

# Grubbs Catalysts Immobilized on Mesoporous Molecular Sieves via Phosphine and Pyridine Linkers

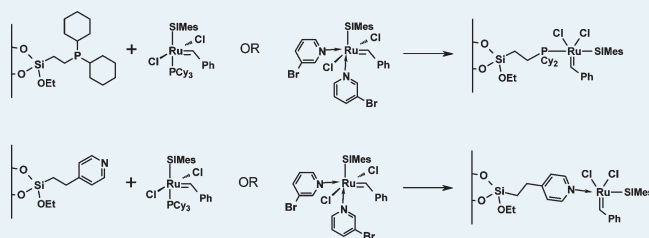
David Bek, Hynek Balcar, Naděžda Žilková, Arnošt Zukal, Michal Horáček, and Jiří Čejka\*

J. Heyrovský Institute of Physical Chemistry, Academy of Sciences of the Czech Republic, Dolejškova 3, 182 23 Prague 8, Czech Republic

Supporting Information

**ABSTRACT:** Hybrid catalysts for olefin metathesis were prepared by the immobilization of Ru alkylidenes (Grubbs catalysts) on mesoporous molecular sieves SBA-15 and MCM-41 having the surface modified with molecules bearing dicyclohexylphosphine (PCy<sub>2</sub>) and pyridine end groups. Hybrid catalysts with Ru attached to the surface via PCy<sub>2</sub> ligands exhibited higher activity and stability than those with Ru attached via pyridine ligands. The former catalysts exhibited a high activity in a series of metathesis reactions (RCM, ROMP, and cross-metathesis) reaching turnover numbers (TONs) from 200 to 2000 and being reusable several times. The filtration tests for all catalysts suggested that the solid catalysts were responsible for catalytic activity during the reactions. Only low Ru leaching was observed. A positive effect of the pore size of the support on catalyst activity was observed for the metathesis of methyl oleate.

**KEYWORDS:** Grubbs catalysts, olefin metathesis, mesoporous molecular sieves, catalyst immobilization, hybrid catalysts



## 1. INTRODUCTION

Olefin metathesis belongs to the important C–C forming reactions having numerous applications in petrochemistry, polymer chemistry, and fine chemical synthesis.<sup>1</sup> The introduction of Ru alkylidene complexes (L<sub>2</sub>Cl<sub>2</sub>Ru=CH–Ar, L = ligand) as robust and heteroatom tolerant metathesis catalysts<sup>2</sup> established olefin metathesis as a powerful tool in the synthesis of chemical specialties such as natural product analogues, pharmaceuticals, and special polymers.<sup>3</sup> The immobilization of these Ru complexes on solid supports (both organic polymers and inorganic) provides hybrid catalysts offering following advantages: (i) catalyst easy separation from products and delivery of products free of catalyst residues, (ii) catalyst reuse, and (iii) the possibility of catalyst application in flow reactors. Therefore, the design of these hybrid catalysts has attracted a particular attention and numerous methods for complex immobilization have been developed.<sup>4–8</sup> Generally, three basic strategies have been used: (i) L ligand exchange (phosphine or N-heterocyclic carbene),<sup>9–13</sup> (ii) chloro ligand exchange,<sup>14–18</sup> and (iii) alkylidene ligand exchange (including chelating alkylidene ligands).<sup>19–26</sup> Complexes with chelating alkylidene ligands when immobilized by direct interaction with silica surface delivered heterogeneous catalysts of high efficiency.<sup>27,28</sup>

For Ru alkylidenes with L = tricyclohexylphosphine or bromopyridine (complexes I–III, Chart 1), the exchange of these ligands by the phosphine or pyridine groups on the support surface offers an efficient method for their immobilization, as (i) the ligand exchange proceeds easily<sup>29</sup> and (ii) the supports with phosphine or pyridine groups are easy available. In spite of that, this possibility has been rarely used. Grubbs et al. reported

the immobilization of RuCl<sub>2</sub>(PCy<sub>3</sub>)<sub>2</sub>(=CH–CH=CPh<sub>2</sub>) on phosphine-derivatized styrene-divinylbenzene.<sup>9</sup> The supported catalyst was found active in metathesis of 2-pentene and in ring-opening metathesis polymerization (ROMP) of norbornene and cyclooctene. However, the reaction rates were reduced in comparison with homogeneous counterparts, in particular because of diffusion limitations. On the other hand, the supported catalyst was long-living and reusable. Kirschning et al.<sup>12</sup> reported on the immobilization of both II and III complexes on poly(vinylpyridine) and the activity of prepared catalysts in various ring-closing metathesis (RCM) reactions (100 °C, turnover number (TON) < 20). The catalyst prepared from III was reused several times with gradually decreasing yields. No data about Ru leaching were given.<sup>11</sup> Verpoort et al.<sup>10</sup> described the immobilization of I on phosphine modified mesoporous molecular sieve MCM-41. The hybrid catalyst prepared was active in ROMP of norbornene and RCM of diallylmalonate and diallylamine (from room temperature to 60 °C, TON ≤ 20 for RCM). Minor leaching was observed (1.2% of the Ru catalyst content). No catalyst reuse was reported.

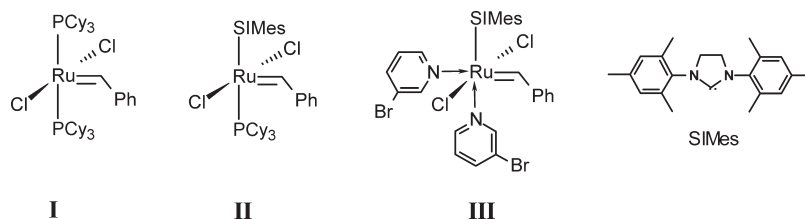
The aim of this contribution is to report on (i) the preparation of hybrid metathesis catalysts by the immobilization of alkylidenes II and III on the mesoporous molecular sieves MCM-41 and SBA-15 modified with molecules bearing dicyclohexylphosphine and

**Special Issue:** Victor S. Y. Lin Memorial Issue

**Received:** February 20, 2011

**Revised:** April 8, 2011

**Published:** May 05, 2011

Chart 1. Grubbs Catalysts<sup>a</sup>

<sup>a</sup>Cy = cyclohexyl.

pyridine end groups (PCy<sub>2</sub> and py linkers) on the surface, (ii) the activity of prepared catalyst in various metathesis reactions, (iii) Ru leaching and the possibility of catalyst reuse, and last but not least (iv) the influence of the support on the catalyst activity. Mesoporous molecular sieves represent siliceous materials with regular architecture, high surface areas and pore sizes in the mesopore region.<sup>30,31</sup> Therefore, they have been used as advanced supports for transition metal catalysts including metathesis ones.<sup>32–34</sup>

## 2. EXPERIMENTAL SECTION

**2.1. Materials and Techniques.** The synthesis of siliceous MCM-41 (surface area  $S_{\text{BET}} = 972 \text{ m}^2/\text{g}$ , void volume  $V = 1.14 \text{ cm}^3/\text{g}$ , and pore size diameter  $D = 4.0 \text{ nm}$ ) was performed as described elsewhere.<sup>35</sup> Mesoporous molecular sieves SBA-15 ( $S_{\text{BET}} = 934 \text{ m}^2/\text{g}$ ,  $V = 0.96 \text{ cm}^3/\text{g}$ ,  $D = 6.9 \text{ nm}$ ) and SBA-15 with large pores (SBA-15 LP,  $S_{\text{BET}} = 610 \text{ m}^2/\text{g}$ ,  $V = 1.67 \text{ cm}^3/\text{g}$ ,  $D = 11.1 \text{ nm}$ ) were prepared according to the literature.<sup>36,37</sup>

