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Metathesis of terpenes using the second generation Grubbs Ru–alkylidene catalysts: Computational modeling

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ABSTRACT

The initiation step, self metathesis of β-pinene (**2**) and its cross metathesis with (*Z*)-3-methylpent-2-ene (**16**) mediated by the second generation Grubbs catalyst have been modeled at PBE/def2-TZVP level of theory using empirical dispersion correction scheme (D3). It has been found that the initiation step leads to the formation of tertiary not primary metalacarbene which undergoes the nonproductive metathesis reaction with β-pinene. The self-metathesis productive reaction path is inhibited by unfavorable kinetic and thermodynamic factors. The first one is related to the high steric hindrances in transition states and the second one with the low stability of formed primary metalacarbene. The free Gibbs activation energies of cross metathesis of **2** and **16** were found to be around 23 kcal/mol.

Introduction

Terpenes are a class of renewable compounds that typically contain carbon atom units built from isoprene molecules, which has the molecular formula C_5H_8. The basic molecular formulae of terpenes are multiples of that, $(C_5H_8)_n$ where *n* is the number of linked isoprene units (Scheme 1).

A wide variety of biobased structures are synthesized by transformation of isoprene monomer units. Monoterpenes, β-carotene, natural rubber, carvone and steroids such as testosterone, cholesterol and estrogen are same of the examples of terpene based compounds (Scheme 1). In plants, terpenes are found as a main component of the essential oils, that are used as medicines, spices and perfumes [1]. Commercial polymers of pinenes prepared usually by Lewis acid catalyzed polymerization are used in many industrial applications for example, as pressure-sensitive adhesives, hot-melt coatings, packaging gum and additives [2,3]. The transformations of terpene based molecules using efficient catalysts are of great interest for the development of new applications for these biomass-derived compounds. In this perspective, metathesis transformations are becoming more attractive as the availability and choice of effective catalysts increased [4]. Experimental and computational studies show that Ru-alkylidene catalysts with strongly σ-donating N-heterocyclic carbene (NHC) ligand are preferred for the metathesis of challenging highly functionalized substituted olefins [5–7]. Recent computational study of α-pinene ring-opening metathesis using the second generation Grubbs catalyst, tungsten based Schrock and Fischer type metalacarbenes revealed the importance of the steric factor in both the metathesis catalyst and the monomer substrate [8]. The metathesis transformations of terpene based compounds using the NHC ligand containing Ru-alkylidene catalysts have been reported [9]. Monoterpenes such as D-limonene and β-pinene have been used in the cross-metathesis reactions with cycloolefins [10] and natural rubber [11] (Scheme 2). Recently, terpene based essential oils have been tested as a cross-metathesis partner and a green solvent for the degradation of natural rubber and polybutadiene in block-copolymers [12].

The goal of this study is the computational modeling of β-pinene cross-metathesis with (*Z*) 3-methyl-2-pentene as a model compound of natural rubber and other terpene based molecules using the NHC containing Ru-alkylidene catalysts.

Computational details

All calculations were carried out using TURBOMOLE 6.4 suit of programs [14]. PBE functional in combination with triple ζ quality pseudopotential basis sets def2-TZVP has been used all calculations. Selected method reproduces remarkably well the PCy_3 dissociation energy for Grubbs II type catalyst (36.4 *vs.* 36.8 kcal/mol) [15] showing MAD error for Ru–Cl, Ru–P, Ru–C, and P–C

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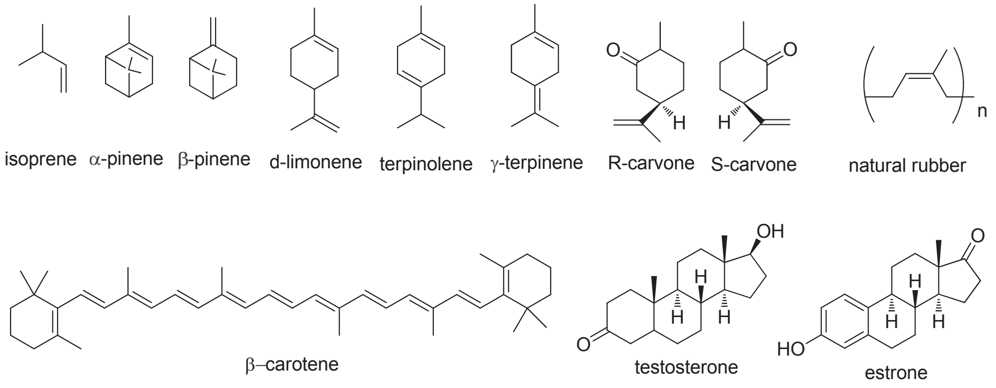


