RESEARCH ARTICLE

Thiol-Ene Polymerization of Natural Monomers: A DFT Study

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This study investigates the thiol-ene reaction mechanism of natural monomers using quantum chemical tools. The structure-reactivity relationship for these monomers is elaborated by the aid of radical stabilization energies (RSEs), intermolecular interactions, the curve-crossing model, Hammond Postulate, and Evans–Polanyi relationships. Geometry optimizations, frequency, and energy calculations are performed at the M06-2X/6-31++G(d,p) level of theory. A crucial parameter for thiol-ene polymerization, which is the ratio of the propagation reaction (k_p) and the chain transfer reaction (k_{ct}) rate constants (k_p/k_{ct}), is calculated in order to elucidate the thiol-ene reaction mechanism. In light of these energetic and kinetic calculations, it is suggested that linalool, d-limonene, terpinolene, and γ-terpinene are considered natural monomer candidates for thiol-ene polymerization due to their almost equal magnitude of the rate constants ($k_p/k_{ct} \approx 1$). The thiol-ene polymerization potential of some specific unsaturated fatty acids is another prominent finding in this study.

1. Introduction

The polymer industry has been steadily growing since the invention of synthetic or semisynthetic polymers. However, polymer-based environmental pollution has rapidly become one of the most fundamental problems of all living creatures. Polymer synthesis strongly depends on fossil resources.[1] Sustainable polymers, which can replace petroleum-derived polymers, are now one of the contemporary challenges in polymer science.[2,3] In recent decades, cellulose, proteins, and vegetable oils as sustainable sources have been attracted attention in green polymer synthesis.[4–6] For example, natural oils are one of the most significant environmentally friendly sources as the natural analogue of synthetic monomers. These natural resources can combine some critical features in one pot for polymerization, such as easy accessibility, biodegradability, sustainability, competitive costs, chemical conversion potential, and nontoxicity.[6,7] Another prominent natural source for the polymer field is terpenes such as d-limonene, representing the high potential for synthesizing bio-based polymers.[8]

It is well known that free-radical polymerization is responsible for almost half of industrial polymer production. However, early gelation, branching, and heterogeneous network structure production are considerable weaknesses of conventional radical polymerization.[9,10] On the other hand, thiol-ene polymerization offers an effective combination of step-growth and chain-growth processes to achieve high monomer conversions, form a homogeneous polymer network, obtain a late gelation point, and narrow glassy temperature (Tg).[11] Although radical reactions of thiol with alkene have been known for more than a century,[12] reactions involving polythioether synthesis have been accelerated in recent decades by the definition of "click chemistry." The click chemistry concept[13] gathers crucial properties for a reaction economy, high yield, short reaction time, solvent tolerance, site selectivity, insensitivity to oxygen, and negligible by-product formation, and easy purification.[14,15] Having these characteristics during a chemical synthesis has led to a rapid interest in electronic chemistry,[16] nanomaterials,[17] dendrimer synthesis,[18] dental materials,[19] drug design,[20–23] and green chemistry.[4,5,24] In the polymerization field, photoinitiated thiol-ene reactions have appeared in the application of photocurable polymers and resins used in coatings and protective films.[25–29] The thiol-ene radical polymerization was examined first by Braun and Murjahn, who obtained a nonvolatile product during the 2-propene-1-thiol preparation attempt.[26,30] Subsequent studies have illustrated that photoinitiated thiol-ene polymerization can be applied under relatively moderate conditions with high efficiency and insensitive to environmental conditions such as oxygen and moisture.[11,28,29,31] Improved mechanical properties, clean and ecological reactions, rapid, site-selective polymerization, and improved degradability can also make thiol-ene polymerization a biomaterial design tool.[11,32,33] More details about the applications of thiol-ene polymerization have been reviewed recently.[14]

A recent studies about the reactivity of thiol-ene reactions have emphasized that the polymerization rate varies greatly depending on the alkene nature.[34–36] In general, electron-rich substrates (such as vinyl ether or norbornene) are highly reactive monomers in thiol-ene polymerization.[37–42] In contrast,

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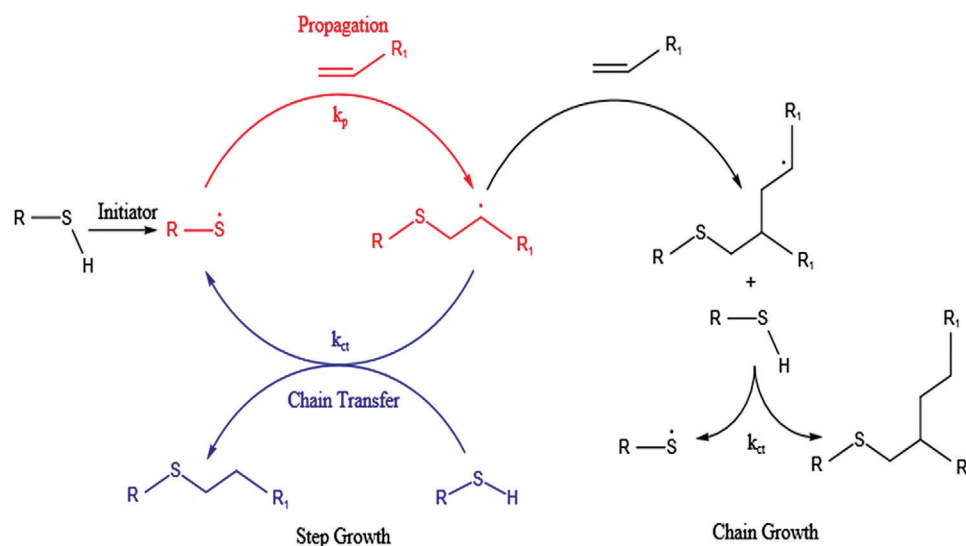Theory and Simulations**

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Figure 1. Schematic representation of the thiol-ene polymerization mechanism.[43]

electron-deficient or conjugated monomers, such as acrylonitrile, styrene, or butadiene, have less reactivity.[43] Besides these assessments, some other studies have suggested that the electronic nature of both alkene and thiol makes a significant contribution to polymerization.[43–46] Especially, the chain transfer reaction step of thiol-ene polymerization can be significantly influenced by aromatic thiol structure. Also, the role of the initiator on polymerization has been elaborated.[47] However, the role of natural monomers in thiol-ene polymerization has not been studied extensively yet. It is necessary to elucidate the mechanism (**Figure 1**) and polymerization kinetics to understand the structure–reactivity relationship of these monomers in polymerization.

