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Spin-Polarized Conceptual Density Functional Theory Study of the Regioselectivity in the [2+2] Photocycloaddition of Enones to Substituted Alkenes

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A study of the regioselectivity of the photochemical [2+2] cycloaddition of triplet enones with a series of ground-state electron-rich and electron-poor alkenes using density functional theory (DFT)-based reactivity descriptors is presented. Using the concepts of local softness combined with a local hard and soft acids and bases principle and a softness matching approach, the regioselectivity of this reaction can only be explained in the case of the interaction of the triplet enones with electron-rich alkenes. In the next part, the regioselectivity was assessed within the framework of conceptual spin-polarized conceptual DFT, considering response functions of the system's external potential v, number of electrons N, and spin number N_S (with N_S being the difference between the number of α and β electrons in the spin-polarized system). Within this theory, the concepts of local spin philicity and donicity are introduced. Using the spin philicity concept, the regioselectivity can almost be completely interpreted as resulting from the interaction of the site on the alkene with the highest spin philicity (i.e., lowest destabilization upon increasing spin number) with the site showing the highest change of spin number on the enone expected to result in the largest stabilization of this species.

1. Introduction

The photochemical [2+2] cycloaddition of α,β-unsaturated carbonyl compounds (enones) to substituted alkenes, shown in Figure 1, is an important, widely used reaction, because it constitutes a particularly useful tool in the synthesis of cyclobutanes.[1] It is, by now, well-established that this photochemical cycloaddition involves the attack of an alkene to the triplet ($\pi-\pi^*$)- excited enone, leading to the formation of an 1,4-biradical intermediate, which, after intersystem crossing to the singlet ground-state potential energy surface, can react to yield the cyclobutane derivative.[1] Next to a vast amount of experimental data,[1] this reaction has also been the subject of many theoretical investigations.[2−10]

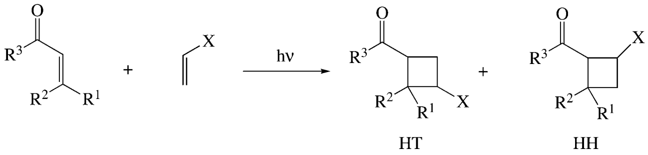

Figure 1. [2+2] Photocycloaddition of a triplet α, β-unsaturated carbonyl compound to a singlet ethylene, with an indication of the head-to-head (HH) and the head-to-tail (HT) regioselectivities.

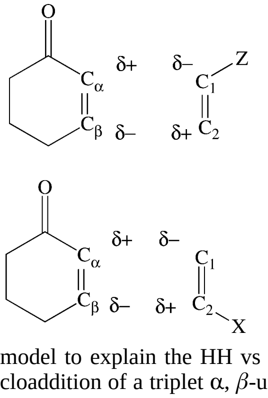

Figure 2. Exciplex model to explain the HH vs HT regioselectivity in the [2+2] photocycloaddition of a triplet α, β-unsaturated carbonyl compound to an electron-deficient (substituent Z) and an electron-rich (substituent X) alkene.

Initially, it was postulated that the reaction proceeded through the interaction of a $^3(n\pi^*)$ excited enone with the alkene, where the regioselectivity would then be determined by the specific electrostatic interaction between reacting molecules in this π complex or exciplex.[1a] This exciplex, shown in Figure 2, will result in the head-to-head (HH) regioselectivity in the case of electron-deficient alkenes (i.e., with an electron-withdrawing substituent Z on the double bond) and the head-to-tail (HT) regioselectivity for electron-rich alkenes (the substituent X on the double bond now being an electron-donating group). The regioselectivity for the first biradical producing step in the addition of 2-cyclohexenone to alkenes was studied by Broeker et al.,[2] using acrolein to model the 2-cyclohexenone. These authors indeed confirmed the $^3(n\pi^*)$ polarity put forward by Corey, but found that the minimum energy triplet is the $^3(\pi\pi^*)$ state of the enone, showing the reverse polarity at the α and β C atoms of the enone. From calculated activation barrier differences, these authors concluded that, in the case of electron-deficient alkenes, the enone attacks the alkene on the least-substituted terminus by its β carbon whereas, in the case of the electron-rich alkenes, this attack occurs via the α carbon of the enone. Suishu et al. investigated the regioselectivity of the

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reaction of some cyclic enones using a frontier molecular orbital (FMO) method.[5] These authors have concluded that the regioselectivities are mainly determined in the initial biradical formation step, in agreement with the conclusions made by Broeker et al.[2] More specifically, the addition to electron-rich alkenes was determined to be well-correlated with the FMO interaction factors associated to the first biradical formation step. In the case of the electron-deficient alkenes, the data suggest that also the reversal of the biradical intermediates is relatively efficient. Very recently, the effect of the alkene ring size on the regioselectivity of the addition of 2-cyclohexenone with 1-cycloalkenecarboxylates was studied using transition-state energies, deformation energies, and an FMO analysis.[6]

Weedon et al.[11] performed biradical trapping experiments[11] for several enone−alkene systems. From the study of the trapped biradical intermediates, they concluded that the regioselectivity of the reaction is governed by the competition of the ring closure step of the biradical and the reversal of this intermediate to the ground-state reagents. The complete reaction path of the cycloaddition of acrolein to ethylene was studied by Wilsey et al.,[7] using the CASSCF method, both for the singlet S_0 ground state and the $\pi\pi^*$ triplet excited-state T_1. In a subsequent contribution, the ground and first triplet excited-state potential energy potential energy surface for the addition of 2-cyclohexenone, methyl acrylate, and methyl crotonate to ethylene was investigated using CASSCF and DFT-B3LYP levels of theory.[8] Next to the competition of the ring closure step and the fragmentation path, these authors have also considered the competition between the deactivation of the $\pi\pi^*$ triplet enone and the reaction of this species with the alkene. It was concluded that the outcome of the reaction is governed by the competition between the deactivation of the $^3(\pi\pi^*)$ enone and its reaction with the alkene, leading to the formation of the 1,4-biradical. In a theoretical analysis of the photochemical addition of chiral and polyfunctional 2-cyclohexenones to 1,1-diethoxyethylene, García-Expósito et al. concluded that the regioselectivity is determined by the relative rate of the biradical formation and not by the relative stabilities of these species.[9] Bertrand et al.[10] also studied the complete reaction profile for the addition of acrolein to ethylene, to model cycloenones, on various theoretical levels to provide guidelines for choosing an appropriate computational method to describe the photochemical [2+2] cycloaddition.