Scheme 1. Terpenes and related molecules.

bonds of **1a** of only 0.016 Å. Frequency calculations were run at 298.15 K for all structures to make sure that a transition state (one imaginary mode) or minimum (zero imaginary modes) is located and to estimate zero point energy correction and thermodynamic properties.

The reaction energies of non polar olefin metathesis reactions in non polar solvents are barely affected by solvation [5b], therefore, all the calculations were carried out in the gas phase. Thus, test single point calculations on gas phase optimized structures using COSMO [16] solvation model and 1,2-dichloroethane as a solvent carried out for the **1** → **9a** and **1** → **9b** transformations (Scheme 3a) only show deviation from gas phase energies of 0.20 and 0.17 kcal/ respectively.

To estimate the effect of steric hindrances on the metathesis activation energy caused by different orientations of β-pinene in transition states, following methodology has been used. The β-pinene moieties in two transition states **TS1** and **TS2** differing only by β-pinene orientation were replaced by hydrogen atoms, The new resulting structures **TS1$_m$** and **TS2$_m$** were optimized with all but new hydrogen atoms frozen. The difference of steric energy contribution between **TS1** and **TS2** is calculated as $(E_{TS1} - E_{TS2}) - (E_{TS1m} - E_{TS2m})$ where E_{TS1} and E_{TS2} are the total electronic energies of **TS1** and **TS2** and E_{TS1m} and E_{TS2m} are the total electronic energies of the modified structures **TS1$_m$** and **TS2$_m$**.

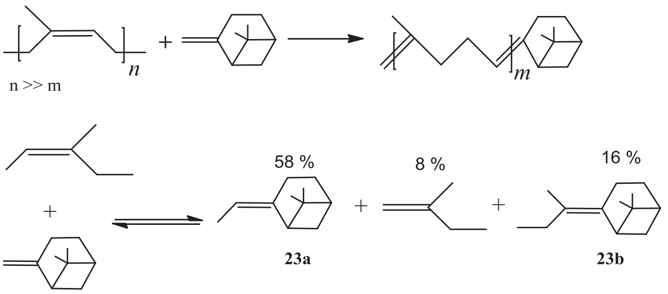
Results and discussion

Scheme 3a–c shows studied reaction routes. It has been discovered that [6f] all three mechanisms: (associative, dissociative, and interchange) are operational for Grubbs–Hoveyda-Type alkene metathesis catalysts. The mechanism is very sensitive to the considered reaction as well as the level of theory. On the other hand, it has been recently shown [6d] that barrier of olefin coordination is smaller than that of cycloaddition step, moreover, it has been recently demonstrated that dissociative mechanism operates for catalyst **1** [6e]. Therefore, taking into account the above the reaction mechanism can be describes as follows: the first is the initiation: the reaction of the second generation Grubbs catalyst **1** with β-pinene (**2**) (Scheme 3a). There are two possible orientations of **2**. The first one giving as a result styrene (**8a**) and tertiary metalacarbene **9a** and the second one producing methylene metalacarbene **9b** and olefin **8b**. Fig. 1 shows the corresponding free Gibbs energy profiles.

