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Regioselectivity in the [2 + 2] cyclo-addition reaction of triplet carbonyl compounds to substituted alkenes (Paterno–Büchi reaction): A spin-polarized conceptual DFT approach

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Abstract. Regioselectivity of the photochemical [2 + 2] cyclo-addition of triplet carbonyl compounds with a series of ground state electron-rich and electron-poor alkenes, the Paterno–Büchi reaction, is studied. Activation barriers for the first step of the triplet reaction are computed in the case of the O-attack. Next, the observed regioselectivity is explained using a series of DFT-based reactivity indices. In the first step, we use the local softness and the local HSAB principle within a softness matching approach, and explain the relative activation barriers of the addition step. In the final step, the regioselectivity is assessed within the framework of spin-polarized conceptual density functional theory, considering response functions of the system's external potential v, number of electrons N and spin number N_s, being the difference between the number of a and b electrons in the spin-polarized system. Although the concept of local spin philicity, introduced recently within this theory, appears less suited to predict the regioselectivity in this reaction, the correct regioselectivity emerges from considering an interaction between the largest values of the generalized Fukui functions f_{ss} on both interacting molecules.

Keywords. Regioselectivity; cyclo-addition of triplet carbonyl compounds; spin-polarized conceptual DFT approach.

1. Introduction

The Paterno–Büchi reaction[1–4] (figure 1), i.e. the formation of oxetanes via photochemical cyclo-addition of aldehydes and ketones to alkenes, is the most general method for the synthesis of four-membered oxygen heterocyclic rings (oxetanes) in a regio- and stereoselective manner. An impressive number of papers, both preparative[5–8] and mechanistic,[9–13] have been published in this field. Mechanistic studies have shown that the cyclo-addition generally proceeds through the attack of an (n, p^*) excited carbonyl compound on a ground-state olefin. For oxetane formation to occur, the excited state energy of the olefin must be higher than that of the ketone so that energy transfer does not dominate the reaction.[14–17] The reaction occurs for both the first singlet and triplet[1,3] (n, p^*) excited state of the carbonyl compounds.[3,4] The reaction is known to proceed via 1,4-diradicals which were detected experimentally in transient spectroscopy studies.[18] The Paterno-Büchi cyclo-addition, proceeding through triplet manifold, exhibits good regio- and stereoselectivity and the most general adopted method to predict the major product is the most stable biradical rule, which was predicted first by Zimmerman.[19] There are exceptions to this rule; special methods were suggested to predict the major product, for example attack on the less hindered side of the molecule, the relative stability of the adducts[20] or kinetic control.[21]

Rationalization of the model of cyclo-addition to unsymmetrical substituted olefins[20] has also led to postulating a nonconcerted mechanism (predominant isomer), and the results show that product ratios are not always simply predicted from the stability of the

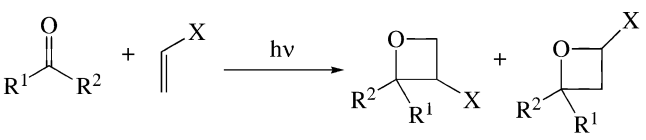

Figure 1. [2+2] Photo-cyclo-addition of a triplet carbonyl compound to a singlet ethylene.

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intermediate radicals. The results suggest that the additions occur via one excited quenchable state, most likely the (n, p^*) triplet state of the carbonyl compounds. Other regio- and stereoselective Paterno–Büchi reactions involve the use of phenylglioxylates as the olefin components[22] and numerous electron-rich and electron-poor alkenes at the olefin side. The results clearly demonstrate that the electron density of the olefins affects the mechanism; the reaction for electron-rich alkenes is rapid, highly regio- and stereoselective, without competitive Norrish type II reactions. When less electron-rich alkenes are used, the Norrish type II reaction becomes competitive. One can predict the regioselectivity with the "biradical rule", the instant of the intersystem crossing determines the stereoselectivity of the products.

In contrast to unsymmetrically substituted allenes, in the case of 9-methyl-1,2-butadiene, lower regioselectivity, but higher stereoselectivity was found.[23] In the reaction between styrene and benzaldehyde[24] there is a p–p overlap which has an impact on the distribution of products because there is *cis*-2,2-diphenyloxetane obtained from the irradiation. For silylated cinnamyl alcohol and benzaldehyde noncovalent tethering was reported (but not p–p overlap) since there is only one stereoisomer obtained and no side reactions. If tethering is involved, then phenyl groups must be held in opposite directions in the coordinated structure due to steric effects. Recently, a couple of studies reported the hydrogen-bond interaction in the excited singlet and triplet states,[25,26] influencing the ratio of regio- and stereoisomers. Palmer *et al*[9] performed a detailed MC-SCF/6-31G* study of the singlet and triplet Paterno–Büchi reaction using formaldehyde and ethylene as model systems, investigating both the formation of the oxetane via carbon–carbon and carbon–oxygen attacks. They found the C–O attack to be non-concerted, the first step of the reaction involving, in the case of the triplet pathway, the direct formation of the diradical intermediate. One of their other conclusions stated that the triplet diradicals generated in this reaction have similar energies and geometries to the singlets. Nguyen *et al*[11] used the Fukui functions, the local softness and the local hard and soft acids and bases principle for the regioselectivity of oxetane formation in the lowest $^3(n, p^*)$ state of carbonyl compounds and their results are in good agreement with the experimental data. In their approach, they considered this reaction to be a concerted one-step cyclo-addition. In 2004, D'Auria *et al*[20] reported that an approach based on the frontier orbitals control is more efficient in explaining the photochemical behavior for furan derivatives than the most stable biradical rule.