In the mechanism, a thiyl radical is formed as a reaction product of hydrogen abstraction from thiol by the initiator radical, which is generated by heat or light exposure to the initiator in the initiation step. A carbon-centred radical (thioether radical) is produced through the thiyl radical addition to the "ene" functionality at the propagation step. The thioether radical can follow two different pathways: a step-growth or a chain-growth mechanism. The formed carbon-centred radical is added to alkene functionality in the chain-growth pathway to achieve classical free radical homopolymerization. In the step-growth case, the carbon-centered radical carries out the chain transfer reaction by hydrogen transferring from a thiol, while a new sulfur-centered radical and a dead polymer chain are formed. As a result, a thiol addition to alkene leads to the anti-Markovnikov configuration in the thioether product.
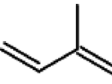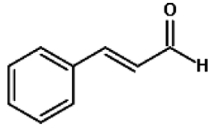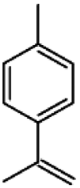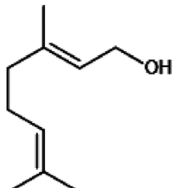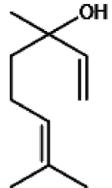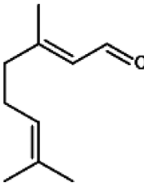
Experimentally, Cramer et al. have focused on the factors underlying the diversity of thiol-ene reactivity.[34–36,48] They have shown that the overall reaction kinetics of the polymerization is controlled by the rate constant ratio of the propagation (k_p) and the chain transfer (k_{ct}) reactions.[48,49] The desired thiol-ene polymerization product is acquired when the reaction rate constants are equal to each other ($k_p = k_{ct}$). The first quantum chemical calculation attempt to enlighten the polymerization mechanism by using methyl thiol as a model for thiol-ene polymerization of

a set of alkenes has demonstrated that all process is exergonic.[43] The calculated activation free energies of propagation reactions vary between 28.4 kJ mol^{-1} (butadiene) and 42.7 kJ mol^{-1} (maleimide) (14.2 kJ mol^{-1} energy difference). On the other hand, the activation free energies for chain transfer reactions range from 32.6 kJ mol^{-1} (vinyl silane) to 72.4 kJ mol^{-1} (butadiene) (39.8 kJ mol^{-1} difference). The chain transfer reaction barrier of electron-deficient monomers is relatively larger than the electron-rich ones. In addition to this, the activation energy of the chain transfer reaction varies more tha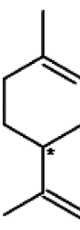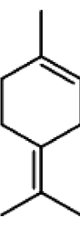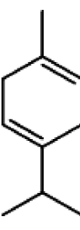n the propagation reaction. As a consequence, it was illustrated that electron-deficient monomers undergo the propagation reaction relatively fast (large k_p), while the chain transfer reaction is slow (small k_{ct}). The opposite is possible for electron-rich monomers. Moreover, due to the wide range of activation barriers for chain transfer reactions, it is also possible to have similar reaction rates, which is desired to obtain the best thiol-ene polymerization product. Although there have been many experimental studies on thiol-ene reactions[50–53] in the field of green chemistry, the mechanism and kinetics have not been elaborated for the thiol-ene polymerization.

This study focuses on expanding investigations of thiol-ene polymerization from synthetic monomers to natural monomers by using quantum chemical tools. In this context, it is aimed to perform analysing the structure–reactivity relationships of the monomers. For this goal, methyl thiol (methyl mercaptan) and a set of alkenes (**Table 1**) were modeled to seek a reasonable pathway for the natural monomer applications in thiol-ene polymerization.

Monomers in Table 1 present a bouquet of chemical properties. 2-butene was considered as an analogue monomer to evaluate the reactivity of unsaturated bonds found in fatty acids. 2,4-hexadiene was considered as an analog to conjugated unsaturated fatty acids and was also preferred to investigate the behavior of isoprene, which bearings conjugated π bond system. Furthermore, isoprene, cinnamaldehyde, p-cymenene, geraniol, linalool, citral, d-limonene, and γ-terpinene were modeled as

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Table 1. Chemical structures of monomers considered in this study.

(1) 2-Butene	(2) 2,4-Hexadiene	(3) Isoprene	(4) Cinnamaldehyde
(5) P-cymenene	(6) Geraniol	(7) Linalool	(8) Citral
(9) D-limonene	(10) Terpinolene	(11) γ-terpinene	(12) Vinyl chloride

a set of natural monomers. In addition to 2-butene and 2,4-hexadiene, vinyl chloride is another synthetic monomer investigated for the first time concerning thiol-ene reactivity in this study.

2. Methodology

All calculations were carried out using the Gaussian 16 B.01 program package.[54] The M06-2X meta-hybrid functional was performed for modeling reactions since it successfully predicts the activation energies and energy of the disulfide exchange reactions.[55] Recent studies have demonstrated that less than 1.5 kcal mol^{-1} error range with the M06-2X functional has been achieved compared to the CBS-QB3 and G3B3 composite methods as reference methods.[56,57] Moreover, M06-2X/6-31++G(d,p) level gas phase calculations show better predictions for elucidating the mechanism.[44] Therefore, conformational analyses were performed at the low basis-set level (6-31+G(d)), while thermodynamic data were obtained by reoptimization of geometries at the higher basis-set level (6-31++G(d,p)). Computational studies were performed at the gas phase with a pressure of 1.0 atm, and 298.15 K. The effect of solvent on the thiol-ene polymerization is well elaborated both experimentally and computationally.[45, 58] These studies have emphasized that its contribution to the propagation is negligible and is limited on the chain transfer reaction. Therefore, for simplicity, all energy calculations were carried out at the gas phase. Multiplicity is defined as doublet for the radical

species and singlet for the closed-shell systems. Reaction rate coefficients were predicted using the transition state theory, which is given by the following equation[58]

$$k = \kappa \frac{k_B T}{h} \left(\frac{p^\theta}{RT} \right)^{1-m} e^{-\Delta G^\ddagger / RT} \qquad (1)$$

