

# Thermodynamic Study of Polyhydroquinoline Synthesis in the Presence of the Catalyst in Ionic Liquid

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**ABSTRACT :** Polyhydroquinolines and its derivatives are an important group of organic Heterocyclic compounds. Due to their applications in pharmaceutical and chemical industries, study of new methods of synthesis is considerably substantial. One of such synthesis methods is the Hantzsch reaction in which numerous factors are used to increase the reaction efficiency. The most critical component includes heterogeneous and reusable catalyst. Therefore, in order to have higher efficiency in shorter time for polyhydroquinolines synthesis using the heterogeneous and reusable catalysts inside ionic liquids, we performed a study on function of different ionic liquids. The test uses B3LYP/6-31g optimization method for polyhydroquinolines synthesis with aromatic aldehyde, dimedone, ethyl acetate and ammonium acetate in the presence of catalyst.

**KEYWORDS:** ionic liquids, DFT, hydroquinoline, Hantzsch reaction

## I. INTRODUCTION

Cyclic organic compounds consist of two categories of carboxyl and heterocycle. The carboxylic circles contain only carbon atoms, but the heterocycle circles have one or more atoms in addition to carbon. Nitrogen (N), Oxygen (O) and Sulfur (S) are some of the most conventional atoms. Contrarily, certain heterocycles may have heteroatoms like P, Si, etc [1,2]. Approximately half of organic compounds comprise at least one heterocycle component. Also, most of the heterocycle compounds are biosynthesized by animals and plants, which are biologically dynamic. Conjugated bases found in DNA and RNA (uracil, guanine, thymine, adenine, cytosine) and most of physiologically active compositions depend upon existence of heteroatoms are typically in form of heterocycles [2,3,4]. Quinoline and isoquinoline are two isomer systems exist as a structure of pyridine compound in its C2 and C3 positions there is a Benzene ring [1]. Quinolines and polyhydroquinolines consist of aromatic double-ringed heterocycle compounds including nitrogen, which have a wide range of biological and pharmaceutical applications [5]. For the first time, Arthur Hantzsch in 1882 synthesized 4,1 symmetrical substituted dihydropyridine by a one-pot reaction of four component condensation of two molecules of ethyl acetoacetate, aromatic aldehyde and ammonia. This technique incorporates the reaction in acetic acid or an ethanolic solvent under the reflux conditions. By far, there are some drawbacks such as longer reaction time, harsh reaction conditions, using volatile organic solvents and generally lower efficiency [4]. Zolfigol et al [4] and Wang [4] used ammonium acetate instead of ammonia in the reaction, which generated a high-efficiency reaction. Using cyclic compounds 1,3 D-ketone in the Hantzsch reaction is another strategy for improvement of the method. In this regard, the investigators used new catalysts for polyhydroquinolines derivatives synthesis [4]. Also, Mobinikhaledi et al [15] and ShengkaiKo [16] applied ionic liquids, microwave irradiation, polymers, heteropolyacid and ceric ammonium nitrate. Khabazzadeh et al (2010) introduced a process for synthesizing polyhydroquinolines derivatives with a four component Hantzsch reaction, aromatic aldehyde, dimedone, ethyl acetoacetate and ammonium acetate in molten salt media as an alternative to hazardous organic solvents using  $\text{Cs}_{2.5}\text{H}_{0.5}\text{PW}_{12}\text{O}_{40}$  as a heterogeneous and reusable catalyst [13].

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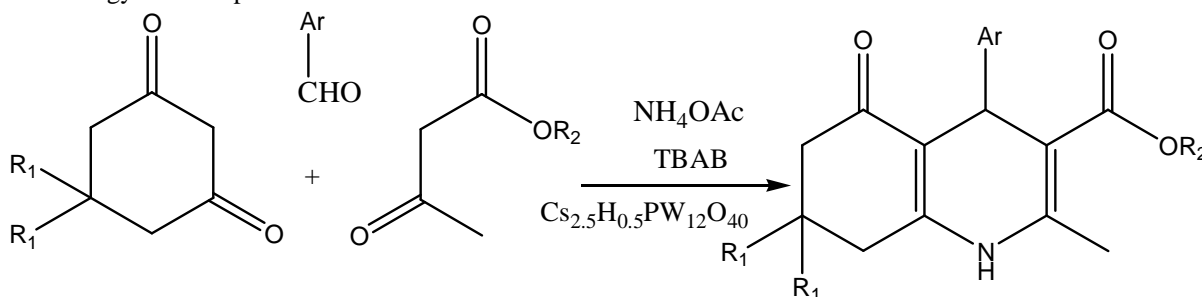
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Nagarapu et al (2007) provided a new process for synthesizing polyhydroquinolines derivatives with a four component reaction of aromaticaldehyde, dimedone, ethylacetoacetate and ammoniumacetate in solvent-free conditions adopting MCM-41 as a heterogeneous catalyst [14]. Mobinikhaledi and colleagues (2009) illustrated that four component Hantzsch reaction can synthesize polyhydroquinolines and its derivatives employing silicasulfuric acid as a heterogeneous and reusable catalyst under thermal control with microwave irradiation [15]. ShengkaiKo et al (2005) reported 1,4-dihydropyridine derivatives synthesis in room temperature via iodine as catalyst [15]. MatloubiMoghaddam and colleagues (2008) presented a process for polyhydroquinolines derivatives and 1,4-dihydropyridine through a four component reaction of aldehydes, ammonium, ethyl acetoacetate, 5,5 dimethyl and 1,3-cyclohexadiene in the presence of ZnO catalyst [17]. Heravi et al (2006) synthesized polyhydroquinolines derivatives via a three component Hantzsch reaction in the presence of some green and cheap catalyst  $K_7PW_{11}CoO_4$  [18].

In 2009, Foroughifar and his colleagues showed that the four component Hantzsch reaction in the solvent-free conditions can be done with sulfamic acid and synthesizes polyhydroquinolines and its derivatives [4]. Rajendran et al (2011) indicated that four component condensation of divergent aromaticaldehydes, cyclic compounds of 1,3-diketone,  $\beta$ -keto ester, ammoniumacetate and catalytic amount from an ionic liquid Tetrabutylammonium, 2-acrylamide, 2-methyl-propane sulfonate (TBA-AMPS) yields polyhydroquinolines derivatives [4]. However, Redi (2008) developed a more simplified and effective technique for polyhydroquinolines synthesis through the four component reaction of aldehydes, dimedone, ethyl acetoacetate and ammoniumacetate in the presence of *p*-Toluenesulfonic acid in ethanolic solvent in room temperature [4]. MahboubBasha and colleagues (2012) synthesized 1,4-dihydropyridines and polyhydroquinolines derivatives through the Hantzsch reaction and using the PEG reagent in solvent-free conditions. The products were directly crystallized with hot methanol. The reaction efficiency with low polyethylene glycol molecular weight was as appropriate as high polyethylene glycol molecular weight [19]. Since Khabazzadeh et al's [13] study was about polyhydroquinolines synthesis via heterogeneous and reusable catalyst  $Cs_{2.5}H_{0.5}PW_{12}O_{40}$  showed high efficiency in short time, so the present paper aims to investigate the theory of the effect of different ionic liquids as solvent molten media by density functional theory method to do polyhydroquinolines synthesis by dimedone, cyclohexa 1,3, aldehyde aryl,  $\beta$ -keto ester, ammoniumacetate solvent of  $Cs_{2.5}H_{0.5}PW_{12}O_{40}$  catalyst.

