SUPPORTING INFORMATION

Acetamide Group-Containing Hoveyda-Grubbs Type Complexes: Synthesis and Activity in Olefin Metathesis Transformations

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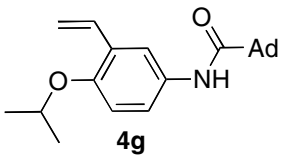
1. General considerations

All reagents were used as purchased. Catalysts **1** and **2a** have been bought from Sigma-Aldrich Co. Catalyst **2c** was generously provided by Prof. Karol Grela (Institute of Organic Chemistry Polish Academy of Sciences). Catalyst **1d** has been bought from Strem Chemical, Inc. The second generation Ru-indenylidene complex **5** is a gift from Umicore A.G: but is also commercially available from Strem Chemicals, Inc.. Dichloromethane (DCM) was dispensed from a solvent purification system from Innovative Technology. Flash column chromatography was performed on silica gel 60 (230-400 mesh). ^{1}H, ^{13}C and ^{19}F Nuclear Magnetic Resonance (NMR) spectra were recorded on a Bruker Avance 400 or 500 Ultrashield NMR spectrometer. High Resolution Mass Spectroscopy (HRMS) analyses were performed at the ICIQ. Elemental analyses were performed at the Universidad Complutense de Madrid. The ICP-MS measurements were performed by UT2A Company, France (http://web.univ-pau.fr/ut2a/). The following compounds have been previously described: **6-27**,[1] **28**,[2] **30**,[3] **31**.[4]

2. Ligands synthesis

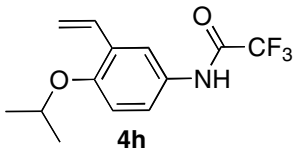
General procedure for ligand synthesis: To a solution of 4-isopropoxy-3-vinylaniline **3**[5] and pyridine (1.5 equiv) in dry DCM, the acylchloride or acid anhydride (1.2 equiv) was added dropwise at 0°C. The reaction mixture was stirred 4 h at room temperature and then diluted with DCM. The organic layer was washed successively with 1N hydrochloric acid solution, saturated solution of sodium carbonate and brine, then dried over magnesium sulfate, filtered and concentrated. The crude product was purified by silica gel chromatography (DCM/Hexanes: 9/1) to afford the product **4**.



4g

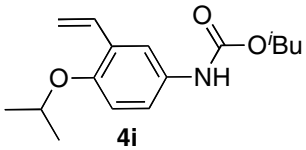
***N*-(4-isopropoxy-3-vinylphenyl)-adamantanamide (4g):** Following the general procedure with adamantane carboxylic acid chloride (26 mg, 0.13 mmol) afforded the title product as pale yellow powder (38 mg, 86% yield). ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS) δ ppm = 7.52 (d, *J* = 2.7 Hz, 1H), 7.34 (dd, *J* = 8.8, 2.7 Hz, 1H), 7.16 (s board, 1H), 6.94 (dd, *J* = 17.8, 11.2 Hz, 1H), 6.76 (d, *J* = 8.8 Hz, 1H), 5.66 (dd, *J* = 17.8, 1.4 Hz, 1H), 5.17 (dd, *J* = 11.2, 1.4 Hz, 1H), 4.40 (sept., *J* = 6.1,

Hz, 1H), 2.06-2.00(m, 3H), 1.92-1.87 (m, 6H), 1.74-1.63 (m, 6H), 1.25 (d, J = 6.1 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS) δ ppm = 176.4, 152.3, 131.9, 131.7, 128.9, 121.3, 118.8, 115.8, 114.9, 72.0, 41.7, 39.7, 36.9, 28.5, 22.6. HRMS (ESI): *m/z*: calcd for $C_{22}H_{29}NO_2$ + Na: 362.2096 [M^++Na]; found 362.2104.



