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Tetrahedron Letters
Tetrahedron Letters 47 (2006) 8617–8620

A new stable Hoveyda–Grubbs catalyst with mixed anionic ligands

Kati Vehlow,[a,b] Simon Maechling,[a] Katrin Köhler[b,†] and Siegfried Blechert[a,*]

[a]*Technische Universität Berlin, Strasse des 17. Juni 135, 10623 Berlin, Germany*
[b]*Merck KGaA, Frankfurter Strasse 250, 64293 Darmstadt, Germany*

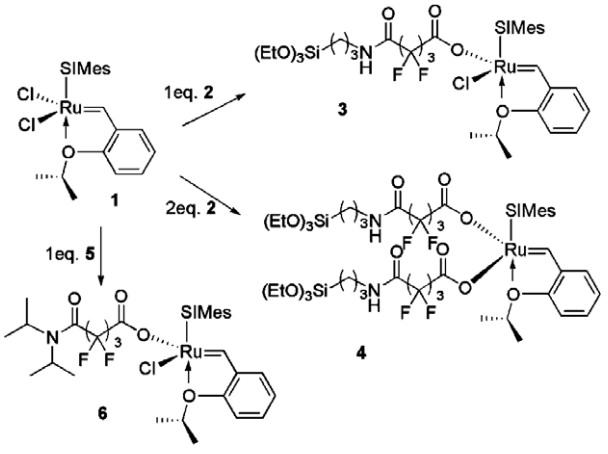
Received 25 August 2006; revised 18 September 2006; accepted 19 September 2006
Available online 16 October 2006

Abstract—The synthesis and characterisation of a new highly active Hoveyda–Grubbs 2nd generation type catalyst is described. Substitution of one chloride ligand with a partially fluorinated trialkoxysilyl substituted carboxylate leads to the stable monocarboxylate ruthenium catalyst (**3**). This catalyst represents the first example of a stable and isolable mono-chloride exchanged carboxylate complex suitable for both homogeneous and heterogeneous metathesis. The reactivity of the new catalyst was tested in representative metathesis reactions and offers an activity comparable to the parent dichloride system (**1**).

In the field of olefin metathesis, ruthenium based carbene complexes play an outstanding role.[1] In particular, the ruthenium (pre)catalysts Grubbs 2nd generation [$RuCl_2$(=CH–C_6H_5)(PCy_3)(SIMes)] (SIMes = 1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-ylidene) and the Hoveyda–Grubbs 2nd generation [$RuCl_2$(=CH-*o*-O–*i*-Pr–C_6H_4)(SIMes)] (**1**) represent reagents of choice for a variety of applications in organic chemistry. During the last few years the modification of ligands have led to metathesis (pre)catalysts with specific characteristics. The variation of the halogen ligands was first examined by Grubbs and co-workers[2] Later the replacement of the chloride ligands by alkoxides,[3] dicarboxylates,[7c] trifluoroacetates[2a] and other strong electron-withdrawing fluorocarboxylates,[4,5] as well as fluorosulfonates[4a] was also investigated. Substitution of the anionic ligands was also used for the immobilisation of Grubbs 2nd generation and Hoveyda–Grubbs 1st and 2nd generation-type catalysts.[4,6,7] However, there are only a few known cases of homogeneous Grubbs and Hoveyda–Grubbs catalysts with mixed anionic ligands.[7c,4a] Typically, the exchange with fluorocarboxylates does not lead to clean monosubstitution. Only nonseparable mixtures of the reactants, bis- and monoadducts could be isolated. Therefore the reactivity of these mixed anionic compounds is more or less unknown.

During our studies on the synthesis of a homogeneous ruthenium catalysts, which could potentially be immobilised on silica gel, we discovered a highly selective mono-substitution of one chloride ligand. This has made possible the direct comparison between mono- and dicarboxylate substituted catalysts and their parent dichloride systems concerning reactivity and stability.

The required silver carboxylate $(EtO)_3Si$–C_3H_6–NH–CO–C_3F_6–COOAg (**2**) was readily synthesised according to the described literature procedure.[8] Initial studies were concerned with monosubstitution of one chloride ligand of **1** with silver carboxylate **2** (Scheme 1). Previous attempts to synthesise similar trifluoroacetate

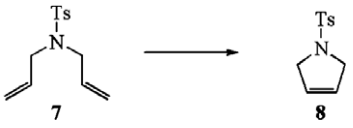


Scheme 1. Synthesis of **3**, **4** and **6**.