Where $\Delta G^\ddagger$ is Gibbs free energy difference between activated complex geometry and reactants (including zero-point vibrational energy correction), T is the temperature (298.15 K), R is the universal gas constant (8.314 J mol^{-1} K^{-1}), κ is the transmission coefficient ($\kappa = 1$ assumed for the propagation reactions), k_B is the Boltzmann constant (1.380 658 × 10^{-23} J K^{-1}), h is the Planck constant (6.6 260 755 × 10^{-34} J s), p^θ is standard pressure (10^5 Pa (1 bar)), and m is molecularity. Quantum tunneling should be considered in the hydrogen abstraction reactions due to transferring the light atom. The quantum tunneling coefficient (κ) was calculated using the Wigner correction based on the following equation[59,60]

$$\kappa(T) = 1 + \frac{1}{24} \left| \frac{h\omega^\ddagger}{k_B T} \right|^2 \qquad (2)$$

where, $\omega^\ddagger$ represents the imaginary frequency of the activated complex geometry during hydrogen abstraction reaction.

The Hammond postulate[61] and Evans–Polanyi relationship[62] were checked to establish structure–reactivity

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Table 2. Calculated energies (kJ mol^{-1}) for the reactions (at the M06-2X/6-31++G(d,p) level, 298.15 K, and 1.0 atm).

Alkene	Propagation			Chain transfer		
	$\Delta H^{\ddagger}$	$\Delta G^{\ddagger}$	ΔH°_{rxn}	$\Delta H^{\ddagger}$	$\Delta G^{\ddagger}$	ΔH°_{rxn}
2-Butene (1)	2.70	47.47	−36.43	−4.09	42.32	−50.67
2,4-Hexadiene (2)	−9.55	35.95	−75.78	24.34	71.21	−0.74
Isoprene (3)	−11.46	32.29	−83.15	21.89	71.34	−7.20
Cinnamaldehyde (4)	−1.07	46.68	−42.45	9.76	56.73	−27.03
P-cymenene (5)	−15.24	33.03	−71.03	4.70	54.55	−12.45
Geraniol (6)	−11.59	36.24	−61.00	10.46	61.84	−17.68
Linalool (7)	−1.00	47.03	−40.40	−2.84	47.87	−47.25
Citral (8)	−6.45	40.22	−39.51	2.92	53.29	−20.52
D-limonene (9)	−7.08	40.89	−44.31	−4.38	44.39	−29.02
Terpinolene (10)	−9.19	41.18	−41.48	−19.11	36.85	−45.14
γ-terpinene (11)	−8.79	44.81	−35.12	−13.74	39.94	−29.51
Vinyl chloride (12)	3.05	47.89	−45.22	1.58	46.43	−43.48

relationships for the reactions. If a reaction set does not obey Evans–Polanyi relationship, the curve-crossing model is used to explain the effects on activation energies of the propagation reactions by polar and nonpolar electronic configurations.[43,63] In this respect, the reactivity of reactants was explained by charge transfer configuration energies (RS$^-$ + ene$^+$ and RS$^+$ + ene$^-$) and the singlet–triplet energy gap (ΔE_{ST}) of substrates based on the curve-crossing model. Charge transfer configuration energies considered the polar interactions, representing electrophilic (RS$^-$ + ene$^+$) or nucleophilic (RS$^+$ + ene$^-$) character of a radical and shows that the energy needed for the electron transfer between radical and alkene species. Furthermore, electrophilic or nucleophilic characteristics of alkyl thiyl radical were elaborated with point charge separation ($\delta^{\ddagger}$) between the radical and ene moieties at the transition state geometry. The ΔE_{ST} as nonpolar interaction represents stabilization effect of π^* of substrate and spin of the radical moiety."

The literature studies have emphasized that the main driving force is the stability of carbon-centered radical intermediate[34] in the chain transfer step of thiol-ene polymerization. To investigate this property, radical stabilization energy (RSE) was calculated by the enthalpy of the following isodesmic reaction[64,65]

$$RH + CH_3\bullet \rightarrow R\bullet + CH_4 \qquad (3)$$

3. Results and Discussions

Thiol-ene polymerization is effectively governed by the propagation and the chain transfer reaction steps that are elaborated in this investigation (Figure 1). Since the initiation step is carried out by photochemical or thermally catalysed, it was not involved in the scope of the investigation. A recent benchmark study has shown that computational estimation in the kinetics of propagation reactions at the M06-2X/6-31++G(d,p) level is well correlated with the experimental results.[44] Therefore, that level of theory was preferred to predict the k_p/k_{ct} ratios in this investigation. The calculated energy data for the considered reactions are presented in **Table 2**.

3.1. Propagation

The calculated energies of the reactions vary significantly with the alkene functionality. Thiyl radical addition to alkenes is exothermic (Table 2) since a strong C−S σ bond replaced the weak C=C π bond. Propagation reaction enthalpies range from −35.12 kJ mol^{-1} (γ-terpinene) to −83.15 kJ mol^{-1} (isoprene). Since there are two double bonds in the structure of some natural monomers considered in this study, each C=C double bond was checked to reveal which one is more reactive for the reaction. Comparing the relative energies of the most stable transition state geometries for each possible double bond is presented in Figure S1 (Supporting Information). The activation barriers and reaction energies belong to the more reactive double bond of monomers presented in Table 2. For d-limonene and terpinolene, one of the double bonds is in the molecule ring (*endo*) and the other in the moiety attached to the ring (*exo*). Both double bonds are in the molecule ring for γ-terpinene. It was computationally demonstrated that the less substituted carbon atom on the *exo* double bonds are preferred for propagation reaction (Figure S1, Supporting Information) for d-limonene and terpinolene. However, the relative activation energy of attacking to the less substituted carbon atom on the *endo* double bond of d-limonene is not so different (1.64 kJ mol^{-1}) than the *exo* addition. The predicted higher reactivity of *exo* addition is consistent with a recent study on d-limonene reactivity[8] on thiol-ene reactions. In addition to this, the energy difference between propagation transition state geometries for both accessible C=C double bonds of γ-terpinene is negligible.

