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Theoretical study on the mechanism of reaction between 3-hydroxy-3-methyl-2-butanone and malononitrile catalyzed by lithium ethoxide

Research Article

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Abstract: The The mechanism of reaction between 3-hydroxy-3-methyl-2-butanone and malononitrile for the synthesis of 2-dicyanomethylene-4, 5, 5-trimethyl-2,5-dihydrofuran- 3-carbonitrile catalyzed by lithium ethoxide was investigated by density functional theory (DFT). The geometries and the frequencies of reactants, intermediates, transition states and products were calculated at the B3LYP/6-31G(d) level. The vibration analysis and the IRC analysis verified the authenticity of transition states. The reaction processes were confirmed by the changes of charge density at the bond-forming critical point. The results indicated that lithium ethoxide is an effective catalyst in the synthesis of 2-dicyanomethylene-4, 5, 5-trimethyl-2, 5-dihydrofuran- 3-carbonitrile from malononi-trile and 3-hydroxy-3-methyl-2-butanone. The activation energy of the reaction with lithium ethoxide was 115.86 kJ·mol^{-1} less than the uncatalyzed reaction. The mechanism of the lithium ethoxide catalyzed reaction differed from the mechanism of the uncatalyzed reaction.

Keywords: *Density functional theory • Lithium ethoxide • Transition state • Reaction mechanism*

1. Introduction

In past years, chromophore-functionalized electro-optic (EO) polymeric materials have been iintensively investigated for their potential applications in high-speed photonic devices [1]. This has led to extensive explorations of 'push-pull' type chromophores with high molecular second-order nonlinearity. Among the three molecular building blocks commonly used for NLO (nonlinear optic) chromophores (electron donor, conjugating bridge and electron acceptor), the development of electron donors and conjugating bridges is already so mature that they can meet most of the synthetic and physical requirements. Therefore, one of the major tasks in this area is to develop novel electron acceptors. 2-dicyanomethylene-4,5,5-trimethyl-2,5-dihydrofuran-3-carbonitrile is a strong electron acceptor for nonlinear optics. It is a molecular building block for NLO material [2-5]. Li et al. has reported its single-crystal structure [6]. The compound has been synthesized using three different catalysts: lithium ethoxide[7], sodium ethoxide [8], and magnesium ethoxide[9]. Lithium ethoxide is an effective catalyst in the synthesis of 2-Dicyanomethylene-4,5,5-trimethyl-2,5-dihydrofuran-3-carbonitrile from malononitrile and 3-hydroxy-3-methyl-2-butanone. However, there is no report on the theoretical study of the microscopic mechanism of its synthesis reaction which is catalyzed by lithium ethoxide. This is an important subject to investigate.

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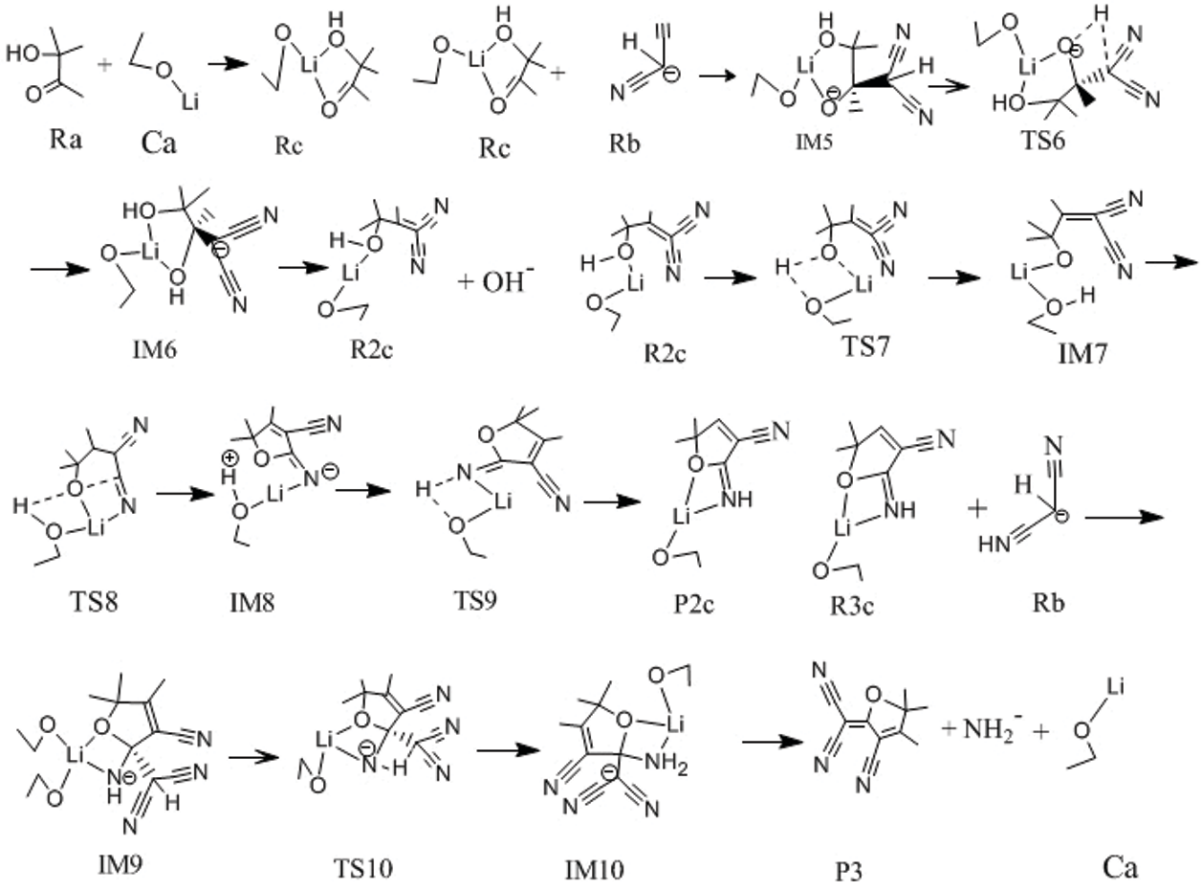