In this contribution, we carry out a high level theoretical study on the regioselectivity of the Paterno–Büchi photocyclo-addition of triplet acetone and acetophenone on a series of substituted alkenes, involving both electron-poor and electron-rich alkenes. Next to the localization of the transition structures of the biradical formation step of this reaction, the regioselectivity is assessed within the framework of both non-spin polarized and spin-polarized conceptual density functional theory.[27]

2. Theory and computational details

Next to the well-established computational advantages, density functional theory (DFT) is the source for the introduction of a series of concepts and principles, readily used by chemists but often defined on an empirical basis. This aspect of DFT, in which chemical quantities are identified with response functions of the system's energy with respect to either the number of electrons N, the external (i.e. due to the nuclei) potential $v(\mathbf{r})$ or both was termed "conceptual DFT" by R G Parr. The first-order derivative of the energy of the system with respect to the number of electrons is the chemical potential μ, identified by Parr *et al*[28,29] with the negative of the electronegativity χ:

$$\mu = -\chi = (\partial E/\partial N)_v. \tag{1}$$

The chemical hardness η of the system[30] was quantified by Parr and Pearson as:[31]

$$\eta = \tfrac{1}{2}(\partial^2 E/\partial N^2)_v, \tag{2}$$

which, in a finite difference approximation, can be written as:

$$\eta \approx (IE - EA)/2, \tag{3}$$

where IE and EA are the vertical ionization energy and electron affinity of the systems respectively. The inverse of the global hardness is the global softness S:[32]

$$S = 1/\eta = (\partial N/\partial \mu)_v \approx 1/(IE - EA). \tag{4}$$

The local counterpart of this quantity, the local softness $s(\mathbf{r})$, is introduced as:[32,33]

$$s(\mathbf{r}) \equiv \left(\frac{\partial r(\mathbf{r})}{\partial m}\right)_v = \left(\frac{\partial r(\mathbf{r})}{\partial N}\right)_v \left(\frac{\partial N}{\partial m}\right)_v = Sf(\mathbf{r}), \qquad (5)$$

where $f(\mathbf{r})$ is the Fukui function, a reactivity index introduced by Parr and Yang.[34] Due to the discontinuity of the electron density with respect to the number of electrons, three different Fukui functions can be introduced, representing the case of a nucleophilic attack (f^+), an electrophilic attack (f^-) or a neutral (radical) attack (f^0):

$$f^+ \equiv (\partial r(\mathbf{r})/\partial N)_v^+ \approx r_{N+1}(\mathbf{r}) - r_N(\mathbf{r}), \qquad (6)$$

$$f^- \equiv (\partial r(\mathbf{r})/\partial N)_v^- \approx r_N(\mathbf{r}) - r_{N-1}(\mathbf{r}), \qquad (7)$$

$$f^0 \equiv (f^+ + f^-)/2 \approx 1/2(r_{N+1}(\mathbf{r}) - r_{N-1}(\mathbf{r}), \qquad (8)$$

where $r_{N+1}(\mathbf{r})$, $r_N(\mathbf{r})$ and $r_{N-1}(\mathbf{r})$ are the electron densities of the $N + 1$, N and $N - 1$ electron system respectively, all obtained at the geometry of the N-electron system, due to the fact that the derivative is taken at a constant external potential. These Fukui functions can be condensed to the nuclei by using an atomic charge partitioning scheme, $N_k(N + 1)$, $N_k(N)$ and $N_k(N - 1)$ representing the electron populations on atom k in the $N + 1$, N and $N - 1$ electron system:[35]

$$f_k^+ \approx N_k(N + 1) - N_k(N), \qquad (9)$$

$$f_k^- \approx N_k(N) - N_k(N - 1), \qquad (10)$$

$$f_k^0 \approx \tfrac{1}{2}(N_k(N + 1) - N_k(N - 1). \qquad (11)$$

The condensed local softness is the product of the global softness S with f_k^i at a given site k:

$$s_k^i = S \cdot f_k^i \qquad (12)$$

where i equals either +, – or 0 depending on whether the system undergoes a nucleophilic, electrophilic or radical attack. A theoretical justification of the HSAB-principle was provided by Chattaraj, Lee and Parr.[36] This principle has been applied many times in recent years, both at the local and the global level, for the rationalisation of regioselectivity and reactivity of many problems.[37]

