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# Development of an Efficient Thionolactone for Radical Ring-Opening Polymerization by a Combined Theoretical/Experimental Approach

Bastien Luzel,<sup>a</sup> Noémie Gil,<sup>a</sup> Patrick Désirée,<sup>a</sup> Julien Monot,<sup>b</sup> Didier Bourissou,<sup>b</sup> Didier Siri,<sup>a</sup> Didier Gimes,<sup>a</sup> Blanca Martin-Vaca,<sup>b</sup> Catherine Lefay<sup>a</sup> and Yohann Guillaneuf<sup>a,\*</sup>

<sup>a</sup> Aix-Marseille Univ, CNRS, Institut de Chimie Radicalaire, UMR 7273, F-13397 Marseille, France.

<sup>b</sup> Univ Toulouse UPS, Lab Heterochim Fondamentale & Appl UMR 5069, CNRS, 118 Route Narbonne, F-31062 Toulouse, France

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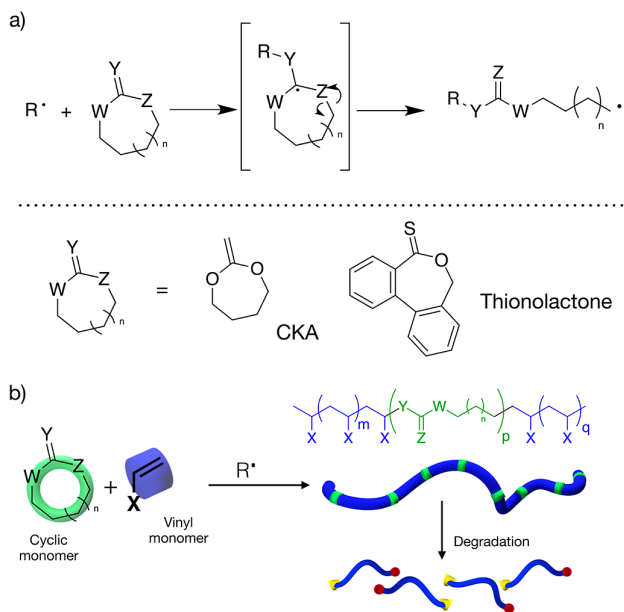
**ABSTRACT:** The environmental impact of plastic waste has been a real problem for the past decades. The incorporation of cleavable bonds in the polymer backbone is a solution to make a commodity polymer degradable. When radical polymerization is used, this approach is made possible by the radical ring-opening polymerization (rROP) of a cyclic monomer that allows the introduction of a weak bond into the polymer backbone. Among the various cyclic monomers that could be used in rROP, thionolactones are promising structures due to the efficiency of the C=S bond to act as radical acceptor. Nevertheless, only few structures were reported to be efficient. In this work, we used DFT calculations to gain better understanding of the radical reactivity of thionolactones and in particular we focused on the transfer rate constant  $k_{tr}$  value and its ratio with the propagation rate constant  $k_p$  of the vinyl monomer. The closer to 1, the better the statistical incorporation of the two comonomers into the backbone. These theoretical results were in good agreement with all the experimental data reported in the literature. We thus used this approach to understand the key parameters to tune the reactivity of thionolactone to prepare random copolymers. We identified and prepared the 7-phenyloxepane-2-thione (POT) thionolactone that led to statistical copolymers with styrene and acrylate derivatives that were efficiently degraded under accelerated conditions (KOH in THF/MeOH, TBD in THF or *m*CPBA in THF), confirming the theoretical approach. The compatibility with RAFT polymerization was established as well as the homopolymerization behavior of POT. This theoretical approach paves the way to the in-silico design of new efficient thionolactones for rROP.

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## INTRODUCTION

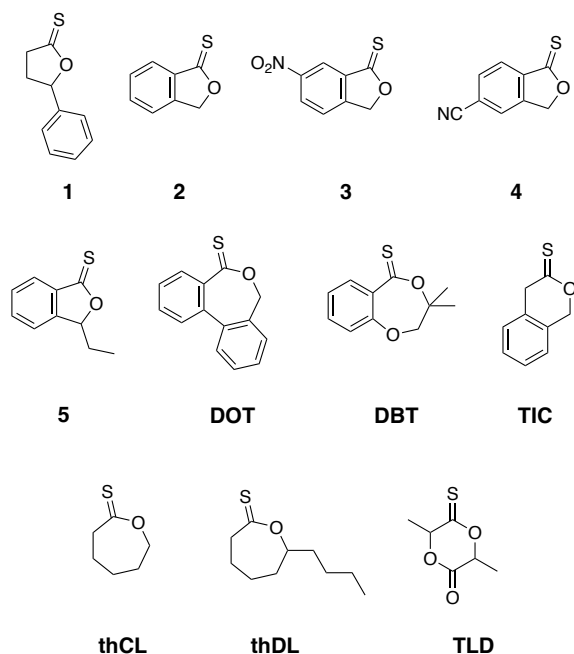
Plastics are omnipresent in everyday life due to their advantages (light weight, low cost, and stability under thermal, chemical, and mechanical solicitations) but they produce large amounts of wastes that accumulate in the environment.<sup>1,2</sup> The microplastics generated thereby have become a major environmental issue.<sup>3,4</sup> This is especially true for polymers having a backbone consisting of carbon-carbon bonds, that do not allow chemical degradation by hydrolysis. For example, polystyrene is a very common plastic due to its thermal properties and its resistance to corrosion but it could be found intact after 32 years in soil.<sup>5</sup> Another example is polyacrylates that are widely used in adhesives, textiles and lubricating oils for their properties of flexibility, low glass transition temperature and tunable hydrophobicity. Since it is very difficult but also very expensive (REACH registration, etc.) to design brand-new materials that could both have the desired properties (mechanical, thermal, solvent resistance, etc.) and that are at the same time either recyclable and/or biodegradable, transforming already known materials to make them biodegradable/recyclable is more interesting.<sup>2,6-8</sup> This approach relies on the introduction of labile bonds into the polymer backbone. The degradation could thus occur from these weak bonds leading to oligomers that could be easily chemically recyclable and/or bio-assimilable. One technique for producing this kind of material is the radical ring-opening copolymerization (rROP) of a cyclic monomer with a common vinyl monomer.<sup>9,10</sup> The polymerization occurs via the addition of radicals onto cyclic monomers bearing an exo-methylene function or equivalent groups followed by a fragmentation of the intermediate cyclic radical to

afford a new radical capable of propagating with a vinyl monomer. This mechanism results in the incorporation of heteroatoms into the C-C backbone and consequently in the introduction of cleavable bonds in the copolymer backbone (Figure 1). The main family of cyclic monomers used in rROP is cyclic ketene acetal (CKA).<sup>10,11</sup> These cyclic monomers have been proposed and extensively studied by Bailey *et al.*<sup>12</sup> in the eighties and their interest has been rejuvenated during the last few years. These monomers are very efficient for the copolymerization with vinyl acetate, maleimide and vinyl ether derivatives. In the case of the copolymerization with (meth)acrylate and (meth)acrylamide derivatives, the difference in reactivity between the comonomers led to a lower insertion of the CKA compared to the initial feed ratio and a compositional drift at high conversion.<sup>13</sup> For styrene and dienes, the high difference in reactivity impedes their practical use to prepare homogeneous copolymers incorporating ester bonds into the backbone.<sup>14</sup>



**Figure 1.** a) Mechanism of rROP. b) Preparation of degradable polymers via rROP

Moreover, the main drawback of CKAs is also related to their sensitivity to protic sources and the competition between the two mechanisms of propagation, *ie* ring-opening and ring-retaining.<sup>15</sup> To circumvent such drawbacks, Roth<sup>16</sup> and Gutekunst<sup>17</sup> recently proposed thionolactones as new cyclic monomers for rROP by taking advantages of the higher reactivity of the C=S bond than the C=C bond as radical acceptor. Among a library of six thionolactones, dibenzo[*c,e*]-oxepane-5-thione (**DOT**, Figure 2) was shown to copolymerize efficiently with acrylate, *N,N*-dimethylacrylamide and maleimide and to produce copolymers with thioester units inserted into the backbone.<sup>16-19</sup>



**Figure 2.** Thionolactones already prepared in the literature.

In the case of MMA and styrene, it was reported that there was no incorporation of **DOT** into the polymer, whereas the