4h

2,2,2-Trifluoro-*N*-(4-isopropoxy-3-vinylphenyl)acetamide (4h): Following the general procedure with trifluoroacetic anhydride (290 µL, 2.03 mmol) afforded the title product as a yellow powder (317 mg, 69% yield). ^{1}H NMR (400MHz, $CDCl_3$, 25°C, TMS): δ ppm = 7.93 (s, 1H), 7.59 (d, ^4J(H,H) = 2.7 Hz, 1H), 7.44 (dd, ^3J(H,H) = 8.9 Hz, ^4J(H,H) = 2.7 Hz, 1H), 7.01 (dd, $^3J_{cis}$(H,H) = 11.2 Hz, $^3J_{trans}$(H,H) = 17.8 Hz, 1H), 6.88 (d, ^3J(H,H) = 8.9 Hz, 1H), 5.74 (dd, $^2J_{gem}$(H,H) = 1.3 Hz, $^3J_{trans}$(H,H) = 17.9 Hz, 1H), 5.28 (dd, $^2J_{gem}$(H,H) = 1.3 Hz, $^3J_{cis}$(H,H) = 11.2Hz, 1H), 4.53 (sept, ^3J(H,H) = 6.1 Hz, 1H), 1.35 (d, ^3J(H,H) = 6.1 Hz, 6H). ^{13}C NMR (100MHz, $CDCl_3$, 25°C, TMS): δ ppm = 155.7 (q, ^2J(C,F) = 37 Hz), 153.3, 131.0, 128.7, 127.9, 121.2, 119.0, 115.8 (q, ^1J(C,F) = 288 Hz), 115.3, 114.7, 71.3, 22.1. ^{19}F NMR (376.5MHz, $CDCl_3$, 25°C, TMS): δ ppm = -76.1 (s). HRMS (ESI): *m/z*: calcd for $C_{13}H_{14}NO_2F_3$ + Na: 296.0874 [M^++Na]; found 296.0863.

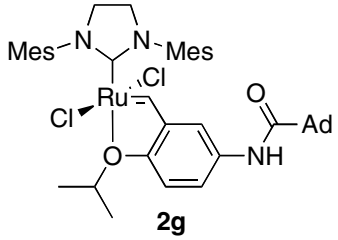


4i

***N*-(4-Isopropoxy-3-vinylphenyl)-isobutylcarbamide (4i):** Following the general procedure with isobutyl chloroformate (27 µL, 0.21 mmol) afforded the title product as pale yellow powder (42 mg, 95% yield). ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS) δ ppm = 7.38 (s broad, 1H), 7.18 (s broad, 1H), 6.94 (dd, J = 17.8, 11.2 Hz, 1H), 6.76 (d, J = 8.9 Hz, 1H), 6.49 (s broad, 1H), 5.64 (dd, J = 17.8, 1.4 Hz, 1H), 5.17 (dd, J = 11.2, 1.4 Hz, 1H), 4.38 (sept, J = 6.1 Hz, 1H), 3.87 (d, J = 6.7 Hz, 2H), 1.94-1.84 (m, 1H), 1.25 (d, J = 6.1 Hz, 6H), 0.89 (d, J = 6.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS) δ ppm = 154.2, 154.1, 151.5, 131.5, 131.2, 128.6, 119.8, 115.6, 114.5, 73.0, 71.6, 28.0, 22.2, 19.0. HRMS (ESI): *m/z*: calcd for $C_{16}H_{23}NO_3$ + Na: 300.1576 [M^++Na]; found 300.1570.

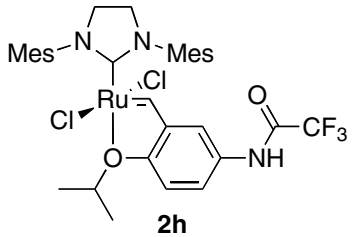
3. Complexes synthesis

General procedure for catalyst formation: To a solution of catalyst **5** and copper chloride (1.1 equiv) in dry DCM (1 mL for 0.02 mmol of Ru-indenylidene complex), **4g-i** (1 equiv) in DCM solution (1 mL for 0.05 mmol of ligand) was added. The resulting mixture was stirred at 35°C for 5 h. Volatiles were removed under reduced pressure, acetone was added to the residue and the solution was filtered on a plug of Celite®. The filtrate was concentrated and purified by chromatography on silica gel (pentane/acetone, 75/25) to yield to catalysts **2g-i** as green microcrystalline solids.



