The Radical Ring-Opening Polymerization of Cyclic Ketene Acetals Revisited: An Experimental and Theoretical Study

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ABSTRACT: Radical Ring-Opening polymerization (rROP) of Cyclic Ketene Acetals (CKAs) combines the advantages of both ring-opening polymerization and radical polymerization thereby allowing the robust production of polyesters coupled with the mild polymerization conditions of a radical process. rROP was recently rejuvenated by the possibility to copolymerize CKAs with classical vinyl monomers leading to the insertion of cleavable functionality into a vinyl-based copolymer backbone and thus imparting (bio)degradation. Such materials are suitable for a large scope of applications, particularly within the biomedical field. The competition between the ring-opening and ring-retaining propagation routes is a major complication in the development of efficient CKA monomers, ultimately leading to the use of only four monomers that are known to completely ring-open under all experimental conditions. In this article we investigate in detail the radical ring-opening polymerization of model CKA monomers and demonstrate by the combination of DFT calculations and kinetic modeling using PREDICI software that we are now able to predict in silico the ring-opening ability of CKA monomers.

Introduction

Recently, the final outcome of synthetic polymers has become a major issue due to the accumulation of wastes that are damaging the environment. To overcome this problem the use of biodegradable polymers such as polyesters, in particular polylactides, has been widely investigated. These polymers are commonly prepared by polycondensation or Ring-Opening Polymerization (ROP). Nevertheless, the majority of commodity and specialty polymers are produced by radical polymerization techniques that impede the introduction of ester linkages into the backbone of the polymer chains. Relatively few studies, initiated by the pioneering work of Bailey et al., have demonstrated that various cyclic monomers bearing vinyl or exomethylene groups could be polymerized radically through a ring-opening process (Scheme 1a).

Radical Ring-Opening Polymerization (rROP) presents the advantages of both ring-opening polymerization and radical polymerization, specifically the production of (co)polymers with the possibility to insert heteroatoms and/or functional groups into the main chain by facile polymerization procedures (Scheme 1a). The ring-opening polymerization of Cyclic Ketene Acetals (CKAs) by free radical or controlled radical mechanisms has attracted considerable interest since it presents an alternative route for the synthesis of functionalized aliphatic polyesters and is a powerful tool for imparting degradability to vinyl polymers by introducing ester linkages into their backbone (Scheme 1b).

Scheme 1. a) Mechanism of Radical Ring-Opening Polymerization (rROP). b) rROP of Cyclic Ketene Acetals (CKAs) and their use in the preparation of functionalized polyester or segmentable vinyl-based polymers.
Even though the rROP has been known since the eighties, very few mechanistic studies have been performed and no clear structure-reactivity relationships have been established for those monomers.\textsuperscript{20, 21} Indeed, the major drawback of this family of monomer is related to the competition between the ring-opening process and the undesired direct vinyl propagation that leads to polyacetal (Scheme 2). Thus, for the majority of CKA monomers, the resultant polymer is a random copolymer of ester and acetal units.

![Scheme 2](image)

Scheme 2. Competition between ring-opening and direct vinylic propagation leading to either ester units or acetal units.