## II. PROCEDURE

First, the researchers optimized entire existing compounds in mechanism of the present reaction including dimedone, 1,3-cyclohexadiene, different substitution donate and demand, ethyl acetoacetate, ammonium acetoacetate and catalyst totally consist of 180 compounds by the Gaussian03 software and through B3LYP/6-31G method. Finally, their sustainable energy was computed.



$R_1 = H$  Or  $CH_3$

$R_2 = Et$  or  $Me$

## FINDINGS

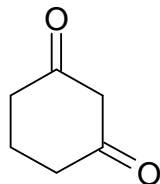
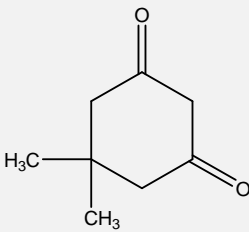
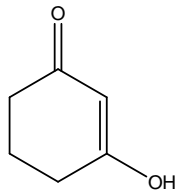
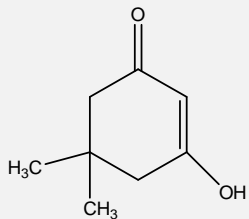
Data for optimization of all entered molecules into the reaction and the sustainable energy are in Table 1 below.

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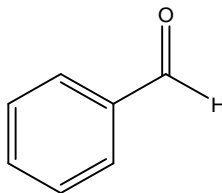
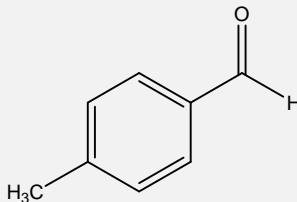
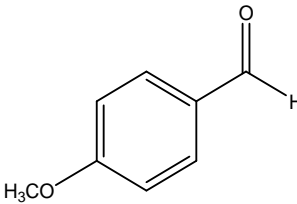
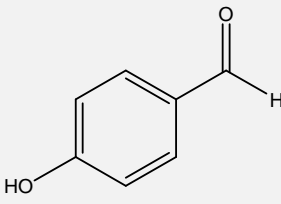
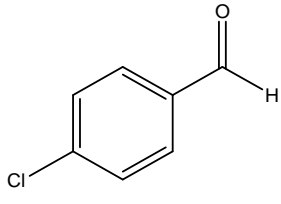
Table 1: optimized structure energy using B3LYP/6-31G method

role	Energy (joule)	compound
Raw material	-1007628.186	
Raw material	-1214019.14	
Raw material(Enol form)	-1007619.274	
Raw material(Enol form)	-1214007.656	

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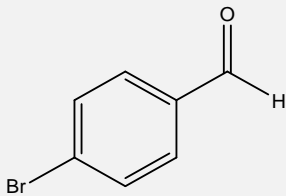
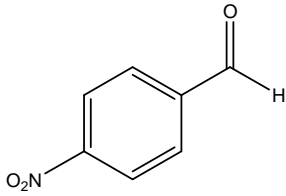
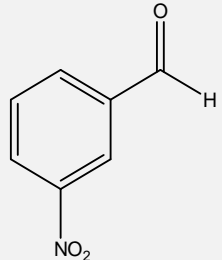
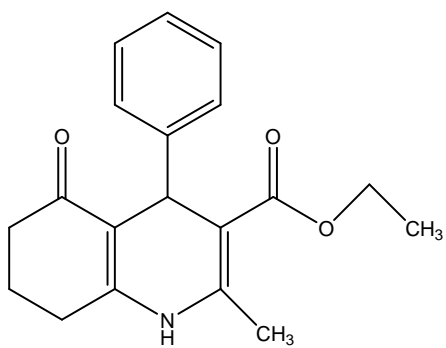
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Raw material	-907070.0897	 <chem>O=Cc1ccccc1</chem>
Raw material	-1010276.803	 <chem>CC1=CC=C(C=O)C=C1</chem>
Raw material	-1207652.637	 <chem>COc1ccc(C=O)cc1</chem>
Raw material	-1206880.299	 <chem>Oc1ccc(C=O)cc1</chem>
Raw material	-2113682.356	 <chem>Clc1ccc(C=O)cc1</chem>

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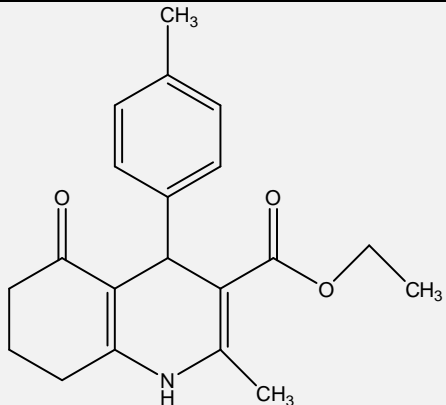
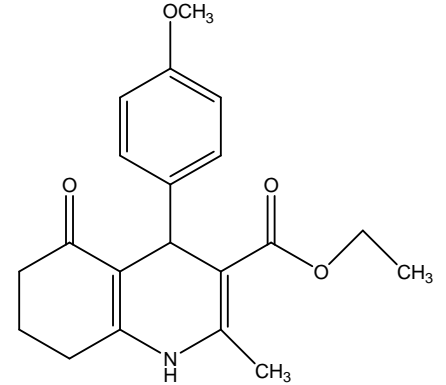
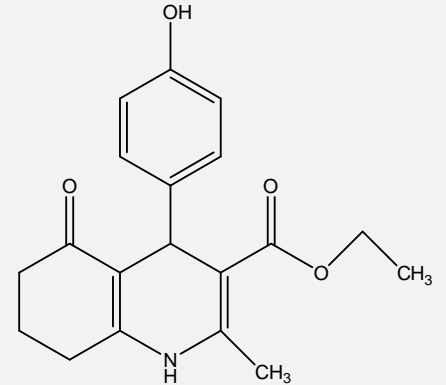
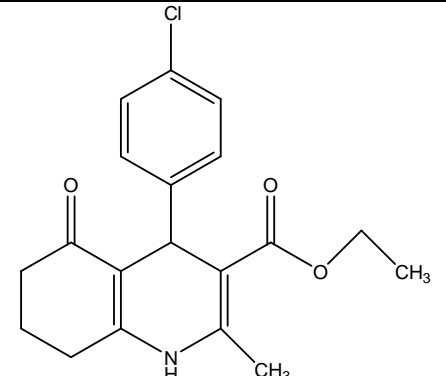
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Raw material	-7657153.986	
Raw material	-1443762.091	
Raw material	-1443764.624	
final product	-2669701.186	

