UNIVERSIDADE DE ÉVORA

Computational Chemistry Modelling and Simulations of Finite Systems

THE DECISIVE ROLE OF GLOBAL ELECTRON DENSITY TRANSFER ON REACTION RATES

AN MEDT INTERPRETATION

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13 September 2023
Évora, Portugal (online)

THE MOLECULAR ELECTRON DENSITY THEORY

"the changes in electron density, but not MO interactions, are responsible for chemical reactivity"

L. R. Domingo, *Molecules* **2016**, *21*, 1319

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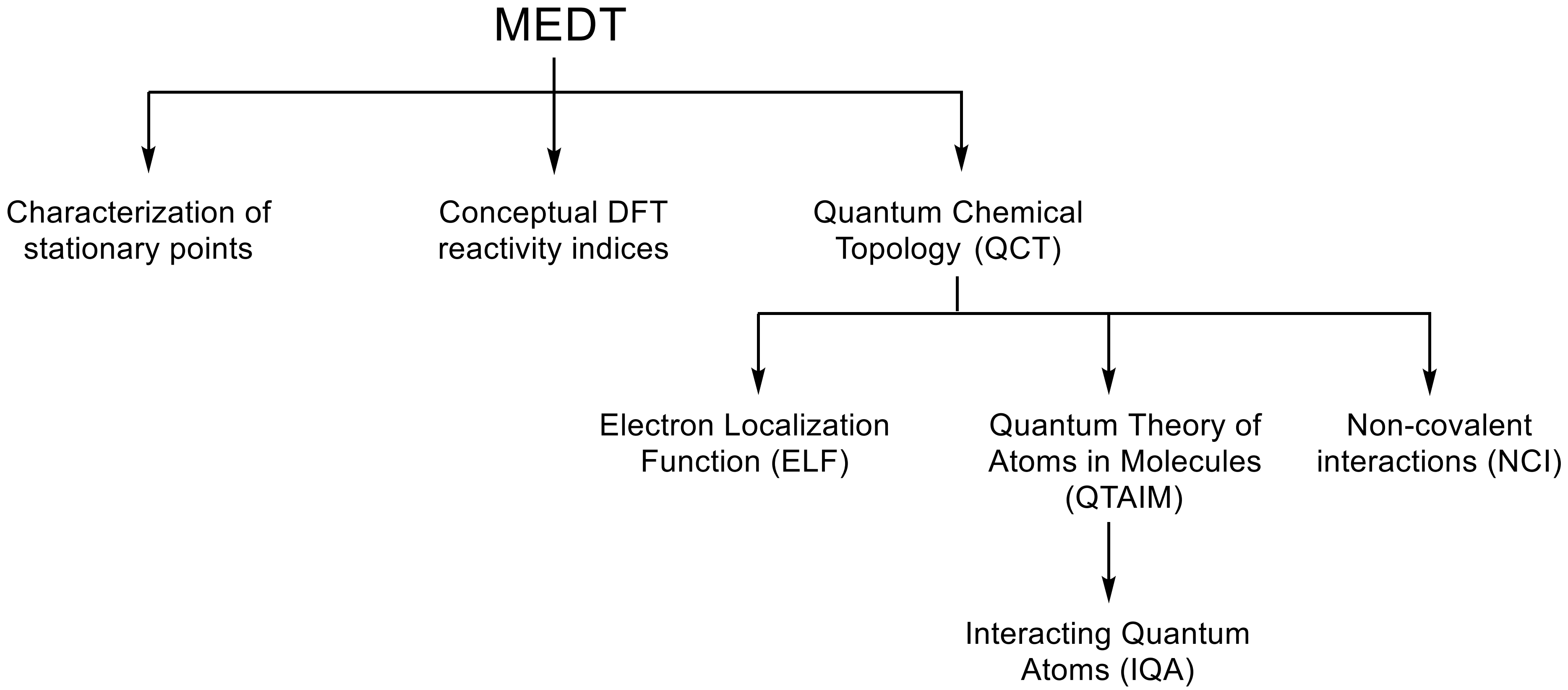

MEDT

Characterization of stationary points

Conceptual DFT reactivity indices

Quantum Chemical Topology (QCT)

Electron Localization Function (ELF)

Quantum Theory of Atoms in Molecules (QTAIM)

Non-covalent interactions (NCI)

Interacting Quantum Atoms (IQA)

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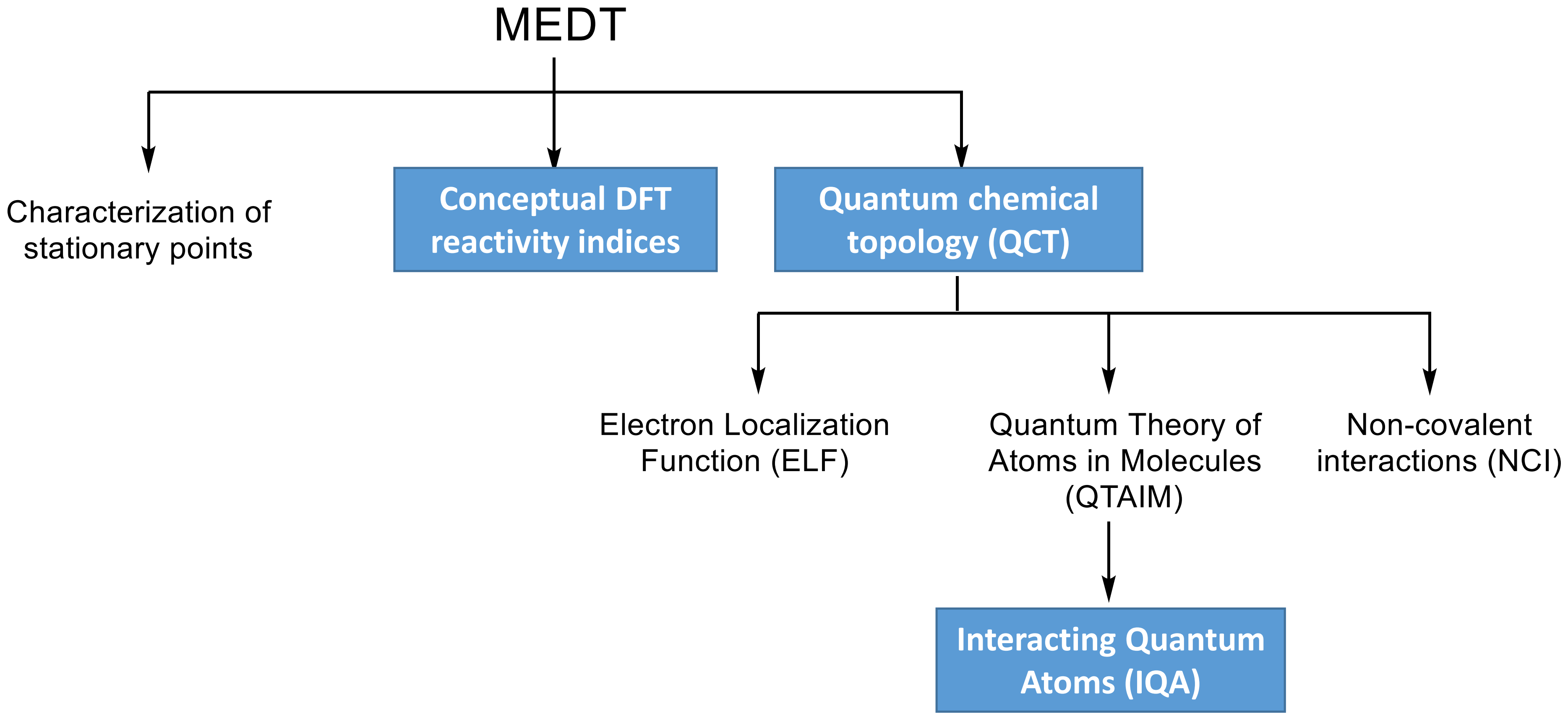

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THE GLOBAL ELECTRON DENSITY TRANSFER

When two molecules with different electronic chemical potentials combine chemically,
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Domingo, L. R.; Ríos-Gutiérrez, M.; Pérez, P. Molecules **2016**, *21*, 748

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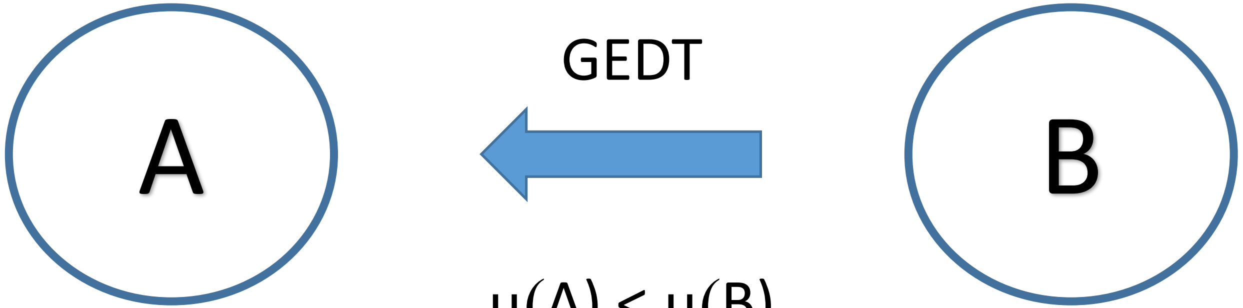