2g

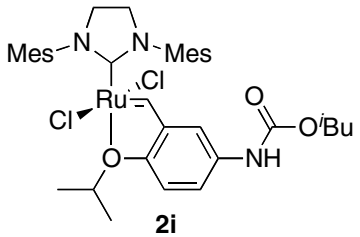
(1,3-Bis(2,4,6-trimethylphenyl)imidazolidin-2-ylidene)(2-isopropoxy-5-(adamantanamido)benzylidene)ruthenium(II) dichloride (2g): Following the general procedure with ligand **4g** afforded the title product (28 mg, 86% yield). ^{1}H NMR (400 MHz, acetone d_6, 25°C, TMS): δ ppm = 16.39 (s, 1H), 8.42 (s, 1H), 7.64 (dd, ^{3}J(H,H) = 8.7 Hz, ^{4}J(H,H) = 2.5 Hz, 1H), 7.61 (d, ^{4}J(H,H) = 2.5 Hz, 1H), 7.07 (s, 4H), 6.92 (d, ^{3}J(H,H) = 8.7 Hz, 1H), 4.90 (sept, ^{3}J(H,H) = 6.1 Hz, 1H), 4.28 (s, 4H), 2.78 (s, 3H), 2.47 (s, 12H), 2.44 (s, 6H), 2.00 (s, 6H), 1.78 (s, 6H), 1.24 (d, ^{3}J(H,H) = 6.1 Hz, 6H). ^{13}C NMR (100 MHz, acetone d_6, 25°C, TMS): δ ppm = 293.3 (d, J(C,Ru) = 11.9 Hz), 210.9, 175.5, 148.1, 144.9, 138.6, 134.3, 129.4, 129.1, 120.7, 114.4, 112.5, 74.6, 51.3, 41.1, 38.8, 36.3, 28.3, 20.6, 20.3. HRMS (ESI): *m/z*: calcd for $C_{42}H_{53}Cl_2N_3O_2Ru$ – Cl + CH_3CN: 908.3135 [M^+-Cl+CH_3CN]; found 809.3161. Elemental analysis calcd (%) for $C_{42}H_{53}Cl_2F_3N_3O_2Ru$: C 62.75, H 6.65, N 5.23; found: C 62.32, H 6.71, N 5.15.



2h

(1,3-Bis(2,4,6-trimethylphenyl)imidazolidin-2-ylidene)(2-isopropoxy-5-(2,2,2-trifluoroacetamido)benzylidene)ruthenium(II) dichloride (2h): Following the general procedure with ligand **4h** afforded the title product (243 mg, 90% yield). ^{1}H NMR (400 MHz, acetone d_6,

25°C, TMS): δ ppm = 16.44 (s, 1H), 7.79 (dd, ^3J(H,H) = 8.8 Hz, ^4J(H,H) = 2.5 Hz, 1H), 7.61 (d, ^4J(H,H) = 2.6 Hz, 1H), 7.08-7.06 (m, 5H), 4.97 (sept, ^3J(H,H) = 6.1 Hz, 1H), 4.28 (s, 4H), 2.47 (s, 12H), 2.43 (s, 6H), 1.26 (d, ^3J(H,H) = 6.1 Hz, 6H). ^{13}C NMR (100 MHz, acetone d_6, 25°C, TMS): δ ppm = 291.3 (d, J(C,Ru) = 12.3 Hz), 209.9, 149.5, 145.0, 138.7, 131.3, 129.1, 121.1, 121.0, 116.0 (q, J(C,F) = 286.7 Hz), 114.2, 114.1, 113.2, 75.3, 51.4, 20.6, 20.3. ^{19}F NMR (376 MHz, acetone d_6, 25°C, TMS): δ ppm = -76.2 (s). HRMS (ESI): *m/z*: calcd for $C_{33}H_{38}Cl_2F_3N_3O_2Ru$ – Cl + CH_3CN: 743.1914 [M^+-Cl+CH_3CN]; found 743.1926.