In this work, the regioselectivity of the [2+2] photocycloaddition of triplet α,β-unsaturated carbonyl compounds to alkenes is investigated using density functional theory (DFT)-based reactivity descriptors. Generally, for systems in the triplet state, the α and β electron densities will be different and one must work within the framework of spin-polarized DFT.[12] Spin-polarized conceptual DFT[13] allows the researcher to obtain more insight into the chemical properties of systems with spin polarization (i.e. with a difference between α − and β-electron density), which is the case for the triplet enones, and properties related to the change in spin number ($N_S = N_\alpha - N_b$), which is the case in this cycloaddition. Within this framework, many response functions have been introduced that can be used to describe the chemical reactivity of spin-polarized systems.[13] In 1988, Galván, Vela and Gázquez introduced spin-polarized conceptual DFT, deriving expressions for the spin potential μ_S, the spin hardness η_{SS} and the Fukui functions f_{NN}, f_{NS}, and f_{SS}.[13a] Pérez et al. defined the concepts spin philicity and spin donicity[14] within this spin-polarized conceptual DFT. In their work, they demonstrated the applicability of these indices in the interpretation of the spin-catalytic effect of some diatomic and triatomic molecules. Oláh et al.[15] investigated a large set of substituted carbenes, silylenes, germylenes, and stannylenes using the spin potential, spin hardness, spin-philicity, and donicity. In this work, next to a study involving the more-traditional DFT-based reactivity indices such as Fukui functions and local softnesses, a local version of spin-philicity and spin-donicity concepts will be derived to investigate the spin coupling in the first biradical formation step of the [2+2] photocycloaddition of triplet enones to substituted alkenes.

2. Theoretical Background

Conceptual DFT[16] offers the possibility to rationalize well-known empirical but rather intuitively defined chemical concepts as hardness,[17,18] softness[17,19] and electronegativity,[20,21] and gives their theoretical definition to calculate them from first principles. For a N-electron system with external potential (i.e., potential due to the nuclei) $v(\mathbf{r})$ and total energy E, Parr et al. showed that the electronegativity[21] could be identified as the negative of the electronic chemical potential μ:

$$\chi = -\mu = -\left(\frac{\partial E}{\partial N}\right)_{v(\mathbf{r})} \approx -\frac{I+A}{2} \tag{1}$$

where I and A are the vertical ionization energy and electron affinity, respectively.

Chemical hardness and softness were introduced by Pearson[17] in 1963 when he was studying and classifying Lewis acid and base interactions. He formulated the hard and soft acids and bases (HSAB) principle “hard acids prefer to bond to hard bases and soft acids prefer to interact with soft bases”.[17] In 1983, Parr and Pearson proposed a quantitative definition of this hardness:[18]

$$\eta = \frac{1}{2}\left(\frac{\partial^2 E}{\partial N^2}\right)_{v(\mathbf{r})} = \frac{1}{2}\left(\frac{\partial \mu}{\partial N}\right)_{v(\mathbf{r})} \approx \frac{I-A}{2} \tag{2}$$

measuring the system’s resistance toward charge transfer.

The softness S is defined as the inverse of the hardness:[19]

$$S = \frac{1}{2\eta} \tag{3}$$

The local counterpart of the softness, the local softness, was introduced by Parr and Yang as[19,22]

$$s(\mathbf{r}) = \left(\frac{\partial \rho(\mathbf{r})}{\partial \mu}\right)_{v(\mathbf{r})} = \left(\frac{\partial \rho(\mathbf{r})}{\partial N}\right)_{v(\mathbf{r})}\left(\frac{\partial N}{\partial \mu}\right)_{v(\mathbf{r})} = Sf(\mathbf{r}) \tag{4}$$

In this equation, $f(\mathbf{r})$ is the Fukui function, which, because of the discontinuity of the $\rho(\mathbf{r})$, with respect to N, can be computed either for nucleophilic ($f^+(\mathbf{r})$) attack, electrophilic ($f^-(\mathbf{r})$) attack, or a radical attack ($f^0(\mathbf{r})$):[23]

$$f^+(\mathbf{r}) = \left(\frac{\partial \rho(\mathbf{r})}{\partial N}\right)^+_{v(\mathbf{r})} \approx \rho_{N+1}(\mathbf{r}) - \rho_N(\mathbf{r}) \tag{5}$$

$$f^-(\mathbf{r}) = \left(\frac{\partial \rho(\mathbf{r})}{\partial N}\right)^-_{v(\mathbf{r})} \approx \rho_N(\mathbf{r}) - \rho_{N-1}(\mathbf{r}) \tag{6}$$

$$f^0(\mathbf{r}) = \frac{f^+(\mathbf{r}) + f^-(\mathbf{r})}{2} \tag{7}$$

where $\rho_N(\mathbf{r})$, $\rho_{N+1}(\mathbf{r})$, and $\rho_{N-1}(\mathbf{r})$ are the densities of the N, $N + 1$, and $N - 1$ electron system, which are computed at the equilibrium geometry of the N_0 electron system (at a constant external potential v).

The theoretical justification of the HSAB principle was given by Chattaraj, Lee, and Parr.[24] Recently, this HSAB principle has been applied, both at the local and the global level, for the rationalization of regioselectivity and reactivity of many problems.[16f,25]

It is important to mention that the aforementioned response functions are governing changes from one ground state to another. The famous Hohenberg−Kohn-theorems,[26] on which DFT is based, were also initially developed for the ground states but later could be generalized to time-dependent electron densities and external potentials.[27,28] Applications of these DFT-based reactivity indices to excited states have, however, been scarce.[15,29]

For atomic and molecular systems in the triplet state, the density of the α and β electron densities will differ and one must work within the framework of spin-polarized DFT.[13] The spin-polarized conceptual DFT was introduced by Galván, Vela, and Gázquez.[13a]

The first-order partial derivative of the energy, with respect to the total number of electrons at constant spin number (μ_N) is the equivalent of the chemical potential μ in the spin-restricted case:[13]

$$\mu_N = \left(\frac{\partial E}{\partial N}\right)_{N_S, v(\mathbf{r}), \boldsymbol{B}} \tag{8}$$

where $\boldsymbol{B}$ is the external magnetic field and N_S is the spin number,

$$N_S = N_\alpha - N_\beta \tag{9}$$

which represents the difference in the number of α electrons (N_α) and β electrons (N_β).

