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ARTICLE TYPE

The Effect of $LiNTf_2$ on the Propagation Rate Coefficient of Methyl Methacrylate

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In the present work we use accurate Pulsed Laser Polymerization (PLP) to measure the influence of various concentrations of lithium bis(trifluromethane) sulfonamide ($LiNTf_2$) on the propagation rate coefficient of methyl methacrylate (MMA). We also perform ^{1}H-NMR analysis to evaluate the effect of $LiNTf_2$ on poly(MMA) stereochemistry. Additionally, we perform high-level quantum-chemical calculations to model the interactions between Li^+ and the MMA monomer and propagating radical. Across a broad range of concentrations, $LiNTf_2$ only slightly increases the isotacticity of the resultant poly(MMA). However, a significant increase in the propagation rate coefficient was noted upon addition of $LiNTf_2$. The magnitude of this increase was found to be dependent on the $LiNTf_2$ concentration and temperature. Theoretical calculations reveal the complexities associated with Lewis acid-mediated stereocontrol. On the basis of this theoretical work, we suggest that the potential stereocontrol afforded by Lewis acids is being hindered by their action as propagation catalysts though non-stereoselective binding modes.

Introduction

The objective of polymer synthesis is to control the assembly of macromolecules to facilitate precise adjustments to their structure and properties. Since they were first employed in radical polymerization over 50 years ago, Lewis acids have been used to alter monomer reactivity and control various aspects of polymer microstructure. Arguably, the most exciting function of these additives is their influence on main-chain stereostructure (tacticity), which is usually poorly regulated in their absence. The integration of effective stereocontrol with living radical polymerization would revolutionise polymer synthesis by providing a convenient radical-based route to precisely controlled stereoregular polymers. Over the last few decades, much pioneering work has sought to realise this goal,[1] which has been described as the *"holy grail"*[2] of radical polymerization.

More than 50 years ago, Bovey examined the effect of low concentrations of zinc chloride ($ZnCl_2$) on the radical polymerization of methyl methacrylate (MMA), noting no significant stereochemical effects.[3] Otsu et al. later reported that employing high concentrations of $ZnCl_2$ slightly increases the isotacticity of the resulting poly(MMA).[4] Subsequently, Matsumoto et al. utilised magnesium bromide ($MgBr_2$) in the radical polymerization of MMA, also noting a slight increase in isotacticity, particularly on the solid surface of the partially insoluble $MgBr_2$.[5] More recently, Okamoto and co-workers successfully synthesised isotactic rich polymers of various methacrylates,[6] α-(alkoxymethyl)acrylates,[7] acrylamides,[8, 9] and methacrylamides[10, 11] by employing rare earth metal triflates ($M(OTf)_3$, M = Sc, Y, Yb, Lu) as stereocontrol agents.

Unfortunately, even with these novel additives, the stereocontrol achieved in most systems is modest, compared with the high stereoregularity of polymers synthesised via anionic or coordination polymerization. Although reasonable isotactic control has been reported for acrylamides[8, 9] and to a lesser extent methacrylamides,[10,11] this stereocontrol has not yet been replicated for other polar monomers, such as methacrylates, acrylates, vinyl esters, vinyl amides and vinyl halides. For instance, the best isotactic control reported for the radical polymerization of MMA is an isotactic triad fraction (*mm*) of 22%,[6] compared to *mm* > 99% via anionic polymerization (albeit under much more demanding reaction conditions).[12] In Lewis acid-mediated radical polymerization, polymer stereochemistry is highly dependent on the reaction conditions (i.e. the identity and concentration of the Lewis acid, ligands, monomer and solvent). Unfortunately, the development of more effective stereocontrol is hindered by a poor understanding of the interactions between the Lewis acid and growing polymer terminus that regulate stereochemistry.

Stereocontrol Mechanism?

In contrast to anionic and coordination polymerization, stereochemistry in radical polymerization is not determined by the orientation of incoming monomer, but by the relative orientation of the terminal and penultimate side-chains of the polymer terminus during propagation (scenario (1) in Scheme 1). The pro-chiral polymer terminus can rapidly interconvert between *pro-meso* and *pro-racemo* conformations, which in the absence of stereocontrol agents, are nearly degenerate and similarly reactive towards propagation. Thus, radical

polymerization is generally not stereoselective and affords atactic polymer. Since it was first proposed by Matsumoto,[5] the literature mechanism of isotactic regulation has been frequently cited,[1, 13, 14] although its complexities and limitations are neither widely appreciated nor well understood. The proposed mechanism of isotactic regulation is via the formation of a kinetically labile chelate complex between the terminal and penultimate side-chains of the polymer terminus and the Lewis acid (scenario (2a) in Scheme 1).[5] It is assumed that such coordination imparts an energetic preference for *meso* propagation; thus leading to isotactic regulation. However, this simplistic mechanism conceals a layer of complexity and so potential modes of failure.

