

Stability of the first-generation Grubbs metathesis catalyst in a continuous flow reactor

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Abstract

Ethylene pretreatment of the $(PCy_3)_2Cl_2Ru=CHPh$ catalyst (**1**) prior to cross-metathesis of ethylene and *cis*-2-butene to form propylene in the continuous flow reactor produced a direct effect on catalyst deactivation. Similar *cis*-2-butene pretreatment of the same catalyst exhibited far less change in the catalyst activity. These results support the assumption that the ruthenium methylidene intermediate generated from ethylene and **1** is unstable and promotes catalyst loss while ruthenium alkylidenes, e.g. derived from 2-butene, exhibit significantly enhanced stability and sustained catalyst integrity. Continuous removal of products in the continuous flow reactor was important for separating the catalyst decay and the catalyst deactivation caused by a terminal olefin, in this case propylene.

The amount of produced propylene during the **1** lifespan was determined in a series of tests using identical catalyst concentrations ($[Ru] = 60$ ppm) in pentadecane while varying the olefin pretreatment times from 0 to 420 min. The catalyst turnover numbers in the cross-metathesis experiments proved inversely proportional to the duration of ethylene treatment prior to the reaction. The activity of **1** pre-exposed to ethylene closely matched with the activity of the catalyst that decayed in the reaction mixture containing ethylene and *cis*-2-butene for the same period of time. A significant contribution of the Ru-methylidene decay to the activity losses in metathesis reactions was demonstrated directly in the cross-metathesis reaction environment. The catalyst proved to be less sensitive to *cis*-2-butene pretreatment and showed turnover numbers for subsequent cross-metathesis essentially similar to the reference cross-metathesis test.

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1. Introduction

Grubbs and co-workers discovered several generations of efficient ruthenium catalysts for olefin metathesis [1,2] and extended them for aqueous [3] and asymmetric [4] reactions. The catalysts exhibited fast rates, proved easy for handling and showed tolerance to a range of functional groups. The catalyst depicted in Fig. 1 was the early member of the Grubbs catalyst family and attracted attention in both academia and industry.

This catalyst exhibited consistently high turnover numbers in the cross-metathesis of olefins [1,2,5]. However, concomitant catalyst deactivation and irreversible degradation [6,7] called for the study of underlying factors in this

process. This is especially important due to emerging industrial applications of the Grubbs catalysts. A number of important papers have addressed the catalyst stability issues [6–10]. According to the accepted mechanism, **1** produces both methylidene and alkylidene complexes in the presence of ethylene and the corresponding olefin such as propylene (Fig. 2).

The methylidene and alkylidene species play a major role in the catalytic cycle, and their longevity determines the number of catalytic turnovers. Previously determined half-lives of the ruthenium methylidene and ruthenium propylidene intermediates in a NMR tube at 55 °C were 40 min and 8 h, respectively [6]. The methylidene complex decomposes mostly via unimolecular pathway [6], forming propylene, butanes, and cyclopropane presumably as a result of β -hydride transfer from a rutenacyclobutane intermediate [7]. The nature of the inorganic degradation products is

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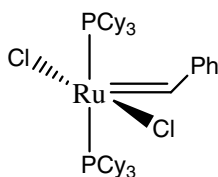


Fig. 1. Structure of the first generation Grubbs catalyst 1.

not known [6]. A striking difference between the methyldene and alkylidene complexes warranted further study.

Also, determination of catalyst deactivation profile in the presence of both ethylene and another olefin to initiate cross-metathesis was important under continuous reaction conditions. Previously methyldene and alkylidene decay was reported in the inert solvent [6].

A continuous flow reactor is a unique set-up for such investigation (Fig. 3). The corresponding tests are performed by constantly feeding olefins to a small reaction vessel, followed by sampling and analyzing the off-gas from the reactor to determine the conversion of the feedstock. The reactor provides a continuous way to measure the

activity, turnover numbers, stability, and selectivity of a homogeneous catalyst [11,12].