$\mu(A) < \mu(B)$

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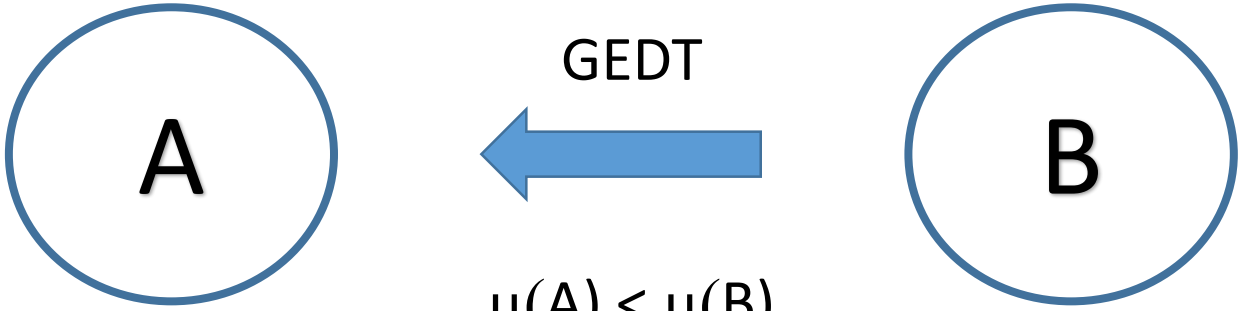

A

GEDT

B

$\mu(A) < \mu(B)$

Electrophile

Nucleophile

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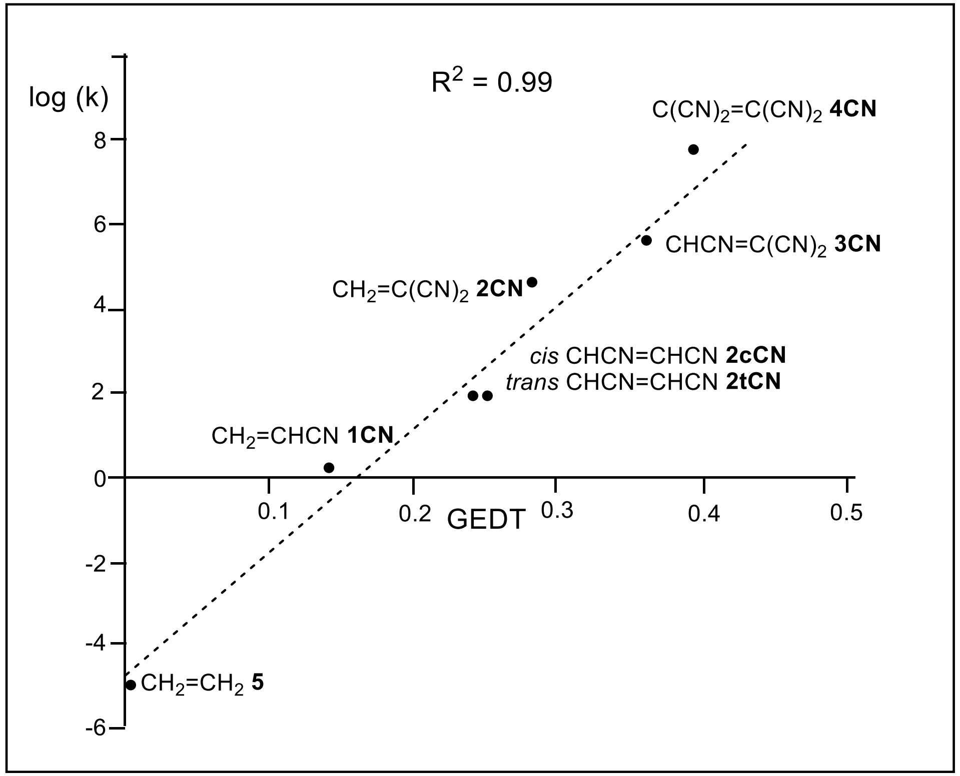
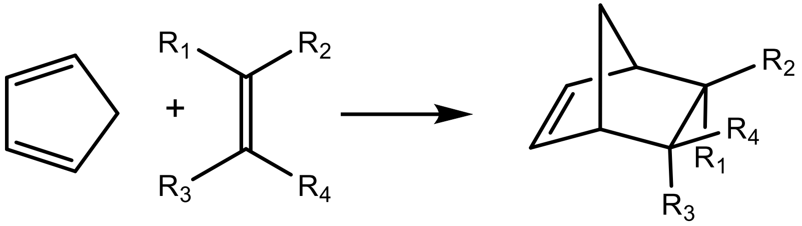
CORRELATION BETWEEN GEDT AND $\Delta E^{\neq}$



Diels-Alder (DA) reaction between cyclopentadiene (Cp) **1** and cyanoethylenes **7**

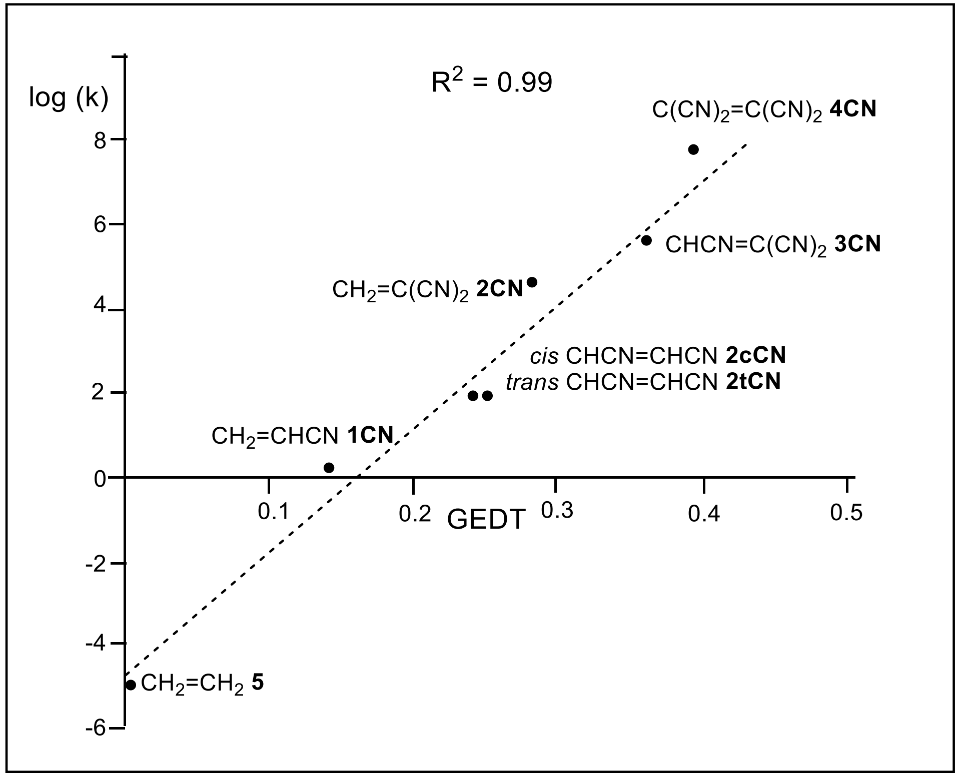


1 **7** **8**

nCN $R_{1\text{-}4}$ = H or CN

L.R. Domingo, M.J. Aurell, P. Perez, R. Contreras. *J. Org. Chem.* **2003**, *68*, 3884

CORRELATION BETWEEN GEDT AND $\Delta E^{\neq}$



Excellent linear correlation between the logarithm of experimental reaction rates and GEDT

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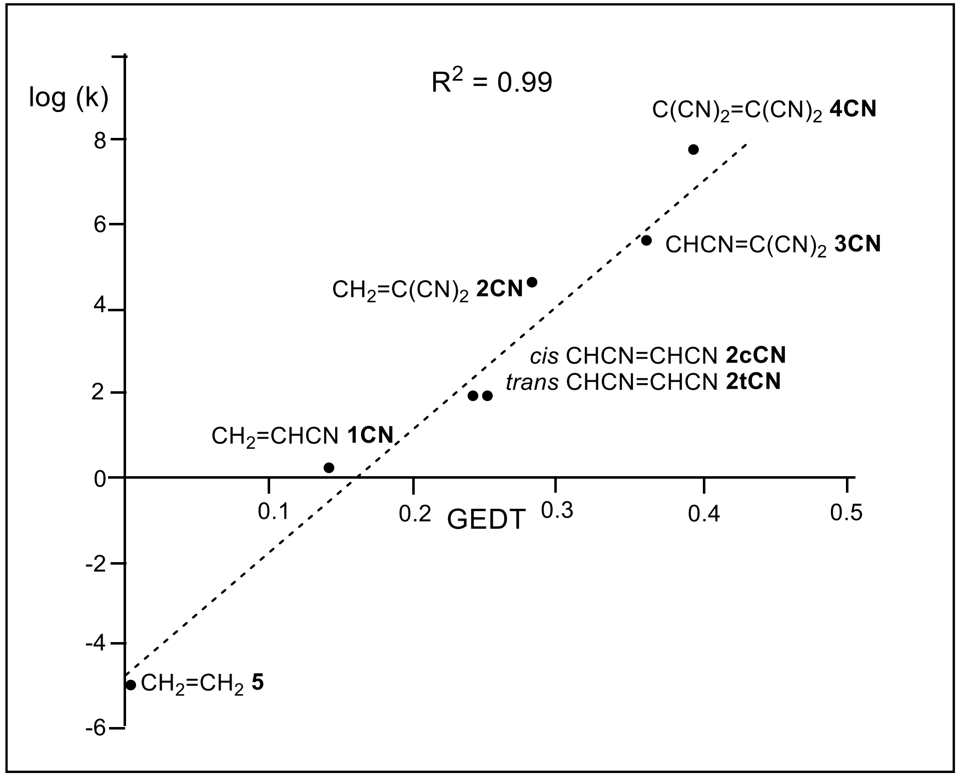

