

New insight into atomic-level interpretation of interactions in molecules and reacting systems[†]

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S1 δg_i isosurfaces for hydrogen atoms in the water dimer

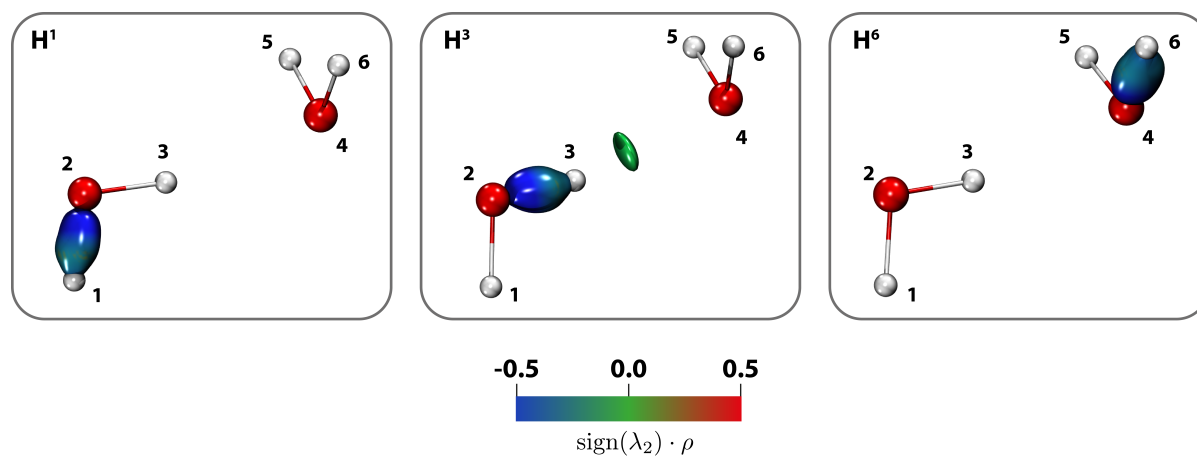


Fig. S1 δg_i isosurfaces associated with atoms H¹ and H³ and H⁶ for the water dimer obtained at the MP2/6-31G** level of theory; isovalues set equal to 40% of the peak in the δg_i fingerprint, i.e. 0.3 a.u. for covalent bonds and 0.045 a.u. for hydrogen-bonding; all the iso-surfaces are colored according to the BGR scheme over the range $-0.5 \text{ a.u.} < \text{sign}(\lambda_2)\rho < 0.5 \text{ a.u.}$

S2 Atomic DOIs computed from the Remdesivir molecule (C₂₇H₃₅N₆O₈P)

atom	DOI (a.u.)	atom	DOI (a.u.)
P1	5.23	O2	2.06
O3	2.51	O4	3.08
O5	2.57	N6	5.21
N7	3.50	O8	2.75
O9	3.15	N10	2.51
O11	2.38	N12	3.19
N13	3.78	C14	4.61
O15	2.76	N16	3.50
C17	4.09	C18	5.31
C19	4.74	C20	4.76
C21	4.86	C22	3.96
C23	4.95	C24	4.57
C25	4.64	C26	4.05
C27	4.14	C28	3.89
C29	4.60	C30	3.86
C31	3.32	C32	4.01
C33	3.89	C34	4.54
C35	4.61	C36	3.91
C37	3.90	C38	3.92
C39	3.94	C40	3.94
C41	3.37	C42	3.34
H43	0.92	H44	0.89
H45	0.90	H46	0.89
H47	0.91	H48	0.97
H49	0.94	H50	0.92
H51	0.92	H52	0.96
H53	0.87	H54	0.85
H55	0.86	H56	0.93
H57	0.84	H58	0.92
H59	0.94	H60	0.91
H61	0.92	H62	0.90
H63	0.86	H64	0.88
H65	0.84	H66	0.83
H67	0.97	H68	0.91
H69	0.86	H70	0.98
H71	0.94	H72	0.94
H73	0.91	H74	0.93
H75	0.99	H76	1.02
H77	0.94		

Table S1 Atomic DOIs (Δg_i) obtained at the M06-2X/6-31G** level of theory.

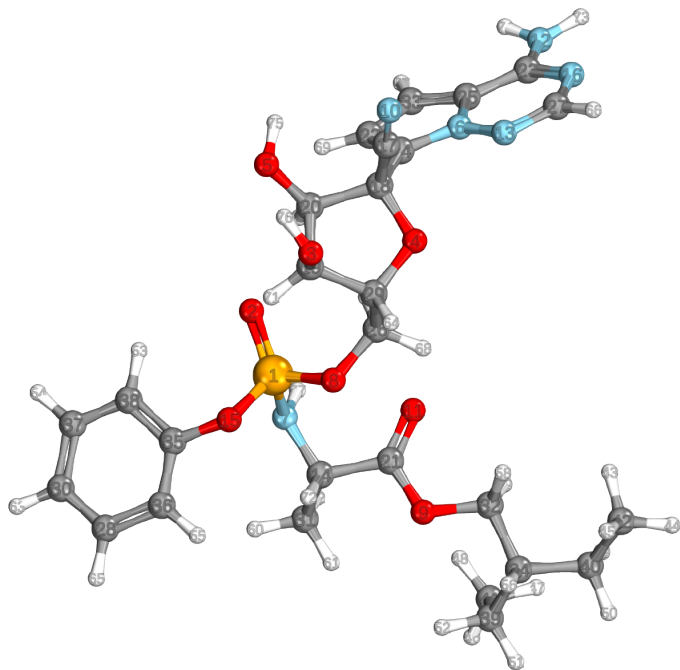


Fig. S2 Remdesivir geometry with atom numbers (level of theory: M06-2X/6-31G**).

S3 Atomic δg_i peak height scale

The δg_i peak height on the atomic (ρ , δg_i) 2D fingerprint-plot allows for ranking the interactions in categories, like for the conventional δg local descriptor. Based on our experience for δg :

- weak non-covalent interactions never (or hardly) exceed δg peak heights of 0.1 a.u.
- vdW interactions rarely extend beyond 0.02-0.03 δg peak heights
- H-bonding generally may extend up to a maximum of δg peak =0.1 a.u. (for instance, the δg peak for H-bond in water is 0.06 a.u. with a QM treatment)
- pure covalent bonding δg peak ranges from 0.2 up to around generally 1.0 in "common" molecules (δg peak for covalent O-H bond in water is 0.9), but it can be as large as 2.5 for exotic species like O_2^{2+}
- metal coordination δg peaks range between 0.1 and 0.6 a.u. (using a QM treatment)

S4 Search for a correlation between atomic DOIs and natural atomic charges for the Remdesivir molecule

The correlation between DOI and natural atomic charges (POP=(FULL,NBO) using Gaussian, level of theory: M06-2X/6-31G**) for the non-hydrogen atoms has been carried out for the Remdesivir molecule.