Firstly, this mechanism assumes terminal-penultimate complexes prearrange the polymer terminus exclusively into *pro-meso* configurations. However, helical polymer conformations could potentially accommodate such chelate complexes in *pro-racemo* configurations, which might competitively propagate and reduce the level of isotactic control (scenario (2) in Scheme 1). [15] Secondly, this mechanism implicitly assumes that the terminal-penultimate complex is formed selectively over other monomer/polymer adducts. However, non-stereoregulating complexes could form and compete with this terminal-penultimate complex to reduce the effectiveness of this stereocontrol. Specifically, coordination of the Lewis acid to the terminal side-chain and incoming monomer (scenario (3) in Scheme 1), exclusively to incoming monomer (scenario (4) in Scheme 1) or to the main polymer chain would not be expected to impart significant isotactic control. Such complexes could readily accommodate both *pro-meso* and *pro-racemo* conformations, as the terminal and penultimate side-chains are not coordinated simultaneously. These conformations would be expected to rapidly interconvert (via rotation about the terminal chain bond) and possess similar stability and reactivity; thus leading to non-stereoselective propagation of the parent complexes. Most of these complications are unique to radical polymerization and are unlikely to be pertinent in synthetic intermolecular radical addition reactions, where coincidently Lewis acids have been utilised to achieve very high diastereoselectivities.[16]

Catalysis?

Intriguingly, in addition to influencing polymer tacticity, Lewis acids can catalyse radical homopolymerizations[3, 6, 17] and alter sequence distribution and composition in copolymerizations.[18-20] Remarkably, some novel Lewis acids facilitate the radical polymerization of 1-alkenes,[21] presumably by catalysing propagation and limiting the degenerative hydrogen transfer reactions which normally impede the production of high polymer. Indeed, such catalysis was first predicted by Clark on the basis of *ab initio* calculations carried out over 25 years ago,[22] prior to being confirmed experimentally by Michl et al.[21] Clark attributed these rate accelerations to electrostatic effects, suggesting such catalysis does not require covalent interaction between Li^+ and the C=C bond and so can be observed even at long distances (> 4.5 Å) when the cation is fully solvated. [23, 24]

Although Clark's theoretical work provides a satisfactory rationale for the catalysis reported in 1-alkenes, the origin of propagation rate enhancement in polar systems, where Lewis acid coordination presumably occurs at the conjugated side-chain rather than the C=C bond, is more speculative. Simultaneous increases in the initial polymerization rate and the polymer's molecular weight confirm that Lewis acids are catalysing propagation, although the extent of these increases is uncertain. Initial polymerization rate is a function of monomer and initiator concentrations and rate coefficients for initiator decomposition, propagation and termination. However, extracting propagation rate coefficients from initial polymerization rate measurements can be problematic as Lewis acids are known to catalyse the thermal decomposition of radical initiators and can even catalyse the addition of 'unconventional' initiators, such as triplet oxygen (O_2[3]), to alkenes.[21] Although Pulsed Laser Polymerization (PLP) can be used to extract very accurate propagation rate coefficients in a relatively model free manner, to date we are unaware of any PLP studies of the effect on Lewis acids on the kinetics of radical polymerization.

Scheme 1 Stereoselectivity during radical polymerization of a mono substituted alkene (CH_2=C(CH_3)R), in the absence (1) and presence (2)-(4) of a Lewis acid (LA): scenarios (2)-(4) illustrate different positions of Lewis acid coordination to the polymer terminus and incoming monomer

Objectives

Undoubtedly, there is a lack of understanding of Lewis acid-mediated polymerization, particularly the mechanistic aspects of stereoselectivity, yet this information is crucial improving stereocontrol. As the mechanism of isotactic regulation is fairly speculative, it is difficult to suggest modifications that could improve existing stereocontrol, which leads to trial and error experimentation rather than rational design of stereocontrol agents. Clearly it would be desirable to clarify the mechanism underlying isotactic regulation; unfortunately doing so would require discriminating between scenarios (2)-(4), which is difficult or even impossible using experimental techniques. Although ^{1}H and ^{13}C NMR has been employed to examine the relative binding affinity of polymer and monomer to Lewis acids,[6] such techniques cannot readily observe coordination to the polymer terminus (such as scenarios (2) and (3) in Scheme 1) because of the very low concentration of radical chain-ends in the polymerising medium. Moreover, it is not clear if the most thermodynamically stable complex would also be the most reactive towards propagation.

This is a situation where theoretical chemistry can provide meaningful insight into the underlying interactions occurring at the polymer terminus, which is inaccessible directly from experiments. In the present work we aim to assess a new potential stereocontrol agent - lithium bis(trifluromethane) sulfonamide ($LiNTf_2$) - in the radical polymerization of MMA and examine its effect on polymerization kinetics using appropriate PLP-SEC analysis. Concurrently, we aim to examine the importance of the proposed binding scenarios (2)-(4) with state-of-the-art quantum-chemical calculations. To the best of our knowledge this is the first time PLP has been used to accurately quantify the effect of Lewis acids on propagation kinetics and additionally the first time theoretical calculations have been used to clarify the mechanisms underlying stereoselectivity in such systems.

Methodology

Materials

Methyl methacrylate (MMA) (Aldrich, 99%) was passed through a column of basic alumina to remove the inhibitor. Benzoin (Aldrich, 98%) was purified by recrystallization from hot ethanol. Lithium bis(trifluoromethanesulfonimide) ($LiNTf_2$) (Aldrich, 99.9%), 2-methyl-4'-(methylthio)-2-morpholinopropiophenone (Aldrich, 98%), Chloroform-*d* (*D* = 99.8%, Cambridge Isotope Laboratories), Methanol (GC grade, Merck), tetrahydrofuran (THF) (GC/GPC grade stabilized with BHT, Honeywell Burdick & Jackson) were used as received.

