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Atom transfer radical addition and enol-ester synthesis catalyzed by Ru–vinylidene complexes

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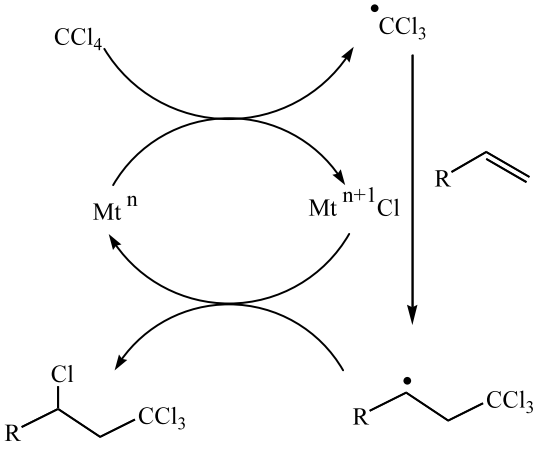
Abstract—Ru–vinylidene complexes, $Cl_2Ru\{=C=C(H)^tBut\}(PCy_3)(L)$ (L = PCy_3 or *N*-heterocyclic carbenes) reveal themselves as a versatile catalyst for the atom transfer radical addition (ATRA) of polyhalogenated alkanes to olefins, such as methylmethacrylate, styrene and 1-octene. Furthermore, these systems are excellent catalysts for the nucleophilic addition of carboxylic acids to terminal alkynes and yielded exclusively alk-1-en-2-yl esters. These complexes can also be transformed to their cationic counterparts by treating the neutral complexes with $AgBF_4$ and their catalytic potential in ATRA and vinylation reaction are investigated.

During the mid 1980s, the atom transfer radical addition (ATRA) reaction emerged from a long period of obscurity to take a leading position in modern synthetic radical chemistry.[1] The formation of polyhalogenated alkanes, lactones and lactams has attracted the attention of synthetic chemists because these compounds are versatile reactants that can act as building blocks in the synthesis of natural products with biological activity such as insecticides and antibiotics.[2,3] Hereby, the redox properties of the transition metal complexes are exploited in order to initiate the reaction by a homolytic cleavage of the carbon–halogen bond and a concomitant creation of a carbon centered radical. Moreover, the termination step introduces a versatile halogen atom into the molecule which can be further functionalized (Scheme 1). Since the transition metal is crucial for the position of the equilibrium and thus for the control of 1:1 adduct formation, a new class of catalysts have been developed to perform ATRA reactions. Among these, a great number are based on ruthenium with $RuCl_2(PPh_3)_3$,[4] $RuCl_2(Ind)(PPh_3)_2$ (Ind = indenyl)[5] and $RuCl(Cp^*)(PPh_3)_2$ (Cp^* = pentamethylcyclo pentadienyl)[6] as the most prominent group.

The development of efficient Ru-catalysts is mainly driven by their tolerance toward functional groups, their ease of preparation and the ability to perform a broad range of selective reactions with one single catalytic system.[7] Another reaction whereby ruthenium cannot be omitted is the enol-ester synthesis also called vinylation reaction. In this reaction, ruthenium complexes orchestrate the selective nucleophilic addition of carboxylic acids to terminal alkynes to produce Markovnikov or *anti*-Markovnikov adducts which are useful synthetic intermediates or polymer precursors (Scheme 2).[8]

Recently, our group[9–11,17] and others[12–14] succeeded in implementing Ru–alkylidene and more readily accessi-



Scheme 1.

Keywords: ATRA; enol-esters; homogeneous catalysis; ruthenium and compounds; olefins.

