## **Electronic Supporting Information**

## A Molecular Electron Density Theory Study of the Enhanced Reactivity of Aza Aromatic Compounds Participating in Diels-Alder Reactions

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# *1. Evaluation of the aromatic character of AACs* **8** – **11** *by analysis of their thermodynamic stability.*

Although several criteria of aromaticity can be found in the literature based on the electronic structure obtained from the wave function, in organic chemistry the concept of aromaticity was defined at the end of the 19<sup>th</sup> century to characterise the unexpected reactivity of aromatic compounds with respect to the unsaturated hydrocarbon compounds, as a consequence of the thermodynamic stability of former.

The thermodynamic stability of aromatic compounds can be experimentally determined through the thermodynamic equation associated with the hydrogenation of an aromatic compound (see Scheme S1). The value of the heat of hydrogenation of benzene **7**, -49.4 in kcal·mol<sup>-1</sup>, which is lower than that of the hydrogenation of a hypothetical hexatriene, -85.5 kcal·mol<sup>-1</sup>, makes it possible to establish the energy stabilisation of benzene **7** by aromaticity at ca. 36 kcal·mol<sup>-1</sup>.

+ 3 H<sub>2</sub> 
$$\longrightarrow$$
  $\Delta H = -49.4 \text{ kcal mol}^{-1}$ 

Scheme S1. Thermodynamic equation associated to the hydrogenation of benzene 7.

On the other hand, isodesmic reactions<sup>1</sup> have also been used to evaluate the thermodynamic stability of organic compounds by aromaticity.<sup>2</sup> In order to estimate the relative stability of the AACs with respect to that of aromatic benzene **7**, the five isodesmic reactions given in Scheme S2 were considered. These isodesmic reactions were chosen considering the structural relation of the corresponding hydrogenated compounds with the cycloadducts obtained from the corresponding ADA reactions. As can be observed, the endothermic character of these isodesmic reactions decreases on going from benzene **7** to tetrazine **11**.



Scheme S2. Isodesmic reactions used for the evaluation of the aromatic character of benzene 7 and AACs 8 - 11. MPWB1K/6-311G(d,p) isodesmic energies are given in kcal·mol<sup>-1</sup>.

A plot of the energies involved in these isodesmic reactions,  $\Delta E_{iso}$ , vs the proposed relative ring electron density (RRED) index of benzene **7** and AACs **8** – **11** is given Figure S1a. As can be seen, the  $\Delta E_{iso}$  of pyridazine **9** experiences a deviation from the expected value. This behaviour might be a consequence of a specific intermolecular interaction taking place at the corresponding 3,6-dihydroderivative. Interestingly, when the value of  $\Delta E_{iso}$  of pyridazine **9** is removed from this series, a completely second-order polynomic correlation between the RRED index, which is a measure of loss of electron density in the aromatic ring of these AACs, and the energies involved in these isodesmic reactions is observed, R<sup>2</sup> = 1.00 (see Figure S1b). Consequently, this analysis makes it possible to stablish a close correlation between the proposed RRED index and the aromatic character of these AACs **8** – **11**.



Figure S1. Plots of the endothermic character of the isodesmic reactions given in Scheme 2,  $\Delta E_{iso}$  in kcal·mol<sup>-1</sup>, vs the RRED index of benzene 7 and AACs 8 – 11. The red points correspond to the estimated  $\Delta E_{iso}$  for pyridazine 9.

From the second-order polynomic correlation given in Figure S1,  $y = 102.59x^2 - 159.49x + 100.84$ , the value of  $\Delta E_{iso}$  of pyridazine **9** due to its aromatic character can be estimated in 41.2 kcal·mol<sup>-1</sup>. Considering this value, the specific intermolecular interaction taking place at 3,6-dihydroderivative of pyridazine **9** can be estimated in 3.1 kcal·mol<sup>-1</sup> (see Figure S1a), a reasonable values for intermolecular interactions.

# 2. Evaluation of the aromatic character AACs 8 – 11 by analysis of the nucleus independent chemical shift (NICS).

Magnetic indices of aromaticity are based on the electron ring current that is induced when the system is exposed to external magnetic fields. The magnitude of the nucleus independent chemical shift (NICS) index, proposed by Schleyer and co-workers,<sup>3-5</sup> is one of the most widely used indicators to characterise aromaticity of rings. The simplest NICS variant computed at the center of the aromatic ring is isotropic NICS, (NICS<sub>iso</sub> or NICS(0)), which can be influenced by shielding or deshielding contributions provided by the core electrons and  $\sigma$ -framework as well as the in-plane shielding tensor components. The sign of the computed NICS(0) values are reversed to conform to the experimental upfield (negative) and downfield (positive) NMR chemical shifts. Negative NICS(0) values estimated at the center of the ring indicate the presence of induced diatropic ring currents (aromaticity), whereas positive NICS(0) values at the same points denote paratropic ring currents (antiaromaticity). Thus, the more negative the NICS(0) value in the ring, the more aromatic is. The NICS(0) values at the center of benzene **7** and AACs **8**–**11**, computed at the MPWB95/6–311+G(d,p) level, are given in Table 1.

**Table 1.** Isotropic NICS(0) values, in ppm, of benzene 7 and AACs 8 - 11, obtained at the (GIAO) MPWB95/6-311+G(d,p) /MPWB95/6-311G(d,p) level of theory.

	NICS(0)
benzene 7	-8.30
pyridine 8	-7.01
diazine 9	-5.42
triazine 10	-3.92
tetrazine 11	-1.68

Benzene 7, as reference, presents a high NICS(0) value, -8.30 ppm. On the other hand, the NICS(0) values of the AACs **8** – **11**, range from –7.01 ppm (pyridine **8**) to –1.68 ppm (tetrazine **11**). These results are closely to those found for the series of AACs studied by Houk et al. at the M06-2X/6–311+G(d,p) computational level.<sup>6</sup> A very good linear correlation between the number of nitrogen nuclei in the AACs and the NICS(0) values of the AACs **8** – **11** is found,  $R^2 = 1.00$  (see Figure S2). As can be seen, a decrease of the NICS(0) value with the inclusion of nitrogen atoms in the benzene aromatic ring is observed.