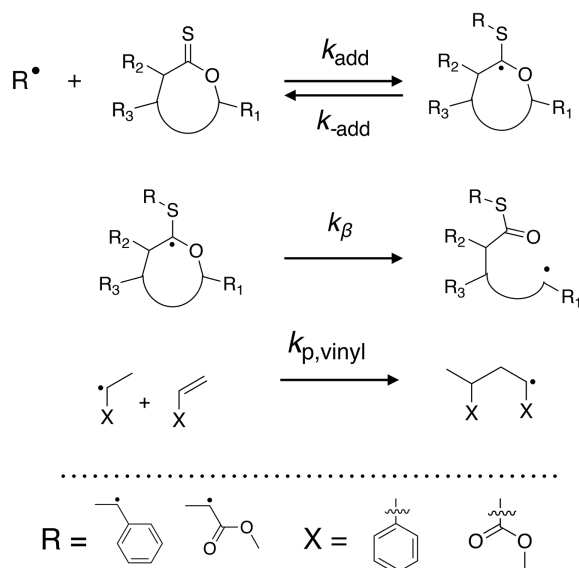
copolymerization with vinyl acetate inhibits the polymerization.<sup>16, 17</sup> Since then, Destarac and Harrison,<sup>20</sup> in parallel with our group,<sup>21</sup> presented thionocaprolactone (**thCL**, Figure 2) as an efficient thionolactone to copolymerize with vinyl acetate. We also started gaining better understanding of the **DOT** reactivity via a joined experimental/theoretical study. We showed that contrary to some data in the literature, the copolymerization with styrene at 80 °C is possible but with a lower reactivity of **DOT** compared to styrene. The reactivity of this couple of monomers could nevertheless be modified at higher temperature (150 °C)<sup>22</sup> with the reactivity ratio of styrene ( $r_S$ ) and **DOT** ( $r_{DOT}$ ) measured at 0.55 and 1.68 respectively. We then succeeded to obtain a poly(*S-co-DOT*) with a high molecular weight ( $M_n = 75,000 \text{ g}\cdot\text{mol}^{-1}$ ) using 5 mol% of **DOT** at 150 °C in bulk. The copolymer presented similar mechanical and thermal properties than polystyrene but could be degraded into oligomers ( $M_n$  below 1,000  $\text{g}\cdot\text{mol}^{-1}$ ) within 1h at room temperature in the presence of a 2.5 wt% solution of 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) in THF.<sup>22</sup> We also recently determined the reactivity ratio of **DOT** ( $r_{DOT} = 1.6$ ) and methyl acrylate ( $r_{MA} = 0.2$ ) during the copolymerization of these two monomers in anisole at 80 °C in the presence of 1 mol% of AIBN as radical initiator.<sup>23</sup> Additionally, **DOT** was recently extended to dispersed media,<sup>24, 25</sup> network<sup>26</sup> and 3D printing<sup>11</sup>. Recently, Roth and coworkers<sup>27</sup> proposed a new thionolactone structure, *ie* the 3,3-dimethyl-2,3-dihydro-5Hbenzo[*e*][1,4]dioxepine-5-thione (**DBT**, Figure 2) that is reported to homopolymerize, to copolymerize with styrene and methacrylate derivatives but not with *tert*-butyl acrylate. Nevertheless, the copolymerization with styrene is not ideal with a tendency to polymerize **DBT** first and styrene in a second time. In the case of methacrylate derivatives, the results are opposite with the incorporation of **DBT** only at the end of the polymerization. Satoh<sup>28</sup> and Destarac<sup>29</sup> developed in parallel thionolactide (**TLD**, Figure 2) as a new monomer for rROP. This compound copolymerizes with styrene and acrylate derivatives but with a high proportion of ring-retained moieties in the backbone. Reineke and coworkers<sup>30</sup> also reported a six-membered thionolactone, the thionoisochromanone (**TIC**, Figure 2), that copolymerizes with styrene but also with an undesired ring-retaining mechanism.

According to these studies, only a few thionolactones are available so far to prepare degradable vinyl-based copolymers, and with a peculiar reactivity that could be worthwhile to more finely tune. In this work, we thus aimed at gaining better understanding of the structure-reactivity relationship leading to efficient rROP for the thionolactone family. This will help to design *in silico* new structures and ultimately, their reactivity may be thereby rationalized tuned. We will focus exclusively on styrene and acrylate derivatives since thionolactones with low, moderate and good reactivity are already reported with these monomers. Reactivity ratios for the copolymerization with styrene and acrylate derivatives closer to 1 at temperature 80-100 °C were targeted to ensure the random incorporation of the weak bonds into the polymer backbone.

## RESULTS AND DISCUSSIONS

**DFT calculations.** The first part of this study was to understand the reactivity of thionolactones via DFT calculations. Our approach is based on the determination of rate constant of the different steps of the radical ring-opening polymerization, that is the addition of the propagating radical onto the C=S bond, the reverse addition that releases the same radical and the original thionolactone and the  $\beta$ -scission of the radical intermediate that leads to the incorporation

of the thioester bond in the polymer chain and the release of a new propagating alkyl radical (Figure 3).



**Figure 3.** Elementary steps relevant to the radical ring-opening copolymerization of thionolactones with vinyl monomers and the corresponding rate constants. With  $k_{\text{add}}$  as addition rate constant,  $k_{-\text{add}}$  as reverse addition rate constant,  $k_{\beta}$  as fragmentation rate constant and  $k_{\text{p}}$  as propagation rate constant.

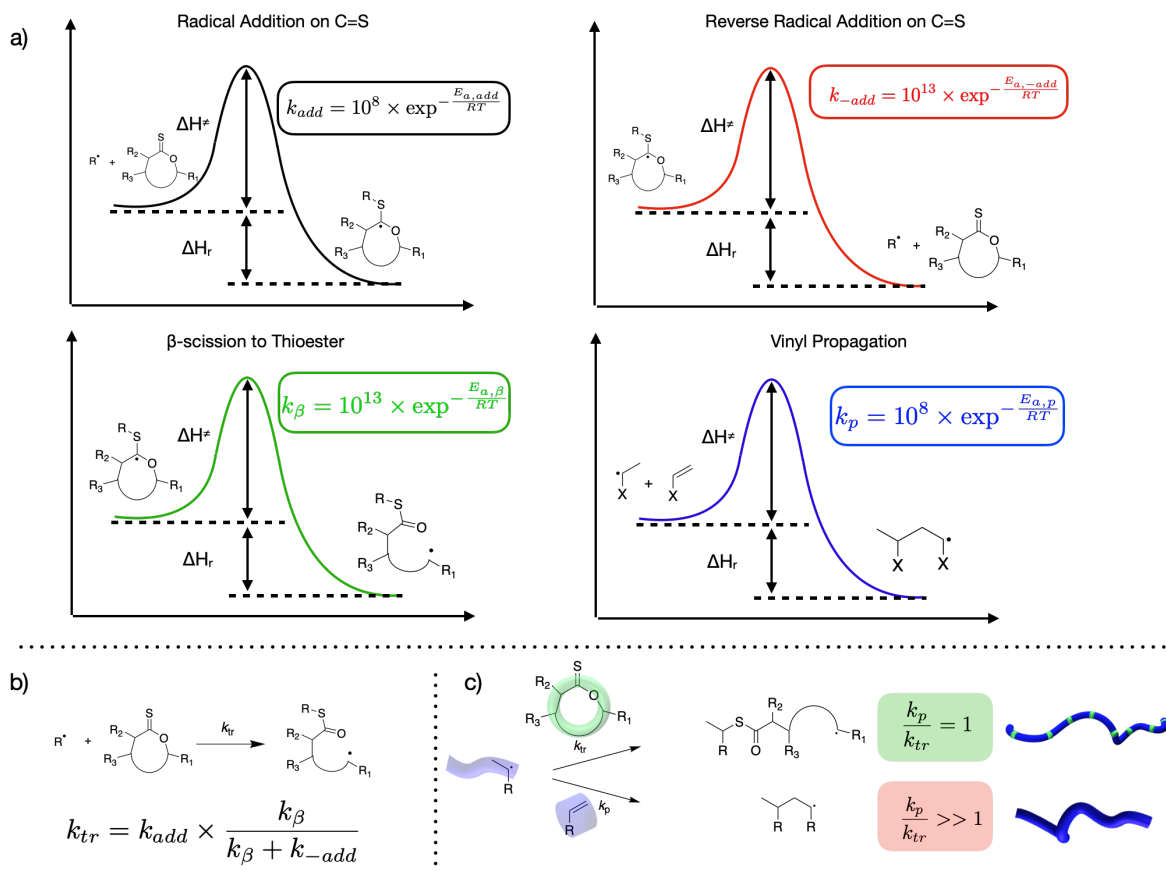
In a previous study, we used the transfer rate constant  $k_{\text{tr}}$  that is a complex rate constant combining the three steps and that describes the addition-fragmentation process.<sup>22</sup> This constant was then compared with the propagation rate constant of the vinyl monomer as a good way to evaluate the reactivity of the comonomer pair (Figure 4) by determining the  $r_{\text{vinyl}}$  reactivity ratio. Indeed, in these materials, the cyclic monomer is usually inserted as an additive (below 10 mol%) and thus the growing macroradicals are mainly the polyvinyl ones. Thereby, we could save computational time and avoid computing the  $r_{\text{thionolactone}}$  reactivity ratios. We showed in particular the negative Arrhenius behavior of such ratio that was experimentally proven in the case of the **DOT**/styrene copolymerization.<sup>22</sup> In this study, we only focused on structures that undergo efficient ring-opening and thus we discarded **TLD**<sup>28, 29</sup> and **TIC**<sup>30</sup> that showed moderate to high ring-retaining propagation. We thus applied the same methodology on three of the six originally prepared thionolactones to validate our approach (Table 1). As previously, we used B3LYP/6-31G(d) as method of DFT calculation because

we already showed that the reactivity of **CKA**<sup>14, 15, 31</sup> and thionolactones<sup>22</sup> was well described with this method and that the use of more sophisticated levels of theory (BMK, G3MP2RAD and a larger dataset) was at the expense of the calculation cost without better correlation with the experimental data. As done already in our previous papers, we used tabulated pre-exponential factors,<sup>14, 15, 22, 31</sup> instead of the one that can be obtained using DFT calculations. Even if the entropy associated for certain vibrations is correct, hindered rotations occurring in cyclic molecules cannot be properly taken into account.