When methyl thiyl radical reacts with a conjugated alkene (2,4-hexadiene, isoprene, and p-cymenene), the exothermicity of the reaction is greater than the other propagation reactions. This trend is governed excessively by the higher stability of radical intermediate due to the delocalization of the radical spin by adjacent π bond systems (**Table 3**). The reaction Gibbs free energy of activation range from 32.29 kJ mol^{-1} (isoprene) to 47.89 kJ mol^{-1} (vinyl chloride). The factors affecting these activation energies are explained by the Hammond postulate[61] and Evans–Polanyi relationship.[62] The relationship between critical bond length (CS) and reaction enthalpy was established ($R^2 = 0.88$, **Figure 2**a).

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Table 3. The charge transfer configuration energies ((RS$^-$+ene$^+$) and (RS$^+$+ene$^-$), in eV), critical bond distances (Å) for the propagation (C–S) and chain transfer (C–H) reactions, the singlet–triplet energy gaps (ΔE_{ST}) of substrates, radical stabilization energies (RSE, kJ mol^{-1}) of thioether radicals, and amount of charge on thiyl ($\delta^{\ddagger}$) radical moiety at the transition state.

Alkene	RS$^-$+ene$^+$	RS$^+$+ene$^-$	ΔE_{ST}	RSE	C–S	C–H	$\delta^{\ddagger a)}$
2-Butene (1)	7.39	11.71	4.54	35.54	2.37	1.57	−0.051
2,4-Hexadiene (2)	6.38	12.20	3.54	85.47	2.53	1.41	−0.048
Isoprene (3)	7.02	11.74	3.60	79.00	2.58	1.42	−0.016
Cinnamaldehyde (4)	7.18	10.20	3.23	59.18	2.47	1.52	0.044
P-cymenene (5)	6.43	11.56	3.86	73.76	2.55	1.43	0.026
Geraniol (6)	6.98	11.49	4.23	68.53	2.49	1.54	0.019
Linalool (7)	7.00	11.53	6.03	38.95	2.38	1.59	0.062
Citral (8)	7.00	11.14	3.47	65.69	2.37	1.57	−0.001
D-limonene (9)	6.84	11.56	6.01	57.18	2.42	1.53	0.058
Terpinolene (10)	6.45	11.60	4.36	41.07	2.38	1.57	0.120
γ-terpinene (11)	6.64	11.57	5.46	56.70	2.33	1.50	0.107
Vinyl chloride (12)	8.33	11.73	4.41	42.73	2.42	1.55	−0.031

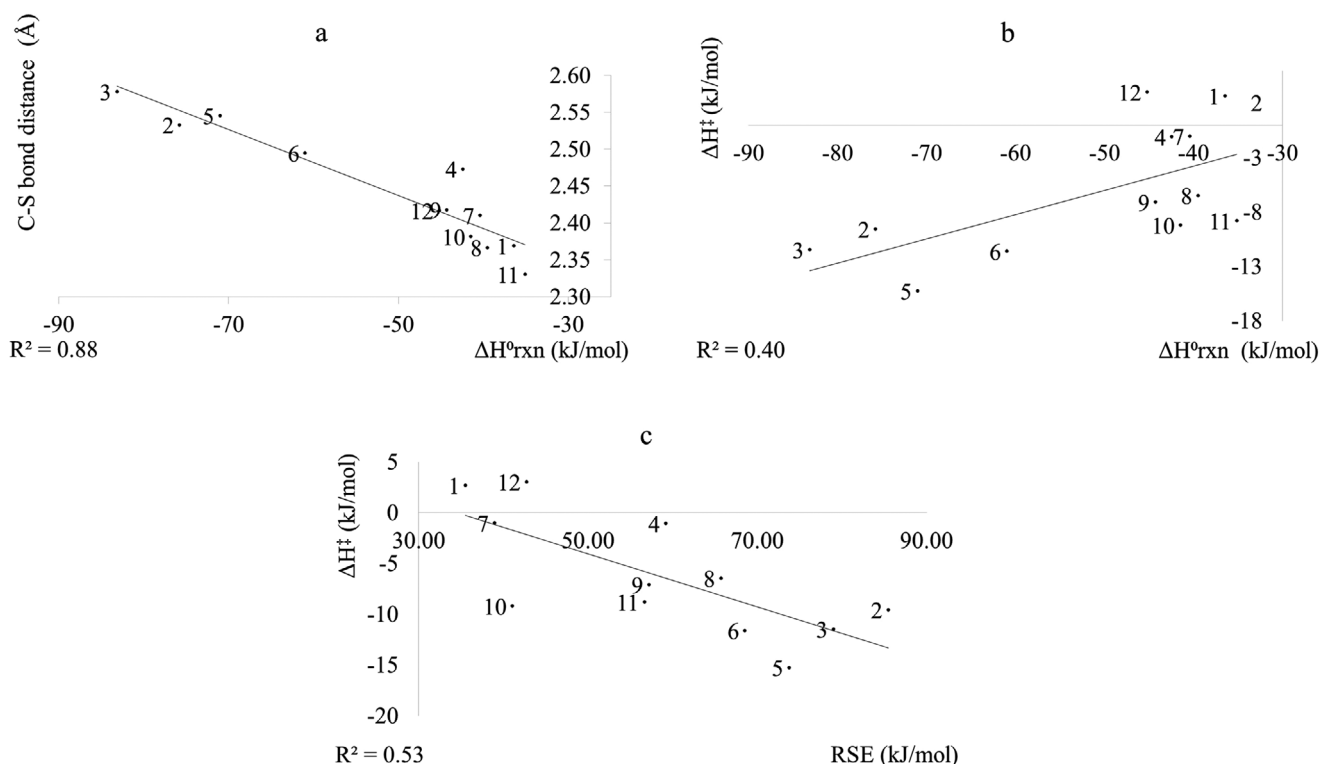a) Mulliken charge on thiyl radical at the transition state geometry.

Figure 2. a) Hammond postulate (without cinnamaldehyde (4), $R^2 = 0.96$), b) Evans–Polanyi relationship, and c) correlation between radical stabilization energy (RSE) of carbon-centered radicals and the activation enthalpies for the propagation reaction.

