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Short Communication

2-Methyltetrahydrofuran: Sustainable solvent for ruthenium-catalyzed olefin metathesis

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ABSTRACT

Applicability of 2-methyltetrahydrofuran for olefin metathesis was examined with a set of ruthenium Hoveyda-type second generation catalysts. Influence of temperature was studied and the results were compared with those obtained in classical solvents for metathesis: dichloromethane and toluene.

1. Introduction

Catalytic olefin metathesis is an efficient synthetic method for the creation of new carbon–carbon double bond [1,2]. Main by-product of the whole catalytic cycle is typically ethylene, thus this process in comparison with other relevant synthetic approaches like Wittig reaction is much more economical and waste reducing. As the catalyst loading in preparative procedures usually does not exceed 1–5 mol% (loadings as low as 50 ppm are also possible [3]) the reaction mixture basically contains relatively pure product dissolved in a solvent. Typically this reaction is carried out in highly environmentally unfriendly solvents like dichloromethane or toluene (other halogenated solvents like 1,2-dichloroethane and fluorinated solvents are also used [4]). On the other hand there are several reports presenting the use of water as a reaction medium [5], but problems associated with solubility of typical olefins and catalysts pose a significant encumbrance. Alternative ionic liquids are considered [6], but their recycling is still a challenge [7]. It is also possible to conduct olefin metathesis in supercritical carbon dioxide ($scCO_2$) [8–10], however this requires pressurized reactors, not always available in research laboratories. The use of other renewable solvents like glycerol [11], polyethylene glycol [12] and methyl decanoate [13] has been also studied. However, the most interesting results concern dimethyl carbonate [14,15].

As olefin metathesis become an important part of industrial processes [16] there is a growing need for the search of eco-friendly solvents applicable in large scale synthesis. We turned our attention to 2-methyltetrahydrofuran (2-MeTHF), derived from renewable resources like oat hulls and corn cobs containing pentoses which after dehydrations give furfural catalytically reduced to 2-MeTHF. This solvent has already a broad application in organic chemistry including pharmaceutical industry [17]. In comparison with tetrahydrofuran, 2-MeTHF have several advantages like lower volatility, relatively high stability towards acids [18], and bases [19], low solubility in water (interestingly, decreasing with increasing temperature) making them easier to recycle than THF. Taking into account the low toxicity [20] and high biodegradability 2-MeTHF is considered as an environmentally friendly compound and their use is advocated by the ACS Green Chemistry Pharmaceutical Roundtable.

To the best of our knowledge, there are no reports on the use of 2-MeTHF as a medium for olefin metathesis reactions. In this study we present performance of selected newly synthesized second generation Hoveyda-type catalysts **5a**–**c** in comparison with commercially available second generation Hoveyda catalyst **6** in 2-MeTHF (Scheme 1). To extensively examine the performance of the catalysts we applied them in a set of model reactions. For comparison the same catalysts were also tested in common solvents used in olefin metathesis: dichloromethane and toluene.

2. Experimental

2.1. Materials

Solvents were dried by conventional methods. Substrates were used as obtained. For details see Appendix A.

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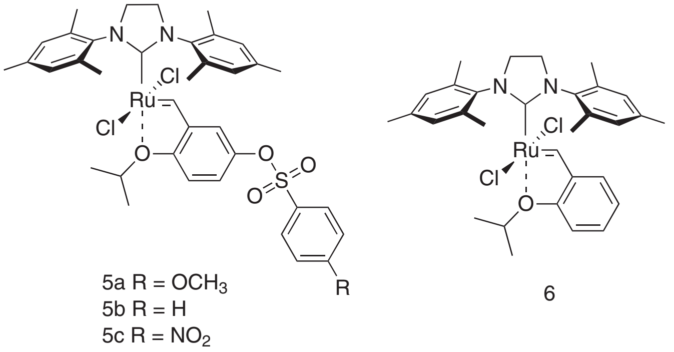


Scheme 1. Newly synthesized second generation Hoveyda-type catalysts **5a**–**c** and second generation Hoveyda catalyst **6**.

2.2. Techniques

All experiments were carried out under argon atmosphere using standard Schlenk technique. NMR spectra were recorded on Agilent 400-MR DD2 400 MHz spectrometer. NMR experiments (reaction profiles for RCM of diethyl diallylmalonate **7**) were carried out using nondeuterated solvents [21] in typical NMR tubes closed with rubber septum and filled under argon with solution of substrate in dry solvent. Solution of catalyst (prepared in dry solvent under atmosphere of argon) was added through rubber septum just prior ^{1}H NMR measurement. The progress of the metathesis reactions was monitored by ^{1}H NMR spectroscopy on Agilent 400-MR DD2 400 MHz spectrometer. Conversions determined by gas chromatography were measured by PE Clarus 580 with InterCap 5MS-Sil column.