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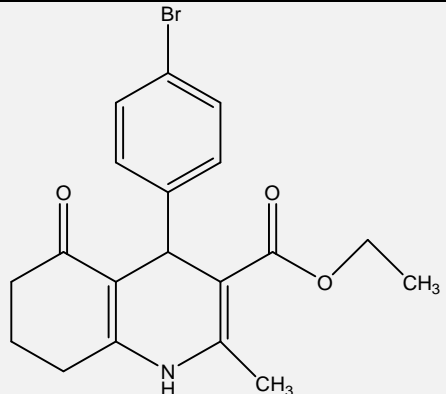
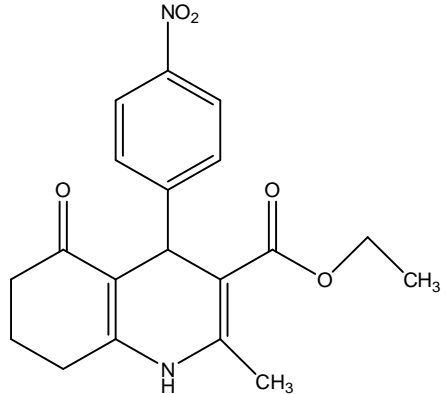
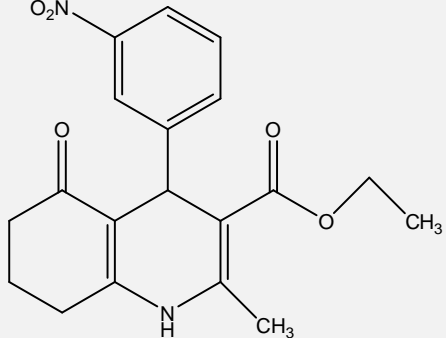
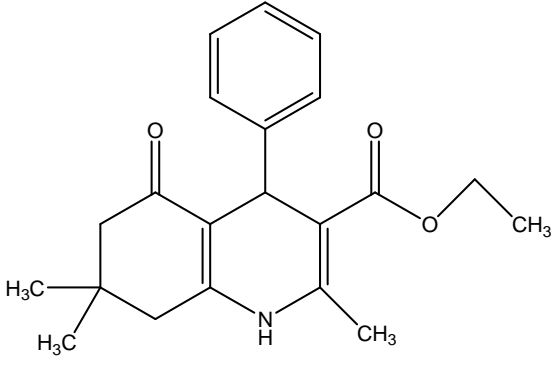
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<p>final product</p>	<p>-2772904.719</p>	
<p>final product</p>	<p>-2970277.736</p>	
<p>final product</p>	<p>-2867112.581</p>	
<p>final product</p>	<p>-3876321.085</p>	

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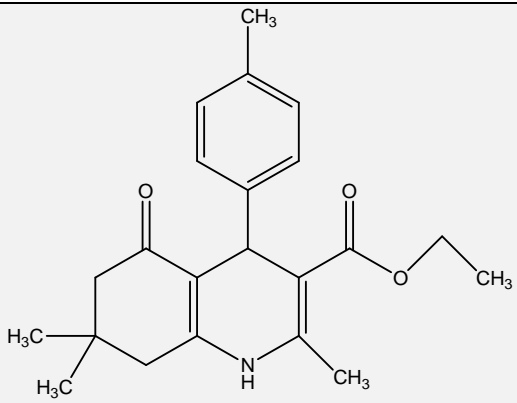
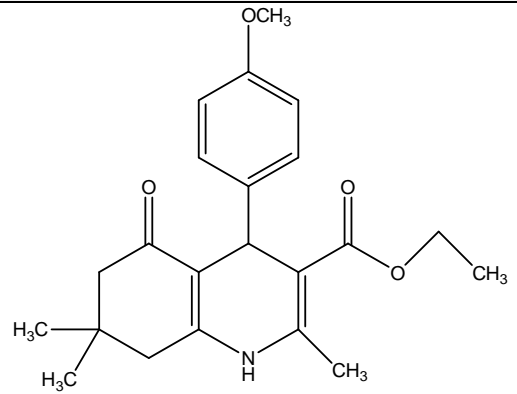
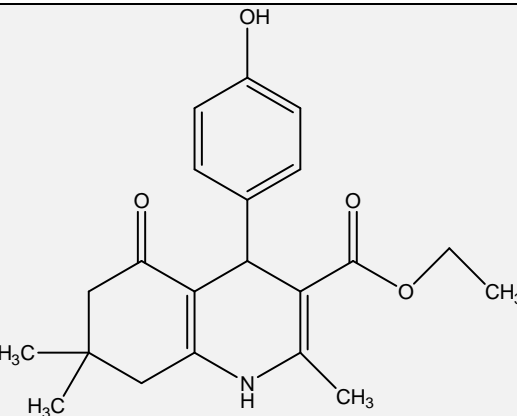
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final product	-9419791.665	
final product	-3206414.590	
final product	-3206418.450	
final product	-2876090.556	

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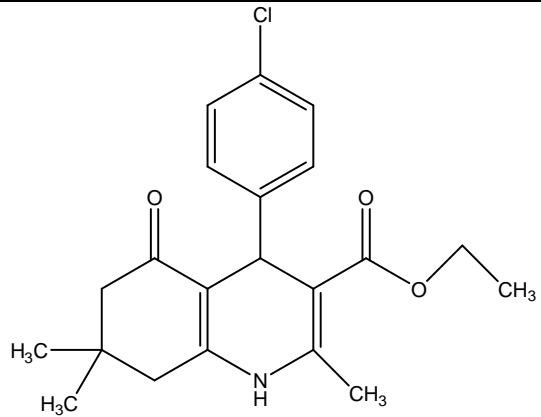
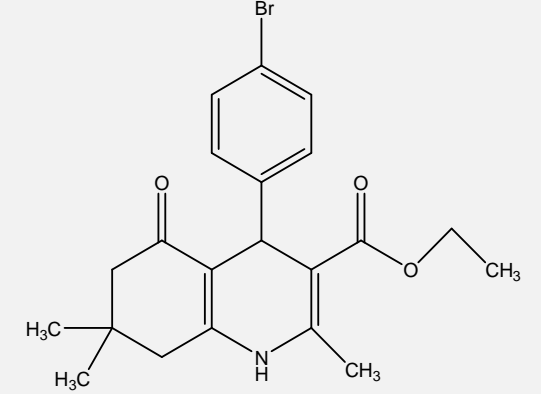
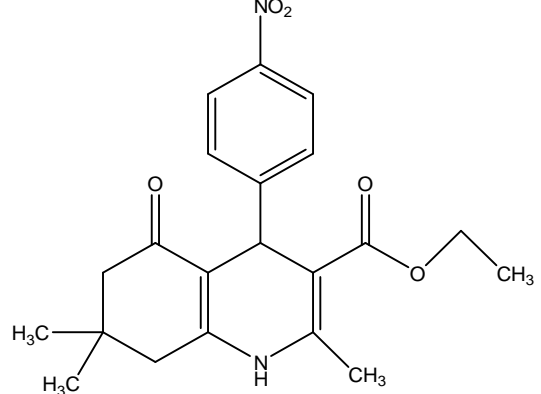
final product	-2979294.036	
final product	-3176667.027	
final product	-3073501.758	