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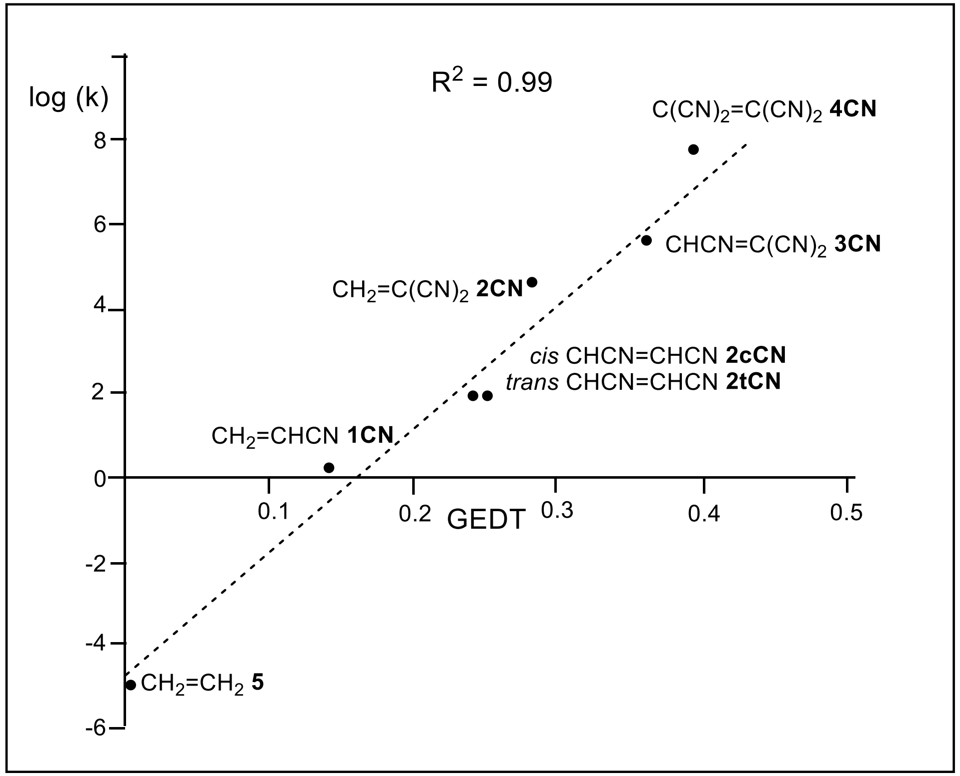

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GEDT is one of the key factors in the activation energy

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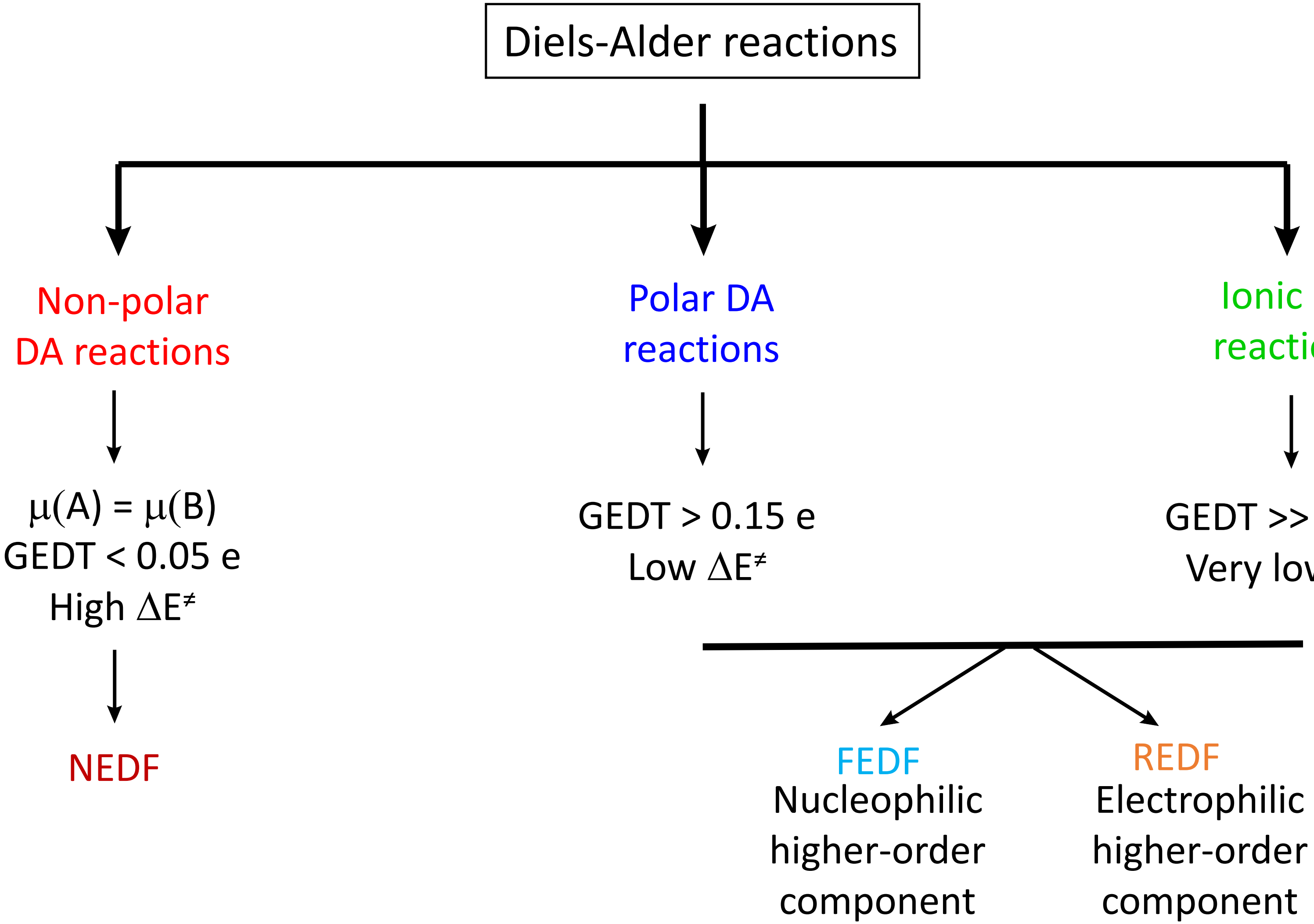
CLASSIFICATION OF DIELS-ALDER REACTIONS



Diels-Alder reactions

Non-polar DA reactions

$\mu(A) = \mu(B)$

GEDT < 0.05 e

High $\Delta E^{\neq}$

NEDF

Polar DA reactions

GEDT > 0.15 e

Low $\Delta E^{\neq}$

Ionic DA reactions

GEDT $\gg 0.20$ e

Very low $\Delta E^{\neq}$

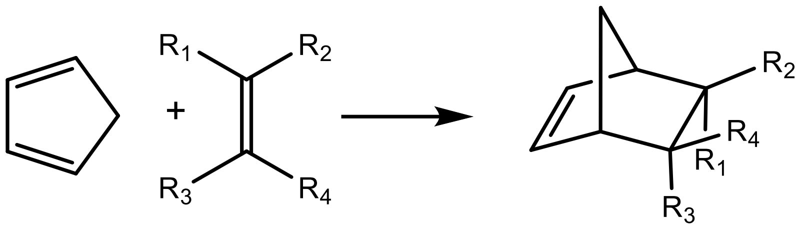
FEDF

Nucleophilic higher-order component

REDF

Electrophilic higher-order component

STUDY OF THE ROLE OF GEDT ON REACTION RATES OF DIELS-ALDER REACTIONS



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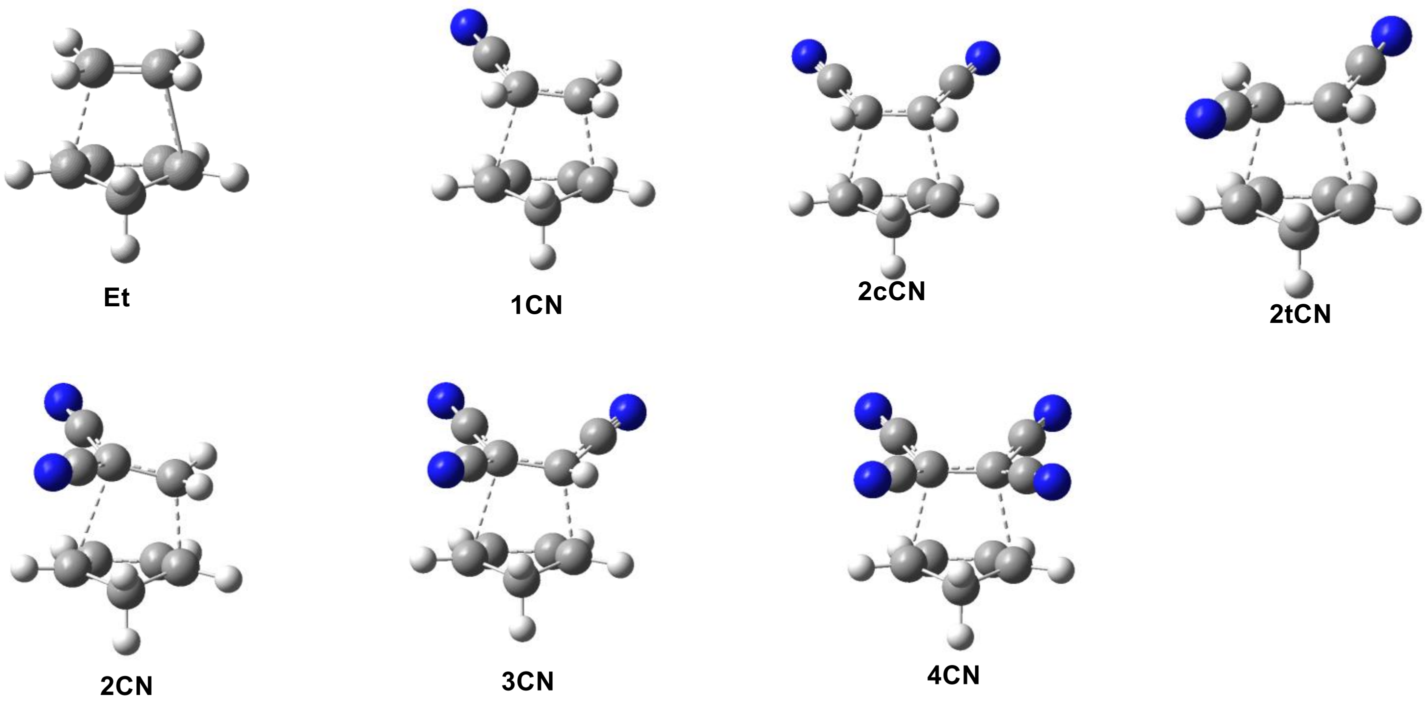
M06-2X/6-311G(d,p) optimized geometries of the TSs



