Copolymerization

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Mechanism-Based Design of a ROMP Catalyst for Sequence-Selective Copolymerization

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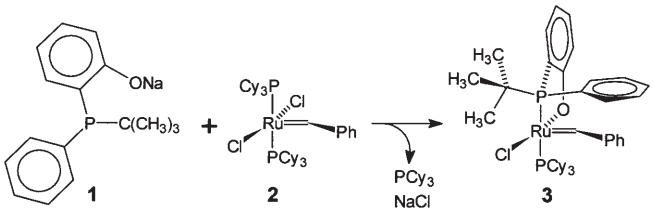
We report here the mechanism-based design of a ring-opening metathesis polymerization (ROMP)[1] catalyst which preferentially assembles a mixture of cyclooctene and norbornene into an alternating copolymer. While there have been reports of regular copolymerizations, highly selective examples are uncommon outside of free-radical polymerization, with the 1:1 alternating copolymers of ethylene and carbon monoxide,[2] or of epoxides and carbon dioxide,[3] being perhaps the most prominent examples. Given that the exemplary functional characteristics of biopolymers, for example, structural or catalytic functions in polypeptides, information storage and transmission in polynucleotides, and molecular recognition in polysaccharides, derive ultimately from sequence-selective copolymerization of simple monomer units, one can presume that synthetic polyolefins, as high-performance materials, would be substantially enhanced if even simple sequence-selective copolymerizations could be achieved routinely. Treating regular copolymerization more generally as a problem in metal-catalyzed organic synthesis, one sees that the issue is not stereoselectivity, or even regioselectivity. We seek to introduce into polymerization catalysts the element of chemoselectivity, which is the most basic kind of selectivity in organic synthesis. We encode the sequence information in the catalyst itself, and in this present study succeed in the most primitive, two-component, alternating sequence of ring-opening metathesis copolymerization.

Phosphine ligand **1** was prepared by sequential alkylation and arylation of phenyldichlorophosphine with *t*BuMgCl and *ortho*-methoxyphenyllithium, isolation by careful distillation, cleavage of the methyl ether by BBr_3, and then deprotonation with NaH. Reaction of one equivalent of **1** and $[(Cy_3P)_2RuCl_2(=CHPh)]$ (**2**, Scheme 1) resulted in phosphine exchange,



Scheme 1. Synthesis of the chemoselective ROMP catalyst **3**. Cy = cyclohexyl.

followed by elimination of NaCl. A similar approach has been reported by Hoveyda and co-workers for the preparation of a tethered, second-generation metathesis catalysts.[4] The resulting carbene complex **3** was purified by column chromatography under rigorous exclusion of oxygen, and checked by ^1H and ^{31}P NMR spectroscopy, as well as ESI-MS, to confirm that a single compound was prepared. Importantly, no other carbene species was present (analytical details and further information on the synthesis of **1** and **3** can be found in the Supporting Information). Polymerization of norbornene, cyclooctene, and mixtures thereof, together with 0.05 mol% catalyst, were conducted under dry N_2 at room temperature in either dichloromethane or cyclooctene as solvent. In experiments with cyclooctene as solvent, the norbornene is consumed quantitatively after 17 h. If a less-coordinating solvent, such as CH_2Cl_2, is used, then norbornene is consumed much more rapidly, with phenomenological rates comparable to those observed with catalyst **2** under the same conditions. The resulting polymer was isolated by removal of solvent at 0.01 mbar pressure until no further weight loss was seen. In copolymerizations with **3**, the weight of the dry polymer corresponded to the weight of norbornene, plus up to one equivalent of cyclooctene. The polymer samples were characterized by ^1H and ^{13}C NMR spectroscopy (Varian Gemini 300 MHz for ^1H, and 75.4 MHz for ^{13}C; $CDCl_3$) and gel

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permeation chromatography (PL-GPC-220, 1,3,5-trichlorobenzene, 180 °C, PLgel 10 μm column) with refractive index and viscometry detection calibrated against polyethylene standards. Reference polymer samples were prepared analogously with $[(Cy_3P)_2RuCl_2(=CHPh)]$ (**2**) for comparison. The ^{13}C resonances were assigned with the help of group equivalents, which gave good predictions for the homopolymers. The relaxation time was set to $t_2 = 5$ s so that reliable integrations could be taken from the ^{13}C NMR spectra.

