[\text{Cp}^*\text{RuCl}]_4$ (2 mol %) in CH_2Cl_2 under an atmosphere of H_2 (1 bar) for 3 h at ambient temperature (Scheme 2). Treatment of the crude material with silica released the corresponding butenolide **3**.^[8] Alternatively, **2** can be alkylated with allyl iodide to give product **4**.^[9] In other cases such as **5–7**, the furan itself was sufficiently stable for isolation. In line with our previous investigations,^[2–4] different propargylic substituents (for example, -OR, -OSiR₃, -OMOM) were found to instigate *gem*-hydrogenation. Gratifyingly though, even substrates devoid of such directing groups led to the formation of butenolides **10** and **11**;^[10] in these cases, the ester itself might serve as a directing group, fostering regioselective carbene formation by *gem*-hydrogenation.^[2a] This effect is not always sufficient, however, as illustrated by the formation of alkene **12** through *trans*-hydrogenation of the corresponding alkyne substrate.^[11] This outcome is not overly surprising since *trans*-hydrogenation has previously been shown to be a facile process downstream

[*] S. Peil, Prof. A. Fürstner
Max-Planck-Institut für Kohlenforschung
45470 Mülheim/Ruhr (Germany)
E-mail: fuerstner@kofo.mpg.de

Supporting information and the ORCID identification number(s) for the author(s) of this article can be found under:
<https://doi.org/10.1002/anie.201912161>.

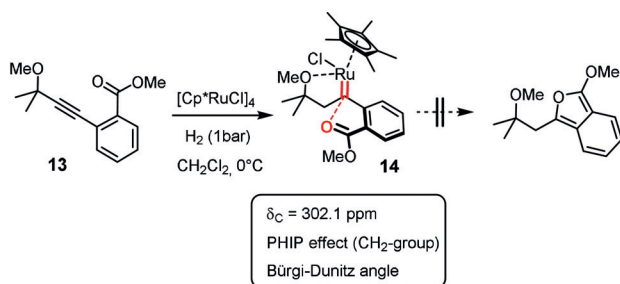
© 2019 The Authors. Published by Wiley-VCH Verlag GmbH & Co. KGaA. This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.



Scheme 2. a) $[\text{Cp}^*\text{RuCl}]_4$ (2 mol%), H_2 (1 atm), CH_2Cl_2 , RT; b) SiO_2 ; c) allyl iodide, NaI, THF, 100 °C; Boc = *tert*-butoxycarbonyl; MOM = methoxymethyl; TBS = *tert*-butyldimethylsilyl.

of an initial *gem*-hydrogenation event (even though **12** could very well originate from a concerted pathway).^[1,2,12]

Although these results are fully consistent with the formation of pianostool ruthenium carbenes by *gem*-hydrogenation in the first place, we sought to confirm this mechanistic interpretation. To this end, we resorted to substrate **13**, which is expected to undergo regular *gem*-hydrogenation but should be resilient to cyclization because heterocycle formation comes at the prize of dearomatization of the phenyl ring (Scheme 3). Indeed, the reaction stopped at



Scheme 3. Interrupted process: *gem*-Hydrogenation without subsequent heterocycle formation.

the stage of the pianostool ruthenium carbene complex **14**. The use of *para*-hydrogen as the reagent leads to a massive amplification of the ^1H NMR signal of the methylene group flanking the carbene center as a result of the PHIP effect (PHIP = *p*-hydrogen induced polarization).^[13,14] This spectroscopic signature provides unambiguous proof that these two H-atoms originate from the same H_2 molecule by pairwise delivery, a characteristic trait of *gem*-hydrogenation.^[2]

The structure of this sensitive complex in the solid state is highly informative (Figure 1). It suggests that the directing