**Figure S2.** Plot of the isotropic NICS(0) values computed at the center of the aromatic ring, in ppm, *vs* the number of nitrogen nuclei n of the AACs.

Figure S3 shows a completely correlation between the proposed RED and the NICS(0) values of benzene **7** and the AACs **8** – **11**,  $R^2 = 1.00$ . Some interesting conclusions can be drawn from this correlation: i) has was commented on, RED comes from the sum of the six ELF disynaptic basins [V(C,C), V(C,N), V(N,N)] belonging to the aromatic ring. Consequently, RED does not distinguish between  $\pi$  and  $\sigma$  electrons; ii) RED ranges between 16.62 e (**7**) and 14.28 e (**11**). These values do not correlate with the Hückel's 4n + 2 rule, for  $\pi$  electrons, proposed for the characterisation of aromatic compounds; and iii) although the RED tetrazine **11** experiences a loss of 2.34 e with respect to that of benzene **7**, it represents a decrease in the aromatic stabilisation with respect to benzene **7** of only 4.4 kcal·mol<sup>-1</sup>, note that the aromatic stabilization of tetrazine **11** has been thermodynamically estimated in 39.6 kcal·mol<sup>-1</sup> (see before section).



Figure S3. Plot of the isotropic NICS(0) values computed at the center of the aromatic ring, in ppm, vs the RED, in e, of benzene 7 and AACs 8 - 11.

Finally, Figure S4 shows a very good lineal correlation between the proposed RRED and the NICS(0) values of benzene 7 and the AACs 8 - 11,  $R^2 = 0.99$ . This correlation makes it possible the use of the proposed RRED as a measure of the aromatic character of this series of AACs.



Figure S4. Plot of the isotropic NICS(0) values computed at the center of the aromatic ring, in ppm, vs the RRED of benzene 7 and AACs 8 - 11.

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#### 3. BET study of the DA reaction between ethylene benzene 7 and ethylene 5.

The BET study the non-polar DA reaction between benzene **7** and ethylene **5** was performed. Lewis-structures rising from ELF topology representing the molecular mechanism along the reaction path is shown in Scheme S3 and, the populations of the most significant valence basins, among other relevant parameters, are included in Table S2.

The non-polar DA reaction between benzene 7 and ethylene 5 takes place along six differentiated phases. The topological features of the ELF at S0 are very similar to those of the isolated reagents showing benzene 7 more delocalised bonds. Along phase I, a depopulation of the C1–C2 bonding region of the ethylene fragment from 3.39 to 3.18 e is performed, while depopulations of the C3–C6[C7] and C4–C5[C8] bonding regions are also observed together to population of the C5[C7]-C6[C8] bonding regions at the benzene moiety. Along *Phase II*, slight electron rearrangements around the entire benzene fragment are observed. At S2, two C3 and C4 *pseudoradical* carbons of the benzene framework are created [see V(C3) and V(C4) in Table S2 and Scheme S3] integrating 0.11 e each one as the consequence of the depopulation of the four adjacent C3–C6[C7] and C4–C5[C8] bonding regions [see V(C3,C6[C7]) and V(C4,C5[C8]) in Table S2]. Along Phase III, two C1 and C2 pseudoradical centers of ethylene moiety, with an initial population of 0.22 e are formed [see V(C1) and V(C2) in Table S2 and Scheme S3]. This electron density mainly comes from the strong depopulation of the C1–C2 bonding region by ca. 0.42 e [see V(C1,C2)]. Along this phase, the population associated to the C3 and C4 pseudoradical centers continues increasing to 0.20 e [see V(C3) and V(C4) in Table S2]. Along *Phase IV*, in which **TS1** is found, the four C1 and C2, and C3 and C4 *pseudoradical* centers increase their population to 0.41 and 0.37 e, respectively, while the population in the C5–C6 bonding region increases to 3.25 e [see V(C5,C6) and V'(C5,C6) in Table S2] and also in the C7–C8 bonding region to 3.26 e [see V(C7,C8) and V'(C7,C8) Table S2]. At S5, the formation of the C1–C4 single bond [V(C1,C4)] takes place and simultaneously, the C2–C3 single bond [V(C2,C3)] is also formed, both integrating 0.95 e.

These electron changes indicate that the formation of the two new single bonds begins at a distance of *ca*. 1.98 Å through a C-to-C coupling of the two C1 and C4 and the two C2 and C3 *pseudoradical* centers. Finally, at the last structure **17**, the populations of C1-C4 and C2-C3 bonding regions are 1.76 e, that of the C1-C2 region is 1.90 e and C3–C6, C3–C7,

C4–C5 and C4–C8 bonding regions also reach populations around 2.0 e, acquiring the expected population for single bonds, while that the C5–C6 and C7–C8 bonding regions reach populations of 3.47 e, characterising double bonds in **17**.

From the BET study of the DA reaction between benzene **7** and ethylene **5** some attractive conclusions can be drawn: i) this non-polar DA reaction takes place along six different phases; ii) the highest energy cost demanded to reach **TS1**, 36.9 kcal·mol<sup>-1</sup> agrees with that found at **S3** involved in *Phase IV* (see Table S2). The activation energy of this non-polar reaction is mainly associated to the continuous depopulation of the C1–C2 bonding regions and electron reorganizations around the C3–C6[C7], C4–C5[C8], C5–C6 and C7–C8 bonding regions; iii) the formation of the two C1–C4 and C2–C3 single bonds takes place simultaneously at a C–C distance of 1.98 Å, by the C-to-C coupling of the two C1 and C4 and the two C2 and C3 *pseudoradical* centers; finally, iv) the non-polar DA benzene **7** and ethylene **5** is entirely synchronic (see Scheme S3).