STUDY OF THE ROLE OF GEDT ON REACTION RATES OF DIELS-ALDER REACTIONS

	ω		ΔG	k_r	GEDT
Et	0.73	**TS-Et**	29.8	1.00E+00	-0.03
1CN	1.74	**TS-1CN**	25.9	8.09E+02	-0.14
2cCN	2.82	**TS-2cCN**	22.3	3.91E+05	-0.23
2tCN	3.01	**TS-2tCN**	22.0	6.54E+05	-0.23
2CN	3.08	**TS-2CN**	18.2	4.45E+08	-0.27
3CN	4.39	**TS-3CN**	15.9	2.31E+10	-0.34
4CN	5.95	**TS-4CN**	12.7	5.62E+12	-0.42

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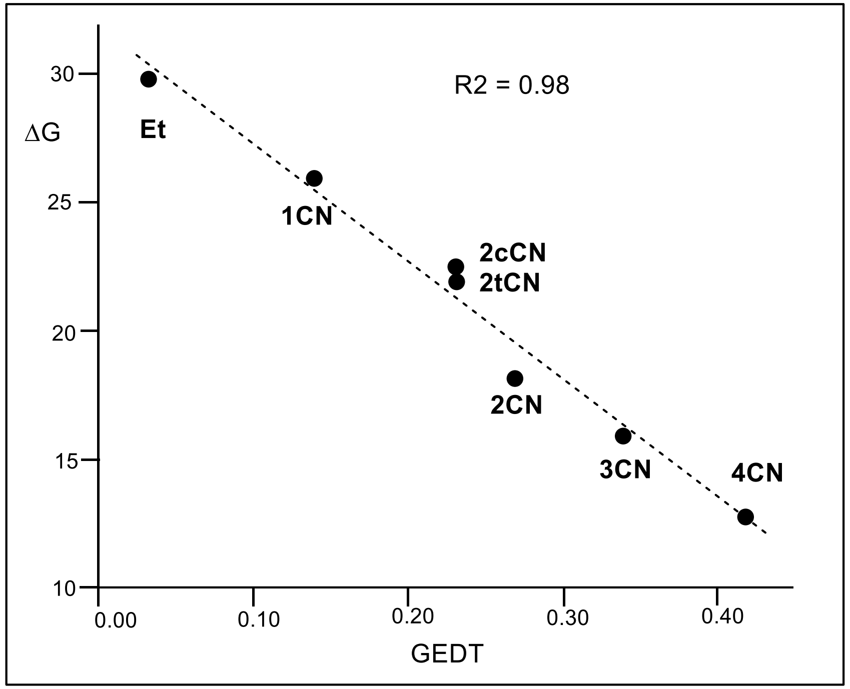

STUDY OF THE ROLE OF GEDT ON REACTION RATES - IQA ANALYSIS

The IQA is a parameter-free and reference-free real-space energy partitioning method based on Quantum Chemical Topology

$$E_{\text{total}} = \sum_{A} E_{\text{intra}}^{A} + \frac{1}{2} \sum_{A} \sum_{B \neq A} V_{\text{inter}}^{AB},$$

M. A. Blanco, A. Martín Pendás, E. Francisco. *J. Chem. Theory Comput.* **2005**, *1*, 1096–1109.

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$$E_{\text{intra}}^{A} = T^{A} + V_{\text{ee}}^{AA} + V_{\text{en}}^{AA} \qquad V_{\text{inter}}^{AB} = \left(V_{\text{nn}}^{AB} + V_{\text{en}}^{AB} + V_{\text{ne}}^{AB}\right) + V_{\text{ee}}^{AB}$$

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Steric hindrance

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electrostatic

covalency

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STUDY OF THE ROLE OF GEDT ON REACTION RATES - IQA ANALYSIS

The IQA terms can be grouped in molecular fragments (the two interacting reagents) and differences between the grouped terms at the TSs and the reagents can be obtained in order to quantify their variation along the activation energy path.

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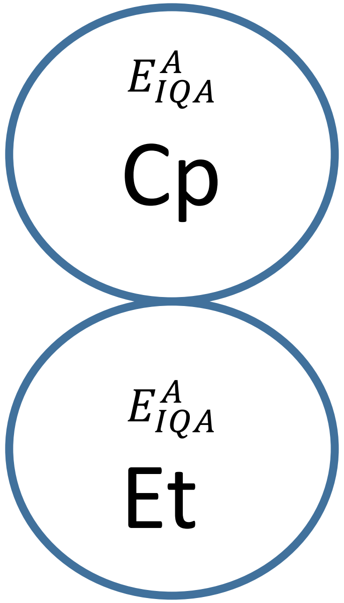
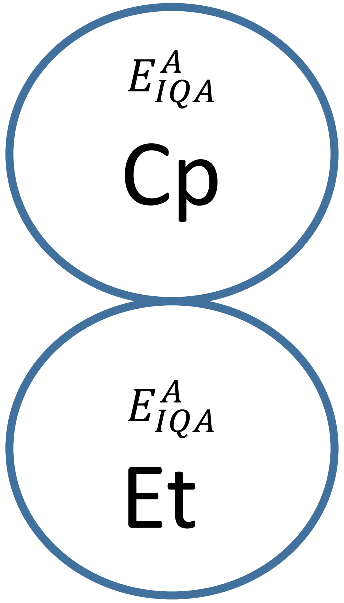


$$E_{IQA}^{A} = E_{intra}^{A} + V_{inter}^{A}$$

STUDY OF THE ROLE OF GEDT ON REACTION RATES - IQA ANALYSIS

		$\sum\Delta E^{A}_{intra}$	$\sum\Delta V^{A}_{inter}$	$\sum\Delta E^{A}_{IQA}$	$\sum\sum\Delta E^{A}_{IQA}$
TS-Et	**Cp**	34.6	-26.8	7.8	15.6
	Et	33.1	-25.3	7.8	
TS-1CN	**Cp**	37.8	-19.9	17.9	11.0
	1CN	34.4	-41.3	-6.9	
TS-2cCN	**Cp**	42.3	-13.6	28.7	8.1
	2cCN	49.4	-70.0	-20.6	
TS-2tCN	**Cp**	41.8	-13.2	28.6	6.9
	2tCN	46.5	-68.2	-21.7	
TS-2CN	**Cp**	41.2	-10.0	31.2	4.0
	2CN	29.3	-56.5	-27.2	
TS-3CN	**Cp**	46.1	-4.4	41.7	1.9
	3CN	54.8	-94.6	-39.8	
TS-4CN	**Cp**	51.9	1.3	53.2	-1.5
	4CN	72.6	-127.3	-54.7	
Standard deviation	**Cp**	10.0	18.2	28.1	
	xCN	20.4	58.1	39.3	



$$E^{A}_{IQA} = E^{A}_{intra} + V^{A}_{inter}$$

STUDY OF THE ROLE OF GEDT ON REACTION RATES - IQA ANALYSIS

		$\sum\Delta E_{intra}^{A}$	$\sum\Delta V_{inter}^{A}$	$\sum\Delta E_{IQA}^{A}$	$\sum\sum\Delta E_{IQA}^{A}$
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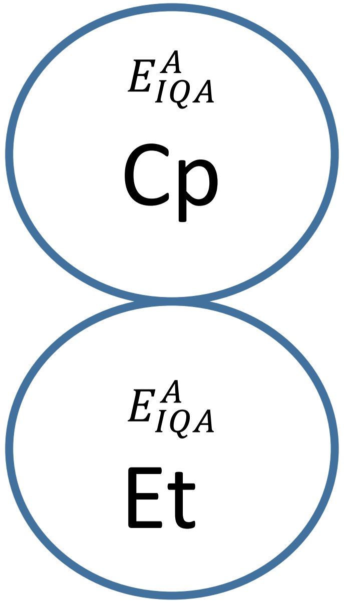
the sum of the energy variation of the two fragments, yields the activation energy