The above mentioned response functions can be used to describe changes from one ground state to another. The Hohenberg–Kohn theorems,[38] on which density functional theory is based, were also initially developed for the ground states but could later on be generalized to time-dependent electron densities and external potentials.[39,40] Applications of these DFT based reactivity indices to excited states have moreover been scarce.[41]

In the present application, one of the reaction partners, i.e. the carbonyl compound, is in its excited triplet state for which the electron densities of the a and b electrons are different, corresponding to a spin-polarized chemical system. We are thus working within the framework of spin-polarized DFT.[42] Galván, Vela and Gázquez have introduced spin-polarized conceptual DFT, deriving expressions for, among others, the spin potential μs, the spin hardness h_{ss} and the Fukui functions f_{ss}.[43a] (For a detailed account of other reactivity indices introduced within this framework, see ref. 43).

The spin potential m_s is introduced as the partial derivative of the energy with respect to the spin number, N_s ($=N_a - N_b$), since it provides a measure for the tendency of the system to change its spin polarization:

$$m_s = (\partial E/\partial N_s)_{N,v(\mathbf{r})\cdot\mathbf{B}}, \qquad (13)$$

where **B** is the external magnetic field.

The second-order partial derivative of the energy with respect to N_s is the spin hardness h_{SS}:

$$h_{SS} = (\partial m_s/\partial N_s)_{N,v(\mathbf{r})\cdot\mathbf{B}} = (\partial^2 E/\partial N_s^2)_{N,v(\mathbf{r})\cdot\mathbf{B}}. \qquad (14)$$

The change of the spin density $r_s(\mathbf{r})$ upon change in spin number N_s is governed by the Fukui function f_{SS}:

$$f_{SS} = (\partial r_s(\mathbf{r})/\partial N_s)_{N,v(\mathbf{r}),\cdot\mathbf{B}}. \qquad (15)$$

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 constant total number of electrons and external potential, can be written up to second order as:

$$\Delta E_{v,N} \approx m_s^0 + \tfrac{1}{2} h_{ss}^0 (\Delta N_s)^2. \qquad (16)$$

In this expression, m_s^0 must always be calculated in a given direction, substituting m_s^0 by m_s^+ when describing changes with increasing spin number, and by m_s^- when the spin number is decreasing. The chemical potentials m_s^+ and m_s^- can be approximated as:

$$m_s^+ \approx (e^a_{\mathrm{LUMO}} - e^b_{\mathrm{HOMO}})/2 \quad (17)$$

and

$$m_s^- \approx (e^a_{\mathrm{HOMO}} - e^b_{\mathrm{LUMO}})/2, \quad (18)$$

where e^a_{HOMO}, e^b_{HOMO}, e^a_{LUMO} and e^b_{LUMO} are the orbital energies of the a and b HOMO and LUMO orbitals respectively. The spin hardness can be evaluated as:

$$h^0_{SS} \approx [m_s^-(M') - m_s^+(M)]/2, \quad (19)$$

where $m_s^-(M')$ is the spin potential of the higher multiplicity (M¢), towards a decrease in the spin number and $m_s^+(M')$ the spin potential of the lower multiplicity (M) towards an increase in N_s. It measures the curvature of the E versus N_S curve in the given interval. Within this framework, Pérez *et al*[44] defined the concepts spin-philicity and spin-donicity. The spinphilicity index w_s^+ of the system can be defined as:[44]

$$w_s^+ \equiv (m_s^+)^2/2h_{SS}. \quad (20)$$

In the direction of a decreasing spin number, the spin-donicity index is given as:

$$w_s^- \equiv (m_s^-)^2/2h_{SS}. \quad (21)$$

Both indices are shown to be interesting quantities in the discussion of spin catalysis phenomena and can be invoked to explain singlet–triplet gaps.[41f,41g] De Proft *et al*[45] introduced the concepts of local spin-philicity and donicity for use in regioselectivity studies. The spin-philicity can be calculated condensed on a atom k in the molecule, as:

$$w^+_{s,k} = [(m_s^+)^2/2h_{SS}]\, f^+_{ss,k}, \quad (22)$$

where f^+_{ss} denotes the spin Fukui function in the direction of increasing spin number. Similarly we define the local spin-donicity, condensed on an atom k, as:

$$w^-_{s,k} = [(m_s^-)^2/2h_{SS}]\, f^+_{ss,k}, \quad (23)$$

f^-_{ss} being the Fukui function for decreasing spin number. Approximations for these spin Fukui functions can be computed using the approximations proposed by Galvan *et al*[43a]:

$$f^+_{ss}(\mathbf{r}) \approx \tfrac{1}{2}[|f_{\mathrm{LUMO},a}|^2 + |f_{\mathrm{HOMO},b}|^2], \quad (24)$$

$$f^-_{ss}(\mathbf{r}) \approx \tfrac{1}{2}[|f_{\mathrm{HOMO},a}|^2 + |f_{\mathrm{LUMO},b}|^2], \quad (25)$$

where $f_{\mathrm{HOMO},a}$, $f_{\mathrm{HOMO},b}$, $f_{\mathrm{LUMO},a}$ and $f_{\mathrm{LUMO},b}$ are respectively the a and b HOMO and LUMO orbitals.