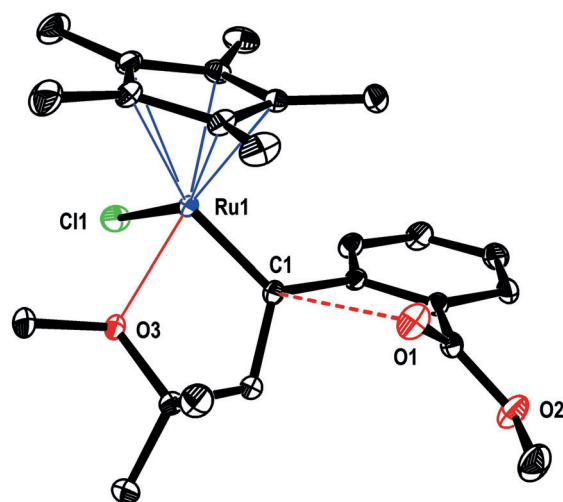
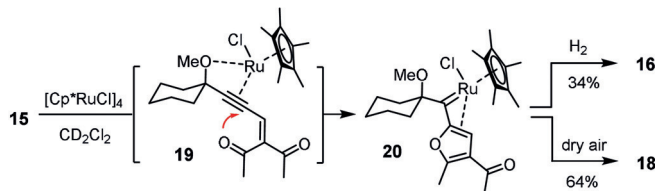
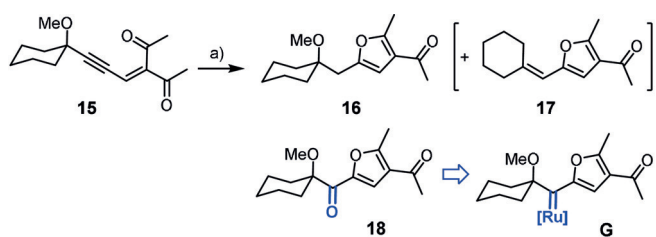


Figure 1. Structure of carbene complex **14** in the solid state. The dotted line indicates that the ester carbonyl oxygen atom O1 adopts a Bürgi–Dunitz trajectory in its approach to the electrophilic carbene site C1; the O1–C1 distance is well below the sum of the van-der-Waals radii.

effect of the methyl ether substituent emanates from its interaction with the Lewis-acidic Ru center at a distance of 2.18 Å; the actual C1–Ru1 carbene bond length (1.883(2) Å) is in the expected range.^[2] The arguably most remarkable structural feature, however, is the orientation of the carbonyl oxygen atom O1 relative to the carbene center C1: the O1–C1 distance (2.983(4) Å) is well below the sum of the van-der-Waals radii of these atoms (ca. 3.22 Å) and the Ru1–C1–O1 angle of 116.0° shows that the ester carbonyl approaches the trigonal carbene center along a Bürgi–Dunitz trajectory.^[15,16] In view of this ideal geometric predisposition for an out-sphere attack, it is reasonable to believe that ring closure stalls because of the unfavorable thermodynamic rendering of this model compound, since loss of aromaticity of the benzene ring would not be compensated by the enthalpic gain of an emerging isobenzofuran. The Bürgi–Dunitz angle is well recognized as a fundamental principle of (dynamic) stereochemistry originating from the particular shape and occupancy of the relevant frontier orbitals.^[17] Yet, complex **14** seems to be the first case of an electrophilic transition metal carbene and its nucleophilic reaction partner, for which this prominent effect has been explicitly recognized as a structure-determining element manifest in the crystallographic data.^[18]

Next, we attempted to extend the novel hydrogenative furan formation to substrates carrying nucleophiles other than an ester group. The readily available diketone derivative **15** gave the expected product **16** but required a reaction temperature of 70 °C (Scheme 4). Surprisingly, small amounts of ketone **18** were also isolated in one run from the crude mixture, which seems to indicate incidental oxidation of an intermediate of type **G** featuring the carbene site proximal to the directing -OMe substituent. Such a regiochemical course violates the mechanistic rationale outlined above for the ester series and is inconsistent with all other available information on alkyne *gem*-hydrogenation,^[1–4] not least with the X-ray structure shown in Figure 1. Formation of **G** might be



Scheme 4. Extension to the ketone series is accompanied by a switch in mechanism: a) $[\text{Cp}^*\text{RuCl}]_4$ (5 mol%), H_2 (1 atm), 1,2-dichloroethane, 70°C , 57% (**16**), $\leq 5\%$ (**17**), $\leq 10\%$ (**18**).

explained, however, by assuming that the π -acidic metal fragment activates the substrate to the extent that attack of the ketone onto the triple bond is faster than binding of H_2 , as necessary for *gem*-hydrogenation to occur. This type of mechanism has ample precedent in the literature for many different carbophilic catalysts,^[19] although rigorous proof for the intervention of discrete carbenes is exceedingly rare.^[20]

