### Initiation of Radical Chain Reactions of Thiol Compounds and Alkenes without any Added Initiator: Thiol-Catalyzed *cis/trans* Isomerization of Methyl Oleate

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**Abstract:** A kinetic study of the dodecanethiol-catalyzed *cis/trans* isomerization of methyl oleate (*cis-2*) without added initiator was performed by focusing on the initiation of the radical chain reaction. The reaction orders of the rate of isomerization were 2 and 0.5 for **1** and *cis-2*, respectively, and an overall kinetic isotope effect  $k_{\rm H}/k_{\rm D}$  of 2.8 was found. The initiation was shown to be a complex reaction. The electron-donor/-acceptor (EDA) complex of dodecanethiol (**1**) and *cis-2* formed in a pre-equilibrium reacts with thiol **1** to give a stearyl and a sulfuranyl radical through molecule-assisted homolysis (MAH) of the sulfur–hydrogen bond. Fragmentation of the latter gives the thiyl radical, which catalyzes the *cis/trans* isomerization. A computational study of the EDA complex, MAH reaction, and the sulfuranyl radical cal-

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culated that the activation energy of the isomerization was in good agreement with the experimental result of  $E_A = 82 \text{ kJ m}^{-1}$ . Overall, the results may explain that the thermal generation of thiyl radicals without any initiator is responsible for many well-known thermally initiated addition reactions of thiol compounds to alkenes and their respective polymerizations and for the low shelf-life stability of *cis*-unsaturated thiol compounds and of mixtures of alkenes and thiol compounds.

### Introduction

The *cis/trans* isomerization of unsaturated fatty acids, that is, oleic acid of lipids, in biological systems is of great importance.<sup>[1]</sup> Chatgilialoglu et al. showed that thiyl radicals are among the most efficient isomerizing agents and studied in detail the kinetics of the *cis/trans* isomerization of oleic acid of phospholipids and methyl oleate with thiol compounds occurring in a radical chain reaction.<sup>[2-4]</sup> The reaction was initiated by either the thermal decomposition of azo compounds.<sup>[2]</sup>  $\gamma$ -irradiation.<sup>[2,3]</sup> or photochemically generated

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thiyl radicals.<sup>[4]</sup> These studies support the mechanism in Scheme 1; however, side reactions are also at work and give the same products but change the rate of reaction. Thus, for

$$RS^{\bullet} + \underset{R^{1}}{R^{2}} \xrightarrow{k_{a}^{Z}} RS \xrightarrow{k_{b}^{E}} R^{2} \xrightarrow{k_{b}^{E}} R^{1} \xrightarrow{R^{2} + RS^{\bullet}} RSSR$$

Scheme 1. Thiyl radical-catalyzed isomerization of mono-unsaturated fatty acid methyl esters.  $^{\left[2-4\right]}$ 

the rather high thiol concentrations of 0.30 and 0.93 M, blank experiments on nonirradiated samples showed some isomerization. This outcome indicates "an unknown additional thermal generation of thiyl radicals", which could be of importance in biological systems.<sup>[3]</sup>

The radical addition of thiol compounds to alkenes initiated photochemically or thermally with radical initiators is a well-known and intensively studied reaction.<sup>[5]</sup> It is well known that certain thiol/ene mixtures are quite thermally unstable at room temperature, and many studies on the related shelf-life stability are available.<sup>[6]</sup> However, only very few investigations on the initiation of this dark reaction have been reported. In the 1980s, Nuyken et al. studied the very efficient thermally initiated radical polymerization of 3-



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and 4-vinylbenzenethiol and dithiol compounds with dienes and diynes without the addition of any special initiator.<sup>[7]</sup> Kinetic evidence was found for the molecule-assisted homolysis (MAH)<sup>[8]</sup> of the S–H bond as an initiation reaction. The activation energy of the addition of thiophenol to styrene as a model reaction was  $E_A = 65 \text{ kJ M}^{-1}$ , which was in good agreement with the calculated activation energy of the bimolecular reaction of thiophenol and styrene to give a thiyl and a 1-phenylethyl radical as an initiation reaction (Scheme 2).<sup>[9]</sup> Klemm and Sensfuß observed the formation