In particular for radical addition reaction, we used  $A_{\text{add}} = 10^8 \text{ L mol}^{-1} \text{ s}^{-1}$  as recommended by Fischer and Radom<sup>32</sup> and for the unimolecular  $\beta$ -fragmentation, a value of  $A_{\beta} = 10^{13} \text{ L mol}^{-1} \text{ s}^{-1}$  was used for the  $\beta$ -scission and inverse radical addition.<sup>33-35</sup> The result of the DFT calculations as well as the  $k_{\text{tr}}$  values and the ratio  $k_{\text{p}}/k_{\text{tr}}$  are summarized in Table 1.

The first observation is that in agreement with the study of Roth,<sup>16</sup> **DOT** is the most efficient thionolactone since its  $k_{\text{p}}/k_{\text{tr}}$  value is roughly close to unity compared to values that are higher by 2-5 order of magnitude for thionolactones **1**, **2** and **5**. Since many approximations (gas phase, model molecules, etc.) were used during these calculations, only relative values between different structures are of interest. Besides this preliminary finding, other conclusions could be done. First, the addition rate constant  $k_{\text{add}}$  is dictated as expected by the group in  $\alpha$  position to the thionocarbonyl, with values one order of magnitude higher when an aromatic group is present (structure **1** compared to **2-5** and **DOT**). The presence of a stabilizing group on the released radical do not affect such value (structures **2** and **5**). For the  $\beta$ -scission, we could observe a drastic increase of the  $k_{\beta}$  between **2** and **5** that is due to the stabilizing properties of the ethyl group. It is more difficult to see the influence of the group in  $\alpha$  position to the thionocarbonyl since both groups were changed between **1** and **5**.

We already showed experimentally using **thCL** and **thDL** that an alkyl group inserted on the released radical did not drastically improve the efficiency of the radical ring-opening polymerization. The  $k_{\text{p}}/k_{\text{tr}}$  for **DBT** is very instructive. Its value for styrene is two orders of magnitude lower than the one for **DOT** and lower than unity, meaning that PS macroradical is more prone to add on **DBT** than on styrene thus indicating higher reactivity of **DBT** than **DOT** on styrene. This theoretical result is in good agreement with the experimental since **DBT** polymerizes non-randomly with **DBT** reacting first and styrene latter.













**Figure 4.** Methodology used to estimate the copolymerization behavior between thionolactones and vinyl monomers. a) DFT Calculations using the B3LYP/6-31G(d) level of theory and tabulated frequency factors.  $E_a = \Delta H^\ddagger(298K) + mRT$  with  $m$  the molarity of the reaction and  $T=353K$ . b) definition of the transfer constant  $k_{tr}$ . c) Determination of the  $k_p/k_{tr}$  ratio to estimate the copolymerization behavior.

**Table 1.** Computed values for the addition rate constant  $k_{add}$ ,  $\beta$ -scission rate constant  $k_{\beta}$ , reverse addition rate constant  $k_{-add}$ , transfer rate constant  $k_{tr}$  all defined in Figure 4 and the ratio between  $k_{tr}$  and the propagation rate constant  $k_p$  of styrene and acrylate derivatives calculated using the same approach for the experimentally prepared thionolactones (80 °C)

	$k_{add} / \text{L}\cdot\text{mol}^{-1}\cdot\text{s}^{-1}$		$k_{\beta} / \text{s}^{-1}$		$k_{-add} / \text{s}^{-1}$		$k_{tr} / \text{L}\cdot\text{mol}^{-1}\cdot\text{s}^{-1}$		$k_p/k_{tr}$		
	$(E_a / \text{kJ}\cdot\text{mol}^{-1})$		$(E_a / \text{kJ}\cdot\text{mol}^{-1})$		$(E_a / \text{kJ}\cdot\text{mol}^{-1})$						
<b>1</b>	$7.84 \times 10^1$ (41.3)	$8.47 \times 10^3$ (27.5)	$1.71 \times 10^5$ (52.5)	$4.91 \times 10^3$ (62.9)	$1.03 \times 10^{11}$ (13.4)	$7.06 \times 10^8$ (28.1)	$1.30 \times 10^{-4}$	$5.89 \times 10^{-2}$	$6.41 \times 10^5$	$1.16 \times 10^5$	
<b>2</b>	$1.53 \times 10^3$ (32.6)	$8.98 \times 10^4$ (20.6)	$3.98 \times 10^{-1}$ (90.6)	$3.75 \times 10^{-1}$ (90.8)	$5.42 \times 10^8$ (28.8)	$6.67 \times 10^8$ (28.2)	$1.12 \times 10^{-6}$	$5.05 \times 10^{-5}$	$7.43 \times 10^7$	$1.35 \times 10^8$	
<b>5</b>	$1.26 \times 10^3$ (33.1)	$1.52 \times 10^5$ (19.1)	$1.51 \times 10^0$ (86.7)	$2.47 \times 10^0$ (85.2)	$5.33 \times 10^8$ (28.9)	$1.66 \times 10^8$ (32.3)	$3.57 \times 10^{-6}$	$1.28 \times 10^{-3}$	$2.33 \times 10^7$	$3.64 \times 10^4$	
<b>DBT</b>	$4.22 \times 10^4$ (22.7)	$7.5 \times 10^5$ (14.4)	$3.37 \times 10^4$ (57.3)	$3.47 \times 10^5$ (50.4)	$1.89 \times 10^6$ (45.5)	$1.02 \times 10^6$ (47.3)	$7.56 \times 10^2$	$1.91 \times 10^5$	0.11	$3.57 \times 10^{-2}$	
<b>DOT</b>	$3.6 \times 10^3$ (30.0)	$1.33 \times 10^6$ (12.7)	$5.53 \times 10^3$ (63.1)	$2.04 \times 10^4$ (59.4)	$6.69 \times 10^6$ (41.7)	$4.34 \times 10^7$ (36.3)	2.52	525	33.12	12.99	

**Table 2.** Theoretical values (80 °C) of the addition rate constant  $k_{\text{add}}$ ,  $\beta$ -scission rate constant  $k_{\beta}$ , reverse addition rate constant  $k_{\text{-add}}$ , transfer rate constant  $k_{\text{tr}}$  all defined in Figure 4 and the ratio between  $k_{\text{tr}}$  and the propagation rate constant  $k_{\text{p}}$  of styrene and acrylate derivatives calculated using the same approach for in-silico designed thionolactones

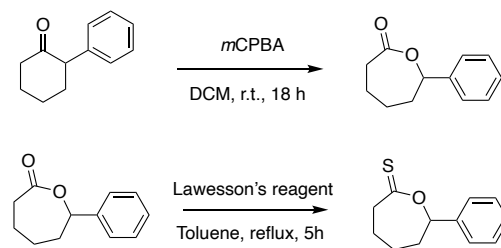
	$k_{\text{add}} / \text{L}\cdot\text{mol}^{-1}\cdot\text{s}^{-1}$		$k_{\beta} / \text{s}^{-1}$		$k_{\text{-add}} / \text{s}^{-1}$		$k_{\text{tr}} / \text{L}\cdot\text{mol}^{-1}\cdot\text{s}^{-1}$		$k_{\text{p}}/k_{\text{tr}}$	
	$(E_{\text{a}} / \text{kJ}\cdot\text{mol}^{-1})$		$(E_{\text{a}} / \text{kJ}\cdot\text{mol}^{-1})$		$(E_{\text{a}} / \text{kJ}\cdot\text{mol}^{-1})$					
										
<b>6</b>	$1.45 \times 10^3$ (32.7)	$1.08 \times 10^5$ (20.1)	$1.68 \times 10^5$ (52.6)	$5.79 \times 10^4$ (55.7)	$6.20 \times 10^8$ (28.4)	$1.07 \times 10^8$ (33.6)	$3.92 \times 10^{-1}$	$5.82 \times 10^1$	$2.13 \times 10^2$	$1.17 \times 10^2$
<b>7</b>	$2.51 \times 10^3$ (31.1)	$7.27 \times 10^5$ (14.5)	$6.35 \times 10^{-1}$ (89.2)	$1.34 \times 10^0$ (87.0)	$1.71 \times 10^7$ (39.0)	$7.23 \times 10^{10}$ (14.5)	$9.34 \times 10^{-5}$	$1.35 \times 10^{-5}$	$8.92 \times 10^5$	$5.05 \times 10^8$
<b>8</b>	$3.00 \times 10^2$ (37.3)	$6.36 \times 10^5$ (14.8)	$7.33 \times 10^3$ (61.8)	$1.64 \times 10^4$ (59.4)	$6.44 \times 10^7$ (35.1)	$2.65 \times 10^9$ (24.2)	$3.41 \times 10^{-2}$	3.95	$2.44 \times 10^3$	$1.72 \times 10^3$
<b>9 (POT)</b>	$5.44 \times 10^2$ (35.6)	$3.22 \times 10^4$ (23.6)	$6.46 \times 10^8$ (28.3)	$1.16 \times 10^8$ (33.4)	$8.92 \times 10^9$ (20.6)	$7.98 \times 10^8$ (27.7)	$3.68 \times 10^1$	$4.08 \times 10^3$	2.27	1.67

The  $k_{\text{p}}/k_{\text{tr}}$  for **DBT** and acrylate derivative is also very informative since this value is one order of magnitude lower than the one with styrene. We could then expect an even more pronounced inhomogeneous incorporation that is observed experimentally with only poly(**DBT**) that is produced without any polymerization of the acrylate derivative. These preliminary results confirmed the already available experimental data but the structural diversity (ring size, presence of a stabilizing group either or both in  $\alpha$  to the thionocarbonyl and on the released radical) of the structures (**1,2,5, DBT** and **DOT**) that have been prepared by Roth and coworkers<sup>16</sup> impede to clearly understand the key parameters to design efficient thionolactones.