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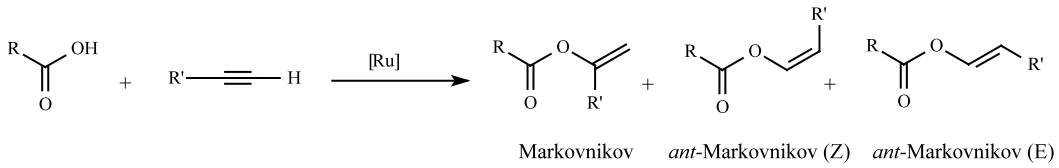

Scheme 2.

ble vinylidene complexes in the world of ATRA, olefin metathesis, atom transfer radical polymerization (ATRP) and vinylation reactions. To further elaborate the expanding scope of these systems, we continuously try to improve and fine-tune our catalytic systems. We now report upon two new members of the vinylidene series which are active in both ATRA and vinylation reactions. Complexes **1** and **2** are prepared according to literature procedures.[15,16] Furthermore, the analogous cationic species (**3** and **4**) are generated in situ by treating complexes **1** and **2** with 1 equiv. of $AgBF_4$ during 30 min at room temperature before the substrate was added (Fig. 1).

Catalysts **1**–**4** are tested for the ATRA of polyhalogenated alkanes to different olefins and the results are summarized in Table 1. The first thing that is directly noticed is the fact that substituting one phosphine ligand in complex **1** with a bulky and strong electron donating *N*-heterocyclic carbene has an enormous impact on the catalytic activity. In this way, the conversion for the addition of CCl_4 to methylmethacrylate and styrene are on average 11% higher with system **2** than the results obtained with complex **1**, whereas for 1-octene the conversion is three times higher. An analogous tendency was observed for the addition of chloroform. This tendency is quite surprising since it is known from literature that ruthenium alkylidene complexes, Ru=CHPh, bearing less bulky and electron donating ligands (PPh_3 versus PCy_3) give access to very active ATRA catalysts.[6] This confirms again that the exact role of the carbene entity in radical reactions is not unambiguous elaborated and is still a main topic in this research. The total conversions for the ATRA of

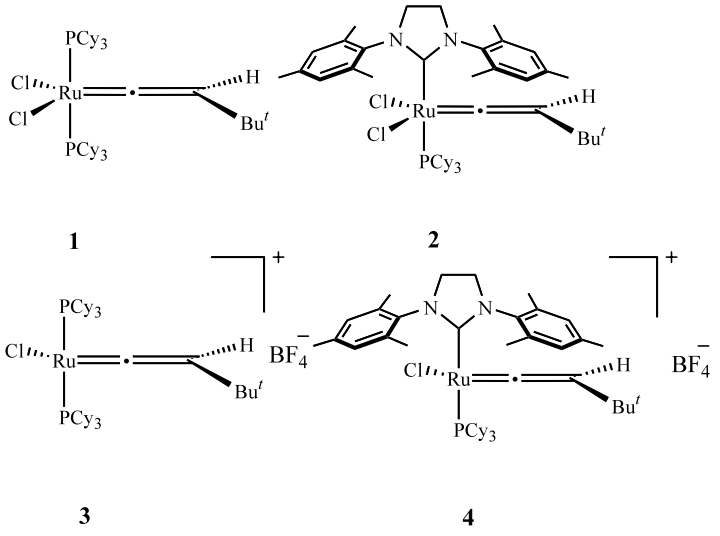

Figure 1.

Table 1. ATRA of halogenated alkanes to olefins catalyzed by neutral and cationic ruthenium complexes **1**–**4**[a]

Olefin	Halide	Time (h)	Yield (%)[b]			
			1	**2**	**3**	**4**
Methylmethacrylate	CCl_4	17	76	85	62	77
Styrene		17	83	92	67	79
1-Octene		24	18	56	11	40
Methylmethacrylate	$CHCl_3$	17	30	44	19	25
Styrene		17	45	60	36	43
1-Octene		24	7	22	13	17

[a] General conditions: The catalyst (0.03 mmol) was dissolved in toluene (1 ml) and subsequently added through the septum of a glass vessel to a mixture of alkene (9 mmol), halide (13 mmol), dodecane (0.25 ml) and toluene (1 ml). Reaction temperature: 80°C.