Scheme S3. Simplified representation of the molecular mechanism of the non-polar DA reaction between benzene 7 and ethylene 5 by Lewis-like structures arising from the topological analysis of the ELF along the reaction path. Atom numbering is included.

**Table S2.** ELF valence basin populations, distances of the forming bonds, relative<sup>a</sup> electronic energies, GEDT and IRC values of the IRC structures, S0 - S5, defining the VI phases characterizing the molecular mechanism of the DA reaction between benzene 7 and ethylene 5. TS1 and 17 are also included. Distances are given in angstroms, Å, GEDT values and electron populations in average number of electrons, e, relative energies in kcal·mol<sup>-1</sup> and IRC values in a.u.

Structures	7	5	<b>S0</b>	<b>S1</b>	<b>S2</b>	<b>S3</b>	TS1	<b>S4</b>	<b>S5</b>	17
Phases			j	!	II .	III	IV	V	v V	Ί
d(C1-C4)			3.558	2.218	2.161	2.117	2.103	2.033	1.978	1.553
d(C2-C3)			3.558	2.213	2.167	2.126	2.116	2.040	1.984	1.553
ΔΕ			0.0	34.6	36.2	36.9	36.9	35.7	33.0	-1.0
GEDT			0.00	-0.02	-0.01	0.01	0.01	0.03	0.04	0.04
IRC			-11.3	-0.72	-0.37	-0.08	0.00	0.49	0.87	3.93
V(C1,C2)		1.69	1.64	3.18	3.20	2.78	2.73	2.48	2.36	1.90
V'(C1,C2)		1.71	1.75							
V(C3,C6)	2.75		2.83	2.52	2.46	2.41	2.39	2.29	2.23	1.97
V(C3,C7)	2.73		2.69	2.66	2.55	2.49	2.48	2.36	2.30	2.02
V(C4,C5)	2.75		2.68	2.60	2.53	2.47	2.46	2.35	2.28	2.02
V(C4,C8)	2.73		2.83	2.58	2.48	2.43	2.40	2.31	2.25	1.98
V(C5,C6)	2.75		2.78	3.07	3.11	3.15	3.17	1.72	1.78	1.71
V'(C5,C6)								1.53	1.53	1.76
V(C7,C8)	2.73		2.78	3.07	3.11	3.15	3.17	1.73	1.78	1.71
V'(C7,C8)								1.53	1.53	1.76
V(C1)						0.22	0.26	0.41		
V(C2)						0.22	0.25	0.41		
V(C3)					0.11	0.20	0.23	0.37		
V(C4)					0.11	0.20	0.23	0.37		
V(C1,C4)									0.95	1.76
V(C2,C3)									0.95	1.76

<sup>a</sup> Relative to the first structure of the IRC, **S0** 

#### 4. BET study of the DA reaction between ethylene 5 and pyridine 8.

A BET study of the non-polar DA reaction of ethylene **5** and pyridine **8** was accomplished. A simplified representation of the molecular mechanism by Lewis-like structures result from the ELF topology is shown in Scheme S4, while the populations of the most significant valence basins, together with other relevant parameters, of selected structures of the IRC are collected in Table S3.

BET study of the bonding changes along the non-polar DA pathway between ethylene 5 and pyridine 8 is topologically characterized by ten differentiated phases. At *Phase I*, the reaction starts with the depopulation of the C1–C2 single bond of 0.20 e at the ethylene moiety [see V(C1,C2) in Table S3] together with depopulations of the C3–N6[C7] bonding regions by ca. 0.15 e, as well as in those associated with the C4-C5[C8] ones [see V(C3,N6[C7]), V(C4,C5[C8]) in Table S3]. Meanwhile, an increase of the population of the C5–N6 and C7–C8 bonding regions by ca. 0.26 e at the pyridine fragment is observed [see V(C5,C6) and V(C7,C8) in Table S3]. At S2, while slight electron reorganizations are observed, a C3 *pseudoradical* center is created at the pyridine fragment, integrating 0.16 e [V(C3)], mainly associated to a depopulation of the C3–C7 bonding region by ca. 0.14 e [see V(C3,C7) in Table S3]. In the following phase, at the pyridine fragment, a second C4 *pseudoradical* center is created with an initial population of 0.11 e [V(C4)] as a consequence of the depopulation of the C4–C8 and C4–C5 bonding regions by 0.09 e and 0.05 e. Along Phase IV, a C2 pseudoradical center at the ethylene moiety is formed integrating 0.23 e [V(C2)] as the outcome of the depopulation of the C4–C8 and C4-C5 bonding regions. Along *Phase V*, in which the **TS2** is found, a C1 *pseudoradical* center at the ethylene fragment is created with a population of  $0.20 \in [V(C1)]$  as result of a strong depopulation of the C1–C2 bonding region by ca. 0.26 e [V(C1,C2)]. Along Phase VI, while the four C1 and C2, and C3 and C4 pseudoradical centers follow increase their populations, an increase of populations in the C7-C8 bonding region by ca. 0.14 [see V(C7,C8) and V'(C7,C8) in Table S3], and a strong depopulation at the C1-C2 bonding region by *ca*. 0.26 e are observed [see V(C1,C2) in Table S3]. At S7, the C2–C3 single bond is formed with an initial population of 1.01 e [see V(C2,C3) in Table S3] at a C–C distance of 1.95 Å by the merger of the C2 pseudoradical center at the ethylene fragment and the C3 pseudoradical ones, located at the pyridine moiety. Along *Phase VIII*, the second C1–C4 single bond with a population of 0.91 e at a C–C distance of 2.00 Å is formed by the merger of the C1 *pseudoradical* center at the ethylene moiety and the C4 ones at the pyridine fragment [see V(C1,C4) in Table S3]. The formation process of C2-C3 and C1-C4 single bonds is given by a C-to-C coupling of the two C2 and C3, and C1 and C4 *pseudoradical* centers. At *Phase IX*, the populations of the C1–C4 and C2–C3 bond regions reach values of 1.30 e and 1.47e, whereas the population of C7–C8 and C5–N6 bonding regions acquiring some character of delocalized double bonds. Finally, at **18**, the populations of C1-C4 and C2-C3 bonding region is 1.90 e, together to that associated to C3–N6[C7] and C4–C5[C8] bonding regions, by *ca.* 2.00 e, are the expected for single bonds, while the populations of C7-C8 and C5-N6 bonding regions, 3.47 e and 3.05 e, predict polarized double bonds.