Figure 1. The mechanism of reaction between 3-hydroxy-3-methyl-2-butanone and malononitrile with catalyst lithium ethoxide.

2. Computational methodology

The mechanism of reaction between 3-hydroxy-3-methyl-2-butanone and malononitrile for the synthesis of 2-dicyanomethylene-4,5,5-trimethyl-2,5-dihydrofuran- 3-carbonitrile catalyzed by lithium ethoxide was investigated by density functional theory (DFT). The geometries and the frequencies of reactants, intermediates, transition states and products were calculated at the B3LYP/6-31G(d) level. Stable structures were obtained. The parameters of geometry configuration are shown in Fig.2(Ra-P3) and in Fig.3(Rc-IM10). The vibration analysis and the IRC analysis proved the authenticity of intermediates and transition states. The reaction processes were confirmed by the changes of charge density at the bond-forming critical point (as shown by the numeric value in the parentheses in Fig. 2 and Fig. 3) [10-11]. All calculations were carried out with the Gaussian 03 program [12].

3. Results and Discussion

The calculated energies (E) and relative energies (E_{rel}) of reactants, intermediates, transition states and products are listed in Table 1. All energies (E) include zero-point energy (ZPE) corrections. Vibration frequencies of reactants, intermediates and products are positive and vibration frequencies of all transition states have only one imaginary frequency. Fig. 4 is a schematic map of energy levels for the reaction. The reaction path Ra'→TS1'→……IM4' is without lithium ethoxide, and the reaction path Ra'→Rc'→……IM10' is with lithium ethoxide.

3.1. The reaction mechanism and energies analysis of the reaction without catalyst

The reaction between 3-hydroxy-3-methyl-2-butanone and malononitrile for the synthesis of P1 is a nucleophilic reaction. In basic solution, the C1 atom of malononitrile with negative charge collides with the carbonyl carbon atom of 3-hydroxy-3-methyl- 2-butanone to form intermediate IM1 through transition state TS1. In TS1,

