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Microwave-Accelerated Ru-Catalyzed Hydrovinylation of Alkynes and Enynes: A Straightforward Approach toward 1,3-Dienes and 1,3,5-Trienes

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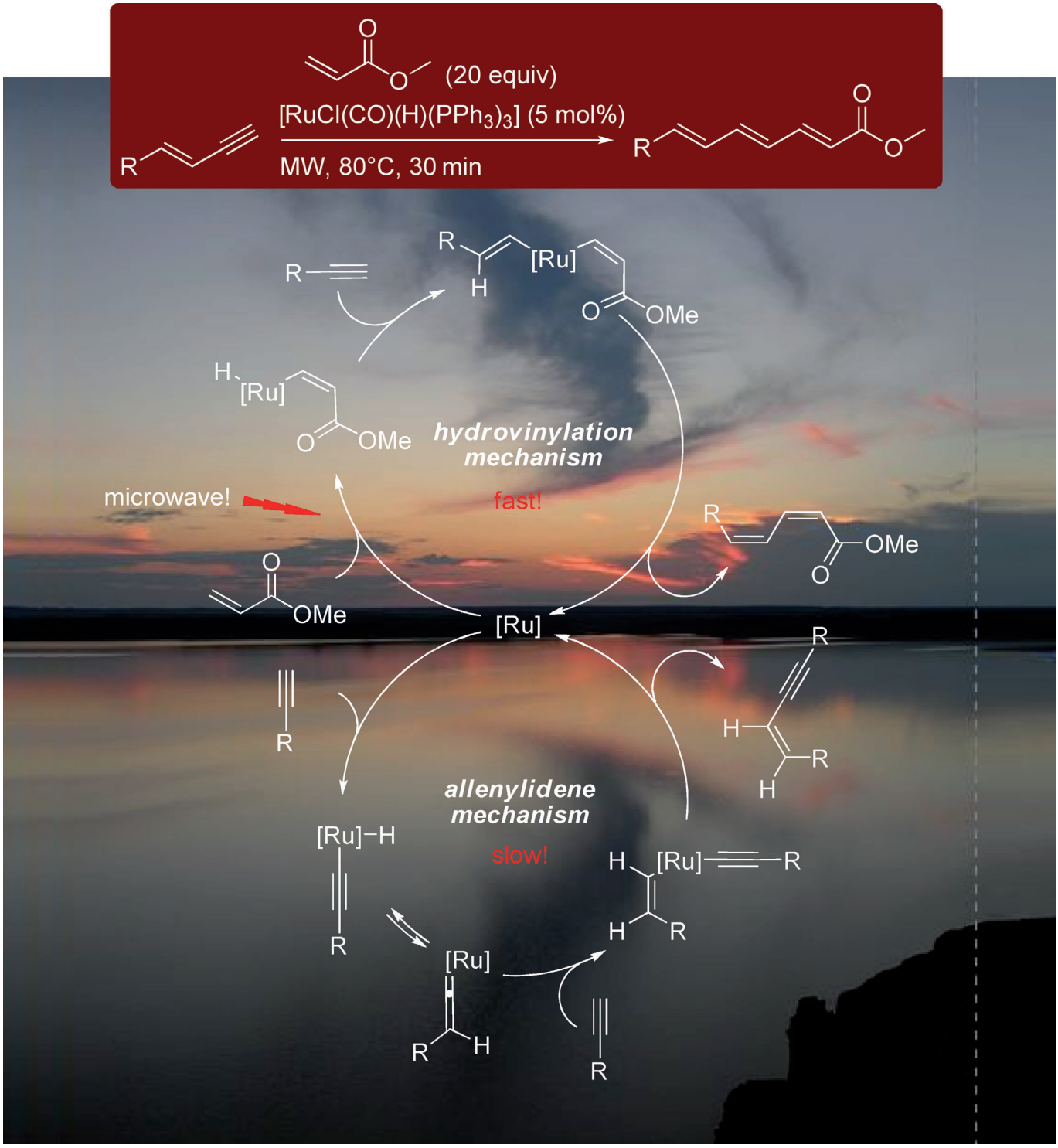
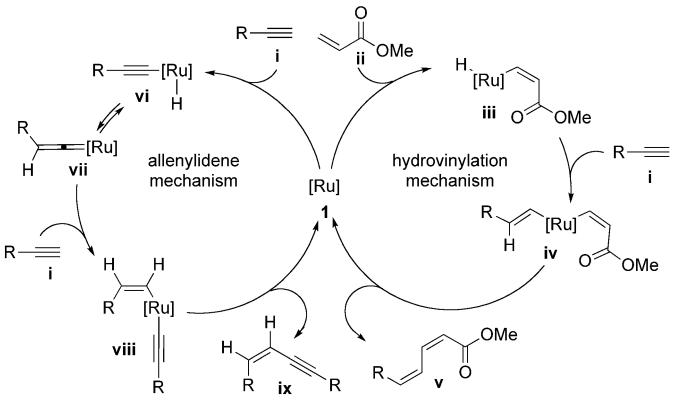


