

Copyright © 2019 by Academic Publishing House Researcher s.r.o.



Published in the Slovak Republic
European Journal of Molecular Biotechnology
Has been issued since 2013.
E-ISSN: 2409-1332
2019, 7(2): 91-99

DOI: 10.13187/ejmb.2019.2.91
www.ejournal8.com



The Use of the Parr Function Would Include the Reactivity of the Carbenes with β -himachalene

Z. Jalil ^a, M. El idrissi ^{b, *}, A. Barhoumi ^b, A. Zeroual ^b, M. Mbarki ^a, A. Tounsi ^c

^a Sultan Moulay Slimane University, Béni-Mellal-23000, Morocco

^b Chouaib Doukkali University, El Jadida, Morocco

^c Moulay Slimane University, Mghila, Béni Mellal, Morocco

Abstract

Cyclopropanes are molecules of great importance since they are present in several biologically active molecules in addition to being powerful intermediates in the synthesis of complex molecules. During this work, we have étudié la régio-sélectivité des réactions de cycloaddition [1+2] des carbènes et β -himachalène par la méthode D.F.T au niveau de la base (basis) 6-31 (d), en utilisant un nouveau descripteur de la régio-sélectivité, c'est la fonction (office) de Parr, nous remarquons d'après cette étude que l'attaque d'une mole de carbènes est préférentiellement faite au niveau de la connexion C6=C7 de β -himachalène de dans les deux possibilités de carbènes (nucléophile ou électrophile). Nous remarquons également que l'interaction entre les orbitales frontières de réactifs (β -himachalène-carbènes) est faite d'une manière faciale, nous remarquons également que les différences de électrophile $\Delta\omega$ (Entre carbènes: { CH(CH₃), :CCl(Ph), :CH(Ph), :CCl(CH₃), :CHF, :CF(Ph), :CF(Cl), :CF₂, :C(Ph)₂, :CH₂, :CHCl, :CCl₂, et :C(Br)₂ } et β -himachalène) varie de 0.162 eV à 3.408 eV; Cela montre que toutes les réactions étudiées ont un caractère polaire, contrairement aux réactions utilisant les carbenes alcoxycarbènes et silane-carbene { :ccl(OCH₃), CF(OCH₃), :C(OCH₃)₂, :C(OH)₂ and :CH(SiH₃). } ont un caractère non-polaire car $\Delta\omega$ est inférieur à 1 ($\Delta\omega < 1$).

Keywords: cycloaddition [1+2], D.F.T, carbenes, nucleophilic power, electrophilic power, polar character, regioselectivity.

1. Introduction

Carbenes are defined as neutral species with divalent carbon with only six electrons of valence. They have long been considered to be very reactive and difficult to isolate transient species (Figure 1). These compounds are highly reactive, usually known to be unstable and have a very limited lifespan. (Cheng et al., 2004; de Frémont et al., 2009, Vignolle et al., 2006). For example, dimethyl carbene (Pezacki et al., 1999; Ford, et al., 1998) and dichlorocarbene (Chateaneuf et al., 1990) have, respectively, a half-life of the order of nanosecond and microsecond while dimethoxycarbene has a half-life of 2 milliseconds (Moss et al., 1988). This difference in the reactivity of dialkoxycarbenes is largely due to the interaction between n-oxygen electrons and the carbon orbital of carbene, increasing the energy of the $p\pi'$ carbene molecular orbital and ΔE value ($p\pi'-\sigma'$). (Figure 1). These interactions thus give dialkoxycarbenes a nucleophilic character (Rondan et al., 1980).

* Corresponding author

E-mail addresses: idrissi_82@hotmail.fr (M. El idrissi)

