Against Ring Walking In Catalyst Transfer Polymerization

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Abstract

The widely-accepted theory that catalyst transfer polymerization (CTP) proceeds through an associative intermediate between M(0) catalysts and the π-system of a conjugated polymer in order to give chain-growth kinetics is flawed. Consensus on this theory has been established over a number of years, allowing weaker and weaker studies to be accepted as evidence of this phenomenon. In this paper I present an alternative theory: that ring-walking is likely not real, certainly not important, and has hindered the progress of CTP.

Introduction

Many living polymerizations have been developed since anionic polymerization of polystyrene in 1956,[1] but cataylst transfer polymerization (CTP) is the only living technique that applies to conjugated polymers.
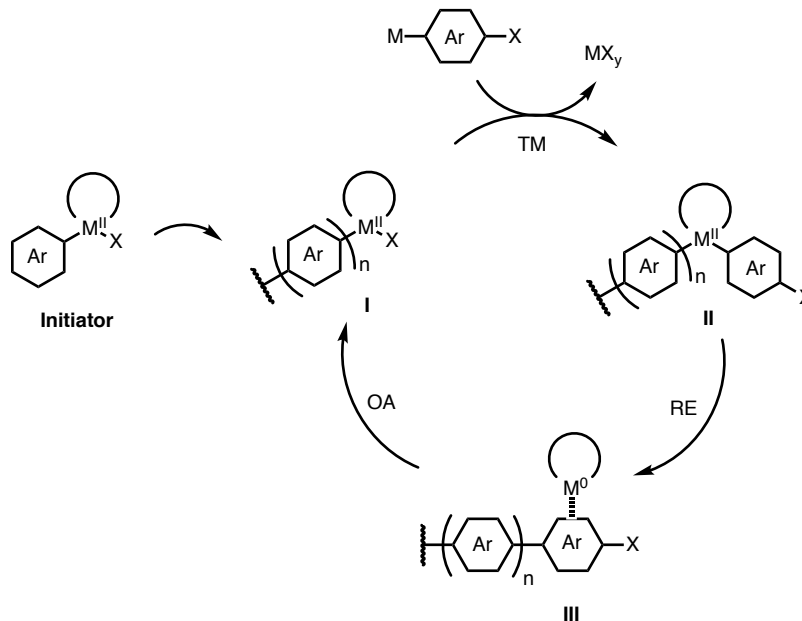

Figure 1: Generalized mechanism of CTP, including π-association. TM, RE, and OA refer to transmetallation, reductive elimination, and oxidative addition, respectively.

The commonly accepted mechanism of CTP is shown in figure 1, where M can represent any metal used for cross-coupling reactions (e.g. MgX,[2] Li,[3] B(OH)$_2$,[4] etc.). The cata-

lyst is most commonly nickel, though palladium[5,6] is occassionally used. The ligand is typically some bidentate phosphine like bis(diphenylphosphino)ethane,[7] but N-heterocyclic carbenes[3,6] and diimine-based ligands[8] have also been used.

The first CTP system reported was the polymerization of 3-hexylthiophene using Ni(dppp)Cl$_2$.[9,10] Ni(dppp) and Ni(dppe)-based catalysts continue to be the most common examples seen in the literature. They are bulky enough to prevent side-reactions and provide reasonable rates of reductive elimination (RE), while also leaving enough room to allow rapid transmetallation (TM). However, the biggest reason these catalysts originally caught on is that they make regioregular P3HT from a combination of 2 and 5-activated 3-hexylthiophene monomers. This occurs because these phosphine ligands are just bulky enough to allow rapid TM with the 5-activated thiophene, but virtually no TM can occur at the 2-position in THF at RT. This somewhat arbitrary "ability" of dppe and dppp is a large part of what makes these ligands the most commonly used in CTP.

What gives CTP living and not step-growth kinetics is that the catalyst has a major preference to oxidatively insert on the same chain it reductively eliminated from. There are some competing theories as to why this is the case, such as decreased rate of oxidative addition (OA) on activated monomers, but the common consensus is that the Ni(0) complex strongly associates with the π system of the conjugated polymer. That is, the catalyst is effectively stuck to the chain until it reaches the end, at which point it oxidatively inserts and the cycle continues. However, this model is at best incomplete.

