Polymer Chain Cleavage

International Edition: DOI: 10.1002/anie.201508531
German Edition: DOI: 10.1002/ange.201508531

Entropy-Driven Selectivity for Chain Scission: Where Macromolecules Cleave

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***Abstract:** We show that, all other conditions being equal, bond cleavage in the middle of molecules is entropically much more favored than bond cleavage at the end. Multiple experimental and theoretical approaches have been used to study the selectivity for bond cleavage or dissociation in the middle versus the end of both covalent and supramolecular adducts and the extensive implications for other fields of chemistry including, e.g., chain transfer, polymer degradation, and control agent addition are discussed. The observed effects, which are a consequence of the underlying entropic factors, were predicted on the basis of simple theoretical models and demonstrated via high-temperature (HT) NMR spectroscopy of self-assembled supramolecular diblock systems as well as temperature-dependent size-exclusion chromatography (TD SEC) of covalently bonded Diels–Alder step-growth polymers.*

Reversible covalent and supramolecular bonding systems are being employed increasingly for the generation of materials with novel characteristics such as, for example, self-healing or otherwise stimuli-responsive abilities, self-assembly into complex molecular architectures, mimicking of proteins, easily recyclable substructures, and self-immolative polymers.[1] In such dynamic systems, a thorough understanding of the numerous factors that influence the binding constants is very important.[2] Moreover, it is not only the binding characteristics of reversible ligation sites that have to be closely considered, but also processes that are less dynamic, as they may be impaired by similar restrictions. Recently, we demonstrated the significance of physical molecular properties in addition to the known chemical effects on reversible and irreversible association and degradation. It was predicted theoretically and demonstrated in diverse experiments that—due to the differences in released entropy—a mass and chain-length effect leads to favored debonding, dissociation, and degradation of heavier or longer species, and, furthermore, the intramolecular mobility (i.e., chain stiffness) also influences reaction equilibria.[3] While this "entropy effect" has so far been utilized to alter the properties of self-healing materials, by its nature it is in principle applicable to all chemically controlled reactions of macromolecular species and must be considered when small-molecule chemistry is transferred to larger systems. In light of these demonstrated entropic effects on bonding and association equilibria, an obvious question is whether, all other factors being equal, the position of a bonding or debonding site in a given molecule could affect the reaction equilibrium. To address this question, in the present work a set of experiments and calculations with a special focus on the selectivity for bond cleavage in the middle versus at the chain end was examined (Scheme 1). As a first proof of concept, we considered a highly simplified chemical model of a polymer comprising a linear string of point masses with arbitrary, yet realistic dimensions. Using standard textbook equations, we calculated the translational (ΔS_{trans}) and rotational (ΔS_{rot}) contributions to the entropy of bond cleavage in the middle and at the end of the chain under otherwise identical conditions (Table 1). Full details of the model used and the calculations are provided in the Supporting Information.

Our choice of a simplified model allowed us to consider much larger chains than would otherwise be possible, and to study the broader chemical trends on these parameters in the absence of the complicating effects of the local chemical nature of the employed ligation sites. Values of the vibrational entropy (ΔS_{vib}) and enthalpy (ΔH) were not calculated

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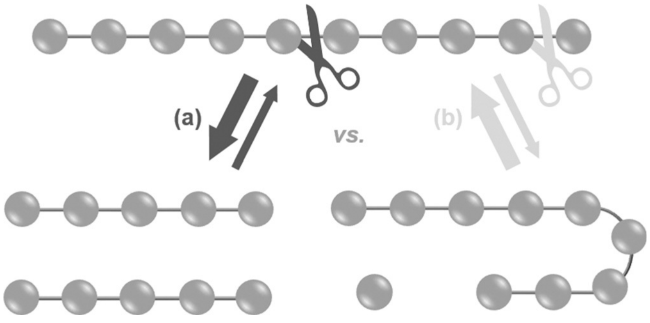
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201508531.



Scheme 1. Schematic view of the theoretical and experimental setup to determine characteristic differences between bond cleavage a) in the middle and b) at the end of a molecule.

Table 1: Values for the translational and rotational entropy[a] for debonding of simple geometric models determined via statistical thermodynamics methods.