These concepts were successfully applied in study of the regioselectivity of the [2 + 2] cyclo-addition of triplet enones on substituted alkenes.[45] All calculations were performed at the (U)B3LYP level[46] using the Gaussian 03 program.[47] The different triplet carbonyl compounds and singlet alkenes studied are given in figure 2. All transition state geometries of the first addition step of the reaction on the triplet energy surface were optimized using the (U)B3LYP level of theory with the 6-31G(d) basis set. The geometries used to compute the DFT based reactivity indices were fully optimized with the 6-311+G** basis set[48] and were confirmed to be minima on the potential energy surface. Molecular properties and reactivity indices were obtained at the 6-311G** level; as can be seen, the diffuse function in the basis set used for the optimization of the reacting molecules was dropped when computing the properties because this was found to be more suitable in the case of the Fukui functions and local softnesses, where anionic metastability is frequently observed (for a detailed account, see ref. [27g]). Atomic populations were obtained using the natural population analysis (NPA),[49] in order to compute the condensed Fukui functions and local softnesses. The Fukui functions f_{ss} were computed

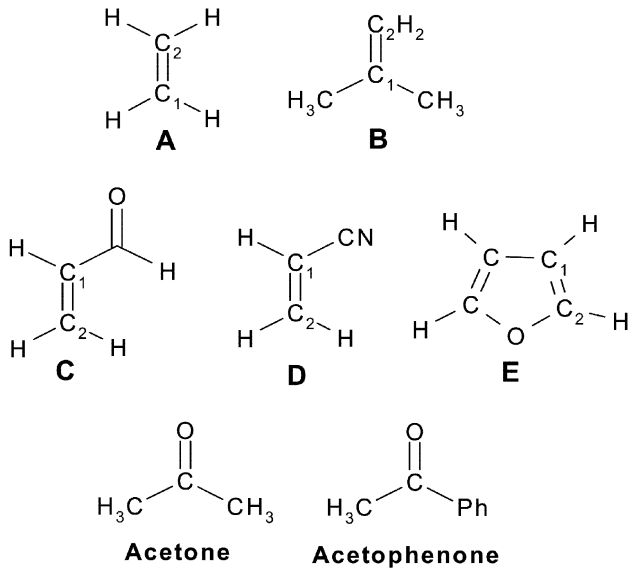

Figure 2. Different compounds investigated in this work: A = ethylene, B = isobutene, C = acrylonitrile, D = acrolein, E = furan.

using approximations (24) and (25); the condensed values of densities of *a* and *b* frontier molecular orbitals on the different atoms were obtained using the Hirshfeld partitioning scheme.[50] This partitioning scheme has also been found particularly useful to compute condensed values of DFT-based reactivity indices.[51]

3. Results and discussion

In the first part of this work, we have investigated the reaction mechanism in some more detail for our series of ketones and substituted ethylenes. The transition state (TS) structures for the first step (figure 3), i.e. the formation of the diradical structures, which are the intermediates of the reaction, were located. In this work, we have only investigated the triplet surface of the attack of the carbonyl oxygen to one of the carbon atoms of the substituted ethylenes. In figure 4, the two different orientations for the carbonyl oxygen attack are depicted: the face-to-face and the face-to-edge attack. In the face-to-face attack, an electron on the carbonyl oxygen and an electron on an olefin carbon are spin-coupled to form a CO bond while the carbonyl and alkene fragments are mutually parallel. When the carbonyl oxygen attacks the olefin in a perpendicular orientation, the face-to-edge attack, the terminal groups on the carbonyl are rotated by approximately 90 degrees. As is generally accepted that the face-to-edge attack correlates electronically with an (*n*, *p**) excited-state carbonyl compound and a ground state olefin, our attention was mainly focussed on this orientation in the optimization of the different transition states. The different arrangements of the transition states for the C–O attack that were considered in this work are presented in figure 5.

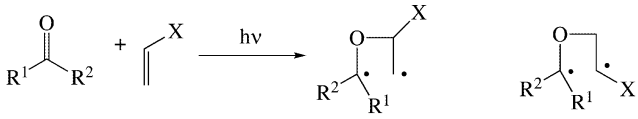

Figure 3. First step (C–O attack) of the [2 + 2] photo-cyclo-addition of a triplet carbonyl compound to a singlet ethylene.

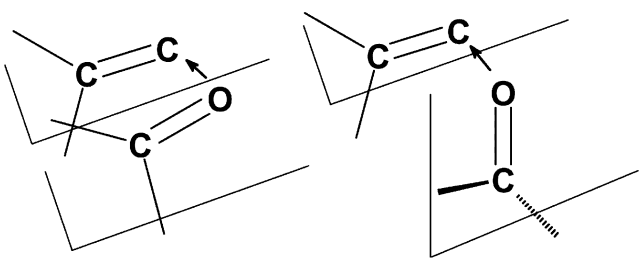

Figure 4. The two different orientations for the carbonyl oxygen attack: the face-to-face (left) and the face-to-edge (right) attack.

