A theoretical approach to the regioselectivity in 1,3-dipolar cycloadditions of diazoalkanes, hydrazoic acid and nitrous oxide to acetylenes, phosphaalkynes and cyanides

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ABSTRACT: The 1,3-dipolar cycloadditions of diazoalkanes (R_2CNN), hydrazoic acid (HNNN) and nitrous oxide (N_2O) to some simple dipolarophiles such as acetylenes, phosphaalkynes and cyanides were studied using quantum chemical calculations at the B3LYP/6–311++G(d,p) level and, in the simplest case, using also the CCSD(T) method. Along with frontier molecular orbital coefficients, the local softness being a DFT-based reactivity criterion is established as a useful tool to predict the regioselectivity in these cycloaddition reactions. Copyright © 2003 John Wiley & Sons, Ltd.
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KEYWORDS: 1,3-dipolar cycloadditions; regioselectivity; hard and soft acids and bases; local softness; density functional theory

INTRODUCTION

1,3-Dipolar cycloaddition reactions play an important role in the syntheses of five-membered heterocyclic compounds; therefore, understanding of their intrinsic reaction mechanism and the origin of their regioselectivity has been the aim of numerous experimental and theoretical studies.[1] It is generally accepted that a 1,3-dipolar cycloaddition includes four π-electrons from the 1,3-dipole and two π-electrons from the dipolarophile. Similarly to Diels–Alder additions, in their concerted approach, these [3 + 2] pericyclic reactions are allowed by frontier orbital interactions.[2] Although there were some discussions in the 1970s about the stepwise diradical and concerted approach,[3] the latter mechanism is now supported by a large number of theoretical and experimental studies.[1,4] It is not our intention to engage in this debate, we rather consider in this work only the concerted single-step reaction.

Diazomethane (H_2CNN) was first isolated in 1894[5] and is described either in the classical closed shell resonance hybrid form **1**[6,7] or in the form **2** recently proposed by Papakondylis and Mavridis.[8]
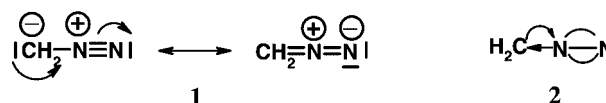
Diazomethane (DZM), known as a 1,3-dipole of the propargyl/allenyl anion types,[7] has been widely studied in its 1,3-dipolar cycloaddition (13DC) reactions with alkenes,[9–14] phosphaalkynes,[15] hydroxamic acids,[16] carbonyls,[1,12,17] etc. However, as far as we are aware, the 13DC of DZM to acetylenes has only been studied theoretically in the unsubstituted case[10] and the regioselectivity of this kind of addition has not been reported. Therefore, it seems reasonable, if not necessary, to investigate the mechanistic aspects, especially the regioselectivity, of the 13DC between DZM and substituted acetylenes, making use of quantum chemical methods.

Moreover, hydrazoic acid (HNNN) and nitrous oxide (N_2O) also belong to the propargyl/allenyl anion types[7] and have been studied as the dipoles in many 13DC reactions.[10,13,15,18,19] In this work we also considered the 13DC of hydrazoic acid to ethylene, acetylene, phosphaalkynes and cyanides. The 13DC of nitrous oxide to acetylenes has been studied in our previous work[19] at the B3LYP/6–31G(d,p) level. For the sake of consistency, we only studied in this work the 13DC of nitrous oxide to

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some dipolarophiles such as ethylene, acetylene, propyne and phosphaalkynes at a higher level, namely the B3LYP/6–311++G(d,p) level.

On the other hand, in relation to our continuing theoretical interest in the application of DFT-based reactivity descriptors[20] to study the regioselectivity of cycloaddition reactions,[19,21] we set out in all reactions considered in this paper to investigate the validity of the local hard and soft acids and bases (HSAB) principle[22] by using the local softness values obtained not only from the natural population analysis (NPA) charges[23] but also from the Hirshfeld ('stockholder') charges[24] that, among others, in view of their DFT-based character[25] and the increasing computational possibility to implement them, have recently attracted renewed interest.[26,27]

THEORY AND COMPUTATION DETAILS

In addition to the widely accepted computational advantages associated with density functional theory, it has also been the source of the sharp definition of a series of concepts, readily known by chemists but mostly introduced on an empirical basis. These concepts emerge as response functions of the system's energy with respect to its number of electrons N or/and its external (i.e. due to the nuclei) potential $v(\boldsymbol{r})$; among the most important ones, we mention the electronegativity (for detailed account of different electronegativity scales see, e.g., Ref. 28), hardness[29] and softness[29] and Fukui's frontier molecular orbital reactivity index.[30]

The electronegativity χ was found to the negative of the chemical potential μ, the derivative of E with respect to N at constant v:[31]

$$\mu = -\chi = \left(\frac{\partial E}{\partial N}\right)_v \qquad (1)$$

Within a finite difference approximation, this equation reduces to

$$\mu \approx \frac{I + A}{2} \qquad (2)$$

where I and A are the vertical ionization energy and electron affinity, respectively. Using Koopmans' approximation[32] within a Hartree–Fock context, this equation is further reduced to

$$\mu \approx \frac{-(\varepsilon_{\text{LUMO}} + \varepsilon_{\text{HOMO}})}{2} \qquad (3)$$

The chemical hardness η was defined as the second derivative of E with respect to the number of electrons N at constant v:[20c]

$$\eta = \frac{1}{2}\left(\frac{\partial^2 E}{\partial N^2}\right)_v = \frac{1}{2}\left(\frac{\partial \mu}{\partial N}\right) \approx \frac{I - A}{2} \qquad (4)$$

Within the framework of Koopmans' theorem, the approximation reduces to half of the HOMO–LUMO gap:

$$\mu \approx \frac{\varepsilon_{\text{LUMO}} - \varepsilon_{\text{HOMO}}}{2} \qquad (5)$$