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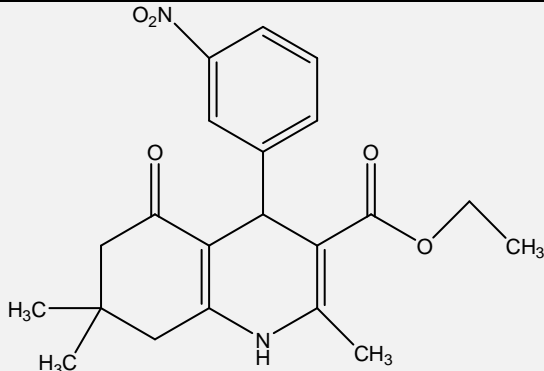
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final product	-4082710.087	
final product	-9626181.058	
final product	-3412803.910	

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final product	-3412798.580	
Ionic liquid	-1835754.929	Tetra-butylammonium bromide
catalyst		$\text{H}^{\oplus}$
catalyst	-749759.2211	$\text{NH}_4\text{OAc}$

### III. REACTION MECHANISM

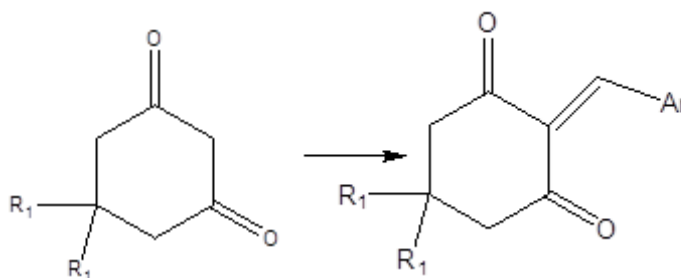
Considering the mechanism and the results of the relationship  $\Delta E = \sum E_{\text{products}} - \sum E_{\text{raw material}}$ , in detailed steps of the reaction listed below, most of the steps particularly the first stage and disclosure of Pyridine circle there exists a positive energy difference. If  $\Delta E$  is positive the reaction does not proceed spontaneously.

Reaction stage #1

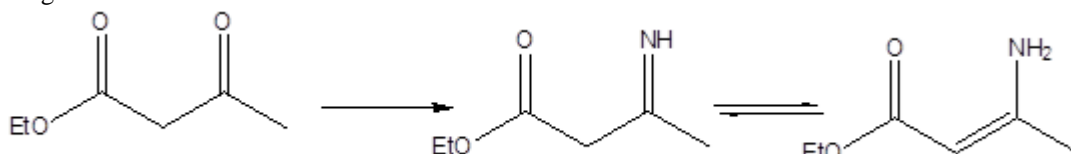
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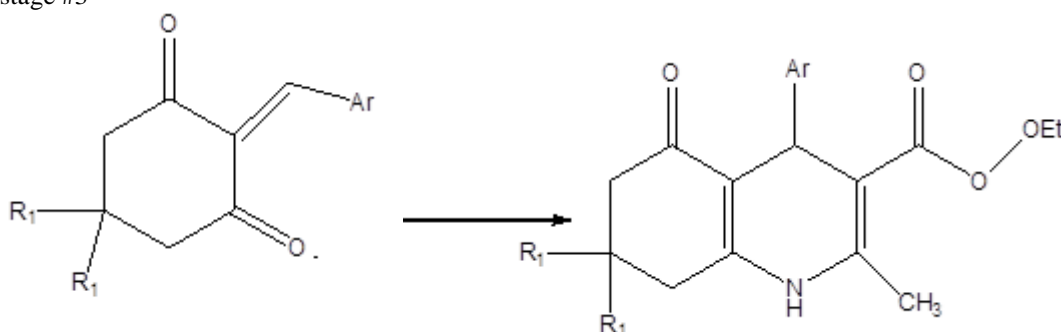
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Reaction stage #2

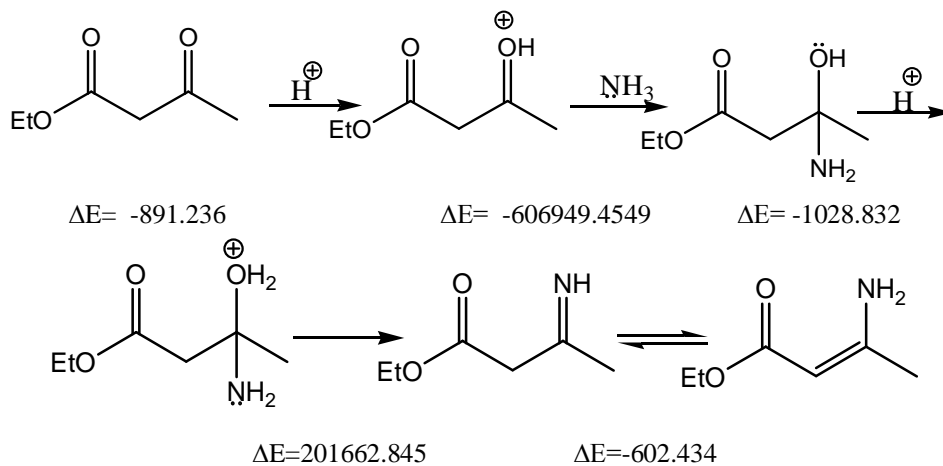


Reaction stage #3



## Energy difference of different stages of reaction

The steps below are similar for all reactions:

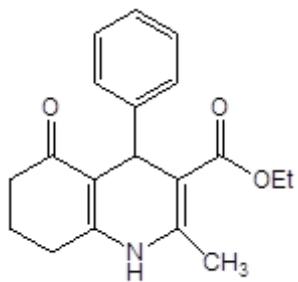
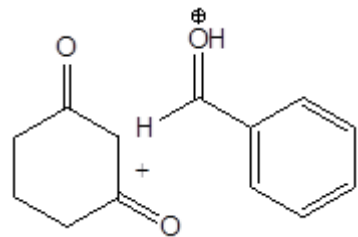