2. Experimental

2.1. Materials

cis-2-Butene, 95%, was obtained from Phillips Petroleum and purified to remove hydroperoxides and residual oxygen using alumina and copper (II) oxide (Aldrich 41,797-1) beds [13]. High-purity ethylene was obtained from Matheson and used as received. Bis(tricyclohexylphosphine)benzylidene ruthenium (IV) dichloride, was obtained from Strem Chemicals and used as received. Pentadecane was obtained from Aldrich and passed through activated alumina under nitrogen prior to use.

2.2. General description

A continuous flow reactor used for the metathesis catalyst testing is shown in Fig. 3. The set contains three such reactors immersed into an oil bath. Every reactor is a

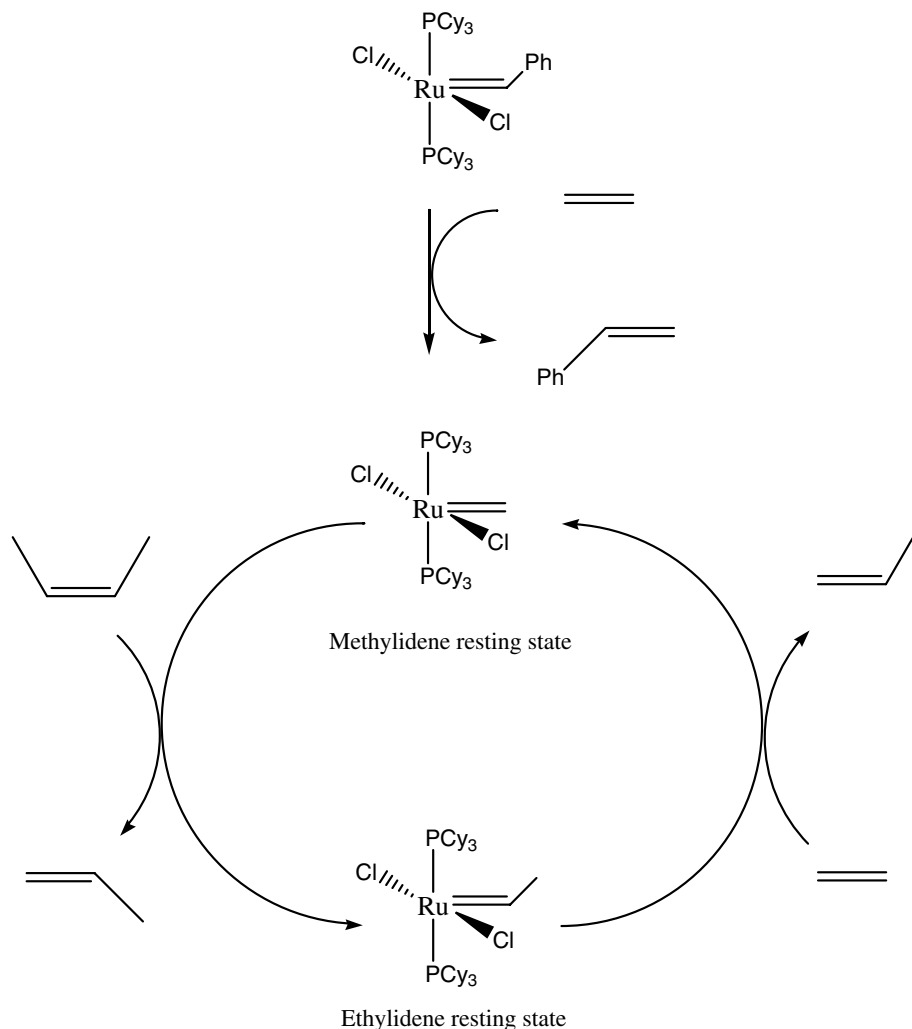


Fig. 2. Formation of the 1 methyldene and ethylidene complexes.