The inverse of the hardness is called the softness S:[33]

$$S = \frac{1}{2\eta} \approx \frac{1}{I - A} \qquad (6)$$

of which the local counterpart, the local softness $s(\boldsymbol{r})$, is introduced as[33]

$$s(\boldsymbol{r}) = \left[\frac{\partial \rho(\boldsymbol{r})}{\partial \mu}\right]_v = S\left[\frac{\partial \rho(\boldsymbol{r})}{\partial N}\right]_v \equiv Sf(\boldsymbol{r}) \qquad (7)$$

i.e. the product of the global softness of the system and the Fukui function $f(\boldsymbol{r})$,[34] a reactivity index, which, as can be seen from Eqn (7), was introduced as the derivative of the system's electron density with respect to the number of electrons at constant external potential. Owing to the discontinuity of $\rho(\boldsymbol{r})$ with respect to N, a left- and a right-hand side derivative can be introduced, corresponding to the case of an electrophilic (f^-) or a nucleophilic (f^+) attack:

$$f^-(\boldsymbol{r}) = \left[\frac{\partial \rho(\boldsymbol{r})}{\partial N}\right]_v^- \approx \rho_N(\boldsymbol{r}) - \rho_{N-1}(\boldsymbol{r}) \qquad (8)$$

$$f^+(\boldsymbol{r}) = \left[\frac{\partial \rho(\boldsymbol{r})}{\partial N}\right]_v^+ \approx \rho_{N+1}(\boldsymbol{r}) - \rho_N(\boldsymbol{r}) \qquad (9)$$

where $\rho_{N+1}(\boldsymbol{r})$, $\rho_N(\boldsymbol{r})$ and $\rho_{N-1}(\boldsymbol{r})$ are the electron densities of the $N+1$, N and $N-1$ electron system, respectively, all at the geometry of the N-electron system. It was shown by Yang *et al.*[35] that f^- and f^+ can, on neglect of orbital relaxation on adding or subtracting electrons, be approximated by the density of the HOMO or the LUMO, respectively. From this, it can be seen that the Fukui function is a generalization of frontier MO theory, both methods, as they deal with the isolated reagents, however describing the onset of the reaction. Discrepancy of both indices from observed regioselectivities is thus often ascribed to the transition state occurring late on the reaction path.

Yang and Mortier[36] proposed a condensed version of these Fukui functions, i.e.

$$f_k^- \approx N_{k,N} - N_{k,N-1} \qquad (10)$$

$$f_k^+ \approx N_{k,N+1} - N_{k,N} \qquad (11)$$

where $N_{k,N+1}$, $N_{k,N}$ and $N_{k,N-1}$ are the electron populations of atom k in the $N+1$, N and $N-1$ electron system, respectively.

In addition to the introduction of these concepts, several chemical principles received theoretical justification. One of these is Pearson's hard and soft acids and bases principle, stating that hard acids prefer to bond to hard bases and soft acids to soft bases. This principle also has a local counterpart, stating that interacting sites of a Lewis acid and base will have local softnesses that are as close as possible. As such, it can be rationalized[37,38] that two molecules containing two possible interaction sites a and a' and b and b' will preferentially interact yielding the smallest of the two Δ values:

$$\Delta_1 = \left(s_a^+ - s_b^-\right)^2 + \left(s_{a'}^+ - s_{b'}^-\right)^2 \qquad (12)$$

$$\Delta_2 = \left(s_{a'}^+ - s_b^-\right)^2 + \left(s_a^+ - s_{b'}^-\right)^2 \qquad (13)$$

Quantum chemical calculations were performed with the aid of the Gaussian 98 set of programs.[39] All structures were fully optimized with the hybrid exchange correlation B3LYP functional and the 6–311++G(d,p) basis set. However, in our experience, the diffuse basis functions can cause some unpredictable errors in calculating the local softness values.[40] For this reason, we only used the B3LYP/6–311G(d,p) method to calculate the characteristics of the reactants in order to probe the regioselectivity in the 13DC reactions considered. Zero-point vibrational energies (ZPEs) were calculated and scaled down by a factor of 0.9806[41] at the B3LYP/6–311++G(d,p) level. In the simplest cases, the relative energies were further refined by single-point electronic energy computations at higher levels such as the B3LYP with the larger aug-cc-pVTZ basis set and coupled-cluster theory, CCSD(T)/6–311++G(d,p) and CCSD(T)/6–311++G(3df,2p). As mentioned above, atomic charges were obtained via natural population analysis using the NPA option in the Gaussian program and via the 'stock-holder' charges using Hirshfeld's partitioning procedure.[24] The orbital coefficients and the orbital shapes are obtained from HF/STO-3G calculations. Throughout this paper, bond distances are given in ångstroms, bond angles in degrees, total energies in hartrees and zero-point and relative energies, unless stated, otherwise in kilocalories per mole (1 kcal = 4.184 kJ).

RESULTS AND DISCUSSION

The 13DC of diazoalkanes

The differences in vertical ionization energies (*II*) and electron affinities (*AA*) obtained from B3LYP/6–311G(d,p) calculations for some simple diazoalkanes and a series of dipolarophiles are presented in Table 1. It turns out that diazomethane (DZM) behaves as a nucleophilic reagent involving its highest occupied molecular orbital (HOMO) in the reactions with ethylene, acetylene (cases 2 and 3) and the group II (cases 8–24) in Table 1, whereas it becomes an electrophilic reagent interacting via its lowest unoccupied molecular orbital (LUMO) in the reactions with the group I (cases 4–7 in Table 1). Table 1 also presents the differences in the vertical ionization energies and electron affinities (*II* – *AA*) for substituted diazoalkanes and H—C≡C—CH₃. While Br₂CNN, Cl₂CNN behave as electrophiles (group I), (CH₃)₂CNN acts as a nucleophile (group II) in their reactions with propyne.