[b] Yields (%) based on GLC using dodecane as internal standard.

chloroform are significantly lower compared to CCl_4. The reason for this can be explained by the preference to form oligomers with this halide which was confirmed by others.[4,13,14] Abstracting a chloride entity in complexes **1** and **2** does not improve their performance since the total yields for all the substrates are lower with both systems. This is quite surprising because an opposite tendency was observed for ATRP reactions.[17] It must be said that an eventually solvent effect on the outcome of the reaction has not yet been investigated. If we compare our results in terms of average turnover frequency (TOF) with the traditional alkylidene system $RuCl_2(=CHPh)(PR_3)$ (R = Ph, **5**, R = Cy, **6**),[12,13] the obtained turnover frequencies in this work are considerably higher for comparable reaction conditions. For example, for 1-octene the TOF for **5** is 0.9 h^{-1} and for **6** a value of 3.25 h^{-1} is reached, while the vinylidene complexes **1** and **2** easily get 2.25 and 7 h^{-1}. Next to the higher activity, the vinylidene complexes have the advantage that they are also easily accessible via commercial available and air-stable compounds.[15]

Complexes **1**–**4** can be implemented in the formation of enol-esters from the reaction of several terminal alkynes with carboxylic acids (Table 2). With phenylacetylene as the substrate nearly quantitative yields are obtained with a preference for the formation of the Markovnikov adduct. It is also seen that the catalytic activity and the regioselectivity (M/*anti*-M >3) increases when the mixed ligand systems containing one *N*-heterocyclic carbene are used. For instance, the addition of benzoic acid to phenylacetylene results in the formation of the (*Z*)-alk-1-en-1-yl ester (M/*anti*-M = 0.21) with system **1**, while catalyst **2** yielded almost exclusively the alk-1-en-2-yl ester (88%). Transforming complexes **1** and **2** into their cationic counterparts has a pronounced effect on the catalytic activity in vinylation reactions. Complexes **3** and **4** give access to the formation of 2-styryl benzoate in quantitative yields in a three times shorter period compared with systems **1** and **2**. The addition of formic acid and acetic acid to phenylacetylene were followed in function of time and an analogous accelerating effect was observed as with benzoic acid (Figs. 2 and 3). A possible explanation is given in Fig. 4. It is known from the literature that the first step involves the dissociation of a phosphine ligand before the acid coordinates.[18] This phosphine entity can compete every moment in the reaction cycle with the incoming acid. When a chloride is abstracted, the acid can directly enter the coordination sphere of the Ru-center and no equilibrium with a competitive phosphine ligand is established.

For the vinylation of the more steric *t*-butylacetylene with acetic acid, globally lower conversions are obtained (55–77%), but again a preference for the Markovnikov product is noticed (M/*anti*-M ≈ 3). The fraction of the alk-1-en1-yl esters consist almost exclu-

Table 2. Vinylation reaction catalyzed by complexes **1**–**4**[a]

Alkyne	Acid	Cat.	Time (h)	% Yield[b]	% M[c]	% *anti*-M[c] (Z)[2]	% *anti*-M[c] (E)[2]	Dimerization[c]
Phenylacetylene	HCOOH	**1**	6	80	66	34	–	–
Phenylacetylene	CH_3COOH	**1**	6	93	70	8	–	22
Phenylacetylene	C_6H_5COOH	**1**	6	97	17	80	–	5
Phenylacetylene	HCOOH	**2**	6	85	75	25	–	–
Phenylacetylene	CH_3COOH	**2**	6	96	76	24	–	–
Phenylacetylene	C_6H_5COOH	**2**	6	98	88	–	–	12
Phenylacetylene	HCOOH	**3**	2	82	89	11	–	–
Phenylacetylene	CH_3COOH	**3**	4	94	87	10	3	–
Phenylacetylene	C_6H_5COOH	**3**	2	95	100	–	–	–
Phenylacetylene	HCOOH	**4**	2	85	77	10	3	–
Phenylacetylene	CH_3COOH	**4**	2	96	89	5	2	4
Phenylacetylene	C_6H_5COOH	**4**	2	100	99	1	–	–
t-Butylacetylene	CH_3COOH	**1**	6	55	67	2	29	2
t-Butylacetylene	CH_3COOH	**2**	6	60	70	–	25	5
t-Butylacetylene	CH_3COOH	**3**	6	68	74	–	26	–
t-Butylacetylene	CH_3COOH	**4**	6	77	76	3	21	–
1,7-Octadiyn[d]	CH_3COOH	**1**	6	72	44	–	14	–
1,7-Octadiyn[d]	CH_3COOH	**2**	6	78	48	4	10	–
1,7-Octadiyn[d]	CH_3COOH	**3**	6	80	52	–	17	–
1,7-Octadiyn[d]	CH_3COOH	**4**	6	83	46	–	15	–
4-Pentynoic acid		**1**	2	100	100	–	–	–
4-Pentynoic acid		**2**	2	100	100	–	–	–
4-Pentynoic acid		**3**	1	100	100	–	–	–
4-Pentynoic acid		**4**	1	100	100	–	–	–