Cleavage site:	Middle ΔS_{trans}	ΔS_{rot}	End ΔS_{trans}	ΔS_{rot}
initial	148.9	82.4	136.1	−2.6
longer chain	148.9	87.6	136.1	−0.7
heavier chain	157.5	99.3	137.4	−0.3

[a] ΔS in $\text{J mol}^{-1}\text{K}^{-1}$ at 298 K.

because, in contrast to ΔS_{trans} and ΔS_{rot}, they are both highly sensitive to the local chemical properties of the employed ligation sites and relatively insensitive to chain-length effects.[3e] From Table 1 it is clear that, in all cases, cleavage in the middle of the chain is strongly favored entropically (i.e., greater positive ΔS, compare $\Delta G = \Delta H - T\Delta S$) due to the reinforcing effects of translational and rotational entropy. Moreover, this preference becomes more pronounced as the chains become heavier and/or longer. In other words, the chain-length and mass effects on ΔS are much more pronounced for cleavage in the middle of a polymer chain than for the equivalent reaction at the chain end, with the former expected to converge much less slowly as a function of chain length than the latter. One immediate consequence of these results is the prediction that rate and equilibrium constants for polymerization reactions in which a growing polymeric species adds to a small molecule (as in chain polymerization) should converge much more quickly with chain length than those in which two growing polymeric species add to each other. Indeed, it is well known that the propagation rate coefficient in free-radical polymerization converges rapidly with chain length (<1000 u),[4] whereas, as noted above, our experimental studies have demonstrated that chain-length and mass effects on the equilibrium constant for step-growth Diels–Alder (DA) polymers extends to high molecular weights (ca. 10^5 u).[3b] As the use of simple geometric models can account for qualitative trends only, the experimental investigation of actual chemical systems is needed to provide a deeper insight into the quantitative characteristics of the position effect. Therefore, we next considered the examination of the temperature-dependent association of different supramolecular diblocks via high-temperature (HT) NMR spectroscopy (see the Supporting Information for synthetic details). While entropic effects are a generally applicable principle and thus not exclusive for polymer systems, such systems allow for a facile adjustment of the molecular parameters in question. A pair of diblocks, each containing two blocks of differing individual, yet approximately same overall length, was self-assembled in an aprotic solvent (tetrachloroethane-d$_2$, $c = 6\ \text{mmol L}^{-1}$) via cyanuric acid (CA) and Hamilton wedge (HW) recognition units to resemble dynamic noncovalent association in the middle or at the end of a macromolecule (Figure 1 a,b). Thus it was possible to examine the two extreme examples when investigating the effect of the position of a ligation site within a molecule.

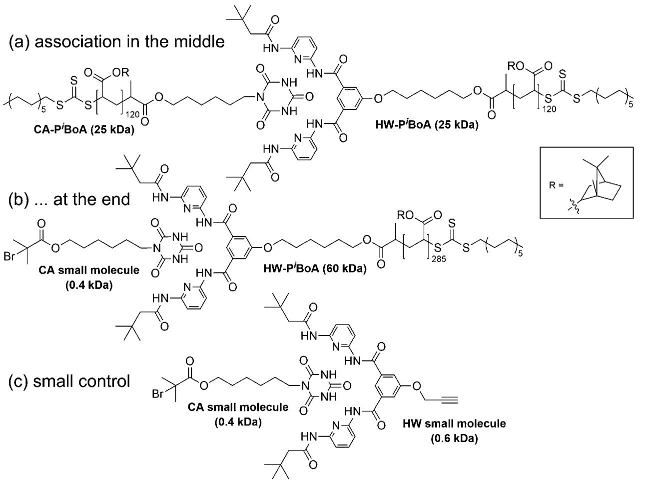


Figure 1. The supramolecular building-block pairings with a) poly(isobornyl acrylate) moieties (with $M_{\text{n,SEC/NMR}} = 25$ kDa on both sides of the ligation site), b) one small-molecule CA unit in combination with a HW functional poly(isobornyl acrylate) ($M_{\text{NMR}} = 60$ kDa), and c) the small-molecule control.