To test this hypothesis, enyne **15** was reacted with stoichiometric amounts of $[\text{Cp}^*\text{RuCl}]_4$ in the presence as well as in the absence of H_2 ; either set-up afforded the very same pianostool ruthenium carbene **20** in less than 30 min reaction time. The structure of this remarkable complex in the solid state shows that the ruthenium atom no longer interacts with the adjacent -OMe group (Figure 2); rather, it is tightly ligated to the electron rich “enol ether” site of the newly formed furan ring as manifested in the observed distances as well as in an elongated C2–C3 bond. The distinctive up-field shift of the NMR signals of C2 ($\delta_{\text{C}} = 132.3$ ppm), C3 ($\delta_{\text{C}} =$

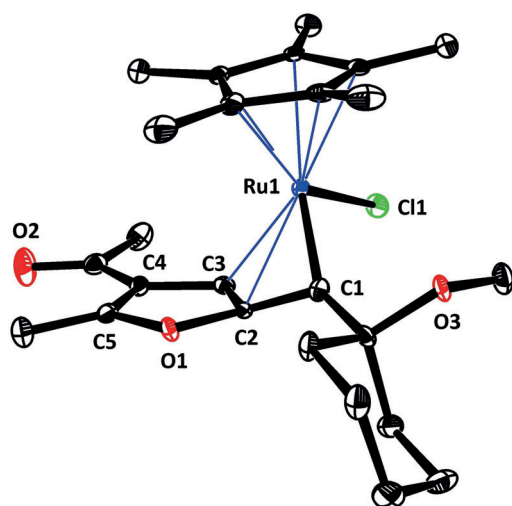
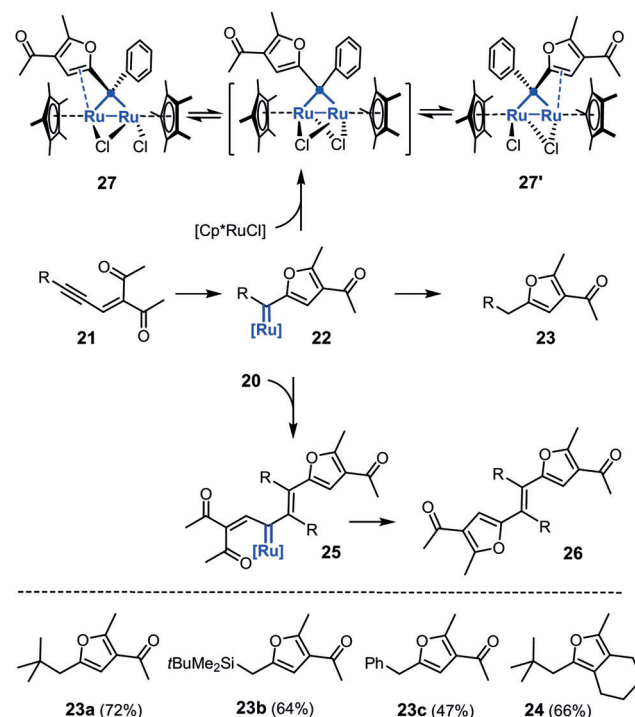


Figure 2. Structure of the furyl carbene **20** in the solid state; selected bond lengths (Å): Ru1–C1 1.890(3), C2–C3 1.399(4), C4–C5 1.363(4), Ru1–C2 2.217(2), Ru1–C3 2.330(2).

89.7 ppm), and the carbene center C1 ($\delta_{\text{C}} = 266.7$ ppm) suggest that this bonding situation persists in CD_2Cl_2 solution.^[21] Despite the stabilizing interaction, **20** is a competent intermediate on the way to product and by-product alike. It reacts with H_2 at 70°C to give furan **16**,^[22] whereas stirring of a solution in air afforded the furyl ketone **18** (Scheme 4).

Since π -bond activation by the carbophilic catalyst does not require assistance by a neighboring directing group,^[23] substrates of type **21** (R = alkyl, aryl) devoid of donor substituents at the propargylic position should react analogously (Scheme 5). As the formation of furans **23a,b** and **24**



Scheme 5. The fate of the pianostool ruthenium carbene formed by carbophilic activation.

shows, this is indeed the case as long as the substituent R shields the transient carbene center in **22**. If not, dimerization with formation of a tetrasubstituted alkene **26** becomes competitive. Thus, substrate **21c** (R = Ph) gave a mixture of the monomeric furan **23c** and olefin **26c** (R = Ph, *E/Z* ca. 1:1),^[24] whereas **21d** (R = *n*-Bu) afforded only traces of the monomeric furan derivative but furnished the product **26d** (R = *n*-Bu) as the major product in the form of a single isomer. The *E*-configuration of the central double bond could only be assigned by crystallographic means.^[21,25] It is assumed that the triple bond of a second substrate inserts into the $[\text{Ru}=\text{C}]$ bond of **22** in an enyne metathesis fashion to furnish a vinylcarbene **25**,^[26] which is then intercepted by the adjacent ketone to close the second furan ring of the resulting dimer **26**.