This situation leads to the predominant use of two cyclic monomers in all of the literature: 2-methylene-1,3-dioxolane (MDO, C\textsubscript{7}, Scheme 3) and the 5,6-benzo-2-methylene-1,3-dioxolane (BMDO, C\textsubscript{7B}, Scheme 3), both known to undergo complete ring-opening polymerization independent of the conditions.\textsuperscript{20} Promising results have been obtained for biomedical applications with these two monomers (gene transfection, etc.).\textsuperscript{20} The development of new CKA monomers that can extend the properties of the corresponding polyester by tuning the mechanical properties, degradation rate, etc. is paramount. To design a monomer for radical ring-opening polymerization, originally two factors were taken into account in order to improve the selectivity of the ring-opening process: (i) the ring strain and (ii) the stabilization of the ring-opened radical. For example, 6-membered ring monomers are recognized to be difficult to polymerize via a ring-opening process. This is usually explained by the low ring-strain of monomers analogous to cyclohexane (whose ring-strain is set to zero). The addition of an aromatic ring close to one oxygen (2-methylene-4-phenyl-1,3-dioxolane, C\textsubscript{6P}, Scheme 3) was also expected to increase the ring-opening ability via the stabilization of the released alkyl radical, but the radical polymerization of such monomers, under both UV at 25–50 °C and thermal initiation at 80 and 120 °C, gave polycetals of high molar mass.\textsuperscript{22} On the contrary, an analogous chemical modification of the 5-membered monomer (2-methylene-4-phenyl-1,3-dioxolane or MPDL, C\textsubscript{5P}, Scheme 3) increases the ring-opening ability.\textsuperscript{23, 24} There are many similar examples showing that the aforementioned factors were not key parameters for rationalizing the reactivity of such monomers.\textsuperscript{20}

These results demonstrate why only a few known monomers are used within the literature and why the versatility of the rROP technique to prepare a wide range of functionalized polyesters has not been extensively investigated. In order to efficiently design new monomers, it would be useful to be able to predict the efficiency of a given monomer in rROP before its synthesis and polymerization. Herein, we propose a theoretical approach that combines quantum calculations and kinetic modeling based on the competitive process described above (scheme 2) to achieve this goal.

More precisely, our strategy is to use Differential Functional Density (DFT) to calculate the various rate coefficients that will be later implemented into a kinetic model to obtain the theoretical composition of ester and acetal units in a polymer backbone. These theoretical results were then experimentally confirmed by studying the radical polymerization of C\textsubscript{5}, C\textsubscript{5H}, C\textsubscript{6} and C\textsubscript{7} CKA monomers (Scheme 3). Such an approach allows the \textit{in silico} prediction of the behavior of new CKA monomers.

![Scheme 3](image)

Scheme 3. Structures of CKA monomers and their corresponding intermediate acetalyl radicals

**Results and discussion**

**Experimental Study**

A significant problem when rationalizing the reactivity of CKA monomers arises from the many experimental condi-
tions that have been reported within the literature (initia-
tor nature and concentration, temperature, etc.). Addi-
tionally, since many of the published studies were per-
formed in the 80-90s, some non-reliable characterization
methods have been used to assess the ratio between acetal
and ester repeating units. To ensure the validity of the ex-
perimental data before implementing the modeling, we
performed the polymerization of monomers C5, C5H, C6
and C7 coupled with careful microstructure analysis to ob-
tain an accurate ratio between the acetal and ester units
for these model CKA polymers.

As was previously stated by Bailey et al., in their pioneer-
ing studies, CKA monomers with 5- and 6-membered rings
are prone to cationic polymerization initiated by contact
with glass making purification steps particularly problem-
atic. This is a crucial issue when attempting to quantify the
ester percentage obtained by radical polymerization as
cationic polymerization typically results in a high quantity
of acetal units, or even pure polyacetal (see ESI Fig. S1).
Thus, in order to prevent spontaneous cationic polymer-
ization contamination during monomer purification, stor-
age, radical polymerization and subsequent analysis, all
glassware was prior rinsed with triethylamine. Additionally,
the storage of the monomers at -18°C over sodium al-
lows the preservation of the monomer for multiple
months. Finally, to avoid cationic processes during the
radical polymerization, 10 wt % pyridine was added to the
mixture and only liquid initiators were used since they are
readily soluble and therefore allow prompt polymeriza-
tion. Under such conditions we are confident that the ob-
tained polymers were prepared from exclusively radical
polymerization.