Experimental Procedures

To determine accurate propagation rate coefficients of MMA in the presence of $LiNTf_2$, we performed PLP-SEC analysis. Particular attention was given to IUPAC-recommended consistency criteria to demonstrate the reliability of the k_p values. [25] Accordingly, the ratio of inflection point positions, L_1/L_2, was found to be close to 0.5, and k_p was shown to be independent of pulse energy, of pulse repetition rate, and of photoinitiator identity and concentration. To measure k_p, solutions of MMA (~ 1.5 mL) containing $LiNTf_2$ (0 - 1.50 M) and photoinitator (1-2 mM) were transferred to a quartz vial and each sealed with a rubber septa. Each sample was purged with nitrogen and then subsequently placed into a temperature controlled sample holder. The temperature was measured directly inside the sample and allowed to reach thermal equilibrium. Polymerization was then initiated by laser pulsing (at 355 nm, ~ 20 mJ/pulse) at repetition rates of up to 25 Hz. During polymerization, the temperature inside the sample was logged and the average temperature during the polymerization was used when determining Arrhenius parameters. The temperatures used were 10, 25°C and 40°C and the variation during an experiment did not exceed 3°C. After polymerization, the sample was poured into methanol to precipitate the polymer generated. Subsequently, excess methanol was decanted and the samples were dried in a vacuum concentrator. The molecular weight distribution of the samples was analysed using (THF-phase) SEC and selected samples were analysed by ^{1}H-NMR (in Chloroform-*d*) to determine triad tacticities. A more detailed description of the experimental procedure, including PLP traces and can be found in the Electronic Supplementary Information.‡

Theoretical Procedures

Discriminating between the binding scenarios proposed above is very difficult, if not impossible via experimental techniques; therefore, we have employed quantum chemistry to determine binding affinities from first principles. Specifically, we used the high-level composite *ab initio* G3(MP2)-RAD method in conjunction with an ONIOM inspired approximation[26, 27] and M06-2X[28] thermochemistry to obtain accurate gas-phase energies. The SMD[29] method was used to model implicit solvation effects using methyl propanoate as the solvent to mimic bulk MMA. Similar methodology has been previously shown to predict accurate values for the kinetics and thermodynamics of a wide range of radical reactions, including propagation.[30-32] We should emphasize that the focus of the present theoretical work is to determine the relative binding affinities of very similar chemical species; thus a large degree of intrinsic error cancelation would be anticipated. All standard *ab initio* molecular orbital theory and density functional theory (DFT) calculations were carried out using Gaussian 09[33] and Molpro 2009[34] software packages. A detailed description of all the computational procedures, conformational searching, as well as full set of obtained results can be found in the Electronic Supplementary Information.‡

Experimental Results

To investigate the effect of $LiNTf_2$ on MMA polymerization kinetics we performed PLP-SEC analysis at varying concentrations and temperatures. An overlay of two typical PLP-SEC traces is shown in in Fig. 1, which illustrates the increases in the molecular weight inflection points upon addition of $LiNTf_2$. The average k_p values across temperature range of 10°C to 40°C and for a ratio of $LiNTf_2$ to MMA of 0 to 0.15 are illustrated in Fig. 2. These results clearly illustrate that k_p increases with increasing $LiNTf_2$ concentration. More detailed data included laser flashing rates, inflection points and conversions can be found in Tables S1-S4 in the Electronic Supplementary Information.‡

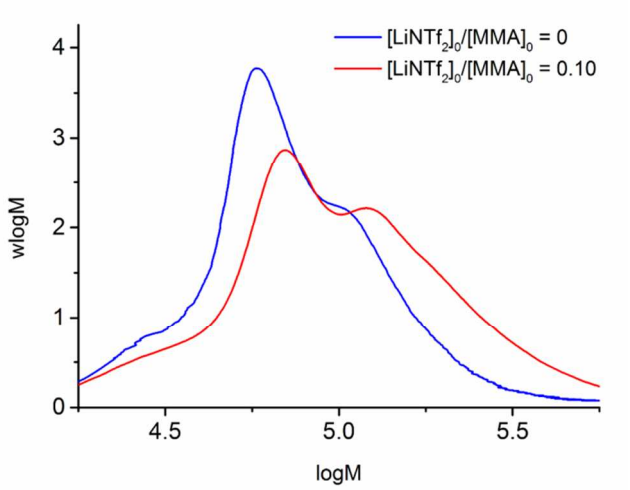

Fig. 1 PLP-SEC traces run at 10 Hz and 40 °C in the presence and absence of $LiNTf_2$.