The bonding in the middle system in combination with a readily available small-molecule control comprising identical recognition units (Figure 1 c) had been studied previously under the said conditions and is indicated for comparison.[3c] Subsequently, the chemical shift values of the CA imide protons enabled the qualitative observation of the temperature-dependent degree of association via their equilibrium-dependent resonance, with higher downfield shift values being related to a higher degree of association (Figure 2 and the Supporting Information, HT NMR Spectra).[1j,3c,5] Competing interactions of acrylate backbones with the employed hydrogen-bonding motifs were excluded by both application of intramolecular spacers and measurements of small-molecule recognition units in the presence of nonfunctionalized polyacrylates.[3c,6] For a quantitative assessment of equilibrium constants, NMR titration experiments were conducted to determine the dissociation constants of the associated individual block pairings (see the Supporting Information, NMR Titration).[7] To circumvent problems of signal isolation due to unfavorable exchange rates or overlapping resonances, a temperature of 100 °C was applied. In accordance with the theoretical considerations, it could be shown that—at a given

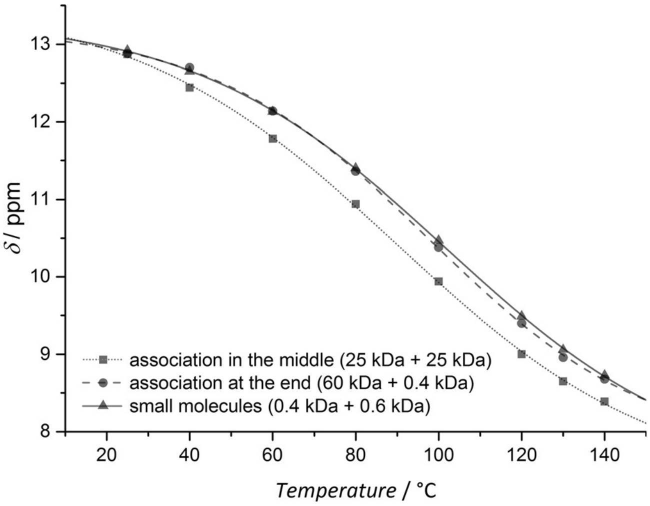


Figure 2. Temperature-dependent CA imide proton resonance in $C_2D_2Cl_4$ for building blocks associated via CA and HW recognition units in the middle (■) or at the end (●) of macromolecules as well as for small-molecule adducts (▲), indicating higher degrees of association for higher downfield shift values.

temperature—dissociation in the middle ($K_{\mathrm{diss,middle}} = (3.7 \pm 0.15) \times 10^{-3}$) is favored by a factor of 2 in comparison with dissociation of a small molecule at the end of a macromolecule ($K_{\mathrm{diss,end}} = (1.9 \pm 0.15) \times 10^{-3}$). Thus, dissociation from the end is comparably unfavorable as the dissociation of two small molecules ($K_{\mathrm{diss,small}} = (1.8 \pm 0.15) \times 10^{-3}$) due to the altered association constants.[3c]

Remarkably, even though large polymer systems were employed, the position effect has not leveled off yet by virtue of a possibly overlapping mass effect, confirming the theoretical prediction of a much higher impact of molecular parameters on central bonding sites and emphasizing the significance of the findings. To gain further knowledge regarding the versatility and specificity of the entropic position effect, an alternative experimental approach was realized via hetero DA step-growth polymers of a cyanodithioester (CDTE) difunctional small-molecule linker and cyclopentadiene (Cp) difunctional macromolecular building blocks comprising poly(methyl acrylate) (PMA), poly(isobornyl acrylate) (P^{i}BoA), or polystyrene (PS) backbones (Figure 3, see the Supporting Information for synthetic details).

