



Research Article

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## Effect of haptotropic rearrangements on reactivity and biological activity in fluorenyl complexes: A DFT Study

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### ABSTRACT

Haptotropic rearrangements  $\pi$ - $\pi$  in fluorenyl complexes are carried out using density functional theory DFT at PBE/TZP level. The calculated activation barriers in  $\eta^6 \rightleftharpoons \eta^5$  of  $(C_{13}H_9)ML$  complexes, ( $M=Mn, Cr$  and  $Fe$ ), ( $L=(CO)_3$  and  $Cp$ ) are (27.731, 63.922 and 63.708  $Kcal.mol^{-1}$  respectively) and in  $\eta^5 \rightleftharpoons \eta^3$  of  $(\eta^5-9-R-C_{13}H_8)Mn(CO)_3$  complexes,  $R=Bu^t$  and  $Ph$  are 28.522 and 69.500  $Kcal.mol^{-1}$  respectively). Thermodynamic parameters of these compounds have been analyzed. The calculated of the redox potentials and the quantum chemical descriptors predict that the iron complex has strong biological activity and strong Lewis acid.

**Keywords:** Haptotropic rearrangements, DFT, activation barriers, redox potentials, biological activity, Lewis acid.

### INTRODUCTION

Haptotropic rearrangement (HR) is a migration of a transition metal fragment from one coordination site to the other on  $\pi$ -conjugated polyene or polyaromatic ligand [1]. Haptotropic migration of a metal fragment over aromatic system has been subject of many experimental and theoretical studies [2-5]. Most theoretical research focused on the  $\eta^6 \rightleftharpoons \eta^5$  rearrangement of  $Cr(CO)_3$  on naphthalene complexes [6] and other polycyclic aromatic hydrocarbons with up to four fused six-membered rings [7]. Haptotropic shifts play an important role in reactions with electronically saturated complexes [8-11] and associative substitution reactions [12,13].

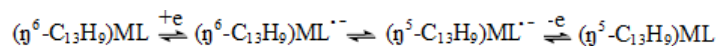
The bio-response of compounds can be the result of several types of interactions between the bioactive compound and the receptor, such as hydrophobic and electrostatic forces, hydrogen bonding and electron donor acceptor complex [14]. These interactions are closely related to physiochemical and structural properties of its component molecules. Therefore it is possible the prediction or explanation of the biological behavior of molecules from their physiochemical properties.

Some electrostatic properties i.e. electron affinity, LUMO's and HOMO's energies can be related to experimental properties such as redox potentials [15]. Furthermore, the latter is known to be related to bio-reduction or bio-oxidation processes of bioactive compounds [16]. The electrochemical response can be experimentally studied, i.e. by polarographic or by cyclic voltammetry techniques [17]. Redox potentials provide information on the feasibility of electron transfer and established relationships between the ease of reduction or oxidation and biological activities demonstrate the relevance of electrochemical studies as tools for the comprehension of drug mechanism of action against various diseases for the prediction of biological activities, and for the design of potentially active compounds [18, 19].

There were several examples for the fluorenyl ligand were qualitatively studied for many transition metals, results in an important specific features of their structures, e.g., unbridged metallocen complexes with fluorenyl ligand constitute precursors of catalysts for homogeneous of  $\alpha$ -olefins [20], in  $[Zr(C_5H_5)(C_{13}H_9)_2Cl](C_7H_8)$  complex facile

changes in hapticity  $\eta^5 \rightleftharpoons \eta^1$  (ring-slippage); this property influence the catalytic activity of this type of compounds [21].

A. I. Yarmolenko and al in 1994-1995 [22, 23] proposed two reactions mechanism  $\eta^6 \rightleftharpoons \eta^5$  and  $\eta^5 \rightleftharpoons \eta^3$  [24] in fluorenyl complexes (Schemes 1 and 2) by cyclic voltammetry in THF. These mechanism described by a catalytic  $E_1CE_2$ -scheme ( $E_1$  corresponds to the reduction process,  $E_2$  to oxidation process, and C to the reaction of haptotropic isomerization). In the first scheme, the existence of the oxidation process  $E_2$  makes possible the catalytic haptotropic isomerization of manganese induced by electron transfer with a current efficiency of more than 100 % [22].