It indeed turns out that the majority of the optimized transition states correspond to a face-to-edge arrangement. In the case of the transition states for the attack of acetone and acetophenone to the substituted carbon atom of the electron poor alkenes, one face-to-edge and one face-to-face (the dihedral angle is $\approx 10°$) transition states are formed. During the face-to-edge attack on C_1 of propenal, in addition to the negative direction of curvature corresponding to forming the C–O bond, there is a force constant for the rotation of the ethylenic terminal methylene. Because of this, the transition structure could not be optimized accurately. The attack of the carbonyl oxygen to the C_1 of isobutene was found to occur via face-to-face orientation. As can be seen for the activation barriers listed in table 1, for all compounds, the lowest activation barrier is observed for the attack of the carbonyl oxygen on the least substituted carbon atom of the olefin, in agreement with experiment (for the case of furan) and Markovnikov's rule.

Table 1. Activation barriers (ΔE and ΔG) for the first step (addition of the carbonyl oxygen to the double bond of the alkenes) in the [2 + 2] photo-cyclo-addition of acetone and acetophenone to the substituted alkenes considered. All values were obtained at the B3LYP/6-311+G**// B3LYP/6-31G* level and are given in kcal/mol.

		Acetone		Acetophenone	
Alkene	Structure	ΔE	ΔG	ΔE	ΔG
Ethylene	A	5·4	17·2	6·1	18·7
Isobutene	B1	5·3	16·3	6·1	19·5
	B2	2·7	15·3	3·2	16·3
Acrolein	C1	4·9	16·4	8·5	21·0
	C2	4·0	15·9	4·4	17·4
	C2′	4·4	16·9	6·6	19·2
Acrylonitrile	D1	5·9	16·8	9·3	21·9
	D1′	5·6	17·0	6·6	19·1
	D2	3·5	16·0	3·5	16·3
	D2′	3·7	16·1	4·3	17·4
Furan	E1	8·5	21·3	7·9	21·5
	E1′	11·1	24·0	10·6	24·0
	E2	2·7	15·3	3·4	16·7
	E2′	4·4	17·0	3·0	16·4

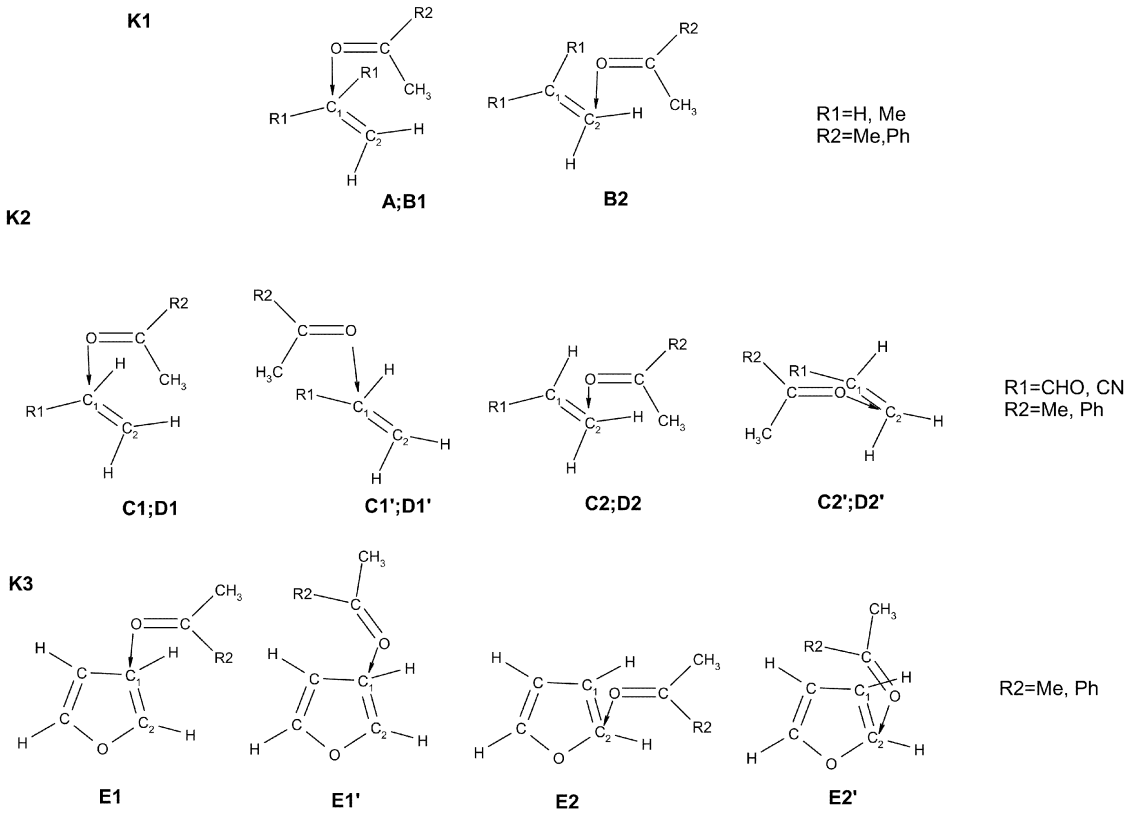

Figure 5. Structures of the different transition states obtained in this work.