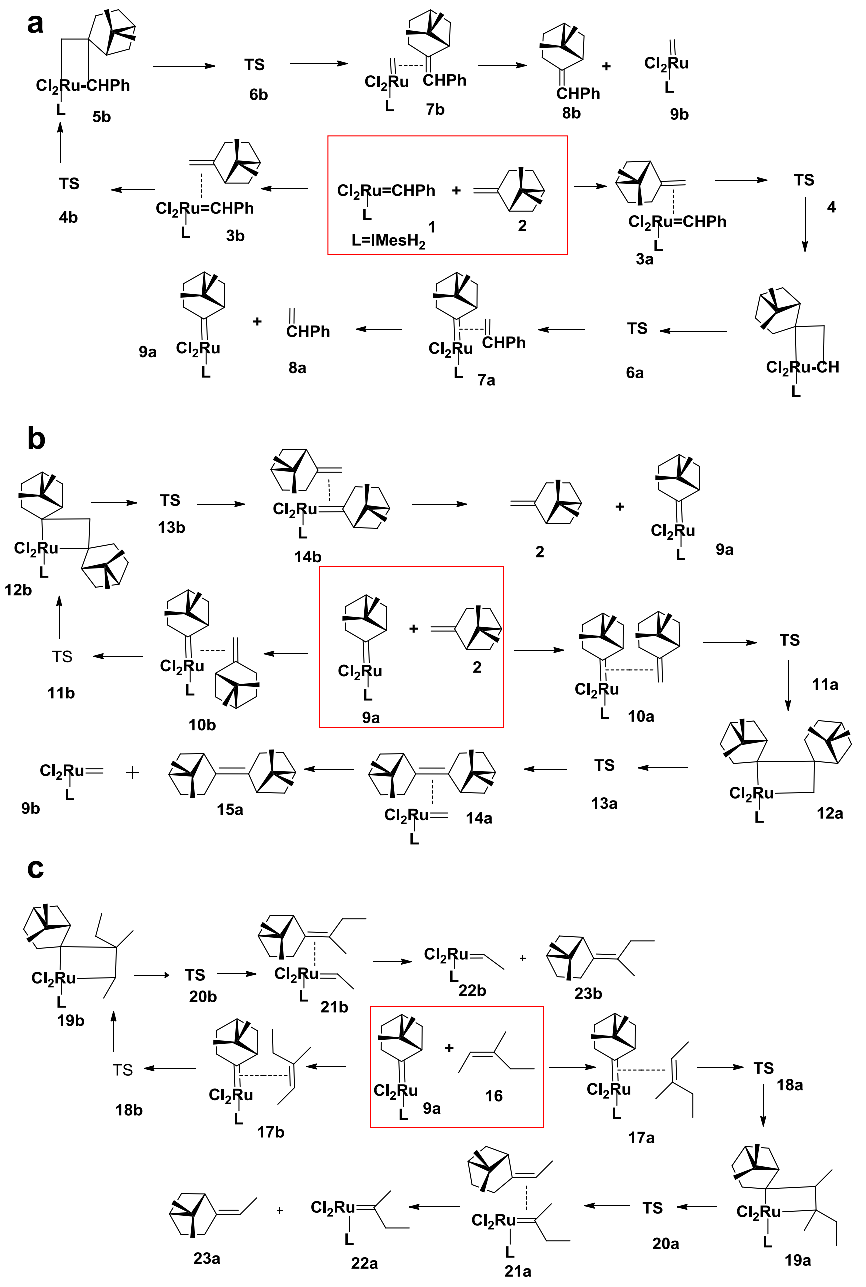
It can be noticed that the first reaction route is the most favorable one kinetically and thermodynamically with only slightly positive reaction energy of 0.6 kcal/mol and the activation energy of 10.1 kcal/mol, while the alternative reaction pathway requires 20.9 kcal/mol showing much more positive reaction energy of almost 10 kcal/mol. Therefore, the only possible way for the initiation step is the formation tertiary carbene **9a**. Such a drastic difference between two reaction pathways is due to two factors acting in the same direction: increased stability of tertiary carbene (**9a**) compared to the primary one (**9b**) and the increase of the activation energy of the metathesis reaction with degree of substitution of formed olefin [8]. As seen from Table 1 the steric factor plays a decisive role in the difference of the activation energies between those two pathways. The same conclusion can be made inspecting the geometry of transition states **6a** and **6b** (Fig. 2), where the olefin bond is slightly larger in **6b**, reflecting repulsion between substituents. Therefore, the most favorable reaction pathway is the formation of less substituted olefin and the most substituted metalacarbene. Since the initiation the most likely leads to the unique metalacarbene **9a**, this metalacarbene has been selected as working metalacarbene.