High correlation shows that reaction enthalpies and transition–state geometries are interrelated. It is seen that the propagation reactions of monomers 2,4-hexadiene (2), isoprene (3), p-cymenene (5), and geraniol (6) have the lowest activation barriers and that the critical bond lengths (C–S) are greater for these monomers (Table 3). They show early transition states and their reaction enthalpies are relatively more exothermic. For example, isoprene (3) has the largest critical bond length (2.58 Å), while the

energy of the propagation reaction of it is the most exothermic ones ($\Delta H^{\circ}_{rxn} = -83.15$ kJ mol^{-1}). Conversely, γ-terpinene (11) has the lowest critical bond length (2.33 Å) at the transition state, which gives the least exothermic reaction (−35.12 kJ mol^{-1}).

If the propagation reaction obeys the Hammond postulate (Figure 2a), the reaction does not fit the Evans–Polanyi relationship (Figure 2b); it shows that there are significant contributions of polar or nonpolar interactions at the transition state

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geometries. The curve-crossing model is used to explain structure-reactivity relationships for these kinds of reactions.[63,66] According to this approach, the reactivity for propagation reaction is elucidated by assessing the charge transfer configuration energies (RS$^-$+ene$^+$ and RS$^+$+ene$^-$) are considered as polar interactions and the ΔE_{ST} of a substrate presents nonpolar interactions.

The energy required for electron transfer from the monomer to the sulfur-centered radical is represented as (RS$^-$+ene$^+$) charge transfer configuration, which shows the electrophilic nature of the thiyl radical, and the energy required for electron transfer from the sulfur-centered radical to monomer is represented as (RS$^+$+ene$^-$) charge transfer configuration, which shows the nucleophilic property of the radical. The relatively less energy for the (RS$^-$+ene$^+$) configuration than the (RS$^+$+ene$^-$) configuration (Table 3) means that the thiyl radical has the electrophilic character. The sulfur-centered radical shows electrophilic nature for the thiol-ene polymerization of interested monomers in this study, consistent with previous theoretical studies on thiol-ene polymerization.[43,44] The low energy of charge transfer configuration due to the electrophilic character of sulfur-centered radical indicates that it can stabilize transition state geometry and lower the activation barrier. This situation is observed particularly for conjugated monomers such as isoprene (Table 3). Its low activation enthalpy (32.29 kJ mol^{-1}) is related to its relatively low (RS$^-$+ene$^+$) configuration energy (7.02 eV). In addition to this, doubly unsaturated carbon bonds containing monomers also show similar behavior. For example, terpinolene has 6.45 eV of the (RS$^-$+ene$^+$) configuration energy and its enthalpy of activation is relatively low (41.18 kJ mol^{-1}). As though adjacent π bond systems to the ene functionality, the other groups also have a crucial effect on the charge transfer configuration energies. The electron-donating property of a moiety attached to the C=C double bond leads to a decrease in the energy of (RS$^-$+ene$^+$) configuration. Contrarily, linalool has comparatively high Gibbs free energy of activation (47.03 kJ mol^{-1}), although its (RS$^-$+ene$^+$) configuration energy value (7.00 eV) is relatively low. Therefore, it is not easy to establish a general trend between electrophilicity of thiyl radical and the enthalpy of the propagation activation ($R^2 = 0.59$, Figure S2a, Supporting Information). However, some relationship is also possible without isoprene, geraniol, and vinyl chloride data ($R^2 = 0.82$, Figure S2b, Supporting Information). As a general assessment, this weak relationship can be attributed to the soft electrophilic nature of the thiyl radical that can be figured out by the amount of charge separation on thiyl (δ‡) radical moiety at the transition state geometry (Table 3). Mulliken charge separation at the activated complex geometries (δ‡) is small or negligible except terpinolene and γ-terpinene. In the case of these two monomers, thiyl radical prefers having positive charge as if it is a nucleophile. On the other hand, still, terpinolene and γ-terpinene have significantly low (RS$^-$+ene$^+$) configuration energies (6.45 and 6.64 eV, respectively) compared to (RS$^+$+ene$^-$) configuration energy. These results show that the polar effect plays an essential role in the activation barrier of the propagation reaction but alone is not sufficient to explain the activation barriers. The singlet–triplet energy gaps of substrates, which is considered nonpolar interactions, can also significantly contribute to the stabilization of activated complex geometries. For example, comparing the (RS$^-$+ene$^+$) configuration energies

with the activation energies of isoprene and linalool exhibits how notable nonpolar interactions are. The (RS$^-$+ene$^+$) configuration energy for isoprene (7.02 eV) is similar to linalool (7.00 eV); interestingly, the activation barrier of isoprene is significantly lower (32.29 kJ mol^{-1}) than linalool (47.03 kJ mol^{-1}). This disparity can be explained by the fact that the singlet–triplet energy gap of isoprene (3.60 eV) is lower than that of linalool (6.03 eV). That means, during the reaction, an electron in π orbital of isoprene is more easily excited to the π^* orbital than linalool, and thus the reaction takes place faster. The ΔE_{ST} of conjugated monomers such as 2,4-hexadiene (3.54 eV), isoprene (3.60 eV), cinnamaldehyde (3.23 eV), p-cymenene (3.86 eV) is slightly lower than the others. As a result, they have relatively less activation energies. However, it is not easy to set up a generalized structure–reactivity relationship between the enthalpy of activation and the ΔE_{ST} of substrates as in the case of electrophilicity characteristic of thiyl radical. Consequently, the factors affecting the activation energies include both the charge transfer configuration energy (RS$^-$+ene$^+$) and the singlet–triplet energy gap (ΔE_{ST}). Furthermore, the stability of carbon-centered radical intermediate contribution to reaction barriers has to be considered for the propagation reactions (Figure 2c). However, small correlation coefficient ($R^2 = 0.53$) between these two parameters reveals that its effect on the activation barriers is limited or negligible. It is well known that the stability of thioether radical intermediate is also a significant feature of chain transfer reactivity.[29]