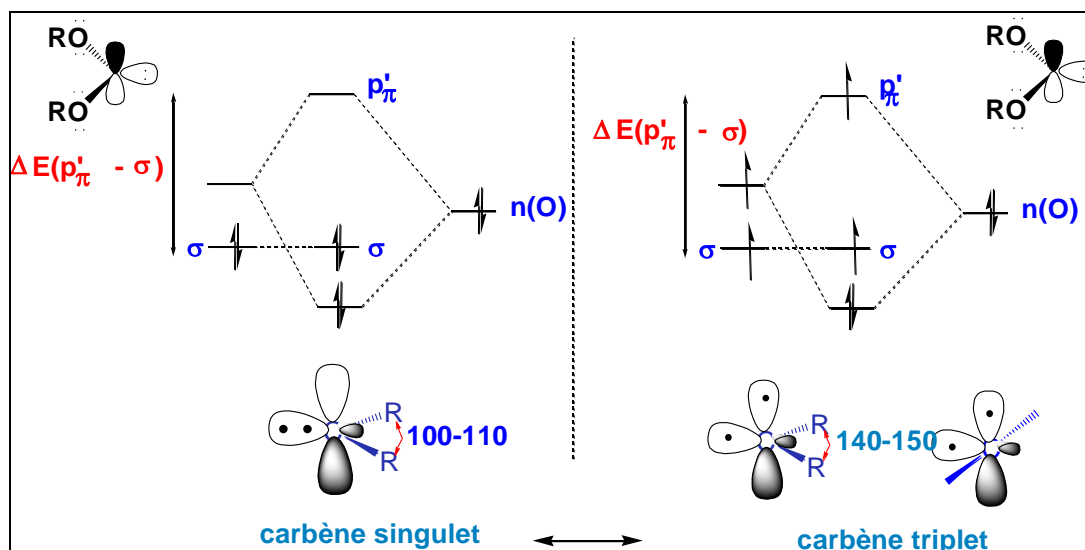


Fig. 1. Molecular orbital borders of a singlet and triplet dialkoxycarbenes

Computational methods

The equilibrium geometries were optimized at the calculation level B3LYP/6-31G(d) (Lee et al., 1988; Becke et al., 1993; Rassolov et al., 2001) using the Gaussian 09 (Schlegel et al., 1994), program using the Bery algorithm (Frisch et al., 2009). The transition states, corresponding to the two modes of alpha and beta epoxidation, were located at B3LYP/6-31G(d). Their existence has been confirmed by the presence of one and only imaginary frequency in the Hessian matrix. The maximum transfer of charges ΔN_{\max} that will allow us to define the electrophilic power of a system defined by: $\Delta N_{\max} = -\frac{\mu}{\eta}$. The global nucleophilicity index ω is defined by the expression (Parr et al., 1999) $\omega = \frac{\mu^2}{2\eta}$ with μ the electronic chemical potential $\mu = \left(\frac{\epsilon_{\text{HOMO}} + \epsilon_{\text{LUMO}}}{2}\right)$ and electronic hardness $\eta = (\epsilon_{\text{LUMO}} - \epsilon_{\text{HOMO}})$ (Parr, Yang, 1989).

Domingo et al (Domingo et al., 2002) proposed that if a molecule is weakly electrophilic, then it is systematically strongly nucleophilic only true for simple molecules. For high nucleophilicity values low values of ionization potentials and vice versa. Used the energies (HOMO) obtained by the Kohn-Sham method (Kohn et al., 1965). The empirical (relative) nucleophilicity (N) index is defined as follows (L. R. Domingo et al., 2002): $N = (E_{\text{HOMO}}(\text{Nu}) - E_{\text{HOMO}}(\text{TCE}))$.

Nucleophilicity is traced to tetra cyano ethylene (TCE) because TCE has the lowest HOMO energy value in the organic molecules series. The local electrophilic index and the local nucleophilicity index were evaluated using the following expressions (Domingo et al., 2013; Gleiter et al., 1968): $\omega_k = \omega \cdot P^+$ and $N_k = N \cdot P^-$ such as P^+ and P^- are the functions of electrophilic and nucleophilic Parr respectively (Hoffmann et al., 1968; Mendez et al., 2011), are obtained from the Mulliken atomic density analysis of the anion and the neutral molecule cation.

2. Results and discussion

Simplistically, the fundamental state of a carbene can be determined by comparing the values of $\Delta E(p\pi' - \sigma')$ to electronic and steric repulsion energies. In the event that the value of $\Delta E(p\pi' - \sigma')$ to the orbital $p\pi'$ to obtain the triplet state becomes more important than the electronic and steric repulsion energies related to the singlet state. A singular fundamental state is then observed. It has been suggested in the past that an existing carbene in the fundamental state singlet had a value of $\Delta E(p\pi' - \sigma')$ greater than 2 eV (46 kcal/mol) while a triplet carbene had a value of $\Delta E(p\pi' - \sigma')$ less than 1.5 eV (35 kcal/mol) (Kassaei et al., 2011; Hirai et al., 2009). These trends were confirmed by Mendez in a theoretical study of the electronic structure of a variety of carbenes. (Geise, Hadad, 2000) the latter has established that the value of ΔE_{ST} (by convention, a negative value of ΔE_{ST} implies a singlet state lower in energy than the triplet state). In the case of dimethoxycarbene, an ΔE_{ST} of -53.0 kcal/mol was calculated (Table 1). In 2011 Kassaei reported similar TSE values of -57 and -55 kcal/mol (Domingo et al., 2008; Domingo et al., 2002).