Alkylidenes **II** and **III** were purchased from Aldrich. Toluene (Lach-Ner, Czech Rep.) was dried overnight over anhydrous  $\text{Na}_2\text{SO}_4$ , then distilled with Na and stored over molecular sieve 4A. Dichloromethane (Lach-Ner) was dried overnight over anhydrous  $\text{CaCl}_2$  then distilled with  $\text{P}_2\text{O}_5$ . 2-(Dicyclohexylphosphino)ethyltriethoxysilane (ABCR, 95%), 2-(4-pyridyl)ethyltriethoxysilane (ABCR, 95%), diethyl diallylmalonate (Sigma-Aldrich, 98%), allylbenzene (Aldrich, 98%), *cis*-1,4-diacetoxy-2-butene (Aldrich, 95%), methyl acrylate (Aldrich, 99%), hexenyl acetate (Aldrich, 97%), (-)- $\beta$ -citronellene (Aldrich, technical,  $\geq 90\%$ ), linalool (Aldrich, 97%), diallyl phthalate (Aldrich, 97%), ethyl vinyl ether (Aldrich, 99%) were used as obtained. *cis*-Cyclooctene (Janssen Chimica, purity 95%) was distilled from  $\text{CaH}_2$  in vacuo. *n*-Nonane (BHD Chemicals,  $\geq 98.5\%$ ) was stored over molecular sieve 4A. Methyl oleate (Research Institute of Inorganic Chemistry, a.s. Czech Republic, purity 94%, methyl palmitate, methyl stearate, and methyl linolate as main impurities) was used as received.

Textural parameters of supports and catalysts were determined from nitrogen adsorption isotherms at  $-196 \text{ }^\circ\text{C}$  with a Micromeritics ASAP 2020 instrument.

UV–vis spectra of catalysts were recorded using a Perkin-Elmer Lambda 950 spectrometer. A Spectralon integration sphere was applied to collect diffuse reflectance spectra of powder samples. Spectralon served also as a reference. Catalyst samples were placed in quartz cuvettes under Ar atmosphere.

Photoelectron spectra of the samples were measured using an ESCA 310 (Scienta, Sweden) spectrometer equipped with a hemispherical electron analyzer operated in a fixed transmission mode. Monochromatic Al K $\alpha$  radiation was used for electron excitation. The spectra were recorded at room temperature. The Si 2p, O 1s, Cl 2p, Br 3d, P 2p, P 2s, N 1s, C 1s, and Ru 3d

photoelectrons were measured. Sample charging was corrected using the Si 2p peak at 103.4 eV as an internal standard. For overlapping C 1s and Ru 3d lines, the contributions of individual components were determined by curve fitting.

<sup>29</sup>Si MAS NMR experiments were carried out on a Bruker Avance 500 MHz (11.7 T) Wide Bore spectrometer using 4 mm o.d.  $\text{ZrO}_2$  rotors with a rotation speed of 7 kHz. For details see Supporting Information.

All manipulations with catalysts and catalytic experiments were carried out under argon atmosphere using standard Schlenk tube technique. A high-resolution gas chromatography Agilent 6890 with DB-5 column (length: 50 m, inner diameter: 320  $\mu\text{m}$ , stationary phase thickness: 1  $\mu\text{m}$ ) and equipped with FID detector was used for reaction product analysis. *n*-Nonane was used as an internal standard if necessary. Individual products were identified by GC/MS (ThermoFinnigan, FOCUS DSQ II Single Quadrupole). Molecular weight of polymer was determined by SEC and values relative to polystyrene standards are reported.

The Ru content was determined by ICP-MS in the Institute of Analytical Chemistry, Institute of Chemical Technology, Prague (for details see Supporting Information). XRF analysis was performed on an Axios sequential WD-XRF spectrometer from PANalytical (in the Laboratory of X-ray diffractometry, Institute of Chemical Technology, Prague).

**2.2. Catalyst Preparation.** The modification of mesoporous molecular sieves (predried in vacuum at 300  $^\circ\text{C}$  for 3 h) by 2-(dicyclohexylphosphino)ethyltriethoxysilane and 2-(4-pyridyl)ethyltriethoxysilane was performed in toluene at room temperature under argon atmosphere.

In a typical modification of SBA-15, 30 mL of toluene was added to 950 mg of SBA-15 in a Schlenk tube, then 890 mg of 2-(dicyclohexylphosphino)ethyltriethoxysilane was added, and the mixture was stirred for 17 h. The product was 5 times washed under argon atmosphere with 15 mL of toluene and finally the rest of toluene was removed by drying of the modified SBA-15 in vacuum at room temperature. The modified sieves were stored under argon atmosphere. The modification of SBA-15LP and MCM-41 was made in the same way. The modification of SBA-15 with 2-(4-pyridyl)ethyltriethoxysilane was made in a similar way (600 mg of SBA-15 and 600 mg of 2-(4-pyridyl)ethyltriethoxysilane was used). The content of P and N in modified sieves was determined by elemental analysis using the ICP-MS method and a Flash EA2000 CHN/O automatic elemental analyzer (Thermo Scientific), respectively. Then, the linker density was calculated using the  $S_{\text{BET}}$  area of parent support.

The immobilization of Grubbs catalysts on modified mesoporous molecular sieves was carried out in toluene at room temperature under argon atmosphere. Preparation of catalyst 2

**Table 1. Amounts of Modified Sieves and Ru Complexes Used for the Preparation of the Catalysts**

catalyst	weight of sieves modified with PCy <sub>2</sub> linkers, mg	type of Ru complex	weight of Ru complex, mg
1	522	II	57
2	624	III	71
2a	261	III	8.2
2b	271	III	17.8
2/SBA-15LP	270	III	30.7
2/MCM-41	179	III	20.4

(for catalysts labeling vide infra): 24 mL of toluene was added to 624 mg of SBA-15 modified with PCy<sub>2</sub> linkers, then 71 mg of **III** was added and the suspension was stirred for 16 h. The product was 3 times washed under argon atmosphere with 15 mL of toluene and 5 times washed with 8 mL of dichloromethane. The rest of the solvent was removed by drying the catalyst in vacuum at room temperature. Catalysts **1**, **2a**, **2b**, **2/SBA-15LP**, and **2/MCM-41** were prepared in a similar way (amounts of sieves and complexes are given in Table 1).

Preparation of catalyst **4**: 12 mL of toluene was added to 345.8 mg of SBA-15 modified with py linkers, then 30.3 mg of **III** was added and the suspension was stirred for 16 h. The product was 3 times washed under argon atmosphere with 10 mL of toluene and 5 times washed with 10 mL of dichloromethane. The rest of the solvent was removed by drying the catalyst in vacuum at room temperature. Catalyst **3** was prepared in a similar way (203.5 mg of modified SBA-15 and 17.1 mg of **II** were used).

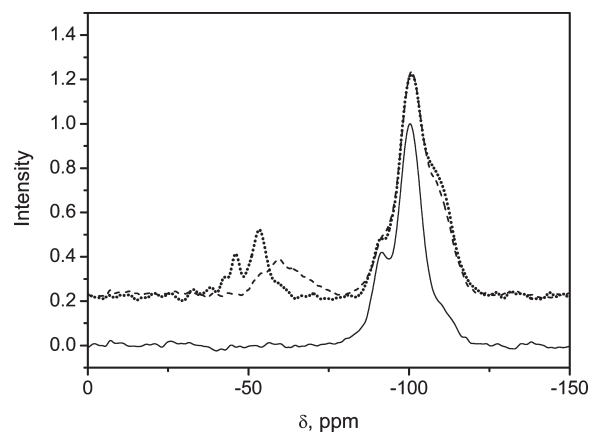
Catalyst loadings were calculated from Ru content in supernatants. All catalysts were stored under argon atmosphere.