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The energy factor that changes the most is $\sum\Delta V_{inter}^{A}$**(xCN)**, associated with the **total interatomic interactions of the ethylene framework**

However, this term contains the **interactions with the other fragment**

STUDY OF THE ROLE OF GEDT ON REACTION RATES - IQA ANALYSIS

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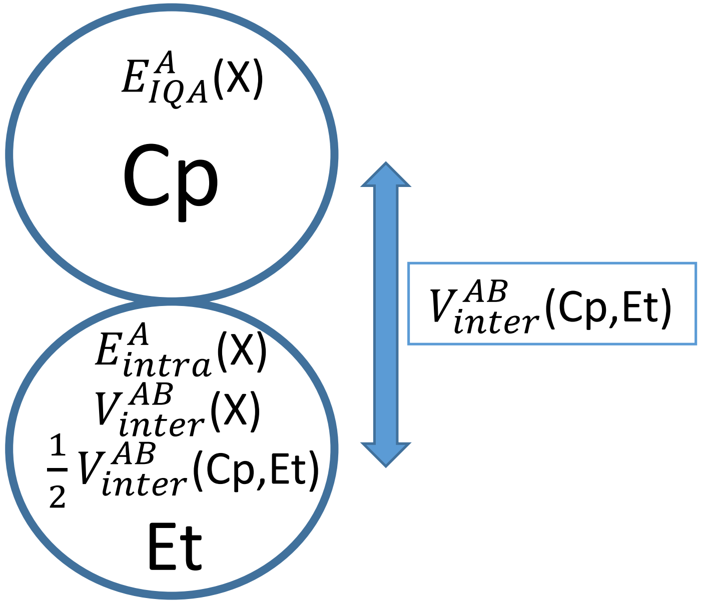

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\begin{aligned}
E^{A}_{IQA}(\mathrm{X}) &= E^{A}_{intra}(\mathrm{X}) + V^{A}_{inter}(\mathrm{X}) \\
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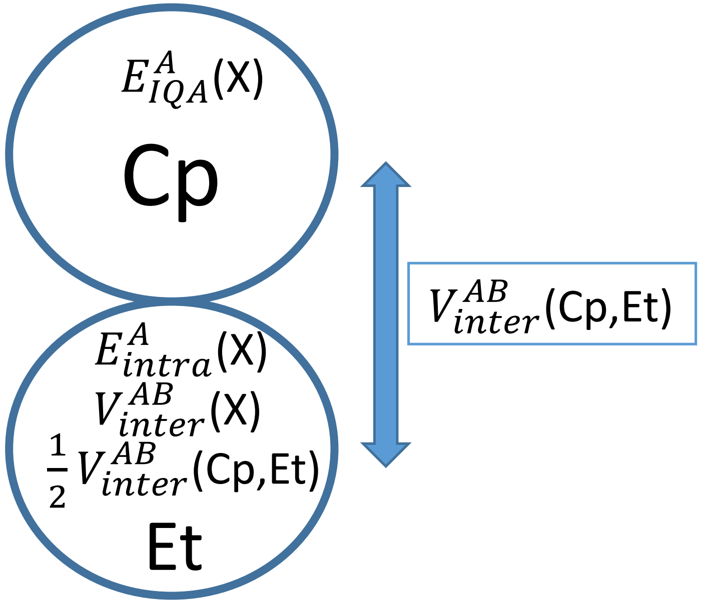
\end{aligned}
$$

STUDY OF THE ROLE OF GEDT ON REACTION RATES - IQA ANALYSIS

In order to gain a more detailed insight into the stabilization of the ethylene derivatives, **the interatomic interactions between the Cp and ethylene frameworks $\sum V_{inter}^{AB}$(Cp,Et), were considered separately** from the interactions that take place within each of them, $\sum V_{inter}^{AB}$(X).



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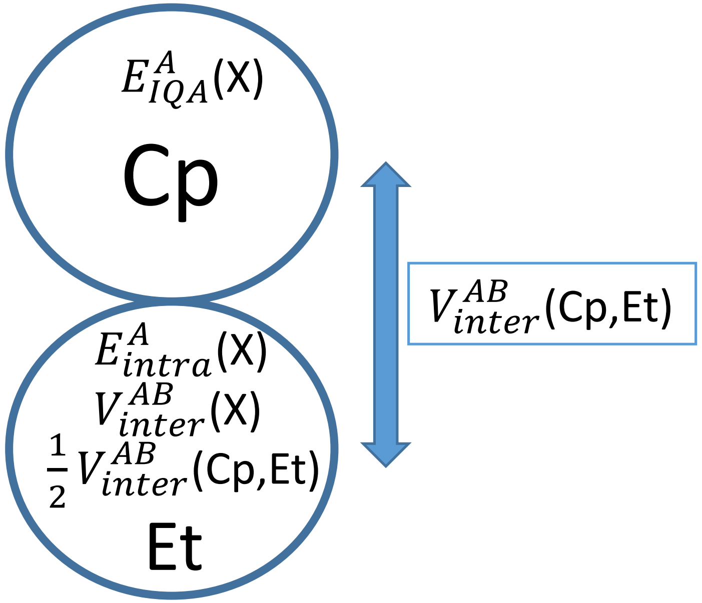
	$\sum V^{AB}_{inter}$(Cp,Et)	$\sum \Delta V^{AB}_{inter}$(Cp)	$\sum \Delta V^{AB}_{inter}$(Et)
TS-Et	-153.7	50.0	51.5
TS-1CN	-160.4	60.4	38.9
TS-2cCN	-167.7	70.3	13.7
TS-2tCN	-168.7	71.1	16.2
TS-2CN	-165.5	72.8	26.3
TS-3CN	-174.1	82.6	-7.6
TS-4CN	-187.3	94.8	-33.6
Deviation	18.9	27.5	48.7



E^A_{IQA}(X)

Cp

V^{AB}_{inter}(Cp,Et)

E^A_{intra}(X)

V^{AB}_{inter}(X)

$\frac{1}{2}V^{AB}_{inter}$(Cp,Et)

Et

$$E^A_{IQA}(X) = E^A_{intra}(X) + V^A_{inter}(X)$$
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the most drastic change with the cyano substitution is the **decrease of the interatomic interactions inside the ethylene fragment $\sum \Delta V_{inter}^{AB}$(Et)**

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Deviation	18.9	27.5	48.7

the most drastic change with the cyano substitution is the **decrease of the interatomic interactions inside the ethylene fragment $\sum \Delta V_{inter}^{AB}$(Et)**

the stabilization of the electrophilic reagent in P-DA reactions via the GEDT is responsible for the increase of reaction rates

STUDY OF THE ROLE OF GEDT ON REACTION RATES - IQA ANALYSIS

In order to gain a more detailed insight into the stabilization of the ethylene derivatives, **the interatomic interactions between the Cp and ethylene frameworks $\sum V_{inter}^{AB}$(Cp,Et), were considered separately** from the interactions that take place within each of them, $\sum V_{inter}^{AB}$(X).

	$\sum V_{inter}^{AB}$(Cp,Et)	$\sum \Delta V_{inter}^{AB}$(Cp)	$\sum \Delta V_{inter}^{AB}$(Et)
TS-Et	-153.7	50.0	51.5
TS-1CN	-160.4	60.4	38.9
TS-2cCN	-167.7	70.3	13.7
TS-2tCN	-168.7	71.1	16.2
TS-2CN	-165.5	72.8	26.3
TS-3CN	-174.1	82.6	-7.6
TS-4CN	-187.3	94.8	-33.6
Deviation	18.9	27.5	48.7

the most drastic change with the cyano substitution is the **decrease of the interatomic interactions inside the ethylene fragment $\sum \Delta V_{inter}^{AB}$(Et)**

the stabilization of the electrophilic reagent in P-DA reactions via the GEDT is responsible for the increase of reaction rates

A more detailed inspection of the V_{cl}^{AB} and V_{xc}^{AB} contributions to $\sum \Delta V_{inter}^{AB}$(Et) indicates that the stabilization of the ethylene is mostly due to the **favourable V_{cl}^{AB} electrostatic interactions**

STUDY OF THE ROLE OF GEDT ON REACTION RATES - IQA ANALYSIS

In 1999, Parr proposed, within the CDFT, the **electrophilicity ω index** as a measure of the electronic stabilization of a species when it acquires a certain amount of electron density from the environment

R.G. Parr, L.v. Szentpály, S. Liu. *J. Am. Chem. Soc.* **1999**, *121*, 9, 1922–1924.