**In-Silico design of new thionolactone.** Other structures were then calculated that will only differ in one feature to investigate in more details the reactivity of the thionolactone family. These structures and their calculated rate constants are presented in Table 2. We first designed and calculated a thionolactone bearing an aromatic group in  $\alpha$  position to the carbonyl moiety and a phenyl stabilizing group on the released radical (**6**) and compared it to the **DOT** structure. Indeed, in this case both compounds will have a stabilizing group for the radical addition and for the released radical. As expected, the compound has a  $k_{\text{p}}/k_{\text{tr}}$  value that is relatively low compared to the thionolactones **1, 2** and **5** prepared by Roth.<sup>16</sup> Nevertheless, the values (164-298) are still higher than the ones of **DOT** (13-31) and thus will impede its use in rROP. To highlight the influence of the various structural parameters, we then focused and calculated seven-membered ring thionolactones with only one phenyl stabilizing group (**7** and **8**). The addition rate in the case of styrene of the propagating radical onto the C=S bond is lower when the aromatic ring in  $\alpha$  position of the carbonyl is removed ( $k_{\text{add}}$  close to  $10^2$  instead of  $10^3$ - $10^4$   $\text{L}\cdot\text{mol}^{-1}\cdot\text{s}^{-1}$ ) but at the same time the selectivity between  $\beta$ -scission and inverse radical addition decreased, leading to higher  $k_{\text{p}}/k_{\text{tr}}$  values. This led to an unexpected low  $k_{\text{p}}/k_{\text{tr}}$  value for thionolactone **8**. With this result, we presumed that increasing the stabilization of the release radical could modify the  $k_{\text{p}}/k_{\text{tr}}$  value. We thus designed thionolactone **9** that possesses a pendant phenyl group at the released radical position, i.e. in epsilon position to enhance the stabilization of the released radical (styryl instead of benzyl like radical) and thus increase the selectivity of the fragmentation. Upon calculation, the thionolactone **9** presents the closest

$k_{\text{p}}/k_{\text{tr}}$  for copolymerization both with styrene and methyl acrylate. Compared to **8**, the  $\beta$ -scission is clearly favored by the better stabilizing effect of the radical and the selectivity between  $\beta$ -scission and inverse radical addition is strongly increased. To confirm experimentally these calculations, the thionolactone **9** was then synthesized and its (co)polymerization with vinyl monomers has been investigated, as described below.

**Synthesis of the thionolactone monomer.** The 7-phenyloxepane-2-thione (**POT, 9**) was prepared in a two steps process (Figure 5). A Baeyer-Villiger oxidation was first performed on phenylcyclohexanone to obtain the corresponding lactone using a published procedure (93 % yield).<sup>36</sup> The second step is the thionation of the lactone using the Lawesson's reagent in anhydrous toluene that gives the **POT** monomer in 50 % yield as a brown oil that solidified upon cooling.

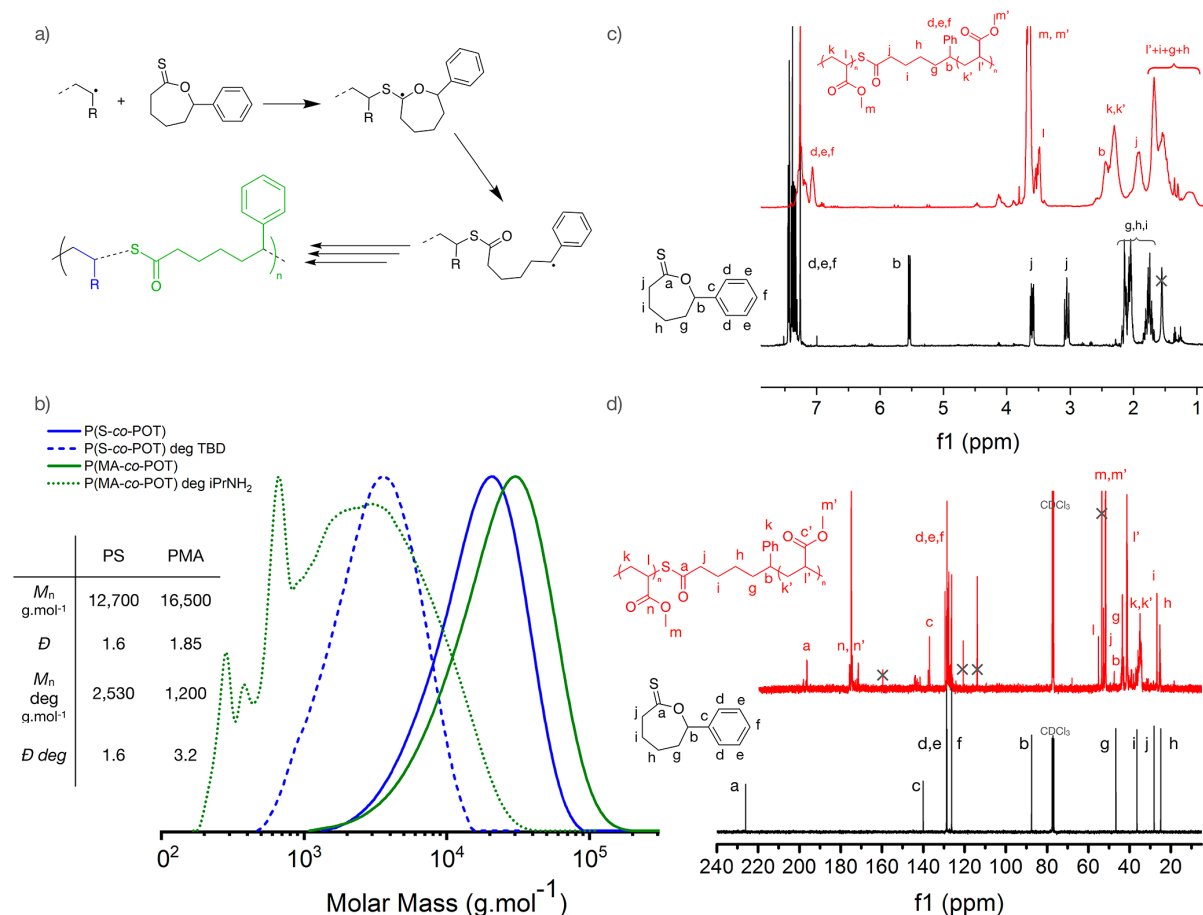


**Figure 5.** Preparation of 7-phenyloxepane-2-thione (**POT**)

The synthetic route is straightforward and allows to prepare easily **POT** in multigram scale. To compare with the synthesis of **DOT** and **POT**, we performed a preliminary economical study using the catalog price of the reactants from our local supplier. The price for preparing **POT** was estimated to be close to 50% lower than that of **DOT**. The detail of the calculation is given in ESI.

The first copolymerizations with styrene and methyl acrylate were then performed at 80 °C with 1 mol% of AIBN as an initiator following the pioneering work of Roth and coworkers.<sup>16</sup> To perform and monitor easily the copolymerization, we used anisole as a solvent (30 mol%) and followed the polymerization by <sup>1</sup>H NMR spectroscopy. In this preliminary study, only 5 mol% of **POT** were used as an additive to impart degradability without changing the

properties of the polymer. After 90 and 60 min respectively for styrene and methyl acrylate, we observed in both cases a color change from brown to pale yellow suggesting the isomerization of the C=S bond from thionoester to thioester occurring via the  $\beta$ -fragmentation process. The conversion determined by  $^1\text{H}$  NMR for styrene and **POT** reached 40 and 50 %, respectively, whereas the conversion of acrylate and **POT** reached 70 and 100%, respectively. The obtained copolymers are in the same range of molar masses, close to  $15,000 \text{ g}\cdot\text{mol}^{-1}$ . The rather similar conversion for both monomers is promising since we could expect a random incorporation of the monomer into the copolymer backbone and thus a rather good degradation profile. The  $^1\text{H}$  NMR spectra before and after polymerization are depicted in Figure 6a with the structure of the polymer obtained after the radical ring-opening copolymerization of **POT** with the vinyl comonomer (styrene or methyl acrylate). It is worth noting that there is no signal originating from ring-retaining polymerization (no  $^{13}\text{C}$  signal between 60-100 ppm).<sup>28-30</sup> The degradation of these two preliminary copolymers was then studied using accelerated conditions.



**Figure 6.** rROP of vinyl monomer (styrene (blue) or methyl acrylate (red)) with the thionolactone **POT**. b) SEC traces of poly(S-*co*-POT) and poly(MA-*co*-POT) before (plain line) and after TBD degradation (dashed and dotted lines).  $^1\text{H}$  (c) and  $^{13}\text{C}$  (d) NMR of **POT** and the poly(MA-*co*-POT).