Insufficient steric shielding of the carbene center can open yet another sidetrack. The NMR data of carbene **22a** (R = *t*Bu, $\delta_{\text{C}} = 285.3$ ppm) correspond to those of **20** and its structure must hence be similar,^[22] but the ruthenium complex

derived from enyne **21c** (R = Ph) and $[\text{Cp}^*\text{RuCl}]_4$ is strikingly different. Whereas **20** and **22a** (R = *t*Bu) are both rather sensitive burgundy-red compounds, a very robust green solid material is formed that does not react with H_2 even at 70°C , is stable towards air and moisture for extended periods of time, and does not catalyze furan formation either; it is hence an off-cycle product. The structure of this complex was determined by X-ray diffraction. As shown in Figure 3, **27** incorporates a bridging rather than terminal carbene moiety; the dimer persists in solution as indicated by the markedly upfield-shifted carbene resonance ($\delta_{\text{C}} = 189.9$ ppm).^[27,28] The distances between C1 and the two Ru atoms are uneven, as are the distances between the bridging chloride Cl2 and the metal atoms. Ru2 benefits from the same stabilizing interaction with the proximal enol site of the furan ring discussed above for **20**, whereas Ru1 carries an additional terminal chloride ligand.

The static picture of the structure in the solid state, however, provides an incomplete description of this complex. Rather, the ^{13}C NMR signals of the two Cp^* rings show

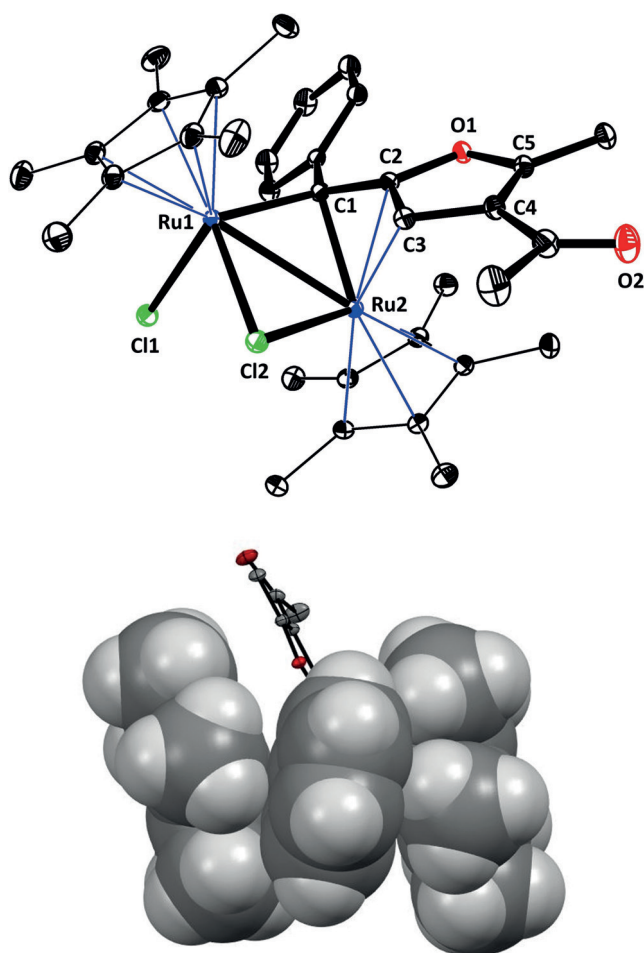
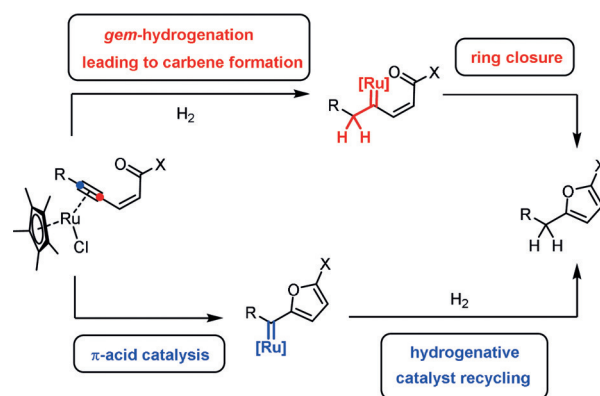


