Reluctant Cross-Metathesis Reactions: The Highly Beneficial Effect of Microwave Irradiation

Antoine Michaut, Thomas Boddaert, Yoann Coquerel, Jean Rodriguez

► To cite this version:

Antoine Michaut, Thomas Boddaert, Yoann Coquerel, Jean Rodriguez. Reluctant Cross-Metathesis Reactions: The Highly Beneficial Effect of Microwave Irradiation. *Synthesis: Journal of Synthetic Organic Chemistry*, 2007, 18, pp.2867-2871. 10.1055/s-2007-983825 . hal-00676779

HAL Id: hal-00676779

<https://hal.science/hal-00676779>

Submitted on 6 Mar 2012

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Reluctant Cross-Metathesis Reactions: a Highly Beneficial Effect of Microwave Irradiation

Antoine Michaut, Thomas Boddaert, Yoann Coquerel,* Jean Rodriguez*

Université Paul Cézanne (Aix-Marseille III), CNRS, UMR 6178, Campus universitaire de St Jérôme, Service 531, 13397 Marseille Cedex 20, France.

Fax: +33 (0)491 28 91 87

E-mail: yoann.coquerel@univ-cezanne.fr and jean.rodriguez@univ-cezanne.fr

Abstract: The beneficial effect of microwave irradiation vs classical thermal conditions is demonstrated through a series of comparative cross-metathesis reactions.

Key words: Carbene complexes, Catalysis, Cross-coupling, Metathesis, Olefination.

The establishment of olefin metathesis as a powerful synthetic tool for C=C bond formation is essentially due to the initial discovery of the Schrock molybdenum-based catalyst, followed by the extensive development of the ruthenium-based catalyst such as **1a,b** and their derivatives introduced by Grubbs and co-workers. More specifically, cross-metathesis (CM) of simple olefins has now become one of the method of choice to access substituted olefins, although its development has been somewhat delayed when compared to Ring Closing Metathesis (RCM) and Ring Opening Metathesis Polymerization (ROMP) due to initial functional group compatibility problems.¹ In some cases, and in particular with electro-deficient olefins, the CM reaction is less effective and requires specific conditions to prevent catalyst deactivation. Among them, addition of Cy₂BCl or Ti(OiPr)₄ have proven useful with substrates bearing a Lewis base functional group.^{2,3h} The CM reactions with reluctant partners such as acrylonitrile derivatives have been the topic of several studies, and specific conditions as well as more reactive phosphine-free catalyst have been developed.³ Recently, some reports appeared on the dramatic improvement in reaction rates and yields in microwave-assisted olefin metathesis reactions.⁴

Figure 1 Metathesis catalysts used.

In connection with our studies on 1,3-dicarbonyl derivatives, we recently prepared a number of allylic derivatives by CM reactions with various functionalized olefins using catalysts **1a,b**. If the desired products could indeed be obtained under classical thermal conditions, reaction times were rather long, and in some cases the yields were modest to very low, probably due to the polar functionalities present on the substrate. With in mind the precedents of microwave (μ W) irradiation during metathesis reactions,⁴ we tested this method of