STUDY OF THE ROLE OF GEDT ON REACTION RATES - IQA ANALYSIS

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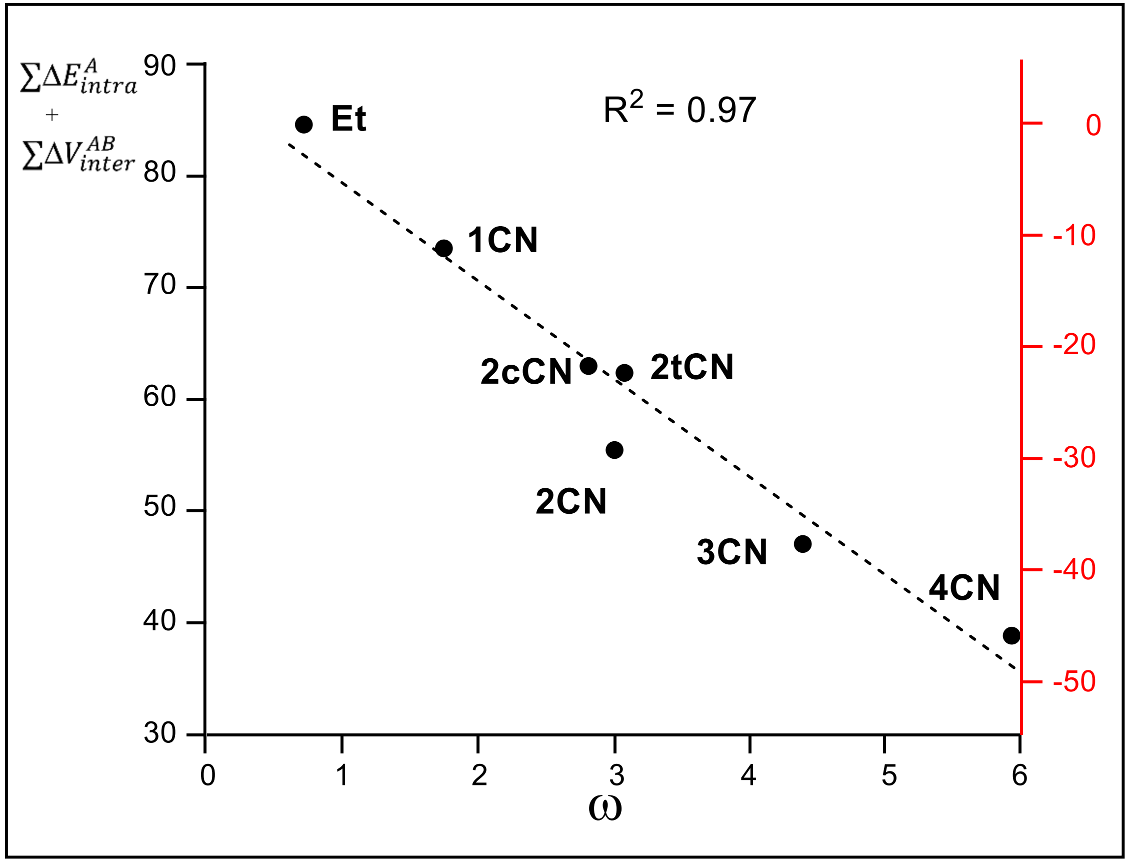

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STUDY OF THE ROLE OF GEDT ON REACTION RATES - IQA ANALYSIS

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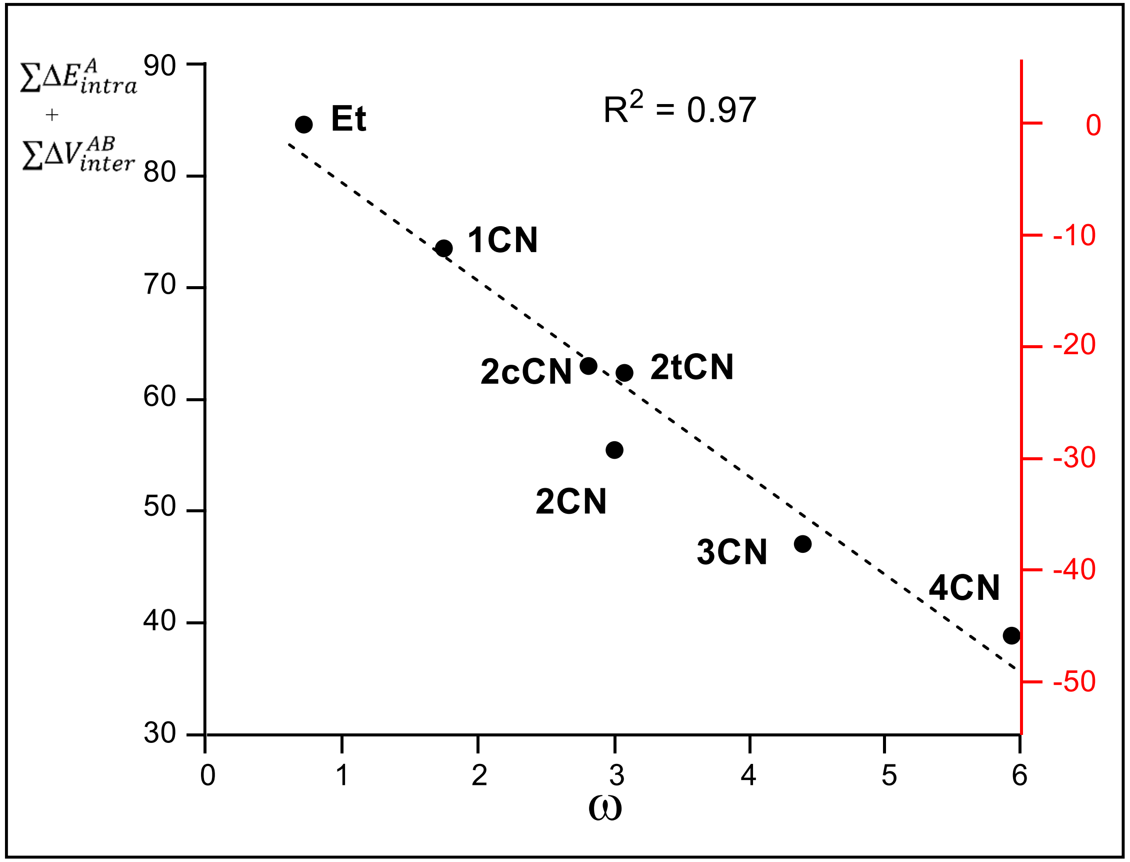


This graph **supports Parr's proposal**; the higher the electrophilicity ω index, the higher the ethylene stabilization at the polar TSs.

Given that the ethylene stabilization via the GEDT is the main factor responsible for the decrease of activation energies, this linear correlation also **validates Parr's electrophilicity ω index as a solid predictor of reactivity in P-DA reactions.**

R.G. Parr, L.v. Szentpály, S. Liu. *J. Am. Chem. Soc.* **1999**, *121*, 9, 1922–1924.

STUDY OF THE ROLE OF GEDT ON REACTION RATES – REG-IQA ANALYSIS

The Relative Energy Gradient (REG) is a method to compute chemical insight at atomistic level.

Combined with IQA, **REG inspects the linear correlation between each partitioned term and the total energy of the system. Then, it ranks all correlations** in an automated fashion **to determine the subset that best describes the behaviour of the total system.** Useful to disern the origin of reaction barriers.

$$E_i(s) = m_{REG,i}E_{total}(s) + c_i$$

Both sign and magnitud of REG values are important.

REG > 0 → the energy term **contributes to** the total behavior of the system
REG < 0 → the energy term **works against** the total behavior of the system

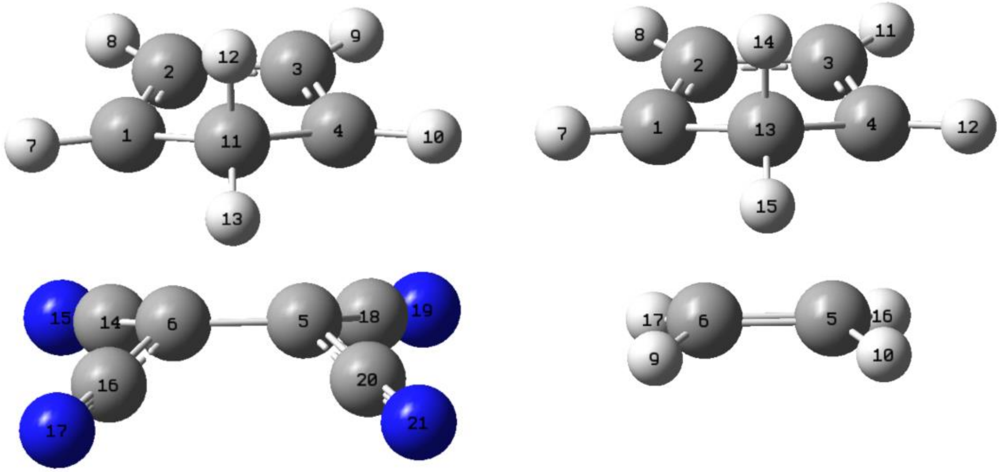
In activation barriers:

REG > 0 → energy terms are unfavorable and contribute to the reaction barrier
REG < 0 → energy terms are favourable and facilitate the reaction.

J.C.R. Thacker, P.L.A. Popelier. *Theor. Chem. Acc.* **2017**, *136*, 86.

