

# A conceptual DFT approach towards analysing feasibility of the intramolecular cycloaddition Diels-Alder reaction of triene amide in Lewis acid catalyst

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**Abstract.** The effect of Lewis acid catalysts,  $\text{TiCl}_4$  and  $\text{Et}_2\text{AlCl}$  on the intramolecular cycloaddition Diels-Alder (IMDA) reaction of triene-amide have been studied theoretically using the DFT (Density Functional Theory) at the 6-31G(d,p) level of theory. The results obtained using the polar model of Domingo, electrophilicity, nucleophilicity indices and thermochemistry computations, demonstrate that these catalysts are coordinated with more nucleophilic atoms of diene fragment (nitrogen and oxygen of amide group). These catalysts affect negatively the feasibility of the reaction as well as the physico-chemical parameters of the IMDA reaction of triene-amide.

**Keywords.** Lewis acid; Diels-Alder; DFT; catalyst; reactivity; intramolecular.

## 1. Introduction

The catalysis of Diels-Alder (DA) reaction by Lewis acids received considerable attention on the part of the experimentalists<sup>1–3</sup> and theoretical chemists.<sup>4–9</sup> Indeed, Lewis acids do not only improve the rate and speed of the DA reaction, they also help increase the high regioselectivity and stereoselectivity compared to the uncatalyzed reactions.<sup>5,6</sup> The first report of catalysis of the DA reaction by Lewis acid appeared in 1960, and *ab initio* studies or application of density functional theory (DFT) on the role of Lewis acids in the DA reaction began to appear in 1990.<sup>4</sup> Garcia *et al.*,<sup>7</sup> have made DFT calculations (B3LYP) to study the role of Lewis acid ( $\text{BF}_3$ ) in the DA reaction between butadiene and acrolein. The results obtained in these studies have confirmed that the method B3LYP/6-31G(d) is an excellent compromise between computational cost and accuracy of the theoretical study Xia *et al.*,<sup>10</sup> also studied the impact of  $\text{AlCl}_3$ ,  $\text{BCl}_3$ ,  $\text{FeCl}_3$ ,  $\text{COCl}_2$ ,  $\text{CuCl}_2$ ,  $\text{CuCl}$ , and  $\text{ZnCl}_2$  in the DA reaction between isoprene and acrolein by using two chemical methods: Computational and conceptual DFT.<sup>11</sup> The use of conceptual DFT, based on

the reactivity indices<sup>11,12</sup> has helped to understand the assessable role of Lewis acids in DA reactions.<sup>13–15</sup>

Currently, Lewis acids of Diethyl Aluminum chloride,  $\text{Et}_2\text{AlCl}$  and Titanium tetrachloride,  $\text{TiCl}_4$  are used in the DA reactions for organic synthesis. In this context, the impact of  $\text{Et}_2\text{AlCl}$  and  $\text{TiCl}_4$  catalysts are used in the intramolecular Diels-Alder reaction (IMDA) of triene-amide to 25°C for the preparation to the Hexahydroindole, which are of interest in chemical and pharmacological industries.<sup>16–19</sup> This reaction has been widely studied previously under thermal conditions (160°C) in a nonpolar solvent (first case: toluene)<sup>17</sup> and in the presence of a polar H-bonding solvent (second case: water) at to 25°C.<sup>18</sup> The studies have shown in the first case that the IMDA reactions of triene-amide are concerted and asynchronous, and giving the exo-product; in the second case, the reaction is unlikely to take place. In this study, we will try to explain theoretically the possible coordination of  $\text{Et}_2\text{AlCl}$  and  $\text{TiCl}_4$  and their role in acceleration of reactivity on the IMDA reactions of triene-amide at ambient temperature (Scheme 1). We have established a greater precision of result with a minimum time of computation in our work on the conceptual DFT.

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## 2. Computational Methods

DFT computations were carried out using the B3LYP<sup>20</sup> exchange-correlation functional, together with the standard 6-31G(d,p) basis set.<sup>21</sup> The optimizations were carried out using the Berny analytical gradient method.<sup>22</sup> All computations were carried out with the Gaussian 09 programs.<sup>23</sup> The global electrophilicity index,  $\omega$ <sup>24</sup> is given by the following expression ( $\omega = \mu^2/2\eta$ ), in terms of the electronic chemical potential,  $\mu$  and chemical hardness,  $\eta$ . Both quantities may be calculated in terms of the one-electron energies of the frontier molecular orbital HOMO and LUMO, as  $\varepsilon_{\text{HOMO}}$  and  $\varepsilon_{\text{LUMO}}$  such as:  $\mu = (\varepsilon_{\text{HOMO}} + \varepsilon_{\text{LUMO}})/2$  and  $\eta = (\varepsilon_{\text{LUMO}} - \varepsilon_{\text{HOMO}})$ , respectively.<sup>25</sup> The nucleophilicity index,  $N$ <sup>26</sup> based on the HOMO energies has been obtained within the Kohn–Sham scheme<sup>27</sup> and defined as:  $N = (E_{\text{HOMO}}(\text{Nu}) - E_{\text{HOMO}}(\text{TCE}))$ . The nucleophilicity is referred to tetracyanoethylene (TCE), because it presents the lowest HOMO energy in a large series of molecules which already investigated in the context of polar cycloadditions.