CTP as a category is quite broad, and in the literature describes both living and non-living polymerizations. For a living polymerization like RAFT, ATRP, or anionic, the active site that reacts with monomers cannot dissociate from the chain it is attached to. By contrast, the catalyst in CTP is not guaranteed to oxidatively insert on the same chain it reductively eliminated. It can instead dissociate and oxidatively insert somewhere else. As the probability of OA approaches 1, the polymerization is considered to be living. As it approaches 0, the kinetics are step-growth. When this probability is somewhere in the middle, the polymerization can be thought of as a step-growth mechanism where instead of joining one monomer at a time, a geometric distribution of monomers is added.

Discussion

In this paper, I will be elaborating on an alternative model: that CTP is successful in the case that the rate of OA of the catalyst into the adjacent C-X bond is so fast that it is essentially diffusion controlled. There may be a weak π-association that slows dissociation by some amount, but the key to optimizing CTP systems is focus on rate of OA while limiting side-reactions like disproportionation.

The term "controlled" is often used to refer to would-be CTP reactions that don't quite work. Even though the CTP field is quite extensive, the amount of systems that truly "work" is quite limited. By "work," I am referring to a polymerization system that follows living kinetics almost perfectly. This does not just mean that the molecular weight of the product decreases with increasing catalyst:monomer ratio, but also that the polymer distribution is Poisson and has quantitative

end group control. To date, the only reported CTP systems with this feature are 3-alkyl thiophenes, selenophenes, tellurophenes,[7] and dialkoxybenzenes.[11] The only other CTP system with end group control is 9,9'-dialkylfluorene,[4] which requires a 3-coordinate Pd catalyst, and appears to be limited to low molecular weights. Figure 2 on page 3 shows the four monomers that we can truly say are controlled (top row), as well as 8 examples of monomers that are purported to be able to by polymerized in a "controlled" manner, but are not actually.
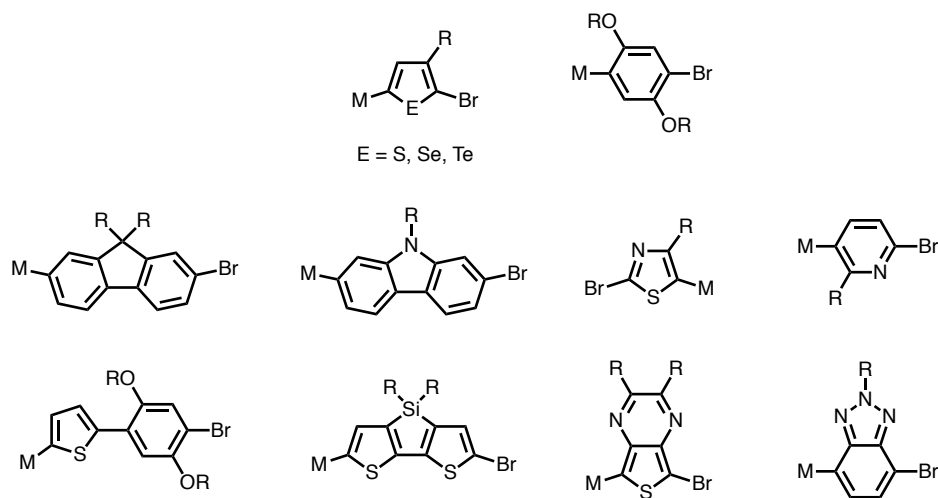