[a] General conditions: The catalyst (0.04 mmol) was dissolved in toluene (1 ml) and subsequently added through the septum of a glass vessel to a mixture of alkyne (4 mmol), carboxylic acid (4.4 mmol), dodecane (0.25 ml) and toluene (2 ml). Reaction temperature 110°C.

[b] The total yield was determined with Raman spectroscopy by following the diminishing intensity of the $\nu_{C\equiv C}$ of the alkyne in combination with appropriate calibration curves.

[c] Selectivities were determined by GC–MS making use of the different fragmentations of the isomers. GC–MS measurements excluded the formation of other products than those reported here. Dimerization products exclusively consist off the (*E*)-enyn.

[d] The rest of the products consist of mono-substituted product (Markovnikov addition).

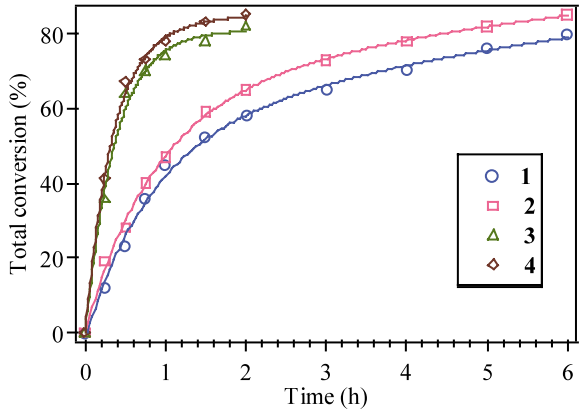

Figure 2. Total conversion versus time for the vinylation reaction of phenylacetylene with formic acid using catalysts **1**–**4**. (Conditions: catalyst:phenylacetylene:formic acid = 1:100:110 in toluene (3 ml). Reaction temperature 110°C.)

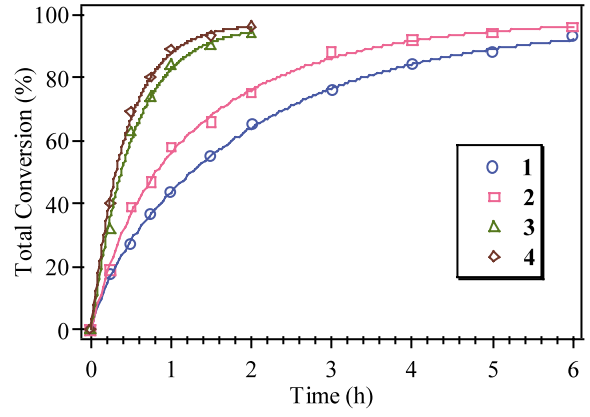

Figure 3. Total conversion versus time for the vinylation reaction of phenylacetylene with acetic acid using catalysts **1**–**4**. (Conditions: catalyst:phenylacetylene:acetic acid = 1:100:110 in toluene (3 ml). Reaction temperature 110°C.)

sively of the (*Z*)-isomer and this is because of sterical reasons. The vinylation reaction of the dialkyne, 1,7-octadiyn, with acetic acid leads to a mixed product distribution containing Markovnikov mono-adduct, Markovnikov disubstituted product and *anti*-Markovnikov disubstituted product and this for all the catalysts. The reaction also demands longer reaction times than with the electrophilic activated phenylacetylene. Cyclisation of 4-pentynoic acid gave, with all the tested catalysts, the *exo*-cyclic product γ-methylene-γ-butyrolactone in excellent yields.