activation in the cases of our reluctant substrates. We observed a highly beneficial effect on the rate of the CM reactions under μ W irradiation, and our results are reported herein (Table 1). It should be noted that μ W-assisted CM reactions have been scarcely reported, and only with ethyl acrylate,^{4q} for the homodimerization of N-allyl amino acids,^{4p} and very recently with peptides.^{4r} We initiated our study with the cross-metathesis of allylic derivatives and allyl(trimethyl)silane (allylTMS, **3a**). The β -ketoamide **2a** is reluctant to undergo CM with allylTMS (**3a**) under classical thermal conditions, resulting in poor conversion leading to a low yield of the desired cross-coupled product, always accompanied by substantial amounts of products resulting from the homocoupling of the substrate and partial isomerisation of the allylTMS (**3a**) to the vinyl silane (Table 1, entry 1). The same reaction performed under μ W irradiation resulted in a dramatic increase in the rate of the CM to give 60% of the expected cross-coupling product (87% conversion) after only 30 seconds at 60°C (entry 1). The isomerisation of allylTMS (**3a**) could be completely suppressed by addition of 10% of 1,4-benzoquinone.⁵ Going down to 0.6 mol% of catalyst is still productive yielding 38% of cross-product after 30 minutes of irradiation (entry 2). A similar accelerating effect was observed for the cross-coupling reactions of the β -ketosulfone **2b** with allylTMS (**3a**) which resulted in 68% yield of the expected olefin after 35 minutes of irradiation compared to 51% after 24 hours under thermal conditions (entry 3). The beneficial effect of μ W irradiation is even more striking with the diketone **2c**, as the CM product is obtained in 75% yield after 10 minutes, while 10% yield is obtained after 16 hours at 100 °C without irradiation (entry 4). The CM of the more sensitive and probably more chelating nitroketone **2d** required the addition of Ti(OiPr)₄ and μ W irradiation to proceed smoothly (entry 5). The cross-coupling of the homoallylic bromide **2e** and allylTMS (**3a**) under thermal conditions gave a very sluggish reaction while μ W irradiation allowed the isolation of the alkene **4e** in 77% yield after only 40 seconds (entry 6). Interestingly, scaling up the reaction to 15 mmol allowed to cut down the amount of catalyst to 0.15% to produce 69% of **4e** after 3 minutes of irradiation (entry 7). This correspond to an exceptionally high TON of 460 for catalyst **1a** in CM.⁶ The nitroalkene **2f** also underwent CM with allylTMS (**3a**) in decent yield after 30 seconds of irradiation (entry 8). Hexene (**3b**) and allyl acetate (**3c**) were also used successfully as CM partners under μ W irradiation with the β -ketoester **2g** to give good Z selectivity in the latter

case (entries 9 and 10). When acrylonitrile (**3d**) is used as the CM partner with the β -ketoester **2h**, catalyst **1b** was by far superior to **1a**,³ as illustrated in entries 11-15. For both thermal and μ W conditions, the reactions were performed at 100 °C with the same catalyst loading and times. Comparable results were obtained in dichloroethane or dichloromethane (compare entries 11 with 12, and 13 with 14). However, with catalyst **1a** (entries 11 and 12) slightly lower yields were obtained

under μ W irradiation, probably due to faster decomposition of the catalyst. The decomposition of catalyst **1b** under the reaction conditions is also evidenced in entries 14 and 15, as for the same total amount of catalyst, better results are obtained by introduction of the catalyst in two portions. As previously reported,³ CM reactions with acrylonitrile (**3d**) exhibit a pronounced *Z* selectivity of the product.

Table 1 Comparative cross-metathesis reactions under thermal and microwave conditions