Table 2. Vertical ionization energies I, electron affinities A, global softnesses S, condensed spin density N_s, Fukui functions f and local softnesses s for triplet acetone and acetophenone obtained at the B3LYP/6-311G**//B3LYP/6-311+G** level.

Molecule	I (eV)	A (eV)	S (a.u.)	Atom	N_s	f^- (a.u.)	f^+ (a.u.)	f^0 (a.u.)	s^- (a.u.)	s^+ (a.u.)	s^0 (a.u.)
Acetone	7·236	1·758	4·967	C	0·705	0·401	0·014	0·207	1·990	0·070	1·030
				O	1·056	0·204	0·562	0·383	1·014	2·791	1·902
Acetophenone	6·209	2·850	8·101	C	0·474	0·252	-0·068	0·092	2·043	–0·549	0·747
				O	1·041	0·103	0·541	0·322	0·835	4·379	2·607

Next, we assess the regioselectivity of the first addition step of the oxygen of the triplet carbonyl compounds to the alkenes using the well-known "non-spin-polarized" DFT based reactivity indices and the local hard and soft acids and bases principle.[37] In this approach, one is looking at the softnesss resemblance of the interacting sites, in this case by considering the smallest absolute value of the difference in local softness between the oxygen of either the triplet acetone or acetophenone on the one hand and one of the carbon atoms of the double bond (C_1 or C_2) in the alkenes on the other, i.e. considering:

$$\sum_0^1 = | s_0 - s_{C1} |, \tag{26}$$

$$\sum_0^2 = | s_0 - s_{C2} |, \tag{27}$$

This approach has been termed "softness-matching".[37]

Within this approach we can either use the s^+/s^--softnesses, considering the interaction to be an interaction between an electrophile and a nucleophile, which was adopted in the work of Nguyen *et al*.[11] We could also perform the softness matching using

Table 3. Vertical ionization energies *I*, electron affinities *A*, global softnesses *S*, Fukui functions *f* and local softnesses *s* for the singlet alkenes obtained at the B3LYP/6-311G**//B3LYP/6-311+G** level.

Molecule	*I* (eV)	*A* (eV)	*S* (a.u.)	Atom	f^- (a.u.)	f^+ (a.u.)	f^0 (a.u.)	s^- (a.u.)	s^+ (a.u.)	s^0 (a.u.)
Ethylene	10·556	–2·761	2·043	C_1=C_2	0·423	0·386	0·404	0·863	0·790	0·826
Isobutene	9·239	–2·639	2·291	C_1	0·268	0·165	0·217	0·615	0·379	0·497
				C_2	0·379	0·322	0·351	0·868	0·739	0·803
Acrylonitrile	10·727	–0·638	2·394	C_1	0·205	0·205	0·205	0·492	0·490	0·491
				C_2	0·321	0·347	0·334	0·768	0·831	0·800
Acrolein	9·903	–0·447	2·629	C_1	–0·018	0·090	0·036	–0·047	0·238	0·095
				C_2	0·194	0·305	0·249	0·510	0·801	0·655
Furan	8·892	–2·556	2·377	C_1	0·120	0·095	0·107	0·285	0·225	0·255
				C_2	0·265	0·247	0·256	0·631	0·587	0·609

Table 4. Transfer energies for one electron from the triplet carbonyl compound to the alkene ($I_{carb} - A_{alkene}$) and vice versa ($I_{alkene} - A_{carb}$), obtained at the B3LYP/6-311G**//6-311+G** level. All values are in eV.

Enone	Alkene	$I_{carb} - A_{alkene}$	$I_{alkene} - A_{carb}$
Acetone	Ethylene	10·00	8·80
	Isobutene	9·88	7·48
	Acrylonitrile	7·87	8·97
	Acrolein	7·68	8·15
	Furan	9·79	7·13
Acetophenone	Ethylene	8·97	7·71
	Isobutene	8·85	6·39
	Acrylonitrile	6·85	7·88
	Acrolein	6·66	7·05
	Furan	8·76	6·04

the local softness for a radical attack s^0 for both reagents, assuming the reaction to be a radical-radical interaction. In tables 2 and 3, the reactivity descriptors for the triplet carbonyl compounds and the singlet alkenes are listed. Using the vertical ionization energy (I) and electron affinity (*A*) one can approximate the energy needed to move an electron from the carbonyl compound to the alkene ($I_{carb} - A_{alkene}$) and the energy needed to move an electron fron the alkene to the enone ($I_{alkene} - A_{carb}$). These transfer energies are listed in table 4. As can be seen, for the interaction of the triplet carbonyl compounds and the electron-rich alkenes, including ethylene, the transfer energy for an electron from the alkene to the excited carbonyl compound is lower that the reverse process, corresponding to an interaction of an electrophilic excited state species with the ground state alkene. In this case, one thus has to consider s^+ on the carbonyl compound and s^- on the alkenes. For the reaction with the electron-poor alkenes (i.e. acrylonitrile and acrolein), the transfer energy for an electron from the triplet carbonyl compounds to the alkenes is the lowest. It thus appears that these alkenes are now operating as electrophilic species, and one thus considers s^+ for these compounds in (26) and (27) together with s- for the triplet carbonyl compounds.