$$R^{1} + S - R \xrightarrow{k_i} R^{1} + S - R$$

Scheme 2. Radical formation by a bimolecular reaction of a thiol and an alkene, a molecule assisted homolysis (MAH).  $^{\left[9\right]}$ 

of an electron-donor/-acceptor (EDA) complex of a thiol and alkene in solution by UV spectroscopic analysis and postulated the formation of a thiyl and an alkyl radical from this EDA complex (Scheme 3).<sup>[10]</sup> This result is equivalent to the MAH reaction postulated by Nuyken et al.<sup>[9]</sup> EDA complexes of thiol compounds and alkenes have also been studied by <sup>1</sup>H NMR spectroscopic analysis.<sup>[11]</sup>

$$\mathbb{R}^{1}$$
 +  $\overset{\mathsf{H}}{\mathsf{S}}$ - $\mathbb{R}$   $\overset{\mathsf{K}_{\mathsf{EDA}}}{\longleftrightarrow}$  [EDA complex]  $\overset{\mathsf{K}_{i}}{\longrightarrow}$   $\mathbb{R}^{1}$  +  $\overset{\mathsf{S}}{\bullet}$ - $\mathbb{R}$ 

Scheme 3. Radical formation via a EDA complex of a thiol and an alkene.  $^{\left[ 10\right] }$ 

Initiation of radical chain reactions by MAH or moleculeinduced homolysis<sup>[12]</sup> have been reported previously, for instance, the thermal initiation of styrene polymerization through the de Mayo mechanism,<sup>[13]</sup> the thermally initiated addition of alkanes to alkenes<sup>[14]</sup> and alkynes<sup>[15]</sup> (i.e., the ane reaction), uncatalyzed transfer hydrogenation and transfer hydrogenolysis,<sup>[16]</sup> and the thermally induced redox reactions of carbonyl compounds and alcohols<sup>[17]</sup> fall into this category. It may be mentioned that this simple elementary reaction of two closed-shell molecules to give two radicals, which is the reverse reaction of the well-known disproportionation reaction of two radicals, has not found an entrance into textbooks and has been remained rather unknown despite being suggested about 50 years ago.<sup>[18]</sup> Recently, Mayer introduced a generalized concept for hydrogen-atom transfer (HAT) that included MAH reactions with a Marcus theory approach.[19]

The radical addition of thiol compounds to alkenes has attracted renewed interest as a "thiol/ene click reaction" because of quantitative yields, rapid reaction rates, mild reaction conditions, and compatibility with water and oxygen.<sup>[20]</sup> It has been demonstrated recently that mixing thiol and methyl 10-undecenoate, a renewable 1-alkene, gave the addition product quantitatively without the use of an initiator and under solvent-free conditions.<sup>[21]</sup> Because a molecule that has an alkyl chain with a *cis*-configured double bond and a thiol functionality should not be stereochemically stable, we wondered about *cis*-octadec-9enethiol, which is commercially available and is "assigned to prepare disordered self-assembled monolayers that may have a significant influence on the fluidity of supported liquid membranes."<sup>[22]</sup>

The question is open as to how the dark reaction of radical addition reactions of thiol compounds to alkenes and the thiol-catalyzed *cis/trans* isomerization of *cis*-alkenes observed by Chatgilialoglu et al.<sup>[3]</sup> may be initiated without any added initiator. To answer this question unambiguously, we performed a kinetic and computational study of the thiol-catalyzed thermal isomerization of methyl oleate because the isomerization reaction is much simpler than the addition reaction and has been studied kinetically in detail.<sup>[2-4]</sup> Most importantly, there is no hydrogen transfer involved in the isomerization reaction. Thus, we could have a chance to verify or exclude unambiguously initiation through MAH<sup>[9]</sup> by performing an appropriate experiment on the kinetic isotope effect  $k_{\rm H}/k_{\rm D}$ .