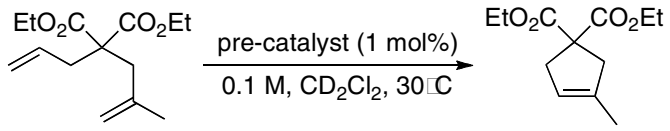
2i

(1,3-Bis(2,4,6-trimethylphenyl)imidazolidin-2-ylidene)(2-isopropoxy-5-(isobutylcarbamido)benzylidene)ruthenium(II) dichloride (2i): Following the general procedure with ligand **4i** afforded the title product (45 mg, 84% yield). ^{1}H NMR (400 MHz, CD_2Cl_2, 25°C, TMS) δ ppm = 16.45 (s, 1H), 7.65 (d, J = 8.7 Hz, 1H), 7.09 (s, 4H), 6.99 (s broad, 1H), 6.78 (d, J = 8.7 Hz, 1H), 6.62 (s broad, 1H), 4.85 (sept, J = 6.0 Hz, 1H), 4.18 (s, 4H), 3.95 (d, J = 6.6 Hz, 1H), 2.45 (s, 18H), 2.02-1.95 (m, 1H), 1.23 (d, J = 6.0 Hz, 6H), 0.99 (d, J = 6.7 Hz, 6H). ^{13}C NMR (125 MHz, CD_2Cl_2, 25°C, TMS): δ ppm = 294.3, 210.4, 153.8, 148.0, 145.0, 139.0, 133.2, 129.2, 119.5, 112.9, 112.5, 75.2, 71.2, 51.1, 29.7, 28.0, 20.8, 18.8. HRMS (ESI): *m/z*: calcd for $C_{36}H_{47}Cl_2N_3O_3Ru$ + Na: 764.1936 [M^++Na]; found 764.1939. Elemental analysis calcd (%) for $C_{36}H_{47}Cl_2N_3O_3Ru$: C 58.29, H 6.39, N 5.66; found: C 58.28, H 6.46, N 5.24.

4. Kinetic Studies

General procedure for kinetic studies at 30°C (figure 3): A NMR tube equipped with a septum was filled with diethylallylmethallyl malonate **6** (25 mg, 0.1 mmol) and CD_2Cl_2 (0.9 mL) under argon. The sample was equilibrated at 30°C in the NMR probe. The sample was locked and shimmed before the catalyst addition (100 µL, 1 µmol, 0.1 M solution of catalyst). The reaction progress was monitored by the periodical acquisition of data over 1 h and integrating the characteristic signals for allylic proton resonances (Table 1).

Table 1: values of the kinetics studies for figure 3

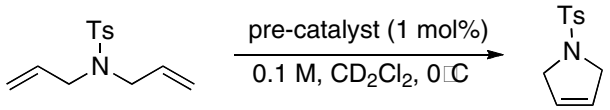


6 **7**

Catalyst **2g**		Catalyst **2h**		Catalyst **2i**	
Time (min)	Conv (%)	Time (min)	Conv (%)	Time (min)	Conv (%)
0.0	0	0.0	0	0.0	0
2.1	2	3.1	11	2.6	6
4.8	7	4.7	19	4.5	12
7.4	12	8.0	36	8.2	25
10.1	17	9.8	44	10.1	31
12.8	21	11.6	52	14.1	43
15.5	25	14.9	62	15.9	48
18.1	29	18.2	69	19.7	57
20.8	32	19.9	73	21.5	60
23.5	36	23.3	78	23.6	64
28.8	41	26.5	81	27.8	69
31.5	44	32.0	86	29.6	72
34.2	47	37.7	89	31.5	74
36.9	49	42.0	90	35.7	78
39.6	51	44.5	91	37.7	79
47.6	56	47.0	91	45.5	85
52.9	59	49.5	92	54.5	88
58.3	61	57.3	93	59.4	90
61.0	63	65.0	95	67.1	92

