

THE USE OF THE PARR FUNCTION FOR UNDERSTANDING THE REACTIVITY OF THE CARBENES WITH β -HIMACHALENE

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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 studied the regio-selectivity of the [1+2] cycloaddition reactions of the carbenes and β -himachalene by the D.F.T method at the level of the basis 6-31 (d), Using a new descriptor of the regio-selectivity concerns the function(office) of Parr. We notice according to this study that the attack of a mole of

carbenes is preferentially realized at the level of the C6=C7 connection of β -himachalene of in both possibilities of carbenes (nucleophile or electrophile). We also notice that the interaction between orbital borders of reactives (β -himachalene-carbenes) is realized in a facial way. The differences of electrophile $\Delta\omega$ between 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} and β -himachalene) vary from 0.162 eV to 3.408 eV. This shows that all studied reactions have a polar character, unlike reactions using alkoxy-carbenes and silane-carbene { :CCl(OCH₃), CF(OCH₃), :C(OCH₃)₂, :C(OH)₂ and :CH(SiH₃). } that have a non-polar character because $\Delta\omega$ is less than 1 ($\Delta\omega < 1$).

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

Introduction

Carbenes have been 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 [1-3]. For example, dimethyl carbene [4-5] and dichlorocarbene [6] have, respectively, a half-life of the order of nanosecond and microsecond while dimethoxycarbene has a half-life of 2 milliseconds [7]. 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). Thus, these interactions thus give dialkoxycarbenes a nucleophilic character [8].

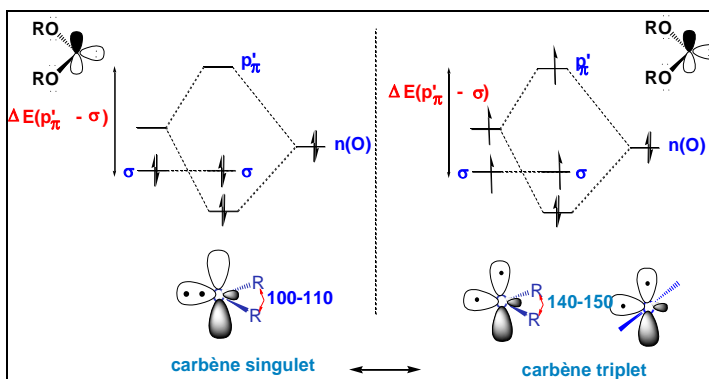


Figure 1: molecular orbital borders of a singlet and triplet dialkoxycarbene

Computational methods

The equilibrium geometries have been optimized at the calculation level B3LYP/6-31G(d) [9-11], using the Gaussian 09 [12], program that uses the Bery algorithm [13]. 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 so that: $\Delta N_{\max} = -\frac{\mu}{\eta}$. The global nucleophilicity index ω is defined by the expression [14] $\omega = \frac{\mu^2}{2\eta}$ with μ the electronic chemical potential $\mu = \left(\frac{\epsilon_{\text{HOMO}} + \epsilon_{\text{LUMO}}}{2}\right)$ and electronic hardness $\eta = (\epsilon_{\text{LUMO}} - \epsilon_{\text{HOMO}})$ [15].

Domingo et al. [16] have proposed that for simple molecules if a molecule is weakly electrophilic, then it is systematically strongly nucleophilic: So, to high nucleophilicity values should correspond low values of ionization potentials and vice versa. Using the energies (HOMO) obtained by the Kohn-Sham method [17] the empirical (relative) nucleophilicity (N) index has been defined as follows [18]: $N = (E_{\text{HOMO}}(\text{Nu}) - E_{\text{HOMO}}(\text{TCE}))$.

Nucleophilicity has been traced to tetra cyano ethylene (TCE) because TCE

since TCE has the lowest HOMO energy value in the organic molecules series. The local electrophilic index and the local nucleophilic index were evaluated using the following expressions [19-20]: $\omega_k = \omega.P^+$ and $N_k = N.P^-$ such as P^+ and P^- are the functions of electrophilic and nucleophilic Parr respectively [21-22] are obtained from the Mulliken atomic density analysis of the anion and the neutral molecule cation.

Results and discussion

In a simple way, 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 $\Delta E(pp-\sigma')$ less than 1.5 eV (35 kcal/mol). [23]. These trends have been confirmed by Mendez in a theoretical study on the electronic structure of a variety of carbenes. [24]. 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 Kassae has reported similar TSE values of -57.0 and -55.0 Kcal/mol [25].