#### Results

In preliminary experiments, we treated dodecanethiol (1) with methyl oleate (*cis-2*) in a ratio of 1.1:1 without a solvent at 118°C (Scheme 4). Analysis of the reaction solution



Scheme 4. Dodecanethiol-catalyzed isomerization of methyl oleate (*cis*-2) to methyl elaidate (*trans*-2).

after 22 hours showed a [*trans*-2]/[*cis*-2] ratio of 2.89:1. The concentration of thiol **1** and the total concentration of *cis*-2 and *trans*-2 was approximately constant over the reaction time. Only very small amounts (i.e., <5%) of the addition products methyl 9- and 10-dodecanethiylstearate were formed. Traces of didodecyldisulfide (7), the expected termination product of the radical chain reaction, were also detected. The ratio of [*trans*-2]/[*cis*-2] at 89°C was 0.83:1 after 24 hours. The addition of AIBN as an initiator showed a [*trans*-2]/[*cis*-2] ratio of 4.28:1 after 15 minutes.

Moreover, we studied the stereochemical stability of *cis*octadec-9-enethiol. A commercial sample<sup>[22]</sup> was used, and the ratio of the *trans* and *cis* isomers, determined by GC after arrival of the sample, was 0.98:1. At room temperature, the isomerization reaction continued (Scheme 5). The [*trans*]/[*cis*] ratio was 4:1 after 10 days and the final ratio of 5.9:1 was obtained after about 38 days (see Figure S1 in the Supporting Information).<sup>[23]</sup> Chatgilialoglu et al. gave a rather similar equilibrium ratio of 5.15:1 at room temperature for methyl oleate.<sup>[4]</sup>



Scheme 5. Isomerization of cis- to trans-octadec-9-enethiol.

The kinetic investigation of the isomerization reaction was performed by mixing the substrates thiol **1** and *cis*-**2**, both freshly distilled under nitrogen, at room temperature under nitrogen without any solvent. A homogeneous solution was obtained. The isomerization reaction was studied at 89, 98, 108, and 118 °C by using a mixture of **1** and *cis*-**2** with concentrations of 1.6 and 1.5 M, respectively, at room temperature in which the temperature dependence of the concentration of **1** and of *cis*-**2** was taken into account (see Figure S2 in the Supporting Information).<sup>[24]</sup> Two experiments at each temperature were performed in two reactors in parallel. The ratio of [*trans*-**2**]/[*cis*-**2**] was determined by GC analysis. The rate of isomerization  $r_{is}$  was constant over the studied range of conversion (Figure 1). Additionally, the de-



Figure 1. Rate of isomerization of methyl oleate (*cis*-2) to *trans*-2 catalyzed by dodecanethiol ([cis-2]/[1]=1:1.1) at 89, 98, 108, and 118 °C.

pendence of the rate of isomerization on the concentration of the reactants was studied at 118 °C by using mixtures of **1** and *cis*-**2** with concentrations of 3.1 and 0.49 M and 0.4 and 2.28 M, respectively (see Figure 2 and Table S1 in the Supporting Information for the results).<sup>[23]</sup>

Evaluation of the dependence of the rate of isomerization on the concentration of **1** and **2** (Figure 2) gives rate Equation (1) with rate constant  $k_{exp}$ . The second reaction order for thiol **1** and 0.5 reaction order for *cis*-**2** seems to be remarkable. Furthermore, monodeuterated dodecanethiol  $C_{12}H_{25}SD$  (D-**1**) was reacted at 118 °C by using a mixture of D-**1** (3.1 M) and *cis*-**2** (0.49 M) to give  $r_{is,D-1}=5.5 \times 10^{-5} \text{ s}^{-1}$ . The experiment was performed in parallel with **1** to give  $r_{is,1}=1.56 \times 10^{-4} \text{ s}^{-1}$  (Figure 4), thus revealing an overall kinetic isotope effect  $k_H/k_D$  of 2.8.





Figure 2. Rate of isomerization of *cis*-2 at 118°C: Dependence on the concentration of 1 and *cis*-2.



Figure 3. Arrhenius presentation of the temperature dependence of the rate constant  $k_{exp.}$  gives  $E_A = 82 \text{ kJ m}^{-1}$  and  $A = 2.0 \times 10^6 \text{ m}^{-1.5} \text{ s}^{-1}$ .



Figure 4. Kinetic isotope effect: Rate of isomerization of *cis*-2 (0.96 M) catalyzed by thiol 1 (3.1 M) and D-1 (3.1 M), respectively  $(r_{is1}=1.56 \times 10^{-4} s^{-1}; r_{isD-1}=5.5 \times 10^{-5} s^{-1})$ .