From the BET study of the non-polar DA reaction between ethylene **5** and pyridine **8** some attractive conclusions can be drawn: i) the non-polar DA reaction of ethylene **5** and pyridine **8** takes place along ten different phases; ii) non polar character (GEDT values are negligible) of this DA reaction process is responsible for the high activation energies; iii) the highest energy cost demanded is to reach **TS2**, 31.3 kcal·mol<sup>-1</sup>. The activation energy of this non-polar reaction is mainly associated to the continuous depopulation of the C1–C2, C4–C5[C8] and C3-N6[C7] bonding regions and ongoing electron reorganizations in the pyridine fragment; iv) the formation of first C2–C3 single bond takes places at a C–C distance of 1.95 Å, while the second C1–C4 single bond takes places at a C–C distance of 2.00 Å, both through the C-to-C coupling of the two C2 and C3 and the two C1 and C4 *pseudoradical* centers. At last, v) the DA reaction between ethylene **5** and pyridine **8** is characterized by a slight synchronic mechanism (see Scheme S4).



Scheme S4. Simplified representation of the molecular mechanism of the non-polar DA reaction between ethylene 5 and pyridine 8 by Lewis-like structures arising from the topological analysis of the ELF along the reaction path.

**Table S3.** ELF valence basin populations, distances of the forming bonds, relative<sup>a</sup> electronic energies, GEDT and IRC values of the IRC structures, **S0** – **S9**, defining the X phases characterizing the molecular mechanism of the DA reaction between ethylene **5** and pyridine **8**. **TS2** and **18** are also included. Distances are given in angstroms, Å, GEDT values and electron populations in average number of electrons, e, relative energies in kcal·mol<sup>-1</sup> and IRC values in a.u.

Structures	8	5	<b>S0</b>	<b>S1</b>	<b>S2</b>	<b>S3</b>	<b>S4</b>	TS2	<b>S</b> 5	<b>S6</b>	<b>S7</b>	<b>S8</b>	<b>S9</b>	18
Phases				Ι	II	III	IV	V	V	<i>יו</i> 1	/II V	'III	IX	Χ
d(C1-C4)			3.511	2.261	2.209	2.188	2.166	2.157	2.140	2.058	2.027	2.000	1.843	1.553
d(C2–C3)			3.407	2.193	2.138	2.115	2.092	2.083	2.065	1.979	1.947	1.919	1.766	1.545
ΔΕ			0.0	29.3	30.8	31.1	31.3	31.3	31.2	29.6	27.4	25.7	11.4	-7.6
GEDT			0.00	0.01	0.02	0.02	0.03	0.03	0.04	0.05	0.06	0.06	0.08	0.07
IRC			-10.42	-0.72	-0.36	-0.21	-0.06	0.00	0.12	0.69	0.90	1.08	2.12	4.22
V(C1,C2)		1.69	1.70	3.17	3.19	3.20	2.98	2.96	2.72	2.46	2.39	2.32	2.07	1.90
V'(C1,C2)		1.71	1.67											
V(C3,N6)	2.33		2.39	2.24	2.17	2.14	2.13	2.11	2.09	1.99	1.95	1.93	1.83	1.81
V(C3,C7)	2.87		2.87	2.71	2.57	2.55	2.50	2.49	2.47	2.34	2.31	2.29	2.16	2.06
V(C4,C5)	2.89		2.86	2.64	2.63	2.54	2.51	2.50	2.48	2.36	2.33	2.30	2.18	2.03
V(C4,C8)	2.73		2.74	2.62	2.59	2.54	2.51	2.49	2.47	2.34	2.30	2.27	2.15	2.02
V(C5,N6)	2.42		2.39	2.65	2.70	2.72	2.73	2.74	2.75	2.83	2.85	2.85	1.45	1.55
V'(C5,N6)													1.49	1.49
V(C7,C8)	2.77		2.74	3.01	3.08	3.10	3.12	3.12	3.15	1.52	1.50	1.54	1.74	1.74
V'(C7,C8)										1.77	1.77	1.77	1.65	1.72
V(N6)	2.69		2.69	2.74	2.74	2.75	2.75	2.75	2.75	2.75	2.77	2.76	2.73	2.74
V(C1)									0.20	0.36	0.40			
V(C2)							0.23	0.25	0.29	0.47				
V(C3)					0.16	0.20	0.25	0.26	0.30	0.45				
V(C4)						0.11	0.15	0.17	0.22	0.38	0.44			
V(C1,C4)												0.91	1.30	1.73
V(C2,C3)											1.01	1.09	1.47	1.81

<sup>a</sup> Relative to the first structure of the IRC, **S0** 

#### 5. BET study of the DA reaction between ethylene 5 and pyridazine 9.

A BET study of the non-polar DA reaction of ethylene **5** and pyridazine **9** was performed. The molecular mechanism which is represented by Lewis-like structures derived from the ELF topology is shown in Scheme S5, while the populations of the most significant valence basins, including other relevant parameters, of selected structures of the IRC are collected in Table S4.