atom	Natural atomic charge	atom	Natural atomic charge
P1	2.61	O2	-1.12
O3	-0.78	O4	-0.56
O5	-0.78	N6	-0.88
N7	-0.58	O8	-0.62
O9	-0.83	N10	-0.15
O11	-1.08	N12	-0.30
N13	-0.84	C14	-0.30
O15	-0.58	N16	-0.17
C17	0.28	C18	0.13
C19	0.05	C20	0.07
C21	0.86	C22	-0.29
C23	0.46	C24	0.12
C25	0.05	C26	-0.14
C27	0.22	C28	-0.23
C29	0.05	C30	-0.26
C31	-0.71	C32	-0.13
C33	-0.30	C34	-0.29
C35	0.30	C36	-0.29
C37	-0.23	C38	-0.29
C39	-0.48	C40	-0.48
C41	-0.71	C42	-0.71
H43	0.23	H44	0.25
H45	0.24	H46	0.25
H47	0.24	H48	0.23
H49	0.24	H50	0.25
H51	0.25	H52	0.25
H53	0.28	H54	0.25
H55	0.26	H56	0.26
H57	0.25	H58	0.24
H59	0.23	H60	0.26
H61	0.26	H62	0.24
H63	0.25	H64	0.27
H65	0.25	H66	0.24
H67	0.24	H68	0.26
H69	0.28	H70	0.26
H71	0.24	H72	0.28
H73	0.44	H74	0.43
H75	0.51	H76	0.52
H77	0.45		

Table S2 Natural atomic charges obtained at the M06-2X/6-31G** level of theory.

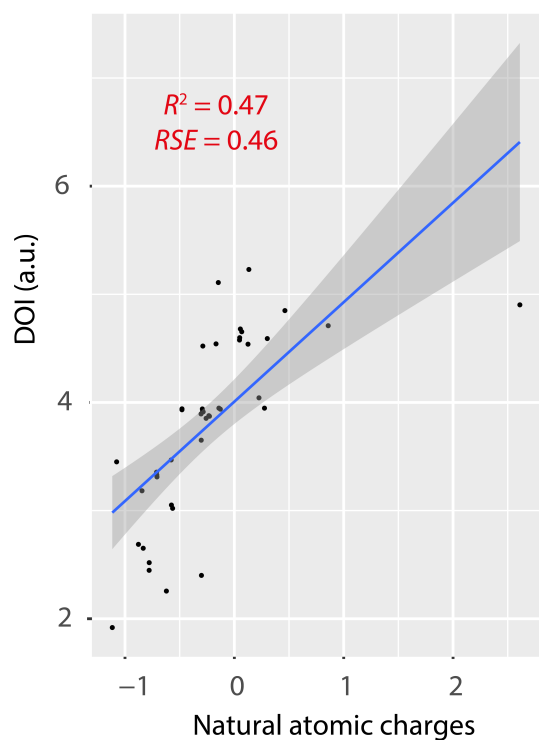


Fig. S3 Correlation between DOI and natural atomic charges for the Remdesivir non-hydrogen atoms.

S5 Search for a correlation between atomic DOIs and NMR chemical shifts for the Remdesivir molecule

The correlation between DOI and $^1\text{H}/^{13}\text{C}$ isotropic chemical shifts (obtained from GIAO method, level of theory: M06-2X/6-31G**) has been investigated for the Remdesivir molecule. The chemical shifts are given relatively to the tetramethylsilane (TMS) at the same level of theory.

Table S3 Atomic DOIs (Δg_i) and NMR shifts for hydrogen atoms of the Remdesivir molecule with respect to tetramethylsilane (TMS) at the same level of theory. IGM calculations have been performed on the M06-2X/6-31G** optimized geometry. For the sake of comparison, NMR shifts have been computed at the same level of theory.

atom	DOI (a.u.)	NMR shift (ppm)
H43	0.92	0.84
H44	0.89	1.06
H45	0.90	0.76
H46	0.89	0.75
H47	0.91	0.76
H48	0.97	0.52
H49	0.94	1.45
H50	0.92	1.23
H51	0.92	1.17
H52	0.96	1.93
H53	0.87	8.64
H54	0.85	8.10
H55	0.86	7.65
H56	0.93	1.90
H57	0.84	6.88
H58	0.92	4.11
H59	0.94	3.80
H60	0.91	0.97
H61	0.92	1.32
H62	0.90	0.53
H63	0.86	7.90
H64	0.88	4.55
H65	0.84	8.03
H66	0.83	8.68
H67	0.97	3.63
H68	0.91	3.38
H69	0.86	7.27
H70	0.98	5.72
H71	0.94	4.85
H72	0.94	3.65
H73	0.91	4.82
H74	0.93	4.75
H75	0.99	1.33
H76	1.02	2.83
H77	0.94	2.19

Table S4 Atomic DOIs (Δg_i) and NMR shifts for carbon atoms of the Remdesivir molecule with respect to tetramethylsilane (TMS) at the same level of theory. IGM calculations have been performed on the M06-2X/6-31G** optimized geometry. For the sake of comparison, NMR shifts have been computed at the same level of theory.

atom	DOI (a.u.)	NMR shift (ppm)
C14	3.78	54.0
C17	4.61	121.9
C18	4.09	78.6
C19	5.31	74.7
C20	4.74	78.1
C21	4.76	181.4
C22	4.86	115.9
C23	3.96	163.1
C24	4.95	135.5
C25	4.57	124.9
C26	4.64	65.0
C27	4.05	157.5
C28	4.14	140.7
C29	3.89	84.8
C30	4.60	135.6
C31	3.86	20.4
C32	3.32	67.5
C33	4.01	104.6
C34	3.89	37.3
C35	4.54	161.8
C36	4.61	130.4
C37	3.91	141.9
C38	3.90	132.5
C39	3.92	25.5
C40	3.94	25.4
C41	3.94	7.6
C42	3.37	13.0