The temperature dependence of  $k_{exp}$  (Figure 3) gives the Arrhenius equation [Eq. (2)] (where  $E_A = 82 \text{ kJ mol}^{-1}$  and  $A = 2.0 \times 10^6 \text{ m}^{-1.5} \text{ s}^{-1}$ ).

$$\log k_{\rm exp} = 6.3 - 4285/T \tag{2}$$

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**Computational results**: We performed DFT calculations with the new dispersion-corrected functional B97D. This approach and several others have been developed with an improved description of weak van der Waals interactions in mind.<sup>[25]</sup> The suitability of B97D for the given problem has been evaluated extensively.<sup>[26,27]</sup>

The structures for all the compounds shown in Scheme 6 have been optimized and their relative enthalpies determined. Spin contamination does not play a significant role in all the structures with unpaired electrons.<sup>[28]</sup> (The complete results are compiled in Table S2 in the Supporting Information).



 $R = C_{12}H_{25}; R^1 = C_8H_{17}; R^2 = C_7H_{14}COOCH_3$ 

Scheme 6. Radical chain mechanism of the thermal isomerization of *cis*-2 catalyzed by thiol 1. Initiation by MAH of thiol 1 and the EDA complex of 1 and *cis*-2 formed in pre-equilibrium (reaction 0) to give alkyl radical 4 and sulfuranyl radical 5 in reaction 1.

The enthalpic difference between cis-2 and trans-2 is calculated to be  $3.8 \text{ kJ}\text{M}^{-1}$ , which is about 1 kJ lower than the experimental results<sup>[3]</sup> and calculations by Chatgilialoglu et al.<sup>[4]</sup> The EDA complex of **1** and *cis*-**2** is formed through a hydrogen bond from thiol 1 to the electron-rich double bond of cis-2 (see Figure S3 in the Supporting Information) and possesses a reaction enthalpy of  $\Delta H_{\rm R} = -39 \, \rm kJ \, \rm M^{-1}$ , but is endergonic because of entropic reasons. The reaction enthalpy of the MAH reaction of thiol 1 and cis-2 is calculated to be 191 kJ m<sup>-1</sup>. In comparison, the reaction enthalpy of the MAH reaction of 1 and the EDA complex is determined to be  $212 \text{ kJ}\text{M}^{-1}$ . With respect to the substrates, this finding gives a remarkably small enthalpy of only 173 kJ m<sup>-1</sup> considering the exothermic formation of the EDA complex (Figure 5). The activation energy of the MAH reaction is approximately equal to the reaction enthalpy because the activation energy of the reverse disproportionation reaction is approximately  $E_A = 0 \text{ kJ } \text{M}^{-1}$ .<sup>[14,16,18]</sup> The energy profile of the initiation reaction is given in Figure 5. In principle, two regioisomeric alkyl radicals 4 with a single electron in the 9 or 10 position (9-4 and 10-4, respectively) can be expected.



Figure 5. Energy profile of the initiation reaction.

However, all the calculated energies of 9-4 and10-4 differ by as little as  $3 \text{ kJ } \text{M}^{-1}$ , so that all the reported numbers refer to the radical at the 10 position. The fragmentation of sulfuranyl radical **5** to thiyl radical **3** and thiol **1** is calculated to be an endothermic but exergonic reaction ( $\Delta H_{\rm R} = 19.4 \text{ kJ } \text{M}^{-1}$ and  $\Delta G_{\rm R} = -31.1 \text{ kJ } \text{M}^{-1}$  at 100 °C).

### Discussion

Chatgilialoglu et al. showed that the thiol-catalyzed rate of isomerization of *cis*-**2** to *trans*-**2** is directly proportional to the steady-state concentration of thiyl radical **3** [Scheme 1; Eq. (3)].<sup>[2-4]</sup>

$$r_{is} = \frac{d([trans-2]/[cis-2])}{dt} = \frac{k_{a}^{Z}k_{f}^{E} + k_{a}^{E}k_{f}^{Z}}{k_{f}^{E}k_{f}^{Z}}[\mathbf{3}] = k_{is}[\mathbf{3}]$$
(3)

The rate of the isomerization of the thermal reaction has a reaction order of two and 0.5 for thiol **1** and *cis*-**2**, respectively, thus giving the first evidence that both substrates are involved in the initiation reaction of the radical chain and the formation of thiyl radical **3**. Moreover, the kinetic isotope effect  $k_{\rm H}/k_{\rm D}$  gives ample evidence that a hydrogentransfer reaction is involved in the rate-determining step of the initiation reaction.