E = S, Se, Te

Figure 2: Some reported CTP monomers

The most commonly accepted evidence of CTP system being "controlled" is that $\bar{X}_n$ has an inverse relationship with catalyst to monomer ratio. That is, higher concentrations of catalyst give lower molecular weights, if nothing else in the system is changed. This is not predicted by a step-growth model, in which one would expect higher conversions and therefore higher $\bar{X}_n$ at any given point in time. However, this is not necessarily the case in CTP. In systems that use an NiX_2 initiator, which includes the majority of studies, two equivalents of the metallated functional group are reacted together to initiate a chain. This immediately causes an imbalance in the proportionality of metallated and halide functional groups, which in a step-growth mechanism would also cause lower molecular molecular weight. This is especially important to consider with CTP, where catalyst:monomer ratios are typically much lower than nonconjugated systems (typically 10 to 100). Alternatively, if disproportionation is the dominant termination mechanism (figure 3 on page 4), we again see the same initiation effect but have the stacked effect of higher catalyst concentrations giving higher rates of chain termination. These two mechanisms are sufficient to explain why the molecular weight is affected by the catalyst concentration, even when it is clear that the polymerization is uncontrolled.

Ignoring for a moment systems that don't work, it's important to understand why the canonical system does. For example:

1. *Question:* Why are nickel catalysts used?
   Conventional: Ni(0) coordinates much better to alkenes than Pd(0) and other common cata-

lysts, which stabilizes the π-association complex.

Alternative: Ni(0) has a much higher rate of oxidative insertion.[12]

2. *Question:* Why use bidentate phosphine ligands with bulky substituents?
   Conventional: Bulky substituents increase the rate of reductive elimination, so that the cycle doesn't get "stuck" at complex **II** (figure 1). Bidentate ligands leave an open side for Ni(0) to coordinate to the polymer.
   Alternative: Bulky substituents discourage disproportionation, the dominant pathway for Ni-based catalysts with small ligands. Bidentate ligands greatly increase the rate of oxidative addition.

3. *Question:* Why does this work for 2-bromo-3-hexylthiophene but not other monomers like 2-bromo-9,9'-dialkylfluorene?
   Conventional: The π-association complex is weaker between Ni(0) and fluorene.
   Alternative: Oxidative addition is much faster on 5-membered rings than it is on 6-membered rings, in addition to being more activated.

4. *Question:* Why are n-type polymers so difficult to polymerize?
   Conventional: Lower electron density in π-system weakens association complex
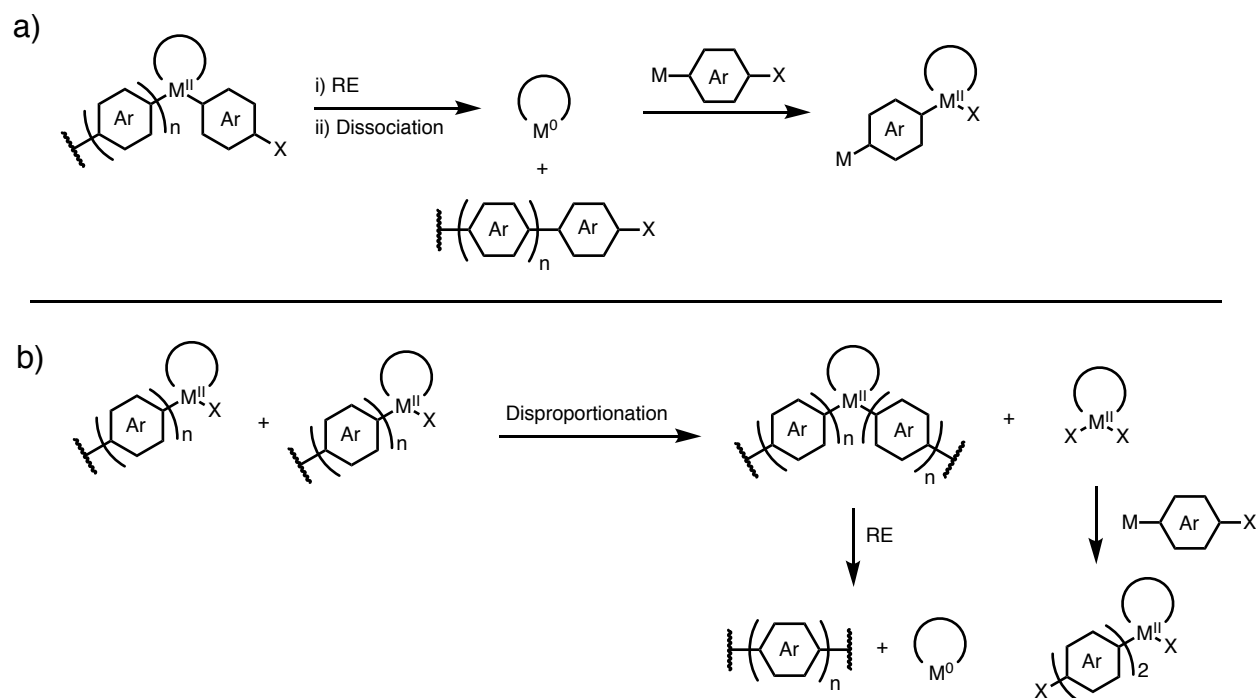   *Alternative:* Lower electron density decreases the rate of oxidative addition.