The BET study of the bonding changes along the DA reaction between ethylene 5 and pyridazine 9 takes place along six different phases. The reaction begins at Phase I, with a depopulation of the C1–C2 bonding region of the ethylene fragment by ca. 0.20 e, (see V(C1,C2) in Table S4), depopulations of the C3-N6[C7] and C4-N5[C8] bonding regions are also observed together with the increase of the populations of the N5–N6 and C7–C8 bonding regions, 0.16 e and 0.22 e, at the pyridazine moiety. At S2, two C3 and C4 pseudoradical carbons of the pyridazine 9 framework are created [see V(C3) and V(C4) in Table S43 and Scheme S5] integrating 0.14 e. Note that the formation of these *pseudoradicals* is mainly consequence of the decrease of populations in C3–N6 and C4–N5 bonding regions by ca 0.16 e (see V(C3,N6) and V(C4,N5) in Table S4). Also note that the adjacent C3–C7 and C4–C8 bonding regions slightly decrease their populations [see V(C3,C7) and V(C4,C8) in Table S4]. Along Phase III, in which the **TS3** is found, two new C1 and C2 *pseudoradical* centers of ethylene fragment are formed, integrating a population of 0.21 e [see V(C1) and V(C2) in Table S4]. This population is mainly provided by the strong depopulation of the C1–C2 bonding region by ca. 0.41 e [see V(C1,C2)] in Table S4]. Along this phase, the population associated to the C3 and C4 pseudoradical centers continues increasing to 0.29 e [see V(C3) and V(C4) in Table S4]. At S4, the four C1 and C2, and C3 and C4 pseudoradical centers increase their populations to 0.38 e and 0.49 e, respectively, while the N5–N6 bonding region slightly increase of population to 2.28 e [see V(N5,N6) in Table S4] and also that in the C7–C8 bonding region to 3.22 e [see V(C7,C8) and V'(C7,C8) Table S4]. At Phase V, the C1 and C4 pseudoradical centers merge creating the new C1–C4 single bond with an initial population of 0.93 e, and concurrently, the C2 and C3 pseudoradical centers merge to form the second C2-C3 single bond, also integrating 0.93 e [see V(C1,C4) and V(C2,C3) in Table S4 and Scheme S5]. These electron changes indicate that the formation of the two new single bonds begins at a distance of *ca*. 1.99 Å through a C-to-C coupling of the two C1 and C4 and the two C2 and C3 pseudoradical centers. Lastly, at the 19 structure, the populations of the C1–C2 and the new C1–C4 and C2–C3 bonding regions are 1.90 e and 1.81 e, respectively,

characterizing single bonds, C3–N6 and C4–N5 bonding regions with populations around 1.75 e showing some polarized single bond character, and C7–C8 bonding region reaching a population of 3.34 e, acquiring the expected population for double bonds, while that the C4–C8 and C3–C7 bonding regions with populations of 2.11 e, being associated to single bonds in **19**. Finally, the N5–N6 bonding region reaches a population of 2.58 e in agreement with the population of a single bond.

From the BET study of the DA reaction between ethylene **5** and pyridazine **9** it can conclude the following: i) this non-polar DA reaction proceeds along six different phases; ii) the highest energy cost demanded is to reach **TS3**, 26.8 kcal·mol<sup>-1</sup> which is found in *Phase III* (see Table S4). The activation energy of this non-polar reaction is mainly associated to the continuous depopulation of the C1–C2 bonding regions and those related with the C3–N6, C4–N5, C4–C8, C3–C7 and C7–C8 bonding regions; iii) the formation of the two C1–C4 and C2–C3 single bonds takes place simultaneously at a C–C distance of 1.99 Å, by the C-to-C coupling of the two C1 and C4 and the two C2 and C3 *pseudoradical* centers. Finally, iv) the non-polar DA ethylene **5** and pyridazine **9** is entirely synchronic (see Scheme S5).



Scheme S5. Simplified representation of the molecular mechanism of the non-polar DA reaction between ethylene 5 and pyridazine 9 by Lewis-like structures arising from the topological analysis of the ELF along the reaction path.

**Table S4.** ELF valence basin populations, distances of the forming bonds, relative<sup>a</sup> electronic energies, GEDT and IRC values of the IRC structures, S0 - S5, defining the six phases characterizing the molecular mechanism of the DA reaction between ethylene 5 and pyridazine 9. TS3 and 19 are also included. Distances are given in angstroms, Å, GEDT values and electron populations in average number of electrons, e, relative energies in kcal·mol<sup>-1</sup> and IRC values in a.u.

Structures	9	5	<b>S0</b>	<b>S1</b>	<b>S2</b>	TS3	<b>S3</b>	<b>S4</b>	<b>S5</b>	19
Phases			Ι	II		III	1	V	V	VI
d(C1–C4)			3.465	2.234	2.178	2.128	2.106	2.001	1.985	1.541
d(C2–C3)			3.478	2.234	2.178	2.128	2.106	2.001	1.985	1.541
ΔΕ			0.0	25.1	26.4	26.8	26.7	23.7	22.4	-14.6
GEDT			0.00	0.03	0.05	0.06	0.07	0.09	0.09	0.08
IRC			-10.62	-0.72	-0.34	0.0	0.16	0.81	0.96	4.07
V(C1,C2)		1.69	1.68	3.15	3.18	3.20	2.77	2.47	2.42	1.90
V'(C1,C2)		1.71	1.70							
V(C3,N6)	2.55		2.57	2.40	2.28	2.22	2.19	2.07	2.05	1.75
V(C3,C7)	2.74		2.75	2.65	2.59	2.53	2.50	2.38	2.35	2.11
V(C4,N5)	2.55		2.57	2.40	2.28	2.22	2.19	2.07	2.05	1.75
V(C4,C8)	2.74		2.75	2.65	2.59	2.53	2.50	2.38	2.35	2.11
V(N5,N6)	1.91		1.94	2.10	2.14	2.19	2.20	2.28	2.31	2.58
V(C7,C8)	2.78		2.79	3.01	3.06	3.10	3.12	1.66	1.50	1.70
V'(C7,C8)								1.56	1.74	1.74
V(N5)	2.75		2.73	2.78	2.80	2.79	2.79	2.77	2.76	2.72
V(N6)	2.76		2.75	2.79	2.79	2.79	2.78	2.77	2.76	2.72
V(C1)							0.21	0.38		
V(C2)							0.21	0.38		
V(C3)					0.14	0.24	0.29	0.49		
V(C4)					0.14	0.24	0.29	0.49		
V(C1,C4)									0.93	1.81
V(C2,C3)									0.93	1.81