The spin potentials and μ_N and μ_S are introduced as the partial derivatives of the energy E, with respect to the number of electrons N (at constant external potential $v(\mathbf{r})$ and spin number N_S) and spin number N_S (at constant external potential $v(\mathbf{r})$ and the number of electrons N), respectively.[13]

$$\mu_N = \left(\frac{\partial E}{\partial N}\right)_{N_S, v(\mathbf{r}), \boldsymbol{B}} \tag{10}$$

$$\mu_S = \left(\frac{\partial E}{\partial N_S}\right)_{N, v(\mathbf{r}), \boldsymbol{B}} \tag{11}$$

μ_N is equivalent to the chemical potential in the spin-restricted case, except that the derivative is taken at constant N_S; the spin potential μ_S is a measure of the tendency of the system to change its spin polarization.[13] The variations in μ_N and μ_S can be expressed as[13]

$$\mathrm{d}\mu_N = \eta_{NN}\,\mathrm{d}N + \eta_{NS}\,\mathrm{d}N_S + \int f_{NN}(\mathbf{r})\delta v(\mathbf{r})\,\mathrm{d}\mathbf{r} - \mu_B \int f_{NS}(\mathbf{r})\delta \boldsymbol{B}(\mathbf{r})\,\mathrm{d}\mathbf{r} \tag{12}$$

and

$$\mathrm{d}\mu_S = \eta_{NS}\,\mathrm{d}N + \eta_{SS}\,\mathrm{d}N_S + \int f_{NS}(\mathbf{r})\delta v(\mathbf{r})\,\mathrm{d}\mathbf{r} - \mu_B \int f_{SS}(\mathbf{r})\delta \boldsymbol{B}(\mathbf{r})\,\mathrm{d}\mathbf{r} \tag{13}$$

where μ_B is the electron Bohr magneton. The hardnesses in these equations are given by[13]

$$\eta_{SS} = \left(\frac{\partial \mu_S}{\partial N_S}\right)_{N, v(\mathbf{r}), \boldsymbol{B}} = \left(\frac{\partial^2 E}{\partial {N_S}^2}\right)_{N, v(\mathbf{r}), \boldsymbol{B}} \tag{14}$$

$$\eta_{SN} = (\eta_{NS}) = \left(\frac{\partial \mu_S}{\partial N}\right)_{N_s, v(\mathbf{r}), \boldsymbol{B}} = \left(\frac{\partial \mu_N}{\partial N_S}\right)_{N, v(\mathbf{r}), \boldsymbol{B}} \tag{15}$$

$$\eta_{NN} = \left(\frac{\partial \mu_N}{\partial N}\right)_{N_S, v(\mathbf{r}), \boldsymbol{B}} \tag{16}$$

Here, η_{NN} is the equivalent of the hardness in the spin-restricted case, except, again, that the derivative is evaluated at a fixed spin number N_S. η_{SS} is called the spin hardness and is evaluated at a constant number of electrons N, and provides information about the different valence states of the system.[13] The different Fukui functions in eqs 12 and 13 are given as[13]

$$f_{NN}(\mathbf{r}) = \left(\frac{\partial \rho(\mathbf{r})}{\partial N}\right)_{N_S, v(\mathbf{r}), \boldsymbol{B}} = \left(\frac{\delta \mu_N}{\delta v(\mathbf{r})}\right)_{N, N_S, v(\mathbf{r})} \tag{17}$$

$$f_{NS}(\mathbf{r}) = \left(\frac{\partial \rho(\mathbf{r})}{\partial N_S}\right)_{N, v(\mathbf{r}), \boldsymbol{B}} = \left(\frac{\delta \mu_S}{\delta v(\mathbf{r})}\right)_{N, N_S, v(\mathbf{r})} \tag{18}$$

$$f_{SN}(\mathbf{r}) = \left(\frac{\partial \rho_s(\mathbf{r})}{\partial N}\right)_{N_S, v(\mathbf{r}), \boldsymbol{B}} = -\frac{1}{\mu_B}\left(\frac{\delta \mu_N}{\delta \boldsymbol{B}(\mathbf{r})}\right)_{N, N_S, v(\mathbf{r})} \tag{19}$$

$$f_{SS}(\mathbf{r}) = \left(\frac{\partial \rho_s(\mathbf{r})}{\partial N_S}\right)_{N, v(\mathbf{r}), \boldsymbol{B}} = -\frac{1}{\mu_B}\left(\frac{\delta \mu_S}{\delta \boldsymbol{B}(\mathbf{r})}\right)_{N, N_S, v(\mathbf{r})} \tag{20}$$

The functions $f_{NS}(\mathbf{r})$, $f_{SN}(\mathbf{r})$, and $f_{SS}(\mathbf{r})$ are the equivalents of the Fukui function $f_{NN}(\mathbf{r})$ of the spin-restricted case (except, again, that the derivative is evaluated at a fixed spin number N_S).[13] As can be seen, $f_{NS}(\mathbf{r})$ and $f_{SS}(\mathbf{r})$ will measure the response of the electron density $\rho(\mathbf{r})$ and the spin density $\rho_S(\mathbf{r})$, relative to changes in the spin number N_S.

After the total energy is known, one can study the energy change as a function of the spin number, the energy change from a ground state to a promoted state of different multiplicity. The total energy of a system can be expanded in a Taylor series around the reference ground state and the energy difference between the ground and promoted state, at a constant number of total electrons and external potential, can be written up to second order as[13,14]

$$\Delta E_{v,N} \approx \mu_S^0 \Delta N_S + \frac{1}{2}\eta_{SS}^0 (\Delta N_S)^2 \tag{21}$$

In this expression, μ_s^0 must always be calculated in a given direction, substituting μ_S^0 by ${\mu_S}^+$ when describing changes with increasing spin number and by ${\mu_S}^-$ when the spin number is decreasing. The chemical potentials ${\mu_S}^+$ and ${\mu_S}^-$ can be approximated as[13]

$${\mu_S}^+ \approx \frac{(\epsilon_{\mathrm{LUMO}}^{\alpha} - \epsilon_{\mathrm{HOMO}}^{\beta})}{2} \tag{22}$$

and

$${\mu_S}^- \approx \frac{(\epsilon_{\mathrm{HOMO}}^{\alpha} - \epsilon_{\mathrm{LUMO}}^{\beta})}{2} \tag{23}$$

where $\epsilon_{\mathrm{HOMO}}^{\alpha}$, $\epsilon_{\mathrm{HOMO}}^{\beta}$, $\epsilon_{\mathrm{LUMO}}^{\alpha}$, and $\epsilon_{\mathrm{LUMO}}^{\beta}$ are the orbital energies of the α and β HOMO and LUMO orbitals, respectively,