Table 2 summarizes the main geometric parameters of the transition and product structures in the 13DC of DZM to ethylene, acetylene, propyne and methinophosphide (HC≡P). The activation energies and reaction energies computed from the full geometry optimizations at B3LYP/6–311++G(d,p), B3LYP/aug-cc-pVTZ, CCSD(T)/6–311++G(d,p) levels and from the single-point calculations at CCSD(T)/6–311++G(3df,2p) level are also listed in Table 2.

Comparing the geometric values of the transition structure (Ts) in Table 2 for the 13DC of DZM to ethylene with the best results obtained from the work of Blavins *et al.*[14] [QCISD/6–31G(d) and CCD/6-31G(d)] and Rastelli *et al.*[11] [MP2/6–31G(d) and B3LYP/6–31G(d)], we can see that the intersystem bond distances R_1 and R_2 are considerably improved when using B3LYP and CCSD calculations with more extended basis sets. Taking the CCSD(T)/6–311++G(d,p) values in the present work as references, the deviation of R_1 amounts to 0.008 Å in B3LYP/6–311++G(d,p) (this work), 0.018 Å in B3LYP/aug-cc-pVTZ (this work), 0.004 Å in QCISD/6–31G(d),[14] 0.002 Å in CCD/6–31G(d),[14] 0.040 Å in B3LYP/6–31G(d)[11] and 0.059 Å in MP2/6–31G(d).[11] Similarly, the differences in R_2 are 0.008 Å in B3LYP/6–311++G(d,p), 0.025 Å in B3LYP/aug-cc-pVTZ (our work), 0.042 Å in QCISD/6–31G(d),[14] 0.039 Å in CCD/6–31G(d),[14] 0.005 Å in B3LYP/6–31G(d)[11] and 0.026 Å in MP2/6–31G(d).[11] Further, in the 13DC of DZM to acetylene, the deviations in the B3LYP calculations of R_1 and R_2, as compared with the CCSD(T) level, are in the same range as in the case of 13DC of DZM to ethylene. It can be seen that the distances of both newly formed bonds in the cycloadducts in both 13DCs of DZM to ethylene and acetylene are nearly equal. However, the bond distances R_1 and R_2 in the transition structures are very similar, although R_1 goes to a larger bond length than R_2. These observations might point to a certain extent of asynchronicity in these concerted 13DC reactions.

The energy barriers, including scaled zero-point energy (ZPE) corrections, computed at the B3LYP levels [19.3 kcal mol⁻¹ using 6–311++G(d,p) and 20.4 kcal mol⁻¹ with aug-cc-pVTZ basis sets] for the ethylene case in Table 2 are close to the values obtained from QCISD/6–31G(d) (20.8 kcal mol⁻¹),[14] CCD/6–31G(d) (19.1 kcal mol⁻¹)[14] and CCD/6–311++G(2d,2p) (19.8

Table 1. Differences (in eV) in $II - AA$ of diazoalkanes and various dipolarophiles

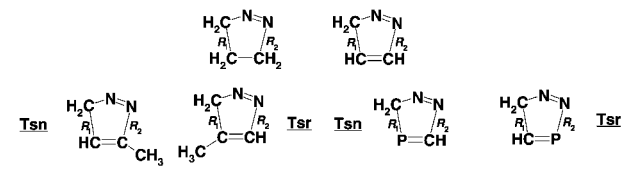| No.	Structure	II^a	AA^a	$II(R) - AA(H_2CNN)$	$II(H_2CNN) - AA(R)$
1	H_2CNN	9.06	−1.38		
2	$CH_2{=}CH_2$	10.56	−2.77	11.94	11.83
3	$H{-}C{\equiv}C{-}H$	11.36	−3.30	12.74	12.36
	Group I—				
4	$H{-}C{\equiv}C{-}CH_3$	10.30	−2.99	11.68	12.05
5	$Br{-}C{\equiv}C{-}CH_3$	9.50	−2.03	10.88	11.09
6	$Cl{-}C{\equiv}C{-}CH_3$	9.74	−2.60	11.12	11.66
7	$F{-}C{\equiv}C{-}CH_3$	10.27	−3.09	11.65	12.15
	Group II—				
8	$H{-}C{\equiv}C{-}Br$	10.22	−1.88	11.60	10.94
9	$H{-}C{\equiv}C{-}Cl$	10.55	−2.55	11.93	11.61
10	$H{-}C{\equiv}C{-}F$	11.28	−3.37	12.66	12.43
11	$H{-}C{\equiv}C{-}CBr_3$	9.94	0.66	11.32	8.40
12	$H{-}C{\equiv}C{-}CCl_3$	10.74	−0.45	12.12	9.51
13	$H{-}C{\equiv}C{-}CF_3$	11.99	−2.21	13.37	11.27
14	$Br{-}C{\equiv}C{-}CBr_3$	9.61	0.76	10.99	8.30
15	$Cl{-}C{\equiv}C{-}CCl_3$	10.33	−0.31	11.71	9.37
16	$F{-}C{\equiv}C{-}CF_3$	11.89	−2.70	13.27	11.76
17	$H{-}C{\equiv}P$	10.76	−0.89	12.14	9.95
18	$Br{-}C{\equiv}P$	9.82	−0.51	11.20	9.57
19	$Cl{-}C{\equiv}P$	10.08	−0.59	11.46	9.65
20	$F{-}C{\equiv}P$	10.58	−1.10	11.96	10.16
21	$CH_3{-}C{\equiv}P$	9.84	−1.07	11.22	10.13
22	$CBr_3{-}C{\equiv}P$	9.77	1.01	11.15	8.05
23	$CCl_3{-}C{\equiv}P$	10.38	0.76	11.76	8.30
24	$CF_3{-}C{\equiv}P$	11.27	0.09	12.65	8.97
No.	Structure	II^a	AA^a	II(propyne) − $AA(R_2CNN)$	$II(R_2CNN)$ − AA(Propyne)
	Group I—				
1	Br_2CNN	8.53	0.63	9.67	11.52
2	Cl_2CNN	8.81	0.49	9.81	11.80
	Group II—				
3	$(CH_3)_2CNN$	7.85	−1.36	11.66	10.84