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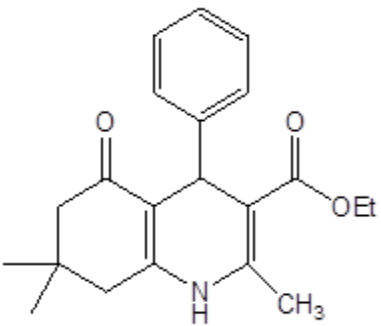
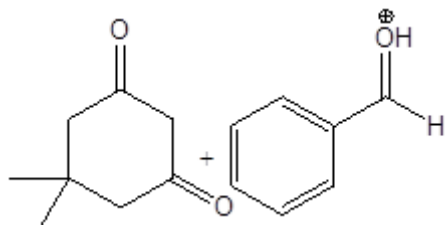
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Calculated energy for polyhydroquinolines synthesis with raw materials cyclohexa-1,-3,benzaldehydo ethyl,-3oxobutanoate

Energy per stage	Final product	Raw material
$\Delta E=21.8103$ $\Delta E=12.8983$ $\Delta E= -954.321$ $\Delta E= -201590.683$ $\Delta E= -983.089$ $\Delta E=1513.488$ $\Delta E= -53.489$ $\Delta E= -953.364$ $\Delta E= 936.836$ $\Delta E= 670.76$		

Calculated energy for polyhydroquinolines synthesis with raw materials dimedone, benzaldehydo ethyl,-3 oxobutanoate

Energy per stage	Final product	Raw material
$\Delta E= 22.214$ $\Delta E= 10.73$ $\Delta E= -950.911$ $\Delta E=201514.24$ $\Delta E= -914.44$ $\Delta E= 206332.691$ $\Delta E=-1043.069$ $\Delta E=1017.403$ $\Delta E=647.144$ $\Delta E= 199913.2$		

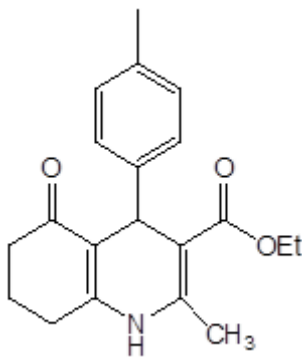
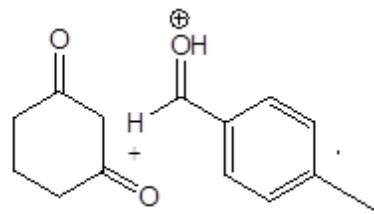
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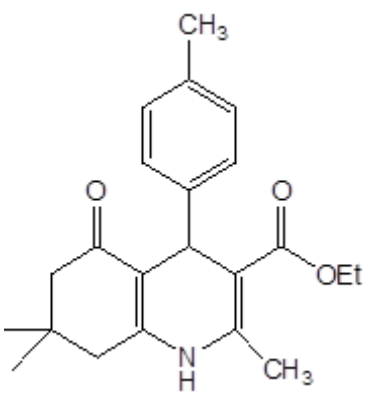
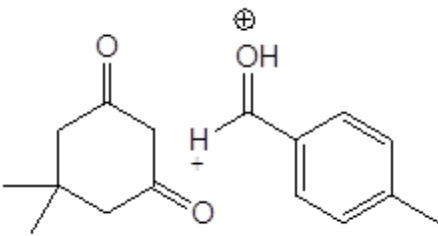
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Considering the energy differences in the first part of reaction, benzaldehyd, cyclohexa -1,-3 and dimedone do not react spontaneously in the present of acid catalyst. Moreover, comparing the energy difference suggests that benzaldehyd reaction with enol forms cyclohexa -1,-3 and dimedone was more negative and consequently the reaction is more spontaneous. In the next steps, the energy differences considerably vary in benzaldehydreaction with cyclohexa -1,-3 and with dimedon reaction. However, the energy difference in other stages of benzaldehyd reaction with cyclohexa -1,-3 is more negative. Although, the disclosure process of pyridine circle and the final reaction stage do not proceed spontaneously, it is more negative compared with dimedon reaction and so, it happens more spontaneously.

Calculated energy for polyhydroquinolines synthesis with raw materials cyclohexa -1,-3,4 methyl benzaldehydoethyl , -3 oxobutanoate

Energy per stage	Final product	Raw material
$\Delta E=2840.404$ $\Delta E= 2831.492$ $\Delta E= -2888.522$ $\Delta E= -201519.199$ $\Delta E=-3.000$ $\Delta E= 614.566$ $\Delta E= -53.366$ $\Delta E=-961.038$ $\Delta E= 941.286$ $\Delta E=663.671$ $\Delta E= 199904.653$		

Calculated energy for polyhydroquinolines synthesis with raw materials dimedone, -4 methyl benzaldehydoethyl,-3 oxobutanoate

Energy per stage	Final product	Raw material
$\Delta E=906.464$ $\Delta E=894.98$ $\Delta E= -1461.535$ $\Delta E= 202027.148$ $\Delta E= -927.779$ $\Delta E= 1537.9$ $\Delta E= 206338.057$ $\Delta E= -1040.265$ $\Delta E= 1021.096$ $\Delta E= 640.64$ $\Delta E= 199920.033$		

As results illustrate, 4- methyl benzaldehyd withcyclohexa -1,-3 and dimedone do not react spontaneously in the present of acid catalyst. in addition, comparing the energy difference indicates that4- methyl benzaldehyd reaction with

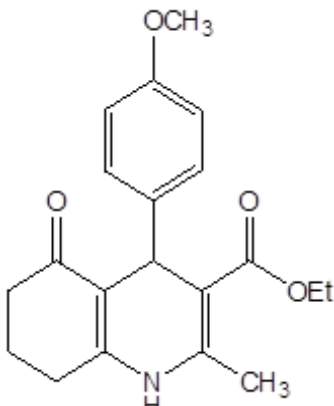
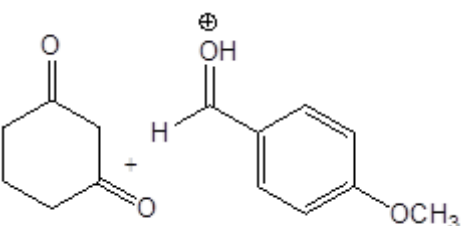
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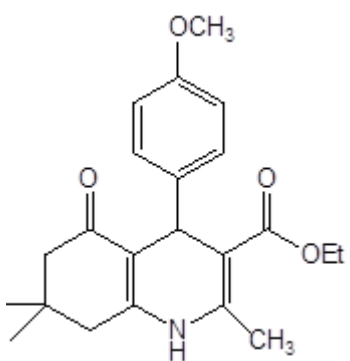
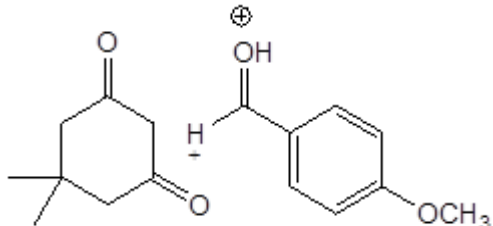
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Calculated energy for polyhydroquinolines synthesis with raw materials cyclohexa -1,-3, Methoxybenzaldehyde-4 and ethyl -3 oxobutanoate raw materials