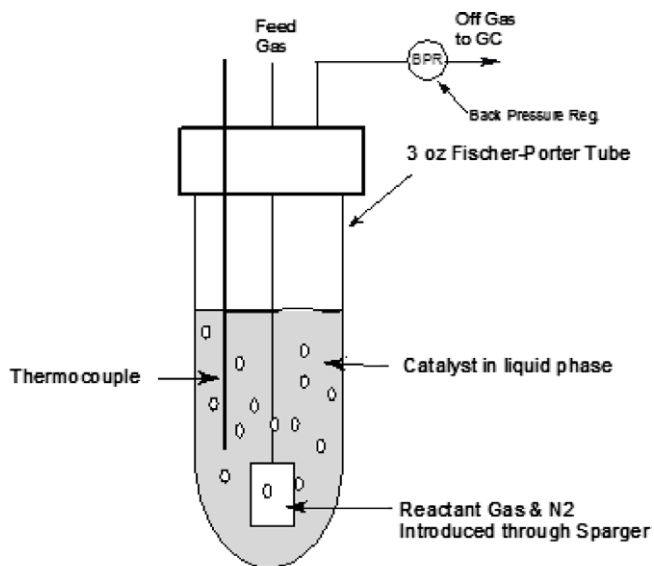


Fig. 3. A conceptual flow diagram and a picture of the continuous flow reactor set-up.

100 mL glass container similar to a Fisher–Porter bottle. Usually, each reactor is charged with approximately 20 mL of a catalyst solution. The reactor temperatures are controlled by a silicone oil bath and the reactor pressures are controlled with back-pressure regulators located on the vent lines. The feed gases are supplied to the reactors at rates that exceed the consumption rates, so there is a vent flow of both unreacted gases and the products. The unreacted ethylene along with nitrogen helps to strip the product out of the reactors. The out-going gases carry the stripped product through the back-pressure regulators into a process GC and then eventually into the hood. The amount of product being generated in a reactor can then be determined from the GC analysis.

2.3. Catalyst preparation

Each catalyst solution was prepared in a nitrogen box using an 80 mL glass bottle with a rubber septum. The catalyst weight was taken using two balances to make sure

that the weight is accurate. Pentadecane was sparged with nitrogen prior to mixing with the catalyst. The mixtures were sonicated for 10–30 min to completely dissolve solids. Catalyst **1** solutions had a typical purple color.

2.4. Ethylene pretreatment test

A solution of **1** was prepared by dissolving 0.0231 g of the catalyst in 60.0 mL of pentadecane. Then 20 mL of this solution was charged to each of three nitrogen purged glass reactors. The solution was sparged with nitrogen at 5 slph (slph = standard liters per hour) at 40 °C for 15 min. Then the catalyst solution was treated with ethylene at 2.75 slph for 30, 60, 100, 200, and 300 min. Upon exposure to ethylene, the mixture changed color from purple to red-orange. *cis*-2-Butene was then charged with the approximate rate of 0.04 mol/h. The total reactor pressure was maintained at 85 psi. The reactor effluent was sampled every 30 min using an on-line GC to determine gas composition. The experiment was monitored for 8–10 h.

2.5. 2-Butene pretreatment test

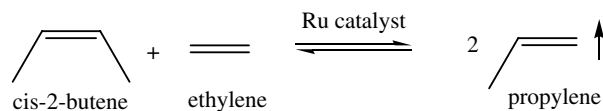
This experiment was conducted similarly to the above with *cis*-2-butene used in place of ethylene in the initial pretreatment, followed by addition of ethylene.

3. Results and discussion

The continuous flow reactor proved to be an excellent tool to study the reactivity loss in metathesis. In this reactor, a flow of *cis*-2-butene and ethylene is continuously passed through a solution of the catalyst **1** in a low volatility solvent such as pentadecane. In addition, nitrogen is a third component sparged into the liquid reaction mixture in order to remove the volatile reactants and products. The homogeneous catalyst system remains in the reactor throughout the experiment. A constant liquid volume in the reactor under steady conditions is achieved by providing enough sparging capacity.