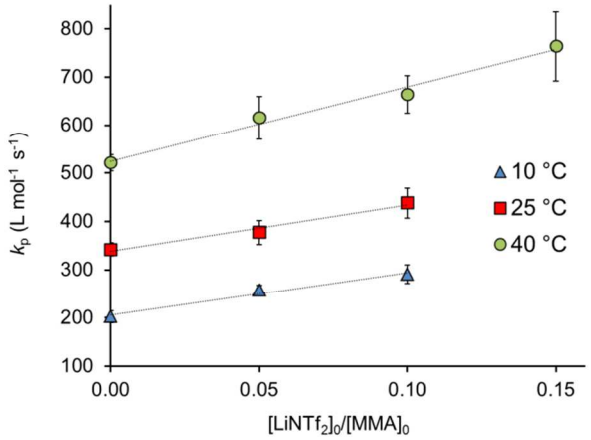

Fig. 2 Average k_p values in the presence and absence of $LiNTf_2$ determined by PLP-SEC. Error bars indicate 95% confidence intervals.

Table 1 MMA tacticity in the presence and absence of $LiNTf_2$

$[LiNTf_2]_0/[MMA]_0$	temp (° C)	triad tacticity (%)			diad (%)
		mm	*mr*	*rr*	*m*
0	10	1.7	26.8	71.4	15.2
0.05	10	1.8	29.5	68.7	16.5
0.10	10	2.2	29.2	68.5	16.9
0	25	2.3	27.5	70.1	16.1
0[a]	25	2.2	29.6	68.2	17.0
0.05	25	2.6	30.4	67.0	17.8
0.10	25	2.9	31.5	65.6	18.7
0	40	3.0	31.7	65.3	18.9
0[a]	40	3.2	31.6	65.2	19.0
0.05	40	3.9	33.4	62.7	20.6
0.10	40	3.7	33.2	63.1	20.3
0.10[a]	40	3.8	32.9	63.3	20.3
0.15	40	3.7	34.2	62.1	20.8

[a] Indicates a duplicate sample was tested.

Unfortunately, the addition of $LiNTf_2$ had little effect on poly(MMA) tacticity across a range of concentrations and temperatures (Table 1). The reasonably consistent tacticities of duplicate samples demonstrates the high precision of this analysis. Disappointingly, across all the conditions studied in this work, the isotactic triad fraction (*mm*) of the resultant poly(MMA) never exceeded 4%.

Theoretical Results and Discussion

From the experimental work undertaken, it is clear that $LiNTf_2$ increases the propagation rate coefficient of MMA, although there is no significant effect on polymer stereochemistry. The presence of propagation catalysis suggests that $LiNTf_2$ is interacting with the pendant ester groups of the polymer terminus and/or incoming monomer during propagation, though the absence of isotactic control indicates that these interactions are not stereoselective. These observations raise several questions regarding the interactions occurring at the polymer terminus: What coordination mode is the most favoured for polar monomers? Is there an electronic preference for coordination to a particular ester moiety within a polymerization? What is the relative binding affinity of monomer, the polymer terminus and the polymer chain? Which scenario (2) – (4) is responsible for the experimentally observed catalysis and perhaps most crucially, why does $LiNTf_2$ have no significance effect on polymer stereochemistry?

To address these questions we have used accurate quantum chemistry to clarify the nature of interactions between Li^+ and the polymer terminus. To perform accurate calculations on these complex systems we need to make some simplifications. Thus, only relatively small oligomeric models are considered so that high levels of theory can be used. These models are too small to allow for a quantitative first principles prediction of tacticity, which would require at least tetramer transition state models. Instead, our objective here is to use theory as a tool to understand the interactions underlying stereoselectivity. We aim to determine if the literature mechanism of isotactic regulation is applicable in the present system and identify the underlying cause of the low stereoselectivity. Results of this computational investigation are now presented and discussed in turn.

Binding Modes

Prior to considering more complex systems, the coordination of Li^+ to MMA monomer was rigorously examined. The coordination of 'hard' Lewis acids, such as Li^+, would be expected to occur predominantly at the O-acyl group of the ester side-chain. Nevertheless for completeness, Li^+ coordination to each ligation site of MMA monomer was investigated: The C=C bond, the O-acyl group and O-methoxy group of the ester and both ester heteroatoms simultaneously in a chelate arrangement (O,O'-bis).

In total six discrete Li^+ monomer complexes were identified: s-trans and s-cis conformations of the O-acyl, O-methoxy and O,O'-bis coordination modes (Fig. 3). Interestingly, no stable minima with Li^+ complexed directly to the C=C bond were found and attempts to optimise reasonable starting geometries afforded O-acyl or O-methoxy bound complexes. The relatively short C-Li distances (< 2.6 Å) in the s-trans O-methoxy complex are suggestive of an interaction between the cation and the C=C bond. Similar screening was performed on unimeric MMA radical Li^+ complexes to investigate the possibility of a direct C radical Li^+ interaction rather than coordination to the ester moiety. No stable minima with Li^+ complexed directly to the radical were found and attempts to optimise reasonable starting geometries afforded similar O bound complexes. Given the large electronic preference for O-acyl coordination in all systems

considered, other sites of ligation were excluded henceforth.