Entry	Substrate	Olefin	Catalyst (%)	Product	Thermal conditions		Microwave irradiation	
					Conditions	Yield (%); <i>E/Z</i> ratio ^a	Conditions ^b	Yield (%); <i>E/Z</i> ratio ^a
1			1a (2)		Neat, 90 °C, 16 h	14; 3:1	Neat, 60 °C, 30 s, 10% 1,4-benzoquinone	60; 3:1
2	2a	3a	1a (0.6)	4a	Not tested	-	Neat, 60 °C, 30 s, 10% 1,4-benzoquinone	38; 1:1
3		3a	1a (3)		Neat, 90 °C, 24 h	51; 1:1	Neat, 60 °C, 35 min	68; 1:1
4		3a	1a (2)		Neat, 100 °C, 16 h	10; 1.8:1	Neat, 90 °C, 10 min	75; 1.8:1
5		3a	1a (4)		CH ₂ Cl ₂ , 40 °C, 15% Ti(OiPr) ₄ , 16 h	40; 1.8:1	CH ₂ Cl ₂ , 60 °C, 15% Ti(OiPr) ₄ , 40 min	62; 1.8:1
6		3a	1a (0.8)		Neat, 90 °C, 8 h	6; nd ^c	Neat, 60 °C, 40 s	77; 1.9:1
7	2e	3a	1a (0.15)	4e	Not tested	-	Neat, 60 °C, 3 min	69; 1.9:1
8		3a	1a (1.5)		Not tested	-	Neat, 60 °C, 30 s	57; 2.3:1
9			1a (2)		Neat, 90 °C, 16 h	50; 4:1	Neat, 60 °C, 75 s	68; 4:1
10	2g		1a (3)		CH ₂ Cl ₂ , 40 °C, 12 h	41; 1:5.7	CH ₂ Cl ₂ , 60 °C, 15 min	78; 1:5.7
11			1a (3+1)		CH ₂ Cl ₂ , 100 °C, 20+10 min	35; 1:3.8	CH ₂ Cl ₂ , 100 °C, 20+10 min	24; 1:3.5
12	2h	3d	1a (3+1)	4i	ClCH ₂ CH ₂ Cl, 100 °C, 20+10 min	24; 1:3.4	ClCH ₂ CH ₂ Cl, 100 °C, 20+10 min	22; 1:3.9
13	2h	3d	1b (3+1)	4i	CH ₂ Cl ₂ , 100 °C, 20+10 min	79; 1:3.1	CH ₂ Cl ₂ , 100 °C, 20+10 min	89; 1:3.3
14	2h	3d	1b (3+1)	4i	ClCH ₂ CH ₂ Cl, 100 °C, 20+10 min	70; 1:3.6	ClCH ₂ CH ₂ Cl, 100 °C, 20+10 min	90; 1:3.0
15	2h	3d	1b (4)	4i	Not tested	-	ClCH ₂ CH ₂ Cl, 100 °C, 30 min	83; 1:3.8

^aYields of isolated homogeneous product. *E/Z* ratio was determined by NMR analysis of the crude mixture.

^bThe times indicated does not include ramp up time (which is 20-80 s depending on conditions)

^cnd = not determined

Paralleling the remark of professor Hoveyda,^{3f} acrylonitrile might be categorised as a Type III olefin with

catalyst **1b** and Type IV with **1a** (although it is not truly spectator to CM) in the Grubbs' categorisation of

olefins.^{1d} Trace amount (< 0.1%) of the (*Z*)-homodimer of acrylonitrile (**3d**) are detected with both catalyst **1a,b**, and a minor amount (< 5%) of the (*E*)-homodimer of the substrate are also observed.

Through this series of comparative CM reactions performed under classical thermal conditions and under microwave irradiation, the beneficial effect of microwave activation is clear, particularly in reluctant cases. However, a microwave effect could not be evidenced.^{4c,q} The better yields and conversions observed under microwave irradiation appear to result from the

Dichloromethane and dichloroethane were dried by refluxing with calcium hydride and then distilled under an argon atmosphere. The reactions were monitored by TLC, which were performed on Merck 60F254 plates and visualised with an ethanolic solution of *p*-anisaldehyde and sulfuric acid or an ethanolic solution of molybdophosphoric acid. Flash chromatography was performed with Merck 40-63 μ m silica gel eluted with diethyl ether or ethyl acetate in petrol ether. NMR data were recorded on a Bruker Avance 300 spectrometer in CDCl₃ and chemical shifts (δ) are given in ppm relative to the residual CHCl₃ signal for ¹H NMR (7.26 ppm) and relative to the deuterated solvent signal for ¹³C NMR (77.0 ppm); coupling constants (*J*) are in Hertz, and the classical abbreviations are used to describe the signal multiplicity. Mass spectra were recorded on a API III Plus Sciex spectrometer, or an Applied Biosystems 3200 Qtrap both equipped with an ESI source. AllylTMS, allyl acetate, 1-hexene, 4-bromo-1-butene, 5-nitro-1-pentene and catalysts **1a,b** were used as received (Aldrich). Acrylonitrile was distilled prior use. **2a-d** and **2g** were obtained by standard allylation methodology from the corresponding activated ketones and allyl bromide (**2b,c** and **2g**: K₂CO₃, acetone; **2a**: LiOH, THF; **2d**: NaH, DMF), and **2h** was obtained by trans-esterification of the corresponding ethyl ester (Aldrich) with 3-buten-1-ol (DMAP, toluene).