General procedure for kinetic studies at 0°C (figure 4): A NMR tube equipped with a septum was filled with 500µL of *N*,*N*-diallyltosylamide **8** solution (25 mg, 0.1 mmol in 4 mL CD_2Cl_2) under argon. The sample was equilibrated at 0°C in the NMR probe. The sample was locked and shimmed before the catalyst addition (100 µL, 1 µmol, 0.1 M solution of catalyst). The reaction progress was monitored by the periodical acquisition of data over 4 h and integrating the characteristic signals for allylic proton resonances (Table 2).

Table 2: values of the kinetics studies for figure 4

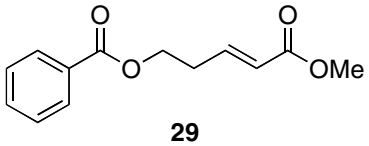


8 **9**

Catalyst **1**		Catalyst **2a**		Catalyst **2c**		Catalyst **2d**		Catalyst **2h**	
Time (min)	Conv (%)	Time (min)	Conv (%)	Time (min)	Conv (%)	Time (min)	Conv (%)	Time (min)	Conv (%)
0.0	0	0.0	0	0.0	0	0.0	0	0.0	0
2.8	1	4.7	3	3.0	16	2.9	14	3.3	13
5.8	1	9.7	4	6.2	24	5.8	20	6.1	17
8.7	1	14.4	7	9.1	30	8.7	25	9.0	21
11.7	1	19.1	9	12.1	35	11.5	29	11.8	24
14.6	1	23.8	11	15.0	41	14.4	34	14.7	28
18.0	2	28.5	13	18.0	45	17.2	38	17.5	31
21.0	2	33.2	15	20.9	49	20.0	42	20.3	35
23.9	4	37.9	17	23.8	53	22.9	46	23.2	37
26.9	5	42.6	19	26.8	56	25.7	50	26.0	40
29.8	6	47.2	21	29.7	60	28.5	52	28.8	43
32.7	7	51.9	23	32.6	63	31.4	56	31.7	45
35.7	8	56.6	25	35.6	65	34.2	58	34.5	47
38.6	9	60.3	27	38.5	68	37.1	61	37.3	49
41.6	10	66.0	28	41.4	69	39.9	64	40.2	51
44.5	11	70.7	30	44.4	72	42.7	66	43.0	53
50.4	12	75.4	32	50.3	75	50.6	71	51.0	57
59.2	15	80.1	33	59.1	80	58.5	75	58.9	62
73.9	19	84.8	35	73.8	85	72.4	82	70.4	66
76.8	19	98.5	36	79.7	88	79.4	85	82.0	71
114.7	29	113.0	44	91.4	90	90.0	87	93.5	74
139.7	34	136.5	50	115.8	93	111.3	92	112.4	78
147.8	36	150.6	54	143.8	96	139.9	95	145.9	83
175.8	41	174.0	58	179.0	97	175.9	97	179.4	86
222.9	49	220.5	67	232.0	99	226.5	99	212.1	88
247.2	52	243.4	70	251.2	99	255.3	99	244.7	89

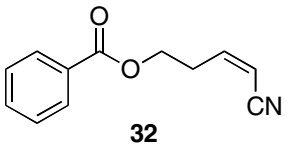
5. Catalysis

General procedure for metathesis reaction: A Schlenk apparatus under argon was filled with the olefin (0.5 mmol) and the solvent (5 mL) (DCM for reaction at rt and 40°C), then pre-catalyst **2h** was added. Of note, for accurate reactions with low catalyst loadings, stock solutions of **2h** were used and RCM were performed on larger scale in a drybox with an opened glassware. Progress of the reaction was monitored by TLC or ^{1}H NMR in integrating the characteristic signals for allylic proton resonances. The solvent was removed under vacuum, and if necessary, the crude residue was purified by flash column chromatography to yield the pure product.