Cross-metathesis of *cis*-2-butene with ethylene in the continuous flow reactor gives propylene (Fig. 4a). Homo-metathesis of *cis*-2-butene leads to the formation of *trans*-2-butene (Fig. 4b).

(a) Cross-metathesis transformations in the continuous flow reactor



(b) Homo-metathesis transformations in the continuous flow reactor

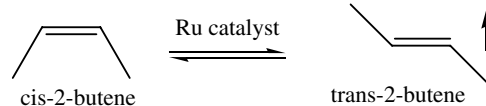


Fig. 4. Metathesis reactions in the continuous flow reactor.

Several important factors contribute to the observed catalyst deactivation. One of them involves the terminal olefin inhibition with accumulation of the product containing a terminal double bond [5]. Another component of deactivation is catalyst decay, leading eventually to complete and irreversible loss of catalytic activity. Use of the continuous flow reactor allows for propylene removal immediately after its formation and thus substantially reduces the catalyst inhibition by terminal olefin. Therefore, continuous flow reactor studies make it possible to practically separate the inhibition effect from authentic catalyst degradation.

Ru-methylidene and Ru-alkylidene are two key catalytic intermediates in cross-metathesis reaction systems [14]. Ru-methylidene could exist in the presence of ethylene or terminal olefins. On the other hand, only Ru-alkylidene could be formed in the presence of an internal olefin. To study the longevity of the two key forms of the catalytic species, namely, Ru-methylidene and Ru-alkylidene in a realistic reaction environment, we exposed the catalyst **1** to ethylene in the continuous flow reactor before feeding *cis*-2-butene. The results are presented in Fig. 5.

In the above experiments, the catalyst **1** (60 ppm Ru) in 20 mL of pentadecane was treated with a flow of ethylene/nitrogen (1:1) at 40 °C and 85 psi for different periods of time (“delay” in Fig. 5) before the addition of *cis*-2-butene. Cross-metathesis starts only when both ethylene and *cis*-2-butene are present in the mixture, so the approximate duration of the catalyst exposure to ethylene could be readily seen in the graph by noting the time when propylene appears in the vapor.

The area under propylene concentration curves in the graph represents the total turnover number (TON) throughout the catalyst life and is a measure of catalyst efficiency for each run. Turnover numbers clearly decline with increasing catalyst exposure to ethylene (Fig. 5). Further, the rate of the propylene formation at any given time could be viewed as a measure of the catalyst activity at that time. The decreasing percentage of propylene in vapor after reaching a peak activity attests to continuous loss of reactivity with time for all runs (Fig. 5). Since the product inhibition component of the reactivity loss is minimized by continuous removal of propylene, it is assumed that the observed activity at any time correlates predominantly with the amount of the active catalyst. Fig. 5 reveals that the peak activities of the pre-exposed to ethylene catalysts are similar to the observed catalyst activities in the reference cross-metathesis run (curve #1) at the corresponding “delay” times. This comparison clearly indicates that the loss rate of active catalyst due to pre-exposure to ethylene matches the catalyst decay in the productive cross-metathesis environment.

Another representation of the above statement is shown in Fig. 6. The corresponding areas for a 210 min “ethylene pretreatment” test (curve #3) and the portion of the reference run (curve #1) starting at 210 min are comparable. Accordingly, the pretreated catalyst has been deactivated close to the level attained over the same time period in the reference cross-metathesis run. The relatively small area difference for these two experiments could be due to the presence of additional, although minor, deactivation pathways.