<sup>a</sup> Relative to the first structure of the IRC, **S0**.

#### 6. BET study of the DA reaction between ethylene 5 and 1,2,4-triazine 10.

A BET study of the polar DA reaction of ethylene **5** and 1,2,4-triazine **10** was carried out. A simplified representation of the molecular mechanism by Lewis-like structures result from the ELF topology is shown in Scheme S6. The populations of the most significant valence basins, including other relevant parameters, of selected structures of the IRC are collected in Table S5.

The bonding changes of ethylene 5 and 1,2,4-triazine 10 along the polar DA pathway by the BET analysis shows eight different phases. The reaction progresses, along Phase I, with a depopulation of the C1–C2 single bond at the ethylene moiety [see V(C1,C2) in Table S5] from 3.39 e to 3.14 e, together with the depopulation, at the triazine fragment, of the C3–N6[N7] and the C4-N5[C8] bonding regions by ca. 0.15 e [see V(C3,N6[N7], V(C4,N5[C8]) in Table S5], while the increase of the population is observed at N5–N6 and N7–C8 bonding regions by ca. 0.13e [see V(N5,N6) and V(N7,C8) in Table S5]. Along Phase II, a C3 pseudoradical center is created at the 1,2,4-triazine moiety, integrating 0.16 e [V(C3)], mainly associated to a depopulation of the C3–N6 bonding region by ca. 0.13 e [see V(C3,N6) in Table S5], while other slight electron reorganizations are also observed. In the following phase, Phase III, a second C4 pseudoradical center is created at the 1,2,4-triazine fragment with an initial population of 0.17 e [V(C4)] mainly by a depopulation of the C4–N5 bonding region by 0.14 e [V(C4,N5)]. Along Phase IV, in which the TS4 is found, a C2 pseudoradical center at the ethylene moiety is formed integrating 0.21 e [V(C2)] as result of a depopulation of the C1–C2 bonding region by 0.21 e. Other relevant electron reorganizations are consistent with bonding changes observed along the reaction progresses. Along *Phase V*, a C1 *pseudoradical* center at the ethylene fragment is created with a population of 0.19 e [V(C1)] as result of a strong depopulation of the C1–C2 bonding region by ca. 0.22 e [V(C1,C2)]. Along Phase VI, the C1 pseudoradical center at the ethylene fragment and the C4 pseudoradical ones located at the 1,2,4-triazine ones merge to form a new C1–C4 single bond with an initial population of 0.88 e [see V(C1,C4) in Table S5] at a C–C distance of 2.01 Å. At the same time, the second C2–C3 single bond with a population of 0.99 e [see V(C2,C3) in Table S5] at a C–C distance of 1.97 Å is also formed by the merger of the C2 *pseudoradical* center at the ethylene moiety and the C3 ones at the 1,2,4-triazine fragment, [see V(C2,C3) in Table S5] while the rearrangement of the populations of the other bond regions progressively continue. The process of formation of C1–C4 single bond can be considered taking

place by a C-to-C coupling of the C1 and C4, and C2 and C3 *pseudoradical* centers. At *Phase VII*, the populations of the C1–C4 and C2–C3 bond regions reach values of 1.38 e and 1.50 e, whereas the population of N7–C8 bonding region increases from 2.79 e to 2.93 e and that of N5–N6 increase by *ca*. 0.16 e. Lastly at **20**, the populations of C1–C4 and C2–C3 bonding regions are 1.78 and 1.84 e, that associated to C3-N6[N7] is around 1.80 e, that of the C4–N5 bonding region is 1.75 e and that of the C4–C8 bonding region is 2.14 e. These populations are the expected for single bonds in **20**. At the same point, the populations N5–N6 and N7–C8 bonding regions reach values of 2.55 e and 2.98 e, predicting polarized double bonds.

The bonding changes along the reaction path of ethylene **5** and 1,2,4-triazine **10** analysed from the point of view of BET show some interesting conclusions: i) DA reaction of ethylene **5** and 1,2,4-triazine **10** takes place along eight different phases. Note that the maximum GEDT occurs along *Phases VI* and *VII* (0.09 e); ii) thus, the polar character in this DA reaction process is responsible for the no so high activation energies; iii) the highest energy cost demanded to reach **TS4**, 20.5 kcal·mol<sup>-1</sup> agrees with that found at **S3** (see Table S5). The activation energy of this polar reaction is mainly associated to the continuous depopulation of the C1–C2, C3–N6[N7], C4–N5[C8] bonding regions and electron density enhancement around the N5–N6 and N7–C8 bonding regions; iv) the formation of the two C1–C4 and C2–C3 single bonds takes places at a C–C distance by *ca*. 1.98 e, in the same phase, through a C-to-C coupling of the C1 and C4 and the C2 and C3 *pseudoradical* centers; and finally, v) the DA ethylene **5** and 1,2,4-triazine **10** is fully synchronic (see Scheme S6).