The local nucleophilicity,  $N_k$ ,<sup>28</sup> is defined as the product of the global nucleophilic index  $N$  and nucleophilic Fukui index  $f_k^-$ .

Thus,  $N_k = N f_k^-$  with  $N = \sum N_k$ . The condensed Fukui functions in a molecule with  $N$  electrons was proposed by Yang and Mortier:<sup>29</sup>

$$f_k^+ = [q_k(N+1) - q_k(N)], \quad \text{for nucleophilic attack}$$

$$f_k^- = [q_k(N) - q_k(N-1)], \quad \text{for electrophilic attack}$$

$q_k(N)$ : Electronic population of the atom  $k$  in the neutral molecule.

$q_k(N+1)$ : Electronic population of the atom  $k$  in the anionic molecule.

$q_k(N-1)$ : Electronic population of the atom  $k$  in the cationic molecule.

We can determine the electrophile ( $\omega_F$ ) and nucleophile ( $N_F$ ) indices of fragments<sup>30</sup> ( $F =$  diene or dienophile) by the equations given below:

$$\omega_F = \omega \sum_{k \in F} f_k^+$$

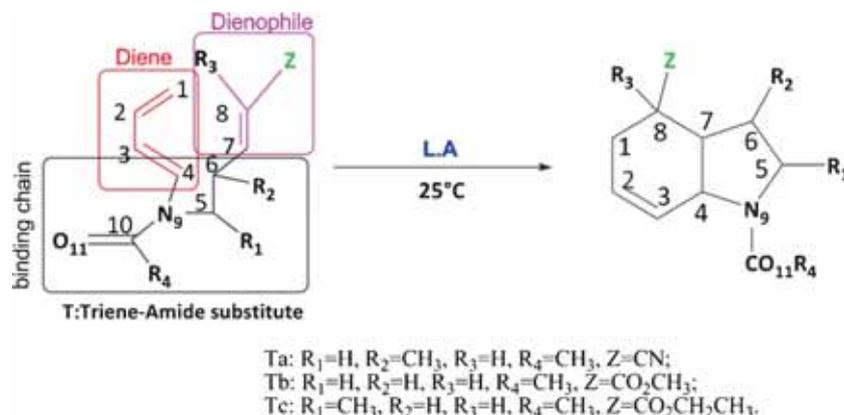
$$N_F = N \sum_{K \in F} f_k^-$$

The calculation of this function has been realized by using the natural of populations analysis (NPA).<sup>31</sup>

## 3. Results and Discussion

### 3.1 Possible coordination of Lewis acids ( $\text{TiCl}_4$ and $\text{Et}_2\text{AlCl}$ ) with atoms in molecule

The coordination of catalyst in the literature<sup>32–34</sup> is usually associated with an atom that has lone pairs. Compound Ta ( $R_1 = \text{H}$ ,  $R_2 = \text{CH}_3$ ,  $R_3 = \text{H}$ ,  $R_4 = \text{CH}_3$ ,  $Z = \text{CN}$ ) (Scheme 1), has lone pairs in the terminal function of nitrile ( $Z = \text{CN}$ ) in dienophile fragment (Dp). In addition, another electron-rich carbonyl (CO) of amide function is present in diene fragment (D), so the coordination of Lewis acid is probably done with these groups. Moreover, for compounds Tb ( $R_1 = \text{H}$ ,  $R_2 = \text{H}$ ,  $R_3 = \text{H}$ ,  $R_4 = \text{CH}_3$ ,  $Z = \text{CO}_2\text{CH}_3$ ) and Tc ( $R_1 = \text{CH}_3$ ,  $R_2 = \text{H}$ ,  $R_3 = \text{H}$ ,  $R_4 = \text{CH}_3$ ,  $Z = \text{CO}_2\text{C}_2\text{H}_5$ ), the situation is different because of existence of two carbonyl groups (carbonyl (CO) of amide function in diene fragment and carbonyl (CO) of ester function in dienophile fragment). The catalysts have two opportunities for coordination. In order to accelerate or improve the reactivity of the intramolecular reactions, the catalyst must be coordinated with dienophile to decrease LUMO energy and to lower the difference of HOMO-LUMO energy. In the triene-amide molecule, there are three atoms bearing lone pairs (nitrogen and oxygen) distributed between