[a] Vertical ionization energies and electron affinities obtained from B3LYP/6–311G(d,p) computations.

kcal mol^{-1}).[14] Owing to the difficulty in the frequency calculation at the CCSD(T)/6–311++G(d,p) level, we only report in Table 2 the energy barriers computed from the optimization process and from the single-point calculation at the CCSD(T)/6–311++ G(3df,2p) level based on the CCSD(T)/6–311++G(d,p) geometry, corrected with the scaled ZPE obtained from B3LYP/6–311++ G(d,p) calculations. In all calculations, the differences in energy barriers between B3LYP and CCSD(T) calculations vary from 2 to 5 kcal mol^{-1} as reported in the literature.[42] However, although the B3LYP slightly underestimates the energy barriers, this computationally low cost approximation gives the same orders of energy barriers in the initial attacks of the 13DC reactions as compared with the CCSD(T) method (cf. Table 2). Therefore, in the rest of this work, the B3LYP/6–311++G(d,p) will be the method of choice to compute the activation energies. It should be kept in mind that in this work, the emphasis is mainly on reproducing trends in activation barriers and not on reproducing the absolute values of the barriers themselves. One can nevertheless see that the differences in reaction energies between both

B3LYP and CCSD(T) levels show larger variations from 7 to 12 kcal mol^{-1}.

In an attempt to probe the regioselectivity, we consider a number of different substituents in the dipolarophiles and also in the DZM dipole. The calculated results are reported in Table 3. Moreover, the criteria used to rationalize the regioselectivity such as the local softness difference obtained from NPA and Hirshfeld charges (Δ) and the classical frontier molecular orbital (FMO) coefficients (C) are also displayed in Table 3.

Let us first consider the monosubstituted cases, namely the methylated $H{-}C{\equiv}C{-}CH_3$ containing an electron-donor group and halogenated $H{-}C{\equiv}C{-}Br$, $H{-}C{\equiv}C{-}Cl$, and $H{-}C{\equiv}C{-}F$ containing an electron-withdrawing group. Compared with the unsubstituted case $H{-}C{\equiv}C{-}H$, we note that the activation energy increases by about 2–4 kcal mol^{-1} when one hydrogen atom is replaced by an electron donor group and decreases by 1–3 kcal mol^{-1} when it is substituted by an electron acceptor group. Such a trend is in line with the experimental kinetic results[43] that showed that electron acceptors on dipolarophiles and electron donors on

Table 2. Selected geometric parameters of the transition structures and cycloadducts in 13DC of H_2CNN and related structures

Structure	B3LYP 6–311++G(d,p)	B3LYP[a] aug-cc-pVTZ	CCSD(T)[a] 6–311++G(d,p)	CCSD(T)[a] 6–311++G(3df,2p)
$H_2C=CH_2$				
Ts—				
$\Delta E^{\neq}$ (kcal mol^{-1})	19.27	20.36	15.00	16.35
R_1 (Å)	2.207	2.197	2.215	
R_2 (Å)	2.337	2.320	2.345	
Product—				
ΔE_r (kcal mol^{-1})	−23.48	−21.93	−33.42	−32.64
R_1 (Å)	1.540			
R_2 (Å)	1.493			
$HC\equiv CH$				
Ts—				
$\Delta E^{\neq}$ (kcal mol^{-1})	19.03	19.79	16.02	17.08
R_1 (Å)	2.203	2.199	2.200	
R_2 (Å)	2.372	2.357	2.358	
Product—				
ΔE_r (kcal mol^{-1})	−42.68	−41.77	−49.06	−49.42
R_1 (Å)	1.487	1.484		
R_2 (Å)	1.433	1.431		
$H—C\equiv C—CH_3$				
$\Delta E^{\neq}$ (Ts$_n$)	21.44		17.13	
$\Delta E^{\neq}$ (Ts$_r$)	23.04		18.06	
$HC\equiv P$				
$\Delta E^{\neq}$ (Ts$_n$)	9.07		6.54	6.82
$\Delta E^{\neq}$ (Ts$_r$)	10.01		8.08	8.01

[a] Including zero-point vibrational corrections (ZPEs) obtained at the B3LYP/6–311++G(d,p) level.

dipoles reduce the activation energies. In the DZM + H—C≡C—CH$_3$ case, the more favored Ts-normal corresponds to the attack of CH$_2$ in DZM on C—H in acetylene, whereas it is the attack of CH$_2$ on the substituted carbon in the halogenated acetylenes.

Similarly, as seen in Table 3, the energy barriers of the Ts-normal approach of the halophosphaalkynes actually decrease on going from Cl—C≡P to Br—C≡P, H—C≡P and F—C≡P. Both Cl and Br atoms clearly behave as global electron donors, presumably through π back-donation in such a way that the P-atoms in Cl—C≡P and Br—C≡P have more negative net charges than that in H—C≡P, so the attack of CH$_2$ in DZM on the P-atom in those substituted cases becomes more difficult, leading to higher activation energies. In the F—C≡P case, owing to the strongest σ-electron withdrawing effect of the fluorine atom, the substituted carbon now has fewer electrons than the P-atom. As a consequence of the reversed polarity, the Ts-normal in this case corresponds to the attack of CH$_2$ in DZM to the C-atom. It is also interesting that in CH$_3$—C≡P the activation energy of the Ts-normal turns out to be higher than that of H—C≡P, in agreement with that observed in the pair acetylene–propyne. Experimentally, all of the