Scheme S6. Simplified representation of the molecular mechanism of the non-polar DA reaction between ethylene 5 and 1,2,4-triazine 10 by Lewis-like structures arising from the topological analysis of the ELF along the reaction path.

**Table S5**. ELF valence basin populations, distances of the forming bonds, relative<sup>a</sup> electronic energies, GEDT and IRC values of the IRC structures, S0 - S7, defining the eight phases characterizing the molecular mechanism of the DA reaction between ethylene 5 and 1,2,4-triazine 10. TS4 and 20 are also included. Distances are given in angstroms, Å, GEDT values and electron populations in average number of electrons, e, relative energies in kcal·mol<sup>-1</sup> and IRC values in a.u.

Structures	10	5	<b>S0</b>	<b>S1</b>	<b>S2</b>	<b>S3</b>	TS4	<b>S4</b>	<b>S5</b>	<b>S6</b>	<b>S7</b>	20
Phases				Ι	II I	II	IV	1	V I	VI V	VII V	'III
d(C1–C4)			3.451	2.270	2.211	2.182	2.168	2.126	2.112	2.011	1.804	1.543
d(C2–C3)			3.394	2.228	2.170	2.141	2.127	2.084	2.069	1.965	1.761	1.537
ΔΕ			0.0	19.1	20.2	20.4	20.5	20.2	19.9	15.8	-3.2	-21.3
GEDT			0.0	0.05	0.07	0.08	0.08	0.09	0.10	0.12	0.12	0.08
IRC			-10.1	-0.68	-0.29	-0.09	0.00	0.29	0.39	1.07	2.44	4.49
V(C1,C2)		1.69	1.69	3.14	3.13	3.14	3.14	2.93	2.71	2.43	2.08	1.89
V'(C1,C2)		1.71	1.70									
V(C3,N6)	2.69		2.65	2.49	2.36	2.33	2.31	2.24	2.22	2.11	1.95	1.82
V(C3,N7)	2.41		2.39	2.33	2.27	2.24	2.22	2.17	2.16	2.05	1.90	1.81
V(C4,N5)	2.55		2.57	2.42	2.43	2.29	2.26	2.20	2.17	2.05	1.91	1.75
V(C4,C8)	2.82		2.81	2.71	2.66	2.63	2.61	2.55	2.53	2.42	2.15	2.14
V(N5,N6)	1.90		1.92	2.05	2.09	2.11	2.12	2.16	2.17	2.25	2.41	2.55
V'(N5,N6)												
V(N7,C8)	2.38		2.46	2.58	2.63	2.65	2.66	2.69	2.70	2.79	1.50	1.48
V'(N7,C8)											1.43	1.50
V(N5)	2.71		2.69	2.77	2.78	2.78	2.78	2.78	2.77	2.77	2.74	2.75
V(N6)	2.77		2.77	2.83	2.81	2.81	2.81	2.81	2.82	2.78	2.75	2.74
V(N7)	2.67		2.66	2.69	2.70	2.71	2.72	2.74	2.75	2.76	2.74	2.75
V(C1)									0.19			
V(C2)								0.21	0.25			
V(C3)					0.16	0.22	0.25	0.33	0.36			
V(C4)						0.17	0.20	0.29	0.32			
V(C1,C4)										0.88	1.38	1.78
V(C2,C3)										0.99	1.50	1.84

<sup>a</sup> Relative to the first structure of the IRC, S0

#### 7. BET study of the DA reaction between ethylene 5 and, 1,2,4,5-tetrazine 11.

A BET study of the polar DA reaction of ethylene **5** and 1,2,4,5-tetrazine **11** was accomplished. The molecular mechanism represented by Lewis-like structures result from the ELF topology is shown in Scheme S7. Populations of the most significant valence basins, including other relevant parameters, of selected structures of the IRC are collected in Table S6.

The BET analysis of the bonding changes along the polar DA pathway between ethylene 5 and tetrazine 11 is characterized by five different phases. Along *Phase I*, a depopulation of the C1–C2 bonding region of the ethylene fragment by 0.21 e is observed [V(C1,C2)] while slight depopulations around the C3-N6[N7] and C4-N5[N8] bonding regions at the tetrazine moiety are performed. At this point, slight populations at the N5–N6 and N7–N8 bonding regions by *ca*. 0.10 e [see V(N5,N6) and V(N7,N8) in Table S6] are also observed at tetrazine fragment, while the N non-bonding electron densities slightly increase [see all V(N<sub>i</sub>)]. Along *Phase II*, slight electron rearrangements around the entire ethylene and tetrazine fragments are observed. At S2, two C3 and C4 pseudoradical centers of the tetrazine moiety are created [see V(C3) and V(C4) in Table S6 and Scheme S7] integrating 0.13 e each one. The formation these *pseudoradical* centers is mainly triggered by the depopulation of the C3-N6[N7] and C4-N5[N8] bonding regions [see V(C3,N6[N7]), and V(C4,N5[N8]) in Table S6]. Along Phase III, in which TS5 is found, two C1 and C2 pseudoradical centers at the ethylene moiety are formed integrating a population of 0.19 e each one [see V(C1) and V(C2) in Table S6]. This electron density is a consequence to the strong depopulation of the C1–C2 bonding region by ca 0.36 e [V(C1,C2)]. Along this phase, the population associated to the C3 and C4 pseudoradical centers increase to 0.37 e [see V(C3) and V(C4) in Table S6]. Along *Phase IV*, while the population associated to C1-C2, C3-N6[N7] and C4-N5[N8] bonding regions decrease and that associated to the N5-N6 and N7-N8 bonding regions slightly increase, the C1 and C4 pseudoradical centers merge to form a new C1–C4 single bond with an initial population of 0.89 e, and concurrently, the C2 and C3 pseudoradical centers also merge giving rise the second C2–C3 single bond, integrating 0.89 e [see V(C1,C4) and V(C2,C3) in Table S6 and Scheme S7]. These electron density changes indicate that the formation of the two new single bonds begins at a distance of 2.0 Å through a C-to-C coupling of the two C1 and C4 and the two C2 and C3 pseudoradical centers. Finally, at the 21 structure, the population of the C1-C2 bonding region is 1.89 e, i.e. the expected polarized value for single bonds, the C3-N6[N7] and C4-N5[N8] bonding regions reach a population by

*ca.* 1.85 e, also acquiring the expected population for single bonds, while that associated to the N5[N7] -N6[N8] bonding regions increase their populations to 2.48 e and that associated to N[5–8] non-bonding electron density reach a population of 2.76 e, characterizing polarized double bonds at **21**.