**Scheme 1.** Intramolecular Diels-Alder reaction of triene-amide catalyzed by Lewis Acid (LA).

diene and dienophile fragments, and consequently the catalysts have two or three opportunities for coordination of same reagents such as N<sub>9</sub>, O<sub>11</sub>, N<sub>13</sub> or O<sub>13</sub> and O<sub>14</sub> (Scheme 1). For adequate coordination, we will try to identify the more nucleophilic atom, using the polar model of Domingo<sup>35</sup> applied to the ground state; this model requires that a good nucleophile reacts with a good electrophile. In order to know the favorite nucleophile, we apply the theoretical approaches. Lewis acid has an empty square (electrophile) so their coordination will be done to atom with a lone pair (nucleophile). The application of the above equations allows us to calculate the nucleophilicity of each atom k (k= N<sub>9</sub>, O<sub>11</sub>, N<sub>13</sub>, O<sub>13</sub>, and O<sub>14</sub>). The results corresponding to the nucleophilicity of Fukui index  $f_k^-$ , the global nucleophilicity index N and the local nucleophilicity index N<sub>k</sub> of atoms N<sub>9</sub>, O<sub>11</sub>, N<sub>13</sub>, O<sub>13</sub> and O<sub>14</sub> are reported in Table 1.

Following the results noted in Table 1, Lewis acid is probably making bonding to the nitrogen (N<sub>9</sub>) and oxygen (O<sub>11</sub>) atoms having the greatest nucleophilic power such as,  $f^-(N_9) > f^-(O_{11}) > f^-(N_{13}) > f^-(O_{13}) > f^-(O_{14})$ . Thereby, N<sub>9</sub> and O<sub>11</sub> atoms of diene fragment are preferable coordination sites. This coordination will

possibly not be useful because Lewis acids decrease the reactivity of diene by reducing HOMO energy (nucleophilicity). To explain the possible effects of Lewis acids, we suppose that the catalyst can make coordination on both the nucleophilic atoms. For this reason, we propose studying the two cases of more nucleophilic atoms O<sub>11</sub> (case A) and N<sub>9</sub> (case B) (Figure 1).

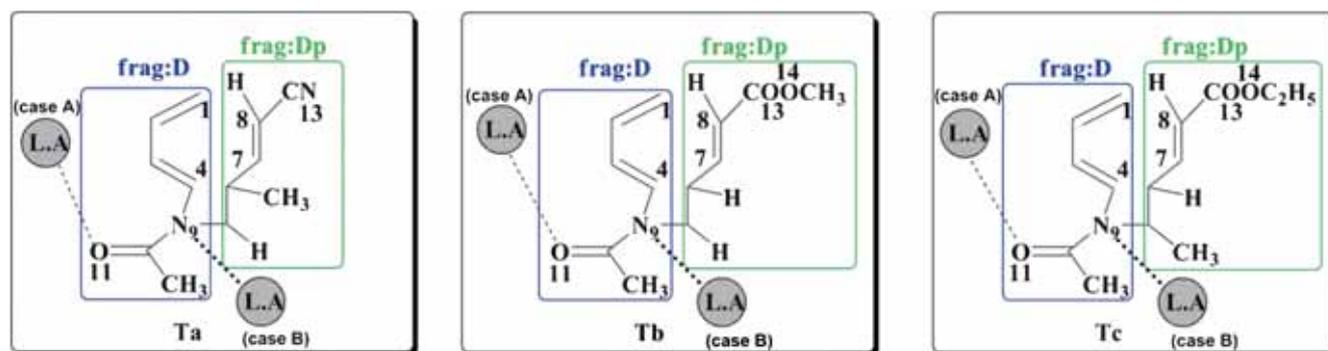
### 3.2 Mechanism of intramolecular reaction of triene amide

In order to know the electronic flux between fragments such as the fragment donor or acceptor of the electron in the intramolecular Diels-Alder reaction, one should calculate the charge transfer (CT) in the transition state of these compounds. To this end, we will assess the two possible cases in the presence of Et<sub>2</sub>AlCl and TiCl<sub>4</sub> catalysts and in the gas phase (without catalyst). This is done by using the natural population analysis (NPA), and the results found are given in Table 2.

Table 2 shows that the charge transfer in IMDA reaction for reagents (Ta, Tb and Tc) in the presence and absence of catalysts has taken place from the diene (D)

**Table 1.** Nucleophilic of Fukui index  $f_k^-$ , global nucleophilic index N and local nucleophilic index N<sub>k</sub> of N<sub>9</sub>, O<sub>11</sub>, N<sub>13</sub>, O<sub>13</sub> and O<sub>14</sub> atoms calculated at the 6-31G(d,p)//B3LYP level in absence of the catalyst. See Scheme 1 for labels and numbers.