The values of $\sum_0^1$ and $\sum_0^2$ obtained for the addition of the triplet carbonyl compounds to the alkenes, computed using (26) and (27), considering either an interaction between a nucleophile and an electrophile (s^+/s^-) or the interaction between two radicals (s^0/s^0) are listed in table 5. As can be seen, the smallest softness difference always occurs for the interaction of the oxygen of the triplet carbonyl compound with carbon atom 2 of the alkenes, in agreement with the computed activation barriers for this first addition step. From table 1, it can indeed be seen that the activation barrier for the addition of the oxygen atom on carbon 2 is always the lowest.

Finally, we investigate the regioselectivity in the different cases studied within the framework of spin-polarized conceptual DFT, as this reaction involves a singlet alkene and a triplet carbonyl compound. In the spin-polarized approach, the first step of this reaction can now be divided into two parts, both at constant external potential *v*, as schematically shown in figure 6. In the first step, a rearrangement of the spin density occurs in both reacting molecules. This amounts to a decrease of the spin number on the excited *a*, *b*-unsaturared carbonyl compound, resulting in stabilisation, and an increase of the spin number on the alkene, resulting in destabilization of the latter. The magnitude of the change of the spin density of the different sites in the interacting molecules upon a change of their total spin number N_s is governed by the generalized Fukui function given in (15); for

Table 5. The values of $\sum_0^i$ for the addition of the triplet carbonyl compounds to the alkenes.
Values computed using (24), considering either an interaction between a nucleophile and an electrophile (s^+/s^-), or the interaction between two radicals (s^0/s^0). All values are in a.u.

		Acetone		Acetophenone	
Alkene		s^+/s^-	s^0/s^0	s^+/s^-	s^0/s^0
Ethylene	$\sum_0^1 = \sum_0^2$	1·927	1·076	3·516	1·781
Isobutene	$\sum_0^1$	2·176	1·405	3·764	2·110
	$\sum_0^2$	1·923	1·099	3·511	1·804
Acrylonitrile	$\sum_0^1$	0·525	1·412	0·345	2·116
	$\sum_0^2$	0·183	1·103	0·004	1·807
Acrolein	$\sum_0^1$	0·777	1·807	0·597	2·512
	$\sum_0^2$	0·214	1·247	0·034	1·952
Duran	$\sum_0^1$	2·506	1·648	4·095	2·352
	$\sum_0^2$	2·160	1·294	3·749	1·998

Table 6. Values of the density of the *a* HOMO, the *a* LUMO, the *b* HOMO and *b* LUMO orbitals, condensed to the O and C_2 atoms of the triplet carbonyl compounds, using the Hirshfeld partitioning scheme.
In the last column, the condensed generalized Fukui function f^-_{ss}, obtained using (24) and (25) is given. All values are in a.u.

Enone	Atom	$\lvert f_{\mathrm{HOMO},a}\rvert^2$	$\lvert f_{\mathrm{LUMO},a}\rvert^2$	$\lvert f_{\mathrm{HOMO},b}\rvert^2$	$\lvert f_{\mathrm{LUMO},b}\rvert^2$	f^-_{ss}
Acetone	C	0·519	0·045	0·149	0·091	0·305
	O	0·219	0·021	0·669	0·718	0·468
Acetophenone	C	0·313	0·007	0·005	0·085	0·199
	O	0·134	0·002	0·009	0·729	0·432

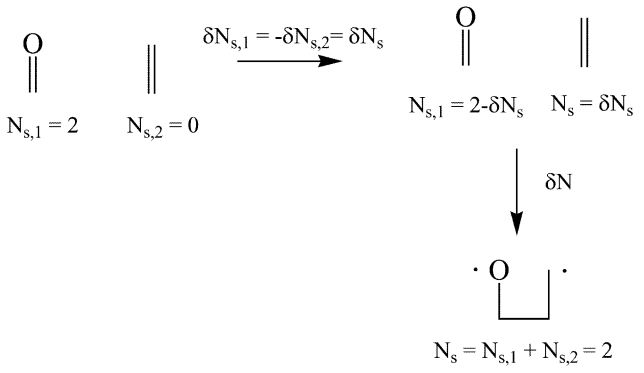

Figure 6. Spin-polarized description of the first step of the Paterno–Büchi reaction (constant external potential). In the first step, a spinpolarization of both reacting molecule occurs (change in N_s), followed by the charge transfer (change in the number of electrons N of both reacting species), forming the 1,4-biradical intermediate of the reaction.