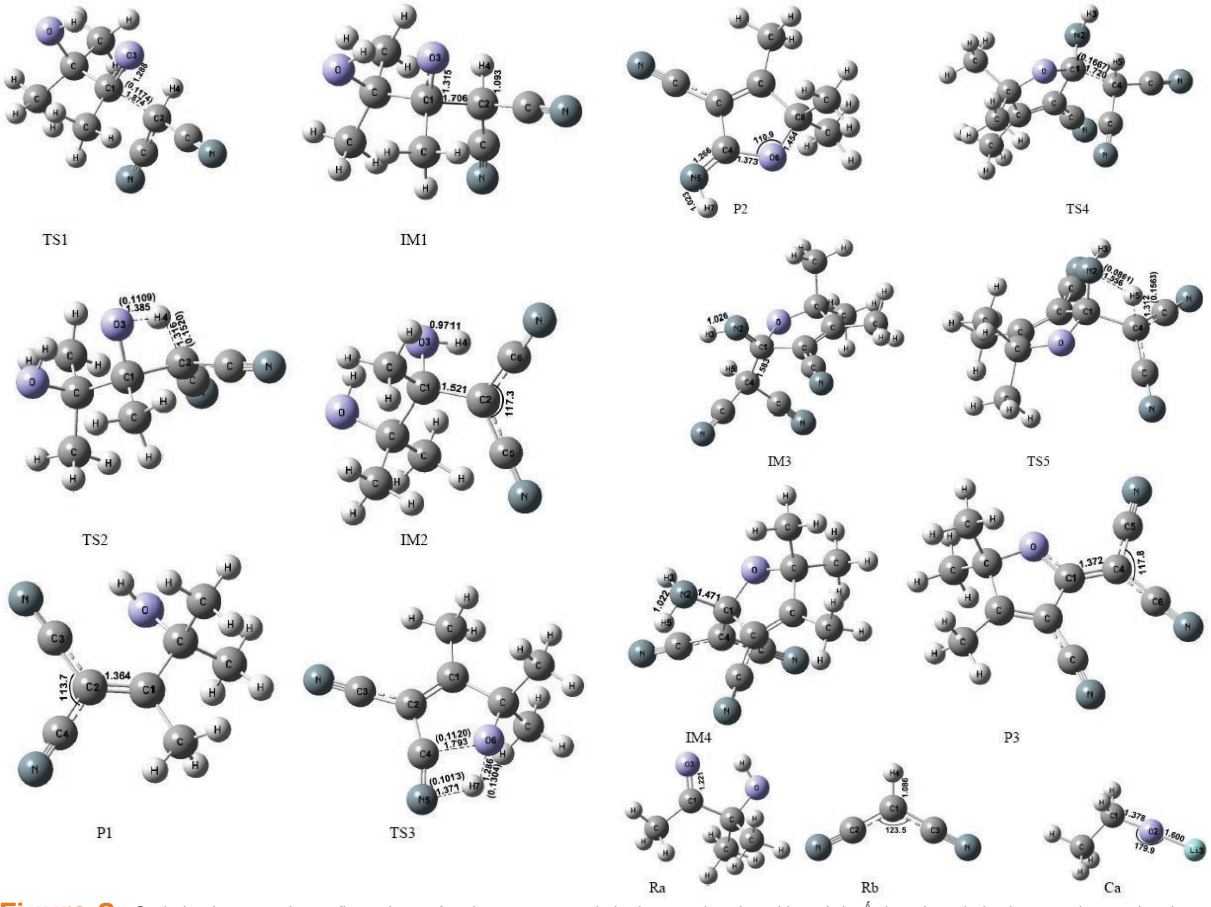

Figure 2. Optimized geometric configurations of various compounds in the reaction: bond length in Å, bond angle in degree, charge density at bond-forming critical point in a.u.

the bond length and the charge density at the bond-forming critical point of C1–C2 are 1.874 Å and 0.1174 a.u. respectively, and the activation energy is 25.89 kJ·mol^{-1}. IM1 forms intermediate IM2 through transition state TS2. This is a hydrogen atom transfer process, which has an activation energy is 82.93 kJ·mol^{-1}. In TS2, the bond length and the charge density at the bond-forming critical point of C2–H4 are 1.306 Å and 0.1520 a.u. respectively, and those of O3-H4 are 1.385 Å and 0.1109 a.u. respectively. Intermediate IM2 decomposes into P1 and hydroxide ion.

P1 forms P2 through transition state TS3. This is a concerted reaction process with the closing of a ring and the transfer of a hydrogen atom. In TS3, the bond length and the charge density at the bond-forming critical points of O6-H7, N5-H7 , C4-O6 are 1.286 Å and 0.1304 a.u., 1.371 Å and 0.1013 a.u., and 1.793 Å and 0.1120 a.u. respectively. The activation energy is 213.29 kJ·mol^{-1}. It is a rate-determining step.