The second step is the properly β-pinene metathesis (Scheme 3b). As seen, similarly to the initiation step there are two different reaction pathways corresponding to two initial orientations of β-pinene in π-complex; complex **10a** and **10b**, respectively. The corresponding free Gibbs reaction energy profiles are depicted in Fig. 3. One pathway is the degenerate metathesis of **2** which has moderately high activation energy of 17 kcal/mol, while the other one is very unfavorable metathesis reaction leading to the formation of tetrasubstituted olefin **15a** and methylene metalacarbene **9b**.

This reaction path implies very high activation barrier of 28.9 kcal/mol with positive reaction energy of 9.5 kcal/mol. A very high activation energy of this reaction pathway is directly related to the formation of tetrasubstituted olefin **15a** resulting in notably strained transition states. This observation supports data of Table 1 where steric factor is shown to be the only one responsible for such a large difference in the activation energies between two reaction



Scheme 2. Cross metathesis of β-pinene with natural rubber and (*Z*) 3-methyl-2-pentene [11].



Scheme 3. Elementary steps of studied reactions: a) Initiation, b) Self -metathesis, c) Cross-metathesis.

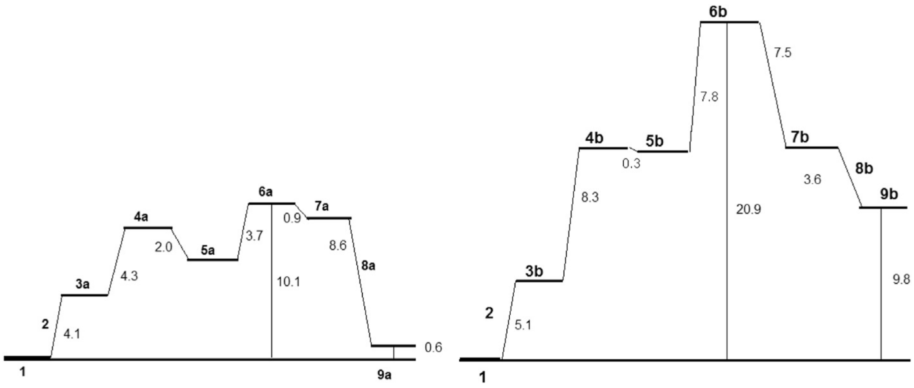


Fig. 1. The free Gibbs energy profile for the reactions **1** with **2** (kcal/mol).

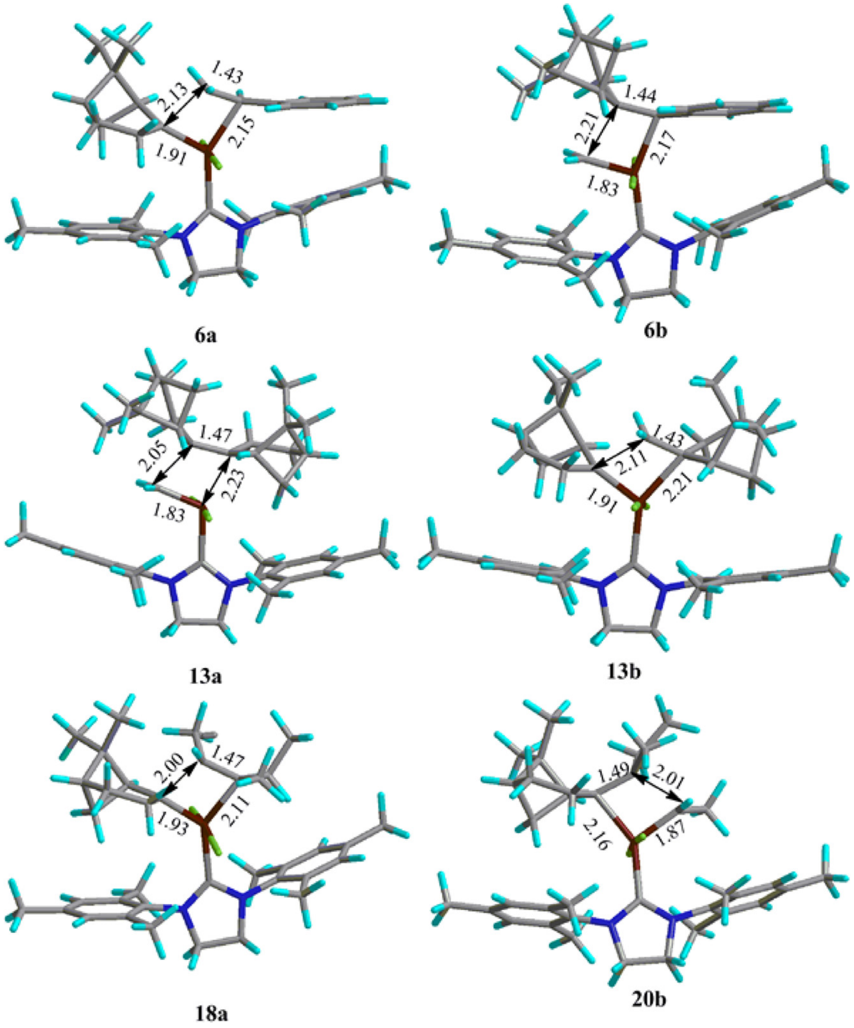
Table 1
The difference of total electronic energies of selected transition states ($E_{\mathbf{TS1}} - E_{\mathbf{TS2}}$), the corresponding modified transition states ($E_{\mathbf{TS1m}} - E_{\mathbf{TS2m}}$) and the difference between them (ΔE) (kcal/mol).