We investigated their retro-DA (rDA) degradation via diverse temperature-dependent size-exclusion chromatography (TD SEC) experiments.[8] Exemplary results are shown for DA-PMA systems; for additional results (PS and P^{i}BoA systems) refer to the Supporting Information. In TD SEC, the DA-PMA was measured in situ at 90 °C, resulting in a chromatogram corresponding to the molecular weight distribution as depicted in Figure 4a, evidencing the beginning of a cleavage process due to the starting rDA reaction (compare Figure S1 for an exemplary initial SEC trace at ambient temperature). After 225 min at 90 °C, a second chromatogram of the same sample was acquired (Figure 4b), which shows the expected shift to higher elution volumes, indicating decreasing molecular weight due to the rDA reaction. It should be expected that the lowest achievable weight corresponds to the chromatogram of the isolated polymer building block (Figure 4d). However, the released species elutes at even higher elution times, implying irrationally low molecular weights. While thermal decomposition could not be evidenced, in liquid chromatography high elution volumes are observed when enthalpic interactions with the column material, originating from highly polar functional groups, lead to additional retention.[9] In fact, such behavior could be attributed to the employed CDTE linker and is also the reason for the apparent occurrence of low-molecular-weight material in the DA polymer (Figure 4a): A polymer building block that is still bound to one (or two) very polar linker units is thus expected to elute later than a block without linker molecules, although the two can have very similar molar masses. To prove this hypothesis and deliberately utilize it to address the question where molecules cleave first, the very same DA polymer sample was heated to 160 °C in order to drive the rDA reaction further, and was then measured at 90 °C to achieve similar measurement conditions. The obtained chromatogram (Figure 4c) clearly shows a shift of the peak, which converges with the signal of the building block (Figure 4d), thus proving that only at higher rDA conversions the bonds at the end cleave. Again, this behavior can be ascribed to the favored scission of bonds in the middle of molecules, while the release of small species at terminal binding sites is disfavored. Similar results could be obtained for a DA-PS (refer to Figure S6 in the Supporting Information). Additional analysis of the decrease of DA-PMA in comparison with the release of the dilinker via deconvolution of chromatograms with suppressed interactions of the polar CDTE linker and the column material via adjusted solvent mixtures confirms these assumptions (see the Supporting Information for experimental details). As the linker signals can now be isolated in the employed solvent mixture, not only the temperature-dependent decrease of the concentration of

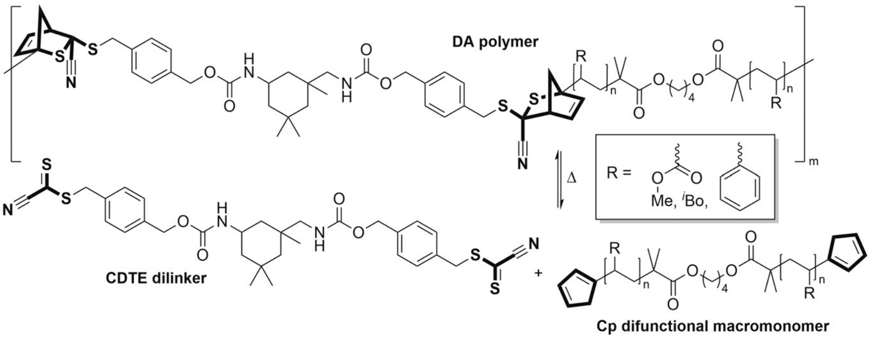


Figure 3. Reaction scheme of the thermoreversible degradation of DA step-growth polymers formed from cyclopentadiene difunctional macromolecular building blocks and a cyanodithioester difunctional linker.

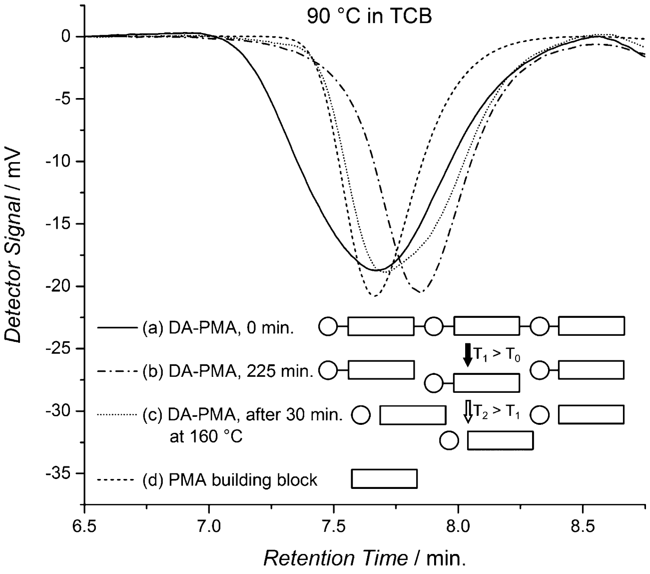


Figure 4. TD SEC chromatogram of a thermoreversible DA-PMA at 90 °C and 160 °C and its corresponding building block in 1,3,5-trichlorobenzene (TCB) as well as a schematic view of the degradation of such DA step-growth polymers, consisting of macromonomers (rectangles) and a small molecular dilinker (circles), at increasing temperatures, here T_0 = ambient temperature, T_1 = 90 °C, T_2 = 160 °C.

the DA polymer species, but also the release of the CDTE linker can be calculated (Figure 5).