Energy per stage	Final product	Raw material
$\Delta E=937.211$ $\Delta E= 928.299$ $\Delta E= -10085.532$ $\Delta E = -187765.821$ $\Delta E=2226.023$ $\Delta E=1091.291$ $\Delta E= -51.121$ $\Delta E= -963.676$ $\Delta E= 941.124$ $\Delta E= 658.055$ $\Delta E= 199909.796$		

Calculated energy for polyhydroquinolines synthesis with raw materials dimedon,  
Methoxybenzaldehyde-4 and ethyl -3 oxobutanoate

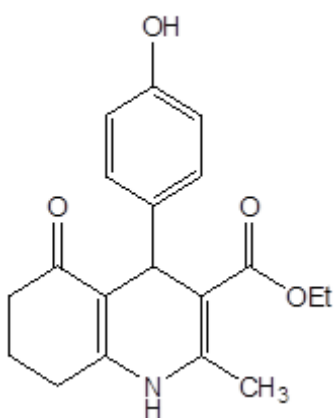
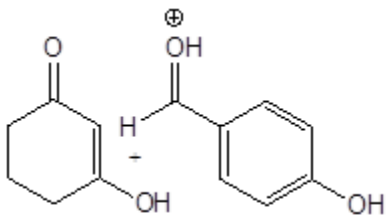
Energy per stage	Final product	Raw material
$\Delta E=931.848$ $\Delta E= 920.364$ $\Delta E= -956.483$ $\Delta E= 201516.132$ $\Delta E= -1445.244$ $\Delta E= 2026.463$ $\Delta E= 206375.995$ $\Delta E= -1050.14$ $\Delta E= 1021.903$ $\Delta E= 634.898$ $\Delta E= 199924.73$		

According to results, 4- methoxybenzaldehydewith cyclohexa -1,-3 and dimedone do not react spontaneously in the present of acid catalyst. additionally, comparing the energy difference indicates that4- methoxybenzaldehydereaction with enol forms cyclohexa -1,-3 and dimedone was more negative and consequently the reaction is more spontaneous. In the next steps , the energy differences considerably vary in 4-methoxybenzaldehyde reaction with cyclohexa -1,-3 and with dimedon reaction. However, the energy difference in other stages of 4- methoxybenzaldehydereaction with cyclohexa -1,-3 is more negative. Although, the disclosure process of pyridine circle and the final reaction stage do not proceed spontaneously, it is more negative compared with dimedon reaction and so, it takes place more spontaneously. Calculated energy for polyhydroquinolines synthesis with raw materials cyclohexa -1,-3,hydroxyl ethylbenzaldehyde-4, -3 oxobutanoate

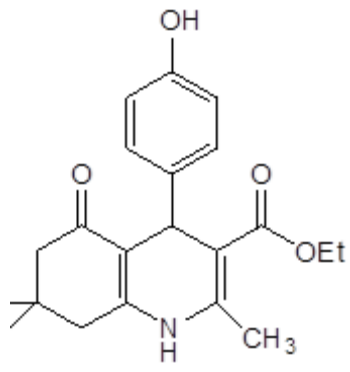
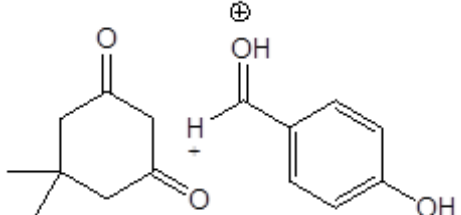
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Energy per stage	Final product	Raw material
$\Delta E=3552.055$ $\Delta E= 3543.143$ $\Delta E= -3585.071$ $\Delta E= -201511.326$ $\Delta E=750.242$ $\Delta E=1910660.076$ $\Delta E= 103139.197$ $\Delta E= -104200.715$ $\Delta E= 937.248$ $\Delta E= 663.485$ $\Delta E= 199903.951$		

Calculated energy for polyhydroquinolines synthesis with raw materials dimedon, hydroxyl ethylbenzaldehyde-4, -3 oxobutanoate

Energy per stage	Final product	Raw material
$\Delta E= 923.282$ $\Delta E= 911.798$ $\Delta E= -952.905$ $\Delta E=201508.609$ $\Delta E=-934.801$ $\Delta E= 491.018$ $\Delta E=310589.297$ $\Delta E= -1028.306$ $\Delta E= 1016.512$ $\Delta E= 640.494$ $\Delta E= 199919.093$		

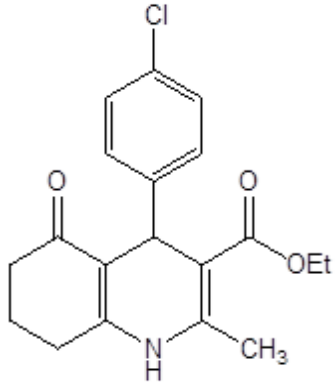
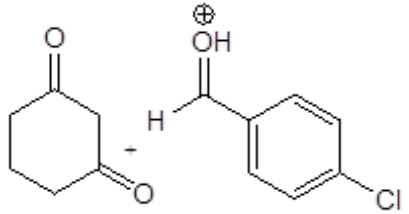
Illustrated in the table above, hydroxyl ethylbenzaldehyde-4 does not react spontaneously with cyclohexa -1,-3 and dimedone in the present of acid catalyst. moreover, comparing the energy difference indicates that hydroxyl ethylbenzaldehyde-4 reaction with enol forms cyclohexa -1,-3 and dimedone was more negative and consequently the reaction is more spontaneous. In the next steps , the energy differences considerably vary in hydroxyl ethylbenzaldehyde-4 reaction with cyclohexa -1,-3 and with dimedon reaction. By far, the energy difference in other stages of hydroxyl ethylbenzaldehyde-4 reaction with cyclohexa -1,-3 is more negative. Although, the disclosure process of pyridine circle and the final reaction stage do not proceed spontaneously , it is more negative compared with dimedon reaction and so, the reaction happens more spontaneously.