Scheme 1

With M=Mn (Mechanism 1), Cr (Mechanism 2) and Fe (Mechanism 3)  
L=CO and Cp



Scheme 2

With R= Bu<sup>t</sup> and Ph

In this work we studied the mechanism of haptotropic rearrangements  $\pi$ - $\pi$  in  $(\text{C}_{13}\text{H}_9)\text{ML}$  complexes and some physiochemical properties related with such biological activity, such as electron donor acceptor, redox potentials and quantum chemical descriptors.

## EXPERIMENTAL SECTION

### Computational Method

DFT calculation were performed with the Amsterdam Density Functional (ADF) program developed by Bearends and al [25] on models  $(\text{C}_{13}\text{H}_9)\text{ML}$ , (M=Mn, Cr and Fe), (L=(CO)<sub>3</sub> and Cp). Electron correlation was treated within general gradient approximation (GGA) with the PBE functional [26], scalar relativistic effects were considered at the level of zero-order regular approximation method (ZORA) [27] with a TZP and the basis set superposition error (BSSE).

## RESULTS AND DISCUSSION

### Mechanism of haptotropic rearrangements

Three models structures bonded to C<sub>6</sub> ring were obtained revealing a  $\eta^6$ -coordination mode differing only in the metallic fragment, and two models of fluorenyl manganese tricarbonyl complexes containing two ligands of different nature R=Bu<sup>t</sup> and Ph, the  $\eta^5$ -structure corresponds to the 18-electrons manganese complexes [24]. The geometries of all complexes were optimized with constraint of symmetry. The selected optimized structures are shown in Fig. 1.

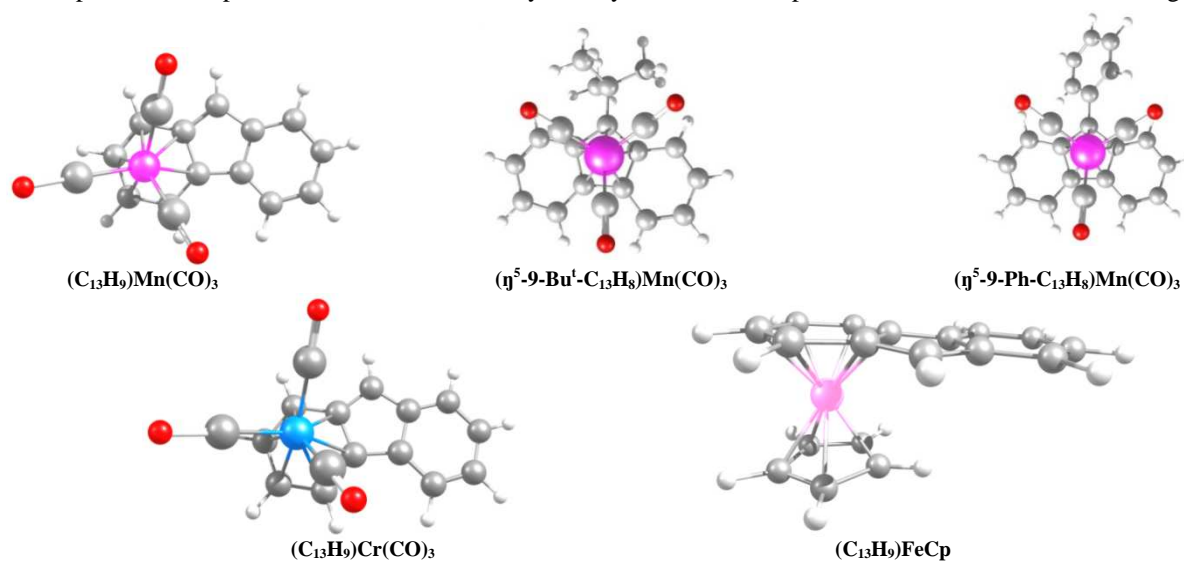


Fig. 1 Optimized geometrical structures of the five fluorenyl complexes

### Complexes of fluorenyl manganese tricarbonyl

In the search of haptotropic rearrangement (HR) reaction pathway, let us begin with the manganese tricarbonyl HR  $\eta^6 \rightleftharpoons \eta^5$  occurring in the  $(\eta^6\text{-C}_{13}\text{H}_9)\text{Mn}(\text{CO})_3$  complex. We found transition state (TS) in a  $\eta^3$ -coordination mode. The calculation activation barrier is  $27.731 \text{ Kcal.mol}^{-1}$ . The energetic profile is depicted in Fig. 2.