General procedure for thermal solvent-free CM reactions (4a-c and 4e,g): Neat **2a-c** or **2e,g** (1.0 mmol), the appropriate alkene **3a,b** (3.0 mmol) and the required amount of catalyst **1a** (see Table 1) were placed in a small sealed tubular reaction vessel (7 mL) equipped with a teflon coated stirring bar under an argon atmosphere. The reaction vessel was placed in a pre-heated oil bath at the required temperature for the desired time (see Table 1). The excess of alkene **3a,b** was evaporated under reduced pressure and the residue was purified by flash chromatography to afford pure **4a-c** or **4e,g**.

General procedure for thermal CM reactions with solvent (4d and 4h,i): A 0.1M solution of **2d** or **2g,h** (0.15 mmol), the appropriate alkene **3a** (0.45 mmol) or **3c,d** (0.30 mmol), Ti(O*i*Pr)₄ (0.023 mmol) in the case of entry 5, and the required amount of catalyst **1a,b** (see Table 1; for entries 11-14, the catalyst was added in two portions: 3 mol% at *t* = 0, and 1 mol% at *t* = 20 min)

rapid heating allowed in the microwave oven, and a faster cross-metathesis reaction relative to catalyst decomposition. In some cases, the latter effect allowed a substantial decrease of the amount of catalyst.

In conclusion, we have demonstrated that microwave irradiation does not only dramatically reduce the reaction times of cross-metathesis, but also allows to obtain higher TON of the catalysts and ultimately render efficient otherwise unproductive reactions.

were placed in a small sealed tubular reaction vessel (7 mL) equipped with a teflon coated stirring bar under an argon atmosphere. The reaction vessel was placed in a pre-heated oil bath at the required temperature for the desired time (see Table 1). The solvent and the excess of alkene **3a** or **3c,d** were evaporated under reduced pressure and the residue was purified by flash chromatography to afford pure **4d** or **4h,i**.

General procedure for microwave assisted CM reactions (4a-i): Microwave irradiations were performed in a CEM Discover 1-300W oven in sealed tubes (10 mL) equipped with a teflon coated stirring bar under argon at the temperature and times shown in Table 1 (mode discover standard). The reaction mixtures were prepared as described above, except in the cases of entries 1 and 2 where 1,4-benzoquinone (0.1 mmol, 10 mol%) was added. The products were purified as described above.

4a: colorless oil; *E/Z* = 3:1

¹H NMR (mixture of isomers) δ : -0.03/-0.01 (s/s, 9H), 1.08 (t, *J* = 7.1 Hz, 6H), 1.40 (d, *J* = 8.0 Hz, 1H), 1.44 (d, *J* = 9.2 Hz, 1H), 1.56-2.06 (m, 3H), 2.06-2.70 (m, 5H), 3.14-3.55 (m, 4H), 5.05-5.25 (m, 1H), 5.33-5.56 (m, 1H).

¹³C NMR ((*E*) isomer) δ : -1.6(CH₃), 13.2(CH₃), 18.9(CH₂), 31.2(CH₂), 33.9(CH₂), 34.0(CH₂), 37.1(CH₂), 41.0(CH₂), 61.2(C), 121.5(CH), 128.4(CH), 168.5(C), 215.5(C).