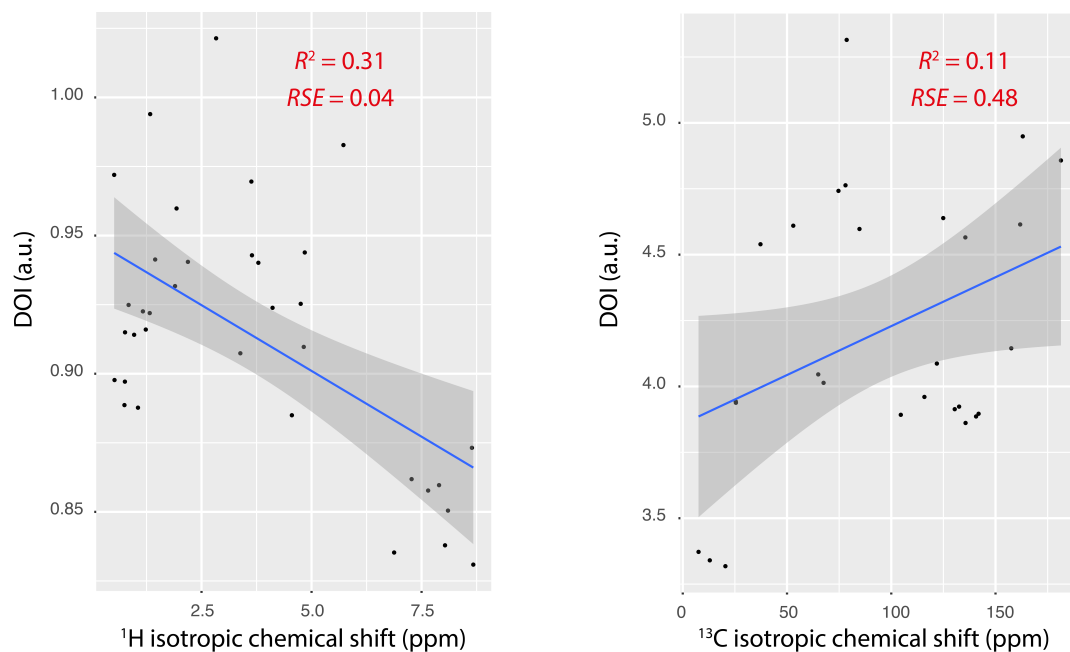


Fig. S4 Correlation between DOI and isotropic chemical shifts for the hydrogen and carbon Remdesivir atoms (GIAO method).

S6 Search for a correlation between atomic DOIs and inter-atomic energies obtained by IQA calculations for several small molecules

The correlation between DOI and inter-atomic energies (obtained from the IQA method, level of theory: M06-2X/Def2-TZVP) has been investigated for the 12 following molecules:

Table S5 Atomic DOIs (Δg_i) and inter-atomic energies (IQA).

	atom	DOI (a.u.)	inter-atomic energy (Ha)
HF	F	0.92	-0.228
	H	0.92	-0.228
NH ₃	N	2.29	-0.595
	H	0.92	-0.147
CH ₄	C	2.63	-0.495
	H	0.87	-0.128
H ₂ O	O	1.71	-0.519
	H	0.95	-0.193
SO ₂	S	4.69	-2.13
	O	2.38	-0.868
PF ₅	P	5.34	-3.72
	F ^{2,3}	1.40	-0.428
	F ⁴⁻⁶	1.22	-0.446
HCN	H	0.73	-0.114
	C	2.99	-0.872
	N	2.34	-0.848
CH ₃ OH	C	3.28	-0.593
	O	2.31	-0.594
	H ^{3,4}	0.87	-0.129
	H ⁵	0.88	-0.127
	H ⁶	0.97	-0.191
	C	4.38	-1.30
formic acid dimer	O ^{2,7}	2.40	-0.772
	O ^{3,8}	2.46	-0.781
	H ^{4,9}	0.78	-0.120
ethene-ethyne complex	H ^{5,10}	0.95	-0.215
	C ^{1,2}	3.21	-0.485
	H ³⁻⁶	0.81	-0.127
	C ⁷	3.01	-0.441
	C ⁸	3.08	-0.440
	H ⁹	0.79	-0.124
NH ₃ BH ₃	H ¹⁰	0.73	-0.121
	N	2.99	-0.833
	B	1.89	-0.122
	H ³⁻⁵	0.88	-0.137
B ₂ H ₆	H ⁶⁻⁸	0.60	-0.264
	B	2.26	-0.109
	H	0.62	-0.276
	H ^{4,5}	0.84	-0.405

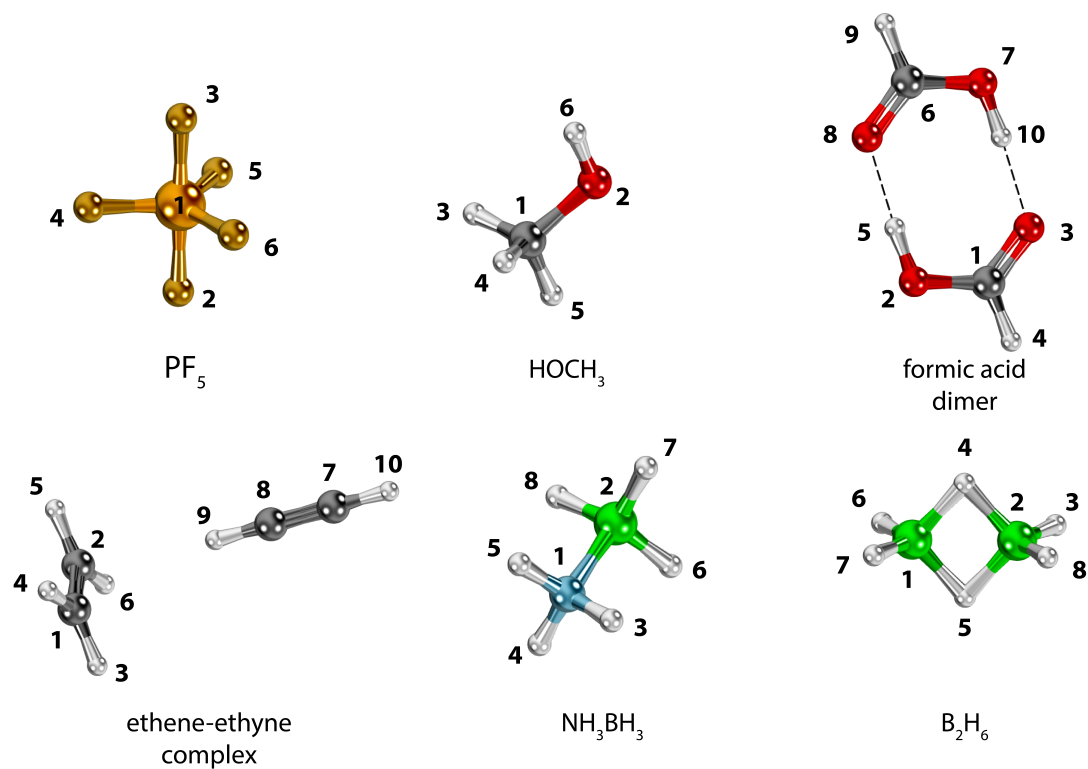


Fig. S5 Geometry and atomic numbers of PF₅, methanol, formic acid dimer, ethene-ethyne complex, NH₃BH₃ and B₂H₆.