In contrast to a purely statistical degradation, it is clearly visible that—while the DA polymer debonds very fast—significant amounts of the linker species can be detected only at high temperatures. Analogous observations are made for the DA-P^{i}BoA systems (refer to Figure S4 in the Supporting Information) and via the inclusion of a UV detector for DA-PS systems (refer to Figure S6 in the Supporting Information), thus completely supporting the herein described effects.

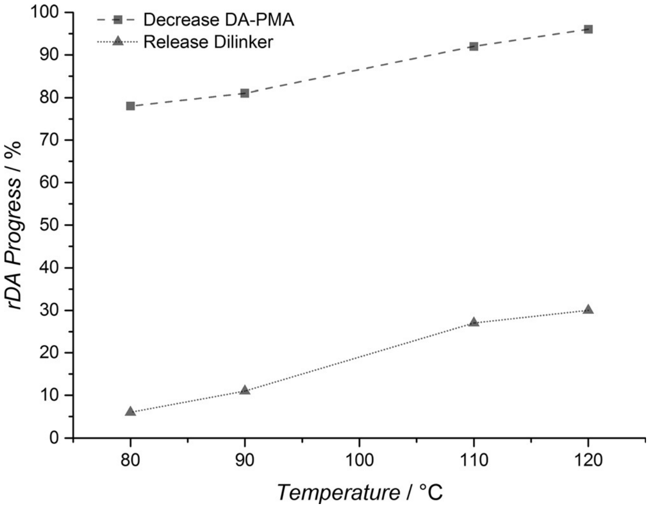


Figure 5. Temperature-dependent decrease of DA-PMA in comparison with the release of the DA dilinker.

In conclusion, we have demonstrated that debonding in the middle of molecules is entropically favored over debonding at the end for both covalent and noncovalent interactions (Scheme 1). Clearly, these findings can be exploited to tune reaction equilibria of known dynamic chemistries and need to be considered when new reversible ligation sites are transferred to other systems. Moreover, being properties of polymer chains rather than the specific chemical reaction involved, these entropic effects are not limited to dynamically bonding self-healing polymers but should have general applicability for chemical reactions involving macromolecular species. Among others, the effects of extended chain length on polymerization rate coefficients are not necessarily restricted to reactions occurring under diffusion control, but need to be considered in chemically controlled bimolecular reactions involving two polymeric species. Such examples could thus include polymer degradation, chain transfer to polymers, and addition of control agents. For equilibrium cases, both the chain cleavage and the corresponding bond formation reactions can be considered via simply reversing the prefixes of the thermodynamic values. In the case of thermal or oxidative polymer degradations, no clear trends besides a mass effect could be deduced from literature, probably due to the generation of radicals via a manifold of reaction channels.[3d,10] Thus, for example, an entropic tendency to undergo midchain homolysis is likely countered by the greater preponderance of unsaturated initiation sites at the chain end.[11] Nonetheless, ultrasonication or general shearing of polymers leads to a favored chain scission in the middle of the molecule.[12] In the case of controlled radical polymerization, the present work suggests that, unlike low-molecular-weight control agents, polymeric control agents are likely to become less reactive to growing polymeric species as a function of their chain length (and hence conversion). In other words, radical addition to polymeric control agents would be expected to become slower and less favorable with increasing chain length of the propagating radical and control agent, while the reverse fragmentation reactions would be expected to become faster and more favorable. Thus, for example in RAFT polymerizations, the addition of polymeric radicals to polymeric RAFT agents is likely to be much less kinetically and thermodynamically favored than the reactions of corresponding low-molecular-weight species. These previously unforeseen extended-chain-length effects may help to account for apparent discrepancies between the kinetic and thermodynamic parameters measured for polymeric species, and those measured or calculated for the corresponding low-molecular-weight compounds.[13]

Acknowledgements

C.B.-K., M.L.C., and A.L. are grateful for continued support from and the excellent collaboration with Evonik Industries. C.B.-K. additionally acknowledges funding from the KIT via the Helmholtz association (BIFTM and STN programs) as well as the German Research Council (DFG). M.L.C. acknowledges generous allocations of supercomputing time on the National Facility of the National Computational

Infrastructure and an Australian Research Council Future Fellowship.

Keywords: cycloadditions · entropic effects · polymers · supramolecular chemistry · thermodynamics

How to cite: *Angew. Chem. Int. Ed.* **2016**, *55*, 1514–1518
Angew. Chem. **2016**, *128*, 1537–1541

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Received: September 11, 2015
Revised: October 30, 2015