**2.3. Metathesis Reactions.** Metathesis reactions were performed under Ar atmosphere in a Schlenk tube equipped with a magnetic stirrer. In a typical RCM experiment, 17.7 mg of the catalyst **2** was placed into the reactor, then 2.9 mL of toluene was added, and the suspension was heated to 80 °C in an oil bath. Then 109 μL of diethyl diallylmalonate (DEDAM) (molar ratio DEDAM:Ru = 250,  $c_{\text{DEDAM}}^0 = 0.15$  mol/L) and 60 μL of *n*-nonane as an internal standard was added under stirring. Samples (0.1 mL) were taken in given intervals after DEDAM addition. Ethyl vinyl ether (terminating agent) was added into each sample, the samples were centrifuged, and the supernatant analyzed by GC and GC-MS.

In a typical cross-metathesis (CM) experiment, 22.0 mg of catalyst **2** was placed into the reactor, then 2.5 mL of toluene was added, and the suspension was heated to 80 °C in an oil bath. Then the mixture of 74 μL of allylbenzene (AllB), 179 μL of *cis*-1,4-diacetoxy-2-butene (DAB) (molar ratio AllB/Ru = 250,  $c_{\text{AllB}}^0 = 0.2$  mol/L,  $c_{\text{DAB}}^0 = 0.4$  mol/L) and 70 μL of *n*-nonane (internal standard) was added under stirring. Termination and sampling for GC proceeded as it was given in the previous example.

In a typical metathesis of methyl oleate (MeOl), 15.0 mg of the catalyst **2** was placed into the reactor, then 2.37 mL of toluene was added, and the suspension was heated to 60 °C in an oil bath. Then 60 μL of *n*-nonane (internal standard) and 131 μL of MeOl (molar ratio MeOl:Ru = 250,  $c_{\text{MeOl}}^0 = 0.15$  mol/L) were added under stirring. Termination and sampling for GC proceeded as it was given previously.

In a typical ROMP experiment, 16.9 mg of catalyst **2** was placed into the reactor, 0.965 mL of toluene was added, and the

**Figure 1.** <sup>29</sup>Si CP MAS NMR spectra of SBA-15 (full line), SBA-15 with PCy<sub>2</sub> linkers (dashed line), and SBA-15 with py linkers (dotted line).

suspension was heated to 80 °C in an oil bath. Then 112 μL of cyclooctene (COE) (molar ratio COE/Ru = 500,  $c_{\text{COE}}^0 = 0.8$  mol/L) was added and the reaction mixture was stirred for 2 h. The reaction mixture was cooled down, the catalyst was separated by centrifugation, and the polymer was precipitated by pouring of supernatant into 6 mL of methanol containing a small amount of 2,6-di-*tert*-butyl-*p*-cresol as an antioxidant. The polymer was dried in a vacuum oven at 60 °C to the constant weight. The yield was determined gravimetrically.

### 3. RESULTS AND DISCUSSION

**3.1. Catalyst Preparation and Characterization.** Modification of mesoporous molecular sieves proceeded via reaction of surface OH groups with ethoxysilyl groups of 2-(dicyclohexylphosphino)ethyltriethoxysilane and 2-(4-pyridyl)ethyltriethoxysilane, respectively. Figure 1 shows <sup>29</sup>Si CP MAS NMR spectra of parent SBA-15 and SBA-15 modified with PCy<sub>2</sub> linkers (1.38 wt % of P according to the elemental analysis) and SBA-15 with py linkers (0.8 wt % of N). The decrease in the intensity of Q<sup>2</sup> and Q<sup>3</sup> signals in comparison with Q<sup>4</sup> (−91, −100, and −110 ppm, respectively) indicates the consumption of surface OH groups. Moreover, the appearance of new signals in the region from −40 to −75 ppm (T<sup>m</sup> sites) confirms the attachment of linkers to the surface by siloxane bridges [(T<sup>m</sup> = RSi(OSi)<sub>m</sub>(OEt)<sub>3−m</sub>, m = 1,2,3]. As for T<sup>1</sup>, T<sup>2</sup>, and T<sup>3</sup>, chemical shifts of −47, −57, −67 are given in the literature;<sup>38–40</sup> we can assume that the py linkers are bound to the surface by T<sup>1</sup> and T<sup>2</sup> sites in contrast to the PCy<sub>2</sub> linkers where the T<sup>2</sup> and T<sup>3</sup> sites prevail. The reason for this difference is not completely clear. The linker densities, calculated from the P and N concentration, are 0.32 PCy<sub>2</sub> linkers per nm<sup>2</sup> and 0.41 py linkers per nm<sup>2</sup>. Taking into account the average OH group concentration of 4.2 OH groups/nm<sup>2</sup> determined from <sup>29</sup>Si MAS NMR spectra of parent SBA-15 (see Supporting Information), it is seen that only about 1/10 of the OH groups was consumed in both cases. A tentative explanation might be a possible formation of hydrogen bonds between pyridine groups and surface OH groups, which may reduce the probability of reaction between OH groups and ethoxysilyl groups under formation of multiple siloxane bridges in the case of modifications with 2-(4-pyridyl)ethyltriethoxysilane.

By immobilization of complexes **II** and **III** on SBA-15 modified with PCy<sub>2</sub> and py linkers hybrid catalysts **1–4** were prepared (Scheme 1). The immobilization is nucleophilic substitution, which is governed by nucleophile strength (PCy<sub>2</sub> linkers > py linkers) and the substitutional lability of replacing ligands (Brpy > PCy<sub>3</sub>). It did not proceed quantitatively. Under conditions applied, different fraction of the starting amounts of complexes **II** and **III** (corresponding to the expected loading between 1.0 and 1.25 wt % Ru in hybrid catalysts) were transferred into catalysts **1, 2, 3, 4** (23.9%, 87%, 29.6%, and 65.8%, respectively) and therefore the catalysts **1, 2, 3, 4** differed in their loadings (0.30, 1.0, 0.34, and 0.62 wt % of Ru, respectively). Taking into account the surface area of the support and the linker density, it can be assumed that not all linkers were consumed even for the highest Ru concentration (1 wt %). The same Ru species are postulated for catalyst pairs **1, 2** and **3, 4** in accordance with the lowering of the coordination number described for complex **III** in similar ligand exchange reactions in the homogeneous phase<sup>29</sup> and on the basis of catalyst spectroscopic characterizations (vide infra).

Textural analysis showed that mesoporous character and regular architecture of supports used were preserved during catalyst preparations. X-ray diffraction (XRD) patterns and N<sub>2</sub> adsorption isotherms of catalysts and parent support (see Supporting Information) are characteristic of high quality SBA-15. The comparison of isotherms of the parent SBA-15 with the isotherms of the catalysts indicates that the surface modification by linkers and Ru complex anchoring did not diminish the structural ordering of the supports. Strong decrease in the surface area S<sub>BET</sub> and void volume V was associated with the catalyst preparation. For instance, S<sub>BET</sub> decreased from 934 m<sup>2</sup>/g for parent SBA-15 to 475 m<sup>2</sup>/g for **2** and 549 m<sup>2</sup>/g for **4**, and V decreased from 0.96 cm<sup>3</sup>/g for parent SBA-15 to 0.62 and 0.71 cm<sup>3</sup>/g for **2** and **4**, respectively. Average pore size diameter decreased from 6.9 nm for parent SBA-15 to 5.3 and 5.6 nm for **2** and **4**, respectively, and the narrow pore size distribution was

preserved, see Figure 2. For catalysts **1** and **3**, the S<sub>BET</sub> values and pore size diameters are assumed to be the same or slightly higher than those for **2** and **4**, because these catalysts consist of the same modified supports and the concentrations of Ru species are lower than for **2** and **4**.