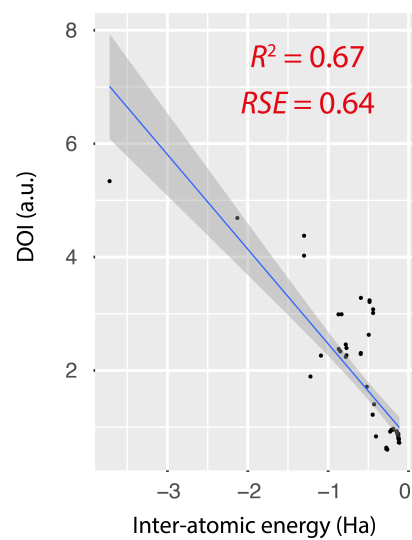


Fig. S6 Correlation between DOI and inter-atomic energies for small molecules (IQA method).

S7 Search for correlations between atomic DOIs and atomic properties computed from the program Multiwfn for the 77 atoms of the Remdesivir molecule (C₂₇H₃₅N₆O₈P)

The comparison of the atomic DOI value Δg_i with 38 real space functions integrated in atomic basins has been performed with the use of **R** via principal components analysis (PCA) for the Remdesivir molecule. 38 properties available in the Multiwfn output have been explored for a set of 77 atoms, among which: electron density (ED), ED laplacian, local Mulliken electronegativity, local hardness, Shannon entropy. A molecular integration grid has been built with the program Multiwfn for every atom, based on the Hirshfeld-I partition. Given a certain local real space property $f(\mathbf{r})$, the integrated real space function I_i is defined as follow for each atom i :

$$I_i = \int_{R^3} w_i(\mathbf{r}) \cdot f(\mathbf{r}) \, d\mathbf{r}. \quad (\text{S1})$$

with w_i the weighting function of atom i , obtained through an iteration process in the Hirshfeld-I method. PCA furnished the following correlation circle presented below:

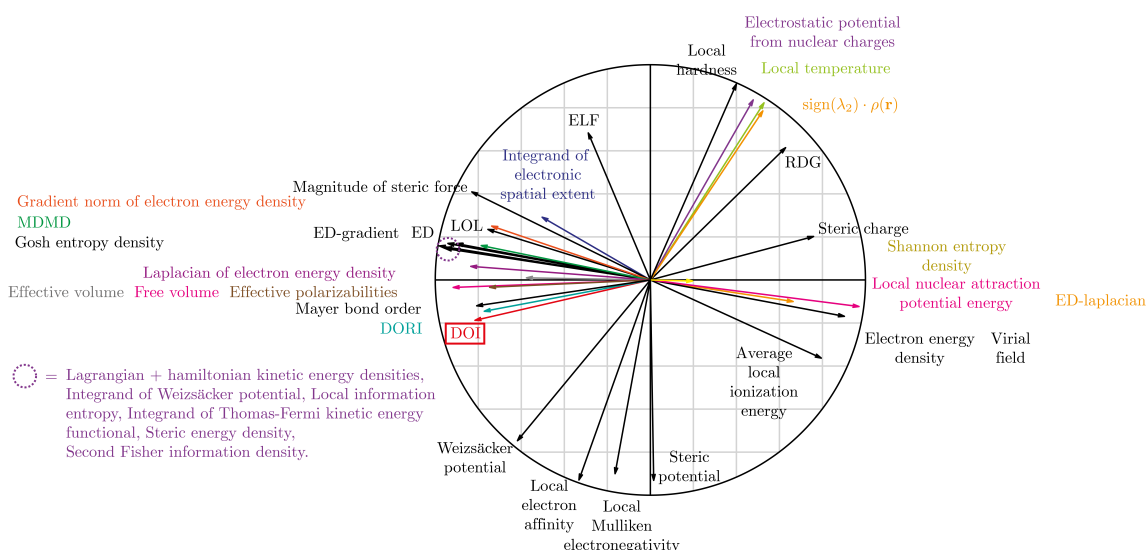


Fig. S7 PCA correlation circle of 38 space functions integrated using the Hirshfeld-I partition of 77 atoms. In addition, atomic valence has also been used in the PCA (calculated as the sum of the Mayer bond orders).

Comparison between DOI and other properties is meaningful as long as the length and orientation of the arrows are similar. Actually, the arrows are in the plane of the circle where the abscissa and the ordinate represent the two optimal components for which the ensemble of variables can be projected onto. Thus, in this case, angle between the different variables can be linked to the correlation coefficient: the more this angle is close to 0°, the more correlated the variables; the more this angle is close to 180°, the more the variables are anti-correlated ; an angle of 90° means a non-correlation between two variables. The correlation circle helped in deciphering the real space functions closest to DOI. Herewith, the following figure summarizing the determination coefficient between DOI and others variables as well as the linear regression between the closest one to DOI determined by PCA.

Even though a relatively large determination coefficient is found in the case of the effective volume, free volume, effective polarizability and atomic valence, none proper correlation could be found with these atomic-integrated functions. Actually, the plots of the residuals versus the considered predictors (see below) reveal a non-random pattern around 0.0 for hydrogen atoms (the corresponding residuals depart from 0 in some systematic manner for hydrogen atoms, being dominantly negative) indicating an improper fit despite a high R^2 value.