After the polymerization of monomers C5, C5H, C6 and C7
and purification by precipitation, the four polymers were
analyzed by 1H and 13C NMR. All 1H and 13C NMR signals
can be assigned and are consistent with the data reported
within the literature. 2D NMR techniques also confirmed
these assignments (see ESI for details, Figure S2 and S3 for
PC5 for example). The analysis of the 13C NMR spectra (Fig.
1 for the polymerization of monomer C5, other NMR spec-
tra are provided in ESI) confirmed the presence of two re-
peating units within the copolymers. These spectra display
peaks in the characteristic zones of both acetal and ester
units, at 100 and 170 ppm, respectively. We also noted a
change in the number (i.e. the presence of diads, see Figure
1) and intensity of these peaks corresponding with the
temperature of polymerization. The acetal peaks were
more intense at low temperatures, while there was an in-
version in the intensity of the two main ester peaks with
temperature. It is clear that an increase in temperature
promotes the presence of ester units, which are highly
prevalent at 150 °C.

After full assignment of the 1H NMR spectrum, quantifica-
tion of the percentage of ester units in PC5 can be per-
formed by focusing on the protons c and q in the region
3.7-4.2 ppm using the formula proposed by Pittman et al.,
who performed a similar study but instead using cationic
polymerization.

\[
%_{\text{ester}} = \frac{I_c}{I_c + I_e/2}
\]

From this formula and others (see ESI for details) using ei-
ther 1H or 13C NMR, we can calculate the percentage of
ring-opening at different temperatures. The results are ex-
tremely close regardless of the applied method (ESI, Table
S2). It should be noted that the difference between the val-
ues is almost negligible at 120 and 150 °C, while it is less
than ± 5% at low temperatures. Accordingly, there is a per-
fectedly linear trend of ring-opening percentage and tem-
perature, allowing a change in ester unit percentage from ca.
50% to 80% by increasing the temperature from 50 to
100 °C. Extrapolating these conditions, the polymerization
of monomer C5 should be performed beyond 200 °C to ob-
tain pure polyester, which is not relevant. These results are
in good agreement with those previously reported in the
literature concerning the trend, but also with ring-opening
percentage values.

![Figure 1](image-url). 1H and 13C NMR spectra and structure of PC5 ob-
tained at different temperatures.

In the case of the C5H polymerization, only acetal units
were observed in the polymer chains by both 1H and 13C
NMR (see Figure S4 and S5), as was previously reported
within the literature. Moreover, unlike the other CKA
monomers, molar masses were found to be very high (>30,000 g.mol⁻¹).

The six-membered ring monomer (C6) was then polymerized at the same temperatures. The quantity of precipitated polymer was lower than in the previous cases and therefore the uncertainty was higher, and thus a sample polymerized at 100 °C was added to compensate. The obtained molar masses were also relatively small when compared to PC5. We noted that the ¹³C NMR spectra had the same basic characteristics as those presented in Figure 1 (the presence of peaks corresponding to both ester and acetal units at all temperatures; an increase in the temperature leading to better ring-opening ability). However, whereas previously the ester peak intensity significantly exceeded the intensity of acetal peaks at temperatures above 120 °C, the intensities are much closer in this case. Moreover, the peak b is almost absent at low temperatures (Figure S6-S8), demonstrating a lower ring-opening ability of such 6-membered CKA monomer when compared to their 5-membered analogues. Nevertheless, the results still demonstrated a linear evolution in the ring-opening percentage in relation to temperature. At 130 °C we calculate 50-60% ester units, which is significantly below the value of 85% reported within the literature (Figure 2).²¹

![Figure 2](image-url)  
**Figure 2.** Ring-opening percentage as a function of temperature for the bulk polymerization of monomers C₅-C₇.

As expected from the literature data, the 7-membered ring monomer (MDO, C₇) provided only polyester regardless of the temperature used (see ESI Figure S9-S10 for details). All of the obtained experimental data is in good agreement with the literature data. Indeed, the order for obtaining polyesters follows the trend: C₆H < C₉ < C₇ < C₅. Nevertheless, we are now able to examine these results in detail. The 5- and 6-membered monomers both have the ability to form aliphatic polyester, their ring-opening ability increasing also linearly with temperature, with an almost identical slope, whatever the monomer. It was also demonstrated that there is a clear difference in the ring-opening ability of the 5- and 6-membered ring CKA monomers, with the 6-membered CKA being less prone to ring-opening. These obtained data were subsequently used as a reference set for the following theoretical modeling.