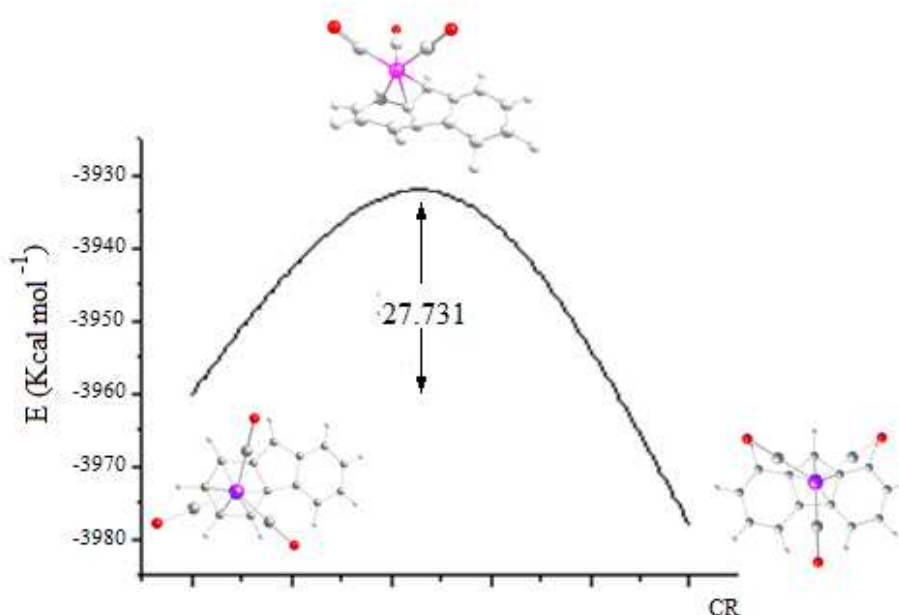


Fig. 2 Energy profile of the haptotropic migration in  $(\eta^6\text{-C}_{13}\text{H}_9)\text{Mn}(\text{CO})_3$  complex

The haptotropic migration  $\eta^5 \rightleftharpoons \eta^3$  of the manganese tricarbonyl was studied in  $(\eta^5\text{-9-R-C}_{13}\text{H}_8)\text{Mn}(\text{CO})_3$  complexes with 9-tert-butylfluorenyl and 9-phenylfluorenyl ligands and with activation barriers ( $28.522$  and  $69.500 \text{ Kcal.mol}^{-1}$  respectively)[24], these results predict a difficult reaction mechanism pathway with 9-phenylfluorenyl ligand compared with 9-hydrogenfluorenyl and 9-tert-butylfluorenyl ligands and explain the important specific features of their structures.

The distance of manganese to the ring center is about  $1.622 \text{ \AA}$ , smaller distance compared to benzene-Mn interaction of  $2.078 \text{ \AA}$ [28]. It is possible to explain the ease or the difficult reaction mechanism pathway from their average angle between the three rings center ( $\text{C}_6\text{-Cp-C}_6$ ).  $\text{Mn}(\text{CO})_3$  fragment rotate by  $5^\circ$  when going from the reactant to the transition state, this average decrease slightly when going from the transition state to the product ( $3^\circ$ ) (Table 1).

Table 1. Angles ( $^\circ$ ) between three rings center of the reactants, transition states and products of the three complexes

Mechanism	Reactants	TS	Products
Mechanism 1	142	147	144
Mechanism 2	150	135	149
Mechanism 3	152	137	144

### Complex of fluorenyl tricarbonylchromium

For the  $(\eta^6\text{-C}_{13}\text{H}_9)\text{Cr}(\text{CO})_3$  complex, it is worth to note that  $\text{Cr}(\text{CO})_3$  haptotropic rearrangement has been the subject of extensive experimental and theoretical investigations and it has more recently been extended to PAH and heteropolycyclic aromatic hydrocarbons such as phenanthrene., [29,30]benzofuran., [31-34] and complexes with more extended arene platforms [35,36]. Thus, the migration of  $\text{Cr}(\text{CO})_3$  from the  $\text{C}_6$  ring to the Cp ring is difficult (activation barrier  $63.922 \text{ Kcal.mol}^{-1}$ ). We located transition state (Fig. 3) in which the Cr is attached to a six carbon atoms in a  $\eta^6$ -fashion. The Cr-coordinated ring are elongated ( $1.724\text{-}1.726 \text{ \AA}$ )[37] in comparison with the distance of Cr-ring center ( $1.702 \text{ \AA}$ ), this value is a sign of lesser interaction of the  $\text{Cr}(\text{CO})_3$  fragment with  $\text{C}_6$  ring than  $(\text{C}_{13}\text{H}_9)\text{Mn}(\text{CO})_3$  complex ( $1.622 \text{ \AA}$ ). The migration of the  $\text{Cr}(\text{CO})_3$  fragment from the reactant to the transition state lead to a decrease in the angle between the three ring center ( $\text{C}_6\text{-Cp-C}_6$ ) ( $15^\circ$ ) and increase when going from the transition state to the product ( $14^\circ$ ), this average is longer than that obtained in  $(\text{C}_{13}\text{H}_9)\text{Mn}(\text{CO})_3$  complex (see Table 1).