Figure 3. Top: Structure of complex **27** in the solid state; selected bond lengths (Å): Ru1–Ru1 2.822(3), Ru1–C1 2.099(1), Ru2–C1 2.118(1), Ru1–Cl1 2.448(3), Ru1–Cl2 2.456(3), Ru2–Cl2 2.393(4), Ru2–C2 2.208(1), Ru2–C3 2.284(1), C2–C3 1.416(2), C3–C4 1.452(2), C4–C5 1.365(2). Bottom: partial space-filling representation (except for the furyl ring in the back), showing the immersion of the phenyl group between the lateral Cp^* rings.

massive line broadening at ambient temperature; a reversible dyotropic process **27/27'** is the likely cause for the equilibration of the two different metal subunits,^[29] a dynamic behavior that can be frozen out by lowering the temperature to -50°C . At the same time, the rotation of the phenyl substituent comes to a halt. Inspection of the space-filling model of **27** shows that this phenyl ring is “sandwiched” between the lateral Cp^* rings. Actually, it is plausible that the complex draws some of its remarkable stability from this peripheral interaction, even though this aspect needs further scrutiny. In any case, only slim substituents will be able to intercalate analogously. Only two related complexes are known in the literature: indeed, they carry H/alkenyl and Me/Me substituents at a bridging ruthenium carbene site between the Cp^* ligands.^[4,30] Sterically demanding branched alkyl residues in lieu of the phenyl group are unlikely to fit into the groove formed by the Cp^* rings and will hence prevent bridging carbene formation from occurring; the structure of the complex **20** discussed above bears witness of this notion.

The subtlety of the transformations described above is deemed remarkable: hydrogenation of enynes carrying a tethered carbonyl group with the help of $[\text{Cp}^*\text{RuCl}]_4$ as the catalyst invariably affords highly substituted furan products (Scheme 6). Depending on the nucleophilicity of the carbonyl



Scheme 6. Conceptual framework featuring two unorthodox roles that hydrogenation can gain in metal carbene chemistry.

substituent, however, the reaction takes place along two distinctly different pathways, each of which involves piano-stool ruthenium carbenes as the key intermediates. These reactive species evolve, however, on the opposite ends of the central alkyne subunit of the substrate. In the first case, the π -complex initially formed binds H_2 , which in turn triggers the unorthodox *gem*-hydrogenation of the triple bond with concomitant formation of a ruthenium carbene;^[1–4] hydrogenation and carbene formation are hence synchronized. Attack of the tethered ester carbonyl onto the electrophilic carbene center delivers the heterocyclic product and, at the same time, regenerates the catalyst.

Alternatively, direct attack of a ketone onto the ligated alkyne outperforms *gem*-hydrogenation.^[31] The ensuing five-*exo-dig* cyclization places the emerging ruthenium carbene away from the incoming nucleophile. In this π -acid catalysis scenario, carbene formation precedes the actual hydrogenation.

tion reaction, which is necessary to regenerate the catalyst and ensure turn-over. Insertions of either free carbenes or metal carbene complexes into H₂ are known;^[32,33] to the best of our knowledge, however, the furan synthesis described herein is the first example in which carbene hydrogenation is essential for the release of the desired product and catalyst recovery alike; it therefore keeps the actual catalytic carbene formation up and running.^[34] From the conceptual viewpoint, the chemistry described herein outlines new strategic roles for catalytic hydrogenation chemistry. Ongoing studies in our laboratory try to leverage some of the opportunities that this unconventional reactivity paradigm may provide.

Acknowledgements

Generous financial support by the MPG is gratefully acknowledged. We thank Dr. M. Leutzsch for the PHIP-NMR experiments, Mr. J. Rust, Mr. J. Nöthling, and Dr. R. Goddard for solving the X-ray structures, and all service groups of our Institute for excellent support.

Conflict of interest

The authors declare no conflict of interest.