From the BET analysis of the polar DA reaction between ethylene **5** and 1,2,4,5-tetrazine **11** some significant conclusions can be drawn: i) this polar DA reaction takes place along five different phases. The maximum of GEDT is proceeds along *Phase IV* (ca. 0.14 e); ii) the **TS5** shows the highest energy of the path, 14.1 kcal·mol<sup>-1</sup>. The activation energy of this reaction is mainly associated to the continuous depopulation of the C1–C2 bonding regions and electron reorganizations around the C3–N6[N7], C4–N5[N8], N5[N7] –N6[N8] bonding regions; iii) the formation of the two C1–C4 and C2–C3 single bonds takes place simultaneously at a C–C distance of 2.00 Å, by the C-to-C coupling of the two C1 and C4 and the two C2 and C3 *pseudoradical* centers; and finally, iv) the DA ethylene **5** and 1,2,4,5-tetrazine **11** is thoroughly synchronic.



Scheme S7. Simplified representation of the molecular mechanism of the non-polar DA reaction between ethylene 5 and 1,2,3,5-triazine 11 by Lewis-like structures arising from the topological analysis of the ELF along the reaction path.

**Table S6**. ELF valence basin populations, distances of the forming bonds, relative<sup>a</sup> electronic energies, GEDT and IRC values of the IRC structures, S0 - S4, defining the five phases characterizing the molecular mechanism of the DA reaction between ethylene 5 and 1,2,4,5-tetrazine 11. TS5 and 21 are also included. Distances are given in angstroms, Å, GEDT values and electron populations in average number of electrons, e, relative energies in kcal·mol<sup>-1</sup> and IRC values in a.u.

Structures	11	5	<b>S0</b>	<b>S1</b>	<b>S2</b>	TS5	<b>S3</b>	<b>S4</b>	21
Phases				Ι	II	III	1	V	V
d(C1–C4)			3.248	2.270	2.209	2.162	2.090	1.998	1.536
d(C2–C3)			3.251	2.279	2.209	2.162	2.090	1.998	1.536
ΔΕ			0.0	13.0	13.9	14.1	13.4	9.6	-29.0
GEDT			0.0	0.08	0.10	0.11	0.13	0.15	0.09
IRC			-8.1	-0.72	-0.31	0.00	0.48	1.09	4.44
V(C1,C2)		1.69	1.75	3.16	3.14	3.14	2.78	2.49	1.89
V'(C1,C2)		1.71	1.62						
V(C3,N6)	2.63		2.63	2.44	2.39	2.31	2.22	2.12	1.85
V(C3,N7)	2.55		2.55	2.49	2.40	2.37	2.28	2.19	1.86
V(C4,N5)	2.52		2.62	2.41	2.36	2.31	2.22	2.13	1.89
V(C4,N8)	2.65		2.56	2.52	2.43	2.37	2.28	2.19	1.84
V(N5,N6)	1.96		1.96	2.06	2.08	2.11	2.17	2.23	2.48
V(N7,N8)	1.96		1.96	2.06	2.08	2.11	2.16	2.23	2.48
V(N5)	2.71		2.71	2.77	2.78	2.78	2.78	2.77	2.76
V(N6)	2.72		2.71	2.77	2.78	2.78	2.78	2.77	2.76
V(N7)	2.71		2.71	2.78	2.78	2.78	2.78	2.77	2.76
V(N8)	2.72		2.71	2.78	2.78	2.78	2.78	2.77	2.76
V(C1)							0.19		
V(C2)							0.19		
V(C3)					0.13	0.22	0.37		
V(C4)					0.13	0.22	0.37		
V(C1,C4)								0.89	1.84
V(C2,C3)								0.89	1.83

<sup>a</sup> Relative to the first structure of the IRC, **S0** 



**Figure S5**. Plot of the ELF RED obtained from the topological analysis of the ELF vs the estimated RED obtained by using EDU indices, in average number of electrons, e.



Figure S6. Plot of the activation energies,  $\Delta E_{act}$  in kcal·mol<sup>-1</sup>, of the DA reactions of benzene 7 and AACs 8 – 11 with ethylene 5 vs the GEDT, in average number of electrons, e, computed at the corresponding TSs.



**Figure S7.** Plot of the activation energies,  $\Delta E_{act}$  in kcal·mol<sup>-1</sup>, of the DA reactions of benzene 7 and AACs 8 – 11 with ethylene 5 vs the number of nitrogen nuclei n of the AACs.

Table S7. MPWB1K/6-311G(d,p) gas phase total electronic energies of the stationary points involved in the DA reactions of benzene 7 and AACs 8 - 11 with ethylene 5.

5	-78.552844
7	-232.173614
8	-248.209643
9	-264.210204
10	-280.245309
11	-296.243263
TS1	-310.668677
TS2	-326.714264
TS3	-342.723080
TS4	-358.768905
TS5	-374.777363
17	-310.728979
18	-326.776375
19	-342.789095
20	-358.835528
21	-374.846035