13DC of diazo compounds to alkylphosphaalkynes (R—C≡P, R = alkyl) proceed regiospecifically and lead almost exclusively to the 3H-1,2,4-diazaphospholes **3** with yields of 90–100%.[44]

(R = Alkyl)

3
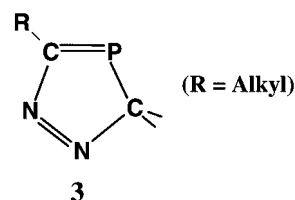
The substituent effects in the dipole are best illustrated when comparing the 13DC of $(CH_3)_2CNN$ and H_2CNN with that of H—C≡C—CH$_3$. The presence of two methyl groups in the dipole reinforces the electron donating capacity of the C-atom in DZM leading to the lower energy barriers (18.8 kcal mol^{-1} in case 25 compared with 21.4 kcal mol^{-1} in case 2 in Table 3). Nevertheless, the presence of two Br- or two Cl-atoms in the dipole does not give rise to a reversed regioselectivity; in fact, the Ts-normal also correspond to the attack of the C-atom in diazoalkanes on C—H in propyne as in the $(CH_3)_2CNN$ case. In this case, this leads to the conclusion that these halogens behave as electron donors, in

Table 3. Different reactivity criteria [energy barriers ΔE (kcal mol^{-1}), local softness differences Δ and FMO coefficients product C] used in explaining the regioselectivity of 13DC of H_2CNN with $R—C\equiv P$ and $R^1C\equiv C—R^2$, and R_2CNN on $H—C\equiv C—CH_3$

Group	No.	Structure	Site of attack in Ts	$\Delta E^{\neq}$	Δ^a	Δ^b	C^c
I	1	$HC\equiv CH$	(CH_2) on C—H	**19.03**[d]			
	2	$H—C\equiv C—CH_3$	(CH_2) on C—H	**21.44**	0.394	0.201	0.170
			(CH_2) on C—CH$_3$	23.04	0.149	0.059	0.195
	3	$Br—C\equiv C—CH_3$	(CH_2) on C—Br	**20.66**	0.725	0.285	0.117
			(CH_2) on C—CH$_3$	22.82	0.166	0.190	0.170
	4	$Cl—C\equiv C—CH_3$	(CH_2) on C—Cl	**20.83**	**0.155**	**0.185**	**0.199**
			(CH_2) on C—CH$_3$	23.20	0.602	0.241	0.176
	5	$F—C\equiv C—CH_3$	(CH_2) on C—F	**17.80**	**0.125**	0.152	**0.134**
			(CH_2) on C—CH$_3$	22.30	0.464	0.137	0.100
II	6	$H—C\equiv C—Br$	(CH_2) on C—H	19.23	1.293	0.586	1.412
			(CH_2) on C—CBr	**18.41**	1.355	0.588	**1.413**
	7	$H—C\equiv C—Cl$	(CH_2) on C—H	19.57	1.543	0.643	1.418
			(CH_2) on C—Cl	**18.62**	**1.507**	0.644	**1.419**
	8	$H—C\equiv C—F$	(CH_2) on C—H	19.02	1.757	0.523	1.407
			(CH_2) on C—F	**15.36**	**1.556**	0.523	**1.411**
	9	$H—C\equiv C—CBr_3$	(CH_2) on C—H	**16.47**	2.256	1.169	0.407
			(CH_2) on C—CBr$_3$	18.28	2.079	1.165	0.424
	10	$H—C\equiv C—CCl_3$	(CH_2) on C—H	**16.12**	**1.572**	**1.200**	**0.469**
			(CH_2) on C—CCl$_3$	16.83	1.891	1.204	0.451
	11	$H—C\equiv C—CF_3$	(CH_2) on C—H	15.21	0.644	0.268	1.065
			(CH_2) on C—CF$_3$	**14.29**	0.818	0.271	1.053
	12	$Br—C\equiv C—CBr_3$	(CH_2) on C—Br	**16.42**	**2.238**	**1.241**	**0.436**
			(CH_2) on C—CBr$_3$	18.31	2.377	1.244	0.418
	13	$Cl—C\equiv C—CCl_3$	(CH_2) on C—Cl	**16.11**	**1.777**	**1.289**	**0.508**
			(CH_2) on C—CCl$_3$	17.15	2.033	1.292	0.490
	14	$F—C\equiv C—CF_3$	(CH_2) on C—F	**11.49**	**0.835**	**0.347**	**1.131**
			(CH_2) on C—CF$_3$	14.30	0.959	0.350	1.113
	15	$H—C\equiv P$	(CH_2) on P	**9.07**	**0.392**	**0.487**	**1.304**
			(CH_2) on C—H	10.01	0.924	0.504	1.298
	16	$Br—C\equiv P$	(CH_2) on P	**11.69**	**0.696**	**0.647**	**1.291**
			(CH_2) on C—Br	13.08	1.359	0.668	1.286
	17	$Cl—C\equiv P$	(CH_2) on P	**12.02**	**0.702**	**0.539**	**1.299**
			(CH_2) on C—Cl	13.26	1.365	0.558	1.294
	18	$F—C\equiv P$	(CH_2) on P	12.23	0.590	0.555	1.278
			(CH_2) on C—F	**10.96**	1.215	0.573	**1.279**
	19	$CH_3—C\equiv P$	(CH_2) on P	**12.52**	**0.676**	**0.523**	**1.236**
			(CH_2) on C—CH$_3$	15.47	1.326	0.541	1.230
	20	$CBr_3—C\equiv P$	(CH_2) on P	**8.11**	**1.156**	**0.518**	**0.802**
			(CH_2) on C—CBr$_3$	11.96	1.861	0.536	0.778
	21	$CCl_3—C\equiv P$	(CH_2) on P	**7.43**	**0.985**	**0.458**	**0.852**
			(CH_2) on C—CCl$_3$	10.18	1.674	0.475	0.826
	22	$CF_3—C\equiv P$	(CH_2) on P	**5.90**	**0.639**	**0.489**	**1.183**
			(CH_2) on C—CF$_3$	6.60	1.272	0.506	1.166
I	23	Br_2CNN	(Br_2C) on C—H	**14.74**	0.583	0.343	0.070
			(Br_2C) on C—CH$_3$	15.94	0.272	0.138	0.090
	24	Cl_2CNN	(Cl_2C) on C—H	**13.21**	0.539	0.355	0.078
			(Cl_2C) on C—CH$_3$	14.23	0.244	0.148	0.098
II	25	$(CH_3)_2CNN$	$(CH_3)_2C$ on C—H	**18.77**	1.981	0.696	**1.176**
			$(CH_3)_2C$ on C—CH$_3$	21.38	1.963	0.632	1.175