a)

b)

Figure 3: CTP chain terminations. a) Chain dissociation, b) Disproportionation

Whether or not the π-association complex exists *in-situ* is less important than whether or not it is vital to designing a CTP system. While it may be possible to gain some insight into the

relative importance of diffusion vs. π-association by investigating chain dissociation as a function of solvent viscosity, as a function of increasing molecular weight of the catalyst (e.g. by using a polymeric ligand), or even measuring chain dissociation as a function of reaction completion rate (i.e. towards the end, the chains will be large and diffuse slower), these studies will not provide much insight into what a functional CTP system actually looks like.

The first piece of evidence against the π-association complex is that it is fleeting. If complex **III** (figure 1) is indeed effectively stuck to the chain, it shouldn't matter how long it "waits" before oxidatively inserting. However, while the polymerization of 2-bromo-3-hexylthiophene (5-position metallated) with Ni(dppe) proceeds with living kinetics, the same is not true when Br is swapped for Cl (2-chloro-3-hexylthiophene).[7] In this case, the catalyst has a non-negligible chance of dissociating from the chain and starting a new one. This can only be explained by the Ni(0) complex having a significant rate of dissociation.

Further evidence for the π association complex is less than compelling. For example, Koeckelberghs[13] showed in 2014 that the presence of a thienothiophene (TT) monomer functionalized with two alkylthio side-chains was able to completely disable a simple Kumada coupling with a Ni(dppp)-based catalyst. While this is said to be due to a very strong π-association complex the TT monomer forms with Ni(0), it is much more easily explained by the Ni(0) coordinating to the two sulfur atoms on either side of the monomer which form a very strong bidentate ligand. The paper mentions that this must not be the case because 3-alkylsulfanylthiophene monomers have been successfully polymerized,[14] the statement ignores the fact that these earlier monomers do not have their sulfur atoms arranged in such a way that they can chelate the metal.

Furthermore, there is no evidence that the π-association complex is so strong that it effectively disables the catalyst. If this were the case, Ni(0) catalysts that "fall off" during polymerization should not be able to start new chains through oxidative insertion on other monomers, but this phenomenon is seen extensively for systems that aren't fully living. This paper should therefore not be seen as evidence for the π-association complex.

Recently, Kennepohl[15] was able to crystallize the complex between Ni[1,2-bis(di-tert-butylphosphino)ethane] and bithiophene, which was said to be direct evidence of the π-association complex during these polymerizations. This study proves that this complex is one enthalpy-minimized conformation these two molecules can have, this fact was never really disputed. Not only was the ligand changed to boost the electron density of the catalyst, the result was achieved at low temperature, and in the absence of any C-X bonds. While this is undoubtedly an impressive feat of chemistry, the result has little relevance to CTP.