¹³C NMR ((*Z*) isomer) δ : -1.8(CH₃), 13.2(CH₃), 18.5(CH₂), 23.0(CH₂), 33.6(CH₂), 7.2(CH₂), 37.3(CH₂), 41.0(CH₂), 61.6(C), 123.1(CH), 130.7(CH), 168.6(C), 215.8(C).

MS (ESI+): *m/z* = 310 [M+H]⁺, 332 [M+Na]⁺, 348 [M+K]⁺.

4b: colorless oil; *E/Z* = 1:1

¹H NMR (mixture of isomers) δ : -0.07 (s, 9H), 1.20-1.45 (m, 2H), 1.50-1.84 (m, 2H), 1.85-2.84 (m, 7H), 3.01, (ddm, *J* = 6.2, 2.4 Hz, 1H), 4.76-5.00 (m, 1H), 5.25-5.62 (m, 1H), 7.42-7.75 (m, 5H).

¹³C NMR (mixture of isomers) δ : -2.0(CH₃), -1.8(CH₃), 18.7(CH₂), 21.4(CH₂), 21.5(CH₂), 23.0(CH₂), 25.1(CH₂), 25.1(CH₂), 29.4(CH₂), 29.5(CH₂), 31.2(CH₂), 37.1(CH₂), 41.6(CH₂), 41.6(CH₂), 75.6(C), 75.8(C), 119.6(CH), 120.7(CH), 128.6(CH), 130.2(CH), 130.2(CH), 130.6(CH), 130.6(CH), 133.0(CH), 134.0(CH), 134.0(CH), 135.4(C), 135.4(C), 204.8(C), 204.8(C).

MS (ESI+): m/z = 365 [M+H]⁺, 382 [M+NH₄]⁺, 387 [M+Na]⁺, 403 [M+K]⁺.

4c: colorless oil; E/Z = 1.8/1

¹H NMR (mixture of isomers) δ : -0.04/-0.02 (s/s, 9H), 1.17-1.27 (m, 4H), 1.38 (d, J = 8.1 Hz, 2H), 1.44 (d, J = 8.1 Hz, 2H), 1.73-1.90 (m, 1H), 2.43-2.51 (m, 2H), 2.52-2.74 (m, 4H), 4.92-5.06 (m, 1H), 5.35-5.57 (m, 1H).

¹³C NMR (mixture of isomers) δ : -1.9(CH₃), -1.6(CH₃), 17.8(CH₃), 17.8(CH₃), 18.5(CH₂), 18.8(CH₂), 19.2(CH₂), 23.2(CH₂), 35.4(CH₂), 38.3(CH₂), 38.4(CH₂), 41.6(CH₂), 65.4(C), 66.2(C), 120.4(CH), 121.4(CH), 130.0(CH), 132.0(CH), 210.0(C), 210.5(C).

MS (ESI+): m/z = 253 [M+H]⁺, 270 [M+NH₄]⁺, 275 [M+Na]⁺, 291 [M+K]⁺.

4d: light brown oil; E/Z = 1.8/1

¹H NMR (mixture of isomers) δ : -0.03/0.00 (s/s, 9H), 1.45 (t, J = 7.0 Hz, 2H), 1.62-1.92 (m, 4H), 1.92-2.14 (m, 1H), 2.46-2.71 (m, 3H), 2.72-2.95 (m, 2H), 5.03-5.24 (m, 1H), 5.41-5.77 (m, 1H).

¹³C NMR (mixture of isomers) δ : -2.0(CH₃), -1.8(CH₃), 18.6(CH₂), 21.4(CH₂), 21.4(CH₂), 23.2(CH₂), 26.8(CH₂), 26.9(CH₂), 32.9(CH₂), 35.8(CH₂), 36.0(CH₂), 39.1(CH₂), 39.7(CH₂), 39.8(CH₂), 96.7(C), 97.3(C), 118.1(CH), 119.3(CH), 131.6(CH), 133.7(CH), 200.5(C), 200.6(C).