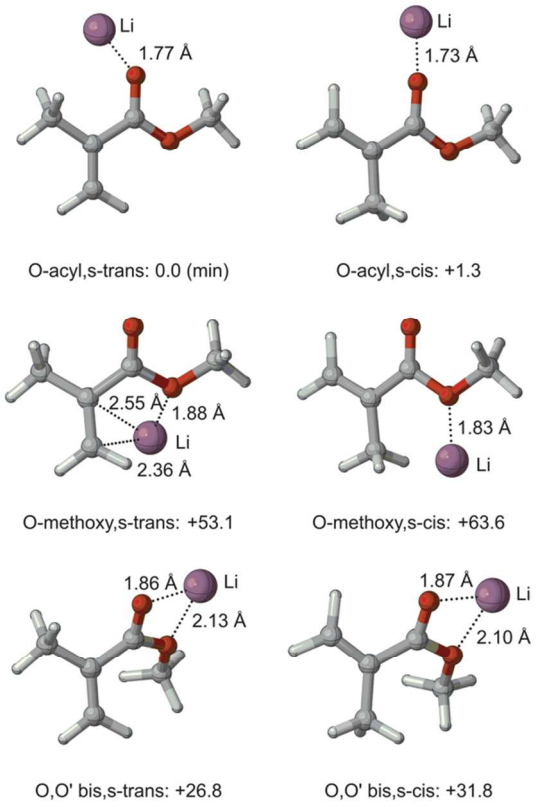

Fig. 3 Optimised geometries and relative free energies (kJ mol^{-1}) of different coordination modes of MMA monomer to Li^+. Contact distances of coordinating atoms are also shown.

Ester Binding Selectivity

It is well known that Lewis basicity is dependent not only on the functional identity of the coordination site but also its extended substitution.[35, 36] In a bulk MMA polymerization, there are 3 functionally distinct methyl ester moieties: those of the monomer, the radical terminus and polymer side-chains. To examine if there was an underlying electronic preference for coordination to a particular ester group, binding enthalpies of various unimeric models (Fig. 4) were calculated as Li^+ was progressively solvated by MMA monomer (Table 2). In the presence of a similarly sized organic ligand, tetrahydrofuran (THF), Li^+ forms a four coordinate complex.[37] Thus, consistent with previous theoretical work,[24] coordination numbers up to four were considered in the present study. As NTf_2^- is weakly coordinating anion, it is expected to be readily displaced from Li^+ by monomer in solution and so was not included in these calculations.

These calculations suggest that there is a modest enthalpic preference for Li^+ coordination to the terminal (radical) ester moiety, which is reduced as the cation is progressively solvated by monomer. The conjugated radical is stabilised by coordination of Li^+ to the ester moiety, with the radical stabilisation energy (RSE) increasing relative to the corresponding uncoordinated species by between 5 to 8 kJ mol^{-1}, depending on the extent of cation solvation (see Table S7 in Electronic Supplementary Information). These results suggest that saturated ester moieties are more basic than comparable α,β-unsaturated esters, which is consistent with previous experimental[35] and theoretical studies.[36] Although these results could be indicative of a modest preference for coordination to the ester group of the polymer terminus, this preference is too modest and the models considered too simplistic to allow for any conclusions regarding the position of Li^+ coordination.

Table 2 Relative binding enthalpies of unimeric MMA models to $Li^+(Mon)_n$.

Model[a]	Rad	Chain	Mon[b]
$n = 0$	0.0 (min)	+ 3.9	+ 10.9
$n = 1$	0.0 (min)	+ 3.6	+ 8.5
$n = 2$	0.0 (min)	+ 5.0	+ 8.3
$n = 3$	0.0 (min)	+ 4.4	+ 4.6

[a] Here n is the number of solvating MMA monomer units. [b] Note that because Mon is also used to solvate Li^+, the product complex can be written as $Li^+(Mon)_{n+1}$. Binding enthalpies were calculated at 25 °C and are reported in kJ mol^{-1}.

Fig. 4 Unimeric models of the MMA polymer terminus (Rad), polymer chain (Chain) and the structure of MMA monomer (Mon).

Polymer Binding Selectivity

To account for the isotactic control of Lewis acids, a chelate terminal-penultimate complex is frequently invoked. [1, 13, 14] Generally, chelate complexes that are composed of five or six membered rings are particularly stable compared with analogous monodentate complexes. However, chelation of adjacent ester groups on a poly(MMA) chain will form a relatively large eight membered ring. Although such large rings are usually enthalpically disfavoured because of transannular strain, all conformations of the highly substituted poly(MMA) chain are strained on the basis of optimal van der Waals radii and bond angles. Thus, in contrast to comparable unsubstituted systems, the enthalpic cost of prearranging poly(MMA) chains into chelating conformations should be minimal. Unfortunately, chelation can occur not only at the polymer terminus, but at any point along the polymer chain. If there is no selectivity for coordination at the polymer terminus, then competitive chelation of the penultimate side-chain in 'mid-chain' complexes will inhibit terminal-penultimate complexation. To examine these aspects of selectivity, the relative binding affinity of dimeric models of the polymer terminus and a polymer mid-chain segment were calculated, as Li^+ was progressively solvated by monomer.