Table 1. Δ EST values calculated for the different carbenes

	Carbene	Δ EST(Kcal/mol)
1	CH(SiH ₃)	23,3
2	CH ₂	13,7
3	CH(CH ₃)	7,9
4	CCl(Ph)	-4,6
5	CHCl	-2,2
6	CH(Ph)	7,1
7	CCl(CH ₃)	-4,9
8	CHF	-12,1
9	CF(Ph)	-13,3
10	CCl ₂	-16,6
11	CF(Cl)	-33,4
12	CCl(OCH ₃)	-36,0
13	CF(OCH ₃)	-51,8
14	CF ₂	-52,1
15	C(OCH ₃) ₂	-53,0
16	C(OH) ₂	-54,5

Prediction of relative reactivity of reagents and polarity of cycloaddition reactions

The polar character of AD reactions can be obtained from the difference in the overall electrophiles of the reagents. This difference was used to determine the polar character of this type of reaction. Indeed, recent studies of AD reactions have shown that DFT-derived reactivity indices are an effective tool for establishing the polar/non-polar character of cycloaddition reactions (El Idrissi et al., 2014). The calculated values of the overall reactivity indices, namely the electronic chemical potential μ , global hardness η , global electrophilic ω , global nucleophilicity N and the overall maximum load transfer ΔN_{max} for reagents are given in Table 2.

Table 2. HOMO/LUMO energies, electronic chemical potential μ , global hardness η , global electrophilicity ω , global nucleophilicity N and maximum overall load transfer/ N_{max} of carbenes 1-18 and β -himachalene

Reactifs	carbene	HOMO	LUMO	μ	η	ω	N	ΔN_{max}
1	CH(SiH ₃)	-6,179	-1,006	-3,592	5,173	1,247	3,353	0,694
2	CH ₂	-6,625	-3,303	-4,964	3,322	3,708	2,907	1,494
3	CH ₂	-5,695	-2,076	-3,885	3,619	2,085	3,837	1,073
4	CH ₂	-5,747	-2,925	-4,336	2,822	3,331	3,785	1,536
5	CH(CH ₃)	-6,708	-3,292	-5	3,416	3,659	2,824	1,463
6	CCl(Ph)	-5,181	-2,666	-3,923	2,515	3,060	4,351	1,559
7	CHCl	-6,206	-2,557	-4,381	3,649	2,630	3,326	1,200
8	CHCl	-6,623	-2,557	-4,59	4,066	2,590	2,909	1,128
9	CH(Ph)	-5,774	-2,457	-4,115	3,317	2,553	3,758	1,240
10	CCl(CH ₃)	-7,357	-3,551	-5,454	3,806	3,907	2,175	1,433
11	CHF	-7,771	-2,998	-5,384	4,773	3,037	1,761	1,128
12	CF(Ph)	-6,669	-1,496	-4,082	5,173	1,610	2,863	0,789
13	CF(Ph)	-6,775	-0,767	-3,771	6,008	1,183	2,757	0,627
14	CCl ₂	-8,088	-2,111	-5,099	5,977	2,175	1,444	0,853
15	CF(Cl)	-5,806	-0,008	-2,907	5,798	0,728	3,726	0,501
16	CF(Cl)	-6,443	-0,137	-3,29	6,306	0,858	3,089	0,521
17	CCl(OCH)	-7,061	-3,600	-5,330	3,461	4,104	2,471	1,540
18	CF(OCH ₃)	-5,533	-3,045	-4,289	2,488	3,696	3,999	1,723
	CF ₂							

	C(OCH ₃) ₂ C(OH) ₂ C(Br) ₂ C(Ph) ₂							
19	β-himachalène	-5,692	0,693	-2,499	6,488	0,696	3,999	0,385