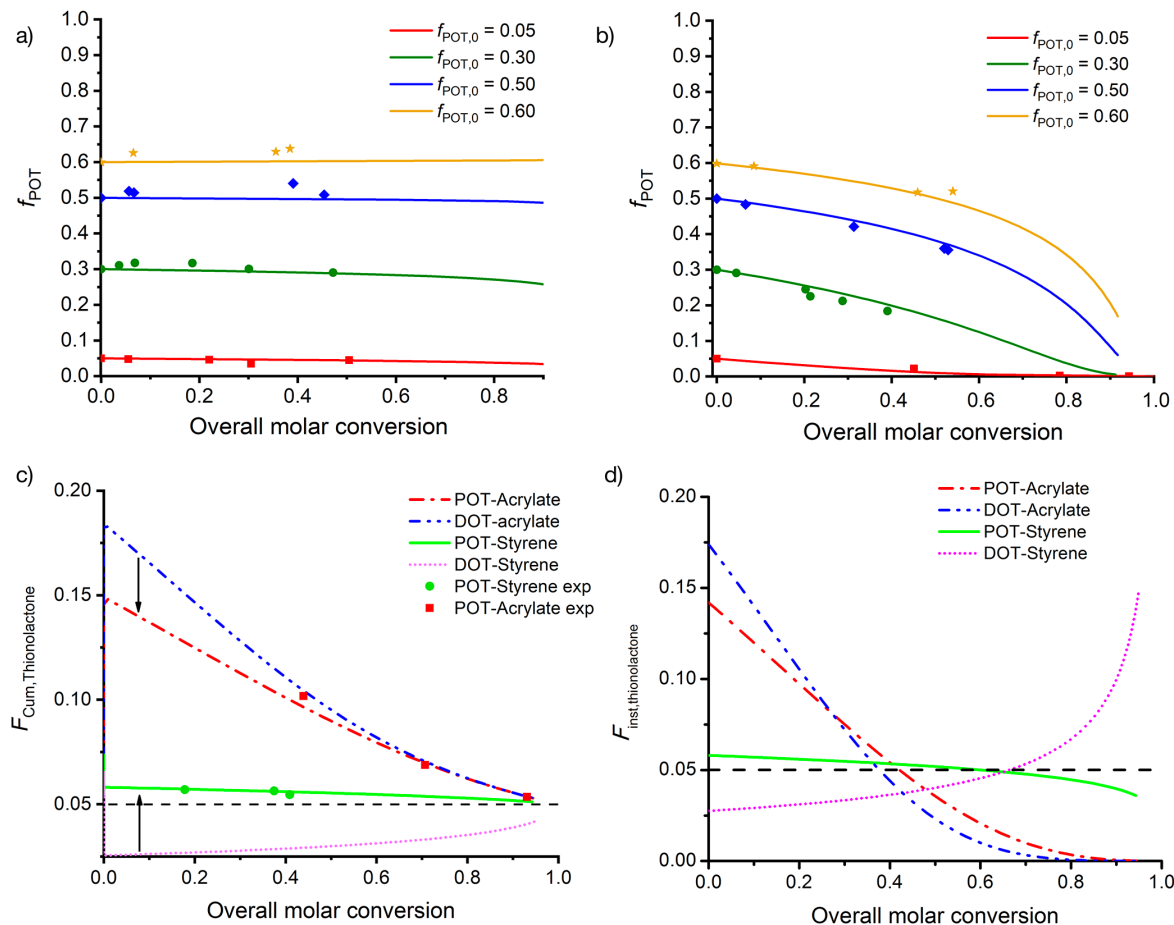
**Copolymerization behavior.** After the proof of concept, the copolymerization behavior of **POT** was further investigated by determining the copolymerization ratios. **DOT** is up to now the most efficient thionolactone to copolymerize with styrene and acrylate with reactivity ratios at 80 °C in the case of styrene:  $r_S = 2.0$  and  $r_{\text{DOT}} = 0.3$  and in the case of methyl acrylate:  $r_{\text{MA}} = 0.2$  and  $r_{\text{DOT}} = 1.6$ . These reactivity ratios led nevertheless to a composition drift with increasing conversion. **POT** was designed to be an alternative of **DOT** and according to the DFT calculations, we could expect a more random incorporation of the two comonomer into the polymer backbone. To validate this hypothesis, we thus measured the

We already showed that the degradation of polystyrene containing thioester moieties required 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) as a base in THF<sup>22</sup> whereas the one of polyacrylate derivatives could be done using either aminolysis or hydrolysis using KOH in a THF/MeOH solvent.<sup>16, 17</sup> The results of the degradation are presented in Figure 6b. A 2.5 wt% solution of TBD in THF was used for the degradation of both poly(S-*co*-POT) during one hour at room temperature and aminolysis using *N*-isopropylamine for poly(MA-*co*-POT). Both polymers showed an important decrease of the  $M_n$  ( $2,500 \text{ g}\cdot\text{mol}^{-1}$ ,  $D = 1.6$ ) and PS oligomers of DP 21-23 were obtained. This value is in good agreement with the theoretical one with 5 mol% of **POT** (theoretical DP=20). For poly(methyl acrylate), the length of oligomers is rather similar but with a higher dispersity, suggesting a lower random incorporation of thioester moieties than during the copolymerization with styrene. This result nevertheless confirmed that statistical incorporation of **POT** occurred during the copolymerization of the two vinylic monomers. This also confirms the better efficiency of **POT** than **DOT** to copolymerize with styrene and acrylate derivatives.

reactivity ratios of **POT** with styrene, and the bulky isobornyl acrylate (IBA) that led to high  $T_g$  acrylate that facilitates purification and handling (Figure 7). Molar mass distribution in case of PIBA were determined using an universal calibration and Mark-Houwink-Kuhn-Sakurada parameters.<sup>37</sup> The polymerizations were done in anisole (50 mol%). The reactivity ratios were then evaluated first by fitting the evolution of the feed ratio versus the overall molar conversion (Figure 7a and 7b) using the Skeist equation and a nonlinear least-squares (NLLS) method (Meyer-Lowry method). We also used the CONTOUR software (see ESI for details) to confirm these values and calculate the 95% joint confidence interval.

The experiments with styrene led to reactivity ratios close to unity ( $r_S = 0.8$ ,  $r_{POT} = 0.9$ ) showing no compositional drift even at high conversion. In the case of IBA, the values are less ideal at  $r_{IBA} = 0.3$  and  $r_{POT} = 1.4$ , indicating a slight decrease of  $F_{POT}$  with conversion (Figure 7b). These reactivity ratios are nevertheless greatly improved for styrene and slightly improved for acrylate derivatives compared to **DOT**. With these reactivity ratios, it is possible to plot the evolution of the instantaneous and the cumulated fraction of inserted thioester bonds into the polymer backbone versus the overall monomer conversion (see ESI for details). Such plot is represented in Figure 7c-d for an initial feed ratio of 5 mol% in thionolactone

and it allows to visualize the compositional drift that occurred during the reaction. The same plot for **DOT** in the same copolymerization system is also reported in the same Figure 7c-d. Experimental data for POT were also added to support the theoretical value (see ESI for details). The impact of **POT** compared to **DOT** is clearly apparent especially for styrene and is less pronounced for acrylate derivatives. In all cases (**DOT** and **POT**) for the polymerization of acrylate derivatives, the conversion has to be kept below 60-70% conversion to still have insertion of thioester moieties into the polymer backbone.



**Figure 7.** Experimental and theoretical POT monomer composition versus overall molar conversion during the solution copolymerization at 80 °C initiated with 0.5 mol% AIBN of **POT** (5 mol%) and : a) Styrene with  $r_S = 0.8$  and  $r_{POT} = 0.9$ ; b) isobornyl acrylate with  $r_{IBA} = 0.3$  and  $r_{POT} = 1.4$ . c) Cumulated average molar composition in thioester of the copolymers. d) Instantaneous average molar composition in thioester of the copolymers.

**Degradation studies.** Since we know that **POT** is efficiently inserted into polymer chains for both styrene and isobornyl acrylate, we then focused on the properties of the materials and in particular their degradation conditions.

Unlike **DOT**,<sup>38</sup> the **POT** monomer is more soluble in both styrene and isobornyl acrylate. We used the procedure already reported by Johnson *et al.*<sup>38</sup> to determine precisely its solubility in styrene. At room temperature, the POT solubility in styrene is 24 mol% that is drastically higher than **DOT** solubility in styrene (2.7 mol%). This will help us to target high molecular weight polymers.