Keywords: Bürgi–Dunitz angle · carbophilic activation · furans · hydrogenation · metal carbenes · ruthenium

How to cite: *Angew. Chem. Int. Ed.* **2019**, *58*, 18476–18481
Angew. Chem. **2019**, *131*, 18647–18652

- [1] A. Fürstner, *J. Am. Chem. Soc.* **2019**, *141*, 11–24.
- [2] a) A. Guthertz, M. Leutzsch, L. M. Wolf, P. Gupta, S. M. Rummelt, R. Goddard, C. Farès, W. Thiel, A. Fürstner, *J. Am. Chem. Soc.* **2018**, *140*, 3156–3168; b) M. Leutzsch, L. M. Wolf, P. Gupta, M. Fuchs, W. Thiel, C. Farès, A. Fürstner, *Angew. Chem. Int. Ed.* **2015**, *54*, 12431–12436; *Angew. Chem.* **2015**, *127*, 12608–12613.
- [3] T. Biberger, C. Gordon, M. Leutzsch, S. Peil, A. Guthertz, C. Copéret, A. Fürstner, *Angew. Chem. Int. Ed.* **2019**, *58*, 8845–8850; *Angew. Chem.* **2019**, *131*, 8937–8942.
- [4] S. Peil, A. Guthertz, T. Biberger, A. Fürstner, *Angew. Chem. Int. Ed.* **2019**, *58*, 8851–8856; *Angew. Chem.* **2019**, *131*, 8943–8948.
- [5] *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds: From Cyclopropanes to Ylides* (Eds.: M. P. Doyle, M. A. McKervey, T. Ye), Wiley, New York, **1998**.
- [6] For structural investigations, see: a) C. Werlé, R. Goddard, A. Fürstner, *Angew. Chem. Int. Ed.* **2015**, *54*, 15452–15456; *Angew. Chem.* **2015**, *127*, 15672–15676; b) C. Werlé, R. Goddard, P. Philipps, C. Farès, A. Fürstner, *J. Am. Chem. Soc.* **2016**, *138*, 3797–3805; c) C. Werlé, R. Goddard, P. Philipps, C. Farès, A. Fürstner, *Angew. Chem. Int. Ed.* **2016**, *55*, 10760–10765; *Angew. Chem.* **2016**, *128*, 10918–10923; d) D. J. Tindall, C. Werlé, R. Goddard, P. Philipps, C. Farès, A. Fürstner, *J. Am. Chem. Soc.* **2018**, *140*, 1884–1893.
- [7] M. El Arba, S. E. Dibrell, F. Meece, D. E. Frantz, *Org. Lett.* **2018**, *20*, 5886–5888.
- [8] However, anaerobic conditions are needed, otherwise partial oxidation is observed.
- [9] J. Chen, S. Ni, S. Ma, *Adv. Synth. Catal.* **2012**, *354*, 1114–1128.
- [10] For the structure of compounds **9** and **11** in the solid state, see the Supporting Information.
- [11] a) K. Radkowski, B. Sundararaju, A. Fürstner, *Angew. Chem. Int. Ed.* **2013**, *52*, 355–360; *Angew. Chem.* **2013**, *125*, 373–378; b) M. Fuchs, A. Fürstner, *Angew. Chem. Int. Ed.* **2015**, *54*, 3978–3982; *Angew. Chem.* **2015**, *127*, 4050–4054.
- [12] The concerted pathway is similar to the mechanism of *trans*-hydrosilylation (stannylation), see: a) L. W. Chung, Y.-D. Wu, B. M. Trost, Z. T. Ball, *J. Am. Chem. Soc.* **2003**, *125*, 11578–11582; b) S. Ding, L.-J. Song, L. W. Chung, X. Zhang, J. Sun, Y.-D. Wu, *J. Am. Chem. Soc.* **2013**, *135*, 13835–13842; c) D.-A. Roşca, K. Radkowski, L. M. Wolf, M. Wagh, R. Goddard, W. Thiel, A. Fürstner, *J. Am. Chem. Soc.* **2017**, *139*, 2443–2455.
- [13] C. R. Bowers, D. P. Weitekamp, *J. Am. Chem. Soc.* **1987**, *109*, 5541–5542.
- [14] For a review, see the following and literature cited therein: S. B. Duckett, R. E. Mewis, *Acc. Chem. Res.* **2012**, *45*, 1247–1257.
- [15] H. B. Bürgi, J. D. Dunitz, J. M. Lehn, G. Wipff, *Tetrahedron* **1974**, *30*, 1563–1572.