In the case of the reaction (1) between β-himachalene and CH(SiH₃) carbenes, the electronic chemical potential of β-himachalene ($\mu = -2.499$ u.a) is higher than that of CH(SiH₃) carbenes ($\mu = -3.592$ u.a); this indicates that the transfer of electrons will take place from β-himachalene to the CH(SiH₃) carbenes. On the other hand, the overall electrophilic index of β-himachalene ($\omega = 0.696$ eV) is lower than that of carbene C(Ph)₂ ($\omega = 1,247$ eV) and therefore CH(SiH₃) carbenes behave like an electrophilic, while β-himachalene behaves like a nucleophile. It is noted that the overall nucleophilicity indices also show that carbene CH(SiH₃) ($N = 3.353$ eV) is less nucleophilic than β-himachalene ($N = 3.427$ eV). In addition, ΔN_{max} , which represents the maximum load ratio that can be acquired by a system of its environment, is maximum for CH(SiH₃) (0,694) and minimum for β-himachalene (0,385).

For the reaction (2) between β-himachalene and CH₂ carbenes, the electronic chemical potential of β-himachalene ($\mu = -2.499$ u.a) is higher than that of CH₂ carbenes ($\mu = -4.964$ u.a); this indicates that the transfer of electrons will take place from β-himachalene to CH₂ carbenes. On the other hand, the overall electrophilic index of β-himachalene ($\omega = 0.696$ eV) is lower than that of carbene CH₂ ($\omega = 3.708$ eV) and therefore carbene CH₂ behaves like an electrophilic, while β-himachalene behaves like a nucleophile. It is noted that the overall nucleophilicity indices also show that CH₂ ($N = 2.907$ eV) is less nucleophilic than β-himachalene ($N = 3.427$ eV). In addition, ΔN_{max} , which represents the maximum load ratio that can be acquired by a system of its environment, is maximum for CH(SiH₃) (0,694) and minimum for β-himachalene (0,385).

For the reaction (2) between β-himachalene and CH₂ carbenes, the electronic chemical potential of β-himachalene ($\mu = -2.499$ u.a) is higher than that of CH₂ carbenes ($\mu = -4.964$ u.a); this indicates that the transfer of electrons will take place from β-himachalene to CH₂ carbenes. On the other hand, the overall electrophilic index of β-himachalene ($\omega = 0.696$ eV) is lower than that of carbene CH₂ ($\omega = 3.708$ eV) and therefore carbene CH₂ behaves like an electrophilic, while β-himachalene behaves like a nucleophile. It is noted that the overall nucleophilicity indices also show that CH₂ ($N = 2.907$ eV) is less nucleophilic than β-himachalene ($N = 3.427$ eV). In addition, ΔN_{max} , which represents the maximum load ratio that a system of its environment can acquire, is maximum for CH₂ (1,494) and minimum for β-himachalene (0,385). It is noted that the same remarks are observed during the reaction of β-himachalene with other carbenes {CH(CH₃), CCl(Ph), CHCl, CH(Ph), CCl(CH₃), CHF, CF(Ph), CCl₂, CF(Cl), CCl(OCH₃), CF(OCH₃), CF₂, C(OCH₃)₂, C(OH)₂, C(Br)₂ and C(Ph)₂}.

In order to show the donor (nucleophilic) or acceptor (electrophilic) character of the two reagents and the polar character of the reactions, we calculated the HOMO/LUMO energy gaps of the reagents and the differences in electrophilicity (Table 3).

Table 2 also shows that the $|E_{HOMO}^{\beta\text{-himachalene}} - E_{LUMO}^{\text{carbene}}|$ are lower than $|E_{HOMO}^{\text{Carbene}} - E_{LUMO}^{\beta\text{-Himachalene}}|$ for 18 reactions.

In conclusion, for the 18 reactions studied, carbenes behave like electrophiles (electron acceptors) and β-himachalene behaves like nucleophiles (electron donors).

Table 2 also shows that electrophilic differences, varies from 0.162 eV to 3.408 eV; showing that all reactions studied have a polar character except reactions where alkoxycarbenes and silane-carbene are used { :CCl(OCH₃) , :CF(OCH₃) , :C(OCH₃)₂ , :C(OH)₂ and :CH(SiH₃) } have a non-polar character because $\Delta\omega < 1$ (El Idrissi et al., 2014).