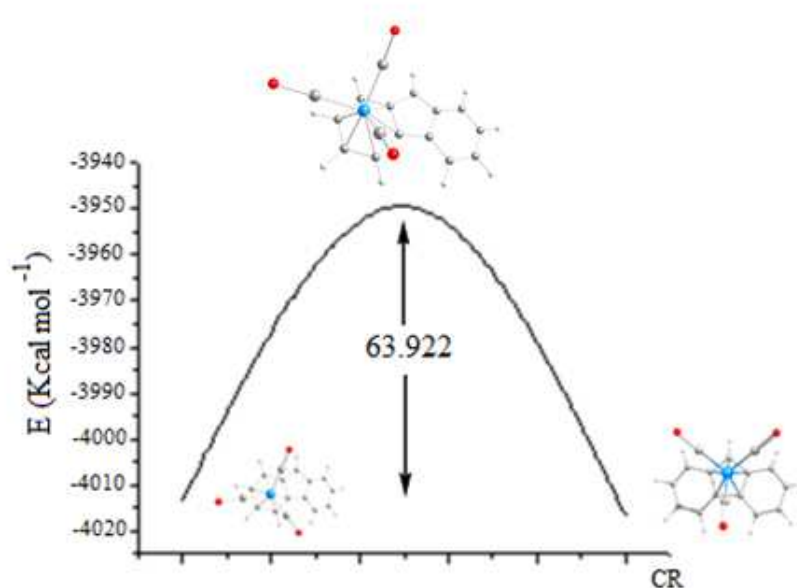


Fig. 3 Energy profile of the haptotropic migration in  $(\eta^6\text{-C}_{13}\text{H}_9)\text{Cr}(\text{CO})_3$  complex

#### Complex of fluorenyl cyclopentadienyliron

The haptotropic migration of FeCp obtained a similar energy barrier of  $63.708 \text{ Kcal.mol}^{-1}$  that the  $(\text{C}_{13}\text{H}_9)\text{Cr}(\text{CO})_3$  system. We found TS in which the FeCp fragment is coordinated to three atoms of the rings of the fluorenyl ligand. The energetic profile of the haptotropic rearrangement  $\eta^6 \rightleftharpoons \eta^5$  is shown in Fig. 4. The Fe-ring center distance of  $1.485 \text{ \AA}$  indicate that this interaction is stronger than that in the manganese and chromium complexes. It can be noted that when the FeCp group migrate from the reactant to the transition state give a same average angle in the  $(\text{C}_{13}\text{H}_9)\text{Cr}(\text{CO})_3$  system ( $15^\circ$ ). The migration from the TS to the product lead to increase in the average angle between the three rings center by  $7^\circ$  (Table 1).