To obtain more detailed information on the initiation reaction, we checked the reaction order for both substrates expected for the initiation reactions suggested in previous reports.<sup>[9,10]</sup> The initiation by alkene-assisted homolysis of the S–H bond in a bimolecular reaction of thiol **1** and *cis*-**2** to give thiyl radical **3** and alkyl radical **4**, a MAH reaction as suggested by Nuyken et al. (Scheme 2),<sup>[9]</sup> would give a reaction order of 0.5 for **1** and *cis*-**2**, which is not in agreement

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with the experimental results (see Scheme S1 in the Supporting Information). Radical formation through a monomolecular fission of the EDA complex of thiol **1** and alkene *cis-***2** formed in a pre-equilibrium (Scheme 3)<sup>[10]</sup> gives the same reaction order for both substrates and can be excluded as well (see Scheme S2 in the Supporting Information).

The experimentally determined reaction order of two for thiol **1** gives an indication that possibly more than one thiol molecule may be involved in the initiation reaction. It could be possible that the EDA complex of thiol **1** and alkene *cis*-**2** may react with another equivalent of thiol **1** in a MAH reaction to give a thiyl and an alkyl radical and thiol **1**. The resulting steady-state concentration of radical **3** and the reaction order of one for **1** was again not in agreement with the experimental results (see Scheme S3 in the Supporting Information).

However, a closer look at the steps in this initiation reaction showed that radical **3** is not obtained directly in the MAH step. In the first step, a sulfuranyl radical **5** may be formed, as shown in reaction step 1, which is the rate-determining step of Scheme 6. The rate of isomerization obtained for a radical chain reaction (as depicted in Scheme 6) is given in Equation (4) and is in perfect agreement with the experimental rate given in Equation (1) (see Scheme S4 in the Supporting Information).<sup>[29,30]</sup> The rate constant  $k_{exp}$  is given in Equation (5).

Intramolecular addition reactions of an alkylthivl radical with an additional SH group to give a cyclic sulfuranyl radical have been detected by laser flash photolysis.[31a,b] In contrast, an intermolecular addition of simple alkylthiyl radicals to thiol or thioether compounds has not been directly observed in solution, which can be explained by the unfavorable equilibrium constant  $K_3$  (Scheme 6). In contrast, the stabilization of alkylthiyl radicals by the formation of sulfuranyl radicals RSS(H)R (R=CH<sub>3</sub>, C<sub>2</sub>H<sub>5</sub>, *i*-C<sub>3</sub>H<sub>7</sub>, *tert*-C<sub>4</sub>H<sub>9</sub>) could be shown by photolysis of thiol compounds in glassy matrices at 77 K.<sup>[31a,c]</sup> Moreover, the reaction of an octadecanethiyl radical with octadecanethiol via a sulfuranyl-type radical to give the perthivl radical was studied within the channel of a thiol/thiourea clathrate.[32] Remarkably, in the example discussed herein, the sulfuranyl radical is directly formed in the initiation reaction 1 (Scheme 6).<sup>[33]</sup> Thus, the rate of isomerization will be proportional to the steady-state concentration of sulfuranyl radical 5 and the concentration of thiyl radical 3 will be steered by equilibrium 3 (Scheme 6), which is strongly shifted to the right, as known from a previous report<sup>[31]</sup> (see Schemes S4 and S5 in the Supporting Information) and shown by our DFT calculations (see Table S2 in the Supporting Information).