TS1	TS2	$E_{\text{TS1}} - E_{\text{TS2}}$	$E_{\text{TS1m}} - E_{\text{TS2m}}$	ΔE
6b	**6a**	10.9	−2.2	13.1
13a	**13b**	17.1	−4.7	21.8
20b	**18a**	1.5	−5.2	6.7

pathways. When revising the geometry of transition states **13a** and **13b** a significant difference of the olefin bond length (0.04 Å) is observed (Fig. 2), reflecting steric hindrances in **13a**. Moreover, the formation of primary metalacarbene **9b** from tertiary one **9a** results in positive reaction energy. Thus, apparently no visible metathesis reaction should occur, and the only viable reaction pathway is degenerate metathesis reaction. However, the cross metathesis reaction is still possible in this case. Many experimental and computational studies show that self-metathesis of α-olefins proceeded via the secondary metalacarbene complex as the most energetically favorable route [13]. The control experiments of β-pinene self-metathesis using the second generation Ru-alkylidene catalyst did not show any evidence of the formation of new productive metathesis olefins [11].These results clearly demonstrated that self-metathesis of β-pinene proceeded via the formation of tertiary Ru–carbene **9a**.

As the model of cross metathesis of β-pinene and natural rubber the reaction of the most abundant metalacarbene **9a** with (*Z*)-3-methylpent-2-ene (**16**) has been modeled (Scheme 3c).

Similarly two previously studied cases, two different reaction pathways are possible in this case corresponding to two distinct orientations of olefin **16** in two different π-complexes **17a** and **17b** (Scheme 3c). One of these pathways leads to the formation of tertiary metalacarbene **22a** and trisubstituted olefin **23a**, while another one results in secondary metalacarbene **22b** and tetrasubstituted olefin **23b**. The corresponding reaction energy profiles are shown in Fig. 3. When analyzing the reaction energy profiles one can see that the first reaction route is slightly more favorable thermodynamically and kinetically. Thus, the first reaction path has 1.2 kcal/mol lower activation energy and 2.4 kcal/mol less positive the free Gibbs reaction energy that make both reaction pathways possible. Slightly more preferable first reaction path compared to the second one is due to two favorable factors: formation of less substituted olefin, on the one hand, and more stable tertiary carbene **22a** compared to secondary one **22b** on the other. The contribution of the steric factor to the activation energy difference between those two reaction pathways is seen from Table 1 where ΔE is positive. Similar conclusion can be made comparing the



6a **6b**

13a **13b**

18a **20b**

Fig. 2. Optimized geometry of located transition states.

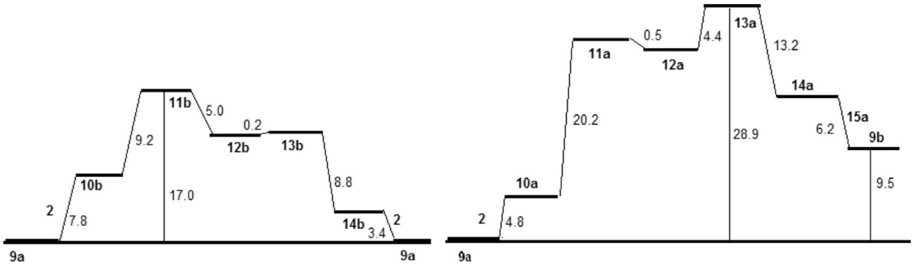


Fig. 3. The free Gibbs energy profile for the reactions **9a** with **2** (kcal/mol).