Keywords: Carboxylate ligands; Metathesis; Ruthenium; Catalysis.
* Corresponding author. Fax: +49 303 31423619; e-mail: blechert@chem.tu-berlin.de
† New address: Sartorius AG, Weender Landstrasse 94-108, 37075 Göttingen, Germany.

0040-4039/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2006.09.096

Table 1. RCM of *N*,*N*′-diallyltosylamide (**7**)[a]



7 **8**

Entry	Cat.	Loading (mol %)	Conv. (%)[b]	TON
1	**1**	0.01	49	4860
2	**1**	0.02	66	3300
3	**3**	0.01	51	5050
4	**3**	0.02	66	3290
5	**4**	0.01	27	2690
6	**4**	0.02	39	1970

[a] Conditions: 0.05 M solution of **7**, CH_2Cl_2, 45 °C, 14 h.
[b] Conversions were determined by HPLC.

derived mono-substituted catalysts, have been met with limited success, affording only an inseparable mixture of products including mono- and di-substituted complexes and starting material.[4a]

We observed that it was possible to achieve a clean conversion to the monosubstituted derivative **3** by utilising a partially fluorinated trialkoxysilyl substituted silver carboxylate. When **1** was treated with 1 equiv of silver carboxylate **2** in CH_2Cl_2, complex **3** could be isolated in high purity as an olive green powder, in 82% yield.[9] Following a similar protocol, both chloro-ligands could be substituted in a clean reaction and **4** was isolated in high purity as a violet powder, by the reaction of **1** with 2 equiv of silver carboxylate **2** (Scheme 1).

In order to investigate the influence of the alkoxysilyl group on the observed monosubstitution we reacted 1 equiv of **1** with 1 equiv of the alkoxysilyl-free $(i\mathrm{Pr})_2$N–CO–C_3F_6–COOAg (**5**) (Scheme 1).[8]

Utilisation of THF in place of CH_2Cl_2 afforded the olive-green complex **6** in 92% yield as an inseperable mixture of 92% of **6**, 4% of the disubstituted catalyst and 4% of **1**. The silyl-free mono-carboxylate complex **6** was found to be unstable in solution, especially in chlorinated solvents and disproportionated. From these results we tentatively assign the stability of **3** to a stabilising Ru–Si(OEt) interaction. This kind of interaction has been also observed for the trialkoxysilyl-functionalised silver(I)-carboxylates.[8]

With the pure complexes **1**, **3** and **4** in hand we were interested in their relative reactivity in the ring closing metathesis (RCM). A meaningful comparison of the activity between the different catalysts can be achieved by determining the turnover numbers (TONs) at the same catalyst loading.[10] Therefore, we tested the three catalysts in the RCM of *N*,*N*′-diallyltosylamide (**7**) (Table 1).

As can be seen from Table 1, the reactivity of the mono-carboxylate complex **3** rivalled with the parent catalyst

Table 2. Representative metathesis reactions utilising **3**[a]

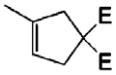
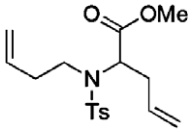
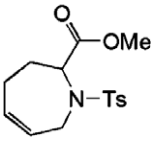
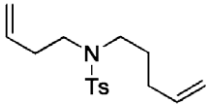
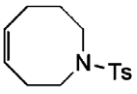
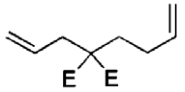
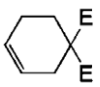
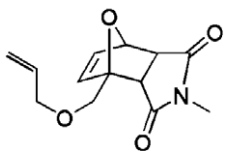
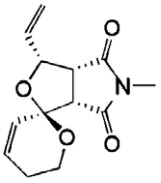
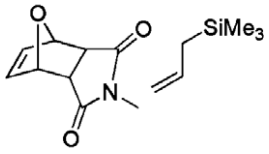
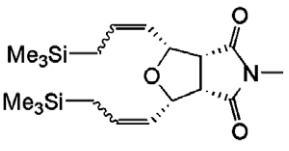
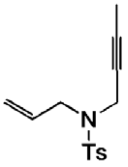
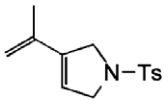
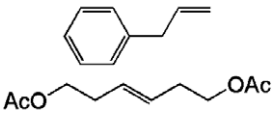
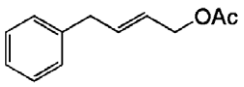
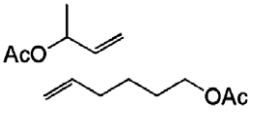
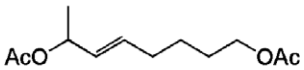
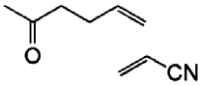
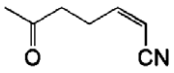
Entry	Substrate[b]	Product[b]	Conv. (*E*:*Z*)[c] (%)	Time (h)	Loading (mol %)
1			>99	2	0.5
2			>99	1	0.5
3			>95	1	0.5
4			>95	3	0.5
5			>99	3	0.5
6			>99	2	0.5