The bond-dissociation energy of the S–H bond of about  $366 \text{ kJ } M^{-1[34]}$  will be decreased by the MAH reaction of **1** and *cis-***2** to about 192 kJ  $M^{-1}$  (see Table S2 in the Supporting Information) because of the simultaneous formation of a C–H bond in alkyl radical **4** with the homolytic dissociation of the S–H bond (Scheme 2). Additionally, the activation energy of the initiation reaction will be decreased by the primary formation of the stabilized sulfuranyl radical **5** in the

rate-determining reaction step 1 (Scheme 6). Interestingly and as further confirmation of the proposed mechanism, the activation energy of the initiation reaction through pre-equilibrium 0 and reaction of EDA and 1 in reaction step 1 (Scheme 6) is calculated to be  $E_A = 173 \text{ kJ M}^{-1}$ , which is about 19 kJ M<sup>-1</sup> lower than the activation energy of 192 kJ M<sup>-1</sup> of the direct MAH reaction of 1 and *cis*-2 (Figure 5). The late transition state of the MAH reaction gives evidence that no or only a very minor steric effect on the rate of reaction 1 (Scheme 6) can be expected.

$$r_{\rm is} = k_{\rm is}[\mathbf{5}] = k_{\rm is} \left(\frac{k_1 K_{\rm EDA}}{2k_t}\right)^{1/2} \frac{1}{K_3} [\mathbf{1}]^2 [\mathbf{2}]^{1/2}$$

$$r_{\rm is} = \frac{d([t-\mathbf{2}]/[c-\mathbf{2}])}{dt} = k_{\rm exp} [\mathbf{1}]^2 [\mathbf{2}]^{1/2}$$
(4)

$$k_{\rm exp} = k_{\rm is} \left( \frac{k_1 K_{\rm EDA}}{2k_{\rm t}} \right)^{1/2} \frac{1}{K_3}$$
(5)

$$E_{\rm A,exp} = E_{\rm A,is} + 0.5 \left( E_{\rm A,1} + \Delta H_0^{\circ} - E_{\rm A,t} \right) - \Delta H_3^{\circ}$$
(6)

To further confirm the validity of this mechanism, the overall activation energy was determined by applying Equation (6). By using the calculated data in Table S2 (see the Supporting Information;  $E_{\rm A,1}=212.5$ ;  $\Delta H^{\circ}=-39.2$ ;  $E_{\rm A,t}=0$ ;  $\Delta H^{\circ}_{_3}=19.4$  kJ m<sup>-1</sup>) and  $E_{\rm A,is}\approx 10$  kJ m<sup>-1</sup>,<sup>[35]</sup> an activation energy  $E_{\rm A,exp}$  of about 77 kJ m<sup>-1</sup> is estimated, which is in good agreement with the experimentally derived activation energy of  $E_{\rm A}=82$  kJ m<sup>-1</sup> [Figure 3, Eq. (2)].

The kinetic isotope effect  $k_{\rm H}/k_{\rm D}$  of the rate of isomerization gives clear evidence that the cleavage of the S–H bond is involved in the rate-determining reaction step. Equations (4) and (5) show that preferentially reaction 1 (Scheme 6), the MAH reaction of the EDA complex and thiol **1**, and, possibly to a small extent, equilibria 0 and 3 (Scheme 6) can contribute to the isotope effect of the overall reaction (i.e.,  $k_{\rm H}/k_{\rm D}=2.8$ ). This result gives a kinetic isotope effect  $k_{\rm 1,H}/k_{\rm 1,D}$  of approximately 7.8 at 118 °C. The kinetic isotope effect of hydrogen abstraction by carbon radicals from thiol compounds has been reported to be  $k_{\rm H}/k_{\rm D}=$ 1.9–6.6.<sup>[36]</sup>

#### Conclusion

The results of our study of the thermal thiol-catalyzed isomerization of *cis*-**2** are in agreement with an initiation of the radical chain reaction by the formation of an EDA complex of a thiol and an alkene compound in a pre-equilibrium reaction and a MAH reaction of an EDA complex and thiol compound to give an alkyl and a sulfuranyl radical. The latter is in equilibrium with the thiyl radical, which catalyzes the isomerization reaction. It can be assumed that this initiation reaction can explain the "unknown additional thermal generation of thiyl radicals" reported by Chatgilialoglu et al.<sup>[3]</sup> Moreover, it can be assumed that this reaction is the initiation reaction of the many well-known thermally initiat-

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ed addition reactions of thiol compounds to alkenes and their respective polymerizations without any initiator. Furthermore, this reaction is the reason for the low shelf-life stability of *cis*-unsaturated thiol compounds and mixtures of alkenes and thiol compounds, thus combining the suggestions of Nuyken et al.<sup>[9]</sup> and Klemm and Sensfuß.<sup>[10]</sup>

### **Experimental Section**

**General:** Dodecanethiol (1) and *cis*-octadec-9-enethiol were purchased from Aldrich (Steinheim, Germany). Methyl oleate (*cis*-2; 91.2% oleic acid, 3.0% palmitic acid, 2.8% linoleic acid, 1.9% stearic acid) was purchased from T+T Oleochemie GmbH (Alzenau, Germany). Compounds 1 and *cis*-2 were distilled under nitrogen by means of a Kugelrohr oven and were stored under nitrogen. *cis*-Octadec-9-enethiol was used as received.