Table 3. Difference between the two possible combinations HOMO/LUMO and $\Delta\omega$ (eV)

Reactions	Carbenes	$ E_{\text{HOMO}}^{\text{Carbene}} - E_{\text{LUMO}}^{\beta\text{-Himachalène}} $	$ E_{\text{HOMO}}^{\beta\text{-himachalène}} - E_{\text{LUMO}}^{\text{carbene}} $	$\Delta\omega$ (eV)
1	:CH(SiH ₃)	6,872	4,6859	0,551
2	:CH ₂	7,318	2,388	3,012
3	:CH(CH ₃)	6,388	3,615	1,389
4	:CCl(Ph)	6,440	2,766	2,635
5	:CHCl	7,401	2,399	2,963
6	:CH(Ph)	5,874	3,025	2,364
7	:CCl(CH ₃)	6,899	3,134	1,934
8	:CHF	7,316	3,134	1,894
9	:CF(Ph)	6,467	3,234	1,857
10	:CCl ₂	8,050	2,140	3,211
11	:CF(Cl)	8,464	2,693	2,341
12	:CCl(OCH ₃)	7,362	4,195	0,914
13	:CF(OCH ₃)	7,468	4,924	0,487
14	:CF ₂	8,781	3,580	1,479
15	:C(OCH ₃) ₂	6,499	5,683	0,032
16	:C(OH) ₂	7,136	5,554	0,162
17	:C(Br) ₂	7,754	2,091	3,408
18	:C(Ph) ₂	6,226	2,646	3,000

According to écarts $|E_{\text{HOMO}}^{\beta\text{-himachalène}} - E_{\text{LUMO}}^{\text{carbene}}|$ and $|E_{\text{HOMO}}^{\text{Carbene}} - E_{\text{LUMO}}^{\beta\text{-Himachalène}}|$ and $\Delta\omega$ mentions in Table 2 it can be concluded that:

- The values of $\Delta\omega$ for reactions 13-15 (experimental data not available) are lower than those of previous reactions 1-12 (experimental data available). Therefore, reactions 13-15 predicted to be more scinetically disadvantaged compared to reactions 1-12;

- The gaps (HOMO/LUMO) for β -himachalene reactions with the following carbenes: :CH(SiH₃), :CCl(OCH₃), :CF(OCH₃), :C(OCH₃)₂, and :C(OH)₂. are greater than those of the β -himachalene reactions with the following carbenes: :CH(CH₃), :CCl(Ph), :CH(Ph), :CCl(CH₃), :CHF, :CF(Ph), :CF(Cl), :CF₂, :C(Ph)₂, :CH₂, :CHCl, :CCl₂, et :C(Br)₂. which shows that the reactions of β -himachalene with the following carbenes: CH(SiH₃), :CCl(OCH₃), :CF(OCH₃), :C(OCH₃)₂, et :C(OH)₂. are more kinetically difficult compared to the reactions of β -himachalene with the following carbenes: CH(CH₃), :CCl(Ph), :CH(Ph), :CCl(CH₃), :CHF, :CF(Ph), :CF(Cl), :CF₂, :C(Ph)₂, :CH₂, :CHCl, :CCl₂, and :C(Br)₂ as already predicted with the values of $\Delta\omega$.

Prediction of the region-chemoselectivity of the cycloaddition reactions studied

The best descriptors for studying local reactivity and regioselectivity of a cycloaddition reaction are local electrophilia and local nucleophilia. In a polar cycloaddition reaction between two replacement reagents. The interaction at two most favourable centres will take place between the most electrophilic centre characterized by the highest value of the local electrophilia index ω_k in the electrophilia, and the most nucleophilic center characterized by the highest value of the N_k local nucleophilia index in the nucleophilia. The local electrophilic powers and local nucleophilic power for 18 carbenes and atoms C2, C3, C6 and C7 of β -himachalene calculated with the function of Parr (Spin Atomic Density) are given in Table 4.