[a] Δ, differences in local softness obtained from NPA charges.
[b] Δ, differences in local softness obtained from stockholder charges.
[c] C, FMO coefficients product calculated at the HF/STO-3G level.
[d] Values in bold correspond to Ts-onrmal and corrected prediction cases by the relevant criteria.

agreement with their negative σ_R values[45] and their higher softness values. It should be noted that we could not locate the Ts for the F_2CNN case owing to the high stability of the difluorocarbene (F_2C) and nitrogen molecule, which invariably leads to dissociation upon geometry optimizations.

The geometric parameters of all the studied Tss (available in the Supplementary Material at the epoc website at http://www.wiley.com/epoc) also suggest that the concerted 13DC of diazoalkanes to acetylenes and phosphaalkynes is a slightly asynchronous process as observed in the unsubstituted cases.

We also use the reactivity indices including the local softness difference Δ and the FMO coefficients to explain the regioselectivity of these 13DC reactions. The definitions of and equations for these criteria can be found elsewhere,[19,21] only the calculated results are listed here in Table 3. It should be stressed that when a diazo derivative behaves as an electrophilic agent (group I), we consider s_k^+ as their local softness and their LUMO coefficients as frontier MOs. In contrast, when they act as nucleophiles (group II) we consider s_k^- and their HOMO coefficients. From the viewpoint of the local HSAB principle[22] and the FMO theory,[46] a lower activation energy is already reflected in a lower local softness difference and higher FMO coefficients product. Table 3 indicates that of the 24 cases considered, the Δ_{NPA} index gives a correct prediction in 15 cases, whereas the $\Delta_{stockholder}$ is successful in 12 cases and the classical FMO coefficient product is able to predict 18 cases.

In summary, the criteria based on the Δ_{NPA} and FMO coefficient products turn out the more useful tools in predicting the regioselectivity in the 13DC reactions, as concluded in our previous work.[19,21] The recently developed 'stockholder' charges do not seem adequate, as also observed in the work of Olah et al.[26] The failed cases of the criteria could be understood by looking at the shapes of the LUMO and HOMO of those compounds, as depicted in Figs 1 and 2. The π-orbitals of C- and N-atoms in diazoalkanes do not correspond to the LUMO, but to the
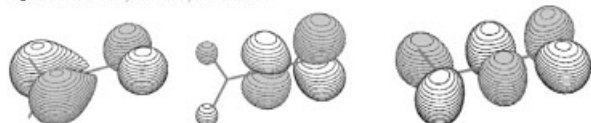
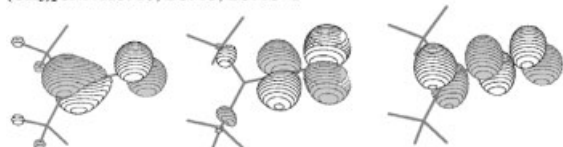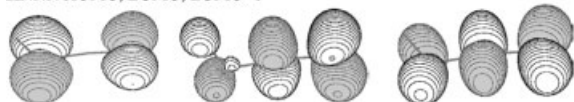**Figure 1.** Selected HOMO and LUMO of related structures (obtained from HF/STO-3G calculations)
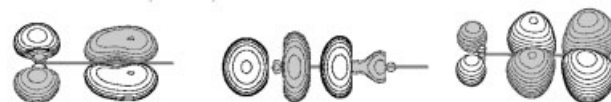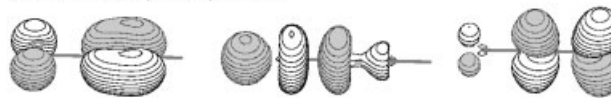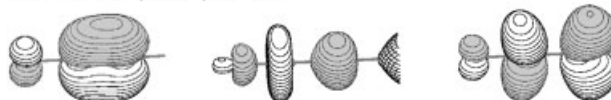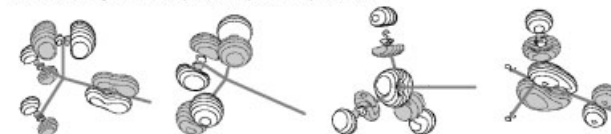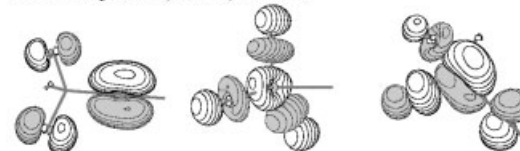
Figure 2. Selected HOMO and LUMO of related structures (continued)

LUMO + 1 or LUMO + 2. Similarly, the π-orbitals of C-atoms in H—C≡C—CBr$_3$ and H—C≡C—Br do not correspond to the HOMO or LUMO, but to the HOMO − 1 or LUMO − 1. The change in orbital energy ordering and thereby the abnormal behavior of the HOMO and LUMO effectively perturb the FMO interaction treatment, leading to a failure of the regioselectivity prediction. When the HOMO − 1 and LUMO + 1 are taken into consideration, a better agreement could be attained. Similarly, the population analysis charges employed to calculate the local softnesses are taken only for the neutral (N electrons), cation ($N − 1$ electrons) and anion ($N + 1$ electrons) species, that do not correspond to the electrons really involved in the electronic reorganization.