MS: m/z = 270 [M+H]⁺, 287 [M+NH₄]⁺, 292 [M+Na]⁺, 308 [M+K]⁺.

4e: colorless oil; E/Z = 1.9/1

¹H NMR (mixture of isomers) δ : 0.00/0.01 (s/s, 9H), 1.44 (d, J = 8.2 Hz, 1.3H), 1.49 (q, J = 7.7 Hz, 0.7H), 2.49-2.62 (m, 2H), 3.35 (t, J = 7.2 Hz, 2H), 5.16-5.32 (m, 1H), 5.46-5.62 (m, 1H).

¹³C NMR ((*E*) isomer) δ : -1.9(CH₃), 23.0(CH₂), 33.6(CH₂), 36.4(CH₂), 124.9(CH), 130.3(CH).

¹³C NMR ((*Z*) isomer) δ : -1.7(CH₃), 19.0(CH₂), 30.9(CH₂), 32.7(CH₂), 123.6(CH), 129.0(CH).

MS: m/z = 221/223 [M+H]⁺, 238/240 [M+NH₄]⁺, 243/245 [M+Na]⁺, 259/261 [M+K]⁺.

4f: colorless oil; E/Z = 2.3/1

¹H NMR (mixture of isomers) δ : -0.02/-0.01 (s/s, 9H), 1.40-1.47 (m, 2H), 2.00-2.12 (m, 4H), 4.32-4.42 (m, 2H), 5.05-5.25 (m, 1H), 5.36-5.54 (m, 1H).

¹³C NMR ((*E*) isomers) δ : -1.9(CH₃), 22.9(CH₂), 27.6(CH₂), 29.4(CH₂), 74.9(CH₂), 125.5(CH), 129.3(CH).

¹³C NMR ((*Z*) isomers) δ : -1.7(CH₃), 18.7(CH₂), 23.7(CH₂), 27.4(CH₂), 75.1(CH₂), 124.2(CH), 128.3(CH).

4g: colorless oil; E/Z = 4/1

¹H NMR ((*E*) isomer) δ : 0.80-0.90 (m, 2H), 1.22 (t, J = 7.2 Hz, 3H), 1.25-1.35 (m, 3H), 1.78-2.09 (m, 6H), 2.10-2.48 (m, 5H), 2.56 (ddd, J = 1.0, 7.2, 13.8 Hz, 1H), 4.12 (q, J = 7.2 Hz, 2H), 5.24 (ttd, J = 1.0, 7.2, 15.4 Hz, 1H), 5.47 (ttd, J = 1.0, 6.7, 15.4 Hz, 1H).

¹³C NMR ((*E*) isomer) δ : 13.9(CH₃), 14.1(CH₃), 19.5(CH₂), 22.2(CH₂), 31.5(CH₂), 32.0(CH₂), 32.3(CH₂), 36.7(CH₂), 38.2(CH₂), 60.3(C), 61.4(CH₂), 124.1(CH), 135.1(CH), 171.1(C), 214.8(C).

MS: m/z = 239 [M+H]⁺, 261 [M+Na]⁺, 277 [M+K]⁺.

4h: colorless oil; E/Z = 1/5.7

¹H NMR ((*Z*) isomer) δ : 1.22 (t, J = 7.2 Hz, 3H), 1.82-1.98 (m, 3H), 2.02 (s, 3H), 2.20-2.32 (m, 1H), 2.32-2.48 (m, 3H), 2.59-2.69 (m, 1H), 4.13 (q, J = 7.2 Hz, 2H), 4.47 (d, J = 4.6 Hz, 2H), 5.63 (m, 2H).

¹³C NMR ((*Z*) isomer) δ : 14.2(CH₃), 19.6(CH₂), 21.0(CH₃), 32.3(CH₂), 36.3(CH₂), 38.1(CH₂), 59.9(C), 61.6(CH₂), 64.7(CH₂), 128.6(CH), 130.0(CH), 170.8(C), 170.9(C), 214.5(C).