Reagent	k	$f_k^-$	N(eV)	N <sub>k</sub> (eV)
Ta	O <sub>11</sub> (Diene fragment)	0.12627	3.29	0.800
	N <sub>9</sub> (Diene fragment)	0.12919		<b>0.190</b>
	N <sub>13</sub> (Dienophile fragment)	0.06216		0.205
Tb	O <sub>11</sub> (Diene fragment)	0.12950	3.40	0.210
	N <sub>9</sub> (Diene fragment)	0.12517		<b>0.620</b>
	O <sub>13</sub> (Dienophile fragment)	0.01260		0.131
	O <sub>14</sub> (Dienophile fragment)	4.81 10 <sup>-3</sup>		0.016
Tc	O <sub>11</sub> (Diene fragment)	0.12112	3.21	0.210
	N <sub>9</sub> (Diene fragment)	0.13198		<b>0.820</b>
	O <sub>13</sub> (Dienophile fragment)	0.02969		0.102
	O <sub>14</sub> (Dienophile fragment)	4.61 10 <sup>-3</sup>		0.015



**Figure 1.** Coordination of Lewis acid by nitrogen and oxygen atoms of amide of the Ta, Tb and Tc compounds.

**Table 2.** Charge transfer in  $e$  (electronic charge), between diene and dienophile fragments of the transition states in the reactants Ta, Tb and Tc.

Reagent		Diene fragment			Dienophile fragment		
		W.C.	Et <sub>2</sub> AlCl	TiCl <sub>4</sub>	W.C.	Et <sub>2</sub> AlCl	TiCl <sub>4</sub>
Ta	Case A	+0.10e	+0.065e	+0.052e	-0.10e	-0.065e	-0.052e
	Case B	+0.10e	+0.041e	+0.037e	-0.10e	-0.041e	-0.037e
Tb	Case A	+0.07e	+0.047e	+0.032e	-0.07e	-0.047e	-0.032e
	Case B	+0.07e	+0.038e	+0.028e	-0.07e	-0.038e	-0.028e
Tc	Case A	+0.06e	+0.036e	+0.029e	-0.06e	-0.036e	-0.029e
	Case B	+0.06e	+0.017e	+0.014e	-0.06e	-0.017e	-0.014e

+ sign: donor of electron; - sign: acceptor of electron; W.C.: Without catalyst.

**Table 3.** HOMO and LUMO energies, chemical potential  $\mu$ , global hardness  $\eta$ , global softness S, electrophilicity index  $\omega$  and nucleophilicity index N in the presence of the catalyst at 298 K.

	Reagent	Catalyst	HOMO (a.u.)	LUMO (a.u.)	$\mu$ (a.u.)	$\eta$ (a.u.)	S (a.u.)	$\omega$ (eV)	N (eV)
CASE A	Ta	W.C.	-0.21670	-0.07000	-0.129	0.170	2.940	1.332	3.288
		TiCl <sub>4</sub>	-0.26080	-0.19300	-0.203	0.114	4.160	4.918	2.024
		Et <sub>2</sub> AlCl	-0.19650	-0.08140	-0.140	0.111	4.134	2.670	3.774
	Tb	W.C.	-0.20884	-0.03716	-0.123	0.172	2.910	1.197	3.400
		TiCl <sub>4</sub>	-0.22129	-0.11000	-0.200	0.117	4.273	4.614	2.093
		Et <sub>2</sub> AlCl	-0.20186	-0.08297	-0.150	0.119	4.202	2.305	3.628
	Tc	W.C.	-0.20921	-0.01200	-0.124	0.171	2.920	1.223	3.210
		TiCl <sub>4</sub>	-0.25150	-0.17700	-0.198	0.113	4.180	4.720	2.203
		Et <sub>2</sub> AlCl	-0.19821	-0.07867	-0.110	0.119	4.202	2.177	3.727
CASE B	Ta	W.C.	-0.21670	-0.07000	-0.129	0.170	2.940	1.332	3.288
		TiCl <sub>4</sub>	-0.26202	-0.12030	-0.210	0.105	4.775	5.711	1.991
		Et <sub>2</sub> AlCl	-0.21682	-0.07198	-0.190	0.140	3.590	2.020	3.221
	Tb	W.C.	-0.20884	-0.03716	-0.123	0.172	2.910	1.197	3.400
		TiCl <sub>4</sub>	-0.21908	-0.11900	-0.205	0.102	4.912	5.628	2.116
		Et <sub>2</sub> AlCl	-0.22033	-0.06997	-0.180	0.113	3.333	1.907	3.125
	Tc	W.C.	-0.20921	-0.01200	-0.124	0.171	2.920	1.223	3.210
		TiCl <sub>4</sub>	-0.20390	-0.13134	-0.168	0.073	6.812	5.260	3.197
		Et <sub>2</sub> AlCl	-0.19232	-0.06261	-0.127	0.130	3.890	1.688	3.888

W.C.: Without catalyst.

to the dienophile (Dp) fragment. Therefore, the diene fragment behaves like electron-releasing (HOMO) and the dienophile fragment behaves like electron-withdrawing (LUMO). Also, the intramolecular cycloaddition Diels-Alder reaction of the triene-amide molecule is controlled by a normal electronic demand in both cases, in the presence and absence of the catalysts. In addition, we have shown that the transfer charge is diminished in compounds catalyzed by Lewis acids, and this can be explained as these catalysts are attractors of charge.