- [16] The array in **19** is very similar to that of a substituted benzophenone derivative in which one of the phenyl rings carries a methyl ester at the *ortho*-position, see: A. Konosonoks, P. J. Wright, M.-L. Tsao, J. Pika, K. Novak, S. M. Mandel, J. A. Krause Bauer, C. Bohne, A. D. Gudmundsdottir, *J. Org. Chem.* **2005**, *70*, 2763–2770.
- [17] a) *Structure Correlation* (Eds.: H. B. Bürgi, J. D. Dunitz), Wiley-VCH, Weinheim, **1994**; b) I. Fleming, *Molecular Orbitals and Organic Chemical Reactions*, Wiley, New York, **2009**.
- [18] We found two hits in the Cambridge Crystallographic Database in which a tethered P=O or C=O group can be seen as adopting a Bürgi–Dunitz angle relative to a transition metal carbene center; in neither case has this aspect been discussed, see: a) C. Ernst, O. Walter, E. Dinjus, *J. Organomet. Chem.* **2001**, *627*, 249–254; b) B. Weberndörfer, G. Henig, H. Werner, *Organometallics* **2000**, *19*, 4687–4689.
- [19] For leading references, see the following and literature cited therein: a) B. Seiller, C. Bruneau, P. H. Dixneuf, *J. Chem. Soc. Chem. Commun.* **1994**, 493–494; b) K. Miki, F. Nishino, K. Ohe, S. Uemura, *J. Am. Chem. Soc.* **2002**, *124*, 5260–5261; c) Y. Xia, S. Qu, Q. Xiao, Z. X. Wang, P. Qu, L. Chen, Z. Liu, L. Tian, Z. Huang, Y. Zhang, J. Wang, *J. Am. Chem. Soc.* **2013**, *135*, 13502–13511; d) H. Cao, H. Zhan, J. Cen, J. Lin, Y. Lin, Q. Zhu, M. Fu, H. Jiang, *Org. Lett.* **2013**, *15*, 1080–1083; e) J. González, J. González, C. Pérez-Calleja, L. A. López, R. Vicente, *Angew. Chem. Int. Ed.* **2013**, *52*, 5853–5857; *Angew. Chem.* **2013**, *125*, 5965–5969; f) J. Ma, H. Jiang, S. Zhu, *Org. Lett.* **2014**, *16*, 4472–4475; g) J. S. Clark, F. Romiti, K. F. Hogg, M. H. S. A. Hamid, S. C. Richter, A. Boyer, J. C. Redman, L. I. Farrugia, *Angew. Chem. Int. Ed.* **2015**, *54*, 5744–5747; *Angew. Chem.* **2015**, *127*, 5836–5839; h) J.-M. Yang, Z.-Q. Li, M.-L. Li, Q. He, S.-F. Zhu, Q.-L. Zhou, *J. Am. Chem. Soc.* **2017**, *139*, 3784–3789; i) D. Zhu, L. Chen, H. Zhang, Z. Ma, H. Jiang, S. Zhu, *Angew. Chem. Int. Ed.* **2018**, *57*, 12405–12409; *Angew. Chem.* **2018**, *130*, 12585–12589; see also: j) F. Nishino, K. Miki, Y. Kato, K. Ohe, S. Uemura, *Org. Lett.* **2003**, *5*, 2615–2617; k) H.-C. Shen, C.-W. Li, R.-S. Liu, *Tetrahedron Lett.* **2004**, *45*, 9245–9247.
- [20] For Fischer-type (2-furyl) chromiumcarbonyl carbene complexes, see: a) K. Miki, T. Yokoi, F. Nishino, K. Ohe, S. Uemura, *J. Organomet. Chem.* **2002**, *645*, 228–234; for gold and copper carbenes with an N,N-disubstituted imidazolone ring in lieu of the furan, see: b) J. Wang, X. Cao, S. Lv, C. Zhang, S. Xu, M. Shi, J. Zhang, *Nat. Commun.* **2017**, *8*, 14625.
- [21] For further details, see the Supporting Information.
- [22] Carbene **22** (R = *t*Bu) was also tested; it reacts more cleanly with H₂ to give the furan derivative **23a** in 86 % yield. In a competition experiment, this reaction showed a kinetic isotope effect of 1.54, which suggests that oxidative insertion of the metal center into