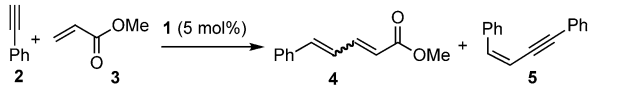
Recently we were able to show that based upon Murai's seminal contribution in the field of Ru-catalyzed C–H activations[1] [Ru(CO)(Ph_3P)$_3$]HCl (**1**) or its corresponding dihydrido species are able to catalyze the hydrovinylation of alkynes with α,β-unsaturated carbonyl compounds.[2] The advantages of this transformation are obvious, the catalyst is readily available in multigram quantities as an air-stable complex in just one step from $RuCl_3$[3] and the transformation is atom economic.[4] However, rather long reaction times of 18 to 48 h and elevated reaction temperatures of 100 °C were required.[2] Furthermore, within an extensive investigation on scope and limitation we observed a serious limitation when functionalized aryl acetylenes were employed in this transformation. Instead of the desired heterocoupling product,[5] the homocoupling product[6–8] was obtained in good to excellent yields. These findings clearly point into the direction of two competing mechanistic manifolds to be operating under thermal conditions (Scheme 1).[2,9]



Scheme 1. Allenylidene versus hydrovinylation mechanism.

Apparently the insertion of the Ru catalyst into the C(sp)–H bond becomes predominant with increasing acidity of this bond.[10] Under standard conditions, this undesired side reaction can be suppressed by employing two equivalents of the acrylate. From a mechanistic point of view the Ru hydride species resulting from the direct insertion into the acrylate β-C–H bond is more reactive in the subsequent hydrometallation of the alkyne. Hence, we speculated that a change in the stoichiometry and a more efficient heating procedure might offer the chance to outcompete the undesired homodimerization of the alkyne. At the outset of our investigations we increased the amount of acrylate systematically under the standard conditions (DMF, 100 °C, 24 h, Table 1).

Table 1. Influence of the solvent and temperature.[a]



Entry	**3** (equiv)	Solvent	*t* [h]	*T* [°C]	**4**/**5** [%][b]
1	2	DMF	24	100	21:23
2	5	DMF	24	100	38:14
3	10	DMF	24	100	47:6
4	20	DMF	24	100	62:–
5	20	DMF	24	120	44:–
6	20	DMF	0.5	100 (MW)	65:–
7	20	–	0.5	100 (MW)	73:–
8	20	–	0.5	80 (MW)	79:–
9	20	–	0.5	60 (MW)	75:–

[a] The reactions were performed under a N_2 atmosphere on a 0.5 mmol scale by using 5 mol% catalyst. [b] Determined by GC integration by using dodecane as an internal standard.

The product ratio changed significantly into the desired direction; however, the long heating periods led to a severe decomposition of the acrylate. At this point we changed the experimental setup and decided to employ microwave heating. This kind of energy supply has been shown to solve problems that are connected with simple thermal heating, in which the energy is absorbed by the solvent and eventually transferred from the solvent to the reaction components.[11] Microwave absorption is only possible by polar molecules. Hence, microwave irradiation of a catalytic reaction, in which usually polar intermediates are involved, in a nonpolar solvent, allows for a directed energy transfer into the reactive intermediates.[11] As a consequence of this directed "heating" shorter reaction times and in certain cases higher yields due to the avoidance of undesired thermal side reactions are observed. We were surprised to find that the concept of microwave irradiation turned out to be a key to the solution of our chemical problem. After only 30 min full conversion was observed by using an excess of acrylate. Under these conditions the addition of DMF as a solvent was not necessary.

A variety of terminal acetylenes were transferred into the corresponding 1,3-dienes without formation of the undesired homocoupling product (Table 2). Good to excellent isolated yields were obtained. The reaction is compatible with functional groups, such as halides, ethers, nitriles, and even heterocycles. Furthermore, no ring opening of the cyclopropyl moiety was observed.

From a mechanistic point of view, the *E*/*Z*-configured 1,3-diene should be the primary product.[4] Due to the thermal conditions we envisioned a subsequent Ru-catalyzed π-bond isomerization into the all-*E*-configured diene to account for the predominant formation of the latter product.[12] The microwave irradiation allows for a decrease in the reaction temperature. From these data it is obvious that the isomerization of the *E*/*Z* into the *E*/*E*-configured product strongly depends on the reaction temperature. To underline the abili-

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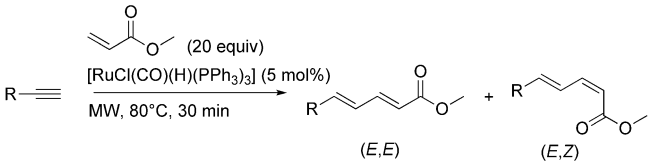
Table 2. Microwave-accelerated hydrovinylation of terminal alkynes.[a]