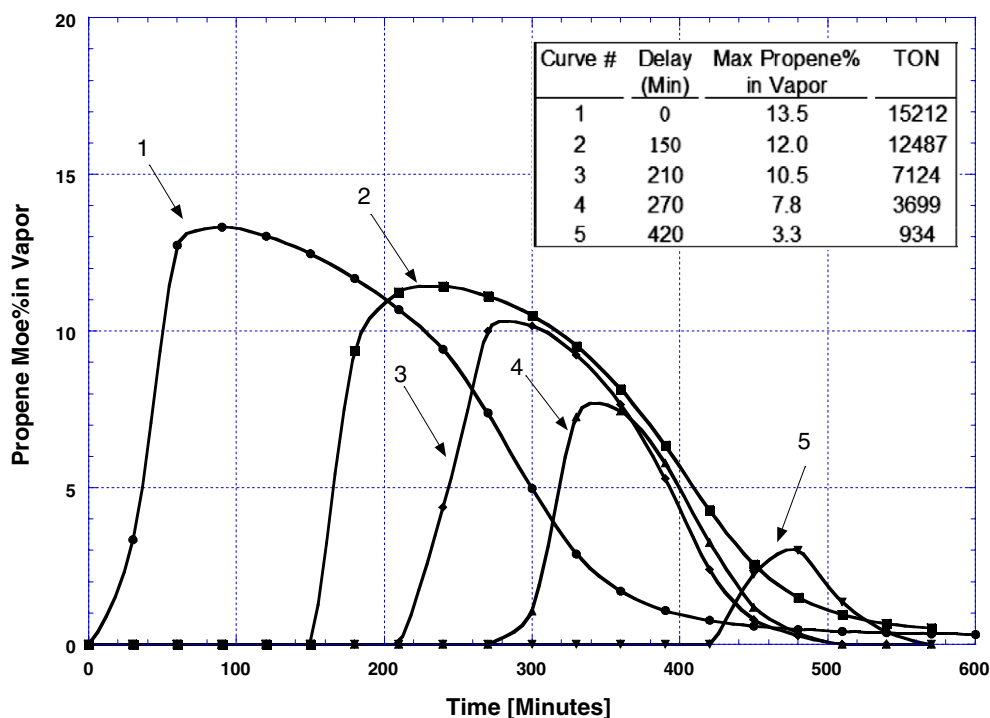


Fig. 5. Pretreatment of **1** with ethylene prior to charging *cis*-2-butene.

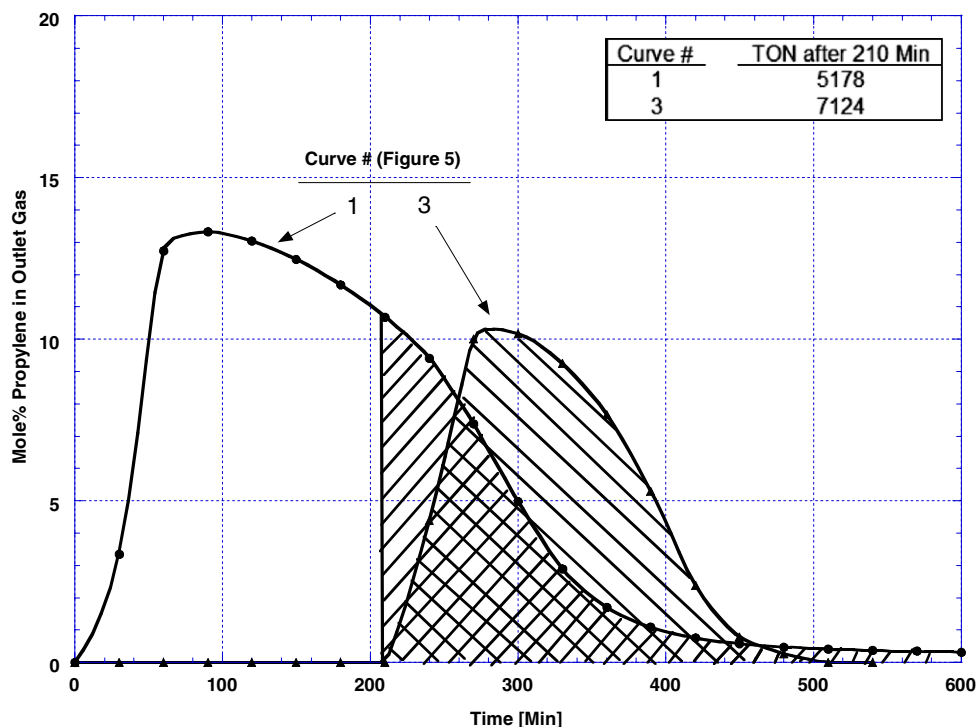


Fig. 6. Propylene formation in the ethylene pretreatment test (curve #3) vs. regular cross-metathesis run (curve #1).