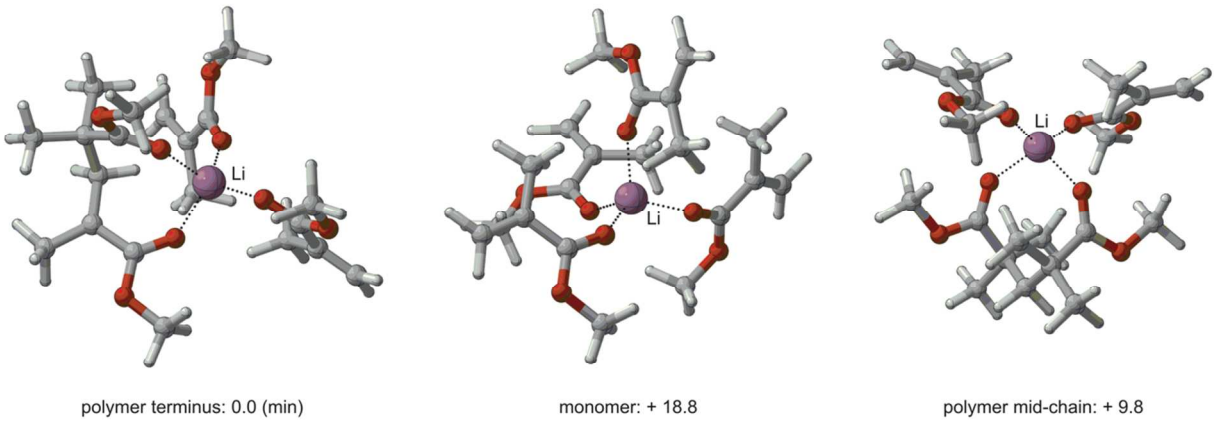

Fig. 5 Optimised geometries and relative binding free energies (kJ mol^{-1}) of $Li^+(Mon)_2$ to models of the polymer terminus, mid-chain and monomer.

These results are summarised in Fig. 5, which illustrates the structures and the best estimates (using a fully solvated cation) of the relative binding affinities (see Table S10 of Electronic Supplementary Information for more detailed results). The calculated thermochemistry is consistent with qualitative arguments presented above, as the energy required to organise the model polymer terminus and polymer segment into precursor conformations for chelate binding is small (> 4 kJ mol^{-1}). However the relatively rigid coordination geometry of these dimeric models leads to lower gas-phase binding enthalpies compared to the corresponding monomer complex. Despite these lower binding enthalpies, the more favourable binding entropies of the dimeric models results in greater overall binding affinities compared with the corresponding monodentate monomer species. There is a clear preference for chelating coordination to the model dimeric polymer terminus compared with chelating coordination to the dimeric mid-chain segment and complete solvation by monomer (Fig. 5).

We should note that the Harmonic Oscillator/ Rigid Rotor (HO/RR) approximation used in this work may overestimate binding entropies, particularly of monomer solvated complexes where rotation around the coordinate bond would probably be more accurately described as a hindered internal rotation. Although it is difficult to quantify this overestimation in the present systems, theoretical assessments of radical propagation reactions (in which the transition states possess a similarly long forming bond) have found the error associated with the HO/RR approximation is generally less than 4 kJ mol^{-1} at 298 K.[30] A more sophisticated (and more accurate) treatment of entropic effects, which would probably require molecular dynamic simulations, is beyond the scope of the present work.

Pro-meso/ *Pro-racemo* Selectivity

Given the apparent preference for coordination to the terminal and penultimate ester groups of the polymer terminus, it is now worth considering if such coordination is selective for *pro-meso* conformations, which is the implicit assumption underlying the literature mechanism of isotactic control. The various conformations of a polymer terminus can be classified as either *pro-meso* or *pro-racemo* depending on the orientation of the terminal and penultimate side-chains with respect to the backbone C_1-C_4 atoms. Considering a simplified linear (antiperiplaner, T) representation of the polymer terminus, such as is depicted in Scheme 1, it is usually assumed that the proximity of the side-chains in the *pro-meso* arrangement would result in a stronger binding affinity. However, the polymer terminus can also position the ester groups in similar proximity in *pro-racemo* arrangements by adopting helical (synclinal, $G^{\pm}$) conformations. The polymer terminus has to be at least trimeric for conformations to be classified as linear (C1-C4: T see Fig. 6) or helical (C1-C4: $G^{\pm}$ see Fig. 6) and more significantly, pro-*meso* or *pro-racemo*. To examine this selectivity, coordination of Li^+ to the terminal and penultimate ester groups of a trimeric polymer terminus was examined. Rigorous assessment of *pro-meso* / *pro-racemo* selectivity would require the calculation of the reactivity of these conformations rather than just their stabilities i.e. an explicit first principles calculation of tacticity. However, given the early position of these transition states and the similar coordination position of Li^+ in these complexes, the relative conformer energies should provide a reasonable estimate for this selectivity.

The geometries and relative energies of the lowest energy pro-*meso* and *pro-racemo* conformations of the chelated terminal-penultimate polymer complex and the parent (uncomplexed) species are illustrated in Fig 6. In the absence of Li^+, the polymer terminus preferentially adopts a linear *pro-racemo* conformation, by approximately 3.8 kJ mol^{-1}, which is consistent with the syndiotactic preference observed for MMA.[38] Chelation of Li^+ at the terminal and penultimate groups reverses this inherent preference of the polymer terminus, favouring a linear *pro-meso* conformation by 5.4 kJ mol^{-1}. If this level of selectivity was retained in the respective transition states, then the corresponding *meso* diad content (*m*) would be 90% and the isotactic triad (*mm*) content of the polymer (assuming Bernoullian statistics) would be approximately 80% at 25 °C. The results presented above suggest that the underlying assumption of the literature mechanism, namely that chelating terminal-penultimate coordination of a Lewis acid favours *pro-meso* conformations, is valid – at least in the present system.