Entry	R	Product	(*E*,*E*)/ (*E*,*Z*)	Yield [%]
1	Ph	**6**	91:9	79
2	*p*-MeOC$_6$H$_4$	**7**	92:8	82
3	*p*-ClC$_6$H$_4$	**8**	86:14	76
4	*p*-F$_3$CC$_6$H$_4$	**9**	81:19	82
5	*p*-MeC$_6$H$_4$	**10**	81:19	83
6	C$_5$H$_{11}$	**11**	76:24	91
6[b]	PhOCH$_2$	**12**	75:25	85
7	4-Cl-C$_4$H$_8$	**13**	74:26	79
8[c]	4-NC-C$_4$H$_8$	**14**	70:30	66
9	cyclopropyl	**15**	81:19	90
10[d]	3-pyridyl	**16**	74:26	74

[a] The reactions were performed under a N_2 atmosphere on a 0.5 mmol scale by using 5 mol% catalyst 80°C. [b] 5 mol% catalyst, 100°C, 1 h. [c] 5 mol% catalyst, 100°C, 1 h, DMF (1 mL). [d] 10 mol% catalyst, 100°C, 30 min.

ty of the Ru catalyst to isomerize π-bonds, isomerically pure *E*/*Z*-configured product **5** was subjected to the reaction conditions at different temperatures (Figure 1).

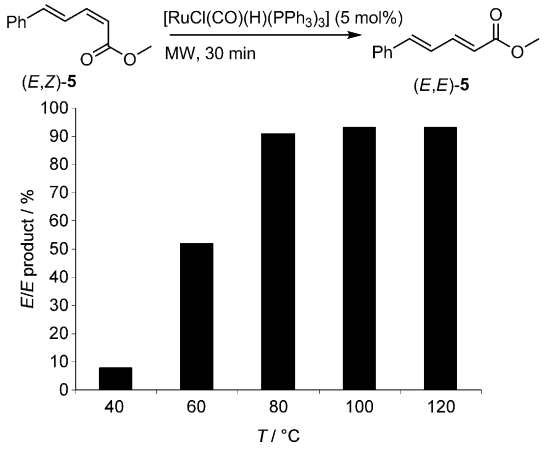


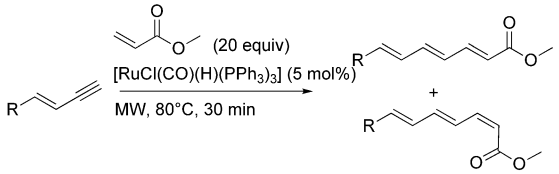
Figure 1. Ru-catalyzed diene isomerization.

From these data it is obvious that the stereoselective course of the hydrovinylation is the consequence of a thermal isomerization rather than of a different mechanism.

After having found suitable reaction conditions that allow for the fast hydrovinylation of different alkynes, we finally set out to employ enynes as starting materials (Table 3).

These starting materials are of interest for several reasons. On the one hand, and from a synthetic point of view, these compounds would allow a preparation of 1,3,5-trienes. On the other hand, and from a mechanistic point of view, the use of a vinylogous alkyne opposes a challenge to the regioselectivity of the hydride transfer. Gratifyingly, this compound class was efficiently transferred into the corresponding trienes by using microwave irradiation (Table 3). A mixture of isomers was observed; however, whereas the geometry of the α,β-double bond displays the thermodynamic equilibrium mixture (Scheme 1) the γ,δ- and ε,ϕ-double bond geometry was only *E* in all cases. Undesired side reactions, such as, for example, benzannulations,[13] were not observed under these conditions.[7–9]

Table 3. Microwave-accelerated hydrovinylation of enynes.[a]



Entry	R	Product	(*E*,*E*,*E*)/(*E*,*E*,*Z*)	Yield [%]
1	Ph	**17**	91:9	79
2	*p*-MeO-C$_6$H$_4$	**18**	92:8	93
3	*p*-*t*Bu-C$_6$H$_4$	**19**	86:14	76
4	*p*-F-C$_6$H$_4$	**20**	81:19	82
5		**21**	76:24	82

[a] The reactions were performed under a N_2 atmosphere on a 0.5 mmol scale by using 5 mol% catalyst 80°C.

In the present manuscript, we report on the beneficial influence of microwave irradiation in Ru-catalyzed hydrovinylation. The interplay of stoichiometry on the one side and the more efficient ("target-oriented") energy transfer by microwaves on the other allows the fast and high yielding atom-economic coupling of monosubstituted alkynes and acrylates to give the corresponding 1,3-dienes. In furtherance of these studies, enynes were employed as a new class of reactive alkynes. The microwave-accelerated hydrovinylation of these compounds provided a straightforward access to 1,3,5-trienes in good yields. This reaction was not possible by using conventional heating technologies. It is our hope that the beneficial influence of microwave irradiation will open up a new perspective in C–H-activation chemistry.[14] Our future investigations will concentrate on this aspect.

Experimental Section

General procedure: A 10 mL-microwave vial was charged at room temperature with [RuCl(CO)(H)(PPh$_3$)$_3$] (5–10 mol%) under a N_2 atmosphere. Methyl acrylate (900 μL) and alkyne (0.5 mmol) were added. The tube was immediately closed and heated for 30 min to the given temperature. After cooling to room temperature the excess acrylate was evaporated and the residue was directly purified by silica gel column chromatography.

Acknowledgements

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Keywords: catalysis · coupling · diene · microwave · ruthenium

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