The reaction between P2 and malononitrile for the synthesis of 2-dicyanomethylene- 4,5,5-trimethyl-2,5-dihydrofuran-3-carbonitrile is also a nucleophilic reaction. First, malononitrile with a negative charge collides with a carbonyl carbon atom of P2 to form intermediate IM3 through transition state TS4. In TS4, the bond length and the charge density at the bond-forming critical point of C1–C4 are 1.720 Å and 0.1667 a.u. respectively, and the activation energy is 88.65 kJ·mol^{-1}. IM3 then forms intermediate IM4 through transition state TS5, This is a hydrogen atom transfer process, and the activation energy is 93.18 kJ·mol^{-1}. In TS5, the bond length and the charge density at the bond-forming critical point C4–H5 are 1.312 Å and 0.1563 a.u. respectively, and those of N2-H4 are 1.556 Å and 0.0861 a.u. respectively. Intermediate IM4 decomposes into the final product P3 and imide ion.

The mechanism of the reaction is: Ra+Rb → TS1 → IM1 → TS2 → IM2 → P1+OH^- → P1 → TS3 → P2 → P2+Rb → TS4 → IM3 → TS5 → IM4 → P3+NH_2^-. Here P1 → TS3 → P2 is a rate-determining step, and activation energy is 213.29 kJ mol^{-1}.

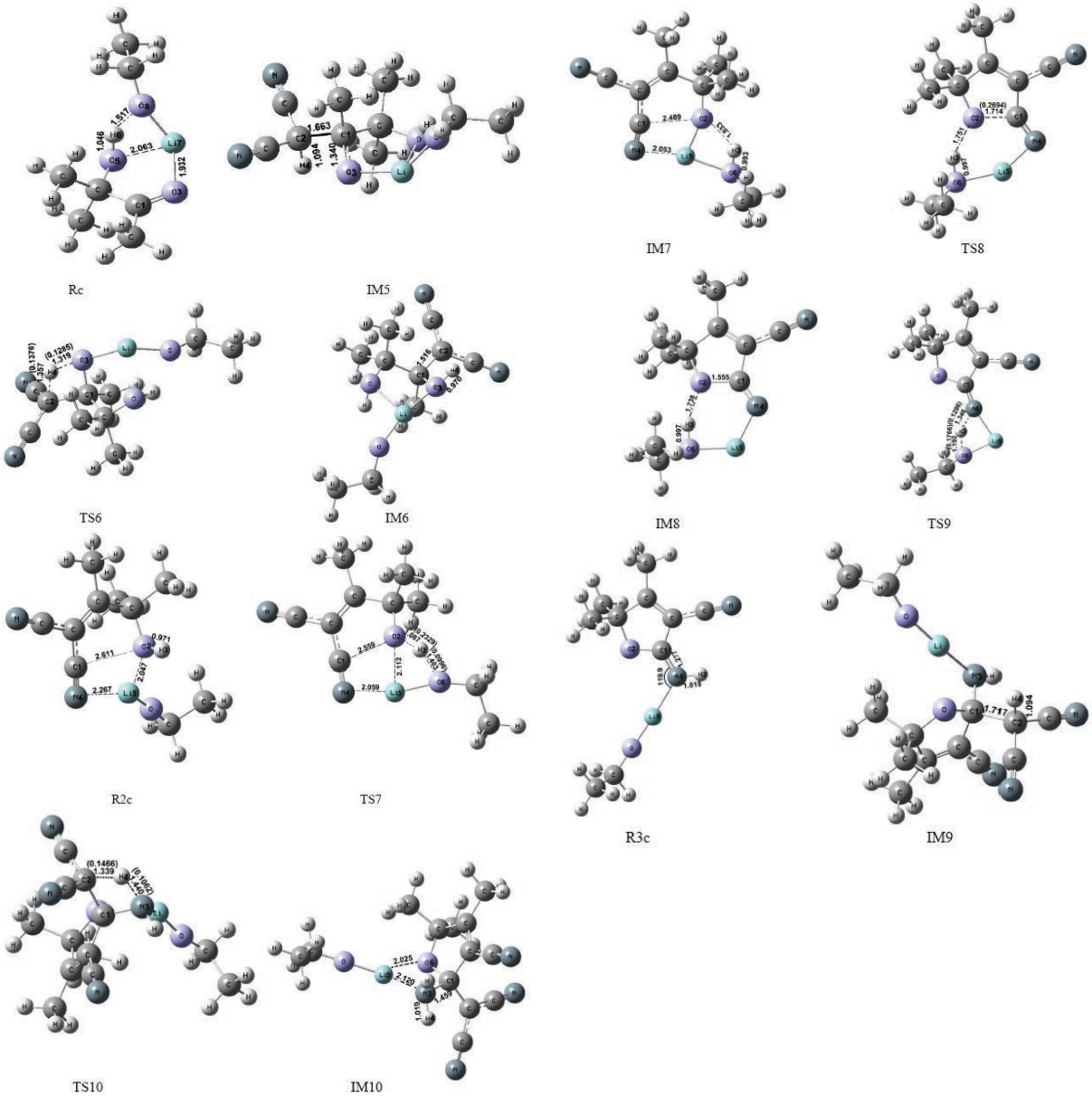

Figure 3. Optimized geometry configurations of various compounds in the reaction: bond length in Å, bond angle in degree, charge density at bond-forming critical point in a.u.