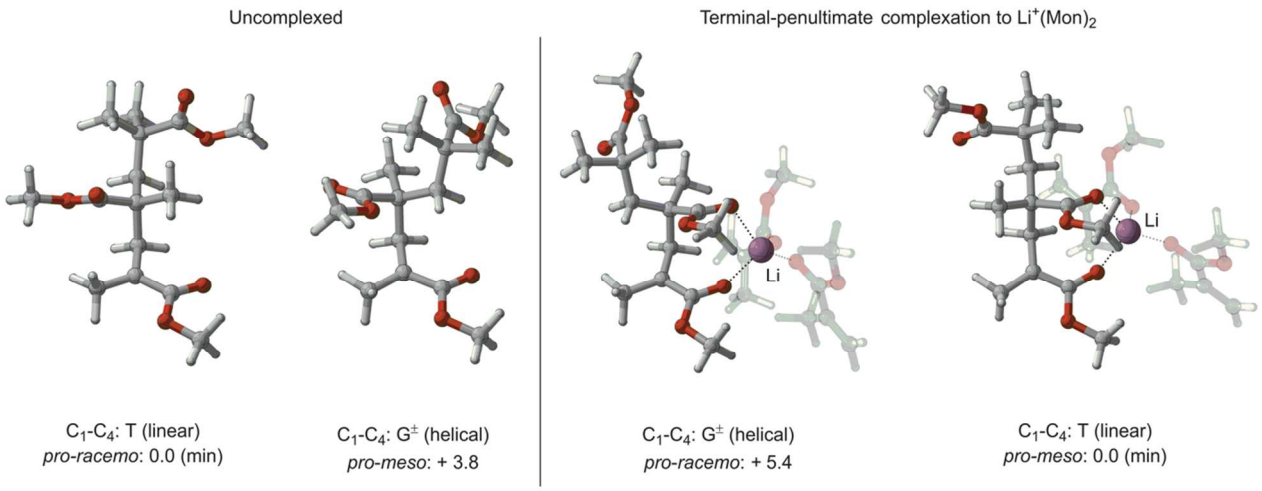

Fig. 6 Optimised geometries and relative free energies (kJ mol^{-1}) of pro-*meso* and *pro-racemo* conformations of the polymer terminus, in the absence of Lewis acid (Uncomplexed, left) and with $Li^+(Mon)_2$ complexed to the terminal and penultimate side-chains (right). Solvating monomer units on Li^+ have been made transparent for clarity.

The Origin of Propagation catalysis

Given that these calculations have demonstrated a binding affinity preference for selective *pro-meso* coordination of Li^+ to the polymer terminus, the poor level of isotactic selectivity found experimentally may initially seem surprising. However, the experimentally observed propagation catalysis indicates that the Li^+ is influencing not only the conformer energies of the polymer terminus but also its reactivity. Thus, it is necessary to consider if a thermodynamically less favourable Li^+ polymer or monomer complex is actually more reactive towards propagation and thus undermining the expected stereocontrol of the terminal-penultimate chelate complex. To investigate the position of Li^+ during monomer addition, the propagation barriers for the terminal-penultimate complex (scenario 2, Scheme 1), terminal-monomer complex (scenario 3, Scheme 1) and the monomer complex (scenario 4, Scheme 1) were calculated. Unfortunately, due to the size of these transition structures no explicit solvating monomer units were included in these calculations, with the exception of the monomer complexation pathway, where 1 solvating monomer unit was used to ensure all pathways had a consistent Li^+ coordination number (of 2).

The calculated kinetics and thermodynamics of these reactions are illustrated in Fig. 7. It should be noted that all energies in this diagram are calculated on the same absolute scale and are directly comparable. It is clear that, while the terminal-penultimate complex is the most stable, this stabilization deactivates it toward propagation to such an extent that it is kinetically disfavoured overall. At the same time, coordination to the Li^+ in the terminal-monomer and complexed-monomer pathways activates the propagation reaction. In the case of the terminal-monomer pathway, this activation is so significant that its propagation becomes the dominant pathway overall, despite the relatively high energy of the precursor complex. This terminal monomer complex is non-stereocontrolling, as it does not directly influence the relative orientation of the terminal and penultimate ester groups. Hence the kinetic favourability of this pathway explains the lack of stereocontrol in this system.

While it is clear that simultaneous coordination of Li^+ to the terminal and monomer chains catalyses propagation, the origin of this catalysis is likely a combination of multiple factors. Li^+ coordination would not only alter underlying polar effects, but our preceding calculations indicate a modest effect on radical stability as well. Additionally, the electrostatic catalysis reported by Clarke, which is based on odd electron interactions and determined by C· and Li^+ proximity, could also contribute to the observed catalysis. Thus the barriers for the reactions considered above probably reflect different contributions from conjugate polar effects, radical stability, odd-electron electrostatic catalysis, chelation and binding geometries. The most successful Lewis acids employed to date, the rare earth metal triflates, are known for their large ionic radii and high coordination numbers, properties that would probably favour a multiple chelation mechanism.