**Computational study**

The different structures of the monomer and adduct radicals have been optimized by the DFT method B3LYP / 6-31G (d), commonly used for its excellent quality of results and calculation times.¹⁵-²⁷,³⁸ Moreover, this method has already been efficiently used in conformational studies of various heterocyclic rings.²⁹,³⁰ The acetal propagating macroradicals has been optimized by simulating the polymer chain using a methyl group (Scheme 3, R₅-R₇ radicals) to mimic steric hindrance without requiring significant calculation costs, while simultaneously reducing energy errors due to free rotation of the chains. In each case, the two C-O bonds susceptible to fragmentation were broken to find the transition state of lowest energy. Here we only show the values for the selected transition state. Concerning the various cyclic radicals having an aromatic substituent (R₅P, R₆P and R₇P) the homolysis is always located on the same side as the substitution, as expected.

There is only scarce experimental data for the β-scission of CKA monomers on which we can base a theoretical approach. The only values originate in a 1982 study where Barclay, Grilling and Ingold³³ studied I₁ and I₂ (Scheme 4) intermediates by EPR and measured their fragmentation rate constant (k_{frag,I₁} (75°C)=7.6·10⁻³ s⁻¹ (with Eₐ=61 kJ.mol⁻¹ and log(A/s⁻¹)=13.0); k_{frag,I₂} (75°C)=1.0·10⁻² s⁻¹ (with Eₐ=67 kJ.mol⁻¹ and log(A/s⁻¹)=13.0).³³ To determine the activation energies we used different quantum methods (i.e., UB3LYP, MO6-2x and G3(MP2)RAD) since it was shown that the particular method applied could lead to drastic differences when compared with experimental data. The results of the calculations are displayed in Figure 3. Importantly, it was observed that calculations performed using the UB3LYP method led to a lower Eₐ than the experiment, while calculations made with G3(MP2)RAD and MO6-2x are slightly and exceedingly higher than the experimental data, respectively. This result is not surprising as the UB3LYP method is known to generally underestimate the energy of structures.³² It is additionally important to note that a difference of 5-8 kJ.mol⁻¹ between the energies of activation for the two species I₁ and I₂ is correctly assessed by all techniques (difference between 3 and 6.5 kJ.mol⁻¹).

![Figure 3](image-url)  
**Figure 3.** Influence of the quantum method on the activation energies of the β-scission reaction of acetalyl-based radicals and their comparison with experimental data.
The values obtained with the method UB3LYP/6-31G(d) are very close but lower than the experimental values with a 3 kJ mol\(^{-1}\) deviation. On the other hand, the use of a larger base (i.e., 6-311+G(3df, 2p)) is not interesting as it further underestimates the energies with a deviation of 5-6 kJ mol\(^{-1}\). The G3(MP2)RAD method,\(^{32, 33}\) known for the quality of its absolute values, is less close to the experimental data than UB3LYP (10-11 kJ mol\(^{-1}\) higher deviation). As the G3(MP2)RAD calculations require much longer and are limited to a few atoms, the UB3LYP/6-31G(d) method appeared to present the best compromise in speed/performance. We already utilized the same DFT method for other quantum calculations of CKA monomers.\(^{15, 34, 35}\)

The activation energy values of \(\beta\)-scission all range between 35 and 70 kJ mol\(^{-1}\) (Figure 4a). All of the 7-membered CKA monomers known to polymerize exclusively by the ring-opening mechanism have an activation enthalpy lower than 40 kJ mol\(^{-1}\), in agreement with the previous calculations of Ochiai and Endo.\(^{21}\) This study also confirmed that the stabilization of the released radical is not a key parameter since there is no direct link between the percentage of ring-opening and the presence of an aromatic ring in the \(\beta\) position to the cyclic acetal functionality. Moreover, these calculations also do not allow a discrimination between a partial and the absence of ring-opening. Thus far, only \(\beta\)-scission reactions have been studied; here and within the literature. This is only a part of the complete mechanism since radical ring-opening polymerization is characterized by the competition between the \(\beta\)-fragmentation and the direct addition. The reactions involved are not of the same order (unimolecular and bimolecular), and thus they are not comparable in terms of thermodynamics or activation energy, such comparisons usually being performed to identify the most-favorable reaction mechanism.