Table 2 (*continued*)

Entry	Substrate[b]	Product[b]	Conv. (*E*:*Z*)[c] (%)	Time (h)	Loading (mol %)
7			35	6	1
8			77 (8:1)	12	3
9			>99 (only *E*)	12	3
10			73 (1:4)	3	5

[a] All reactions were performed in refluxing CH_2Cl_2.
[b] E=CO_2Et.
[c] Conversions determined by ^{1}H NMR.

1. In contrast the reactivity of the dicarboxylate catalyst **4** is clearly reduced.

Finally, the activity of **3** was tested in a series of metathesis reactions and the results are summarised in Table 2. It is clear to see that **3** is capable of performing a variety of metathesis reactions.

Catalyst **3** showed a high activity at a low catalyst loading (0.5 mol %) for RCM (entries 1–4), including a more sterical substrate (entry 1). Entries 5 and 6 represent examples of metathesis sequences; that is, ring rearrangement metathesis (RRM) and ring opening cross metathesis (ROM/CM) respectively. Starting from the endo-educts, the corresponding products were formed in high yields (>99%), using only 0.5 mol % catalyst. Another useful feature is the highly selective cross-metathesis (entries 8 and 9) yielding the products in high yield as would generally be expected. And also the electron-poor acrylonitrile may be used for CM in a good yield (73%) at 5 mol % catalyst loading (entry 10). Although for enyne metathesis (entry 7) **3** performed poorly offering only 35% conversion after 6 h.

In summary, we present a stable and isolable monocarboxylate ruthenium metathesis complex (**3**). This (pre)catalyst is functionalised with one partially fluorinated trialkoxysilyl carboxylate. The synthesis of the disubstituted catalyst **4** allows a direct comparison between mono- and disubstitution concerning reactivity and stability. Compound **3** shows similar activity in RCM of **7** compared to the parent dichloride system (**1**), meanwhile the reactivity of **4** is significantly lower. Furthermore, catalyst **3** displays an excellent activity for various metathesis reactions, even at low catalyst loading. Investigation of the selectivity chloride exchange at other ruthenium systems as well as immobilisation is in progress.

Acknowledgements

We are grateful to the analytical department of Merck KGaA for NMR, IR and GF-AAS spectroscopic measurements and C, H and N analyses and the Graduiertenkolleg 'Synthetische, mechanistische und reaktionstechnische Aspekte von Metallkatalysatoren' for financial support.