3.2. The mechanism and energies analysis of the reaction with lithium ethoxide

The mechanisms of the reaction between 3-hydroxy-3-methyl-2-butanone and malononitrile with catalyst lithium ethoxide for the synthesis of 2-dicyanomethylene- 4,5,5-trimethyl-2,5-dihydrofuran-3-carbonitrile are shown in Fig. 1.

In the first part, 3-hydroxy-3-methyl-2-butanone reacts with lithium ethoxide to form the complex Rc, and the system energy decreases by 147.63 kJ mol^{-1}. Rc is an h-bond complex with O8-H6 h-bond length 1.517 Å. Intermediate Rc reacts with Rb to forms IM5 directly without need of activation energy. The bond length of C1-C2 is 1.663 Å in IM5. IM5 then forms intermediate IM6 through transition state TS6 This is a hydrogen atom transfer process, and the activation energy is 97.43 kJ mol^{-1}. In TS6, the bond length and the charge density at the bond-forming critical point C2–H4 in TS6 are 1.357 Å and 0.1376 a.u. respectively, and those of O3-H4 are 1.319 Å and 0.1285 a.u. respectively. Intermediate IM6 decomposes into the intermediate R2c and hydroxide ion.

The second part is composed of a series of processes consisting of transferring hydrogen atoms and ring closings in the presence of lithium ethoxide catalyst. Firstly the hydrogen atom of hydroxyl in R2c

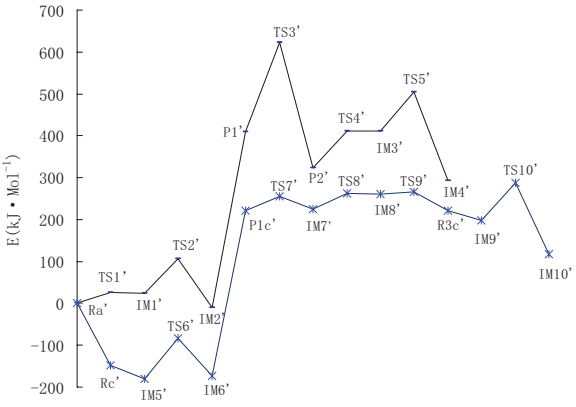

Figure 4. Schematic map of energy levels in the reaction.

is transferred and forms bonds with the oxygen atom of the lithium ethoxide catalyst through transition state TS7, forming Intermediate IM7. In TS7, the bond length and the charge density at the bond-forming critical point of O2–H3 are 1.087 Å and 0.2329 a.u., and those of O6-H3 are 1.403 Å and 0.0996 a.u. respectively. The activation energy is 34.18 kJ·mol^{-1}. IM7 then forms intermediate IM8 through transition state TS8, which is a ring closing process. In TS8, the bond length and the charge density at the bond-forming critical point of C1–O2 are 1.714 Å and 0.2694 a.u., and the activation energy is 37.25 kJ mol^{-1}. IM8 then forms intermediate R3c through transition state TS9, which is a hydrogen atom transfer process. In TS9, the bond length and the charge density at the bond-forming critical point of N4–H3 are 1.346 Å and 0.1296 a.u. respectively, and those of O6-H3 are 1.192 Å and 0.1766 a.u. respectively. The activation energy is 5.32 kJ mol^{-1}.

There are two reaction paths: P1' → TS3' → P2', and P1c' → TS7' → IM7' → TS8' → IM8' → TS9' → R3c' → P2c' → which are illustrated in Fig.4. In the latter path hydrogen atom transfer is easier than the uncatalyzed reaction, because the Li atom, O atom and N atom form coordinate bond in these intermediates. It has been shown that: (1) the activation energy of ring closure processes catalyzed by lithium ethoxide are greatly decreased compared toactivation energies of reactions withoutlithium ehtoxide catalysis.; (2) The mechanism of the reaction with lithium ethoxide catalysis differs from the mechanism in the absence of lithium ethoxide catalysis. The former reaction consists of a ring closure step; the latter reaction consists of three steps. (3)This is the position in which lithium ethoxide catalysis brings a special efficacy.