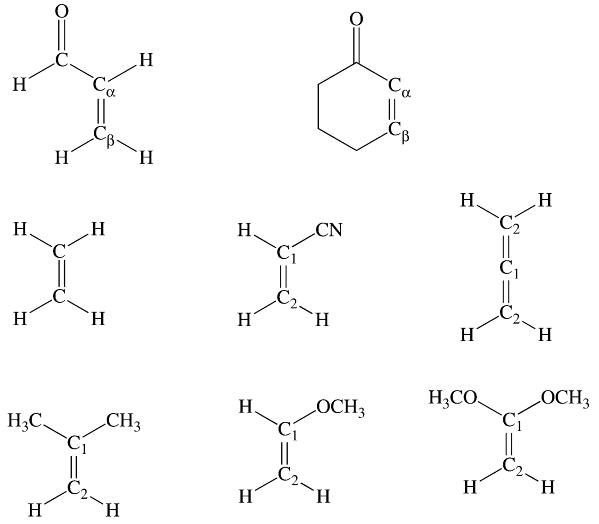

Figure 3. Molecular structures of the different compounds investigated in this work.

computed for the ground state of the system. The spin-hardness can be evaluated as[13]

$$\eta_{SS}^{0} \approx \frac{\mu_S^{-}(M') - \mu_S^{+}(M)}{2} \qquad (24)$$

where $\mu_S^{-}(M')$ is the spin potential of the higher multiplicity (M'), toward a decrease in the spin number and $\mu_S^{+}(M)$ the spin potential of the lower multiplicity (M) toward an increase in N_S. It measures the curvature of the E vs N_S curve in the given interval.

3. Computational Details

All calculations were performed at the (U)B3LYP level[30] using the Gaussian 03 program.[31] The regioselectivity in the [2+2] cycloaddition of $^3(\pi\pi^*)$ acrolein and $^3(\pi\pi^*)$ 2-cyclohexenone to the alkenes ethylene, allene, methyl vinyl ether, acrylonitrile, 1,1-dimethoxyethylene, and isobutene (Figure 3) was investigated. All geometries were fully optimized with the 6-311+G** basis set[31] and were confirmed to be minima on the potential energy surface. All reactivity indices considered in this work were calculated by single point calculations on these geometries with the 6-311G** basis set.[32] As can be seen, no diffuse functions are present in the basis set to compute the reactivity indices, because this turned out to be more suitable in the case of the calculations of the Fukui functions and local softness f^+ and s^+, where anionic metastability is frequently observed.[33]

Atomic populations were obtained using the Natural Population Analysis (NPA)[34] to compute the condensed Fukui functions and local softnesses. Next to its modest basis-set dependence, this orbital-based population analysis was shown to be a reliable method to compute the Fukui function and local softnesses for a series of test systems, including ambident anions.[35] Moreover, in a performance study of DFT methods in the calculation of atomic populations, NPA turned out to be the only orbital-based methods, which yield charges that approximate topological methods.[36]

4. Results and Discussion

TABLE 1: Regioselectivity of the [2+2] Photocycloaddition of Triplet Acrolein and 2-Cyclohexenone to a Set of Singlet Ethylenes Studied in This Work[a]

	Regioselectivity[b]	
	acrolein	2-cyclohexenone
ethylene	C_β	C_β[c]
acrylonitrile	$C_\beta-C_2$ (HH)	HH
allene	$C_\beta-C_2$ (HH)	HH
methyl vinyl ether	$C_\alpha-C_2$ (HT)	HT
isobutene	$C_\alpha-C_2$ (HT)	HT
1,1-dimethoxyethylene		HT[d]

[a] In the case of acrolein, the regioselectivity was determined from the computed relative activation barriers of the C_α and C_β atoms of acrolein to the C_2 atom of the alkenes,[2] assuming that the final regioselectivity is determined in this first step of the reaction. In the case of 2-cyclohexenone, the regioselectivities are listed,[1a,5] as determined from experimental head-to-head (HH)/(head-to-tail) HT product ratios. [b] Head-to head (HH) vs head-to-tail (HT). [c] Taken from ref 8. [d] This entry corresponds to the experimentally observed regioselectivity. In ref 9, García-Expósito et al. concluded from ab initio calculations that the first bond formed is between C_α of the enone and C_2 of the alkene, confirming the experimentally observed HT regioselectivity.

From experimental studies, it is known that the photocycloaddition of cyclohexenones to alkenes yield the head-to-head (HH) adducts in the case of electron-deficient alkenes (i.e., where the double bond is substituted by an electron-accepting group), whereas in the case of electron-rich alkenes (the substituent on the double bond being an electron-releasing group), the head-to-tail (HT) adduct is formed predominantly.[1a,5] Broeker et al.,[2] using acrolein as a model system, confirmed these regioselectivities by computations of the activation barriers for the first bond-making step.[2] They considered the triplet enone to be a nucleophilic alkyl radical at the β carbon, linked to the more-electrophilic α-acyl radical at the α-position. As a result, the β carbon will attach to the least-substituted site of the electron-deficient alkenes (i.e., the formation of a bond between C_β of the enone and C_2 of the alkene) resulting in a HH adduct after ring closure of the biradical. In the case of electron-rich alkenes, the α carbon of the enone will be attached to the least-substituted site of the alkene ((i.e., the formation of a bond between C_α of the enone and C_2 of the alkene), yielding the HT compound after ring closure. For the addition of acrolein and 2-cyclohexenone to ethylene, the lowest activation barrier occurs for the bond formation with the β carbon of the enone.[8] A summary of the previously obtained regioselectivities for the compounds studied in this work is given in Table 1; for each combination of an enone with an alkene, the main reaction adduct, i.e., head to head (HH) or head to tail (HT), is given.

In a first part, we have studied this regioselectivity using the well-known "non-spin-polarized" DFT-based reactivity indices and the local HSAB principle.[25] In this approach, one is looking at the resemblance of the two interacting sites of the enone with the two sites on the alkene, by considering the smallest quadratic difference in local softness between the different interacting sites. To explain these regioselectivities, the local HSAB principle, using two different approaches, was invoked. In a first approach, the local softness difference between the α or β carbon (C_α and C_β, respectively) of the enone and one of the two unsaturated carbons of the alkene (either C_1 or C_2), leading to four possibilities ($C_\alpha-C_1$, $C_\alpha-C_2$, $C_\beta-C_1$, or $C_\beta-C_2$), was computed. When applying this approach, one thus assumes that the formation of the 1,4-biradical will determine the geometry of the final adduct, thus assuming that the second ring closure step of the reaction is fast, in comparison to the formation step of the biradical. This would then yield the HH adducts in the cases where the first bond formed is the bond between C_α and C_1 or between C_β and C_2. The HT adduct is predicted in the case when the initial bond formation occurs between C_α and

TABLE 2: Vertical Ionization Energies, Electron Affinities, Global Softnesses, Fukui Functions, and Local Softnesses for the Triplet Acrolein and 2-Cyclohexenone, Obtained at the B3LYP/6-311G//B3LYP/6-311+G** Level**