the H–H bond is product-determining. Only minute amounts of the cross-over product were observed ($\leq 0.8\%$) when the reaction was carried out under a H_2/D_2 (1:1) atmosphere, thus proving that hydride scrambling before or during the reaction is marginal; for details, see the Supporting Information.

- [23] a) A. Fürstner, P. W. Davies, *Angew. Chem. Int. Ed.* **2007**, *46*, 3410–3449; *Angew. Chem.* **2007**, *119*, 3478–3519; b) A. Fürstner, *Angew. Chem. Int. Ed.* **2018**, *57*, 4215–4233; *Angew. Chem.* **2018**, *130*, 4289–4308.
- [24] As expected, the ratio **23c:26** is strongly concentration-dependent; for details, see the Supporting Information.
- [25] A closely related compound with R = hexyl has previously been misassigned, see: a) Y. Zhou, J. Ma, K. Chen, H. Jiang, S. Zhu, *Chem. Commun.* **2016**, *52*, 13345–13348. For related dimerization reactions with formation of olefinic products, see ref. [19h] and the following: b) J. González, J. González, C. Pérez-Calleja, L. A. López, R. Vicente, *Angew. Chem. Int. Ed.* **2013**, *52*, 5853–5857; *Angew. Chem.* **2013**, *125*, 5965–5969; c) P. Liu, J. Sun, *Org. Lett.* **2017**, *19*, 3482–3485.
- [26] The proposed insertion mirrors the behavior of Grubbs carbenes in enyne metathesis, cf: a) *Handbook of Metathesis* (Eds.: R. H. Grubbs, D. J. O’Leary), 2nd ed., Wiley-VCH, Weinheim, **2015**; b) S. T. Diver, *Coord. Chem. Rev.* **2007**, *251*, 671–701; for a pertinent example from this laboratory, see: c) A. Fürstner, P. W. Davies, C. W. Lehmann, *Organometallics* **2005**, *24*, 4065–4071.
- [27] R. H. Crabtree, *The Organometallic Chemistry of the Transition Metals*, 4th ed., Wiley, Hoboken, **2005**.
- [28] For representative and fully characterized examples, see the following and literature cited therein: a) X. Dai, T. H. Warren, *J. Am. Chem. Soc.* **2004**, *126*, 10085–10094; b) P. Hofmann, I. V. Shishkov, F. Rominger, *Inorg. Chem.* **2008**, *47*, 11755–11762; c) G. Seidel, B. Gabor, R. Goddard, B. Heggen, W. Thiel, A. Fürstner, *Angew. Chem. Int. Ed.* **2014**, *53*, 879–882; *Angew. Chem.* **2014**, *126*, 898–901; d) A. G. Tskhovrebov, R. Goddard, A. Fürstner, *Angew. Chem. Int. Ed.* **2018**, *57*, 8089–8094; *Angew. Chem.* **2018**, *130*, 8221–8226.
- [29] a) M. T. Reetz, *Angew. Chem. Int. Ed. Engl.* **1972**, *11*, 130–131; *Angew. Chem.* **1972**, *84*, 163–163; b) I. Fernández, F. P. Cossio, M. A. Sierra, *Chem. Rev.* **2009**, *109*, 6687–6711.
- [30] M. R. Gagné, R. H. Grubbs, J. Feldman, J. W. Ziller, *Organometallics* **1992**, *11*, 3933–3935.
- [31] Ref. [19c,d] also found that ketones are better nucleophiles than esters towards alkynes activated by carbophilic catalysts.
- [32] For reactions of free carbenes with H_2 , see the following and literature cited therein: a) P. S. Zuev, R. S. Sheridan, *J. Am. Chem. Soc.* **2001**, *123*, 12434–12435; b) G. D. Frey, V. Lavallo, B. Donnadiou, W. W. Schoeller, G. Bertrand, *Science* **2007**, *316*, 439–441; c) S. Henkel, W. Sander, *Angew. Chem. Int. Ed.* **2015**, *54*, 4603–4607; *Angew. Chem.* **2015**, *127*, 4686–4690.
- [33] For reactions of Grubbs carbenes with H_2 (or silanes), see: a) J. Louie, C. W. Bielawski, R. H. Grubbs, *J. Am. Chem. Soc.* **2001**, *123*, 11312–11313; b) S. D. Drouin, G. P. A. Yap, D. E. Fogg, *Inorg. Chem.* **2000**, *39*, 5412–5414; for a review, see: c) B. Alcaide, P. Almendros, A. Luna, *Chem. Rev.* **2009**, *109*, 3817–3858.
- [34] The arguably closest example is the hydrogenative metathesis recently described by our group (ref. [4]), in which the hydrogenation of the ruthenium carbene is critically important for catalyst recycling but has nothing to do with product release.

Manuscript received: September 23, 2019

Accepted manuscript online: October 14, 2019

Version of record online: November 6, 2019