Intermediate P2c reacts with malononitrile to form IM9 directly. Intermediate IM9 then forms intermediate IM10 through transition state TS10, which is a process of hydrogen atom transfer. The bond length and the charge density at bond-forming critical point C2–H4 in TS10 are 1.339 Å and 0.1466 a.u. respectively, and those of N3-H4 are 1.440 Å and 0.1062 a.u. The activation energy is 89.76 kJ mol^{-1}. Intermediate IM10 decomposes into the final product P3, imide ion and lithium ethoxide catalyst.

Table 1. Energies(E) and relative energies(Erel) of various species and imaginary frequency of transitions.

Species	-E (a.u.)	E_{rel} (kJ·mol^{-1})	v/cm^{-1}	Species	-E(a.u.)	E_{rel} (kJ·mol^{-1})	v/cm^{-1}
Ra'(Ra+2Rb)	795.633899	0		Ra'(Ra+Ca+2Rb)	957.560694	0.00	
TS1'(TS1+Rb)	795.624039	25.89	166i	Rc'(Rc+2Rb)	957.616925	-147.63	
IM1'(IM1+Rb)	795.624802	23.88		IM5'(IM5+Rb)	957.629304	-180.14	
Ts2'(TS2+Rb)	795.593217	106.81	1571.8i	TS6'(TS6+Rb)	957.592196	-82.71	1613.2i
IM2'(IM2+Rb)	795.637630	-9.8		M6'(IM6+Rb)	957.626371	-172.43	
P1'(P1+Rb+ OH$^-$)	795.477700	410.1		P1c'(P1c+ OH$^-$+Rb)	957.476412	221.28	
TS3'(TS3+Rb+ OH$^-$)	795.396461	623.39	2098.6i	R2 c'(R2 c+ OH$^-$+Rb)	957.476412	221.28	
P2'(P2+Rb+ OH$^-$)	795.510856	323.05		TS7'(TS7+ OH$^-$+Rb)	957.463394	255.46	13.3i
TS4'(TS4+ OH$^-$)	795.477101	411.67	184.8i	IM7'(IM7+ OH$^-$+Rb)	957.474767	225.60	
IM3'(IM3+ OH$^-$)	795.477495	410.64		TS8'(TS7+ OH$^-$+Rb)	957.460581	262.85	156.7i
TS5'(TS5+ OH$^-$)	795.442003	503.82	1531.1i	IM8'(IM8+ OH$^-$+Rb)	957.461580	260.22	
IM4'(IM4+ OH$^-$)	795.522178	293.32		TS9'(TS8+ OH$^-$+Rb)	957.459557	265.54	1050.2i
				P2c'(P2c+ OH$^-$+Rb)	957.476412	221.28	
				R3c'(P2c+ OH$^-$+Rb)	957.476412	221.28	
				IM9'(IM9+ OH$^-$)	957.485182	198.26	
				TS10'(TS9+ OH$^-$)	957.450993	288.02	1615.8i
				IM10'(IM10+ OH$^-$)	957.515667	118.22	

The reaction of IM5 → TS6 → IM6 is a rate-determining step, and its activation energy is 97.43 kJ mol^{-1}. The activation energy of its reaction with lithium ethoxide decreased by 115.86 kJ mol^{-1} compared with that of its reaction without lithium ethoxide. As above, the rate-determining step of its reaction with lithium ethoxide is changed compared with that of its reaction without lithium ethoxide.

4. Conclusions

The mechanism of reaction between 3-hydroxy-3-methyl-2-butanone and malononitrile in the synthesis of 2-dicyanomethylene-4,5,5-trimethyl-2,5-dihydrofuran-3-carbonitrile catalyzed by lithium ethoxide in the absence of lithium was investigated by density functional theory (DFT). The activation energy with lithium ethoxide decreased by 115.86 kJ mol^{-1} compared with that of the reaction without it. The mechanism of reaction using lithium ethoxide catalyst differs from its mechanism without it. Lithium ethoxide is an effective catalyst in the synthesis of 2-dicyanomethylene- 4,5,5-trimethyls the same -2,5-dihydrofuran-3-carbonitrile from malononitrile and 3-hydroxy- 3-methyl-2-butanone. It is identical with Tao et al.'s conclusions [9], and the mechanism of the reaction according to Knoevenagel [13-18].

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