### 3.3 Effect of Lewis acid on the global chemical groups

Lewis acids may change the physico-chemical parameters of the studied compounds, because of their attractive

effect on electrons in the case of coordination. Consequently, the new features corresponding to the HOMO and LUMO energies of the diene and dienophile, respectively, chemical potential energy  $\mu$ , global hardness  $\eta$ , global softness S, electrophilicity index  $\omega$  and nucleophilicity index N in the presence of TiCl<sub>4</sub> and Et<sub>2</sub>AlCl catalysts at 25°C (298 K) are given in Table 3.

According to this result, we can conclude that the chemical potential  $\mu$  become less important in comparison to the uncatalyzed systems. As regards to the electrophilicity index  $\omega$ , it is known to increase with TiCl<sub>4</sub> and Et<sub>2</sub>AlCl catalysts, as well as the nucleophilicity known to decrease with TiCl<sub>4</sub> and a slight increase with Et<sub>2</sub>AlCl catalyst (TiCl<sub>4</sub> is purely electrophilic). Generally, after this result, the electrophilicity increases and the nucleophilicity reduces, thus the Lewis acids are electron withdrawing.

**Table 4.** Regional electrophilicity ( $\omega_D$ ,  $\omega_{Dp}$ ) and regional nucleophilicity ( $N_D$ ,  $N_{Dp}$ ) of diene and dienophile fragments.

			Diene Fragment (D)				Dienophile Fragment (Dp)			
			$\sum_{K \in D} f_K^+$	$\omega_D$ (eV)	$\sum_{K \in D} f_K^-$	$N_D$ (eV)	$\sum_{K \in D} f_K^+$	$\omega_{Dp}$ (eV)	$\sum_{K \in D} f_K^-$	$N_{Dp}$ (eV)
CASE A	Ta	W.C.	0.18622	0.740	0.86625	2.811	0.97300	0.591	0.09012	0.297
		TiCl <sub>4</sub>	0.21211	1.080	0.19600	1.101	0.03728	0.183	0.15976	0.323
		Et <sub>2</sub> AlCl	0.82032	1.999	0.16017	0.606	0.10132	0.219	0.01899	0.072
	Tb	W.C.	0.18900	0.662	0.89192	3.079	0.72170	0.164	0.09664	0.332
		TiCl <sub>4</sub>	0.18114	0.860	0.21670	1.227	0.04090	0.191	0.18992	0.270
		Et <sub>2</sub> AlCl	0.83274	1.919	0.16017	0.212	0.11837	0.273	0.01870	0.140
	Tc	W.C.	0.16005	0.611	0.93198	3.195	0.99950	0.205	0.07692	0.264
		TiCl <sub>4</sub>	0.28920	1.367	0.13660	1.116	0.03133	0.165	0.19120	0.150
		Et <sub>2</sub> AlCl	0.78285	1.704	0.11968	0.760	0.09201	0.208	0.03698	0.110
CASE B	Ta	W.C.	0.18622	0.740	0.86625	2.811	0.97300	0.591	0.09012	0.297
		TiCl <sub>4</sub>	0.23850	1.376	0.36200	0.680	0.01987	0.325	0.18003	0.321
		Et <sub>2</sub> AlCl	0.67790	1.230	0.21289	0.805	0.21930	0.121	0.08320	0.190
	Tb	W.C.	0.18900	0.662	0.89192	3.079	0.72170	0.164	0.09664	0.332
		TiCl <sub>4</sub>	0.22359	1.221	0.32893	0.708	0.06214	0.370	0.26918	0.210
		Et <sub>2</sub> AlCl	0.67296	1.283	0.29711	0.928	0.22170	0.930	0.01374	0.121
	Tc	W.C.	0.16005	0.611	0.93198	3.195	0.99950	0.205	0.07692	0.264
		TiCl <sub>4</sub>	0.33110	1.789	0.11670	1.375	0.04040	0.216	0.08850	0.163
		Et <sub>2</sub> AlCl	0.59968	1.012	0.39760	1.311	0.22191	0.670	0.07880	0.290

**Table 5.** Activation energy  $E_a$ , free energy  $\Delta G$  and the heat of formation  $\Delta H$  of IMDA reaction of Ta, Tb and Tc compounds at 25°C.