3.2. Chain Transfer

The generated carbon radical (thioether radical) intermediate in the propagation step of thiol-ene polymerization captures a hydrogen atom from a thiol, producing a new sulfur-centered radical (thiyl radical) in the chain transfer step. At the same time, the growing chain is terminated, which produces a thioether product (Figure 1). The stability of the thioether radical intermediate is crucial for elaborating the progress of thiol-ene polymerization. This point has been outlined as a notable factor affecting the chain transfer reaction in both experimental[34,35,48] and theoretical studies.[43–45] Conjugated alkenes such as 2,4-hexadiene and isoprene undergo delocalization, forming more stable radical intermediates (Table 3). For example, it was calculated as 85.47 kJ mol^{-1} for 2,4-hexadiene. Related to this stability of radical intermediates, the Gibbs free energy barrier for the chain transfer reaction is relatively large (71.21 kJ mol^{-1}). The most unstable radicals are produced from 2-butene and linalool in this set of monomers; their RSE values were calculated as 35.54 and 38.95 kJ mol^{-1}, respectively. Related with this property, their activation energies are relatively low (42.32 and 47.87 kJ mol^{-1}, respectively). This study illustrates that reaction barriers in Gibbs free energy are relatively high for conjugated monomers (71.21 kJ mol^{-1} for 2,4-hexadiene, 71.34 kJ mol^{-1} for isoprene). In addition to these monomers, the high activation energies of chain transfer reaction for geraniol (61.84 kJ mol^{-1}) can be correlated with the high stability of radical intermediate (68.53 kJ mol^{-1}), although radical spin delocalization does not occur. In contrast, for P-cymenene, this barrier is relatively low, 54.55 kJ mol^{-1}. Interestingly, some enthalpy of activations is significantly submerged, such as terpinolene and γ-terpinene (−19.11 and

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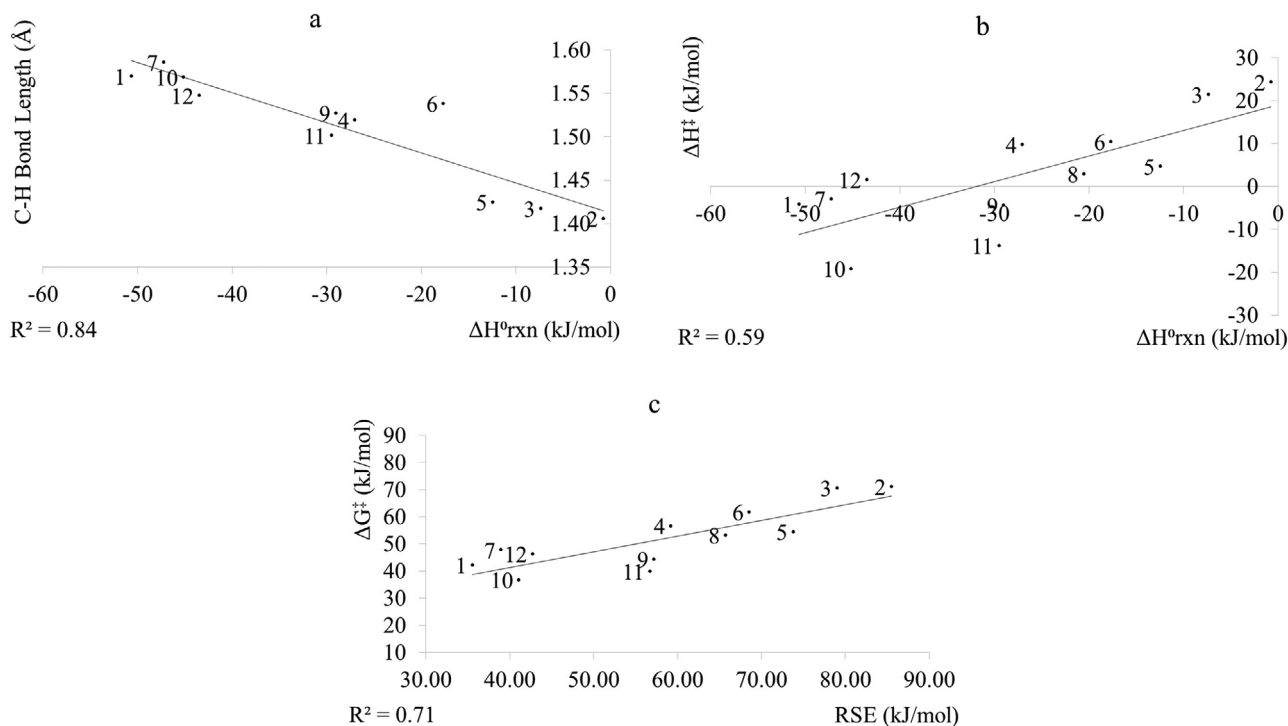Theory and Simulations

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Figure 3. a) Hammond postulate (without geraniol (6), $R^2 = 0.95$). b) Evans–Polanyi relationship, and c) relationship between RSE and the Gibbs free energy of activation for the chain transfer reaction.

-13.74 kJ mol^{-1}, respectively). In the literature studies, these barriers have been experienced for the fast reactions with very accurate composite methods like CBS-QB3 and G3X(MP2)-RAD for similar reactions.[43,67] In general, the reaction enthalpies are exothermic due to the relatively stable sulphur radical forming at the exchange of the unstable carbon radical.[65] However, for chain transfer reactions in which radical intermediate is stable, reaction enthalpies are usually very close to endothermic (for 2,4-hexadiene, isoprene, and p-cymenene, it ranges from -0.74 to -12.45 kJ mol^{-1}).

The reactivity of thioether radicals appears to be very different due to the nature of starting alkenes and, therefore, likely to affect the overall progress of the reaction. The Gibbs free energy barriers of the hydrogen abstraction reactions range from 36.85 kJ mol^{-1} (terpinolene) to 71.34 kJ mol^{-1} (isoprene). To understand the structure–reactivity relationship for the chain transfer reaction step, we first checked the Hammond postulate and Evans–Polanyi relationship. Some correlation ($r^2 = 0.84$, without the outlier citral (8)) was obtained with the Hammond postulate (**Figure 3**a). However, a well correlation could not be established between enthalpy of reaction and activation energies in the Evans–Polanyi relationship (Figure 3b), which shows that intermolecular interactions are significantly involved in the activated complex geometries.[44,45] This result is consistent with a literature study that has extensively focused on the hydrogen abstraction reaction of the carbon-centered radicals from thiols by utilizing the expensive G3X(MP2)-RAD level of theory.[67] Therefore, the relationship between the radical intermediate stability and reaction energy barriers was also examined (Figure 3c). As a result, a relatively high correlation ($R^2 = 0.71$) reveals that the rad-

ical intermediate stability is one of the important contributors to the chain transfer activation energy. This result is consistent with Bowman's suggestions and Northrop's findings.[34,43]