Table 4. Local electrophilic and nucleophilic power for the 18 carbenes and β -himachalene obtained by a Parr function calculus (atoms C2, C3, C6 and C7 of β -himachalene)

Carbenes	Reactifs	P^+	P^-	ω_k	N_k
1	CH(SiH ₃)	0,953	0,95	1,188	3,185
2	CH ₂	1,092	0,989	4,049	2,875
3	CH(CH ₃)	1,044	0,925	2,176	3,549
4	CCl(Ph)	1,01	0,535	3,364	2,024
5	CHCl	1,014	0,84	3,710	2,372
6	CH(Ph)	1,135	0,545	3,473	2,371
7	CCl(CH ₃)	0,963	0,783	2,532	2,604
8	CHF	0,983	0,84	2,545	2,443
9	CF(Ph)	0,98	0,533	2,501	2,003
10	CCl ₂	0,974	0,674	3,805	1,465
11	CF(Cl)	0,914	0,691	2,775	1,216
12	CCl(OCH ₃)	0,894	0,703	1,439	2,012
13	CF(OCH ₃)	0,873	0,737	1,032	2,031
14	CF ₂	0,899	0,769	1,955	1,110
15	C(OCH ₃) ₂	0,85	0,723	0,618	2,693
16	C(OH) ₂	0,916	0,932	0,785	2,878
17	C(Br) ₂	0,66	0,638	2,708	1,576
18	C(Ph) ₂	1,087	0,606	4,017	2,423
β -himacha-ène	C2	0,08	0,14	0,05	0,47
	C3	0,13	0,09	0,09	0,30
	C6	0,27	0,25	0,18	0,85
	C7	0,28	0,27	0,19	0,92

Static evidence of local electrophilia ω_k and N_k local nucleophilia are reliable descriptors for the prediction of the interaction electrophilia-nucleophilia most favoured for the formation of a chemical bond between two atoms. The values of local electrophilia ω_k for carbenes and N_k local nucleophilia for atoms C2, C3, C6 and C7 of β -himachalene, calculated with the function Parr (Spin Atomic Density) are reported in Table 4. The results show that the most favoured interaction will take place between the carbon atom of the carbene (having the highest value of ω_k) and the atoms C6 and C7 of the β -himachalene (having the highest value of N_k). Therefore, the experimentally observed regioselectivity is correctly predicted by the Parr functions.

For carbenics 15 and 16 the electrophilic power decreases, which indicates that carbenic C(OCH₃)₂ ($\omega = 0.728$ eV) is the least electrophilic system of this series. Therefore, Carbenes 15 and 16 can play the role of a nucleophile, so two approaches can be classified:

Interactions between β -himachalene HOMO and carbenes LUMO Figure 2.

The electrophilic attack of carbenes on β -himachalene takes place on the C6=C7 bond and allows to form cyclopropane, a study shows that the reaction of an equivalent of dichlorocarbene with an equivalent of β -himachalene is highly regio-selective, the interaction is between β -himachalene HOMO and carbene LUMO in a facial way (Figure 2).

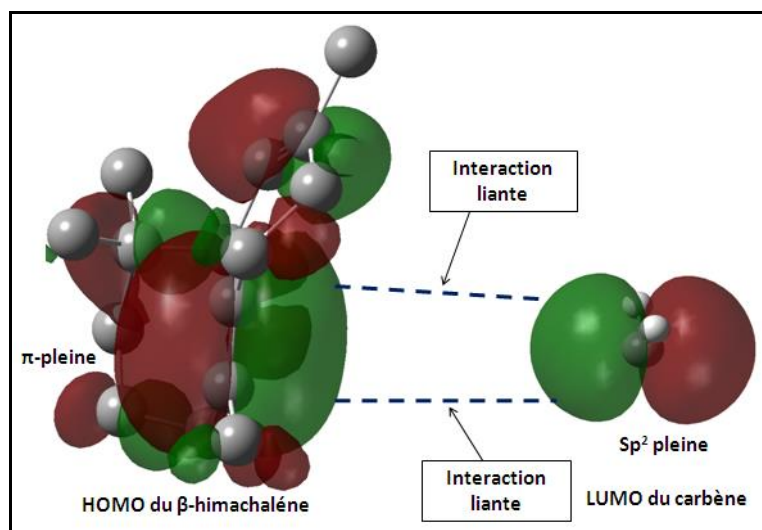


Fig. 2. Optimized structures and HOMO densities of β -himachalene and LUMO carbene density calculated by the B3 lyp/6-31 G(d) method

Interactions between β -himachalene LUMO and carbene HOMO [Figure 3](#).

The nucleophilic attack of the carbene (nucleophilic power of the carbenes is greater than the nucleophilic power of the β -himachalene) takes place at the level of the C6=C7 link because the local electrophilic power of the sites C6 and C7 is at the site of the sites C2 and C3, and the interaction between the Homo orbital of the carbene and Lumo of the β -himachalene and we find that the attack is facial ([Figure 3](#)).