For elucidating the structure of the Ru species on the catalyst surface a combination of UV–vis, X-ray photoelectron spectroscopy (XPS), and X-ray fluorescence (XRF) were used. Figure 3a displays UV–vis spectrum of complex **II** in CH<sub>2</sub>Cl<sub>2</sub> and UV–vis reflection spectra of catalysts **1** and **2**. All spectra exhibit the same band (probably metal-to-ligand charge-transfer) at 335 nm and shoulder at 490 nm, suggesting the similar ligand arrangement in Ru coordination sphere. Similarly, Figure 3b shows UV–vis spectra of **III**, its pyridine analogue [RuCl<sub>2</sub>py<sub>2</sub>(SIMes)(=CHPh)] - **IIIpy**, prepared according to ref 29, and UV–vis reflection spectra of **3** and **4**. **IIIpy**, **3**, and **4** have the same spectra with a band at 342 nm; for **III** this band is slightly red-shifted to

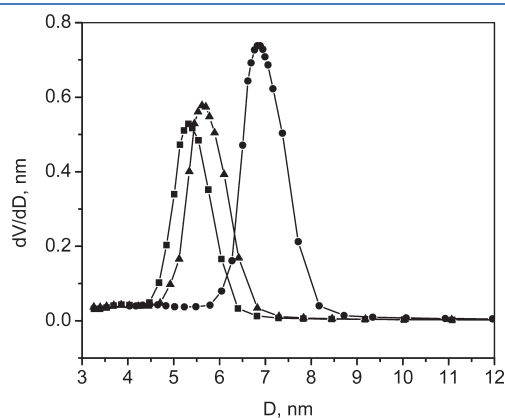
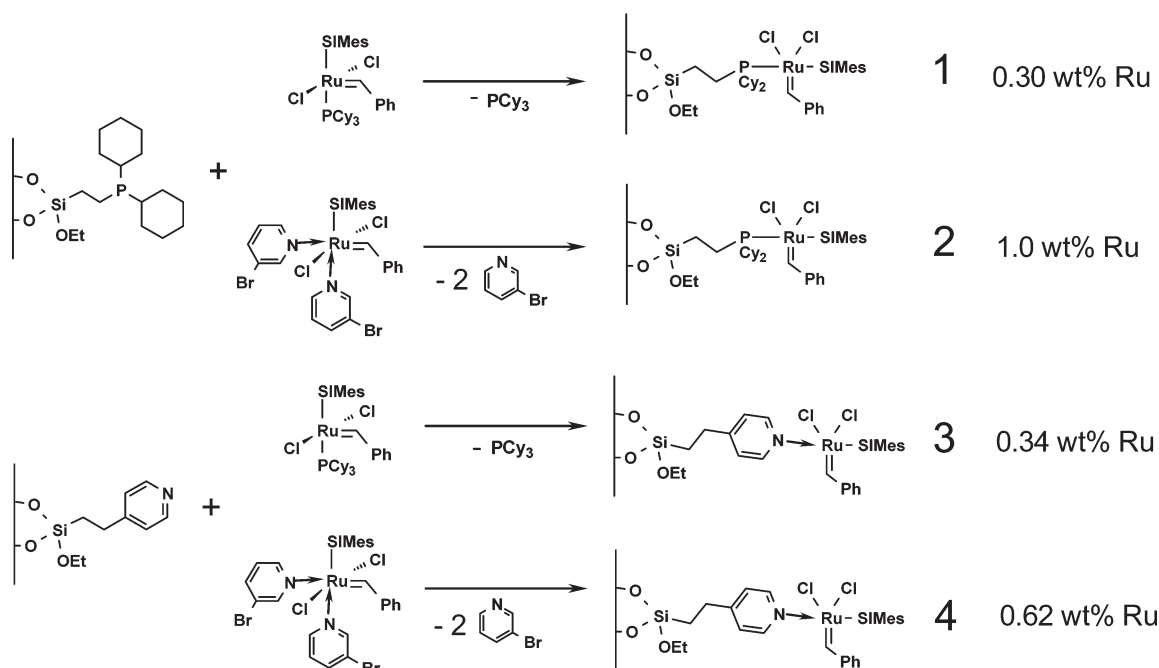
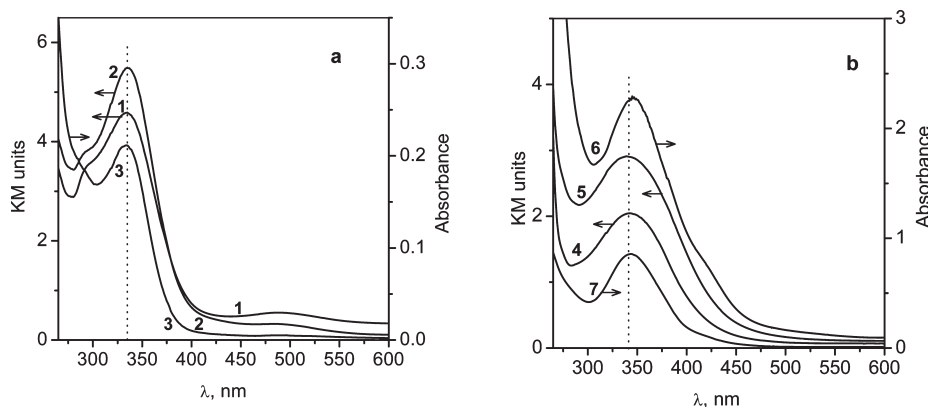


Figure 2. Pore size distribution for parent SBA-15 (●), catalyst **2** (■), and catalyst **4** (▲).

### Scheme 1. Immobilization of **II** and **III** on SBA-15 Modified with PCy<sub>2</sub> and Pyridine Linkers, Respectively





**Figure 3.** UV-vis spectra of (a) **1**, **2** (curves 1,2) and **II** (in  $\text{CH}_2\text{Cl}_2$ ,  $c = 0.00016$  mmol/mL) (curve 3),  $l = 0.2$  cm; (b) **3**, **4** (curve 4,5), **III** ( $\text{CH}_2\text{Cl}_2$ ,  $c = 0.0012$  mmol/mL) (curve 6), and **IIIpy** ( $\text{CH}_2\text{Cl}_2$ ,  $c = 0.0003$  mmol/mL) (curve 7),  $l = 0.2$  cm.

**Table 2.** XPS Binding Energies ( $\pm 0.2$  eV) for Complexes and Catalysts Used<sup>a</sup>

sample	Ru 3d <sub>5/2</sub>	N 1s	Cl 2p	P 2s
<b>II</b>	281.3	400.2	198.3	188.4
<b>III</b>	281.2	400.0	198.8	
<b>IIIpy</b>	281.2	400.0	198.2	
<b>1</b>	280.6	400.0	198.5	190.1
<b>2</b>	280.8	n.m.	n.m.	n.m.
<b>3</b>	280.6	399.6	198.2	
<b>4</b>	280.4	399.1 400.0	198.5	

<sup>a</sup> The line C 1s (285.0 eV) was used as a reference for spectra calibration, FWHM were in the range 2.3–4.3 eV, n.m. = not measured.

347 nm. The coincidence of the spectra also indicates the similarity in Ru species.

The XPS binding energies for complexes **II**, **III**, and **IIIpy** and catalysts **1–4** are provided in Table 2. The values of binding energies for **II** are in accord with literature values<sup>41</sup> (the difference in the C 1s line value used as a reference in ref 41 should be taken into account). Interestingly, **II**, **III**, and **IIIpy** do not differ in the binding energies of Ru 3d<sub>5/2</sub> in spite of the difference in  $\sigma$  electron donating ability of PCy<sub>3</sub> and py ligands (expressed by their pK<sub>a</sub> values) and observed substitutional lability of py linkers.<sup>29</sup> However, the complex geometry is different for complexes **II** and **III**. The Ru 3d<sub>5/2</sub> binding energies of catalysts **1–4** do not differ significantly from each other; however, they all are lower on average by 0.6 eV in comparison with the parent complexes **II** and **IIIpy**. This shift could be due to the change of the initial charge state as well as the final state effects in photoemission related to coordination environment surrounding Ru atom in the complex in crystal and the complex located in mesoporous channels.