The 13DC of hydrazoic acid and nitrous oxide

In this section we will examine the 13DC of the simplest azide and nitrous oxide to some simple dipolarophiles. Our objective is to obtain additional information necessary for a more general rationalization of the regioselectivity in this kind of 13DC.

Table 4. Differences (in eV) in $II - AA$ of hydrazoic acid (HNNN), nitrous oxide (N_2O) and related dipolarophiles

No.	Structure	II^{a}	AA^{a}	$II(R) - AA(HNNN)$	$II(HNNN) - AA(R)$
1	HNNN	10.77	−1.97		
2	$CH_2{=}CH_2$	10.56	−2.77	12.53	13.54
3	$H{-}C{\equiv}C{-}H$	11.36	−3.30	13.33	14.07
4	$H{-}C{\equiv}N$	13.73	−3.52	15.70	14.29
5	$Br{-}C{\equiv}N$	11.80	−1.10	13.77	11.87
6	$Cl{-}C{\equiv}N$	12.33	−1.92	14.30	12.69
7	$F{-}C{\equiv}N$	13.49	−4.24	15.46	15.01
8	$CH_3{-}C{\equiv}N$	12.24	−2.55	14.21	13.32
9	$H{-}C{\equiv}P$	10.76	−0.89	12.73	11.66
10	$Br{-}C{\equiv}P$	9.82	−0.51	11.79	11.28
11	$Cl{-}C{\equiv}P$	10.08	−0.59	12.05	11.36
12	$F{-}C{\equiv}P$	10.58	−1.10	12.55	11.87
13	$CH_3{-}C{\equiv}P$	9.84	−1.07	11.81	11.84

No.	Structure	II^{a}	AA^{a}	$II(R) - AA(NNO)$	$II(NNO) - AA(R)$
1	NNO	12.90	−2.91		
2	$CH_2{=}CH_2$	10.56	−2.77	13.47	15.67
3	$H{-}C{\equiv}C{-}H$	11.36	−3.30	14.27	16.20
4	$H{-}C{\equiv}C{-}CH_3$	10.30	−2.99	13.21	15.89
5	$H{-}C{\equiv}P$	10.76	−0.89	13.67	13.79
6	$CH_3{-}C{\equiv}P$	9.84	−1.07	12.75	13.97

[a] Vertical ionization energies and electron affinities obtained from B3LYP/6–311G(d,p) computations.

Table 4 presents the differences ($II - AA$) for hydrazoic acid, nitrous oxide and related compounds. It has again been observed that hydrazoic acid behaves as an electrophile in the reactions with ethylene and acetylene, whereas it acts as a nucleophile when approaching phosphaalkynes (except for $CH_3C{\equiv}P$ and probably alkyl derivatives) and cyanides. For its part, nitrous oxide always behaves as an electrophile in the reactions considered.

Similarly to the 13DC of diazo compounds, we also computed the energy barriers and reaction energies at higher levels for the 13DC of hydrazoic acid to the simplest structures, ethylene and acetylene. The energy barriers obtained from the optimization procedures at B3LYP/6–311++G(d,p), B3LYP/aug-cc-pVTZ levels and also from the single-point calculations at CCSD(T)/6–311++G(d,p) level are recorded in Table 5. Geometric parameters of the transition structures and also the product structures in the simplest cases in the 13DCs of

hydrazoic acid and nitrous oxide are given in Tables S3 and S4 in the Supplementary Material at the epoc website at http: //www.wiley.com/epoc.

It is noted from Table 5 that the differences in calculated barrier heights between B3LYP and CCSD(T) methods vary from 0.1 to 1.3 kcal mol^{-1}, which are smaller than that in the 13DC of DZM (cf. Table 2). On the other hand, the reaction energy differences between the two methods again show a larger variation from 2–7 kcal mol^{-1}. In general, the performance of the B3LYP functional seems to depend considerably upon the reaction type, as already reported in the literature.[42] In the 13DC case considered here, B3LYP performs fairly well, giving energy barriers close to the CCSD(T) or CASPT2 counterparts.[47]

Table 6 displays the energy barriers of the transition structures in the 13DC of hydrazoic acid to phosphaalkynes and cyanides and in the 13DC of nitrous oxide to

Table 5. Barrier heights $\Delta E^{\neq}$ and reaction energies ΔE_r in 13DC of HNNN to ethylene and acetylene[a]

Structures	B3LYP 6–311++G(d,p)	B3LYP aug-cc-pVTZ	CCSD(T) 6–311++G(d,p)
$H_2C{=}CH_2$			
Ts—			
$\Delta E^{\neq}$ (kcal mol^{-1})	22.48		21.27
Product—			
ΔE_r (kcal mol^{-1})	−13.82		−21.05
$HC{\equiv}CH$			
Ts—			
$\Delta E^{\neq}$ (kcal mol^{-1})	21.69	23.04	21.76
Product—			
ΔE_r (kcal mol^{-1})	−56.38	−55.16	−58.54

[a] Including zero-point vibrational corrections (ZPEs) obtained at the B3LYP/6–311++G(d,p) level.