3.3. Reaction Kinetics

Propagation (k_p) and chain transfer (k_{ct}) reaction kinetics were calculated to elucidate the thiol-ene reactivity of some natural monomers. All produced kinetic data for the forward and reverse reactions are tabulated in **Table 4**. The propagation rate constants (k_p) ranged from 6.26E+05 M^{-1} s^{-1} (vinyl chloride) to 3.39E+08 M^{-1} s^{-1} (isoprene), while the chain transfer rate constants (k_{ct}) range from 1.21E+02 M^{-1} s^{-1} (2,4-hexadiene) to 8.51E+07 M^{-1} s^{-1} (terpinolene) with greater variability.

The magnitude of calculated propagation rate coefficient for 2-butene ($k_p = 7.42$E+05 M^{-1} s^{-1}) is similar with experimentally observed kinetic data ($k_p = 2.9$E+05 M^{-1} s^{-1}) for thiyl radical addition to methyl oleate.[68,69] Moreover, the propagation reaction of 2-butene is reversible, and the chain transfer reaction is irreversible like propene.[43] This finding is also consistent with experimental[70,71] and theoretical[72] investigations on *cis-trans* isomerization of fatty acids by thiyl radicals. Experimentally estimated the β-scission rate constant of thiyl radical from formed intermediate carbon radical of methyl oleate is 6E+06 s^{-1},[71] which is predicted as 1.03E+06 s^{-1} within the experimental error range with 2-butene in this study. The calculated chain transfer rate constant ($k_{ct} = 9.73$E+06 M^{-1} s^{-1}) has similar magnitude with experimentally observed ones ($k_{ct} = 1.0$E+07 M^{-1} s^{-1}).[68] The calculated ratio between the reaction rate constants (7.62E-02) is

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Table 4. Forward and reverse reaction kinetic data for 12 molecules at M062X/6-31++G(d,p) level of theory.

Alkene	k_p [$M^{-1} s^{-1}$]	k_{p_r} [s^{-1}]	k_{ct} [a] [$M^{-1} s^{-1}$]	k_{ct_r} [a] [$M^{-1} s^{-1}$]	k_p / k_{ct} [a]
2-Butene (1)	7.42E+05	1.03E+06	9.73E+06	1.24E-01	7.62E-02
2,4-Hexadiene (2)	7.77E+07	5.17E+01	1.21E+02	5.11E+02	6.43E+05
Isoprene (3)	3.39E+08	2.98E+00	1.26E+02	1.81E+01	2.69E+06
Cinnamaldehyde (4)	1.02E+06	9.20E+05	4.05E+04	6.64E+00	2.52E+01
P-cymenene (5)	2.52E+08	1.21E+03	8.82E+04	2.27E+04	2.86E+03
Geraniol (6)	6.90E+07	5.42E+04	3.68E+03	5.86E+01	1.87E+04
Linalool (7)	8.87E+05	1.54E+06	9.94E+05	7.80E-02	8.93E-01
Citral (8)	1.39E+07	1.55E+07	1.13E+05	9.94E+02	1.23E+02
D-limonene (9)	1.06E+07	1.27E+06	4.37E+06	1.25E+03	2.43E+00
Terpinolene(10)	9.39E+06	6.50E+07	8.51E+07	2.69E+01	1.10E-01
γ-terpinene(11)	2.17E+06	1.07E+08	2.73E+07	2.01E+01	7.94E-02
Vinyl chloride (12)	6.26E+05	4.24E+04	2.02E+06	3.25E+00	3.11E-01

[a] Wigner tunneling correction was carried out. Imaginary frequencies ($\omega^{\ddagger}$) and tuneling coefficients ($\kappa(T)$) for the chain transfer reactions of the monomers is given in Table S1 (Supporting Information).

relatively close to the theoretically suggested ratio (1.00) for this monomer but less than it. These results show that monomers containing an aliphatic chain with internal C=C double bonds can give thiol-ene polymerization. In line with these findings, it is predicted that unsaturated fatty acids containing unconjugated C=C double bonds, such as linoleic acid or oleic acid, have the potential to give thiol-ene products.

The calculated propagation reactions of 2,4-hexadiene (2) and isoprene (3) monomers occur rapidly and irreversibly, as in a literature study about butadiene.[43] Chain transfer reactions are prolonged and reversible compared to propagation reactions. The calculated ratios (k_p/k_{ct}) are much greater than 1.00 in both monomers. These findings show that aliphatic conjugated natural systems, such as conjugated linoleic acid or retinol are unsuitable for obtaining a homogeneous thiol-ene product.

One of the interested natural monomers in this study is cinnamaldehyde (4). Its propagation reaction is fast ($k_p = 1.02E+06$ $M^{-1} s^{-1}$) and it is strongly reversible ($k_{p\_r} = 9.20E+05$ s^{-1}). This reversibility is striking since its intermediate radical stability is relatively high (59.18 kJ mol), but β-cleavage is inevitable as if formed carbon-centered radical is highly unstable. Moreover, the chain transfer reaction is relatively slow ($k_{ct} = 4.05E+04$ $M^{-1} s^{-1}$). Therefore, the reaction rate constants ratio ($k_p/k_{ct} = 2.52E+01$) is a bit higher than the targeted value, 1.0. This ratio can be mitigated by using different thiols suggested in theoretical studies in the literature.[44–46] On the other hand, cinnamaldehyde is expected to give heterogeneous thiol-ene polymer product due to the very fast propagation reaction and possessing quite high the ratio k_p/k_{ct}. P-cymenene (5) is a natural derivative of synthetic monomer styrene. The propagation reaction of this monomer is similar to styrene;[43] the forward reaction rate is almost in the diffusion limit ($k_p = 2.52E+08$ $M^{-1} s^{-1}$), and reverse propagation is relatively slow. Therefore, it can be taken into account as a nonreversible reaction. However, its chain transfer reaction has a different nature from its styrene counterpart, which is strongly reversible. The high stability of the radical intermediate (73.76 kJ