\[\text{Scheme 4. Complex mechanism to theoretically determine the ester/acetal ratio in a polymer backbone.}\]

The correct method to understand the role of the different reactions is to achieve a kinetic model using not only the energy of activation but also the rate coefficients \(k_\beta\) and \(k_{\text{add, closed}}\) (Scheme 4).

**Figure 4.** Enthalpies of activation \(\Delta H^\ddagger\) and reaction \(\Delta H_r\) for the ring-opening reaction (left) and the different radical addition (acetalyl-based radical, middle) and open-type radical (right).
Indeed, to describe the macroscopic result (the ratio between the acetal and ester units in the polymer backbone) we need to compute the number of the two propagation events that occurred during the polymerization process, and thus the addition reaction after opening $k_{add,open}$ is also mandatory. Since our interest is focussed on the propagation steps, we used classic initiation and termination steps and disregarded all side reactions such as chain transfer reactions that are known to occur during the polymerization of MDO, as an example. To make an accurate estimate of the addition rate constant of macroradicals onto monomers it is recommended to model dimers or trimers instead of unimers. However, this work involves relatively large molecules that have between 15 and 33 atoms, which after addition can go up to more than 60 atoms. Thus, we chose to directly use the rate constant of simple addition reactions to limit computing time. In addition, in the case of the addition of radicals after ring-opening, the penultimate effect was not envisioned since the previous unit is at minimum 5 atoms away. In the case of the radical addition of acetalyl-based radicals, it is assumed that the effects of steric hindrance and the specificity of such radicals are well above any potential penultimate effect.

Concerning the addition of ring-opened radicals, the growing number of possible rotations along the length of the aliphatic chains gives access to a very large amount of possible geometries. In this way, there is too great an uncertainty in the values of calculated energies. To avoid this limitation, simple representative radicals mimicking the macroradical were modelled i.e. the ethyl radical for monomers C5-C7 and the styryl- or methyl-benzyl-type radical for the C5P-C7B monomers (Figure 4b). The work of Fisher and Radom which was dedicated to modeling additions of radical reactions by DFT indicates that in the case of relatively large systems the B3LYP method is appropriate and has a good compromise between time and result, also later confirmed by Moscatelli. Thus, and also to be consistent in the various calculations (addition and β-scission), this method was chosen to be applied.

The results for the addition of ring-opened radicals onto the CKA monomers are described in Figure 3b. Since in all cases the polarity of both adding radicals and CKA are similar, thus the rate of addition is dependent only on the stabilization of the alkyl radical (primary, secondary or tertiary alkyl radicals or the presence of a stabilizing aromatic ring). For example, the activation enthalpies of primary alkyl radicals are centered around $28 ± 5$ kJ.mol$^{-1}$, while are higher in the case of secondary radicals ($35.5$ kJ.mol$^{-1}$ for C5H). For aromatic-based monomers, the benzyl type radical has a lower activation enthalpy (43 kJ.mol$^{-1}$ for C7B) than styryl-based radicals (48±1 kJ.mol$^{-1}$ for C5P and C6P).

These obtained values can be compared to the values described by Fischer and Radom dealing with the addition of methyl and benzyl radicals onto vinyl ethers. In this case, activation energies of 25 and 40 kJ.mol$^{-1}$ were given, respectively, that are both 3 kJ.mol$^{-1}$ lower than the values that we obtained for CKA, which are vinyl ethers in which an additional oxygen atom is located in the α position to the vinyl functionality. Moreover, for the C5 monomer Coote and coworkers proposed a value of $30 ± 5$ kJ.mol$^{-1}$ via high level ab initio calculations for the propagation rate constant that is coherent with our value. From all these results we could conclude that the ring-size does not greatly affect the activation enthalpies for similar structures (C5-C6-C7 and C5P and C6P).