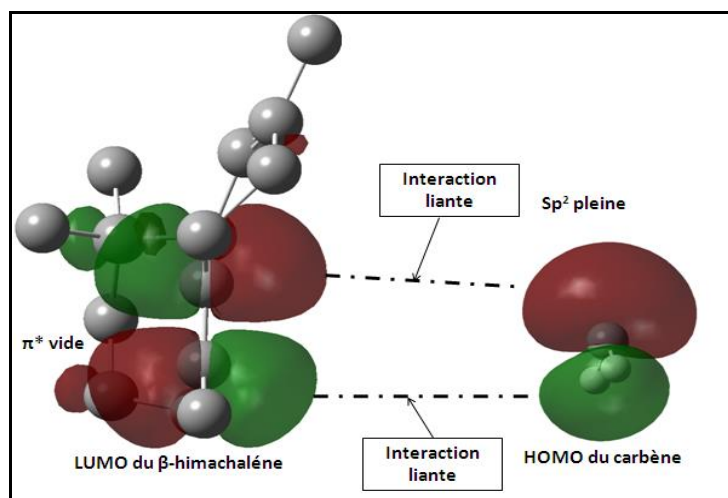


Fig. 3. Optimized structures and densities of β -himachalene and HOMO carbene density calculated by the B3 lyp/6-31 G(d) method

As mentioned above, the interaction between the orbital boundaries of the reagents is done in a facial way, one reagents approach each other the groupings substituted to the carbenes rotates out of the formed cyclopropanation to minimize steric congestion.

5. Conclusion

The regioselectivities of β -himachalenein cycloaddition reactions [1+2] have been studied using the index of local nucleophilia recently proposed by Domingo, P. Pérez and J. A. Sáez (Parr functions). Our results show that the experimental regioselectivities are correctly reproduced with this empirical index which proves to be more reliable than the net loads. Indeed, the index of local

nucleophilia predicts that the double link C6=C7 is more reactive than the link C2=C3 in both cases where β -himachalene plays the role of an electrophile or a nucleophile.

The difference in electrophilia between β -himachalene and carbenes makes it possible to classify these cycloaddition reactions into two categories: non-polar reactions where the following carbenes are used: (:CH(SiH₃), CCl(OCH₃), :CF(OCH₃), C(OCH₃)₂, :C(OH)₂).

Polar reactions if the following carbenes are used: (:CH₂, :CH(CH₃), :CCl(Ph), :CHCl, :CH(Ph), :CCl(CH₃), :CHF, :CF(Ph), , CCl₂, :CF(Cl), :CF₂, :C(Ph)₂).