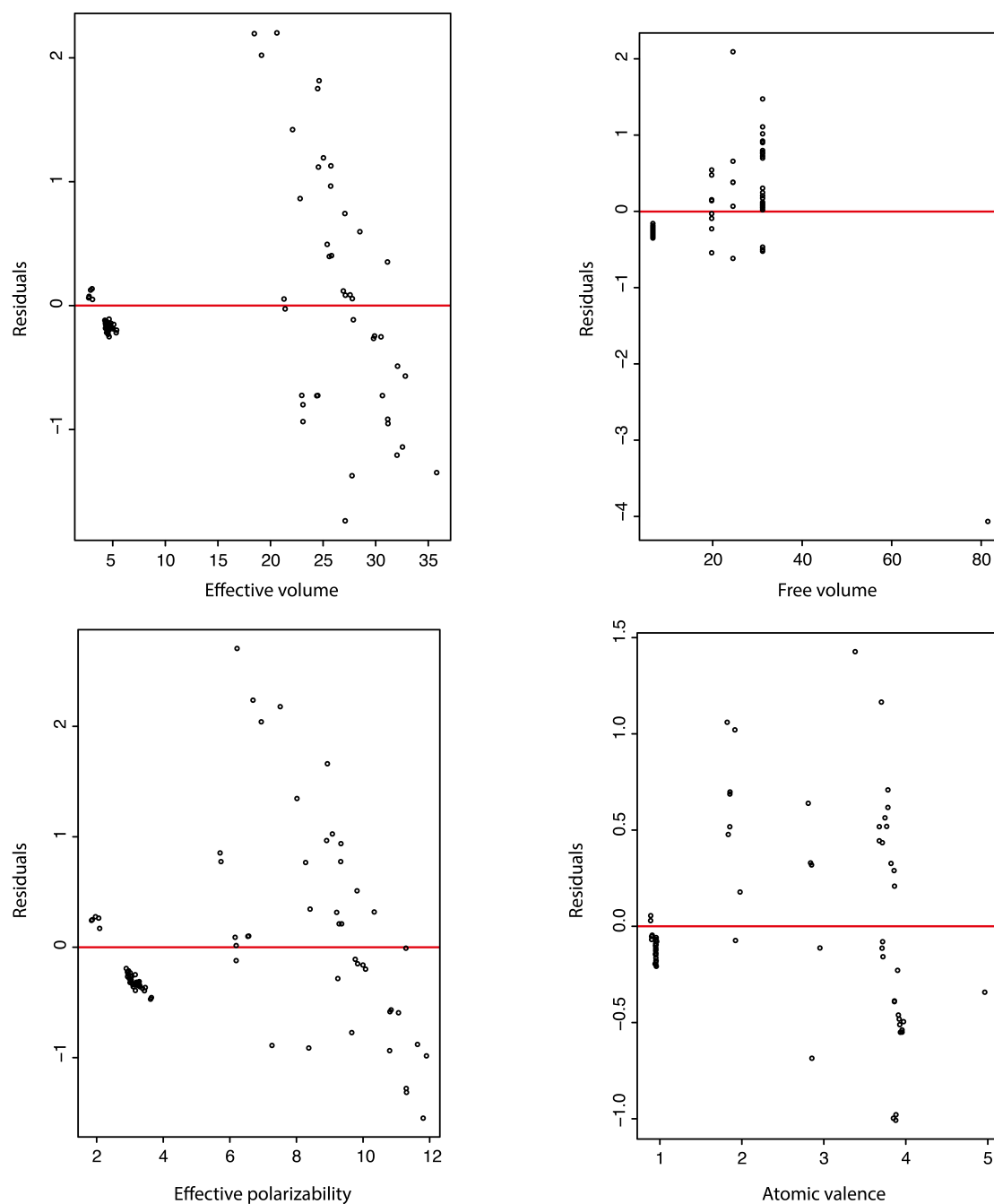


Fig. S9 Residuals versus the examined descriptor for the effective volume, free volume, effective polarizability and atomic valence of the Remdesivir molecule ($C_{27}H_{35}N_6O_8P$).

Determination coefficients of DOI value of non-hydrogen atoms versus real space functions are presented below:

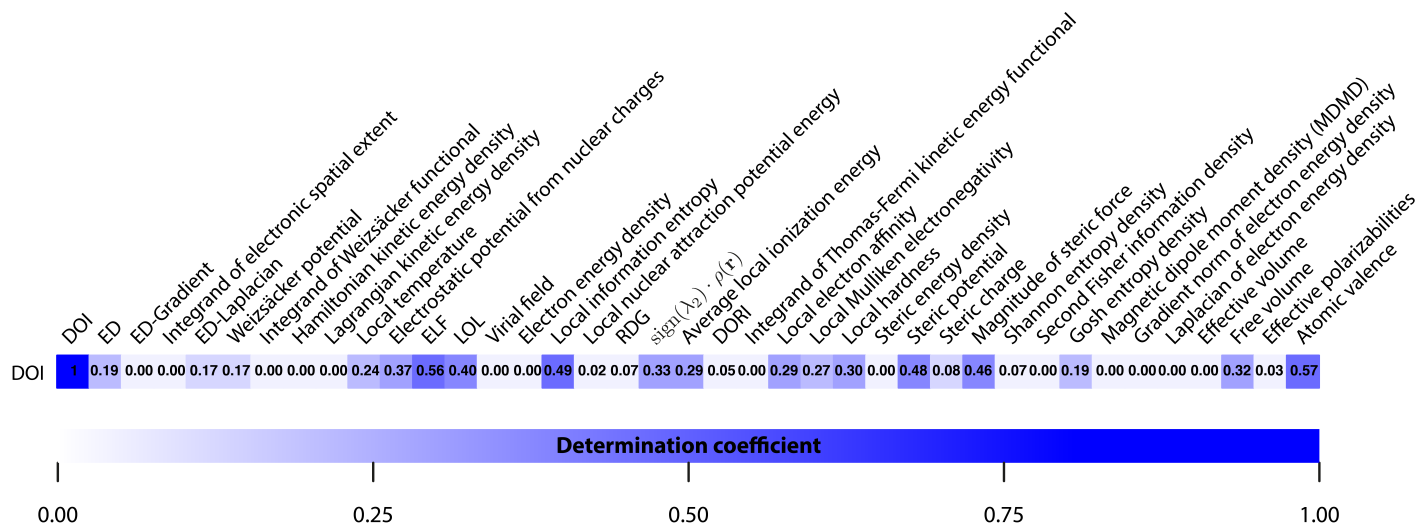
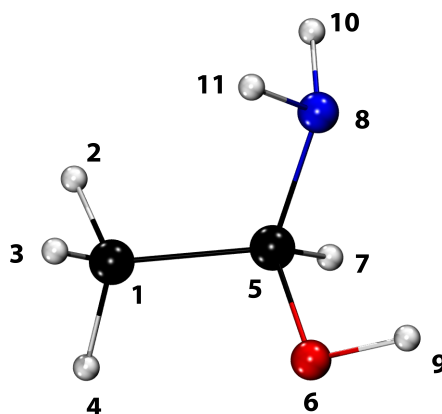


Fig. S10 Determination coefficients between the considered 38 real space functions and DOI for the non-hydrogen atoms of Remdesivir.

S8 Grid increment influence on atomic DOI

Table S6 Influence of the grid step size ("INCREMENTS" option in IGMPlot) on the atomic DOI value (Δg_i) for the atoms of CH3CH(OH)(NH2). IGM calculations have been performed on the M06-2X/6-31G** optimized geometry.

Grid step size (in Å)	0.01	0.025	0.05	0.1	0.25
C1	3.34	3.34	3.34	3.34	3.36
H2	0.90	0.90	0.90	0.90	0.91
H3	1.01	1.01	1.01	1.01	1.03
H4	0.80	0.80	0.80	0.80	0.80
C5	5.13	5.13	5.13	5.13	5.12
O6	2.72	2.72	2.72	2.72	2.72
H7	0.96	0.96	0.96	0.97	0.95
N8	3.16	3.16	3.16	3.15	3.14
H9	1.16	1.16	1.16	1.16	1.17
H10	1.00	1.00	1.00	1.00	0.98
H11	1.10	1.10	1.10	1.09	1.09



S9 Influence of the QM method on atomic DOI

Table S7 Influence of the QM method on the atomic DOI (a.u.) for selected radicals, using the 6-31G** basis set. IGM calculations have been performed on the M06-2X/6-31G** geometry. Mean, Standard Deviation (SD) and Relative SD(%) are reported as well.