mol^{-1}) and low exothermicity (-12.45 kJ mol^{-1}) of the reaction can play a crucial role in the reversibility of this reaction. As a consequence, this monomer is not a suitable option for sustainable thiol-ene polymerization since the ratio of reaction rates (2.86E+03) for p-cymenene is quite high, like styrene. Although geraniol (6) is not a conjugated monomer, its thiol-ene polymerization behaves similar to p-cymenene. The forward propagation reaction is quite fast ($k_p = 6.90E+07$ $M^{-1} s^{-1}$), and it is nonreversible, or its reversibility is negligible. The forward chain transfer reaction is relatively slow ($k_{ct} = 3.68E+03$ $M^{-1} s^{-1}$) and is also highly reversible. In addition to this, the ratio of the reaction rates (1.87E+04) is the largest one in this set of monomers. Therefore, its thiol-ene polymerization behavior is predicted to be the same as conjugated monomers such as 2,4-hexadiene or isoprene. The propagation reaction of linalool (7) is strongly reversible, and its forward reaction is relatively slow ($k_p = 8.87E+05$ $M^{-1} s^{-1}$). In addition to this, the rate constant of chain transfer reaction has similar magnitude with propagation ones ($k_{ct} = 9.94E+05$ $M^{-1} s^{-1}$), and it is not reversible. Therefore, it is expected that this monomer can yield a desired thiol-ene polymerization product since its calculated k_p/k_{ct} ratio is very close to 1.0 (8.93E-01). Similar to geraniol (6), the propagation reaction rate of citral (8) is large ($k_p = 1.39E+07$ $M^{-1} s^{-1}$); in contrast to geraniol, this reaction is strongly reversible. As in the case of geraniol, the forward chain transfer reaction is relatively slow (1.13E+05 $M^{-1} s^{-1}$), and it is reversible. Consequently, citral can be considered unsuitable for the polymerization as in geraniol.

In this monomer set, vinyl chloride is another synthetic monomer, and it has a relatively slow propagation reaction ($k_p = 6.26E+05$ $M^{-1} s^{-1}$). The rate coefficient of carbon-centered radical attacking this monomer is in the order of four.[63] Therefore, homopolymerization inevitably accompanies thiol-ene reaction since relatively slow and reversible propagation reaction. Although the chain transfer reaction is irreversible and the ratio of the reaction rate constants is close to 1.0 (3.11E-01), it was predicted that vinyl chloride-like unconjugated "diene" derivatives,

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such as Z,Z-dichloroalkene[73] would yield a heterogeneous thiol-ene product.

The propagation reaction of *d*-limonene, terpinolene, and *γ*-terpinene are very fast; their rate coefficients are 1.06E+07 M^{-1} s^{-1}, 9.39E+06 M^{-1} s^{-1}, and 2.17E+06 M^{-1} s^{-1}, respectively. Alkyl substituted substrate structures of these monomers have similarities with 2-butene. They are electron-rich monomers, and their addition products are highly unstable compared to conjugated monomers (Table 3). For this reason, the reverse reactions that occur by breaking the C–S bond (*β*-scission) are quite fast, and the propagation reaction of these monomers are reversible. The instability of intermediate radical is one of the crucial factors of thiol-ene reactions, and it enhances fast chain transfer reaction. Therefore, *d*-limonene, terpinolene, and *γ*-terpinene have large chain transfer rate coefficients as significant as in the propagation reactions. Moreover, the ratio of reaction rates for *d*-limonene is very close to 1.0 (2.43E+00), it is a little bit lower than 1.0 for terpinolene and *γ*-terpinene (1.10E-01 and 7.49E-02, respectively). Based on these findings, the chain transfer reaction is a rate-limiting step for *d*-limonene, and it is propagation reaction for terpinolene and *γ*-terpinene.

As a result of this kinetic evaluation, we can suggest that derivatives of linalool and *d*-limonene are the best candidates for thiol-ene polymerization in this set of monomers. Moreover, derivatives of 2-butene, terpinolene, and *γ*-terpinene monomers can give thiol-ene polymer products with some heterogeneity. Finally, the others in this set of monomers are not suitable for the tihol-ene polymerization by using aliphatic thiols. Based on in silico findings at the M06-2X/6-31++G(d,p) level of theory, these natural candidates can pave the way for sustainable thiol-ene polymerization, and they need further investigations by in vitro studies.

4. Conclusions

In this study, the thiol-ene polymerization behavior of natural monomers was elucidated by using quantum chemical tools. The relationship between structure and reactivity on thiol-ene polymerization of natural monomers was clarified with methyl thiol. The M06-2X/6-31++G(d,p) level of theory was used for estimating the propagation (k_p) and chain transfer (k_{ct}) rate coefficients. It was found out that the propagation reaction of thiol-ene polymerization is partially affected by the electrophilic characteristics of the sulfur-centred radicals (RS^-+ene^+ configuration stability) and the ΔE_{ST} of the alkenes. The stability of the formed thioether radical also involves stabilizing the transition state geometries of propagation reaction. In addition to this, chain transfer reaction is significantly governed by the stability of carbon-centered radical intermediate.

This study emphasized that alkene functionality plays a significant role in the k_p/k_{ct} ratio, regulating thiol-ene polymerization processes. In addition, for the polymerization, electron-rich (linalool, *d*-limonene, terpinolene, and *γ*-terpinene) alkenes are highly reactive compared to conjugated alkenes (2,4-hexadiene, isoprene, cinnamaldehyde and p-cymenene) due to the former ones having the k_p/k_{ct} ratio close to 1.0, and the latter ones having large the k_p/k_{ct} ratio.

It was anticipated that cinnamaldehyde, geraniol, and citral as natural monomers would not work well in thiol-ene polymer-ization to be carried out with aliphatic thiols. Among the natural monomers, it is envisaged that 2-butene, which is an analog to unsaturated fatty acids, linalool, *d*-limonene, terpinolene, and *γ*-terpinene monomers, can be good candidates for sustainable thiol-ene polymerization. Beyond forming the thiol functionality of natural products, this study shows that fatty acids and terpenoids have the potential for thiol-ene polymerization. This field of study needs further investigations for the future of green polymer synthesis utilizing the thiol-ene reaction mechanism.

Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

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