Conclusions

In the present work, we have accurately quantified the rate-enhancing effect of $LiNTf_2$ on the free radical polymerization of polar monomer (MMA) by PLP. Significant increases in the propagation rate coefficient, k_p, were observed across varying $LiNTf_2$ initial concentrations. In addition, we determined that $LiNTf_2$ is essentially ineffective, across the broad range of concentrations examined, for isotactic control in the radical polymerization of MMA (*mm* < 4% under all conditions investigated). Whilst this result is disappointing from the perspective of improving stereocontrol in free-radical polymerization, the propagation catalysis is likely to be useful in its own right to enhance other aspects of structural control. In particular, enhancing propagation relative to termination should improve controlled radical polymerization, at least with non-coordinating control agents, while enhancing propagation relative to transfer could help to suppress chain branching.

We have also examined this system in detail using *ab initio* molecular orbital theory. We find that there is significant thermodynamic preference for Li^+ binding to the terminal-penultimate groups of the growing MMA chain end, compared to

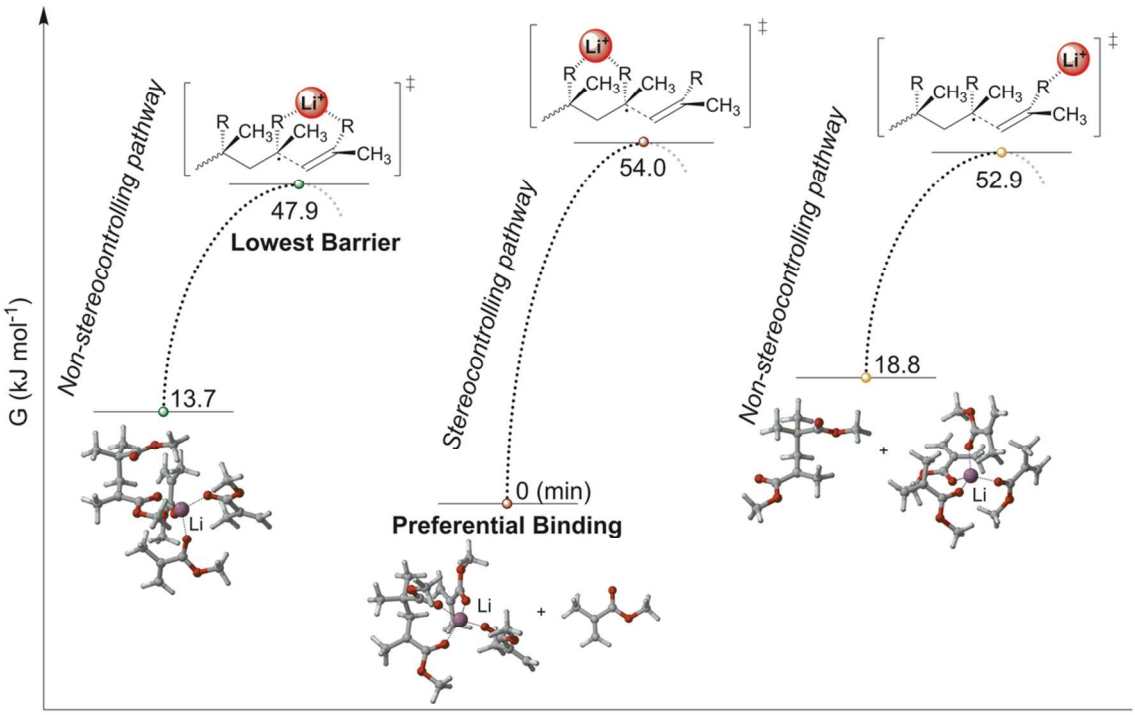

Fig. 7 Relative free energies (kJ mol^{-1}) of four coordinate Li^+ complexed polymer terminus and monomer with estimates of the propagation barriers based on two coordinate Li^+ calculations.

the main polymer chain and monomer. Furthermore this terminal-penultimate complexation of Li^+ selectively orientates these groups into the *pro-meso* configuration required for isotactic propagation, with chelated *pro-racemo* arrangements significantly higher in energy. Crucially however this significant thermodynamic preference for the "correct" binding mode for isotactic propagation fails to result in stereocontrol because of its strong thermodynamic preference. That is, this binding mode is anti-catalytic: it stabilizes the growing radical to an extent that its subsequent propagation rate coefficient is significantly reduced. Instead, propagation predominantly occurs via (pseudo)cyclization of a Li^+ bridged terminal-monomer complex. As this mode does not simultaneously bind the terminal and penultimate side-chains, no significant stereocontrol is anticipated. While this binding mode is less thermodynamically favoured than terminal-penultimate complexation, it activates the monomer toward propagation to such an extent that the overall propagation step is actually catalyzed relative to the other binding modes. On the basis of this work we suggest that strategies for effective stereocontrol need to be re-considered and reagents that simultaneously active monomer while binding to the terminal and penultimate groups offer more promise.

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Notes and references

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† Electronic Supplementary Information (ESI) available: Additional tables, figures and schemes, details of computational procedures and full set of obtained results, individual energy components and optimised geometries (in the form of Gaussian archive entries) for all species in this study. Includes a detailed deccription of the experimental methodology and PLP traces. See DOI: 10.1039/b000000x/

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$LiNTf_2$ catalyses the propagation step of methyl methacrylate radical polymerization but this catalysis hinders stereocontrol.