While the ordinary ruthenium carbene complex **2** polymerizes both norbornene and cyclooctene efficiently, complex **3** shows almost no reactivity with cyclooctene alone under the conditions of the experiment, but is nevertheless as active (qualitatively) as **2** in ROMP of norbornene. More interesting is the behavior with respect to copolymerization. Polymerization catalyzed by **3** in cyclooctene with various amounts of norbornene proceeds until the norbornene is exhausted and then stops, but the resultant polymer ($M_w \approx 10^6$, $M_w/M_n \approx 5$) contains increasingly long stretches of alternating copolymer as the ratio of norbornene to cyclooctene decreases. GPC analysis indicates that the polymer is not a physical mixture of the homopolymers of norbornene and cyclooctene. Both the viscosity and refractive index traces show a single, smooth, monomodal peak at the same retention time, which is significant because norbornene homopolymer would not appear in the latter trace, its refractive index being coincidentally the same as that of the 1,3,5-trichlorobenzene solvent. Moreover, the ^{13}C NMR spectra (Figure 1) of the homopolymers of norbornene and cyclooctene, as well as the copolymers with various ratios of the two monomers, demonstrate that alternate incorporation of cyclooctene and norbornene is preferred for complex **3** but not for ROMP catalyst **2**.

Catalyst **2** in norbornene/cyclooctene mixtures forms predominantly norbornene homopolymer until the norbornene is exhausted, and then proceeds to homopolymerize cyclooctene. As the norbornene is increasingly dilute, the ^{13}C NMR signals arising from its homopolymer disappear because of the increasing preponderance of cyclooctene polymer. Catalyst **3**, on the other hand, displays an increasing preference for the production of the alternating copolymer as the amount of norbornene, relative to cyclooctene, is decreased, with about two-thirds of the olefinic linkages in the copolymer comprising the alternating stretches in the best cases seen so far. Preliminary results for the negative control with a symmetrical analogue of **3** having two *tert*-butyl groups instead of one phenyl and one *tert*-butyl show that the symmetrical catalyst **4** (see Supporting Information for synthesis and characterization) homopolymerizes norbornene well and cyclooctene poorly. No alternating copolymer is formed in the negative control for mixtures of norbornene and cyclooctene.

The design concept for **3** derives from our earlier mechanistic work on olefin metathesis. Secondary deuterium isotope effects, measured in the gas phase, indicated that the structure of the rate-determining transition state for the metathesis reaction catalyzed by the first-generation ruthenium catalyst was a metallacyclobutane.[5] Computational work from our own research group,[6,7] as well as others,[8,9]

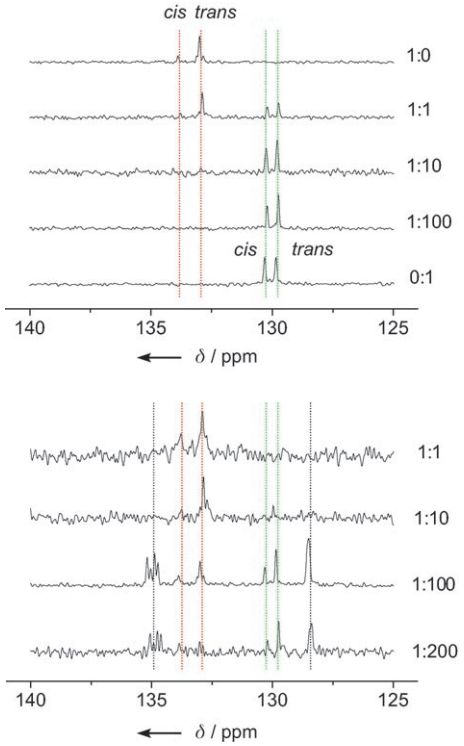
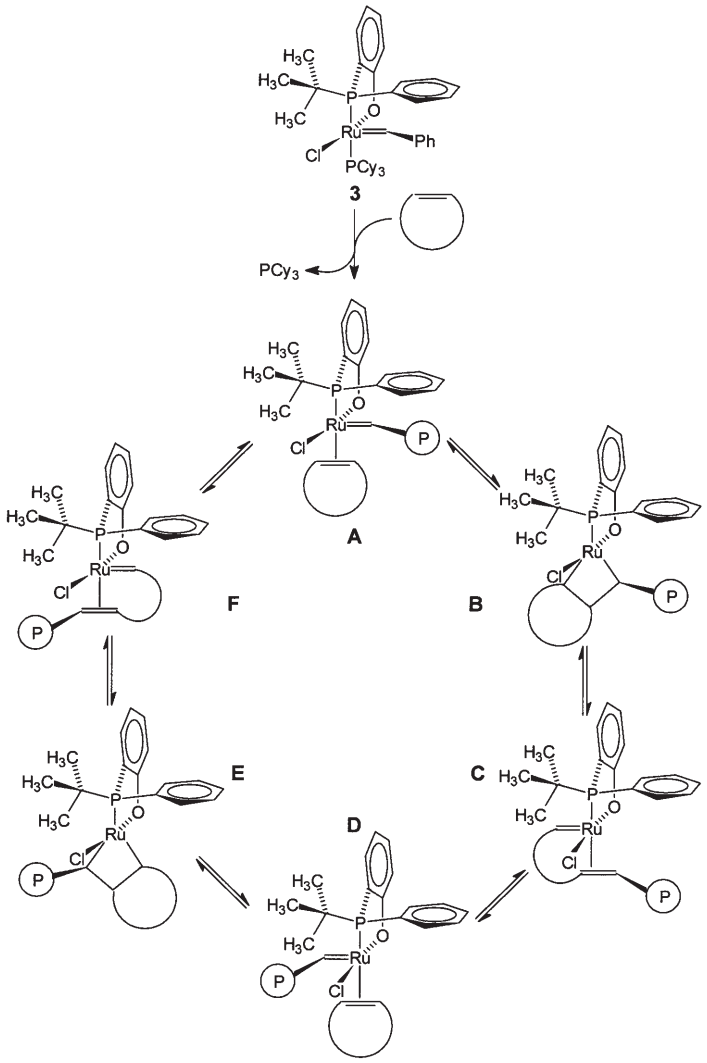