	Method	HF	MP2	MP4(SDQ)	CCSD	M06-2X	B3LYP	Mean	SD	RSD(%)
CH ₃	C1	2.23	2.21	2.20	2.20	2.21	2.24	2.22	0.02	0.74
	H2	0.84	0.84	0.83	0.83	0.84	0.85	0.84	0.01	0.90
	H3	0.88	0.86	0.86	0.86	0.86	0.88	0.87	0.01	1.19
	H4	0.85	0.84	0.83	0.83	0.84	0.86	0.84	0.01	1.39
OH	O/H	0.93	0.93	0.93	0.93	0.95	0.93	0.93	0.008	0.87
HO ₂	H	0.93	0.93	0.93	0.93	0.94	0.97	0.94	0.02	1.71
	O1	2.71	2.70	2.68	2.67	2.78	2.80	2.72	0.05	1.98
	O2	1.95	1.93	1.91	1.90	2.00	1.99	1.95	0.04	2.12
CN	C/N	2.25	2.58	2.46	2.26	2.41	2.39	2.39	0.12	5.22

S10 Influence of the basis set on atomic DOIs

Table S8 Influence of the basis set on the atomic DOI value (Δg_i) for the atoms of CH₃CH(OH)(NH₂). Basis sets avdz, avtz, avqz, mavtz, jnvtz, jltz stand for aug-cc-pVDZ, aug-cc-pVTZ, aug-cc-pVQZ, may-cc-pVTZ, jun-cc-pVTZ, and jul-cc-pVTZ, respectively. IGM calculations have been performed on the M06-2X/6-31G** geometry to avoid any geometrical bias. Mean, Standard Deviation (SD) and Relative SD (RSD1) have been calculated by removing the outlying avdz result, not reflecting the general trend in the series. To compare with, RSD2 has been calculated by including avdz values.

Basis set	C1	H2	H3	H4	C5	O6	H7	N8	H9	H10	H11
6-31G	3.27	0.88	0.87	0.85	4.68	2.32	0.84	3.02	0.93	0.93	0.93
6-31G**	3.35	0.91	0.90	0.90	4.67	2.36	0.89	3.10	1.00	0.98	0.98
6-31++G**	3.41	0.89	0.88	0.88	4.71	2.40	0.89	3.08	1.03	0.96	0.96
6-311G**	3.22	0.88	0.88	0.88	4.62	2.33	0.85	3.00	1.02	0.96	0.97
6-311++G**	3.31	0.89	0.88	0.87	4.74	2.37	0.86	3.01	1.05	0.94	0.94
def2SVP	3.22	0.93	0.93	0.93	4.44	2.28	0.91	3.02	1.03	1.03	1.05
def2TZVP	3.30	0.89	0.88	0.88	4.45	2.30	0.88	2.95	0.97	0.94	0.95
def2QZVP	3.37	0.89	0.90	0.89	4.41	2.26	0.90	3.08	1.04	0.95	0.98
avdz	3.51	1.38	1.33	1.34	5.18	2.58	1.32	3.25	1.19	1.20	1.19
avtz	3.26	0.81	0.85	0.83	4.56	2.52	0.88	3.26	1.24	1.16	1.18
avqz	3.70	0.79	0.85	0.77	4.67	2.23	0.89	3.12	1.04	0.93	0.97
matz	3.25	0.90	0.91	0.90	4.37	2.39	0.87	3.01	1.08	0.99	1.01
jntz	3.09	0.80	0.81	0.84	4.26	2.43	0.81	2.98	1.11	0.99	0.99
jltz	3.27	0.84	0.85	0.87	4.42	2.42	0.82	3.05	1.11	1.03	1.03
pvdz	3.15	0.94	0.94	0.94	4.42	2.24	0.93	2.97	1.02	1.04	1.05
pvtz	3.31	0.93	0.92	0.92	4.37	2.29	0.89	3.03	1.03	1.00	1.00
pvqz	3.32	0.88	0.87	0.90	4.32	2.20	0.90	3.06	0.97	0.95	0.97
mean	3.30	0.88	0.88	0.88	4.51	2.33	0.88	3.05	1.04	0.99	1.00
SD	0.13	0.05	0.03	0.04	0.15	0.09	0.03	0.07	0.07	0.06	0.06
RSD1(%)	4.03	5.20	3.83	4.76	3.44	3.67	3.71	2.43	6.83	5.96	6.04
RSD2(%)	4.18	14.27	12.47	13.16	4.88	4.35	12.45	2.85	7.40	7.71	7.41

Table S9 Influence of the basis set on the atomic DOI value (Δg_i) for the atoms of methyl radical. Basis sets avdz, avtz, avqz, mavtz, jnvtz, jlvtz stand for aug-cc-pVDZ, aug-cc-pVTZ, aug-cc-pVQZ, may-cc-pVTZ, jun-cc-pVTZ, and jul-cc-pVTZ, respectively. IGM calculations have been performed on the M06-2X/6-31G** geometry to avoid any geometrical bias. Mean, Standard Deviation (SD) and Relative SD (RSD1) have been calculated by removing the outlying avdz result, not reflecting the general trend in the series. To compare with, RSD2 has been calculated by including avdz values.

Basis set	C	H	H	H
6-31G	2.13	0.81	0.81	0.81
6-31G**	2.21	0.84	0.86	0.84
6-31++G**	2.18	0.82	0.85	0.82
6-311G**	2.12	0.81	0.83	0.81
6-311++G**	2.12	0.81	0.84	0.81
def2SVP	2.17	0.84	0.87	0.84
def2TZVP	2.16	0.82	0.84	0.82
def2QZVP	2.14	0.79	0.82	0.79
avdz	2.52	1.23	1.22	1.22
avtz	2.14	0.74	0.77	0.75
avqz	2.07	0.71	0.75	0.70
matz	2.27	0.86	0.87	0.87
jntz	2.17	0.80	0.82	0.82
jlz	2.16	0.79	0.81	0.81
pvdz	2.14	0.84	0.87	0.85
pvtz	2.27	0.86	0.87	0.87
pvqz	2.08	0.77	0.79	0.78
mean	2.16	0.81	0.83	0.81
SD	0.06	0.04	0.03	0.04
RSD1(%)	2.6	5.2	4.2	5.2
RSD2(%)	4.7	13.17	11.77	12.84

Table S10 Influence of the basis set on the atomic DOI value (Δg_i) for the atoms of hydroxyl radical. Basis sets avdz, avtz, avqz, mavtz, jnvtz, jlvtz stand for aug-cc-pVDZ, aug-cc-pVTZ, aug-cc-pVQZ, may-cc-pVTZ, jun-cc-pVTZ, and jul-cc-pVTZ, respectively. IGM calculations have been performed on the M06-2X/6-31G** geometry to avoid any geometrical bias. Mean, Standard Deviation (SD) and Relative SD (RSD1) have been calculated by removing the outlying avdz result, not reflecting the general trend in the series. To compare with, RSD2 has been calculated by including avdz values.