References

- Becke et al., 1993 – Becke, Axel D. (1993). A new mixing of Hartree-Fock and local density-functional theories. *J. Chem. Phys.* Vol. 98, pp. 1372-1377.
- Chateaufneuf et al., 1990 – Chateaufneuf J.E., Johnson, R.P., Kirchnoff, M.M. (1990). *J. Am. Chem. Soc.* 112: 3217-3218.
- Cheng et al., 2004 – Cheng, Y. Meth-Cohn, O. (2004). Heterocycles Derived from Heteroatom-Substituted Carbenes. *Chem. Rev.* 104: 2507-2530.
- de Frémont et al., 2009 – de Frémont, P., Marion, N., Nolan, S.P. (2009). Carbenes: Synthesis, properties, and organometallic chemistry. *Coord. Chem. Rev.* 253: 862-892.
- Domingo et al., 2002 – Aurell, M.J., Perez, P., Contreras, R. (2002). Quantitative Characterization of the Global Electrophilicity Power of Common Diene/Dienophile Pairs in Diels-Alder Reactions. *Tetrahedron.* Vol. 58, pp. 4417-4423.
- Domingo et al., 2002 – Aurell, M.J., Pérez, P., Contreras, R. (2002). Quantitative characterization of the local electrophilicity of organic molecules. Understanding the regioselectivity on Diels–Alder reactions. *A.J. Phys. Chem.* Vol. 106, pp. 6871-6875.
- Domingo et al., 2008 – Chamorro, E., Perez, P. (2008). Understanding the reactivity of captodative ethylenes in polar cycloaddition reactions. A theoretical study. *J. Org. Chem.* 73 : 4615.
- Domingo et al., 2013 – Domingo, L.R., Pérez, P., Sáez, J.A. (2013). Understanding the local reactivity in polar organic reactions through electrophilic and nucleophilic Parr functions. *RSC Adv.* 3: 1486.
- El Idrissi et al., 2014 – Zeroual, A., Benharref, A. El Hajbi, A. (2014). Theoretical study of regioselectivity and stereoselectivity of condensation of β -himachalene with dichlorocarbene using density functional theory (DFT). *International Journal of Innovation and Applied Studies.* Vol. 5, pp. 120-130.
- Ford et al., 1998 – Ford, F., Yuzama, T., Platz, M.S., Matzinger, S., Fülscher, M. (1998). *J. Am. Chem. Soc.* 120: 4430-4438.
- Frisch et al., 2009 – Frisch, M.J. (2009). Gaussian, Inc., Wallingford CT.
- Geise, Hadad, 2000 – Geise M., Hadad, C.M. (2000). Computational Study of the Electronic Structure of Substituted Phenylcarbene in the Gas Phase. *J. Org. Chem.* 65: 8348-8356.
- Gleiter et al., 1968 – Gleiter R., Hoffmann, R. (1968). *J. Am. Chem. Soc.* 90: 5457-5460.
- Hirai et al., 2009 – Itoh, T. Tomioka, H. (2009). *Chem. Rev.* 109: 3275-3332.
- Hoffmann et al., 1968 – Hoffmann, R. (1968). Triethylene and addition of methylene to ethylene. *J. Am. Chem. Soc.* 90: 1475-1485.
- Kassaei et al., 2011 – Kassaei, M.Z., Ghambarian, M., Shakib, F.A., Momeni, M.R. (2011). Carbenes with reduced heteroatom stabilization: a computational approach. *J. Phys. Org. Chem.* 24: 351-359.
- Kohn et al., 1965 – Kohn, W., Sham, L. (1965). Self-Consistent Equations Including Exchange and Correlation Effects. *J. Phys. Rev.* 140: 1133-1338.
- Lee et al., 1988 – Lee, C.T., Yang, W.T., Parr, R.G. (1988). Density-Functional Exchange-Energy Approximation with Correct Asymptotic Behavior. *Phys. Rev. B.* Vol. 37, pp. 785-789.
- Mendez et al., 2011 – Mendez F., Garcia-Garibay, M.A. (2011). A hard–soft acid–base and DFT analysis of singlet–triplet gaps and the addition of singlet carbenes to alkenes. *J. Org. Chem.*, 64: 7061-7066.
- Moss et al., 1988 – Moss, R.A, Wlostowski, M., Shen, S., Krogh-Jespersen, K., Matro, A. (1988). Dimethoxycarbene: direct observation of an archetypal nucleophilic carbene. *Journal of the American Chemical Society.* 110 (13): 4443-4444.
- Parr et al., 1999 – Parr, R.G., von Szentpaly, L., Liu, S. (1999). Electrophilicity index. *J. Am. Chem. Soc.* 121, 1922-1924.

[Parr, Yang, 1989](#) – Parr, R., Yang, W. (1989). Density Functional Theory of Atoms and Molecules; Oxford University Press: New York.

[Pezacki et al., 1999](#) – Pezacki, J., Couture, P., Dunn, J.A., Warkentin, J., Wood, P.D., Luszyk, J., Ford, F., Platz, M.S. (1999). *J. Org. Chem.* 64: 4456-4464.

[Rassolov et al., 2001](#) – Rassolov, V.A., Ratner, M.A., Pople, J.A., Redfern, P.C., Curtiss, L.A. (2001). "6-31G* Basis Set for Third-Row Atoms. *J. Comp. Chem.* Vol. 22, pp. 976-984.

[Rondan et al., 1980](#) – Rondan, N.G., Houk, K.N., Moss, R.A. (1980). *J. Am. Chem. Soc.* 102: 1770-1776.

[Schlegel et al., 1994](#) – Schlegel, H.B. et al. (1994). Geometry Optimization on Potential Energy Surface. In: D.R. Yarkony (Ed.), *Modern Electronic Structure Theory*, World Scientific, Singapore.

[Vignolle et al., 2006](#) – Cattoën, X., Bourissou, D. (2006). Stable Noncyclic Singlet Carbenes. *Chem. Rev.* 109: 3333-3384.