Table 7. Spin potentials of the singlet ground state $m^+(S_0)$, the triplet excited state $m^-(T_1)$, the spin hardnesses h^0_{SS} and the spin philicities w^+_s of the singlet alkenes.
All values are in a.u.

Alkene	$m^-(T_1)$	$m^+(S_0)$	h^0_{SS}	w^+_s
Ethylene	0·0257	0·1404	–0·0573	–0·1718
Isobutene	0·0283	0·1327	–0·0522	–0·1687
Acrylonitrile	0·0221	0·1162	–0·0470	–0·1436
Acrolein	0·0204	0·0952	–0·0374	–0·1212
Furan	0·0346	0·1169	–0·0412	–0·1660

the triplet carbonyl compound, this Fukui function has to be computed in the direction of decreasing N_s, whereas for the singlet alkenes, the direction of increasing N_s has to be considered. These condensed generalised Fukui functions, computed using the approximations given in (24) and (25), are given in table

Table 8. Values of the density of the *a* HOMO (= *b* HOMO) and the *a* LUMO (= *b* LUMO) orbitals, condensed to the C_1 and C_2 atoms of the singlet alkenes considered in this work, using the Hirshfeld partitioning scheme.
In the last two columns, the condensed generalized Fukui function f^+_{SS}, obtained using (36) is given, together with the local spin-philicities w^+_s. All values are in a.u.

Alkene	Atom	$\lvert f_{\mathrm{HOMO},a}\rvert^2$	$\lvert f_{\mathrm{LUMO},a}\rvert^2$	f^+_{ss}	w^+_s
Ethylene	C_1	0·439	0·398	0·418	–0·072
	C_2	0·439	0·398	0·418	–0·072
Isobutene	C_1	0·312	0·315	0·314	–0·053
	C_2	0·433	0·347	0·390	–0·066
Acrylonitrile	C_1	0·245	0·245	0·245	–0·035
	C_2	0·316	0·363	0·340	–0·049
Acrolein	C_1	0·087	0·161	0·124	–0·015
	C_2	0·015	0·292	0·154	–0·019
Furan	C_1	0·149	0·124	0·136	–0·023
	C_2	0·296	0·243	0·269	–0·045

6 for the triplet carbonyl compounds (f^-_{ss}) and in table 8 for the singlet alkenes (f^+_{ss}). As can be seen, f^+_{ss} is always the largest on the carbonyl oxygen atom of the triplet carbonyl compounds, in agreement with the NPA spin density values N_s given in table 2 for these compounds. In the case of the alkenes, f^+_{ss} is always higher on the C_2 atom of the double bond. It thus appears that the correct regioselectivity can be predicted by presuming a spin coupling (first step in figure 6) of these two sites that exhibit the largest values of the generalized Fukui function. This finding seems to be remeniscent of some kind of hard and soft acids and bases principle within the context of spin-polarized DFT.

Table 7 lists the spin potentials, spin hardnesses and the global spin-philicities of the singlet alkenes studied in this work. As can be seen, all the spin-philicities are negative, in agreement with the fact that the energy change when going from the singlet state, the ground state, to the first excited triplet state (i.e. a change with $\Delta N_s = 2$) is positive. In previous work, this quantity has been proven to correlate with the singlet-triplet gaps of a series of singlet ground state carbenes, silylenes, germylenes and stannylenes. Recently, this correlation was confirmed by Olah *et al*[41g] for a series of nitrenes and phosphinidenes. Table 8 lists the local spin-philicities of the different alkenes studied in this work. As can be seen, the most negative spin-philicities occur on C_2, in agreement with the fact that the condensed value of is f^-_{ss} always the largest on this atom. The local contribution of this atom in the energy rise due to the increase of the spin number can thus considered to be larger than the contribution of C1. In this case however, this does not seem to be the decisive factor in prediction of the regioselectivity.

4. Conclusions

In this contribution, we have presented a study of the regioselectivity of the photochemical [2 + 2] cyclo-addition of carbonyl compounds with ground state alkenes, the Paterno–Büchi reaction, using DFT-based reactivity descriptors.

In a first part, we have located the different transition states for the first radical coupling step on the triplet surface for the reaction of triplet acetone and acetophenone with a series of electron-rich and electron-poor alkenes, focussing our attention exclusively on the O-attack. Next, we have investigated the regioselectivity using the local softness within the framework of the local hard and soft acids and bases principle. Within this approach, the interaction was investigated as either the interaction between a nucleophile and an electrophile or the interaction of two radicalar species on the other hand. Both approaches systematically yield a regioselectivity that is completely in agreement with the computed activation barriers.

Finally, the regioselectivity of this reaction was investigated using chemical concepts introduced within the framework of spin-polarized conceptual DFT. In this case, the local spin-philicity does not appear the

determining factor for the observed regioselectivity. The correct regioselectivity emerges from considering an interaction between the sites that undergo the largest change in spin number when the total spin number of the molecule is changing.

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