			$E_a$ (kcal/mol)	$\Delta G_r$ (kcal/mol)	$\Delta H_r$ (kcal/mol)
CASE A	Ta	W.C.	29.8	-11.8	-19.3
		TiCl <sub>4</sub>	32.3	-10.2	-16.1
		Et <sub>2</sub> AlCl	30.9	-10.9	-18.1
	Tb	W.C.	27.9	-12.2	-20.1
		TiCl <sub>4</sub>	30.9	-10.7	-17.2
		Et <sub>2</sub> AlCl	29.0	-11.1	-18.6
	Tc	W.C.	26.1	-15.3	-24.0
		TiCl <sub>4</sub>	28.9	-14.2	-19.8
		Et <sub>2</sub> AlCl	27.6	-15.1	-20.2
CASE B	Ta	W.C.	29.8	-11.8	-19.3
		TiCl <sub>4</sub>	—	55.7	52.9
		Et <sub>2</sub> AlCl	—	37.8	37.9
	Tb	W.C.	27.9	-12.2	-20.1
		TiCl <sub>4</sub>	—	66.2	61.4
		Et <sub>2</sub> AlCl	—	65.3	61.9
	Tc	W.C.	26.1	-15.3	-23.9
		TiCl <sub>4</sub>	—	42.2	19.0
		Et <sub>2</sub> AlCl	—	11.8	33.3

— : not found; W.C.: without catalyst

Subsequently, in presence of these catalysts, the reactivity decreases. This is explained by the chemical potential results such as:  $\mu(\text{uncatalyzed}) > \mu(\text{Et}_2\text{AlCl}) > \mu(\text{TiCl}_4)$ . Nevertheless, the nucleophilic and electrophilic groups of intramolecular reaction do not give deep explanations of inter-fragment reactivity.

In order to know the impact of catalysts to the chemical reactivity of diene and dienophile fragments of IMDA reaction, we will try to identify the nucleophilicity

and electrophilicity of diene and dienophile fragments towards these catalysts (Figure 1). The results are given in Table 4.

Following the results in Table 4, we note that the electrophilicity and nucleophilicity characters of diene fragment are changed in the presence of TiCl<sub>4</sub> and Et<sub>2</sub>AlCl catalysts. We observe again an increase of electrophilicity and a decrease of nucleophilicity. Therefore, these catalysts play a role of attractor of electrons in diene

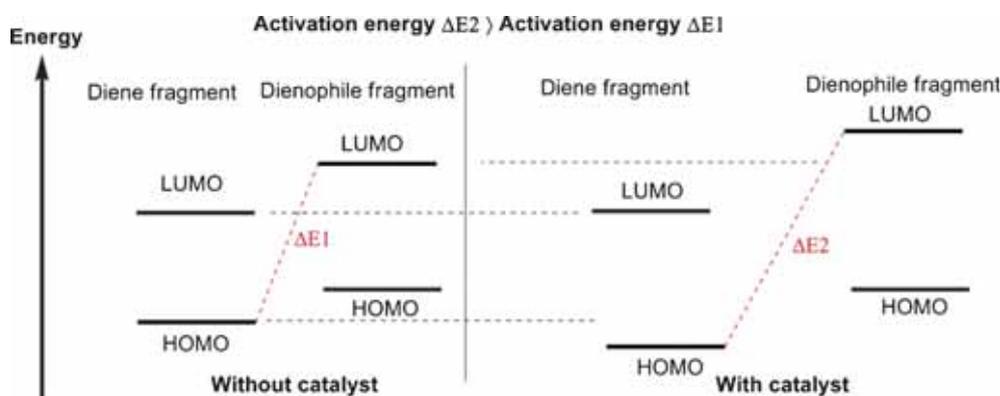
fragment. In addition, the electrophilicity of dienophile fragment decreases for both catalysts and nucleophilicity increases for  $\text{TiCl}_4$  and slightly decreases for  $\text{Et}_2\text{AlCl}$ . Hence, the effect of  $\text{TiCl}_4$  catalyst on the IMDA reaction is large compared to  $\text{Et}_2\text{AlCl}$ . So, the nucleophilicity and electrophilicity of diene and dienophile fragments, respectively, will be changed negatively by the Lewis acid.

Consequently, the catalysts decrease the electron donating power of diene fragment and decrease the electron withdrawing power of dienophile fragment, accordingly decreasing the chemical reactivity.

### 3.4 Effect of Lewis acid on the energy barriers

Lewis acids are known for their catalytic power towards organic reactions, speed, yield and efficiency. Subsequently, these catalysts minimize activation energy. In this context, we calculated the thermodynamic properties of these reactions for normal conditions in the presence and absence of the catalyst. Values of energy barriers of Ta, Tb and Tc compounds in the absence and in the presence of  $\text{TiCl}_4$  and  $\text{Et}_2\text{AlCl}$  catalyst at  $25^\circ\text{C}$  are given in Table 5.

In case A, when the catalyst is coordinated by the oxygen atom ( $\text{O}_{11}$ ), we have remarked that IMDA