Table 6. Different criteria [energy barriers $\Delta E^{\neq}$ (kcal mol^{-1}), local softness differences Δ and FMO coefficients product C] used in explaining the regioselectivity of the 13DC of HNNN to R—C≡N and R—C≡P and N$_2$O to H—C≡C—CH$_3$, H—C≡P and CH$_3$—C≡P

No.	Structure	Site of attack in TS	$\Delta E^{\neq}$	Δ^a	Δ^b	C^c
13DC of HNNN—						
1	H—C≡N	(NH) on C—H	**27.57**[d]	**0.155**	**0.525**	**1.409**
		(NH) on N	34.27	0.202	0.529	1.403
2	Br—C≡N	(NH) on C—Br	**27.06**	**0.617**	0.335	**0.362**
		(NH) on N	34.82	0.621	0.328	0.333
3	Cl—C≡N	(NH) on C—Cl	**26.65**	**0.588**	0.343	**0.410**
		(NH) on N	34.75	0.629	0.338	0.383
4	F–C≡N	(NH) on C—F	**21.07**	**0.247**	**0.130**	**1.400**
		(NH) on N	31.32	0.264	0.150	1.385
5	CH$_3$—C≡N	(NH) on C—CH$_3$	**30.92**	1.823	0.790	**1.274**
		(NH) on N	37.42	1.744	0.785	1.273
6	H—C≡P	(NH) on P	**11.17**	**0.448**	**0.520**	**1.329**
		(NH) on C—H	14.08	0.806	0.595	1.318
7	Br—C≡P	(NH) on P	**15.42**	**0.737**	**0.658**	**1.315**
		(NH) on C—Br	18.02	1.183	0.747	1.306
8	Cl—C≡P	(NH) on P	**15.75**	**0.738**	**0.550**	**1.323**
		(NH) on C—Cl	17.98	1.184	0.632	1.314
9	F—C≡P	(NH) on P	15.70	0.645	0.578	1.300
		(NH) on C—F	**15.60**	1.065	0.660	**1.302**
10	CH$_3$—C≡P	(NH) on P	**14.54**	**0.705**	**0.524**	**1.260**
		(NH) on C—CH$_3$	17.49	1.142	0.606	1.248
13DC of N$_2$O—						
11	H—C≡C—CH$_3$	(O) on C—H	30.01	0.162	0.086	0.449
		(O) on C—CH$_3$	**28.66**	**0.037**	**0.006**	**0.461**
12	H—C≡P	(O) on P	**19.51**	0.771	0.904	0.668
		(O) on C—H	23.39	0.413	0.502	0.675
13	CH$_3$—C≡P	(O) on P	**22.26**	0.818	0.869	0.644
		(O) on C—CH3	23.21	0.317	0.402	0.667

[a] Δ, differences in local softness obtained from NPA charges.
[b] Δ, differences in local softness obtained from stockholder charges.
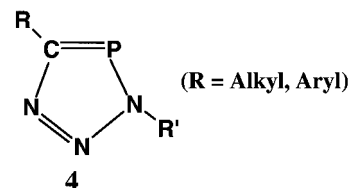[c] C, FMO coefficients product.
[d] Values in bold correspond to Ts-normal and corrected predictions of criteria.

propyne, methinophosphide (HC≡P) and ethylidyne-phosphine (CH$_3$C≡P). The local softness differences and the FMO coefficients are also listed in Table 6.

Accordingly, an approach through a Ts-normal invariably corresponds to an attack of the terminal NH in hydrazoic acid on the C-atom in cyanides and the P-atom in phosphaalkynes (except for FC≡P). In the same vein, a Ts-normal corresponds to the attack of the O-atom in nitrous oxide on the C—H in propyne or the P-atom in phosphaalkynes. It is clear that these approaches follow the difference in electronegativity of both atoms in each dipolarophile. The C-atom is less electronegative than the N in cyanides; a reversed polarity holds in phosphaalkynes. Therefore, the C-atom is more able to receive electrons from the NH terminus in hydrazoic acid that this approach is more favored. The presence of an electron acceptor group (Br, Cl, F) enhances the electron deficiency of the C-atom, and as a consequence tends to decrease the energy barriers from 27.6 kcal mol^{-1} in HC≡N to 27.1 kcal mol^{-1} in BrC≡N, 26.7 kcal mol^{-1} in ClC≡N and 21.1 kcal mol^{-1} in FC≡N. In contrast, an electron donor group (CH$_3$) increases the energy barrier to 30.9 kcal mol^{-1} in CH$_3$C≡N. It is interesting

that the substituent effect in the 13DC of hydrazoic acid to phosphaalkynes is closely analogous to that of diazomethane to phosphaalkynes. The presence of halogen atoms tends to increase the energy barriers and the Ts-normal also corresponds to the attack to C—F instead of the P-atom in FC≡P (cf. the previous sub-section). The regioselectivity in the 13DC of CH$_3$C≡P to hydrazoic acid is also comparable to that of diazomethane. Similarly to diazo compounds, azides undergo regiospecific [3 + 2] cycloadditions with alkyl- and arylphosphaalkynes producing 3H-1,2,3,4-triazaphospholes **4** as the sole primary cycloadducts.

(R = Alkyl, Aryl)

4

Moreover, the number of correct predictions on the utilized criteria, namely 9/13 cases for Δ_{NPA}, 7/13 cases for $\Delta_{stockholder}$ and 11/13 cases for FMO coefficient products (cf. Table 6), lend further support to our conclusion

on the usefulness of the reactivity indices in explaining, rationalizing and predicting the regioselectivity (cf. the previous sub-section).

CONCLUSIONS

The 13DC reactions of diazoalkanes, hydrazoic acid and nitrous oxide to the polar dipolarophiles considered are essentially orbital-controlled. This observation is supported by the successful prediction of the regioselectivity based on reactivity criteria that are basically generalized forms of FMO theory.

The local softness differences and FMO coefficient products remain the criteria of choice in predicting the regioselectivity of cycloaddition reactions. The 'stockholder' charges are less efficient than the NPA charges in supporting the local HSAB principle.

Supplementary material

Additional information containing all optimized geometrics used in this work is available at the epoc website at http://www.wiley.com/epoc.

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