Based on prior studies, the methylidene is expected to accumulate in cross-metathesis reactions and will be present at relatively high concentrations [5]. This is consistent with the continuous flow reactor results presented above because in both cross-metathesis and catalyst exposure to ethylene, methylidene is the prevalent catalytic species governing the catalyst life. In fact, limiting the catalyst species

to the alkylidene intermediate should lead to a direct increase in catalyst life. However, formation of every molecule of the cross-metathesis product requires generation of the methylidene in the catalyst cycle.

Generation of methylidene species by delaying the *cis*-2-butene feed while exposing the metathesis catalyst to ethylene revealed that the methylidene life and stability was

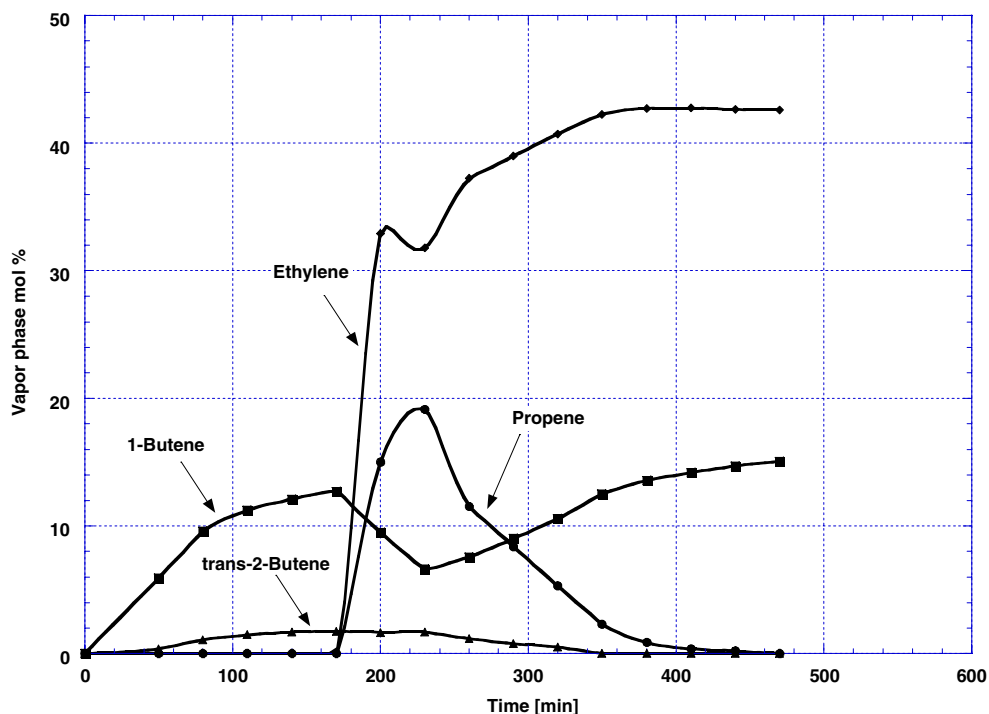


Fig. 7. Pretreatment of the $(\text{PCy}_3)_2\text{Cl}_2\text{Ru}=\text{CHPh}$ catalyst with *cis*-2-butene (internal olefin) prior to charging ethylene to initiate cross-metathesis.