				Fukui Functions			Local Softnesses		
vertical ionization energy, I (eV)	electron affinity, A (eV)	global softness, S (au)	atom	f^+ (au)	f^- (au)	f^0 (au)	s^+ (au)	s^- (au)	s^0 (au)
			acrolein						
9.159	1.132	3.394	O	0.270	0.286	0.278	0.915	0.970	0.943
			C_α	0.474	−0.016	0.229	1.608	−0.053	0.779
			C_β	−0.039	0.415	0.188	−0.132	1.409	0.639
			2-cyclohexenone						
7.609	1.555	4.501	O	0.217	0.205	0.211	0.976	0.923	0.949
			C_α	0.369	0.019	0.194	1.662	0.086	0.874
			C_β	0.122	0.333	0.227	0.550	1.498	1.024

TABLE 3: Vertical Ionization Energies, Electron Affinities, Global Softnesses, Fukui Functions, and Local Softnesses for the Singlet Ethylenes Obtained at the B3LYP/6-311G//B3LYP/6-311+G** Level**

				Fukui Functions			Local Softnesses		
vertical ionization energy, I (eV)	electron affinity, A (eV)	global softness, S (au)	atom	f^+ (au)	f^- (au)	f^0 (au)	s^+ (au)	s^- (au)	s^0 (au)
			ethylene						
10.568	−2.764	2.044	$C_1{=}C_2$	0.386	0.422	0.404	0.788	0.863	0.826
			acrylonitrile						
10.741	−0.638	2.394	C_1	0.205	0.205	0.205	0.491	0.491	0.491
			C_2	0.346	0.321	0.333	0.829	0.768	0.798
			allene						
10.061	−2.565	2.158	C_1	0.143	0.205	0.174	0.308	0.443	0.376
			C_2	0.217	0.260	0.238	0.467	0.561	0.514
			methyl vinyl-ether						
8.745	−2.893	2.341	C_1	0.279	0.110	0.194	0.653	0.257	0.455
			C_2	0.300	0.380	0.340	0.703	0.889	0.796
			isobutene						
9.251	−2.643	2.291	C_1	0.165	0.269	0.217	0.379	0.616	0.497
			C_2	0.322	0.377	0.350	0.738	0.864	0.801
			1,1-dimethoxyethylene						
8.362	−2.726	2.454	C_1	0.006	0.065	0.036	0.014	0.160	0.087
			C_2	0.014	0.462	0.238	0.034	1.134	0.584

C_2 or between C_β and C_1. The corresponding differences in the local softnesses Σ_1^α, Σ_2^α, Σ_1^β, and Σ_2^β can be defined as

$$\Sigma_i^k = (s_i - s_k)^2 \tag{25}$$

where s_i is the condensed local softness of atom C_i on the singlet alkene ($i = 1$ or 2) and s_k the condensed local softness of atom C_k on the triplet enone ($k = \alpha$ or β). In the second approach, which was also adopted in the work of Nguyen et al.[29d] in the study of the addition of triplet carbonyl compounds to alkenes, the local softness difference between two pairs of C atoms was investigated, combining the α carbon of the enone with the C_1 carbon of the alkene *and* the β carbon of the enone with the C_2 of the alkene and vice versa. In this way, the reaction is considered to be a one-step, concerted reaction, similar to the work by Nguyen et al.[29d] on the [2+2] photocycloaddition between an excited carbonyl and an alkene, leading to oxetane derivations.

Within this approach, two values can be defined ($\Sigma_{12}^{\alpha\beta}$ and $\Sigma_{21}^{\alpha\beta}$):

$$\Sigma_{ij}^{kl} = (s_i - s_k)^2 + (s_j - s_l)^2 \tag{26}$$

where s_i and s_j are the condensed local softnesses on atoms C_i and C_j of the singlet alkene and s_k and s_l the condensed local softnesses on the atoms C_k and C_l of the enone.

Within both approaches, one can use the s^+/s^--softnesses, looking at the electrophilic−nucleophilic interaction, again similar to the work by Nguyen et al.,[29d] or using s^0 for both reagents, assuming a radical−radical interaction.

In Tables 2 and 3, the reactivity descriptors for the triplet enones and the singlet alkenes are listed. As can be seen in Table 2, the Fukui functions and local softnesses indeed confirm the model used by Broeker et al. to assess the regioselectivity. The Fukui function f^- and local softness s^- are the highest on the β carbon and thus predict that an electrophilic attack will occur on the β carbon of the enone, so that it can be considered to be the nucleophilic site in the molecule. Note also that f^-—and, as a consequence, s^-—is even slightly negative on the α carbon. The negativity of condensed and noncondensed Fukui functions, also with respect to the population analysis method used in their computation, has been discussed in a series of contributions.[37] The Fukui function f^+ and local softness s^+ are the highest on the α carbon and thus predict that a nucleophilic attack will occur on the α carbon of the enone, so that it can, in turn, be considered as the electrophilic site in the molecule.

Note again the slightly negative Fukui function f^+ now on the β atom. No negative values are encountered in the condensed reactivity indices of the alkenes.

Using the vertical ionization energy (I) and electron affinity (A), one can approximate the energy needed to move an electron from the enone to the alkene ($I_{\text{enone}} - A_{\text{alkene}}$) and the energy needed to move an electron from the alkene to the enone ($I_{\text{alkene}} - A_{\text{enone}}$). These energies are listed in Table 4. As can be seen, with the exception of the reaction of acrylonitrile with 2-cyclohexenone, the energy for the transfer of an electron from

TABLE 4: Transfer Energies for One Electron from the Enone to the Alkene ($I_{\mathrm{enone}} - A_{\mathrm{alkene}}$) and Vice Versa ($I_{\mathrm{alkene}} - A_{\mathrm{enone}}$), Obtained at the B3LYP/6-311G//6-311+G** Level**

enone	alkene	$I_{\mathrm{enone}} - A_{\mathrm{alkene}}$ (eV)	$I_{\mathrm{alkene}} - A_{\mathrm{enone}}$ (eV)
acrolein	ethylene	11.93	9.44
acrolein	acrylonitrile	9.80	9.62
acrolein	allene	11.72	8.93
acrolein	methyl vinyl ether	12.05	7.61
acrolein	isobutene	11.80	8.12
acrolein	1,1-dimethoxyethylene	11.89	7.23
2-cyclohexenone	ethylene	10.37	9.01
2-cyclohexenone	acrylonitrile	8.25	9.19
2-cyclohexenone	allene	10.17	8.51
2-cyclohexenone	methyl vinyl ether	10.50	7.19
2-cyclohexenone	isobutene	10.25	7.70
2-cyclohexenone	1,1-dimethoxyethylene	10.34	6.80