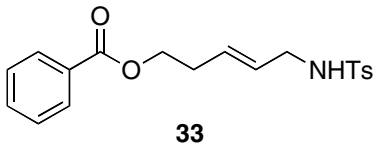
29

(*E*)-5-methoxy-5-oxopent-3-enyl benzoate (29): The general procedure yielded after flash chromatography on silica gel (pentane/diethyl ether, 95/5) the title compound as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS): δ ppm = 8.03 (d, ^3J(H,H) = 8.2 Hz, 2H), 7.59-7.55 (m, 1H), 7.46-7.43 (m, 2H), 7.03 (dt, ^3J(H,H) = 15.7 Hz, ^4J(H,H) = 6.8 Hz, 1H), 6.00 (d, ^3J(H,H) = 15.7 Hz, 1H), 4.45 (t, ^3J(H,H) = 6.5 Hz, 2H), 3.75 (s, 3H), 2.69 (dt, ^3J(H,H) = 6.8 Hz, ^3J(H,H) = 6.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS): δ ppm = 166.6, 166.3, 144.4, 133.1, 129.9, 129.6, 128.4, 123.3, 62.8, 51.5, 31.6. HRMS (ESI): *m/z*: calcd for $C_{13}H_{14}O_4$ + Na: 257.0787 [M^++Na]; found 257.0790.



32

(*Z*)-4-Cyanobut-3-enyl benzoate (32): The general procedure yielded after flash chromatography on silica gel (pentane/diethyl ether, 95/5) the title compound as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS) δ ppm = 8.06-8.02 (m, 2H), 7.62-7.58 (m, 1H), 7.49-7.45 (m, 2H), 6.61 (dt, ^3J(H,H) = 10.9 Hz, ^4J(H,H) = 7.5 Hz, 1H), 5.49 (d, ^3J(H,H) = 10.9 Hz, 1H), 4.47 (t, ^3J(H,H) = 6.3 Hz, 2H), 2.91 (dt, ^3J(H,H) = 7.5 Hz, ^3J(H,H) = 6.3 Hz, 2H).^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS) δ ppm = 166.3, 151.1, 133.3, 129.7, 129.6, 128.5, 128.4, 102.4, 62.3, 31.4. HRMS (ESI): *m/z*: calcd for $C_{12}H_{11}NO_2$ + Na: 224.0690 [M^++Na]; found.224.0687.



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(*E*)-5-tosylpent-3-enyl benzoate (33): The general procedure yielded after flash chromatography on silica gel (pentane/ethyl acetate, 90/10) the title compound as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS) δ ppm = 8.01 (d, ^{3}J(H,H) = 7.1 Hz, 2H), 7.74 (d, ^{3}J(H,H) = 8.3 Hz, 2H), 7.55 (d, ^{3}J(H,H) = 7.1 Hz, 1H), 7.45 (d, ^{3}J(H,H) = 7.2 Hz, 2H), 7.28 (d, ^{3}J(H,H) = 8.3 Hz, 2H), 5.66-5.45 (m, 2H), 4.74 (t, ^{3}J(H,H) = 6.1 Hz, 1H), 4.26 (t, ^{3}J(H,H) = 6.6 Hz, 2H), 3.57 (t, ^{3}J(H,H) = 6.1 Hz, 2H), 2.42 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS): δ ppm = 166.5, 143.5, 137.1, 133.0, 129.8, 129.7, 129.5, 128.4, 127.6, 127.1, 63.8, 45.1, 31.6, 21.5. HRMS (ESI): *m/z*: calcd for $C_{19}H_{21}NO_4S$ + Na: 382.1105 [M^++Na]; found.382.1113.

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