As can be observed from Table 3, catalytic system **4** is a very promising system for the synthesis of alk-1-en-2-yl esters as they can compete with well-established catalysts such as $RuCl_3{\cdot}3H_2O/PBu_3$, Ru(η^5-cyclooctadienyl)/PBu_3/maleic anhydride and $RuCl_2$(*p*-cymene)(PMe_3). Although, the formation of α-methylenebenzyl formate from the reaction of phenylacetylene and formic acid catalyzed by $RuCl_2$(*p*-cymene)(PPh_3) resulted in higher yields. However, taking into consideration that the Ru–vinylidene complexes are readily available from commercial products and taking into account that the last complex is inactive for the Kharasch addition, it is reasonable to state that our systems act as versatile catalysts for a broad avenue of transformations and provide access to an array of fine chemicals such as: alk-1-en-2-yl esters and polyhalogenated alkanes.

In conclusion, the ruthenium vinylidene complexes (**1**–**4**) showed a moderate to good activity for the ATRA of CCl_4 and chloroform to different olefins. Furthermore, these complexes are efficient vinylation catalysts which result in the formation of alk-1-2-yl esters in high yields and selectivity. Especially, the cationic complex bearing a 4,5-dihydroimidazol-2-ylidene entity can compete with the best Ru systems known so far for this reaction.

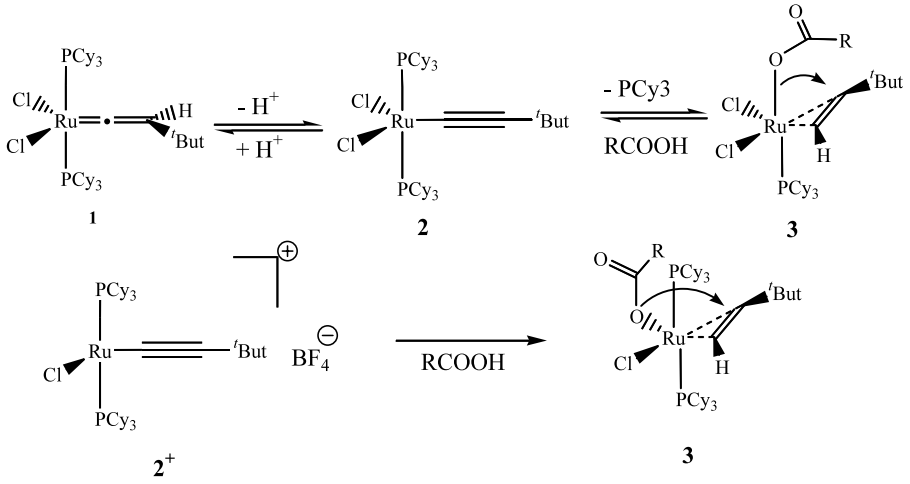

Figure 4.

Table 3. Markovnikov addition of carboxylic acids toward phenylacetylene in the presence of various ruthenium complexes

Catalyst	Reaction conditions	Yield (%)			Ref.
		CH_3COOH	HCOOH	PhCOOH	
$RuCl_3 \cdot 3H_2O/PBu_3$	1.96 mol%/120°C/15 h	54	–	63	19
Ru(η^5-cyclooctadienyl)/PBu_3/maleic anhydride	0.99 mol%/80°C/12 h	40	–	–	20
$RuCl_2$(*p*-cymene)PPh_3	0.79 mol%/80°C/15 h	–	95	–	21
$RuCl_2$(*p*-cymene)PMe_3	1.96 mol%/120°C/15 h	46	–	68	19
4	0.99 mol%/110°C/2 h	85	65	99	–

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