For catalyst **4**, two different values for N 1s line were distinguished (399.1 and 400 eV); the lower one corresponds to N atoms in free pyridine linkers on the surface, the higher one to N atoms in the coordination sphere of Ru. Their concentration ratio 2:1 indicates that a major part of the py linkers remained free (noncoordinated).

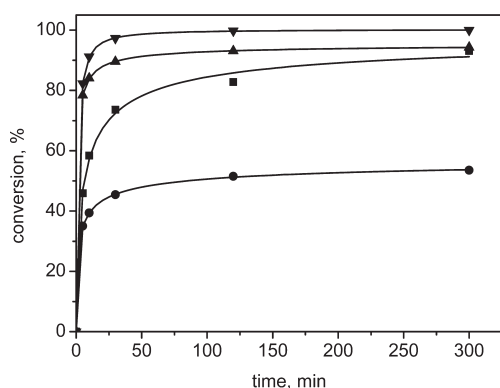
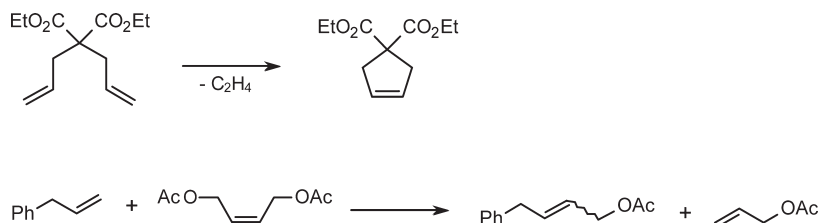
The surface stoichiometry measured for **1** and **3**, Ru<sub>1.0</sub>N<sub>2.0</sub>-P<sub>8.3</sub>Cl<sub>1.7</sub>C<sub>132</sub> and Ru<sub>1.0</sub>N<sub>10.6</sub>Cl<sub>1.8</sub>C<sub>119</sub>, respectively, is in agreement with the catalyst structures depicted in Scheme 1. It also confirms that both linkers were only partially used to attach Ru

complexes. Bromine was not found in **2** and **4** suggesting the complete loss of bromopyridine ligands during immobilization. To overcome the presumption that the bromopyridine ligands were lost by dissociation in vacuum during XPS measurement<sup>29</sup> we measured the Br content in **4** by XRF under He atmosphere. The Br/Ru ratio found was less than 0.1.

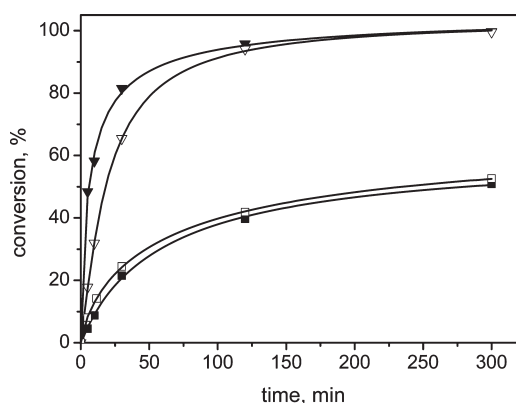
**3.2. Catalyst Activity in Metathesis Reactions.** All catalysts were tested in the RCM of DEDAM and CM of AllB with DAB (Scheme 2).

Figures 4 and 5 show conversion curves for RCM of DEDAM with catalysts **1–4** in the temperature range from 60 to 100 °C. Conversions achieved decreased depending on the catalyst used in the order: **2** > **4** > **1** > **3**. Higher loaded catalyst **2** and **4** achieved higher conversions than their lower loaded counterparts **1** and **3** in spite of the same Ru concentration in the reaction (for discussion of this phenomenon vide infra). High selectivity (94–100%) was observed in all cases. The product of cycloisomerization (diethyl 3-methyl-4-methylenecyclopentane-1,1-dicarboxylate) was observed as the only side product. As concerns a temperature dependence of catalyst activity, there is a difference between catalysts bound to the support by PCy<sub>2</sub> linkers **1**, **2** and those bound by py linkers **3**, **4**. For the former ones, the strong increase in the initial reaction rates with increasing temperature was observed, and high, nearly total conversions were achieved in most cases. On the other hand, the catalyst **3** and **4** exhibited very high initial reaction rates, but the reaction rates ceased quickly before reaching complete conversion. This behavior is probably connected with the initiation phase of the catalytic reaction and the thermal stability of the catalysts. Initiation with the Grubbs catalysts is known to start by phosphine or pyridine ligand dissociation under formation of coordinatively unsaturated 14 electron species (catalytically active species) capable to coordinate a substrate molecule.<sup>42</sup> Dissociation of pyridine ligands is known to proceed more quickly than the dissociation of phosphine ligands.<sup>43</sup> As the main path for catalytically active species decomposition is a bimolecular decay,<sup>44</sup> the increased concentration of catalytically active species accelerates their decomposition and reaction termination at incomplete conversions.

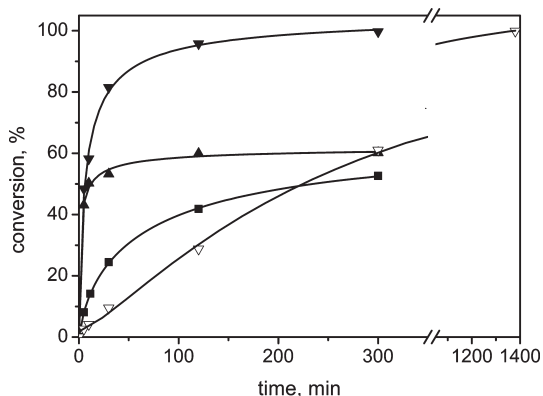
Figure 6 shows conversion curves for RCM of DEDAM using catalysts with PCy<sub>2</sub> linkers differing in Ru loadings **1**, **2**, **2a**, and **2b**. Catalysts **2a** and **2b** were prepared similarly to catalyst **2** (i.e., from **III** and SBA-15 modified with PCy<sub>2</sub> linkers) using a lower concentration of **III** so that loadings of **2a** and **2b** were 0.65 wt %

Scheme 2. RCM of Diethyl Diallylmalonate and CM of Allylbenzene with *cis*-1,4-Diacetoxy-2-butene

**Figure 4.** RCM of DEDAM with catalysts **1** (■), **2** (▼), **3** (●), and **4** (▲). 100 °C, Ru/DEDAM = 1:250, toluene,  $c_{\text{DEDAM}}^0 = 0.15$  mol/L.

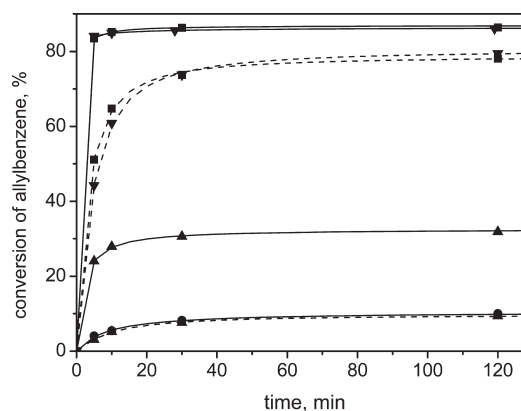


**Figure 6.** Conversion curves for RCM of DEDAM with catalysts of different loading, toluene, 80 °C, Ru/DEDAM = 1:250,  $c_{\text{DEDAM}}^0 = 0.15$  mol/L. Catalyst **1** (■), catalyst **2** (▼), catalyst **2a** (0.65 wt % Ru, ▽), catalyst **2b** (0.33 wt % Ru, □).



**Figure 5.** RCM of DEDAM with catalysts **1** (■), **2** (▼), **4** (▲) at 80 °C, and with **2** at 60 °C (▽). Ru/DEDAM = 1:250, toluene,  $c_{\text{DEDAM}}^0 = 0.15$  mol/L.