Table 1: ΔE_{ST} values calculated for the different carbenes

	Carbene	ΔE_{ST} (Kcal/mol)
1	CH(SiH3)	23,3
2	CH2	13,7
3	CH(CH3)	7,9
4	CCl(Ph)	-4,6
5	CHCl	-2,2
6	CH(Ph)	7,1
7	CCl(CH3)	-4,9
8	CHF	-12,1
9	CF(Ph)	-13,3
10	CCl2	-16,6
11	CF(Cl)	-33,4
12	CCl(OCH3)	-36,0
13	CF(OCH3)	-51,8
14	CF2	-52,1
15	C(OCH3)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[26]. The calculated values of the overall reactivity indices, namely the electronic chemical potential μ , global hardness η , global electrophilicity 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(CH ₃)	-5,695	-2,076	-3,885	3,619	2,085	3,837	1,073
4	CCl(Ph)	-5,747	-2,925	-4,336	2,822	3,331	3,785	1,536
5	CHCl	-6,708	-3,292	-5	3,416	3,659	2,824	1,463
6	CH(Ph)	-5,181	-2,666	-3,923	2,515	3,06	4,351	1,559
7	CCl(CH ₃)	-6,206	-2,557	-4,381	3,649	2,63	3,326	1,2
8	CHF	-6,623	-2,557	-4,59	4,066	2,59	2,909	1,128
9	CF(Ph)	-5,774	-2,457	-4,115	3,317	2,553	3,758	1,24
10	CCl ₂	-7,357	-3,551	-5,454	3,806	3,907	2,175	1,433
11	CF(Cl)	-7,771	-2,998	-5,384	4,773	3,037	1,761	1,128
12	CCl(OCH)	-6,669	-1,496	-4,082	5,173	1,61	2,863	0,789
13	CF(OCH ₃)	-6,775	-0,767	-3,771	6,008	1,183	2,757	0,627
14	CF ₂	-8,088	-2,111	-5,099	5,977	2,175	1,444	0,853

15	C(OCH3)2	-5,806	-0,008	-2,907	5,798	0,728	3,726	0,501
16	C(OH)2	-6,443	-0,137	-3,29	6,306	0,858	3,089	0,521
17	C(Br)2	-7,061	-3,6	-5,33	3,461	4,104	2,471	1,54
18	C(Ph)2	-5,533	-3,045	-4,289	2,488	3,696	3,999	1,723
19	β- himachalne	-5,692	----	-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 carbeneC(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 carbeneCH(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 carbeneCH2($\omega= 3.708$ 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).

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 electrophilia (Table 3).

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

Reactions	Carbenes	A	B	$\Delta\omega(\text{eV})$
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)	6,44	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	8,05	2,14	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	3,58	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

**A: $|E_{\text{HOMO}}^{\text{Carbene}} - E_{\text{Lumo}}^{\beta\text{-Himachalene}}|$ and B: $|E_{\text{HOMO}}^{\beta\text{-himachalene}} - E_{\text{Lumo}}^{\text{carbene}}|$

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

In conclusion, for the 18 reactions studied, carbenes behave like electrophiles (electron acceptors) and β -himachalenebe has 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 alkoxy-carbenes and silane-carbene are used $\{:\text{CCl}(\text{OCH}_3), :\text{CF}(\text{OCH}_3), :\text{C}(\text{OCH}_3)_2, :\text{C}(\text{OH})_2 \text{ and } :\text{CH}(\text{SiH}_3)\}$ have a non-polar character because ρ is less than 1 ($\Delta\omega < 1$) [27].

According to the differences in terms of $|E_{\text{HOMO}}^{\beta\text{-himachalene}} - E_{\text{LUMO}}^{\text{carbene}}|$ and $|E_{\text{HOMO}}^{\text{carbene}} - E_{\text{LUMO}}^{\beta\text{-Himachalene}}|$ 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 have been predicted to be more kinetically disadvantaged compared to reactions 1-12;