TABLE 5: Values of Σ_i^k for the Addition of the Triplet Enones to the Alkenes, Computed Using eq 25, Considering Either an Interaction between a Nucleophile and an Electrophile (s^+/s^-) or the Interaction between Two Radicals (s^0/s^0)

	acrolein		2-cyclohexenone	
	s^+/s^- (au)	s^0/s^0 (au)	s^+/s^- (au)	s^0/s^0 (au)
ethylene				
$\Sigma_1^\alpha = \Sigma_2^\alpha$	0.555	0.002	0.638	0.002
$\Sigma_1^\beta = \Sigma_2^\beta$	0.988	0.035	0.098	0.039
acrylonitrile				
Σ_1^α	1.248	0.082	0.164	0.146
Σ_2^α	0.707	0.000	0.551	0.006
Σ_1^β	0.387	0.022	1.013	0.283
Σ_2^β	0.808	0.025	0.448	0.051
allene				
Σ_1^α	1.357	0.162	1.484	0.248
Σ_2^α	1.096	0.069	1.211	0.129
Σ_1^β	0.330	0.069	0.011	0.420
Σ_2^β	0.479	0.016	0.000	0.259
methyl vinyl ether				
Σ_1^α	1.827	0.104	1.974	0.176
Σ_2^α	0.518	0.000	0.597	0.006
Σ_1^β	0.150	0.034	0.086	0.324
Σ_2^β	1.040	0.025	0.115	0.052
isobutene				
Σ_1^α	0.985	0.079	1.094	0.142
Σ_2^α	0.554	0.001	0.636	0.005
Σ_1^β	0.557	0.020	0.004	0.278
Σ_2^β	0.990	0.026	0.099	0.050
1,1-dimethoxyethylene				
Σ_1^α	2.098	0.477	2.255	0.619
Σ_2^α	0.225	0.038	0.278	0.084
Σ_1^β	0.085	0.305	0.151	0.877
$\Sigma_{2'}^2$	1.600	0.003	0.341	0.193

TABLE 6: Values of Σ_{ij}^{kl} for the Addition of the Triplet Enones to the Alkenes, Computed Using eq 26, Considering Either an Interaction between a Nucleophile and an Electrophile (s^+/s^-) or the Interaction between Two Radicals (s^0/s^0)

	acrolein		2-cyclohexenone	
	s^+/s^- (au)	s^0/s^0 (au)	s^+/s^- (au)	s^0/s^0 (au)
ethylene				
$\Sigma_{12}^{\alpha\beta} = \Sigma_{21}^{\alpha\beta}$	1.927	0.037	0.736	0.041
acrylonitrile				
$\Sigma_{12}^{\alpha\beta}$	1.927	0.026	0.612	0.057
$\Sigma_{21}^{\alpha\beta}$	2.176	0.104	1.564	0.430
allene				
$\Sigma_{12}^{\alpha\beta}$	1.923	0.085	1.484	0.389
$\Sigma_{21}^{\alpha\beta}$	0.525	0.231	1.222	0.668
methyl-vinyl-ether				
$\Sigma_{12}^{\alpha\beta}$	0.183	0.025	2.089	0.058
$\Sigma_{21}^{\alpha\beta}$	0.777	0.138	0.683	0.499
isobutene				
$\Sigma_{12}^{\alpha\beta}$	0.214	0.027	1.193	0.055
$\Sigma_{21}^{\alpha\beta}$	2.506	0.099	0.640	0.420
1,1-dimethoxyethylene				
$\Sigma_{12}^{\alpha\beta}$	2.160	0.480	2.596	0.812
$\Sigma_{21}^{\alpha\beta}$	1.927	0.343	0.429	0.961

the alkene to the enone is less than the energy required for the reverse process. The alkene will thus act as an nucleophile and the enone as an electrophile. Consequently, to study the local HSAB principle, f^- and s^- should be used for the alkene and f^+ and s^+ should be used for the enone.

The results using eqs 25 and 26 for the electrophile–nucleophile interaction are listed in Tables 5 and 6. In the case of acrolein, an HT addition is predicted in the case of the electron-rich compounds (i.e., lowest values of either Σ_2^α or Σ_1^β). Only in the case of isobutene, an initial bond formation between C_α and C_2 on the alkene, as put forward by Broeker et al., is predicted. In the case of the reaction of 2-cyclohexenone with allene and acrylonitrile, one finds a HH regioselectivity whereas for methyl vinyl ether, isobutene, and 1,1-dimethoxyethylene, we find a HT regioselectivity, which is in agreement with the experimental data (see Table 1). Also, the bond formation with ethylene through the β carbon is reproduced.

The results within the second approach, by looking at the cyclobutane formation as a single step reaction, are listed in Table 6. In this case, the correct regioselectivity is only recovered again for the electron-rich alkenes.

However, note that this reaction has a radicalar character, because the first step involves the attack of a triplet (biradicalar) structure on an unsaturated double bond. Because the reaction has a radical character, the regioselectivity can be studied using the s^0 local softness, which is arbitrary chosen as the average between s^+ and s^-, using both eqs 25 and 26. These results are listed in Tables 5 and 6. Looking at Table 5 for the reaction with 2-cyclohexenone we only find the correct regioselectivity for the reactions with electron-rich alkenes, all the results now predicting the formation of the first bond between C_β on the enone and C_2 on the alkene. The same conclusion can be drawn for the reaction with acrolein. These findings are in agreement with the work of Suishi et al.[5] considering the interaction of both the HOMO and LUMO of the alkene with the lowest singly occupied molecular orbital (LSOMO) and highest singly occupied molecular orbital (HSOMO) of the enone, respectively, thus stressing the radical nature of this reaction.

Because this reaction involves a singlet alkene and a triplet α, β-unsaturated carbonyl compound, the regioselectivity will be also be studied using the reactivity indices introduced within the framework of spin-polarized conceptual DFT. We will thereby invoke the concept of spin philicity.[14] Based on the energy expansion described in eq 21, the maximum energy change upon increasing spin number can be derived to be[14]

$$\Delta E_{\max} = -\frac{(\mu_S^{+})^2}{2\eta_{SS}} \tag{27}$$

As such, one can define the spin-philicity index (ω_S^{+}) of the system as[14]

$$\omega_S^{+} \equiv \frac{(\mu_S^{+})^2}{2\eta_{SS}} \tag{28}$$

In the direction of a decreasing spin number, the spin-donicity index (ω_S^{-}) is given as[14]

$$\omega_S^{-} \equiv \frac{(\mu_S^{-})^2}{2\eta_{SS}} \tag{29}$$

Both indices were shown to be interesting quantities in the discussion of spin catalysis phenomena and could be invoked to explain singlet−triplet gaps.[14,15] However, these spin-philicity and spin-donicity indices are global indices, so they cannot be used for the study of aspects of regioselectivity. We will now introduce local versions of these global indices. In a first step, eq 28 can be rewritten as

$$\omega_S^{+} = \frac{(\mu_S^{+})^2}{2\eta_{SS}} = \frac{(\mu_S^{+})^2}{2(\partial\mu_S/\partial N_S)_{N,v}} = \frac{(\mu_S^{+})^2}{2}\left(\frac{\partial N_S}{\partial\mu_S}\right)_{N,v} \tag{30}$$