Basis set	O/H
6-31G	0.93
6-31G**	0.95
6-31++G**	0.97
6-311G**	0.97
6-311++G**	0.98
def2SVP	0.96
def2TZVP	0.90
def2QZVP	0.98
avdz	1.03
avtz	1.06
avqz	0.98
matz	1.00
jntz	1.01
jlz	1.02
pvdz	0.92
pvtz	0.94
pvqz	0.86
mean	0.96
SD	0.05
RSD1(%)	5.08
RSD2(%)	5.17

Table S11 Influence of the basis set on the atomic DOI value (Δg_i) for the atoms of peroxy radical H-O1-O2. Basis sets avdz, avtz, avqz, mavtz, jnvtz, jlvtz stand for aug-cc-pVDZ, aug-cc-pVTZ, aug-cc-pVQZ, may-cc-pVTZ, jun-cc-pVTZ, and jul-cc-pVTZ, respectively. IGM calculations have been performed on the M06-2X/6-31G** geometry to avoid any geometrical bias. Mean, Standard Deviation (SD) and Relative SD (RSD1) have been calculated by removing the outlying avdz result, not reflecting the general trend in the series. To compare with, RSD2 has been calculated by including avdz values.

Basis set	H	O1	O2
6-31G	0.88	2.63	1.85
6-31G**	0.94	2.78	2.00
6-31++G**	0.98	2.65	1.85
6-311G**	0.95	2.80	1.99
6-311++G**	0.98	2.69	1.88
def2SVP	0.96	2.77	1.97
def2TZVP	0.92	2.67	1.93
def2QZVP	0.99	2.67	1.87
avdz	1.04	3.04	2.23
avtz	1.06	2.87	2.04
avqz	0.99	2.51	1.78
matz	1.02	2.75	1.94
jntz	1.03	2.88	2.07
jlvtz	0.99	2.84	1.96
pvdz	0.94	2.70	1.93
pvtz	0.95	2.69	1.92
pvqz	0.92	2.57	1.83
mean	0.97	2.72	1.93
SD	0.05	0.10	0.08
RSD1(%)	5.16	3.83	4.23
RSD2(%)	5.26	4.64	5.55

Table S12 Influence of the basis set on the atomic DOI value (Δg_i) for the atoms of cyano radical. Basis sets avdz, avtz, avqz, mavtz, jnvtz, jlvtz stand for aug-cc-pVDZ, aug-cc-pVTZ, aug-cc-pVQZ, may-cc-pVTZ, jun-cc-pVTZ, and jul-cc-pVTZ, respectively. IGM calculations have been performed on the M06-2X/6-31G** geometry to avoid any geometrical bias. Mean, Standard Deviation (SD) and Relative SD (RSD1) have been calculated by removing the outlying avdz result, not reflecting the general trend in the series. To compare with, RSD2 has been calculated by including avdz values.

Basis set	C/N
6-31G	2.38
6-31G**	2.41
6-31++G**	2.47
6-311G**	2.32
6-311++G**	2.42
def2SVP	2.34
def2TZVP	2.32
def2QZVP	2.21
avdz	2.51
avtz	2.56
avqz	2.26
matz	2.29
jntz	2.45
jlvtz	2.56
pvdz	2.26
pvtz	2.19
pvqz	2.15
mean	2.35
SD	0.12
RSD1(%)	5.24
RSD2(%)	5.34

S11 Influence of the grid step on the DOI, DOI first derivative and DOI second derivative along the H_2+H reaction path