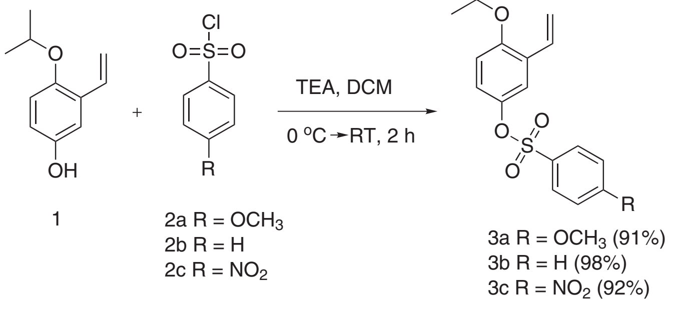
2.3. Catalyst preparation and reactivity studies

The styrene **1** was prepared according to the Yao procedure [22]. The reactions of **1** with appropriate arenesulphonyl chloride **2a**–**c** gave styrenes **3a**–**c** (Scheme 2).

The new Hoveyda-type second generation catalysts **5a**–**c** were obtained in the reaction of the appropriate styrenes **3a**–**c** with indenylidene ruthenium complex **4** in the presence of CuCl (Scheme 3).

2.3.1. Synthesis of *5a*

To a mixture of **3a** (80.9 mg, 0.232 mmol) and CuCl (25.3 mg, 0.253 mmol) dry toluene (5 mL) was added under atmosphere of Ar. Then reaction mixture was warmed up to 70 °C and **4** (200 mg, 0.211 mmol) was added. After 20 min the mixture was cooled down to room temperature and toluene was evaporated. The residue was purified by column chromatography (10% EtOAc/*c*-hexane and then 20% EtOAc/*c*-hexane). Then solvents were evaporated and product was crystallized two times from CH_2Cl_2/CH_3OH mixture, and once from CH_2Cl_2/*n*-hexane mixture, to afford **5a** (152 mg, 89%) as green crystals.



Scheme 2. Synthesis of styrenes **3a**–**c**.

^{1}H NMR (400 MHz, CD_2Cl_2): $\delta = 16.21$ (s, 1H), 7.79–7.64 (m, 2H), 7.18 (dd, $J = 8.9, 2.8$ Hz, 1H), 7.06–6.93 (m, 6H), 6.72 (d, $J = 8.9$ Hz, 1H), 6.50 (d, $J = 2.8$ Hz, 1H), 4.81 (sept, $J = 6.1$ Hz, 1H), 4.15 (s, 4H), 3.90 (s, 3H), 2.41 (s, 12H), 2.38 (s, 6H), 1.20 (d, $J = 6.1$ Hz, 6H). ^{13}C NMR (100 MHz, CD_2Cl_2): $\delta = 291.5$, 209.1, 164.3, 150.2, 145.3, 144.8, 139.0 (ovl.), 130.8, 129.2, 126.2, 126.1, 122.2, 115.1, 114.4, 113.2, 76.1, 55.9, 51.6, 20.9, 20.9, 19.2. IR (KBr): $\nu = 3055$, 3042, 3002, 2979, 2957, 2917, 2845, 2735, 1594, 1577, 1495 cm^{-1}. Anal. Calcd. for $C_{38}H_{44}Cl_2N_2O_5RuS \cdot 2/5CH_2Cl_2$: C 54.47, H 5.33, N 3.31, S 3.79, Cl 11.72; Found: C 54.52, H 5.56, N 3.19, S 3.75, Cl 11.87.

2.3.2. Synthesis of *5b*

To a mixture of **3b** (70.0 mg, 0.220 mmol) and CuCl (24.0 mg, 0.240 mmol) dry toluene (5 mL) was added under atmosphere of Ar. Then mixture was warmed up to 70 °C and **4** (190 mg, 0.200 mmol) was added. After 15 min the mixture was cooled down to room temperature and toluene was evaporated. The residue was purified by column chromatography (10% EtOAc/*c*-hexane and then 20% EtOAc/*c*-hexane). After evaporation of solvents product was crystallized two times from CH_2Cl_2/CH_3OH, and once from CH_2Cl_2/*n*-hexane, to afford **5b** (138 mg, 88%) as green crystals.