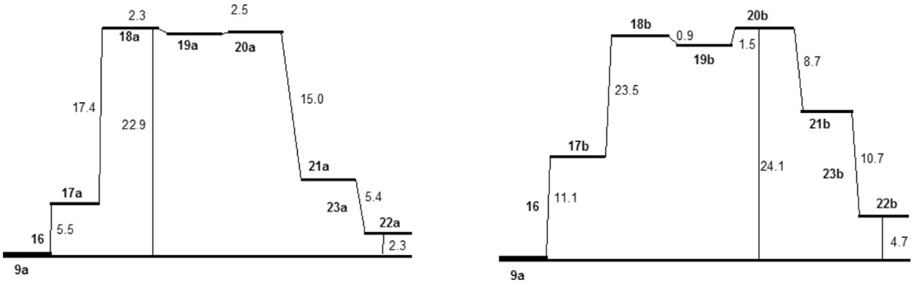


Fig. 4. The free Gibbs energy profile for the reactions **9a** with **16** (kcal/mol).

geometries of the transition states **18a** and **20b**, where olefin bond is 0.02 Å larger in the latter. However, both reaction paths are thermodynamically and kinetically viable to produce the corresponding olefins **23a** and **23b**. Supposing that the reaction pathways shown in Scheme 3c are the only important to generate olefins **23a** and **23b**, then, their relative abundance under equilibrium conditions can be estimated using the free Gibbs formation energies shown in Fig. 3. Therefore, another possible reaction route for the formation of **23a** and **23b** involving the reaction of **1** with **16** followed by the reaction of formed metalacarbenes **22a** and **22b** with **2** is irrelevant due to the formation methylene metalacarbene **9b** which is quite unstable (Fig. 1). The calculated free Gibbs reaction energies for the alternative pathways are of 6.7 and 6.2 kcal/mol for **23a** and **23b**, respectively. Those values are noticeably higher than these shown in Fig. 4, allowing one to neglect this reaction pathway. The results of calculations qualitatively agree with experimental observation (Scheme 2). The most important product of the cross metathesis of β-pinene is olefin **23a**, the experimental ration **23a**/**23b** is 3.6. Considering thermodynamic control the **23a**/**23b** product ratio was found to be of 50, much higher than experimental data, on the other hand, assuming kinetic control the **23a**/**23b** product ratio was found to be of 7, much closer to the experiment. Those estimations suggest that the experimental data of Ref. [11] are obtained under kinetic control.

The relatively high activation energies of cross metathesis of **2** and **16** (about 29 kcal/mol) compared to the metathesis of **16** itself, using catalyst **1** (about 18 kcal/mol [5a]) should slow down the total reaction rate on the addition of **2** to the reaction mixture of **1** and **16**, which is observed experimentally [11].

Conclusions

The calculations demonstrated that the nonproductive metathesis of β-pinene definitely occurs in the presence of second generation Grubbs catalyst. The self-metathesis proceeds via metalacarbene **9a** not **9b** due to kinetic and thermodynamic factors. Self-metathesis of β-pinene mediated by **9a** is inhibited both kinetic and thermodynamic factors. The formation of hydrocarbon **15a** requires very high activation energy due to strong steric hindrances in the transition states, at the same time the formation of metalacarbene **9b** is thermodynamically unfavourd. The calculations carried out for the cross metathesis of β-pinene and (*Z*)-3-methylpent-2-ene as a model of natural rubber agreed well with experiment and revealed that both olefins **23a** and **23b** are formed in the metathesis reaction. The formation of **23a** is slightly more favored by higher stability of tertiary carbene **22a** and less hindered transition state for this reaction path. The cross metathesis of β-pinene and (*Z*)-3-methylpent-2-ene proceeded more slowly than metathesis of (*Z*)-3-methylpent-2-ene itself, due to increase of the activation energies of the cross metathesis steps.

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