Figure 1. Olefinic regions of the ^{13}C NMR spectra of the polymer samples prepared from norbornene/cyclooctene mixtures at different mole ratios. The top spectra show results for catalyst **2**; spectra for catalyst **3** are at the bottom. The olefinic carbon resonances for the ring-opening metathesis polymer of norbornene are marked with red dotted lines, the resonances for the polymer from cyclooctene are marked in green. The black dotted lines mark the resonances for the alternating copolymer. There are at least two partially resolved signals in the high-field resonance, assigned to the end of the double bond derived from cyclooctene (*cis* and *trans*), whereas there are four signals in the low-field resonance, assigned to the end derived from norbornene. One presumes that, not only the *cis* and *trans* configuration of the double bond, but also the *cis* and *trans* configuration of the next double bond, causes the splitting.

however, found minima at the metallacyclobutane structure. Experimental observation of the olefin π complex by Snapper and co-workers[10] and a ruthenacyclobutane intermediate by Romero and Piers[11] supported the DFT calculations. In our computations, we did find, however, that the rate-determining transition step for olefin metathesis by **2** was a rotation of the tricyclohexylphosphine ligand in a metallacyclobutane structure,[6] which is in fact consistent with the isotope effect studies, the other computational work, and the solution-phase observations. For a degenerate metathesis reaction, the rotation is required by microscopic reversibility. If the rotation were, however, to be prevented, and, furthermore, the phosphine were to bear two different substituents, then the mechanism would require that the active site would swing back and forth with each productive metathesis step between two distinct states in a motion reminiscent of a windshield wiper. The two sites can be made sterically or electronically different enough so that chemoselectivity in an appropriate mixture of two substrates can be achieved. Scheme 2 depicts the catalytic cycle for ROMP of cycloalkenes by **3**. The carbene moiety in the propagating species can lie either on



Scheme 2. Catalytic cycle for ROMP of cycloalkenes with catalyst **3**.

the right, as in species **A**, or on the left, as in species **D**. Molecular modeling studies indicate that **A** is much less sterically crowded than **D**, which breaks what would have been a degeneracy in the more usual case of a rotatable phosphine or a phosphine with at least two identical substituents.

If we consider the productive direction around the catalytic cycle for ROMP (**A**→**B**→**C**→**D**→**E**→**F**→**A**) with each step reversible, it would be expected that the forward reaction **A**→**B**→**C** would only occur if there is a large strain release in the **B**→**C** step so that the intermediate metallacyclobutane **B** would preferentially partition forward to **C** rather than return to **A**. On the other hand, the reaction **D**→**E**→**F** should proceed in the forward direction for any cycloalkene, strained or not, because the metallacyclobutane **E** should partition forward to the sterically less hindered carbene **F**. Consequently, the intermediate **A** can only incorporate norbornene into the growing chain, but intermediate **D** can take either norbornene or cyclooctene, the probability being largely determined by the relative concentrations. Accordingly, dilute concentrations of norbornene in a cyclooctene solution yields a largely 1:1 alternating copolymer.

Complex **3** is the simplest implementation of the general concept. It is a dual-site catalyst in which one site shows chemoselectivity and the other not, which, together with a concentration difference between the two monomers, constitutes the bare minimum case for an alternating copolymerization. Selectivity at both sites would eliminate the need for widely divergent concentrations of the two monomers, but even such a restriction can be easily accommodated by slow addition of one monomer into a neat solution of the other. One might expect similar behavior from an unsymmetrically substituted N-heterocyclic carbene complex reported by Mol and co-workers,[12] but the complex did not even polymerize norbornene well, presumably because of the much-too-large adamantyl substituent. One should note that a similar example of a dual-site catalyst can be found in the C_1- or C_s-symmetric metallocene catalysts for syndiotactic polypropylene.[13] In these systems, the activated catalyst alternately selects for the *re* and *si* face of the single monomer, propylene, but there is no documented case where selective copolymerization has been reported with these catalysts. The alternating selectivity has other potential uses as well. Selective oligomerization and selective ring-closing metathesis should be achievable with the new, designer catalyst architecture. Furthermore, while the designed structure demonstrates the target selectivity, no optimization of the catalyst has been attempted yet. Further work in this direction is underway.

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