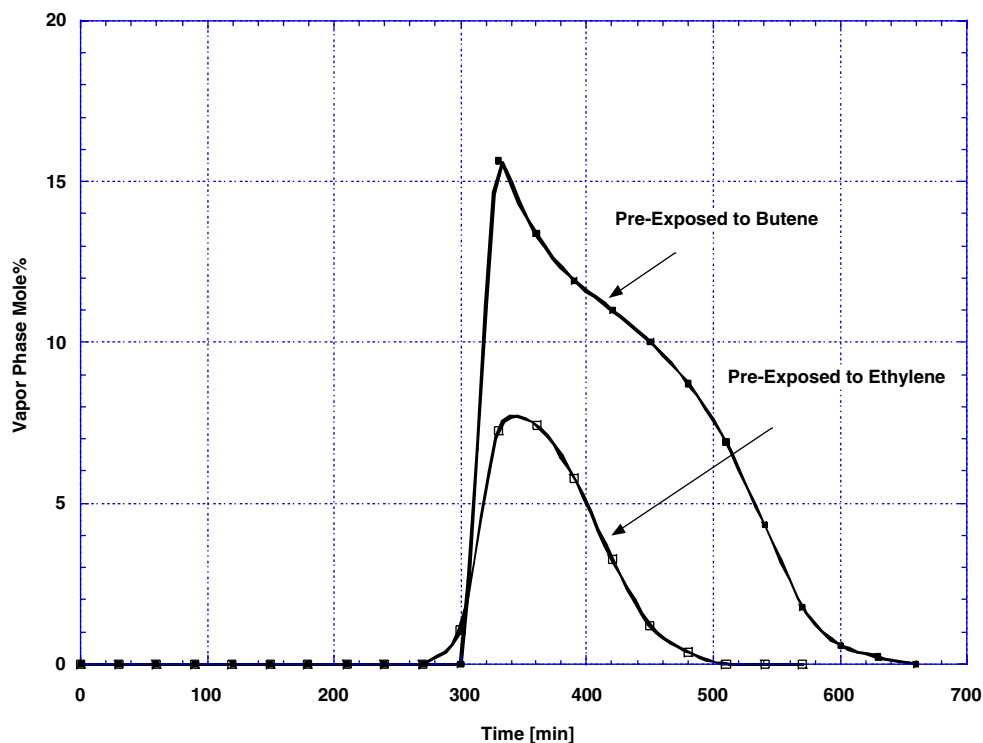


Fig. 8. Comparison of catalyst pretreatment tests with ethylene and *cis*-2-butene.

comparable to that of the overall catalyst life in cross-metathesis. This suggested a prediction that the isolated alkylidene would exhibit a significantly higher stability and lifetime. This was confirmed as discussed in the following.

The continuous flow reactor run exposing the metathesis catalyst to *cis*-2-butene prior to feeding ethylene is shown in Fig. 7.

The presence of the alkylidene in the reaction mixture for more than 5 h, resulting in steady formation of *trans*-2-butene (see Fig. 4), is conspicuous on the graph in Fig. 7. Also, it is readily observed that a flow of ethylene initiates robust cross-metathesis activity even though the catalyst remained in the reaction environment for 3 h in the form of alkylidene.

Fig. 8 depicts the propylene formation profiles for two runs in which the catalyst has been pre-exposed to either ethylene or *cis*-2-butene for about the same period of time. The areas under the curves reflect the corresponding turnover numbers, which are 3700 and 12 500 for the ethylene and *cis*-2-butene pre-exposure tests, respectively. Thus, the superior stability of the alkylidene versus the methyldene is evident.

4. Conclusions

The continuous flow reactor is a viable and efficient tool for the study of homogeneous catalysis processes, in particular, metathesis. Ethylene pretreatment of the catalyst **1** prior to cross-metathesis in the continuous flow reactor shows a direct correlation with catalyst deactivation. On

the other hand, pretreatment of the catalyst **1** with *cis*-2-butene shows no significant change in the catalyst activity. All tests mimic realistic reaction environment.

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Appendix A. Supporting information

Tables of GC data for the performed tests are included in the supporting information. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jorganchem.2006.08.031.

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