The most compelling evidence of an association complex is through small-molecule experiments, wherein there are competing inter and intra molecular pathways to different products (figure 4). When the intramolecular pathway is shown to be dominant, the a π-association complex is assumed.[6,16,17] McNeil reported in 2015 that these experiments do not necessarily prove an intramolecular pathway.[18] The study explains that in many cases, the prevalence of the difunctionalized product is not necessarily due to an intramolecular catalyst transfer, but instead simply due to the monofunctional product being more reactive to oxidative insertion than the starting material (e.g. path B is favoured over path C). This alternative pathway can be differentiated experimentally

by quenching the experiment at low conversions, showing a buildup of the monofunctional product before they react later on to give only difunctional product. By contrast, a true intramolecular mechanism does not at any point have a significant concentration of monofunctional product.
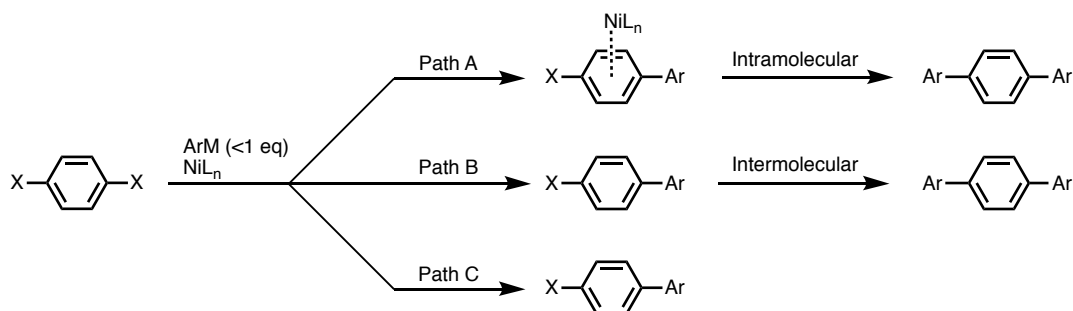

Figure 4: Small molecule experiment showing inter and intramolecular pathways. Ratio of difunctionalized to monofunctionalized starting material is taken to be evidence for intramolecular pathway, which ignores path B.

In 2018, McNeil reported an improved version of this kind of experiment, where the small molecule is replaced by a polymer with a catalyst already inserted at one end.[11] This experiment is illustrated in figure 5. When the same experiment is repeated with the H/Br polymer and separate catalyst, the tolyl-capping is not observed. While extended ring-walking is one way to explain this result, this explanation contradicts some basic CTP principles. Firstly, while it may be possible that ring-walking consistently occurs across one or two monomers, the catalyst association complex would have to be very strong in order for it to cross an entire polymer with > 90% yield. The contradiction is that the same result is observed for both Ni(dppp) and Pd(IPr), but Pd(IPr) does not polymerize 3-hexylthiophene in a living manner.[6,19] If the Pd(IPr) association complex is not strong enough to reliably cross a single monomer unit, it cannot also be possible that it is strong enough to traverse an entire polymer. The fact that the experimental results do not distinguish between the living (Ni(dppp)) and non-living (Pd(IPr)) catalysts is an issue.
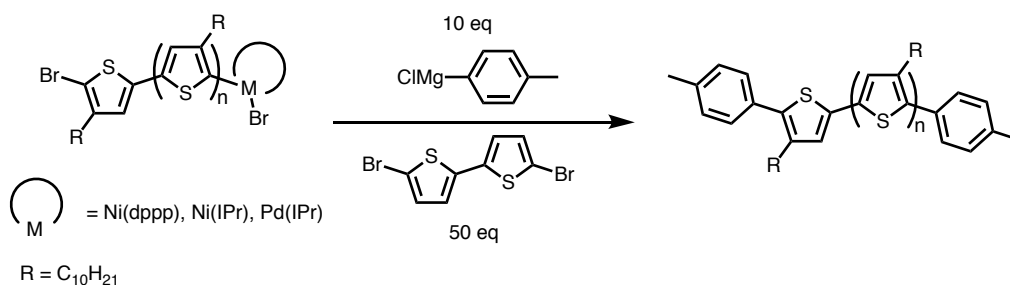

Figure 5: Ring-walking experiment. The excess of 5,5'-dibromo-2,2'-bithiophene is thought to act as an M(0) scavenger, implying that the product can only be made through ring-walking.