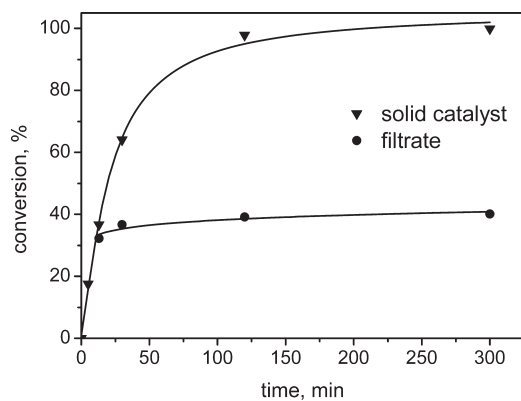
and 0.33 wt %, respectively. The conversion curves for **1** and **2b** are practically identical confirming the notion of the same Ru species formed by the immobilization of both **II** and **III** on the SBA-15 modified with PCy<sub>2</sub> linkers. Although overall Ru concentrations in the reaction mixtures are the same, the initial reaction rate decreases with decreasing Ru loading. The explanation may lie in the increasing excess of free phosphine ligands with decreasing Ru loading. The catalytically active species formed by phosphine dissociation are retrapped by free phosphine ligands,<sup>43,45</sup> so the increasing concentration of free phosphine ligands may lead to the decrease in actual concentration of catalytically active species. Moreover, the phosphine ligands may also participate in an irreversible deactivation of active species.<sup>46</sup> For the lowest loading, the rates of termination reactions<sup>44,46</sup>



**Figure 7.** Conversion curves for catalysts **1** (■), **2** (▼), **3** (●), and **4** (▲) in CM of AllB and DAB. toluene, reaction temperatures = 100 °C (full line) and 80 °C (dashed line), Ru/AllB molar ratio = 1:250,  $c_{\text{AllB}}^0 = 0.2$  mol/L,  $c_{\text{DAB}}^0 = 0.4$  mol/L.

may prevail upon the rate of initiation, which leads to the low overall reaction rate and low conversion.

In CM of AllB with DAB (molar ratio 1:2) (Figure 7), 86% conversion of AllB (equilibrium conversion)<sup>47</sup> was reached in 10 min at 100 °C with both **1** and **2** catalysts. In contrast, catalysts **4** and **3** exhibited considerably lower conversions (32% and 10%, respectively) at the same temperature, probably because of the catalysts decomposition. At 80 °C, about 75% conversion was achieved in 30 min with both **1** and **2** (the reaction rates were surprisingly similar for both these catalysts while substantial



**Figure 8.** Filtration test for catalyst 2. Toluene, 80 °C, Ru/DEDAM = 1:250,  $c_{\text{DEDAM}}^0 = 0.15$  mol/L.

difference in the reaction rates in RCM of DEDAM were observed for the same catalysts, Figure 6). However, only 10% conversion was reached with 4. As concerns the selectivity, only negligible amount of ALLB homometathesis product was found over these catalysts (see Supporting Information).

From all catalytic experiments described, it can be concluded that the catalysts with PCy<sub>2</sub> linkers delivered better results in both RCM and CM testing reactions than the catalysts with py linkers. For RCM of DEDAM at 80 °C, nearly complete conversions were reached with 2 and 2a unlike 4 (conversion 60% only, see Figure 5). Similarly, for CM of AllB and DAB considerably higher conversions were achieved with 1 and 2 in comparison with 3 and 4.

**3.3. Catalyst Leaching and Reusing.** A filtration test is often used in the examination of heterogeneity in transition metal catalyzed reactions.<sup>48</sup> It helped to distinguish whether catalytic activity can be ascribed to the solid phase or to the transition metal species leached into liquid phase. RCM of DEDAM was used for these filtration tests. A typical filtration test is shown in Figure 8. After 10 min of the reaction, half of liquid phase was filtered off at the reaction temperature and transferred into a parallel reactor, where it was kept under the same conditions as the reaction mixture in the original reactor. The analysis showed that in the original reactor, where the liquid phase was in the contact with the solid catalyst, reaction continued until nearly 100% conversion, whereas in the reactor with the liquid phase only, the reaction stopped just after separation. For all catalysts, filtration tests gave the same results suggesting the solid catalyst is responsible for the catalytic activity during reaction. Therefore, the catalytically active species, formed by linker dissociation according to the generally accepted mechanism,<sup>42</sup> remained attached to the support by repeating the dissociation–association process.

For all catalysts, the Ru leaching in RCM of DEDAM was determined. At the end of the reaction, a solid catalyst was removed from the reaction mixture by filtration, and Ru content in the filtrate was determined by ICP-MS. The results are provided in Table 3. For 3 and 4 the catalyst leaching is very low. It means that despite rapid py linker dissociation, the catalytically active species and/or products of their decomposition were recaptured on the surface practically completely. For the PCy<sub>2</sub> linker containing catalysts 1 and 2, the Ru leaching is evidently higher, but it can be reduced by decreasing the temperature and moreover the Ru content in the products can

**Table 3.** Catalyst Leaching<sup>a</sup>

catalyst	reaction		maximum Ru content in products, <sup>c</sup> ppm
	temperature, °C	Ru leaching, <sup>b</sup> %	
1	100	7.7	162
2	80	5.3	105
	60	1.6	29.7
3	60	2.4 <sup>d</sup>	5.8
	100	0.18	6.5
4	100	0.18	3.7

<sup>a</sup>RCM of DEDAM, toluene, Ru/DEDAM = 1:250,  $c_{\text{DEDAM}}^0 = 0.15$  mol/L, reaction time 5 h. <sup>b</sup>With respect to the starting content of Ru in the catalyst. <sup>c</sup>Calculated from the amount of products present in the reaction mixture. <sup>d</sup>Ru/DEDAM = 1:2000.

**Table 4.** Reusing of Catalyst 2<sup>a</sup>

	round					
	1	2	3	4	5	6
conversion, %	94	76	70	56	48	29
						63 (23 h)

<sup>a</sup>RCM of DEDAM, 80 °C, 5 h, toluene, Ru/DEDAM = 1:200,  $c_{\text{DEDAM}}^0 = 0.15$  mol/L.

be reduced to the acceptable level of <10 ppm<sup>8,49</sup> by minimization of the amount of catalyst.

Catalyst 2 reuse was studied in RCM of DEDAM. After 5 h of the reaction, the catalyst was separated by filtration, washed with toluene and new portions of toluene, and DEDAM were added. Catalyst was successfully reused 6 times (Table 4); however, the gradual decrease in the conversion was observed evidently because of the decrease in the concentration of catalytically active species. In the last round, the conversion of 63% was achieved after 23 h. Catalysts 3 and 4 were not reusable under the conditions adopted. The reason for it should be a rapid decomposition of catalytically active species.

**3.4. Versatility of Catalyst 2.** Catalyst 2 as the most active and reusable catalyst was used in the following metathesis reactions (Table 5). RCM of citronellene and diallyl phthalate proceeded with high conversions and more than 90% selectivity, in the case of linalool the selectivity to RCM products was less than 60% only, because of dehydration leading to methylcyclopentadiene as a side-product (the selectivity varies in individual experiments). In the case of CM of 5-hexenyl acetate (HexAc) with methyl acrylate (MeA) 2-fold excess of MeA was used. The selectivity to CM product was more than 95%. Metathesis of methyl oleate (MeOl) proceeded quickly to the equilibrium (55% conversion of methyl oleate), with selectivity more than 90%. ROMP of COE delivered a high molecular weight polymer ( $M_w = 110\,000$ ,  $M_n = 56\,000$ ) in 87% yield.