**Figure 2.** The activation energy diagrams in the presence and in the absence of the catalyst.

**Table 6.** Local electrophilicity  $\omega$  (eV) and local nucleophilicity  $N$  (eV) of active centre sites.

	k	Ta		Tb		Tc		
		$\omega_k$	$N_k$	$\omega_k$	$N_k$	$\omega_k$	$N_k$	
CASE A	W.C.	1	0.112	0.601	0.133	0.620	0.124	0.610
		4	0.092	0.239	0.082	0.213	0.083	0.211
		7	0.162	-0.121	0.129	-0.119	0.111	-0.109
		8	0.109	0.111	0.060	0.119	0.067	0.084
	$\text{TiCl}_4$	1	0.284	0.263	0.226	0.291	0.277	0.212
		4	0.127	0.199	-0.120	0.191	-0.800	0.276
		7	-0.087	0.028	-0.182	0.005	-0.664	0.186
		8	0.101	0.079	0.116	0.026	0.113	0.063
	$\text{Et}_2\text{AlCl}$	1	0.301	0.211	0.273	0.223	0.236	0.193
		4	0.122	-0.016	0.070	-0.009	0.072	-0.029
		7	-0.030	-0.088	-0.029	-0.099	0.019	-0.093
		8	0.071	0.063	0.062	0.083	0.019	0.080
CASE B	W.C.	1	0.112	0.602	0.133	0.620	0.124	0.610
		4	0.096	0.238	0.082	0.213	0.084	0.211
		7	0.162	-0.121	0.129	0.119	0.111	0.109
		8	0.109	0.111	0.060	0.119	0.067	0.084
	$\text{TiCl}_4$	1	0.313	0.181	0.374	0.171	0.310	0.231
		4	-0.177	0.074	-0.132	0.027	-0.004	0.282
		7	-0.182	0.001	-0.192	0.004	0.112	0.112
		8	0.114	0.109	0.162	0.123	0.100	0.071
	$\text{Et}_2\text{AlCl}$	1	0.263	0.321	0.221	0.268	0.273	0.327
		4	0.182	0.010	0.120	0.126	0.113	0.060
		7	0.092	-0.097	0.073	-0.096	0.081	-0.111
		8	0.106	0.077	0.070	0.077	0.014	0.120

reaction is delayed. This is confirmed by values of increased enthalpy and Gibbs free energy of reaction. There is also an increase of activation energy ( $E_a$ ) at 25°C. For that reason, these systems need more energy compared to uncatalyzed systems. This means that IMDA reaction of the studied systems is disadvantaged at this temperature in this case. Otherwise, for case B, when catalyst is coordinated by nitrogen atom (N<sub>9</sub>), we have shown that the energy barriers and free enthalpy of reaction are greater than 0 ( $\Delta G > 0$  and  $\Delta H > 0$ ), which means that IMDA reaction is not possible in this case.

Consequently, IMDA reaction of triene-amide catalysed by TiCl<sub>4</sub> and Et<sub>2</sub>AlCl in ambient temperature, no acceleration or improved selectivity. On the contrary, IMDA reaction is disadvantaged because the coordination was done with atoms having the biggest nucleophilicity of diene fragment and not with the dienophile fragment. Lowering of the nucleophilicity in diene fragment, and thus HOMO (diene)-LUMO (dienophile) difference becomes very large and the activation energy becomes higher, which is shown schematically in Figure 2.

### 3.5 Effect of Lewis acid on the local electrophilic and nucleophilic groups of active centre sites

In order to confirm the results revealed in Tables 2, 3 and 4, we calculated the local nucleophilicity and electrophilicity groups of active centre sites (1, 4, 7 and 8). The results are given in Table 6.

In Table 6, we notice that the nucleophilicity of centres (1) and (4) of diene fragment are observed to decrease by comparing with the results for uncatalyzed systems. This decrease corresponds to an increase in electrophilicity. Therefore, centres (7) and (8) of dienophile fragment are known to decrease both electrophilicity and nucleophilicity groups when using TiCl<sub>4</sub> and Et<sub>2</sub>AlCl catalysts. Changes in active site characters (decrease in nucleophilicity of 1 and 4 sites in diene fragment) and decrease in electrophilicity of 7 and 8 sites in dienophile fragment) affect chemical reactivity, negatively and greatly. This conceptual DFT study showed that Lewis acid is unsuccessful to improve or increase speed, yield and efficiency of the IMDA reaction.

## 4. Conclusions

This study was conducted to estimate the effect of Lewis acids TiCl<sub>4</sub> and Et<sub>2</sub>AlCl on the intramolecular Diels-Alder reaction of triene amide (Ta, Tb and Tc) compounds, and to know their capacity and

efficiency on the chemical reactivity. The study was performed at all susceptible sites to coordinate with Lewis acids (oxygen of ester group, carbonyl and nitrogen of amide group). A study through the polar model of Domingo showed that the oxygen and nitrogen atoms having lone pairs of amide group are the preferred coordination sites for Lewis acid due to their high nucleophilicity. The results showed that the nucleophilicity and electrophilicity of fragments and active sites are reduced in the presence of these catalysts and consequently, the chemical reactivity is diminished. In parallel, the thermochemistry studies demonstrated, on the one hand, when Lewis acid is coordinated to the oxygen atom, IMDA reaction is delayed. On the other hand, when Lewis acid is coordinated to the nitrogen atom, the IMDA reaction is not possible.