MS: m/z = 286 [M+NH₄]⁺, 291 [M+Na]⁺, 307 [M+K]⁺.

4i: colorless oil; E/Z = 1:2.4

¹H NMR (mixture of isomers) δ : 1.78-1.91 (m, 1H), 2.04-2.18 (m, 1H), 2.20-2.33 (m, 4H), 2.55 (pseudo q, J = 6.4 Hz, 1.4H), 2.74 (pseudo q, J = 6.4 Hz, 0.6H), 3.12 (dd, J = 9.2, 9.0 Hz, 0.7H), 3.13 (dd, J = 9.5, 9.0 Hz, 0.3H), 4.08-4.30 (m, 2H), 5.43 (dd, J = 10.8, 1.3 Hz, 0.7H), 5.44 (dd, J = 16.4, 1.5 Hz, 0.3H), 6.68 (ddd, J = 16.4, 7.1, 6.9 Hz, 0.7H), 6.52 (ddd, J = 10.8, 7.7, 7.4 Hz, 0.3H).

¹³C NMR ((*Z*) isomer) δ : 20.8(CH₂), 27.1(CH₂), 31.1(CH₂), 37.9(CH₂), 54.6(CH), 62.4(CH₂), 102.0(CH), 115.4(C), 149.9(CH), 169.0(C), 212.0(C).

¹³C NMR ((*E*) isomer) δ : 20.7(CH₂), 27.0(CH₂), 32.4(CH₂), 37.8(CH₂), 54.5(CH), 62.2(CH₂), 102.3(CH), 116.8(C), 150.7(CH), 169.0(C), 211.8(C).

MS (ESI+): m/z = 208 [M+H]⁺, 230 [M+Na]⁺, 246 [M+K]⁺.

Acknowledgment

We thank the French Research Ministry for fellowship awards to T.B. and A.M., the Université Paul Cézanne, the CNRS (UMR 6178) and the Conseil Général des Bouches du Rhône for financial support.

References

- (1) For reviews on CM, see: (a) Vernall, A. J.; Abell, A. D. *Aldrichimica Acta* **2003**, *36*, 93-105. (b) Connon, S. J.; Blechert, S. *Angew. Chem., Int. Ed.* **2003**, *42*, 1900-1923. (c) Blackwell, H. E.; O'Leary, D. J.; Chatterjee, A. K.; Washenfelder, R. A.; Bussmann, D. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **2000**, *122*, 58-71. For a general model for selectivity in olefin CM, see: (d) Chatterjee, A. K.; Choi, T.-L.; Sanders, D. P.; Grubbs, R. H. *J. Am. Chem. Soc.* **2003**, *125*, 11360-11370.
- (2) Vedrenne, E.; Dupont, H.; Oualef, S.; Elkaïm, L.; Grimaud, L. *Synlett* **2005**, 670-672.
- (3) (a) Randl, S.; Gessler, S.; Wakamatsu, H.; Blechert, S. *Synlett* **2001**, 430-432. (b) Love, J. A.; Morgan, J. P.; Trnka, T. M.; Grubbs, R. H. *Angew. Chem., Int. Ed.* **2002**, *41*, 4035-4037. (c) Rivard, M.; Blechert, S. *Eur. J. Org. Chem.* **2003**, 2225-2228. (d) Michrowska, A.; Bujok, R.; Harutyunyan, S.; Sashuk, V.; Dolgonos, G.; Grela, K. J.