**Analytical equipment**: Analytical GC was performed on a Varian 3400 chromatograph with an flame ionization detector (FID) and fused-silica capillary column SP 2380-FAME (60 m; I.D. = 0.25 mm;  $d_F$  = 0.20 µm; Supelco). Mass spectra were recorded on a Finnigan MAT 95 spectrometer. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded in CDCl<sub>3</sub> on a Bruker DRX 500 spectrometer at 300 K with a residual nondeuterated solvent (<sup>1</sup>H NMR) or CDCl<sub>3</sub> (<sup>13</sup>C NMR) as internal standards.

**Dodecanethiol-D**<sub>1</sub> (D-1): Compound 1 (5 g) and ethanol-D<sub>1</sub> (12 mL) were heated to reflux for 20 min. Ethanol-D<sub>1</sub> was removed in vacuo. This procedure was repeated two times. The product was distilled in vacuo (4.3 g, 86%). <sup>1</sup>H NMR spectroscopic analysis showed a degree of deuteration of >98%.

**Kinetic measurements:** A Schlenk-type reactor (I.D. = 12 mm, height = 45 mm, volume = 5 mL) with a septum, stirring bar, and heating mantle connected to a circulation thermostat was used. Appropriate amounts of 1 and *cis*-2 were charged under nitrogen and mixed at room temperature by stirring (1000 rpm). The mixture was heated in <2 min to the preselected reaction temperature and stirring was stopped. Two experiments at each temperature and concentration were performed in two reactors in parallel. Samples (1  $\mu$ L) for GC analysis were removed by using a syringe through the septum at preselected reaction times and were diluted immediately with CH<sub>2</sub>Cl<sub>2</sub>. The [*trans*-2]/[*cis*-2] ratio was determined by GC analysis.

**Isomerization of** *cis***-octadec-9-enethiol**: *cis*-Octadec-9-enethiol (100 mg) was placed in a vial with a septum under nitrogen. Samples (1  $\mu$ L) for GC analysis were removed by using a syringe through the septum at preselected reaction times.

**Computational details**: Most of the calculations were performed by using the program package Gaussian09.<sup>[37]</sup> DFT with the dispersion-corrected B97D functional<sup>[38]</sup> and the triple-zeta basis set  $6-311+G(d,p)^{[39]}$  was used for the optimization of the ground-state geometries in the gas phase and thermochemical calculations. Additional single-point calculations employed the M06–2X functional.<sup>[40]</sup> The necessary URCCSD(T)/6–31G(d) calculations for the G3(MP2)-RAD level of theory employed the program package MOLPRO.<sup>[41]</sup> The default convergence criteria and integration grid of the program were used. Stationary points were verified as ground states by calculating the number of imaginary harmonic vibrational frequencies at the same level of theory.

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reaction energies usually within 5 kJ mol $^{-1}$  (see the Supporting Information for full details).

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- [28] The influence of spin contamination was additionally probed for at the UHF/6–311+G(d,p) level of theory as DFT methods sometimes inaccurately calculate this property; again, no significant contamination of the wavefunction with higher spin states has been found.
- [29] Interestingly, an analogous rate equation that is in agreement with the experimental rate given in Equation (1) is obtained by assuming a MAH reaction of a hydrogen-bonded thiol dimer **12** and **2** (see Scheme S5 in the Supporting Information); it is not possible to differentiate both possibilities kinetically; dimerization constants of primary alkylthiol compounds  $K_{dimer}=0.01$  have been reported;<sup>[30]</sup> the association constant of cyclohexene and 4-chlorothiophenol was determined to be  $K_{EDA}=0.1$ .<sup>[11]</sup>
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