In this equation, the quantity $(\partial N_S/\partial\mu_S)_{N,v}$, which is the inverse of the spin hardness, is called the spin softness of the system (S_{SS}). Similar to the local softness given in eq 4, we introduce the local spin softness $s_{SS}(\mathbf{r})$ as

$$s_{SS}(\mathbf{r}) \equiv \left(\frac{\partial\rho_S}{\partial\mu_S}\right)_{N,v} = \left(\frac{\partial\rho_S}{\partial N_S}\right)_{N,v}\left(\frac{\partial N_S}{\partial\mu_S}\right)_{N,v} = f_{SS}(\mathbf{r})S_{SS} \tag{31}$$

As can be seen from eq 31, the local spin softness yields the global softness upon integration:

$$\int s_{SS}(\mathbf{r})\,\mathrm{d}\mathbf{r} = S_{SS} \tag{32}$$

and combining eqs 30, 31, and 32, one finds

$$\omega_S^{+} = \frac{(\mu_S^{+})^2}{2\eta_{SS}} = \frac{(\mu_S^{+})^2}{2\left(\dfrac{\partial\mu_S}{\partial N_S}\right)_{N,v}} = \frac{(\mu_S^{+})^2}{2}S_{SS}\int f_{SS}^{+}(\mathbf{r})\,\mathrm{d}\mathbf{r} \tag{33}$$

We can now define the local spin philicity as

$$\omega_S^{+}(\mathbf{r}) \equiv \frac{(\mu_S^{+})^2}{2}S_{SS}f_{SS}^{+}(\mathbf{r}) = \frac{(\mu_S^{+})^2}{2}s_{SS}^{+}(\mathbf{r}) = \frac{(\mu_S^{+})^2}{2\eta_{SS}}f_{ss}^{+}(\mathbf{r}) \tag{34}$$

where $f_{SS}^{+}(\mathbf{r})$ is the Fukui function for increasing spin number. Integration of the local spin philicity gives the global spin philicity.

Using the condensed approach, the spin philicity can be calculated condensed on an atom k in the molecule, as

$$\omega_{S,k}^{+} = \frac{(\mu_S^{+})^2}{2\eta_{SS}}f_{SS,k}^{+} \tag{35}$$

TABLE 7: Spin Potentials of the Singlet Ground-State $\mu^{+}(S_0)$, the Triplet Excited-State $\mu^{-}(T_1)$, the Spin Hardness ($\eta_{SS}{}^{o}$) Values, and the Spin Philicity (ω_S^{+}) Values of the Singlet Alkenes Considered in This Work

alkene	$\mu^{-}(T_1)$ (au)	$\mu^{+}(S_0)$ (au)	$\eta_{SS}{}^{o}$ (au)	ω_S^{+} (au)
ethylene	0.0257	0.1404	−0.0573	−0.1718
acrylonitrile	0.0221	0.1162	−0.0470	−0.1436
allene	0.0469	0.1403	−0.0467	−0.2107
methyl vinyl ether	0.0273	0.1251	−0.0489	−0.1600
isobutene	0.0283	0.1327	−0.0522	−0.1687
1,1-dimethoxyethylene	0.0430	0.1325	−0.0477	−0.1964

Similarly, we define the local spin donicity as

$$\omega_S^{-}(\mathbf{r}) \equiv \frac{(\mu_s^{-})^2}{2}S_{SS}f_{SS}^{-}(\mathbf{r}) = \frac{(\mu_s^{-})^2}{2}s_{SS}^{-}(\mathbf{r}) = \frac{(\mu_s^{-})^2}{2\eta_{SS}}f_{SS}^{-}(\mathbf{r}) \tag{36}$$

or condensed on an atom k:

$$\omega_{S,k}^{-} = \frac{(\mu_S^{-})^2}{2\eta_{SS}}f_{SS,k}^{-} \tag{37}$$

Approximations for these spin Fukui functions can be computed using the approximations proposed by Galvan et al.:[13a]

$$f_{SS}^{+}(\mathbf{r}) \approx \frac{1}{2}\lfloor|\phi_{\mathrm{LUMO},\alpha}|^2 + |\phi_{\mathrm{HOMO},\beta}|^2\rfloor \tag{38}$$

$$f_{SS}^{-}(\mathbf{r}) \approx \frac{1}{2}\lfloor|\phi_{\mathrm{HOMO},\alpha}|^2 + |\phi_{\mathrm{LUMO},\beta}|^2\rfloor \tag{39}$$

where $\phi_{\mathrm{HOMO},\alpha}$, $\phi_{\mathrm{HOMO},\beta}$, $\phi_{\mathrm{LUMO},\alpha}$, and $\phi_{LUMO,\beta}$ are the α and β HOMO and LUMO orbitals, respectively. The condensed values of densities of these orbitals on the different atoms were obtained using the Hirshfeld partitioning scheme.[38] This partitioning scheme has also been found particularly useful to compute condensed values of DFT-based reactivity indices.[39]

The global spin-polarized reactivity indices for the singlet alkenes are listed in Table 7. As can be seen, the global spin philicities for these compounds are all negative, corresponding to a destabilization upon increasing the spin number from 0 to 2. This is in agreement with the fact that the singlet state is indeed the ground state of these compounds. Moreover, we have shown that the global spin philicities for singlet ground-state molecules can be used to explain the magnitude of singlet−triplet gaps.[15] From the data in Table 7, it can thus be invoked that acrylonitrile possesses the lowest singlet gap, whereas allene has the highest gap.