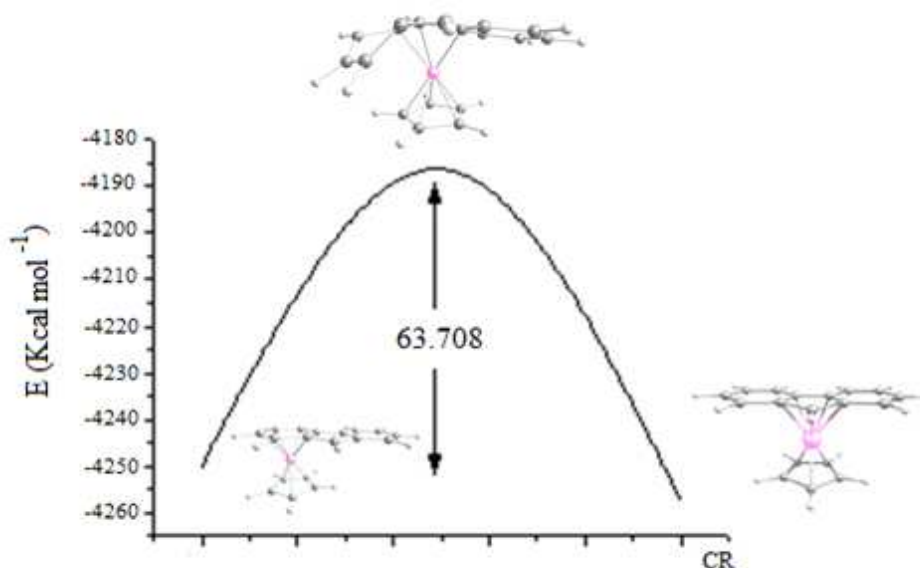


Fig. 4 Energy profile of the haptotropic migration in  $(\eta^6\text{-C}_{13}\text{H}_9)$  FeCp complex

#### Frontier molecular orbitals analysis

DFT molecular orbital diagrams (Fig. 5) display that the HOMO/LUMO gaps of three systems of Mn, Cr and Fe are ( $1.743 \text{ eV}$ ,  $1.998 \text{ eV}$  and  $1.093 \text{ eV}$  respectively), suggestive a good stability for these complexes. Furthermore,

these molecular orbital diagrams predict that these complexes contributed in the oxidation with energetics gaps (1.331eV for the manganese complex, 0.824eV for the chromium complex and 1.467eV for iron complex). The chromium complex oxidizes easily causes by high HOMO's energies. The complexes of Mn and Fe undergo to the ease reduction process with a similar frontier molecular orbitals.

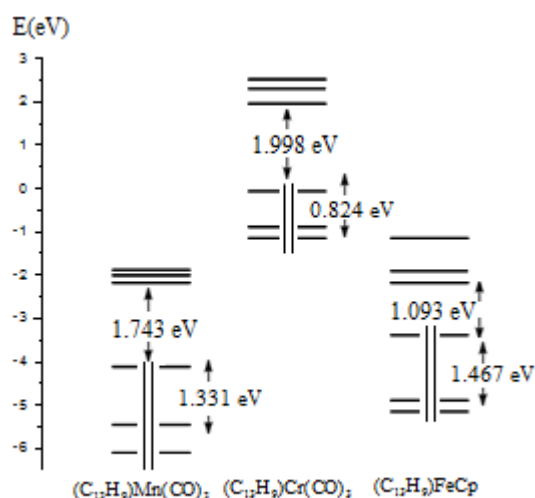


Fig. 5 DFT molecular orbital diagrams of the three complexes

### Thermodynamic parameters

Thermodynamic parameters of this haptotropic rearrangement are given in Table 2. A general observation can be to give an explication about the reaction mechanism pathway. A comparison between the kinetic and thermodynamic parameters reveals that the complex of Mn give a good results, lower activation barrier (27.731 Kcal.mol<sup>-1</sup>) and thermodynamically favored ( $\Delta_rG = -24.265$  Kcal.mol<sup>-1</sup>). In this mechanism, the reduction process is the determinate step, this observation can be to give an explication for the ease reduction process in the Mn complex (lower LUMO energy (-2.394 eV)). These results can be correlated to the results obtained in the molecular orbital diagrams.

Table 2. Thermodynamic parameters  $\Delta_rG$ ,  $\Delta_rH$  (in Kcal.mol<sup>-1</sup>) and  $\Delta_rS \times 10^{-3}$  (in Kcal.mol<sup>-1</sup>.K<sup>-1</sup>) in the three mechanism

Mechanism	$\Delta_rG$	$\Delta_rH$	$\Delta_rS$
Mechanism 1	-24.265	-22.155	7.468
Mechanism 2	-5.275	-5.275	0.123
Mechanism 3	-12.132	-12.132	2.302

### Redox potentials and Koopmans' theorem

Lastly, theoretically computed HOMO or LUMO energies of molecules are closely associated with the respective oxidation and reduction potentials of molecules [38].

Experimental oxidation and reduction potentials are obtained by means of cyclic voltammetry (CV), which is by far the most effective electro-analytical technique for the study of electro-active species.

In general, reduction potentials ( $E_{red}$ ), i.e. where neutral species are turned into corresponding anions, are expected to correlate with electron affinity (EA) while oxidation potentials ( $E_{ox}$ ) are to correlate with ionization potential (IP) [39].