We then prepared two virgin polymers of PS and PIBA with 5 mol% of **POT** at 80°C. The polymerizations were first performed for 15 h at 80°C initiated with 0.2 mol% AIBN to increase the molecular weight. The polymerization of styrene was performed in bulk whereas the one of isobornyl acrylate was performed with 30 mol% of anisole. Conversions were close to 94% for styrene and

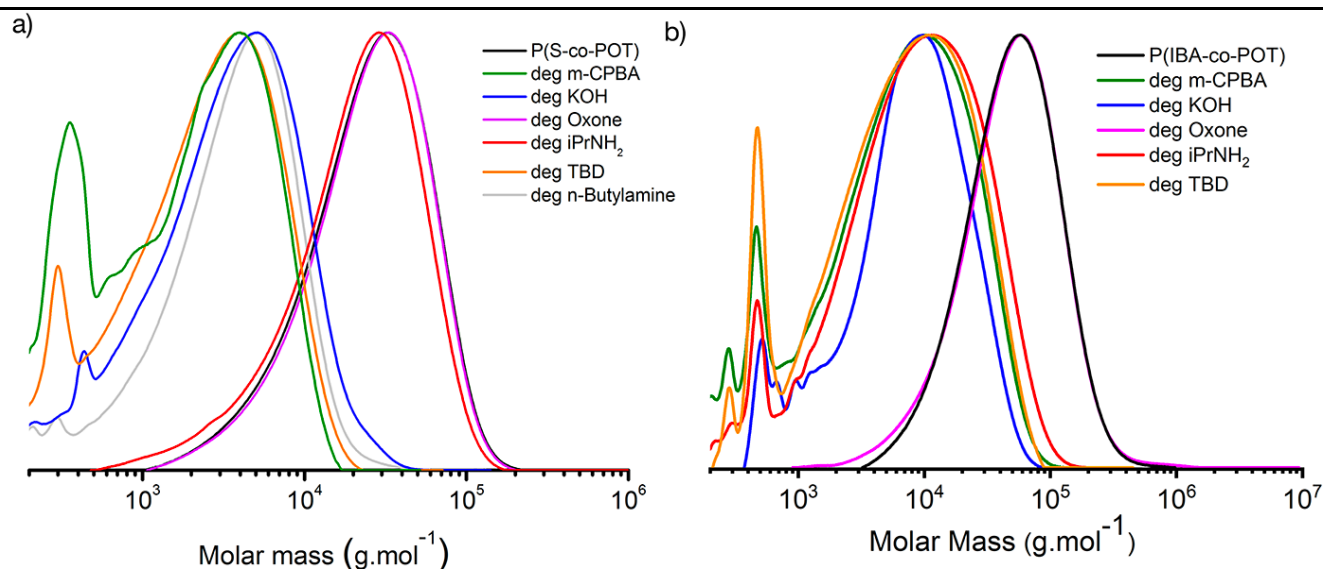
85% for IBA. The characteristics of the polymers are gathered in Table 3. The degradation of the copolymers was then studied using accelerated chemical conditions. The result of the degradation is presented in Figure 8. We first used the classic basic degradation using KOH 5 wt% in THF/MeOH for 17 hours. For both copolymers, we observed a complete degradation that led to oligomers of  $M_n = 3,100 \text{ g}\cdot\text{mol}^{-1}$  (DP=28) and  $6,400 \text{ g}\cdot\text{mol}^{-1}$  (DP=30) for PS and PIBA, respectively. Aminolysis of PIBA via *i*PrNH<sub>2</sub> following the protocol of Roth<sup>16</sup> gives similar degraded products. Unlike P(*S-co*-**DOT**), the incorporation of **POT** in polystyrene led to partial aminolysis using the same protocol. The better degradation could be due to an enhanced accessibility due to more flexible C4 alkyl moiety compared to the rigid bis-aromatic structure of **DOT**. When more drastic conditions (100 % *n*-butylamine at 50°C for 15 hours) were used for aminolysis, we observed similarly to **DOT**, the total degradation of the P(*S-co*-**POT**). We then explored the oxidative



degradation of the copolymers and tested the oxone degradation conditions that were reported by Roth.<sup>39</sup>

**Table 3.** Characterization of S/POT and IBA/POT copolymers prepared at 80°C and 120°C before and after TBD degradation.

	Monomer: POT	$M_n$ (g.mol <sup>-1</sup> )	$M_w$ (g.mol <sup>-1</sup> )	$D$	$T_g$ (°C)	Degradation conditions	$M_n$ (g.mol <sup>-1</sup> ) degradation	$M_w$ (g.mol <sup>-1</sup> ) degradation	$D$ degradation
P(S- <i>co</i> -POT) 80°C	95:5	16,000	33,000	2	87,4	TBD 2.5 wt% in THF	2,400	4,100	1.7
P(IBA- <i>co</i> - POT) 80°C	95:5	25,000	51,000	2	72	TBD 2.5 wt% in THF	5,500	13,450	2.5
P(S- <i>co</i> -POT) 120°C	97.5:2.5	47,000	100,000	2.1	92	TBD 2.5 wt% in THF	6,200	10,900	1.75
P(IBA- <i>co</i> - POT) 120°C	97.5:2.5	51,800	98,000	1.9	77	TBD 2.5 wt% in THF	8,100	12,600	1.6



**Figure 8.** Evolution of the molar mass distribution of a) P(S-*co*-POT) and b) P(IBA-*co*-POT) prepared at 80°C and 5%POT before and after various degradation conditions.

It has to be noted that similar oxidative degradation conditions were also reported by Destarac and coworkers<sup>29</sup> with bleach on PVAc. In both cases, the oxidants were placed in water solutions.

When the copolymer is water-soluble, the degradation was very rapid<sup>39</sup> and when PVAc was tested due certainly to its hydrophobic nature, weeks<sup>29</sup> were necessary to observe degradation. We started with oxone degradation conditions and monitored the evolution of  $M_n$  versus conversion for one day. We did not observe any degradation whatever the copolymer used. To speed-up the degradation, we then moved from water-soluble oxidant to organo-soluble oxidant and selected *meta*-chloroperbenzoic acid (*m*CPBA). Both PS and PIBA copolymers were efficiently degraded at room temperature for 17 hours in a solution of THF containing 2.5 mol% of *m*CPBA whereas the polymers without thionolactone was not impacted (see Figure S8). These new degradation conditions present the advantage to selectively degrade thioester moieties without using a strong base that could lead to side-reactions.

In all successful conditions, the molar mass distributions of oligomers are rather similar with average values of 3,000 and 6,000 g.mol<sup>-1</sup> for PS and PIBA respectively. The nature of the chain-end,

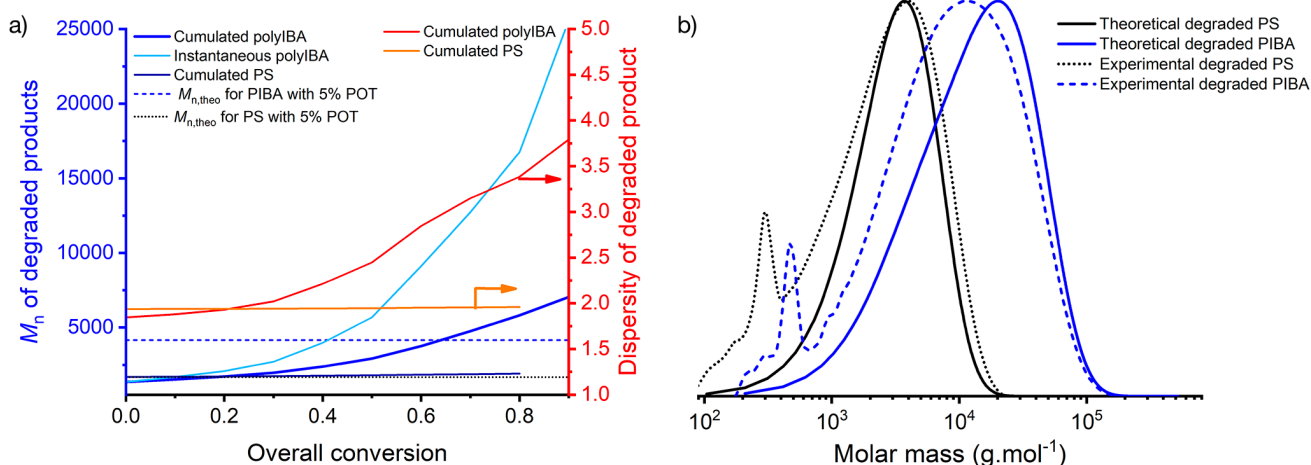
the presence of impurities in the degradation peak and the purification conditions are responsible for such small differences. To investigate the random character of the **POT** insertion, we used the analytical approach developed from Van Herk and coworkers<sup>40</sup> that allow to theoretically create molar mass distribution using reactivity ratio and feed ratio as input parameters. By using 10% conversion increment and addition of the different mass distribution it is possible to simulate the cumulative distribution of the degraded products (see ESI section 8 for details). The evolution of the  $M_n$  and  $D$  of the degraded products were presented on Figure 9a. When similar reactivity ratios were used, the  $M_n$  of the degraded products and  $D$  were constants, whereas during the compositional drift, the  $M_n$  increased as well as the dispersity (from 2 to 3 above 60% conversion). Such theoretical distributions were then compared with experimental ones on Figure 9b (The degradation using TBD was chosen for styrene and aminolysis for PIBA). In both case there is a rather good agreement between experimental and theoretical data. The theoretical and experimental degradation in the case of **POT** – Styrene was very similar confirming the very good homogeneity of the degradation products. The one for **POT** – IBA was less similar,

which could come from some branching<sup>41</sup> (occurring at moderate or high conversion) or molar mass determination accuracy that could happen using universal calibration for oligomers.