To our knowledge, there is no data within the literature reporting the radical addition of acetalyl-type radicals, especially onto cyclic ketene acetalts. The obtained results are summarized in Figure 4c. The data shows that the calculated energy values do not differ significantly, i.e. all the activation enthalpies being centered around $27 ± 5$ kJ.mol$^{-1}$ and the reaction enthalpies around -66 ± 8 kJ.mol$^{-1}$. It can be observed that only the ring size seems to influence such values since C5, C5H and C5P are similar, and such behavior holds true for 6- and 7-membered ring CKA monomers. It should be noted that these values are of the same order of magnitude as the addition of primary alkyl radicals on the CKA while the acetalyl radicals here are tertiary, showing the specific reactivity of such radicals.

The activation energies calculated for different reactions are not directly comparable to know whether a monomer is more likely to propagate directly or undergo β-scission. Indeed, there are different order reactions; i.e. monomolecular and bi-molecular. Therefore, kinetic modeling is required. Kinetic modeling is performed from the rate coefficients of the various reactions. These rate coefficients $k$ can be obtained precisely by knowing the free energy of activation $\Delta G^\ddagger$ or from the Eyring equation through the various components of enthalpy and entropy of activation ($\Delta H^\ddagger$ and $\Delta S^\ddagger$, respectively). However, DFT methods are known to give erroneous evaluations of entropy.

Indeed, the Gaussian software treats all vibrations like harmonic oscillators. This is correct for certain vibrations, but the entropy associated with certain hindered rotations is not properly taken into account. In the cyclic ketal intermediate, such hindered rotations are important and thus $\Delta S^\ddagger$ leads to erroneous results. The use of the Arrhenius equation simplifies the problem. Indeed, the pre-exponential factor $A$ contains the component of entropy and its value is rather similar for the same type of reaction in a narrow range of temperatures. For the addition of open radicals, the values of $\log A$ that are recommended are 7.5, 8, and 8.5 depending on whether the groups are tertiary, secondary or primary, respectively. However, no value for the addition of tertiary acetalyl-based radicals exist in the literature, the presence of more oxygen atoms appears to increase the value of $\log A$ in different cases. Therefore, we chose to use the average value of 8 for such acetalyl radicals. In the case of the ring-opening reaction, it is recommended to take a $\log A$ value of 13.

Kinetic modeling was then performed using PREDICI software. This software is based on the deterministic Galerkin h-p-method has been widely used for describing molecular weight distributions and polymer reaction kinetics for a large range of polymer processes. The kinetic scheme
and the coefficients used are shown in Scheme 5 and Table S7 and S8, respectively.

![Kinetic model used in the PREDICI software.](image)

**Scheme 5.** Kinetic model used in the PREDICI software.

For the different reactions of the initiating step, (dissociation rate constant $k_d$, dimerization of two initiators $k_{d}m$ and first radical addition $k_{ad}$) we used conventional values. Indeed, the initiation theoretically has no influence on the competition between the different propagation reactions, and thus values corresponding to a typical radical polymerization were selected. All the termination reactions that could occur were additionally modeled. As the propagating radicals are alkyl or aromatic derivatives, recombination rate constants of $1.0 \times 10^9$ and $1.0 \times 10^8$ L.mol$^{-1}$s$^{-1}$ were chosen, respectively. Termination reactions by disproportionation have not been included as there is no data on the termination mode of these monomers and this parameter does not influence the structure of the polymer chains. To simplify the model, chain transfer reactions have not been taken into account. Although such reactions should occur for alkyl-based propagating monomers it was considered that chain transfer do not interfere in the kinetic competition, which is the main focus of this study.