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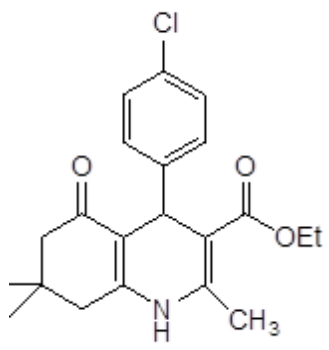
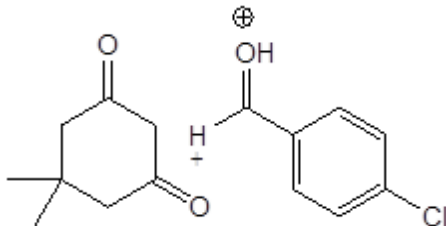
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Calculated energy for polyhydroquinolines synthesis with raw materials cyclohexa -1,-3, chlorobenzaldehyde-4, 3-oxobutanoate

Energy per stage	Final product	Raw material
$\Delta E = 875.35$ $\Delta E = 866.438$ $\Delta E = -895.623$ $\Delta E = -201502.471$ $\Delta E = -941.249$ $\Delta E = -57.375$ $\Delta E = 1500.381$ $\Delta E = -940$ $\Delta E = 922.149$ $\Delta E = 686.401$ $\Delta E = 199881.157$		

Calculated energy for polyhydroquinolines synthesis with raw materials dimedon, chlorobenzaldehyde-4, 3-oxobutanoate

Energy per stage	Final product	Raw material
$\Delta E = 875.543$ $\Delta E = 864.059$ $\Delta E = -938.025$ $\Delta E = 201499.904$ $\Delta E = -900.332$ $\Delta E = 1505.491$ $\Delta E = 206332.328$ $\Delta E = -1017.83$ $\Delta E = 1000.861$ $\Delta E = 662.997$ $\Delta E = 199896.729$		

As the results show, chlorobenzaldehyde-4 does not react spontaneously with cyclohexa -1,-3 and dimedone in the presence of acid catalyst. Furthermore, comparing the energy difference indicates that chlorobenzaldehyde-4 reaction with enol forms cyclohexa -1,-3 and dimedone was more negative and consequently the reaction is more spontaneous. In the next steps, the energy differences considerably vary in chlorobenzaldehyde-4 reaction with cyclohexa -1,-3 and with dimedone reaction. Contrarily, the energy difference in other stages of chlorobenzaldehyde-4 reaction with cyclohexa -1,-3 is more negative. Although, the disclosure process of pyridine circle and the final reaction stage do not proceed spontaneously, it is more negative compared with dimedone reaction and so, the reaction happens more spontaneously.

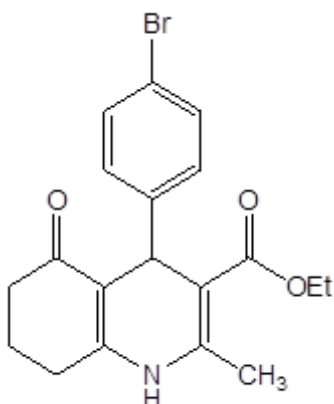
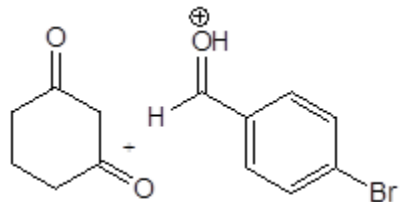


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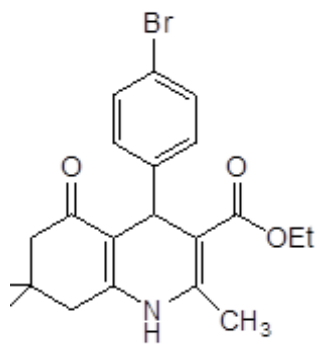
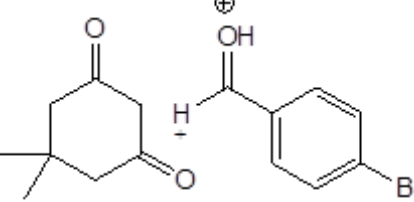
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Calculated energy for polyhydroquinolines synthesis with raw materials cyclohexa -1,-3,bromobenzaldehyde-4, 3-oxobutanoate

Energy per stage	Final product	Raw material
$\Delta E = 882.521$ $\Delta E = 874.609$ $\Delta E = -944.075$ $\Delta E = -1487719.873$ $\Delta E = -128711.68$ $\Delta E = -57.254$ $\Delta E = 8466623.931$ $\Delta E = -942.461$ $\Delta E = 924.618$ $\Delta E = 683.249$ $\Delta E = 1998884.363$		

Calculated energy for polyhydroquinolines synthesis with raw materials dimedon, bromobenzaldehyde-4, 3-oxobutanoate

Energy per stage	Final product	Raw material
$\Delta E = 883.724$ $\Delta E = 872.24$ $\Delta E = -906.089$ $\Delta E = 201502.181$ $\Delta E = -940.685$ $\Delta E = 1512.212$ $\Delta E = 206332.42$ $\Delta E = 1003.827$ $\Delta E = -1020.122$ $\Delta E = 659.787$ $\Delta E = 199899.483$		

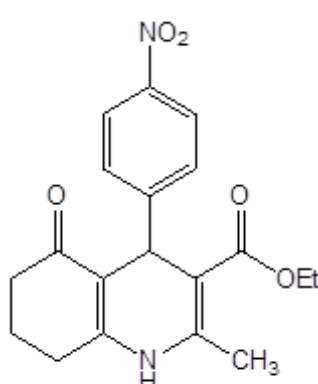
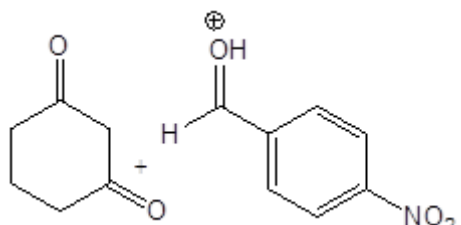
According to the results, bromobenzaldehyde-4 does not react spontaneously with cyclohexa -1,-3 and dimedone in the presence of acid catalyst. In addition, comparing the energy difference indicates that bromobenzaldehyde-4 reaction with enol forms cyclohexa -1,-3 and dimedone was more negative and consequently the reaction is more spontaneous. In the next steps, the energy differences considerably vary in bromobenzaldehyde-4 reaction with cyclohexa -1,-3 and with dimedone reaction. By far, the energy difference in other stages of bromobenzaldehyde-4 reaction with cyclohexa -1,-3 is more negative. Although, the disclosure process of pyridine circle and the final reaction stage do not proceed spontaneously, it is more negative compared with dimedone reaction and so, the reaction happens more spontaneously.

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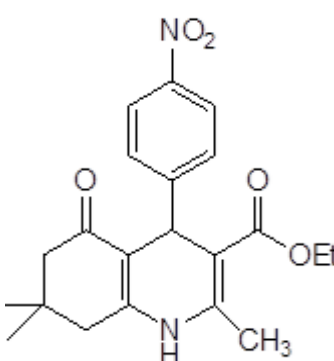
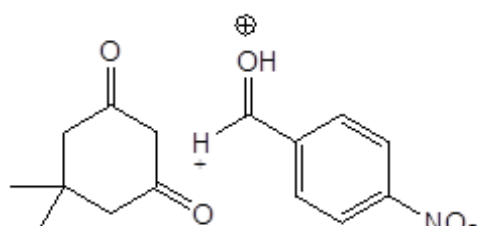
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Calculated energy for polyhydroquinolines synthesis with raw materials cyclohexa -1,-3,nitrobenzaldehyde-4, 3-oxobutanoate