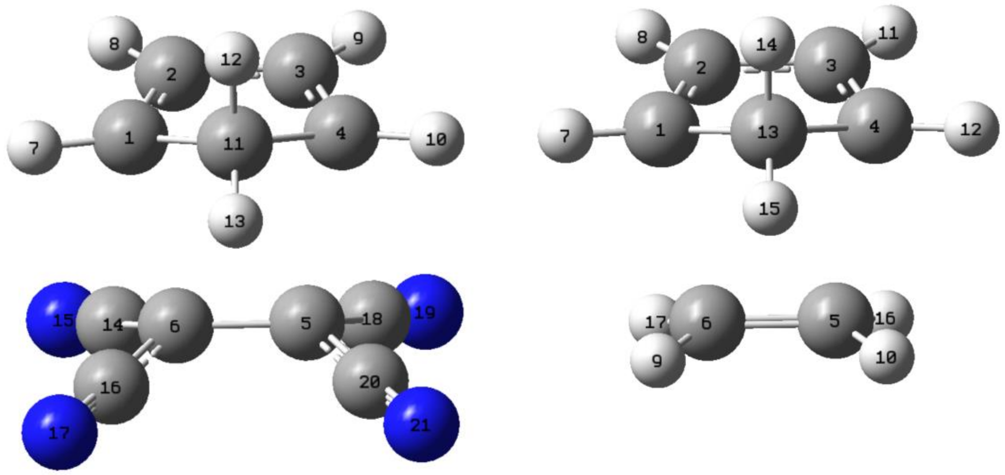
STUDY OF THE ROLE OF GEDT ON REACTION RATES – REG-IQA ANALYSIS

TCE			Ethylene			
TERM	REG	REG*Ea	TERM	REG	REG*Ea	Δ(REG*Ea)
Vxc(c5,c6)	3.9	40.4	Vxc(c5,c6)	2.5	45.1	4.7
Vxc(c3,c4)	3.8	40.2	Vxc(c3,c4)	2.1	37.5	-2.7
Vxc(c1,c2)	3.8	40.2	Vxc(c1,c2)	2.1	37.5	-2.7
Eintra(c1)	0.9	8.9	Eintra(c1)	0.5	9.0	0.1
Eintra(c4)	0.9	8.9	Eintra(c4)	0.5	9.0	0.1
Eintra(c6)	0.4	4.7	Eintra(c6)	0.5	9.5	4.8
Eintra(c5)	0.4	4.6	Eintra(c5)	0.5	9.5	4.8
Vcl(c1,c2)	-0.7	-7.7	Vcl(c1,c2)	-0.4	-7.4	0.3
Vcl(c3,c4)	-0.7	-7.7	Vcl(c3,c4)	-0.4	-7.4	0.3
Vcl(c5,c6)	-1.2	-12.2	Vcl(c5,c6)	-0.5	-9.2	3.0
Vxc(c1,c6)	-3.2	-33.8	Vxc(c1,c6)	-2.0	-36.2	-2.4
Vxc(c4,c5)	-3.2	-33.8	Vxc(c4,c5)	-2.0	-36.2	-2.4
Vxc(c2,c3)	-3.3	-35.0	Vxc(c2,c3)	-1.8	-33.0	2.0
Ea		10.5			18.1	



STUDY OF THE ROLE OF GEDT ON REACTION RATES – REG-IQA ANALYSIS

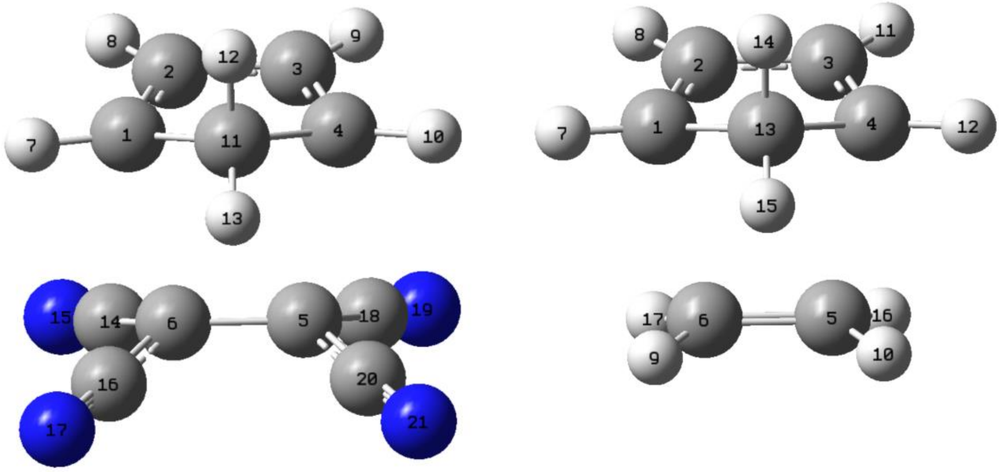
TCE			Ethylene			
TERM	REG	REG*Ea	TERM	REG	REG*Ea	Δ(REG*Ea)
Vxc(c5,c6)	3.9	40.4	Vxc(c5,c6)	2.5	45.1	4.7
Vxc(c3,c4)	3.8	40.2	Vxc(c3,c4)	2.1	37.5	-2.7
Vxc(c1,c2)	3.8	40.2	Vxc(c1,c2)	2.1	37.5	-2.7
Eintra(c1)	0.9	8.9	Eintra(c1)	0.5	9.0	0.1
Eintra(c4)	0.9	8.9	Eintra(c4)	0.5	9.0	0.1
Eintra(c6)	0.4	4.7	Eintra(c6)	0.5	9.5	4.8
Eintra(c5)	0.4	4.6	Eintra(c5)	0.5	9.5	4.8
Vcl(c1,c2)	-0.7	-7.7	Vcl(c1,c2)	-0.4	-7.4	0.3
Vcl(c3,c4)	-0.7	-7.7	Vcl(c3,c4)	-0.4	-7.4	0.3
Vcl(c5,c6)	-1.2	-12.2	Vcl(c5,c6)	-0.5	-9.2	3.0
Vxc(c1,c6)	-3.2	-33.8	Vxc(c1,c6)	-2.0	-36.2	-2.4
Vxc(c4,c5)	-3.2	-33.8	Vxc(c4,c5)	-2.0	-36.2	-2.4
Vxc(c2,c3)	-3.3	-35.0	Vxc(c2,c3)	-1.8	-33.0	2.0
Ea		10.5			18.1	



The contributions of the energy factors of the most relevant regions involved in the reaction to activation energies are **very similar**

STUDY OF THE ROLE OF GEDT ON REACTION RATES – REG-IQA ANALYSIS

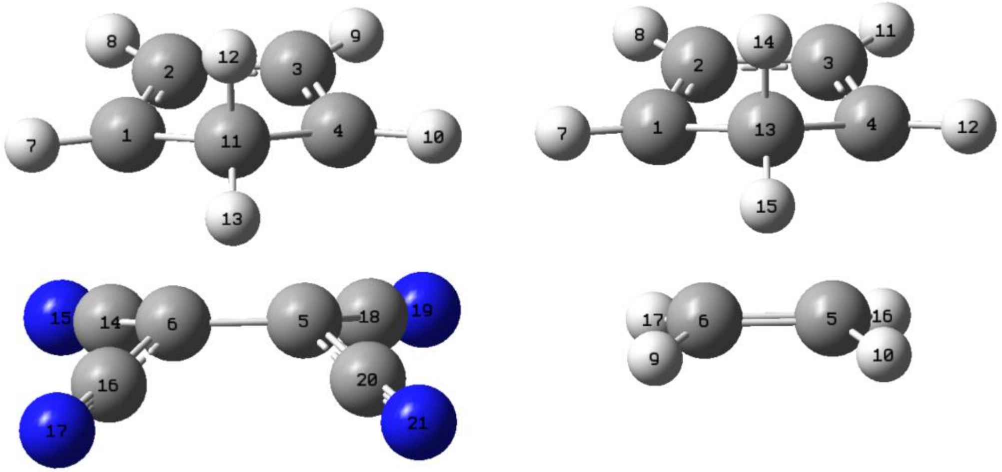
TCE			Ethylene			
TERM	REG	REG*Ea	TERM	REG	REG*Ea	Δ(REG*Ea)
Vxc(c5,c6)	3.9	40.4	Vxc(c5,c6)	2.5	45.1	4.7
Vxc(c3,c4)	3.8	40.2	Vxc(c3,c4)	2.1	37.5	-2.7
Vxc(c1,c2)	3.8	40.2	Vxc(c1,c2)	2.1	37.5	-2.7
Eintra(c1)	0.9	8.9	Eintra(c1)	0.5	9.0	0.1
Eintra(c4)	0.9	8.9	Eintra(c4)	0.5	9.0	0.1
Eintra(c6)	0.4	4.7	Eintra(c6)	0.5	9.5	4.8
Eintra(c5)	0.4	4.6	Eintra(c5)	0.5	9.5	4.8
Vcl(c1,c2)	-0.7	-7.7	Vcl(c1,c2)	-0.4	-7.4	0.3
Vcl(c3,c4)	-0.7	-7.7	Vcl(c3,c4)	-0.4	-7.4	0.3
Vcl(c5,c6)	-1.2	-12.2	Vcl(c5,c6)	-0.5	-9.2	3.0
Vxc(c1,c6)	-3.2	-33.8	Vxc(c1,c6)	-2.0	-36.2	-2.4
Vxc(c4,c5)	-3.2	-33.8	Vxc(c4,c5)	-2.0	-36.2	-2.4
Vxc(c2,c3)	-3.3	-35.0	Vxc(c2,c3)	-1.8	-33.0	2.0
Ea		10.5			18.1	



In both cases, the activation barrier is due to the energy cost for the **rupture of the double bonds**