A final approximation relates to the monomer concentration in the polymerization medium. By weighing a defined volume of the monomer C7B, we determined that the molar concentration of the monomer should be approximately 7.5 mol.L$^{-1}$. Not having the density data of all the various monomers, and to compare the simulation results without changing several parameters simultaneously, we set the concentration identical for all the monomers, to an average of 8 mol.L$^{-1}$. This value appeared to be a suitable intermediate for other more or less dense monomers. For comparison, the molar concentration of styrene is 8.7 mol L$^{-1}$.

The propagating species are simply either closed or open type. The assumption is made that the rate coefficients are independent to the chain length because we consider propagation as being equal to the addition of simple molecules. It has been already stated that the chain length was not taken into account because the larger molecular size requires too much computation time. Moreover, by modeling propagating radicals in the form of dimers or trimers, the penultimate unit would be different according to the previous addition (e.g. closed-closed, open-closed, closed-open or open-open dimers), which would complexify the system and thus would require many additional calculations that are not necessarily useful in this particular case.

Counters have been inserted into the model to quantify the amount of ester and acetal functions introduced in the copolymer. The acetal counter was increased when there is an addition of a closed-type radical. The ester counter increased when ring-opening occurred. In that way, it does not include counting when there is an addition of an open-type radical since the resulting chain end is then of a closed type and can therefore react in both ways. At the end of the modelling, the number of acetal and ester counters were recorded and compared to determine the percentage of ester units in the final polymer backbone.

The result of the modeling is depicted in Figure 5. A good agreement between the experimentally obtained values and those obtained from the model can be observed in the case of simple monomers C5, C6 and C7. Indeed, Figure 5 shows relatively identical behavior between the simulation and the experimental observations for these monomers; C7 monomer gives only ester units at 50 °C while C5 and C6 form copolymers. Moreover, the difference in ability between C5 and C6 to form polyesters is also in good agreement with the experimental results, with 75% and 45% polyester at 100 °C, respectively (on average 20% more for C5 than C6) and an increase in percentage of polyester with an increase in temperature. In contrast, the slope defining the increase in ester percentage depending on the temperature is slightly steeper for the simulation results in comparison to the experimental data. This discrepancy could originate from the assumptions made regarding chain length independency of the various kinetic rate constants. Nevertheless, this modeling approach provides an interesting and relatively accurate tool to describe the reactivity of CKA monomers.

We additionally performed such modeling on more complex monomers. With C5P, C7B and C8O, the model gives complete ring-opening, in accordance to the literature data. In contrast to experimental data, the model predicts that C5H should contain some ester units even if such a monomer has a lower tendency to ring-open. The results obtained for C6P (Figure 6) is not in agreement with the literature data since the modeling showed an enhancement in the ring-opening ability in comparison to the C6 CKA monomer (75 instead of 25% at 70 °C).
Figure 5. Theoretical (plain symbol and straight line) and experimental (empty symbol and dashed-dotted line) ring-opening percentage as a function of the temperature for top: the bulk polymerization of monomers C$_5$ (■), C$_6$ (■) and C$_7$ (■); bottom: the bulk polymerization of C$_5$H (▼) and C$_6$P (▼) monomer.

The discrepancy between the theoretical results and the literature data can be explained by cationic polymerization that was not inhibited. This explanation is further supported by a study on C$_6$ CKA derivatives bearing methyl groups on the carbon in the $\alpha$ position relative to the cyclic acetal functionality. In that case, using base to prevent cationic polymerization, they obtained 89% ester units at $120^\circ$C.

Another parameter that could be used to increase the ring-opening ability of CKA monomers is to decrease the monomer concentration in order to favor the unimolecular reaction compared to the undesired bimolecular acetal propagation. To simulate the monomer dilution, the ring-opening percentage of the C$_6$ monomer at different concentrations and temperatures was modeled (Figure 6). As expected, an evolution towards the production of more polyester at high dilution was observed. On the other hand, the curves level out at the limit values of around 10 and 50% polyester at 50 and 120 °C, respectively for a concentration of 8 mol.L$^{-1}$, confirming that the value we used in previous simulations is representative of the bulk polymerization.