In the spin-polarized approach, the first step of the reaction can now be divided into two parts, both at constant external potential v, as schematically shown in Figure 4. In a first step, a rearrangement of the spin density occurs in both reacting molecules. This amounts to a decrease in the spin number on the excited α, β-unsaturated carbonyl compound, resulting in a stabilization, and an increase of the spin number on the alkene, resulting in a destabilization of the latter. If one assumes that this first spin-coupling step will determine the regioselectivity of the reaction, one thus expects an initial combination of the site on the α, β-unsaturated carbonyl compound, which undergoes the largest change in spin number locally when the global spin number of the molecule is decreased (largest value of f_{SS}^{-}), with the site on the alkene that exhibits the smallest destabilization upon increasing spin number, corresponding to the spin coupling of the sites with the highest spin philicities and donicities. As can be seen from Table 8, f_{SS}^{-} is always the largest

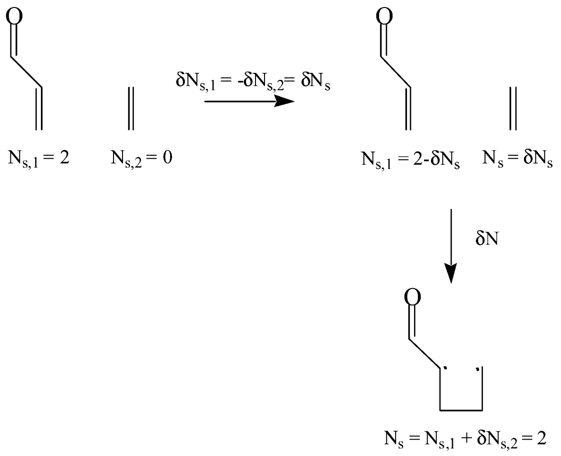

Figure 4. Spin-polarized description, at constant external potential, of the first reaction step of the [2+2] photocycloaddition of a triplet α, β-unsaturated carbonyl compound to a singlet ethylene. In the first step, a spin polarization of both reacting molecules occurs (change in N_S), followed by the charge transfer (change in the number of electrons N of both reacting species), forming the 1,4-biradical intermediate of the reaction.

TABLE 8: Values of the Density of the α HOMO, α LUMO, β HOMO, and β LUMO Orbitals, Condensed to the O, C_α, and C_β Atoms of the Triplet Enones Considered in this Work, Using the Hirshfeld Partitioning Scheme

atom	$\lvert\phi_{HOMO,\alpha}\rvert^2$ (au)	$\lvert\phi_{LUMO,\alpha}\rvert^2$ (au)	$\lvert\phi_{HOMO,\beta}\rvert^2$ (au)	$\lvert\phi_{LUMO,\beta}\rvert^2$ (au)	f_{SS}^{-a} (au)
			acrolein		
O	0.0967	0.2137	0.6858	0.2647	0.1807
C_α	0.0959	0.1805	0.0738	0.4294	0.2627
C_β	0.5704	0.0372	0.0175	0.0644	0.3174
			2-cyclohexenone		
O	0.0948	0.1916	0.6375	0.1954	0.1451
C_α	0.1793	0.1641	0.0766	0.3903	0.2848
C_β	0.4255	0.0302	0.0258	0.1521	0.2888

[a] In the last column, the condensed generalized Fukui function f_{SS}^-, obtained using eq 39 is given.

TABLE 9: Values of the Density of the α Homo (= β HOMO) and the α LUMO (= β LUMO) Orbitals, Condensed to the C_1 and C_2 Atoms of Singlet Alkenes Considered in This Work, Using the Hirshfeld Partitioning Scheme

atom	$\lvert\phi_{HOMO,\alpha}\rvert^2$ (au)	$\lvert\phi_{LUMO,\alpha}\rvert^2$ (au)	f_{SS}^+ (au)	ω_S^+ (au)
		ethylene		
C_1	0.4386	0.3981	0.4183	−0.071
C_2	0.4386	0.3981	0.4183	−0.071
		allene		
C_1	0.3404	0.3317	0.3361	−0.071
C_2	0.2599	0.2207	0.2403	−0.050
		isobutene		
C_1	0.3122	0.3153	0.3138	−0.053
C_2	0.4330	0.3466	0.3898	−0.066
		methyl vinyl ether		
C_1	0.2161	0.3498	0.2829	−0.045
C_2	0.3857	0.3351	0.3604	−0.058
		1,1-dimethoxyethylene		
C_1	0.1858	0.0242	0.1050	−0.021
C_2	0.4608	0.0751	0.2680	−0.053
		acrylonitrile		
C_1	0.2455	0.2445	0.2450	−0.035
C_2	0.3157	0.3634	0.3396	−0.049

[a] In the last two columns, the condensed generalized Fukui function f_{SS}^+, obtained using eq 38 is given, together with the local spin philicities ω_S^+.

on the C_β atom of the enones, with the values on both the O and C_α atoms always being smaller. This indeed indicates that, upon a global change in the spin number, the change of the spin density on C_β is the largest, and the exchange of spin with the alkene, resulting in a stabilization of the enone, will, thus, predominantly be through this atom. In the case of the 2-cyclohexenone, however, the values on C_α and C_β are very similar to each other. It can be anticipated that, in this case, the charge-transfer process, which occurs after the spin coupling of the two reagents, between the sites will determine the regioselectivity.

The condensed generalized Fukui functions f_{SS}^+, obtained using eq 38, are listed in Table 9. It is interesting to note that, because these compounds are singlet compounds computed within a spin-restricted framework, this approximation corresponds to the approximation for f^0, which is the Fukui function for a radical attack. This is not unsurprising, because this reaction basically consists of the attack of a triplet biradical to the double bond of the ethylenes. Also listed in this table are the values of the local spin philicities for these compounds condensed to the two sp^2 C atoms of the double bond. The regioselectivity can now be explained when it is assumed that the site with the smallest negative value for this quantity (i.e. the site exhibiting the smallest destabilization upon an increase of the global spin number of the alkene) will initially couple with the C_2 atom of the enone (the first step in the scheme depicted in Figure 4). The only exception is found in the case of acrylonitrile, where this approach predicts a HT regioselectivity, in contract with the observed HH selectivity.

5. Conclusion

In this contribution, we have presented a study of the regioselectivity of the photochemical [2+2] cycloaddition of triplet enones with ground-state alkenes, using density functional theory (DFT)-based reactivity descriptors. In a first part, we have investigated the regioselectivity using the local softness within the framework of the local Hard and Soft Acids and Bases (HSAB) principle. Within this approach, the reaction was considered to be either a two-step reaction or a one-step concerted reaction. Moreover, the interaction was also investigated as the interaction between a nucleophile and an electrophile on one hand and the interaction of two radicalar species on the other hand. However, all approaches indicate that the regioselectivity can only be explained in the case of the interaction of the enones with electron-rich alkenes.

In a next step, we have introduced, within the framework of conceptual spin-polarized conceptual DFT, the concepts of the local spin philicity and spin donicity. Using the local spin-philicity concept, the regioselectivity can be interpreted as resulting from the spin coupling of the local site on the alkene with the highest spin philicity (i.e., the smallest destabilization upon a global increase of the spin number of the molecule) with the site of the highest change in spin number upon a decreasing global multiplicity of the enone.

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