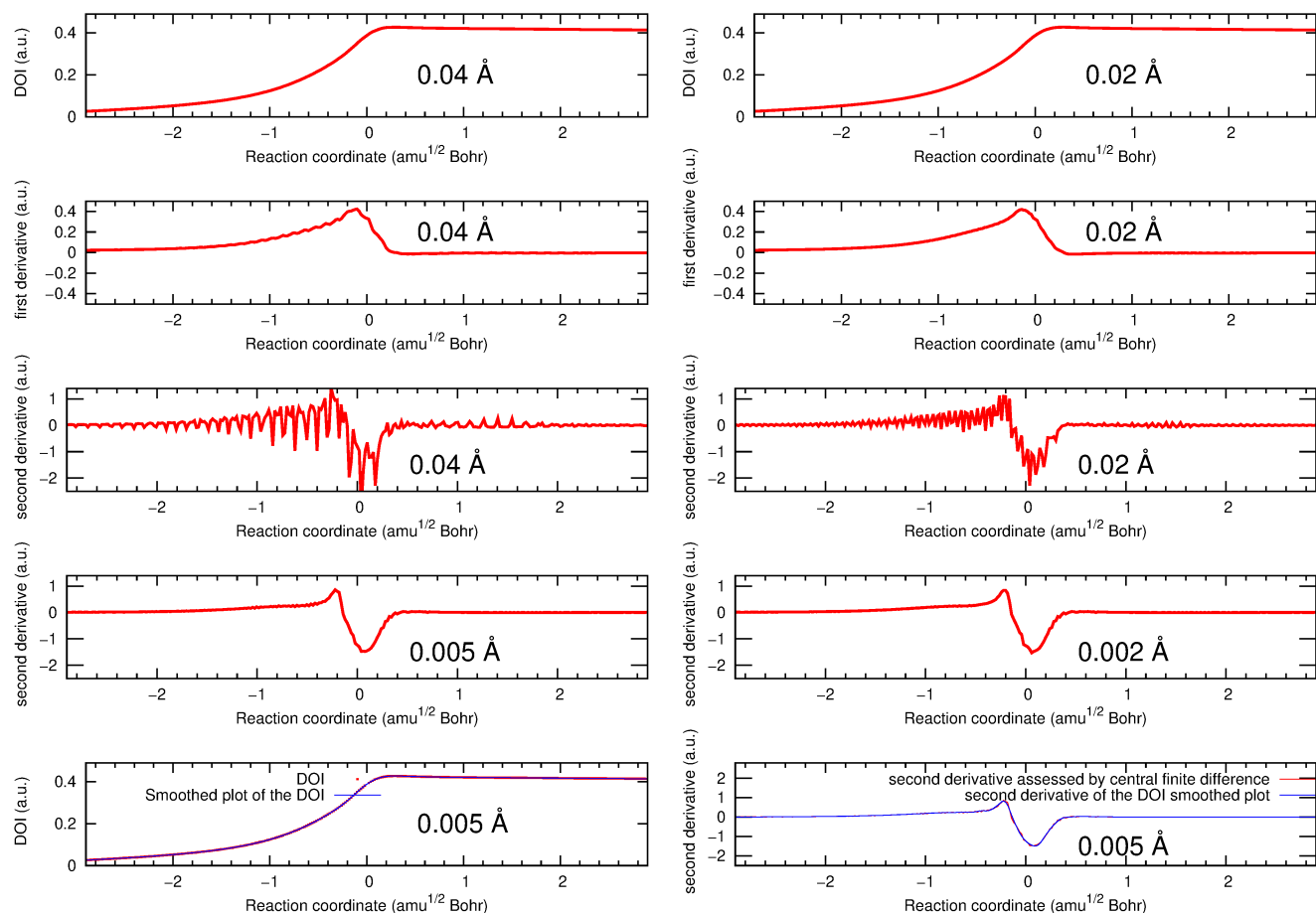


Fig. S11 DOI, DOI first derivative, and DOI second derivative along the H_2+H reaction path for the incoming radical atom H^3 . Row 1: DOI obtained with two grid increments 0.04 and 0.02 Å; Row 2: DOI first derivative obtained with two grid increments 0.04 and 0.02 Å; Rows 3 and 4: DOI second derivative obtained with four grid increments 0.04, 0.02, 0.005 and 0.002 Å; Row 5 left: DOI obtained with grid increment 0.005 Å and the corresponding smoothed plot; Row 5 right: DOI second derivative calculated by a central finite difference from the DOI obtained with grid increment 0.005 Å compared with the DOI second derivative obtained from the DOI smoothed plot.

S12 DOI: an instrument to probe the electronic structure

In complement with atomic partial charges, the atomic DOIs can for instance be employed to probe pure electronic effects upon oxidation of a molecule. For this purpose, we selected the prototypical molecule reported on the following figure. Upon oxidation, this triazolone is known to form a stable radical cation with altered photophysical properties (electrofluorochromism)[1].

First, the singlet ground state electronic structure was determined at the DFT(wB97XD)/Def2TZVP level of theory. Next, the oxidised state (removing an electron to the system, leading to the cation doublet state) was addressed at the same level of theory and using the same geometry as the singlet state. The two resulting wave functions (two wfx files, for the singlet and doublet states) were used to compute the NBO atomic partial charges and atomic DOIs. Next, the NBO atomic charge change and the DOI change upon oxidation for each atom were calculated and reported in color in the following figure. It allows an intuitive representation of the electronic modification occurring after the oxidation process of this molecule in terms of electron distribution and of the resulting degree of attachment.

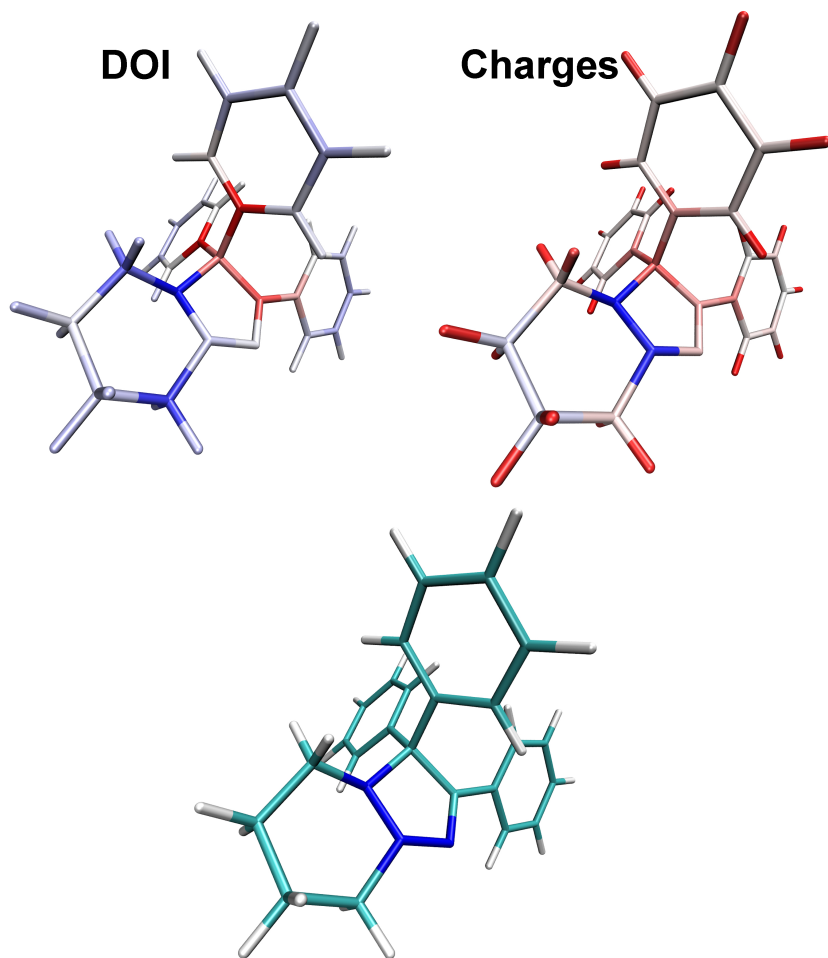


Fig. S12 Substituted triazolone; left: the atomic DOIs change upon oxidation ($-1 e^-$) is reported according to a BWR color scale in the range $[-0.11:+0.10]$ (a.u.); right: the NBO atomic partial charges change upon oxidation ($-1 e^-$) is reported according to a RWB color scale in the range $[-0.12:+0.42]$ (e^-); bottom: the molecular structure.

As can be seen, the oxidation process (without geometry relaxation at this stage) mainly lowers the degree of attachment of one nitrogen atom at the ring junction and two carbons (in blue color). In return, the oxidation increases the degree of attachment of the sp^3 carbon and its three sp^2 carbon neighbours. On the other hand, the NBO atomic charge analysis

discloses the increase of the partial charges of the two nitrogen atoms at the ring junction while it emphasises pronounced changes altering the hydrogen atoms (their charge decreases upon oxidation). For the two nitrogen atoms at the ring junction, the sp^3 carbon and its three sp^2 carbon neighbours, the net-electron loss or gain revealed by the NBO analysis is in line with the attachment loss or gain, respectively, detected by the DOI analysis. But, differences between the two analyses are observed for other atoms, mainly for the hydrogen atoms. A complete study would require to (1) investigate the geometrical change occurring after the geometry relaxation triggered by the oxidation (2) assess the subsequent electron reorganisation of the radical cation by means of the DOI or NBO charge changes after geometry relaxation (3) investigate a link between atoms pointed out by the DOI analysis and the atoms involved in the observed fluorescence. But this is beyond the scope of our study.

[1] Abdusalom A. Suleymanov, Albert Ruggi, Ophélie Marie Planes, Anne-Sophie Chauvin, Rosario Scopelliti, Farzaneh Fadaei Tirani, Andrzej Sienkiewicz, Alberto Fabrizio, Clémence Corminboeuf, and Kay Severin, *Chem. Eur. J.* 2019, 25, 6718 – 6721.