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9. Synthesis of the catalysts was performed under an argon atmosphere by standard Schlenk techniques or in an Argon-mediated dry-box (Labmaster 130, Mbraun, Germany). Solvents were dried before use, employing standard drying agents. [RuCl((EtO)$_3$Si–C$_3$H$_6$–NH–CO–C$_3$F$_6$–COO) (=CH–*o*-O–*i*-Pr–C$_6$H$_4$)(SIMes)] (**3**): A solution of **2** (100.4 mg, 159.6 μmol, 1 equiv) in dry CH_2Cl_2 (40 ml) was slowly added to a stirred solution of **1** (100.0 mg, 159.6 μmol, 1 equiv) in dry CH_2Cl_2 (10 ml). While stirring was continued for 60 min a white disperse precipitate formed. The precipitate was filtered and the filtrate was evaporated to dryness. The residue was dissolved in CH_2Cl_2 (2 ml) and *n*-hexane (6 ml) added. The precipitate was removed by filtration and the solvent was removed in vacuo. Drying under high vacuum afforded 135.3 mg (130.9 μmol, 82.0%) of a olive green powder. ^{1}H NMR (250 MHz, CD_2Cl_2): δ 17.14 (s, 1H, C*H* = Ar), 7.48 (dt, $J = 7.8$ Hz, 1.8 Hz, 1H, aromat. C*H*), 7.17, 7.07 (s, 4H, mes.-C*H*), 7.02 (dd, $J = 7.5$ Hz, 1.8 Hz, 1H, aromat. C*H*), 6.94 (t, $J = 7.1$ Hz, 1H, aromat. C*H*), 6.76 (br s, 1H, NH), 6.76 (d, $J = 8.3$ Hz, 1H, aromat. C*H*), 4.69 (septet, $J = 6.1$ Hz, 1H, *i*-Pr–C*H*), 4.14 (s, 4H, imidazole–CH_2), 3.80 (q, $J = 7.0$ Hz, 6H, Si–OCH_2), 3.20 (q, $J = 6.7$ Hz, 2H, CH_2NH), 2.46 (s, 6H, mes.-*o*-CH_3), 2.43 (s, 6H, mes.-*p*-CH_3), 2.25 (s, 6H, mes.-*o*-CH_3), 1.57 (m, 2H, Si–CH$_2$–CH_2), 1.21 (t, $J = 7.0$ Hz, 9H, Si–OCH$_2$–CH_3), 1.02 (d, $J = 6.1$ Hz, 3H, *i*Pr–CH_3), 0.98 (m, 3H, *i*-Pr–CH_3), 0.57 (t, $J = 8.0$ Hz, 2H, SiCH_2). ^{19}F NMR (235 MHz, CD_2Cl_2): δ −124.5, −124.3 (2s, 2F, CF_2), −119.7, −119.4 (2t, 2F, CF_2CONH), −115.1, −114.8 (dt, t, 2F, CF_2COORu). ^{13}C NMR (75.5 MHz, CD_2Cl_2): δ 307.4 (*C*H=Ar), 210.7 (imidazole–*N*–*C*–N), 161.3 (*C*OO), 158.7 (*C*ONH), 153.4 (aromat. *C*), 144.6 (aromat. *C*), 139.6 (mes.-*p*-*C*), 139.5, 139.1 (mes.-*o*-*C*), 135.7 (mes.-*C*–N), 130.3 (aromat. *C*H), 129.9 (mes.-*C*H), 123.0 (aromat. *C*H), 122.7 (aromat. *C*H), 112.7 (aromat. *C*H), 111.3 (*C*F$_2$CONH), 109.7 (*C*F$_2$COORu), 108.1 (*C*F$_2$), 75.6 (*i*-Pr–*C*H), 58.9 (SiO*C*H$_2$), 51.9 (imidazole–*C*H$_2$), 42.5(*C*H$_2$NH), 22.7 (Si–CH$_2$–*C*H$_2$), 21.3 (mes.-*p*-*C*H$_3$), 20.5 (*i*-Pr–*C*H$_3$), 19.2 (br s, mes.-*o*-*C*H$_3$), 18.7 (mes.-*o*-*C*H$_3$), 18.5 (Si–OCH$_2$–*C*H$_3$), 8.0 (Si–*C*H$_2$). IR (KBr): *v* 3072 (w), 2976 (m), 2925 (m), 2895 (w), 1772 (w), 1717 (vs), 1700 (vs), 1592 (w), 1577 (w), 1540 (m), 1482 (m), 1455 (m), 1399 (w), 1387 (m), 1377 (w), 1355 (w), 1297 (w), 1266 (s), 1215 (w), 1157 (vs), 1113 (s), 1100 (s), 1078 (s), 1038 (w), 940 (m), 851 (w), 841 (m), 798 (m), 749 (m). EA for $C_{45}H_{60}ClF_6N_3O_7RuSi_2$ (1033.573) (found (calcd.)): C 52.2 (52.29), H 5.9 (5.85), N 4.0 (4.07).
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