Koopmans' theorem [38] is an important tool in electronic structure theory because it provides a simple and computationally efficient way to extract information about the successive ionization potentials of a system from correlated electronic structure methods. Koopmans' theorem has been explored as a method for computing the change in electron density from electron removal / attachment (the so-called Fukui function [40-42] and other reactivity indicators in DFT-based chemical reactivity theory [43]. According to this theorem, ionization energy is equal to the HOMO energy of a molecule, but of opposite sign, with the sequence that oxidation potentials may be related to HOMO energies. In the same way LUMO energy is related to reduction potentials. Both HOMO and LUMO energies may easily be calculated theoretically.

The aim of this work was to investigate the correlation between the redox potentials obtained and biological activities of the fluorenyl complexes studied. According to the scheme 1 and Fig.2, 3 and 4 we can separated the

reactions mechanism on two steps, the first step corresponds to reduction process started from the reactants to the transition states, and the second step corresponds to oxidation process, from the transition states to the products. Finally we calculate the reduction potentials ( $E_{red}$ ) of the reactants (LUMO energy), the oxidation potentials ( $E_{ox}$ ) of the transition states (HOMO energy) and the redox potentials ( $E_{redox}$ ). LUMO and HOMO energies were obtained directly from geometry optimized structure without further processing.

It is to be noted that biological activity decrease in the same order in which redox potential decrease. The redox potentials determined decrease significantly when going from the iron complex to manganese complex to the chromium complex (see Table 3). This observation can be suggests that the iron complex has stronger biological activity than the two others complexes.

**Table 3. Potentials redox (eV) of manganese, chromium and iron complexes**

Complex	$E_{red}$	$E_{ox}$	$E_{redox}$
$(\eta^6\text{-C}_{13}\text{H}_9)\text{Mn}(\text{CO})_3$	-2.394	-4.430	0.540
$(\eta^6\text{-C}_{13}\text{H}_9)\text{Cr}(\text{CO})_3$	1.668	-5.262	0.317
$(\eta^6\text{-C}_{13}\text{H}_9)\text{FeCp}$	-2.275	-3.552	0.640

### Calculation of quantum-chemical descriptors

The values of quantum chemical descriptors [44-46] are shown in Table 4. The greater chemical hardness and electronic chemical potential are explained by the higher HOMO energy. Thus,  $(\eta^6\text{-C}_{13}\text{H}_9)\text{Cr}(\text{CO})_3$  complex present a higher capacity to donate electrons than the two others complexes. For the electrophilicity values,  $(\eta^6\text{-C}_{13}\text{H}_9)\text{FeCp}$  complex present a higher capacity to accept electrons. On the other hand, there are similar correlations between the DFT molecular orbital diagrams (Fig. 5) and the quantum chemical descriptors.

**Table 4. Quantum chemical descriptors (eV) in the three complexes**

Complex	$\mu$	$\eta$	$\omega$	HOMO	LUMO
$(\eta^6\text{-C}_{13}\text{H}_9)\text{Mn}(\text{CO})_3$	-3.265	0.871	6.121	-4.137	-2.394
$(\eta^6\text{-C}_{13}\text{H}_9)\text{Cr}(\text{CO})_3$	0.669	0.999	0.223	-0.330	1.668
$(\eta^6\text{-C}_{13}\text{H}_9)\text{FeCp}$	2.821	0.546	7.287	-3.368	-2.275

### CONCLUSION

The DFT study of the geometric parameters shows that the average angle in the  $(\eta^6\text{-C}_{13}\text{H}_9)\text{Cr}(\text{CO})_3$  and  $(\eta^6\text{-C}_{13}\text{H}_9)\text{FeCp}$  complexes is very long than in the  $(\eta^6\text{-C}_{13}\text{H}_9)\text{Mn}(\text{CO})_3$  complex. This result can be correlated to the importance results obtained in the haptotropic rearrangements  $\pi\text{-}\pi$ , when the manganese complex give a lower activation barrier ( $27.731\text{Kcal.mol}^{-1}$ ) and thermodynamically favored ( $\Delta_rG = -24.265\text{Kcal.mol}^{-1}$ ) and an easier reduction process with lower LUMO energy (-2.394 eV).

For the manganetricarbonyl complexes, the values of the activation barriers predict a difficult reaction mechanism pathway with 9-phenylfluorenyl ligand compared with 9-hydrogenfluorenyl and 9-tert-butylfluorenyl ligands and explain the important specific features of their structures.

The calculated of the physiochemical descriptors  $E_{ox}$ ,  $E_{red}$ ,  $E_{redox}$  and the quantum chemical descriptors predict that the iron complex has strong biological activity and strong Lewis acid.

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