Furthermore, the MALDI spectra in the SI of the paper indicate significant amounts of H/H end groups after the reaction. This means that the tolyl Grignard reagents are metathesizing with

the Br end-groups of the polymer, which must mean that they must also be metathesizing with some of the Br atoms on the M(0) scavenger. This is likely the source of some of the chaotic resultant polymer distributions by MALDI. More importantly, it is unexplained why 10 eq of p-tolylmagnesium chloride is used in these experiments. If the catalysts remain associated with the polymer after the first reductive elimination, the result should be the same if 2 eq of Grignard is used instead.

The pilot reactions also overlook an important termination mechanism: disproportionation. Consider a 2017 study by McNeil,[8] in which small-molecule reactions were run with a nickel-diimine catalyst. By gas chromatography, the difunctional product was present in 75% yield and the monofunctional product was barely observed. This was taken to be strong evidence of an associative intermediate, but 75% is quite low. It's worth asking what happened to the other 25%. Because the products were quantified by GC, disproportionation products would have been unidentified. In the same paper, a second competition study was done between brominated thiophene and terthiophene with a 3-hexylthiophene Grignard. A MALDI of the products of this experiment shows a number of unidentified peaks between 400 and 600 Da, at least some of which are plausibly disproportionation products. This is further supported by the fact that a number of these unidentified peaks appear to be about 85 Da apart, roughly the weight of one thiophene unit. In terms of molecular weight distributions and end groups, polymerizations that fail by disproportionation can be virtually indistinguishable from those where dissociation is dominant. This has generally been overlooked in the literature.

This perspective on CTP implies that a great number of monomers must be effectively impossible to polymerize in a controlled manner without a total redesign, such as a catalyst that has an appendage that ensures a mechanical linkage between the polymer chain and catalyst (e.g. by using a large crown ether). This primarily includes monomers with a large distance between the metallated site and the carbon halide bond on the opposite side, but also monomers with carbon-halide bonds that are deactivated to a degree where no catalyst is capable of oxidatively inserting at the required rate while also meeting all other criteria (e.g. no side reactions, fast reductive elimination). It also implies that there is a hard limit on the diversity of monomers that any one catalyst can polymerize in a controlled manner. Because the monomers themselves are an important part of the steric bulk required to prevent disproportionation reactions, large monomers requires small ligands and vice versa. None of these points are denied by the π-association model, but they are important to consider regardless.

1 Summary

A summary is best represented in bullet points, as it is the result of a number of discrete observations:

- Dispersity is a poor and unintuitive measure of polymer heterogeneity. Furthermore, size exclusion chromatography (SEC) systems commonly used to measure conjugated polymer

distributions mischaracterize samples as having significantly higher dispersities due to diffusive broadening (e.g. Đ of 1.02 measured as 1.10), which makes it much more difficult to say by SEC characterization that one polymerization is controlled and another is not.

- A CTP system should only be described as controlled if the products are approximately Poisson distributed and have quantitative end-group control. These systems comprise a small fraction of CTP literature. These systems are not chain-growth polymerizations, but are instead best visualized as a combination of step-growth and chain-growth.

- Successful CTP systems work because it is statistically unlikely for the catalyst to diffuse away from the polymer before it oxidatively inserts on the chain end. This does not necessarily require the existence of a π-association complex. Future studies may gain some insight into these competing explanations by measuring the likelihood of dissociation as a function of solvent viscosity, or by increasing the molecular weight of the catalyst without changing its electronics (e.g. by using polymeric appendages of different molecular weight).

- If it is determined that the chain termination mechanism in a CTP system is primarily dissociation, the system can be improved by increasing the rate of oxidative addition. This can be accomplished largely by decreasing the size of the ligand, less so by increasing the electron density of the ligand.

- The primary mechanism of chain termination in CTP systems already using small ligands (e.g. 1,2-bis(diethylphosphino)ethane) is disproportionation. This has been overlooked in the literature because the products these systems generate are very similar to those where the catalyst dissociates. This causes researchers to move in the opposite direction of the solution (i.e. by concluding that the π-association must be too weak), when the correct course of action is to increase bulk around the catalyst.

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