Figure 6. Theoretical ring-opening percentage as a function of temperature and monomer concentration for the C$_6$ monomer.

Although relatively simple, the kinetic model we have developed appears robust enough to allow an approximation of the behavior of a CKA monomer. The model requires the determination of three activation energies to investigate the reactivity of new CKA monomers. According to the calculations performed for the addition reactions, it appeared possible to approximate the rate of acetal-based addition according to the monomer ring size and the rate of addition of open-type alkyl radicals by using previously determined values for the addition of model alkyl radicals onto simple CKA monomers. Using such an approach, only the $\beta$-scission of the intermediate acetalyl-radical has to be calculated. Secondly, we performed the modeling using the parameters used for C$_6$ and C$_8$O monomers (i.e. the monomers that have the highest and lowest activation energies for ring-opening) and determined the percentage of ester units in the polymer backbone versus a constant $K$ that is determined by the ratio $k_{\beta}/k_{\text{add, closed}}$ (Figure 7).

Figure 7. Theoretical ring-opening percentage as a function of the $K$ parameter.
Interestingly all the data followed a master curve. A threshold value of $1 \times 10^3$ seems mandatory to obtain pure polyester. Using this threshold and the values of the pre-exponential factors, we can estimate that a CKA monomer should have a difference between the activation energies of ring-opening and addition of the ring-retaining acetaldehyde lower than 13-15 kJ.mol$^{-1}$ to efficiently obtain polyester. If we assume that the radical addition of the acetaldehyde intermediate is only determined by the ring size, this approach gives an upper limit for the $\beta$-scission reaction depending of the ring size (Table 1).

**Table 1.** Upper values for the enthalpy of activation for the ring-opening reaction to obtain pure polyester according to CKA ring size

<table>
<thead>
<tr>
<th>CKA Monomer Size</th>
<th>Average $\Delta H_{\text{add, closed}}$ (kJ.mol$^{-1}$)</th>
<th>$\Delta H_{\beta \text{ max}}$ (kJ.mol$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>27</td>
<td>40</td>
</tr>
<tr>
<td>6</td>
<td>24</td>
<td>37</td>
</tr>
<tr>
<td>&gt;7</td>
<td>31</td>
<td>44</td>
</tr>
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</table>

**CONCLUSION**

The competitive process of ring-retaining propagation is a major obstacle in the development of efficient CKA monomers. In this study we investigated this key parameter by a combination of experimental and theoretical approaches. First, it was demonstrated that the ratio between ester and acetal units in the polymer backbone is linearly correlated to the polymerization temperature, with the ease of ring-opening following the order $C_7 > C_5 > C_6$. DFT calculations of the ring-opening reaction showed that complete ring-opening behavior could be obtained with a $\Delta H^\beta$ below 40 kJ.mol$^{-1}$ but it was not possible to discriminate or quantify the behavior for other monomers. By further utilizing the kinetic modeling software PREDICI the behavior of all CKA monomers was able to be rationalized by considering the impact of the addition of acetaldehyde and open-type radicals onto the CKA monomer.

Although relatively simple, the developed kinetic model is based on relevant values and seems robust enough to allow for an approximation of the behavior of a CKA monomer after completing the necessary energy calculations. Furthermore, this model allows an attempt at the rationalization of behavioral differences between the monomers through structure-reactivity relationships. The analysis of molecular orbitals is also predicted to be an excellent method for this because it can separate the contributions due to hyper-conjugation and those due to other energy contributions such as steric and electrostatic interactions. This will be the subject of a subsequent study.

**ASSOCIATED CONTENT**

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website. $^1$H NMR and $^{13}$C NMR spectra of the various polymers, kinetic rate constants used in the modeling part, DFT Calculation details

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**Author Contributions**

The manuscript was written through contributions of all authors.

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