➤ The gaps (HOMO/LUMO) for β -himachalene reactions with the following carbenes: $:\text{CH}(\text{SiH}_3), :\text{CCl}(\text{OCH}_3), :\text{CF}(\text{OCH}_3), :\text{C}(\text{OCH}_3)_2,$ and $:\text{C}(\text{OH})_2$ are greater than those of the β -himachalene reactions with the following carbenes: $:\text{CH}(\text{CH}_3), :\text{CCl}(\text{Ph}), :\text{CH}(\text{Ph}), :\text{CCl}(\text{CH}_3), :\text{CHF}, :\text{CF}(\text{Ph}), :\text{CF}(\text{Cl}), :\text{CF}_2, :\text{C}(\text{Ph})_2, :\text{CH}_2, :\text{CHCl}, :\text{CCl}_2,$ and $:\text{C}(\text{Br})_2$. These results show that the reactions of β -himachalene with the following carbenes: $\text{CH}(\text{SiH}_3), :\text{CCl}(\text{OCH}_3), :\text{CF}(\text{OCH}_3), :\text{C}(\text{OCH}_3)_2,$ and $:\text{C}(\text{OH})_2$ are more kinetically difficult compared to the reactions of β -himachalene with the following carbenes: $\text{CH}(\text{CH}_3), :\text{CCl}(\text{Ph}), :\text{CH}(\text{Ph}), :\text{CCl}(\text{CH}_3), :\text{CHF}, :\text{CF}(\text{Ph}), :\text{CF}(\text{Cl}), :\text{CF}_2, :\text{C}(\text{Ph})_2, :\text{CH}_2, :\text{CHCl}, :\text{CCl}_2,$ and $:\text{C}(\text{Br})_2$ 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 [28] and local nucleophilia [27]. 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 the 18 carbenes and atoms C2, C3, C6 and C7 atoms of β -himachalene calculated using 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	Reagents	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	3,71	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	1,11
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 -himachalene	C2	0,08	0,14	0,05	0,47
	C3	0,13	0,09	0,09	0,3
	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 [29], the interaction is between HOMO β -himachalene and LUMO carbene in a facial way (Figure 2).

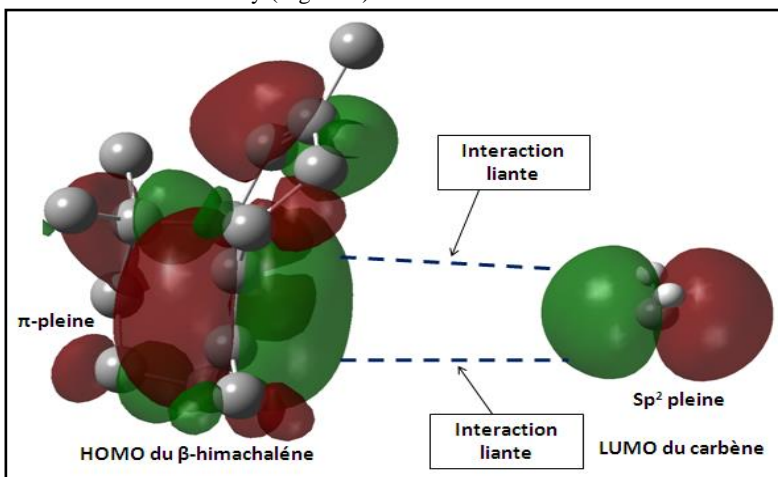


Figure 2: Optimized structures and HOMO densities of β -himachalene and LUMO carbene density calculated by the B3 lyp/6-31 G(d) method.

- 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).

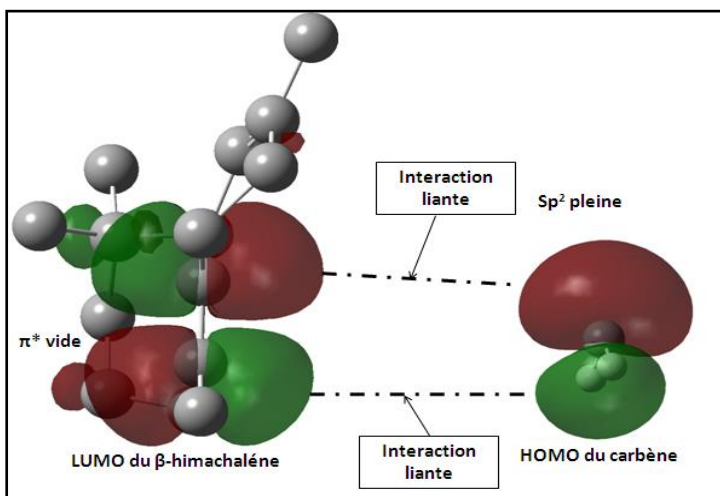


Figure 3: Optimized structures and densities of β -himachalene and HOMO carbene density calculated by the B3 lyp/6-31 G(d) method.

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.

Conclusion.

The regioselectivities of β -himachaleneincycloaddition reactions [1+2] have been studied using the index of local nucleophilicity 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 nucleophilicity 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 -himachaleneandcarbenes 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).

Conflict of interest

The authors declare that there is no conflict of interests regarding the publication of this paper. Also, they declare that this paper or part of it has not been published elsewhere.

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