To increase the differences between the virgin and degraded materials, we tried to increase the molecular weight of the polymers by preparing them at higher temperature. Our calculations on  $k_p/k_{tr}$  values showed a low temperature dependence (see ESI Table S22 for details) and we could thus expect to have the same reactivity and therefore random copolymers with these conditions. We thus performed the copolymerization of **POT** with styrene and IBA at 120 °C without initiator and with 2.5 mol% of **POT**. In both cases, we obtained 99% conversion of **POT**, 90 % conversion of IBA and 99 % of S. The  $M_n$  increased up to 40-50,000 g.mol<sup>-1</sup> (see Table 3 for details). Under the same degradation conditions, oligomers of DP in rather good agreement with the amount of incorporated **POT** could be obtained (Figure S9). This confirms that the length of the oligomers is not impacted by the chain length of the polymer but

only by the amount of initial **POT** added in the polymerization medium. With higher  $M_n$  for the pristine copolymer, the percentage of  $M_n$  reduction is higher and reached 85% and 89% for the polystyrene and PIBA respectively.

**Compatibility with RAFT polymerization.** We showed that the **POT** could be a valuable alternative to **DOT** to obtain degradable organic polymers. We thus investigated its compatibility with RDRP (reversible-deactivation radical polymerization) technique, and we chose to test RAFT polymerization since this process is compatible with the temperature we already tested. The preliminary studies of Roth<sup>16</sup> and Gutekunst<sup>17</sup> combined **DOT** copolymerization and RAFT but do not compare the block copolymer efficiency with and without thionolactone. Later, Guillaneuf<sup>22</sup> and Johnson<sup>38</sup> showed that **DOT** copolymerization is also compatible with NMP. To ensure the compatibility of **POT** and RAFT, we aimed at preparing block copolymers with styrene and IBA.



**Figure 9.** a) Evolution of  $M_n$  and  $D$  for the degraded products from PS and PIBA containing **POT** copolymer using the analytic approach from Reference <sup>40</sup>. b) Experimental and theoretical molar mass distribution of the PS and PIBA degraded products.

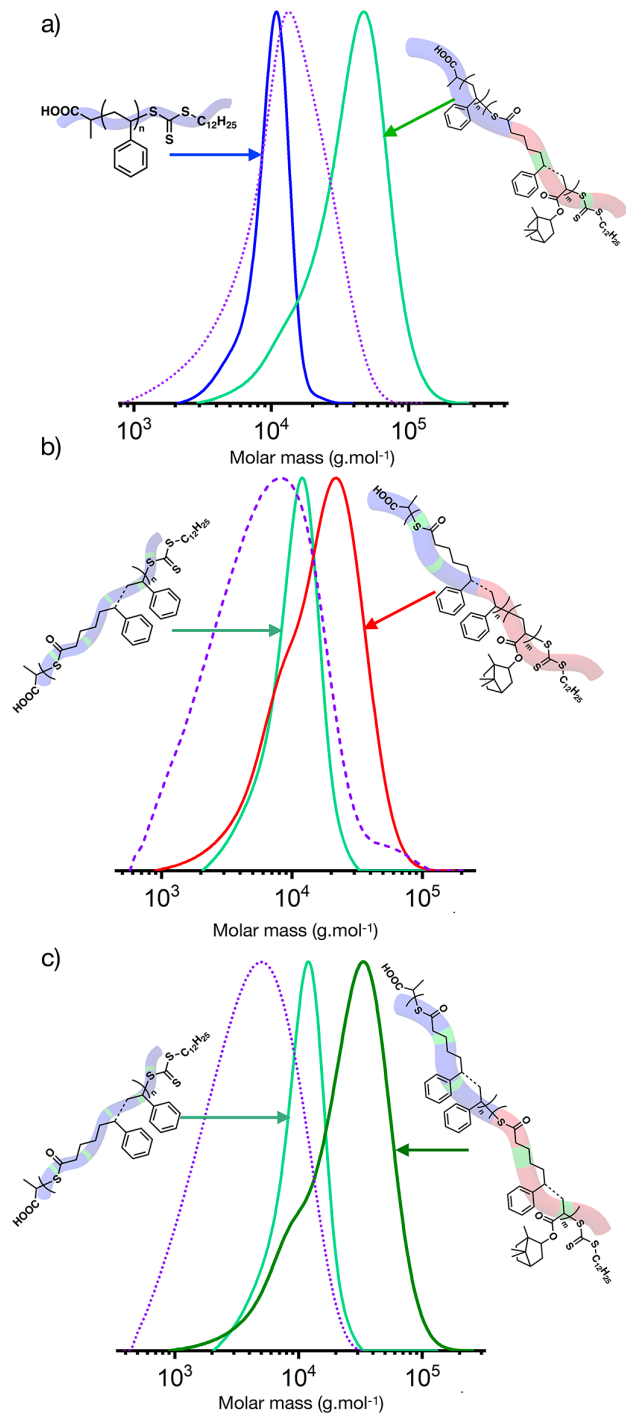
In the case of these monomers, the best order to prepare diblock copolymer is to synthesize first a PS macroinitiator to reinitiate the polymerization of IBA. As **POT** is compatible with both monomers, we added either **POT** in the first block or in the second block or both (Figure 10). Two PS macroinitiators were prepared having or not 5 mol% of **POT**. We used the 2-(dodecylthiocarbonothioylthio) propionic acid (DoPAT) as RAFT agent and performed the polymerization in bulk at 80°C for 20 hours. Macroinitiators with  $M_n$  close to 9,000 g.mol<sup>-1</sup>. were obtained (see ESI for details). A closer analysis of the molar mass distribution of the macroinitiators with and without **POT** showed a broadening of the distribution ( $D$  from 1.13 for PS-RAFT to 1.28 for P(S-co-POT)-RAFT, Figure S4). Similar results were already observed in the case of **DOT** - styrene copolymerization made via NMP.<sup>22</sup> Since the C=S bond of the RAFT agent absorbs at 290 nm, the livingness of the polymers was investigated by double detection SEC (DRI and UV at 290 nm). The UV signal of the P(S-co-POT)-RAFT presented also a broad chromatogram that suggested two kinds of polymer chains (Figure S5). The majority of polymer chains are low  $D$  polymer chains end-functionalized by the dithioester functionality and some chains still have the dithioester functionality but seems deactivated. Similar results were obtained by NMP (see ESI section 6 for details). This result could be explained by the irreversible trapping of the **POT** intermediate by the RAFT end-group. Such side-reaction has been already reported in the case of CKA – NMP polymerization<sup>42</sup> and it has been reported that the cyclic thionocaprolactone (**thCL**) intermediate could be involved in the propagation of the **thCL** – vinyl acetate pair depending of the experimental conditions,<sup>20,21</sup> showing

its ability to add on thCL or vinyl monomers To confirm such hypothesis, polymerization with various amounts of solvent were performed and as expected the higher amount of solvent led to the minimal amount of side reaction (Figure S6). However, at high dilution it was not possible to obtain high conversion and high molar mass PS, thus 50 mol% of anisole was used as an optimal amount of solvent. From these two macroinitiators PS-RAFT and P(S-co-POT)-RAFT, the polymerization of IBA without or with 1 mol% of **POT** was then performed.

We chose this amount of **POT** since it will allow an insertion of thioesters units above to 2 mol% up to 45% conversion Figure S3). All the details of the polymerization are given in the ESI in Table S33 and S34. In all cases, there is a rather good re-initiation efficiency of the polymerization of IBA with block copolymers having  $M_n$  in the range of 20,000 g.mol<sup>-1</sup>.

A tailing of the molar mass distribution is nevertheless observed when the P(S-co-POT) was used as expected due to the side-reaction described above. Increasing the amount of **POT** in the second block synthesis do not impact significantly the tailing (see Figure S7 for detail). The degradation using TBD at room temperature for 1 hour was then performed on all the block copolymers and showed the expected degradation profiles. The molar mass distributions before and after degradation via TBD are shown in Figure 10. The reference P(S-*b*-IBA) was not impacted by this degradation conditions (Figure S10). When a pure PS block was used and POT was inserted only in the second block, the degradation of the block copolymer led to a polymer with a  $M_n$  close to the first PS block that is attached to the residual PIBA Degraded PIBA chains are then

mixed with the first PS block and this could explain the rather broad distribution of the degraded products (see ESI section 8.2 for detail).