^{1}H NMR (400 MHz, CD_2Cl_2): $\delta = 16.23$ (s, 1H), 7.87–7.78 (m, 2H), 7.78–7.70 (m, 1H), 7.64–7.51 (m, 2H), 7.17 (dd, $J = 8.9, 2.8$ Hz, 1H), 7.04 (s, 4H), 6.72 (d, $J = 8.8$ Hz, 1H), 6.53 (d, $J = 2.8$ Hz, 1H), 4.81 (sept, $J = 6.1$ Hz, 1H), 4.15 (s, 4H), 2.42 (s, 12H), 2.38 (s, 6H), 1.20 (d, $J = 6.1$ Hz, 6H). ^{13}C NMR (100 MHz, CD_2Cl_2): $\delta = 291.2$, 209.1, 150.3, 145.3, 144.8, 139.0 (ovl.), 135.1, 134.4, 129.3, 129.3, 128.5, 122.1, 114.9, 113.3, 76.2, 51.6, 20.9, 20.9, 19.1. IR (KBr): $\nu = 2980$, 2961, 2917, 2736, 1606, 1586 cm^{-1}. Anal. Calcd. for $C_{37}H_{42}Cl_2N_2O_4RuS \cdot 3/5CH_2Cl_2$: C 54.17; H 5.22; N 3.36; S 3.85; Cl 13.61; Found: C 54.24, H 5.52, N 3.32, S 3.99, Cl 13.36.

2.3.3. Synthesis of *5c*

To a mixture of **3c** (79.9 mg, 0.220 mmol) and CuCl (24.0 mg, 0.240 mmol), dry toluene (5 mL) was added under atmosphere of Ar. Then reaction mixture was warmed up to 70 °C and **4** (190 mg, 0.200 mmol) was added. After 25 min the mixture was cooled down to room temperature and toluene was evaporated. The residue was purified by column chromatography (10% EtOAc/*c*-hexane and then 20% EtOAc/*c*-hexane). Then solvents were evaporated and product was crystallized two times from CH_2Cl_2/CH_3OH, and once from CH_2Cl_2/*n*-hexane to afford **5c** (107 mg, 65%) as dark-green crystals.

^{1}H NMR (400 MHz, CD_2Cl_2): $\delta = 16.27$ (s, 1H), 8.49–8.28 (m, 2H), 8.12–7.90 (m, 2H), 7.16 (dd, $J = 9.0, 2.9$ Hz, 1H), 7.04 (s, 4H), 6.75 (d, $J = 8.9$, 1H), 6.63 (d, $J = 2.8$, 1H), 4.83 (sept, $J = 6.1$ Hz, 1H), 4.17 (s, 4H), 2.42 (s, 12H), 2.39 (s, 6H), 1.21 (d, $J = 6.1$ Hz, 6H). ^{13}C NMR (100 MHz, CD_2Cl_2): $\delta = 290.4$, 208.7, 151.1, 150.5, 145.4, 144.4, 140.7, 139.0 (ovl.), 130.1, 129.3, 124.5, 121.5 (ovl.), 114.7, 113.5, 76.4, 51.6, 20.9, 20.9, 19.1. IR (KBr): $\nu = 3108$, 3098, 3073, 3021, 2978, 2918, 2739, 1690, 1607, 1533 cm^{-1}. Anal. Calcd. for $C_{37}H_{41}Cl_2N_3O_6RuS \cdot 3/5CH_2Cl_2$: C 51.39, H 4.84, N 4.78, S 3.65, Cl 12.91; Found: C 51.23, H 5.01, N 4.74, S 3.69, Cl 12.96.

The second generation Hoveyda catalyst **6** was prepared according to our procedure [23].

Catalysts **5a**–**c** and **6** (1 mol% loading) were tested in standard RCM reaction performed in DCM, toluene and 2-MeTHF with initial concentration of diethyl diallylmalonate **7** equal to 0.1 M (Scheme 4). The formation of only one product was observed.

2.3.4. General procedure for RCM and Ene–Yne reactions (Table 1, entries 1–4)

The comparative experiments with model substrates (Table 1, entries 1–4) were performed in 2-MeTHF at 70 °C with initial concentration of substrates c = 0.1 M and catalyst loadings 1 mol% (entries 2 and 3) or 2 mol% (entries 1 and 4). To a stirred solution of substrate (1 eq) and durene (1 eq, used as internal standard) in dry 2-MeTHF