For bulky substrates, the catalyst activity may depend on catalyst pore size because in this case the pore size can strongly affect the rates of substrate and product diffusions in the catalyst pores. Figure 9 shows the effect of catalyst pore size on the conversion curves in metathesis of methyl oleate. In addition to the catalyst 2, catalysts 2/MCM-41 and 2/SBA-15LP, prepared in a similar way as 2 with MCM-41 ( $D = 4.0$  nm) and SBA-15LP ( $D = 11.1$  nm) as supports, were used. The loadings of 2/MCM-41 and 2/SBA-15LP were 1.1% Ru and 0.96%, respectively. The

Table 5. Application of Catalyst 2 in Various Metathesis Reactions<sup>f</sup>

reactant	products	conditions	Conversion
		standard	99 %
		standard	99 %
		a)	80 %
		b)	95 % to HexAc
		c)	55 %
		d)	87 % <sup>e)</sup>

<sup>a</sup> Reaction time 5 h. <sup>b</sup>  $c_{\text{HexAc}} = 0.2$  mol/L,  $c_{\text{MeA}} = 0.4$  mol/L, Ru/HexAc = 1:250. <sup>c</sup>  $t = 60$  °C, <sup>d</sup> Ru/COE = 1:500,  $c_{\text{COE}}^0 = 0.8$  mol/L. <sup>e</sup> Isolated polymer yield. <sup>f</sup> Standard conditions: toluene,  $t = 80$  °C, Ru/substrate = 1:250,  $c_{\text{substrate}} = 0.15$  mol/L, reaction time 2 h.

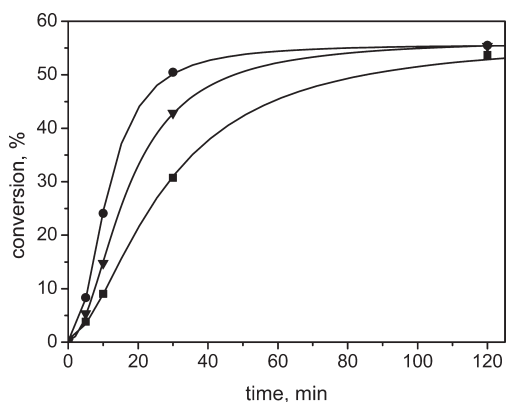


Figure 9. Effect of catalyst pore size on conversion in metathesis of MeOl. Toluene, 60 °C, Ru/MeOl = 1:250,  $c_{\text{MeOl}}^0 = 0.15$  mol/L, catalysts 2 (▼), 2/SBA-15LP (●), 2/MCM-41 (■).

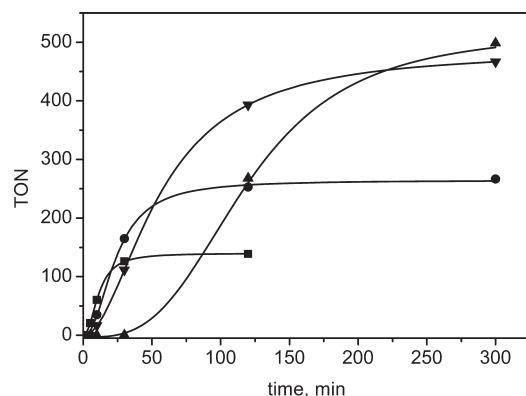


Figure 10. Metathesis of MeOl with 2/SBA-15 LP Toluene, 60 °C, MeOl:Ru = 250 (■), 500 (●), 1000 (▼), 2000 (▲),  $c_{\text{MeOl}}^0 = 0.15$  mol/L.

beneficial effect of increasing pore size is clearly seen. The maximum reaction rate (rate at the inflection point of individual curves)

increased with increasing pore size of catalyst support (in the order MCM-41 < SBA-15 < SBA-15 LP). The filtration experiment for 2/SBA-15LP (see Supporting Information) indicates that the catalytically active species are kept in the catalyst pore regardless of the increase in pore size.

From the practical point of view, the achievement of high TON is very important. For RCM of DEDAM, TONs of nearly 2000 were achieved with catalyst 2 (toluene, 80 °C, Ru/DEDAM = 2000,  $c_{\text{DEDAM}}^0 = 0.15$  mol/L, reaction time 2 h). For the metathesis of methyl oleate with catalyst 2/SBA-15LP, the influence of decreasing amount of catalyst (and consequently increasing molar ratio MeOl/Ru) on TON development in time is given in Figure 10. It is seen that with decreasing Ru concentration (in the gross) the initial TOF decreased and induction period appeared. However, TON increased with increasing MeOl/Ru molar ratio and reached the value TON = 500 at least.

#### 4. CONCLUSIONS

Hybrid catalysts for olefin metathesis were prepared by immobilization of alkylidene complexes **II** and **III** on mesoporous molecular sieves SBA-15 and MCM-41 modified on their surface with PCy<sub>2</sub> and py linkers. From both **II** and **III** complexes, catalysts with the same Ru species on the surface were formed. The employment of complex **III** is preferable because catalysts with high loading are achieved more easily. The mesoporous character and narrow pore size distribution of supports were preserved in the hybrid catalysts.

The catalyst activity was tested in RCM of DEDAM and CM of allylbenzene with 1,4-diacetoxy-2-butene. Catalysts with PCy<sub>2</sub> linkers exhibited high activity and stability reaching high TON (up to 2000) at nearly 100% selectivity (2 h, 60–100 °C) and being reusable for several times. On the other hand, catalysts with py linkers tended to the rapid decomposition at incomplete conversions.

The filtration experiments suggested the solid catalyst was responsible for the catalytic activity. Ru leaching established from final reaction mixture was very low for catalysts with PCy<sub>2</sub> linkers



(from 1.6 to 7.7% of starting amount of Ru in catalyst according to the reaction conditions) and even negligible for catalyst with py linkers (0.18%). Despite that dissociation of phosphine and pyridine ligands is a prerequisite for the formation of catalytically active species (14 electron Ru species), these active species can be easily recaptured by PCy<sub>2</sub> and py groups of free linkers (which are in excess), and we believe the metathesis reaction proceeds in the catalyst pores, where active species are held in by a repetitive dissociation–reassociation cycle.

In addition to the testing reaction given above, the catalysts with PCy<sub>2</sub> linkers were successfully applied in RCM of citronellene, linalool, and diallylphtalate, metathesis of methyl oleate, CM of 5-hexenyl acetate with methyl acrylate, and in ROMP of cyclooctene. TONs achieved in these reactions were from 200 to 500.

In metathesis of methyl oleate, the positive effect of catalyst pore size on reaction rate was found. The initial reaction rate was found to increase with increasing pore size of catalyst support in the order MCM-41 (*D* = 4.0 nm) < SBA-15 (6.8 nm) < SBA-15 LP (11.1 nm), which probably reflects the increasing rate of reactant and product diffusion in the pores.

## ■ ASSOCIATED CONTENT

**S Supporting Information.** XRD patterns, N<sub>2</sub>-adsorption isotherms, analytical procedures and GC records of products. This material is available free of charge via the Internet at <http://pubs.acs.org>.

## ■ AUTHOR INFORMATION

### Corresponding Author

\*E-mail: [jiri.cejka@jh-inst.cas.cz](mailto:jiri.cejka@jh-inst.cas.cz).

### Funding Sources

Financial support from the Grant Agency of the Academy of Science of the Czech Republic (IAA400400805), and the Academy of Sciences of the Czech Republic (KAN100400701) is gratefully acknowledged. D.B. thanks the Grant Agency of the Czech Republic for the support (203/08/H032).

## ■ ACKNOWLEDGMENT

The authors thank Z. Bastl, and J. Dědeček (both from J. Heyrovský Institute) for XPS and NMR measurements, respectively, and J. Sedláček (Department of Physical and Macromolecular Chemistry, Charles University in Prague) for the determination of polymer molecular weights by SEC.