Energy per stage	Final product	Raw material
$\Delta E=824.448$ $\Delta E= 815.536$ $\Delta E= -909.907$ $\Delta E= -175221.426$ $\Delta E= 24736.302$ $\Delta E= 2113.697$ $\Delta E=-36.856$ $\Delta E= -944.437$ $\Delta E= 902.736$ $\Delta E=709.21$ $\Delta E= 199858.19$		

Calculated energy for polyhydroquinolines synthesis with raw materials dimedone, nitrobenzaldehyde-4, 3-oxobutanoate

Energy per stage	Final product	Raw material
$\Delta E= 824.453$ $\Delta E= 812.969$ $\Delta E= -868.275$ $\Delta E= 201486.618$ $\Delta E= -919.624$ $\Delta E=1463.911$ $\Delta E= 206352.98$ $\Delta E= -1001.229$ $\Delta E= 980.579$ $\Delta E= 685.765$ $\Delta E= 199873.454$		

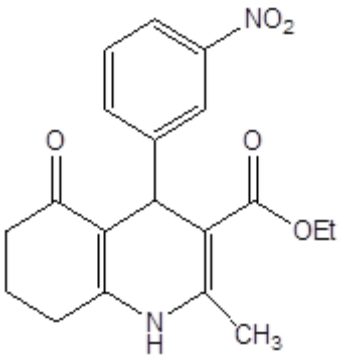
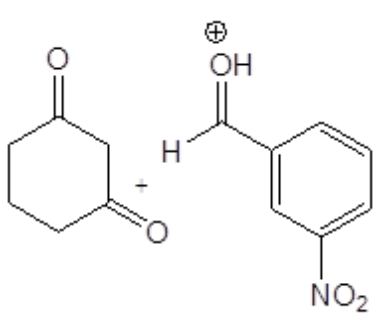
As results show, nitrobenzaldehyde-4 does not react spontaneously with cyclohexa -1,-3 and dimedone in the present of acid catalyst. additionally, comparing the energy difference indicates that nitrobenzaldehyde-4 reaction with enol forms cyclohexa -1,-3 and dimedone was more negative and consequently the reaction is more spontaneous. In the next steps , the energy differences considerably vary in nitrobenzaldehyde-4 reaction with cyclohexa -1,-3 and with dimedone reaction. But, the energy difference in other stages of bromobenzaldehyde-4 reaction with cyclohexa -1,-3 is more negative. Although, the disclosure process of pyridine circle and the final reaction stage do not proceed spontaneously , it is more negative compared with dimedone reaction and so, the reaction proceeds more spontaneously.

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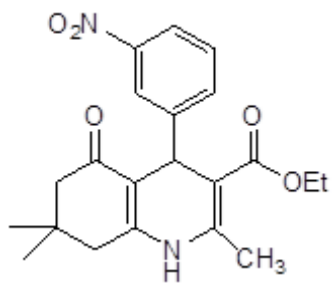
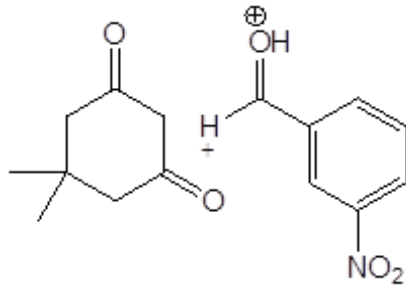
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Calculated energy for polyhydroquinolines synthesis with raw materials cyclohexa -1,-3,nitrobenzaldehyde ethyl-3, 3-oxobutanoate

Energy per stage	Final product	Raw material
$\Delta E=818.134$ $\Delta E= 809.225$ $\Delta E= -1456.117$ $\Delta E= -202035.535$ $\Delta E= -866.222$ $\Delta E=147.740$ $\Delta E= -67.428$ $\Delta E= -985.150$ $\Delta E= 936.238$ $\Delta E= 709.005$ $\Delta E= 199856.063$		

Calculated energy for polyhydroquinolines synthesis with raw materials dimedon,nitrobenzaldehyde ethyl-3, 3-oxobutanoate

Energy per stage	Final product	Raw material
$\Delta E= 822.103$ $\Delta E= 810.619$ $\Delta E= -894.701$ $\Delta E=201411.552$ $\Delta E= -816.145$ $\Delta E=1418.628$ $\Delta E=206385.168$ $\Delta E= -920.4$ $\Delta E=887.237$ $\Delta E=682.139$ $\Delta E=199884.177$		

Considering the results, nitrobenzaldehyde-3 does not react spontaneously with cyclohexa -1,-3 and dimedone in the presence of acid catalyst. also, comparing the energy difference indicates that nitrobenzaldehyde-3 reaction with enol forms cyclohexa -1,-3 and dimedone was more negative and consequently the reaction is more spontaneous. In the next steps, the energy differences considerably vary in nitrobenzaldehyde-3 reaction with cyclohexa -1,-3 and with dimedon reaction. However, the energy difference in other stages of nitrobenzaldehyde-3 reaction with cyclohexa -1,-3 is more negative. Although, the disclosure process of pyridine circle and the final stage of reaction do not proceed spontaneously,  $\Delta E$  for disclosure process of pyridine circle in the presence of dimedon is more negative, but  $\Delta E$  of the last stage of reaction in the presence of cyclohexa -1,-3 gets more negative. In this case, according to rest of reaction stages, the nitrobenzaldehyde-3 reaction with cyclohexa -1,-3 is more negative. To compare groups donate and demand electron, we analyzed the disclosure section of pyridine circle in the cyclohexa -1,-3 and dimedon reaction with substitutions of benzaldehyde. In all groups of electron donate and electron demand of benzene circle,  $\Delta E$  was positive and the reaction did not proceed spontaneously in the presence of  $H^+$  catalyst. But, among the groups of electron -donate OH showed a more negative value and proceeded more spontaneously than other groups. However, of groups of electron -demand in reacting with dimedon,  $NO_2$  locates in a meta more negative condition in reaction with cyclohexa -1,-3,  $NO_2$  places in a para more negative situation and greater spontaneous compared with other groups. It also demonstrated lower rate of energy difference between entire groups of electron- donate and electron-demand.

Conclusion

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After precise study of polyhydroquinolines synthesis through the Hantzsch reaction in the presence of heterogeneous catalyst  $Cs_{2.5}H_{0.5}PW_{12}O_{40}$ , which two surface hydrogen atoms or cesium function as catalyst. After optimization and measurement of energy, converting it into unit of joule and finally calculation of  $\Delta E$  for entire reaction stages, we concluded that the energy difference of majority of steps particularly stage 1 and disclosure stage of heterocyclic circle, the reaction is positive. Finally, we understood that the Hantzsch reaction does not progress spontaneously for polyhydroquinolines synthesis either with hydrogen  $H^+$  or in the room temperature or at  $383^\circ K$ . Therefore, the polyhydroquinolines synthesis in the present study via the Hantzsch reaction is catalyzed by cesium metal atom  $Cs^+$  and promotes the reaction.

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