## References

1. Yates P and Eaton P 1960 *J. Am. Chem. Soc.* **82** 4436
2. Kagan H B and Riant O 1992 *Chem. Rev.* **92** 1007
3. Pindur U, Lutz G and Otto C 1993 *Chem. Rev.* **93** 741
4. Birney D M and Houk K N 1990 *J. Am. Chem. Soc.* **112** 4127
5. Yamabe S, Dai T and Minato T 1995 *J. Am. Chem. Soc.* **117** 10994
6. Sbai A, Branchadell V, Ortuño R M and Oliva A 1997 *J. Org. Chem.* **62** 3049
7. Garcia J I, Martinez-Merino V, Mayoral J A and Salvatella L 1998 *J. Am. Chem. Soc.* **120** 2415
8. Yambe S and Minato T 2000 *J. Org. Chem.* **65** 1830
9. Alves C N, Carneiro A S, Andrés J and Domingo L R 2006 *Tetrahedron* **62** 5502
10. Xia Y, Yin D, Rong C, Xu Q and Liu S 2008 *J. Phys. Chem. A.* **112** 9970
11. Geerlings P, Proft F D and Langenaeker W 2003 *Chem. Rev.* **103** 1793
12. Chattaraj P K, Sarkar U and Roy D R 2006 *Chem. Rev.* **106** 2065
13. Domingo L R, Asensio A and Arroyo P 2002 *J. Phys. Org. Chem.* **15** 660
14. Domingo L R and Sáez J A 2009 *J. Org. Biomol. Chem.* **7** 3576
15. Ess D H, Jones G O and Houk K N 2006 *Adv. Synth. Catal.* **348** 2337
16. Garmes H 1995 In *Triene-amides synthesis from homoallylic azides, Diels-Alder cycloaddition* Thesis (El Jadida: Chouaib Doukkali University)
17. Benallou A, Garmes H and El Alaoui El Abdallaoui H 2014 *Mor. J. Chem.* **2** 181
18. Benallou A, Garmes H and El Alaoui El Abdallaoui H 2016 *Tetrahedron* **72** 76
19. Benallou A, Garmes H and El Alaoui El Abdallaoui H 2014 *IJJAS* **8** 685
20. Becke A D 1993 *J. Chem. Phys.* **98** 5648

21. Hehre W J, Radom L, Schleyer P von R and Pople J A (Eds.) 1986 In *Ab Initio Molecular Orbital Theory* (New York: Wiley)
22. Schlegel H B 1982 *J. Comput. Chem.* **3** 214
23. Frisch M J, Trucks G W, Schlegel H B, Scuseria G E, Robb M A, Cheeseman J R, Scalmani G, Barone V, Mennucci B, Petersson G A, Nakatsuji H, Caricato M, Li X, Hratchian H P, Izmaylov A F, Bloino J, Zheng G, Sonnenberg J L, Hada M, Ehara M, Toyota K, Fukuda R, Hasegawa J, Ishida M, Nakajima T, Honda Y, Kitao O, Nakai H, Vreven T, Montgomery J A, Peralta J E, Ogliaro F, Bearpark M, Heyd J J, Brothers E, Kudin K N, Staroverov V N, Kobayashi R, Normand J, Raghavachari K, Rendell A, Burant J C, Iyengar S S, Tomasi J, Cossi M, Rega N, Millam J M, Klene M, Knox J E, Cross J B, Bakken V, Adamo C, Jaramillo J, Gomperts R, Stratmann R E, Yazyev O, Austin A J, Cammi R, Pomelli C, Ochterski J W, Martin R L, Morokuma K, Zakrzewski V G, Voth G A, Salvador P, Dannenberg J J, Dapprich S, Daniels A D, Farkas O, Foresman J B, Ortiz J V, Cioslowski J and Fox D J 2009 In *Gaussian, Revision A.02* (Wallingford CT: Gaussian Inc.)
24. Parr R G, Szentpaly L V and Liu S 1999 *J. Am. Chem. Soc.* **121** 1922
25. Parr R G and Pearson R G 1983 *J. Am. Chem. Soc.* **105** 7512
26. Domingo L R and Pérez P 2011 *Org. Biomol. Chem.* **9** 7168
27. Kohn W and Sham L J 1965 *Phys. Rev.* **140** 1133
28. Domingo L R and Sáez J A 2009 *Org. Biomol. Chem.* **7** 3576
29. Yang W and Mortier W J 1986 *J. Am. Chem. Soc.* **108** 5708
30. Soto-Delgado J, Domingo L R and Contreras R 2010 *Org. Biomol. Chem.* **8** 3678
31. Reed A E, Weinstock R B and Weinhold F 1985 *J. Chem. Phys.* **83** 735
32. Snider B B and Ron E 1985 *J. Am. Chem. Soc.* **107** 8160
33. Singleton D A and Hang C 2000 *J. Org. Chem.* **65** 895
34. Loncharich R J and Houk K N 1987 *J. Am. Chem. Soc.* **109** 6947
35. Domingo L R, Chamorro E and Pérez P 2008 *J. Org. Chem.* **73** 4615