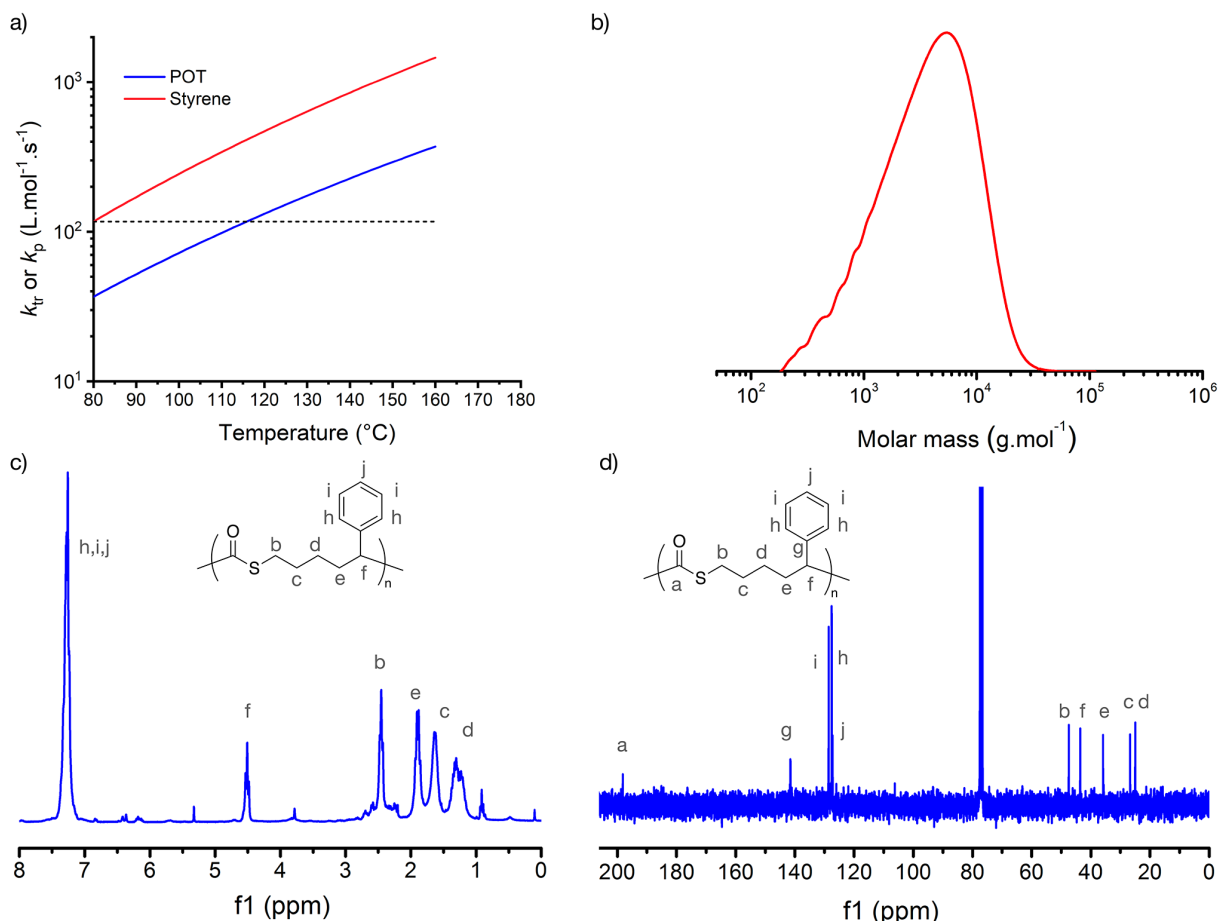


**Figure 10.** Evolution of the molar mass distribution before and after TBD degradation of a) PS-*b*-(PIBA-*co*-POT) diblock

copolymers prepared from a PS-macroRAFT agent, b) P(S-*co*-POT)-*b*-(PIBA) diblock copolymers prepared from a P(S-*co*-POT) macroRAFT agent, c) P(S-*co*-POT)-*b*-(PIBA-*co*-POT) diblock copolymers prepared from a P(S-*co*-POT) macroRAFT agent. The P(S-*co*-POT) macroRAFT agent was prepared using 5 mol% of POT and the reinitiation with IBA was done with and without 1 mol% of POT.

When POT is inserted into the first block and not in the second block, the degradation released only the second block PIBA whose  $M_n$  value is close to the one obtained by subtracting the  $M_n$  of the first block to the one of the copolymer (diblock  $M_n = 14,900 \text{ g.mol}^{-1}$ ,  $M_n$  of the PIBA block =  $7,750 \text{ g.mol}^{-1}$ ). A dual detection SEC confirmed the absence of a UV signal at 254 nm and thus in that case PS was discarded in the mixture (Figure S11 in ESI). When POT was inserted into the two blocks, the degradation products have the smaller  $M_n$  confirming the degradation of both blocks and the rather good efficiency of this technique. More studies are nevertheless required to investigate in detail the living character and compatibility of thionolactone and RDRP polymerization,

**Homopolymerization of thionolactone.** The last point to investigate concerning the development of a new monomer for radical ring-opening polymerization concerns its ability to homopolymerize. CKAs and in particular 2-methylene dioxepane (MDO) are known to readily homopolymerize to obtain polyesters. There is only few data concerning the homopolymerization of thionolactones. Roth *et al.* reported the difficult homopolymerization of DOT with less than 10% conversion in 7 days at  $60^\circ\text{C}$ .<sup>19</sup> The same authors also reported the AIBN-initiated free-radical polymerization of DBT that reached 35% conversion after heating at  $70^\circ\text{C}$  overnight.<sup>27</sup> The polymer was characterized by NMR but not by SEC due to solubility issues. The homopolymerization of TIC was also reported but similarly to DOT, the polymerization proceeded slowly with 75% conversion reached after eight days at  $70^\circ\text{C}$  in DMF. In addition, the produced polythioester has a low  $M_n$  ( $2,000\text{--}7,500 \text{ g.mol}^{-1}$ ). Since the ring-opening of POT produces a styryl like radical, the predicted  $k_{tr}$  value could be seen as a theoretical propagation rate coefficient  $k_p$ . At  $80^\circ\text{C}$ , the value is very low compared to styrene and thus can only allow to prepare small oligomers. To find a more efficient  $k_p$  value to reach acceptable polymerization kinetics, we plotted on Figure 11a the evolution of  $k_{tr}$  (that is in this case the  $k_p$  value of POT) with temperature and compared it with the  $k_p$  of styrene determined using the same level of theory. To have an efficient propagation rate constant, the use of  $120^\circ\text{C}$  seems a better temperature to perform the polymerization since we could expect a similar  $k_p$  value for POT than the  $k_p$  value of styrene at  $80^\circ\text{C}$ . We thus investigated the homopolymerization of POT at this temperature. The polymerization was performed in the presence of anisole (33 mol%) to solubilize the VAM-111 azo initiator (0.5 mol%). The polymerization was followed by  $^1\text{H}$  NMR spectroscopy (see Figure S13). After 22 hours, the conversion was complete, and a waxy polymer was obtained. A polythioester with a  $M_n$  of  $5,500 \text{ g.mol}^{-1}$  with a  $D$  of 2 and a  $T_g$  of  $1\text{--}2^\circ\text{C}$  was obtained. These preliminary results confirmed the interest of POT as a possible route to prepare poly(thioester)s. This will be investigated in detail in a further study.



**Figure 11.** a) Theoretical evolution of the  $k_{tr}$  value (Styrene – POT) versus temperature and its comparison with the theoretical  $k_p$  value of styrene. b) Molecular weight distribution of poly(POT), c)  $^1\text{H}$  NMR analysis of poly(POT). d)  $^{13}\text{C}$  NMR analysis of poly(POT).

## CONCLUSION

Thionolactones have been recently introduced as new promising monomers for radical ring-opening polymerization. Nevertheless only two structures were really efficient and only one (dibenzo[c,e]-oxepane-5-thione (**DOT**)) could be used for the activated monomers (styrene, acrylate, acrylamide derivatives). In this work, we showed that estimation of the  $k_p/k_{tr}$  by DFT calculations help to understand the peculiar reactivity of thionolactones. Thanks to this approach experimental results previously reported for a series of thionolactones could be rationalized. Secondly the better understanding of the thionolactone reactivity allowed us to design a new efficient thionolactone, *i.e.* the 7-phenyloxepane-2-thione (**POT**). An experimental study confirmed the good copolymerization behavior of this thionolactone with styrene and isobornyl acrylate as a model for acrylate derivatives. A detailed kinetic analysis led to reactivity ratios of  $r_S = 0.8$  and  $r_{POT} = 0.9$  for the **POT** - Styrene monomers and  $r_{IBA} = 0.3$  and  $r_{POT} = 1.4$  for the **POT** - isobornyl acrylate monomers, both for solution copolymerization at 80 °C in anisole (50 mol%) initiated with 0.5 mol% AIBN. With these reactivity ratios, a more homogeneous incorporation of thioesters into the polymer chains could be obtained. Good chemical degradation profile was demonstrated with the already used degradation conditions (aminolysis, KOH, TBD) and we also presented a new efficient oxidative degradation procedure using *m*CPBA in THF at RT. The good degradation properties of the obtained copolymers are an indirect proof of the random incorporation of thioester moieties into the backbone that is essential for a homogeneous degradation.

In addition, feasibility of POT polymerization using RAFT was evidenced by preparing a library of block copolymers with thioesters

units that could be inserted in one or both blocks. A side reaction between the thionolactone and the RAFT agent reduced the livingness of the copolymerization. Although a more detailed study is required to have a better understanding of this side reaction, the degradation was effective and confirmed the interest of this technology to prepare block copolymers with one or two blocks that could be degraded. Homopolymerization of **POT** was also demonstrated. p(POT), a new polythioester of moderate  $M_n$  prepared via a radical mechanism could be obtained with full conversion and complete ring-opening mechanism.

In conclusion, this work confirms the interest of our approach that uses the combination of theoretical and experimental experiments to rationally identify new structures or polymerization conditions for radical ring-opening polymerization. This approach is currently used in our laboratories to extend the library of vinyl monomers that are compatible with thionolactones and diversify the structures of thionolactone used.

## ASSOCIATED CONTENT

The Supporting Information is available free of charge on the ACS Publications website.  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra of the monomer and the copolymers, details of the calculations,

## AUTHOR INFORMATION

### Corresponding Author

\* [yohann.guillaneuf@univ-amu.fr](mailto:yohann.guillaneuf@univ-amu.fr)

### Author Contributions

The manuscript was written through contributions of all authors.

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