## ■ REFERENCES

- (1) Ivin, K. J.; Mol, J. C. *Olefin Metathesis and Metathesis Polymerization*; Academic Press: London, 1997.
- (2) Grubbs, R. H., Ed.; *Handbook of Metathesis*; Wiley-VCH: Weinheim, Germany, 2003; Vol. 1, Catalyst development.
- (3) Grubbs, R. H. *Angew. Chem., Int. Ed.* **2006**, *45*, 3760–3765.
- (4) Buchmeiser, M. R. *Catal. Today* **2005**, *105*, 612–617.
- (5) Dragutan, I.; Dragutan, V. *Platinum Met. Rev.* **2008**, *52*, 71–82.
- (6) Copéret, C.; Basset, J.-M. *Adv. Synth. Catal.* **2007**, *349*, 78–92.
- (7) Buchmeiser, M. R. *Chem. Rev.* **2009**, *109*, 303–321.
- (8) Clavier, H.; Grela, K.; Kirschning, A.; Mauduit, M.; Nolan, S. P. *Angew. Chem., Int. Ed.* **2007**, *46*, 6786–6801.
- (9) Nguyen, S. T.; Grubbs, R. H. *J. Organomet. Chem.* **1995**, *497*, 195–200.

- (10) Melis, K.; De Vos, D.; Jacobs, P.; Verpoort, F. *J. Mol. Catal. A: Chem.* **2001**, *169*, 47–56.
- (11) Mayr, M.; Buchmeiser, M. R.; Wurst, K. *Adv. Synth. Catal.* **2002**, *344*, 712–719.
- (12) Mennecke, K.; Grela, K.; Kunz, U.; Kirschning, A. *Synlett* **2005**, 2948–2952.
- (13) Park, K. H.; Kim, S.; Chung, Y. K. *Bull. Korean Chem. Soc.* **2008**, *29*, 2057–2060.
- (14) Nieczypor, P.; Buchowicz, W.; Meester, W. J. N.; Rutjes, F. P. J. T.; Mol, J. C. *Tetrahedron Lett.* **2001**, *42*, 7103–7105.
- (15) Halbach, T. S.; Mix, S.; Fischer, D.; Maechling, S.; Krause, J. O.; Sievers, C.; Blechert, S.; Nuyken, O.; Buchmeiser, M. R. *J. Org. Chem.* **2005**, *70*, 4687–4694.
- (16) Krause, J. O.; Nuyken, O.; Wurst, K.; Buchmeiser, M. R. *Chem.—Eur. J.* **2004**, *10*, 777–784.
- (17) Vehlow, K.; Maechling, S.; Köhler, K.; Blechert, S. *J. Organomet. Chem.* **2006**, *691*, 5267–5277.
- (18) Bek, D.; Žilková, N.; Dědeček, J.; Sedláček, J.; Balcar, H. *Top. Catal.* **2010**, *53*, 200–209.
- (19) Kingsbury, J. S.; Garber, B.; Giftos, J. M.; Gray, B. L.; Okamoto, M. M.; Farrer, R. A.; Fourkas, J. T.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2001**, *40*, 4251–4256.
- (20) Zarka, M. T.; Nuyken, O.; Weberskirch, R. *Macromol. Rapid Commun.* **2004**, *25*, 858–862.
- (21) Yao, Q.; Motta, A. R. *Tetrahedron Lett.* **2004**, *45*, 2447–2451.
- (22) Fischer, D.; Blechert, S. *Adv. Synth. Catal.* **2005**, *347*, 1329–1332.
- (23) Elias, X.; Pleixats, R.; Man, M. W. C. *Tetrahedron* **2008**, *64*, 6770–6781.
- (24) Lim, J.; Lee, S. S.; Ying, J. Y. *Chem. Commun.* **2010**, *46*, 806–808.
- (25) Elias, X.; Pleixats, R.; Man, M. W. C.; Moreau, J. J. E. *Adv. Synth. Catal.* **2007**, *349*, 1701–1713.
- (26) Connon, S. J.; Dunne, A. M.; Blechert, S. *Angew. Chem., Int. Ed.* **2002**, *41*, 3835–3838.
- (27) Van Berlo, B.; Houthoofd, K.; Sels, B. F.; Jacobs, P. A. *Adv. Synth. Catal.* **2008**, *350*, 1949–1953.
- (28) Balcar, H.; Shinde, T.; Žilková, N.; Bastl, Z. *Beilstein J. Org. Chem.* **2011**, *7*, 22–28.
- (29) Sanford, M. S.; Love, J. A.; Grubbs, R. H. *Organometallics* **2001**, *20*, 5314–5318.
- (30) Beck, J. S.; Vartuli, J. C.; Roth, W. J.; Leonowicz, M. E.; Kresge, C. T.; Schmitt, K. D.; Chu, C.-W.; Olson, D. H.; Sheppard, E. W.; McCullen, S. B.; Higgins, J. B.; Schlenker, J. L. *J. Am. Chem. Soc.* **1992**, *114*, 10834–10843.
- (31) Márquez-Alvarez, C.; Žilková, N.; Pérez-Pariente, J.; Čejka, J. *Catal. Rev.* **2008**, *50*, 222–286.
- (32) De Vos, D. E.; Dams, M.; Sels, B. F.; Jacobs, P. A. *Chem. Rev.* **2002**, *102*, 3615–3640.
- (33) Martín-Aranda, R. M.; Čejka, J. *Top. Catal.* **2010**, *53*, 141–153.
- (34) Balcar, H.; Čejka, J. *Macromol. Symp.* **2010**, *293*, 43–47.
- (35) Topka, P.; Balcar, H.; Rathouský, J.; Žilková, N.; Verpoort, F.; Čejka, J. *Microporous Mesoporous Mater.* **2006**, *96*, 44–54.
- (36) Zhang, H.; Sun, J.; Ma, D.; Weinberg, G.; Su, D. S.; Bao, X. *J. Phys. Chem. B* **2006**, *110*, 25908–25915.
- (37) Zukal, A.; Šiklová, H.; Čejka, J. *Langmuir* **2008**, *24*, 9837–9842.
- (38) Dufaud, V.; Davis, M. E. *J. Am. Chem. Soc.* **2003**, *125*, 9403–9413.
- (39) Warad, I.; Al-Othman, Z.; Al-Resayes, S.; Al-Deyab, S. S.; Kenawy, E.-L. *Molecules* **2010**, *15*, 1028–1040.
- (40) Zhao, S.; Zhao, J.; Lou, L.-L.; Liu, S. *Microporous Mesoporous Mater.* **2011**, *137*, 36–42.
- (41) Jarzemska, K.; Seal, S.; Woźniak, K.; Szadkowska, A.; Bieniek, M.; Grela, K. *ChemCatChem* **2009**, *1*, 144–151.
- (42) Sanford, M. S.; Love, J. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **2001**, *123*, 6543–6554.
- (43) Love, J. A.; Morgan, J. P.; Trnka, T. M.; Grubbs, R. H. *Angew. Chem., Int. Ed.* **2002**, *41*, 4035–4037.
- (44) Ulman, M.; Grubbs, R. H. *J. Org. Chem.* **1999**, *64*, 7202–7207.

(45) Sanford, M. S.; Ulman, M.; Grubbs, R. H. *J. Am. Chem. Soc.* **2001**, *123*, 749–750.

(46) Hong, S. H.; Wenzel, A. G.; Salguero, T. T.; Day, M. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2007**, *129*, 7961–7968.

(47) Ritter, T.; Hejl, A.; Wenzel, A. G.; Funk, T. W.; Grubbs, R. H. *Organometallics* **2006**, *25*, 5740–5745.

(48) Phan, N. T. S.; Van Der Sluys, M.; Jones, C. W. *Adv. Synth. Catal.* **2006**, *348*, 609–679.

(49) Guideline on the specification limits for residues of metal catalysts or metal reagents, European Medicines Agency; [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Scientific\\_guideline/2009/09/WC500003586.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003586.pdf).