- Am. Chem. Soc.* **2004**, *126*, 9318-9325. (e) Bujok, R.; Bie-niek, M.; Masnyk, M.; Michrowska, A.; Sarosiek, A.; Ste-powska, H.; Arlt, D.; Grela, K. *J. Org. Chem.* **2004**, *69*, 6894-6896. (f) Hoveyda, H. R.; Vézina, M. *Org. Lett.* **2005**, *7*, 2113-2116. (g) Bai, C.-X.; Zhang, W.-Z.; He, R.; Lu, X.-B.; Zhang, Z.-Q. *Tetrahedron Lett.* **2005**, *46*, 7225-7228. (h) Bai, C.-X.; Lu, X.-B.; He, R.; Zhang, W.-Z.; Feng, X.-J. *Org. Biomol. Chem.* **2005**, *3*, 4139-4142. For CM of acrylonitrile with molybdenum based catalyst, see: (i) Crowe, W. E.; Goldberg, D. R. *J. Am. Chem. Soc.* **1995**, *117*, 5162-5163.
- (4) For reviews on microwave-assisted synthesis, see: (a) Kappe, C. O. *Angew. Chem., Int. Ed.* **2004**, *43*, 6250-6284. (b) Hayes, B. L. *Aldrichimica Acta* **2004**, *37*, 66-77. (c) de la Hoz, A.; Diaz-Ortiz, Á.; Moreno, A. *Chem. Soc. Rev.* **2005**, *34*, 164-178. For microwave-assisted RCM, see: (d) Varray, S.; Gauzy, C.; Lamaty, F.; Lazaro, R.; Martinez, J. *J. Org. Chem.* **2000**, *65*, 6787-6790. (e) Mayo, K. G.; Nearhoof, E. H.; Kiddle, J. J. *Org. Lett.* **2002**, *4*, 1567-1570. (f) Garbacia, S.; Desai, B.; Lavastre, O.; Kappe, C. O. *J. Org. Chem.* **2003**, *68*, 9136-9139. (g) Thanh, G. V.; Loupy, A. *Tetrahedron Lett.* **2003**, *44*, 9091-9094. (h) Grigg, R.; Martin, W.; Morris, J.; Sridharan, V. *Tetrahe-dron Lett.* **2003**, *44*, 4899-4901. (i) Balan, D.; Adolfsson, H. *Tetrahedron Lett.* **2004**, *45*, 3089-3092. (j) Comer, E.; Organ, M. G. *J. Am. Chem. Soc.* **2005**, *127*, 8160-8167. (k) Nosse, B.; Schall, A.; Jeong, W. B.; Reiser, O. *Adv. Synth. Catal.* **2005**, *347*, 1869-1874. (l) Appukkuttan, P.; Dehaen, W.; Van der Eycken, E. *Org. Lett.* **2005**, *7*, 2723-2726. (m) Collins, S. K.; Grandbois, A.; Vachon, M. P.; Côté, J. *Angew. Chem., Int. Ed.* **2006**, *45*, 2923-2926. (n) Yang, Q. Y.; Li, X.-Y.; Wu, H.; Xiao, W.-J. *Tetrahedron Lett.* **2006**, *47*, 3893-3896. (o) Chapman, R. N.; Arora, P. S. *Org. Lett.* **2006**, *8*, 5825-5828. For microwave-assisted CM, see: (p) Poulsen, S.-A.; Bornaghi, L. F. *Tetrahedron Lett.* **2005**, *46*, 7389-7392. (q) Bargiggia, F. C.; Murray, W. V. *J. Org. Chem.* **2005**, *70*, 9636-9639. (r) Morris, T.; Sandham, D.; Caddick, S. *Org. Biomol. Chem.* **2007**, *5*, 1025-1027.
- (5) Hong, S. H.; Sanders, D. P.; Lee, C. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2005**, *127*, 17160-17161.
- (6) As the CM is a reversible process, the TON (turnover number) represents the *average* number of substrate mole-cules converted into the cross-product per molecule of cata-lyst. A typical loading of **1a,b** in CM reaction is 2-10%, which correspond to a maximum TON of 10-50. For a re-cent TON study in ruthenium carbene catalyzed ring-closing metathesis, see: Maechling, S.; Zaja, M.; Blechert, S. *Adv. Synth. Catal.* **2005**, *347*, 1413-1422.