STUDY OF THE ROLE OF GEDT ON REACTION RATES – REG-IQA ANALYSIS

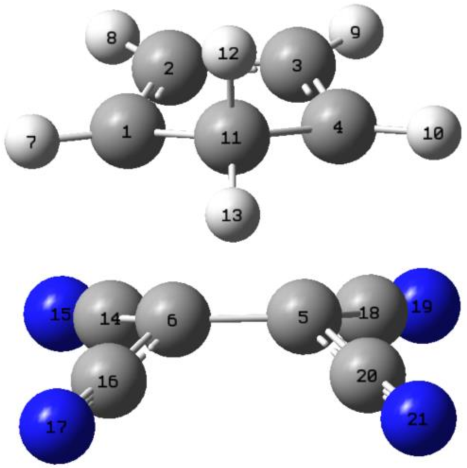
TCE			Ethylene			
TERM	REG	REG*Ea	TERM	REG	REG*Ea	Δ(REG*Ea)
Vxc(c5,c6)	3.9	40.4	Vxc(c5,c6)	2.5	45.1	4.7
Vxc(c3,c4)	3.8	40.2	Vxc(c3,c4)	2.1	37.5	-2.7
Vxc(c1,c2)	3.8	40.2	Vxc(c1,c2)	2.1	37.5	-2.7
Eintra(c1)	0.9	8.9	Eintra(c1)	0.5	9.0	0.1
Eintra(c4)	0.9	8.9	Eintra(c4)	0.5	9.0	0.1
Eintra(c6)	0.4	4.7	Eintra(c6)	0.5	9.5	4.8
Eintra(c5)	0.4	4.6	Eintra(c5)	0.5	9.5	4.8
Vcl(c1,c2)	-0.7	-7.7	Vcl(c1,c2)	-0.4	-7.4	0.3
Vcl(c3,c4)	-0.7	-7.7	Vcl(c3,c4)	-0.4	-7.4	0.3
Vcl(c5,c6)	-1.2	-12.2	Vcl(c5,c6)	-0.5	-9.2	3.0
Vxc(c1,c6)	-3.2	-33.8	Vxc(c1,c6)	-2.0	-36.2	-2.4
Vxc(c4,c5)	-3.2	-33.8	Vxc(c4,c5)	-2.0	-36.2	-2.4
Vxc(c2,c3)	-3.3	-35.0	Vxc(c2,c3)	-1.8	-33.0	2.0
Ea		10.5			18.1	



The factors whose weights change the most are precisely those **belonging to the ethylene structure**, in agreement with the previous IQA analysis at the TSs.

STUDY OF THE ROLE OF GEDT ON REACTION RATES – REG-IQA ANALYSIS

A closer look into the favorable terms with REG < 0 shows:



	REG
Vcl(c5,c18)	-0.9
Vcl(c6,c14)	-0.9
Vcl(c5,c20)	-0.9
Vcl(c6,c16)	-0.9
Vcl(c16,n17)	-0.9
Vcl(c18,n19)	-0.9
Vcl(c20,n21)	-0.9
Vcl(c14,n15)	-0.9

TCE			Ethylene			
TERM	REG	REG*Ea	TERM	REG	REG*Ea	Δ(REG*Ea)
Vxc(c5,c6)	3.9	40.4	Vxc(c5,c6)	2.5	45.1	4.7
Vxc(c3,c4)	3.8	40.2	Vxc(c3,c4)	2.1	37.5	-2.7
Vxc(c1,c2)	3.8	40.2	Vxc(c1,c2)	2.1	37.5	-2.7
Eintra(c1)	0.9	8.9	Eintra(c1)	0.5	9.0	0.1
Eintra(c4)	0.9	8.9	Eintra(c4)	0.5	9.0	0.1
Eintra(c6)	0.4	4.7	Eintra(c6)	0.5	9.5	4.8
Eintra(c5)	0.4	4.6	Eintra(c5)	0.5	9.5	4.8
Vcl(c1,c2)	-0.7	-7.7	Vcl(c1,c2)	-0.4	-7.4	0.3
Vcl(c3,c4)	-0.7	-7.7	Vcl(c3,c4)	-0.4	-7.4	0.3
Vcl(c5,c6)	-1.2	-12.2	Vcl(c5,c6)	-0.5	-9.2	3.0
Vxc(c1,c6)	-3.2	-33.8	Vxc(c1,c6)	-2.0	-36.2	-2.4
Vxc(c4,c5)	-3.2	-33.8	Vxc(c4,c5)	-2.0	-36.2	-2.4
Vxc(c2,c3)	-3.3	-35.0	Vxc(c2,c3)	-1.8	-33.0	2.0
Ea		10.5			18.1	

STUDY OF THE ROLE OF GEDT ON REACTION RATES – REG-IQA ANALYSIS

A closer look into the favorable terms with REG < 0 shows:

Substitution has a relevant role in the stabilization of the electrophilic ethylene derivative as a consequence of the GEDT taking place in polar reactions.

TCE			Ethylene			
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Eintra(c1)	0.9	8.9	Eintra(c1)	0.5	9.0	0.1
Eintra(c4)	0.9	8.9	Eintra(c4)	0.5	9.0	0.1
Eintra(c6)	0.4	4.7	Eintra(c6)	0.5	9.5	4.8
Eintra(c5)	0.4	4.6	Eintra(c5)	0.5	9.5	4.8
Vcl(c1,c2)	-0.7	-7.7	Vcl(c1,c2)	-0.4	-7.4	0.3
Vcl(c3,c4)	-0.7	-7.7	Vcl(c3,c4)	-0.4	-7.4	0.3
Vcl(c5,c6)	-1.2	-12.2	Vcl(c5,c6)	-0.5	-9.2	3.0
Vxc(c1,c6)	-3.2	-33.8	Vxc(c1,c6)	-2.0	-36.2	-2.4
Vxc(c4,c5)	-3.2	-33.8	Vxc(c4,c5)	-2.0	-36.2	-2.4
Vxc(c2,c3)	-3.3	-35.0	Vxc(c2,c3)	-1.8	-33.0	2.0
Ea		10.5			18.1	

STUDY OF THE ROLE OF GEDT ON REACTION RATES – REG-IQA ANALYSIS

A closer look into the favorable terms with REG < 0 shows:

Substitution has a relevant role in the stabilization of the electrophilic ethylene derivative as a consequence of the GEDT taking place in polar reactions.

This stabilization is mostly due to **favourable electrostatic interactions** in the substituents.

TCE			Ethylene			
TERM	REG	REG*Ea	TERM	REG	REG*Ea	Δ(REG*Ea)
Vxc(c5,c6)	3.9	40.4	Vxc(c5,c6)	2.5	45.1	4.7
Vxc(c3,c4)	3.8	40.2	Vxc(c3,c4)	2.1	37.5	-2.7
Vxc(c1,c2)	3.8	40.2	Vxc(c1,c2)	2.1	37.5	-2.7
Eintra(c1)	0.9	8.9	Eintra(c1)	0.5	9.0	0.1
Eintra(c4)	0.9	8.9	Eintra(c4)	0.5	9.0	0.1
Eintra(c6)	0.4	4.7	Eintra(c6)	0.5	9.5	4.8
Eintra(c5)	0.4	4.6	Eintra(c5)	0.5	9.5	4.8
Vcl(c1,c2)	-0.7	-7.7	Vcl(c1,c2)	-0.4	-7.4	0.3
Vcl(c3,c4)	-0.7	-7.7	Vcl(c3,c4)	-0.4	-7.4	0.3
Vcl(c5,c6)	-1.2	-12.2	Vcl(c5,c6)	-0.5	-9.2	3.0
Vxc(c1,c6)	-3.2	-33.8	Vxc(c1,c6)	-2.0	-36.2	-2.4
Vxc(c4,c5)	-3.2	-33.8	Vxc(c4,c5)	-2.0	-36.2	-2.4
Vxc(c2,c3)	-3.3	-35.0	Vxc(c2,c3)	-1.8	-33.0	2.0
Ea		10.5			18.1	

STUDY OF THE ROLE OF GEDT ON REACTION RATES – REG-IQA ANALYSIS

A closer look into the favorable terms with REG < 0 shows:

Substitution has a relevant role in the stabilization of the electrophilic ethylene derivative as a consequence of the GEDT taking place in polar reactions.

This stabilization is mostly due to **favourable electrostatic interactions** in the substituents.

This validates the individual IQA analysis at the TSs and reagents, but REG-IQA provides more information about the mechanism.

TCE			Ethylene			
TERM	REG	REG*Ea	TERM	REG	REG*Ea	Δ(REG*Ea)
Vxc(c5,c6)	3.9	40.4	Vxc(c5,c6)	2.5	45.1	4.7
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Eintra(c5)	0.4	4.6	Eintra(c5)	0.5	9.5	4.8
Vcl(c1,c2)	-0.7	-7.7	Vcl(c1,c2)	-0.4	-7.4	0.3
Vcl(c3,c4)	-0.7	-7.7	Vcl(c3,c4)	-0.4	-7.4	0.3
Vcl(c5,c6)	-1.2	-12.2	Vcl(c5,c6)	-0.5	-9.2	3.0
Vxc(c1,c6)	-3.2	-33.8	Vxc(c1,c6)	-2.0	-36.2	-2.4
Vxc(c4,c5)	-3.2	-33.8	Vxc(c4,c5)	-2.0	-36.2	-2.4
Vxc(c2,c3)	-3.3	-35.0	Vxc(c2,c3)	-1.8	-33.0	2.0
Ea		10.5			18.1	

CONCLUSIONS

The increase of reaction rates is due to the stabilization of the ethylene framework by favourable electrostatic interactions at the cyano substitutents as a consequence of the GEDT

IQA is a parameter-free and reference-free real-space energy partitioning method that does not suffer from process-dependency of their energy components, like traditional EDAs.

REG-IQA is a solid and well defined tool to understand the origin of reaction barriers.

CONCLUSIONS

The increase of reaction rates is due to the stabilization of the ethylene framework by favourable electrostatic interactions at the cyano substitutents as a consequence of the GEDT

IQA is a parameter-free and reference-free real-space energy partitioning method that does not suffer from process-dependency of their energy components, like traditional EDAs.

REG-IQA is a solid and well defined tool to understand the origin of reaction barriers.

ACKNOWLEDGEMENTS

Spanish MICIU, project PID2019-110776GB-I00 (AEI/FEDER, UE)

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MINISTERIO DE CIENCIA, INNOVACIÓN Y UNIVERSIDADES

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