

Supporting Information

Influence of First and Second Coordination Environment on Structural Fe(II) Sites in MIL-101 for C-H Bond Activation in Methane

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S1. Additional data on A and AB

In Table S1 and Table S5, electronic and geometrical parameters for the catalysts in their reduced (**A**) and active form (**AB**) are reported for comparison. **AB** corresponds to the structure in the intermediate **B** with the removal of the N₂ molecule. For the clusters **AB**, their catalytic activity was evaluated as their hydrogen atom affinity of the oxoferryl defined as:¹

$$E_H = E(M_m O_x H_{y+1}) - E(M_m O_x H_y) - \frac{1}{2} E(H_2O) + \frac{1}{4} E(O_2) \quad (1)$$

Table S1. Spin densities ρ and charges q on the divalent Fe and on the central oxygen in the node Oc and their distance $d(Fe-Oc)$ (in Å) for all the *meta-A* clusters as obtained at the UM06-L/def2-TZVP level in their ground spin state. Spin densities are expressed as the difference between the α and β electron densities.

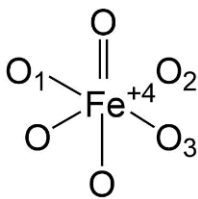
<i>meta-A</i>	2S + 1	$q(Fe)$	$q(Oc)$	$\rho(Fe)$	$\rho(Oc)$	$d(Fe-Oc)$
-H	15	0.86	-0.58	4.03	0.60	1.867
-NH ₂	15	0.84	-0.58	3.99	0.60	1.903
-OH	15	0.86	-0.58	4.01	0.60	1.868
-Br	15	0.84	-0.58	3.98	0.60	1.904
-F	15	0.86	-0.58	4.02	0.60	1.867
-COOH	15	0.87	-0.58	4.04	0.60	1.863
-CF ₃	15	0.86	-0.58	4.01	0.60	1.869
-SO ₃ H	15	0.88	-0.58	4.05	0.60	1.862
-NO ₂	15	0.84	-0.58	3.98	0.60	1.905

Table S2. Spin densities ρ and charges q on the divalent Fe and on the central oxygen in the node Oc and their distance $d(\text{Fe-Oc})$ (in Å) for all the **up-A** clusters as obtained at the UM06-L/def2-TZVP level in their ground spin state. Spin densities are expressed as the difference between the α and β electron densities.

up-A	$2S+1$	$q(\text{Fe})$	$q(\text{Oc})$	$\rho(\text{Fe})$	$\rho(\text{Oc})$	$d(\text{Fe-Oc})$
-H	15	0.86	-0.58	4.03	0.60	1.867
-NH ₂	15	0.85	-0.58	4.00	0.60	1.867
-OH	15	0.85	-0.58	4.00	0.60	1.867
-Br	15	0.84	-0.58	3.99	0.60	1.903
-F	15	0.84	-0.58	3.99	0.60	1.905
-COOH	15	0.87	-0.58	4.04	0.60	1.864
-CF ₃	15	0.84	-0.58	3.99	0.60	1.906
-SO ₃ H	15	0.85	-0.58	4.00	0.60	1.904
-NO ₂	15	0.84	-0.58	3.99	0.60	1.907

Table S3. Spin densities ρ and charges q on the divalent Fe and on the central oxygen in the node Oc and their distance $d(\text{Fe-Oc})$ (in Å) for all the **hb-A** clusters as obtained at the UM06-L/def2-TZVP level in their ground spin state. Spin densities are expressed as the difference between the α and β electron densities.

hb-A	$2S+1$	$q(\text{Fe})$	$q(\text{Oc})$	$\rho(\text{Fe})$	$\rho(\text{Oc})$	$d(\text{Fe-Oc})$
-SO ₂ NH ₂	15	0.86	-0.58	4.01	0.60	1.873
-CH ₂ NH ₂	15	0.84	-0.58	3.99	0.60	1.901
-CH ₂ CH ₂ NH ₂	15	0.85	-0.57	4.09	0.58	1.911
-CONH ₂	15	0.86	-0.58	4.02	0.60	1.868
-CONHOH	15	0.86	-0.58	4.02	0.60	1.872
-NH ₂	15	0.85	-0.58	4.01	0.60	1.867
-NHSO ₃ H	15	0.86	-0.58	4.01	0.60	1.868
-NHCH ₃	15	0.85	-0.58	4.00	0.60	1.866
-NHNH ₂	15	0.85	-0.58	4.00	0.60	1.867
-NHOH	15	0.85	-0.58	4.01	0.60	1.867
-NHCOOH	15	0.84	-0.58	4.00	0.60	1.863
-NHCOCH ₂ NH ₂	15	0.83	-0.58	4.02	0.60	1.885
-NHCOCOOH	15	0.86	-0.58	4.02	0.60	1.878
-NHCONH ₂	15	0.84	-0.58	4.00	0.60	1.864
-NHCOSO ₃ H	15	0.84	-0.58	4.00	0.60	1.874



Scheme S1. Torsional angle $\theta(\text{Fe-O}_{\text{axial}})$ in the tables is defined as $\theta(\text{Fe-O}_1\text{-O}_2\text{-O}_3)$ as labeled here.

Table S4. Spin densities ρ and charges q on the tetravalent Fe, on the oxygen of the ferryl group O_{oxo} and on the central oxygen of the node Oc for all the *meta-AB* clusters as obtained at the UM06-L/def2-TZVP level in their ground spin state. The distance of the tetravalent iron center from them are also reported, $d(\text{Fe-O}_{\text{oxo}})$ and $d(\text{Fe-Oc})$ (in Å). Torsional angle $\theta(\text{Fe-O}_{\text{axial}})$ as defined in Scheme S1 is reported in degrees. Spin densities are expressed as the difference between the α and β electron densities. The hydrogen affinity E_{H} of the clusters (in kJ mol^{-1}) expressed as in Eq. 1 is also reported along with that of the methyl radical.

<i>meta-AB</i>	$2S+1$	$q(\text{Fe})$	$q(\text{O}_{\text{oxo}})$	$\rho(\text{Fe})$	$\rho(\text{O}_{\text{oxo}})$	$d(\text{Fe-Oc})$	$d(\text{Fe-O}_{\text{oxo}})$	$\theta(\text{Fe-O}_{\text{axial}})$	E_{H}
-H	16	0.88	-0.40	3.18	0.56	2.019	1.617	2.5	-81.8
-NH ₂	16	0.88	-0.40	3.18	0.56	2.011	1.617	3.2	-83.5
-OH	16	0.88	-0.40	3.18	0.56	2.011	1.617	2.7	-81.8
-Br	16	0.88	-0.39	3.18	0.57	2.014	1.617	2.8	-82.3
-F	16	0.88	-0.39	3.18	0.56	2.015	1.617	2.5	-82.3
-COOH	16	0.88	-0.40	3.18	0.55	2.028	1.618	2.8	-81.2
-CF ₃	16	0.88	-0.39	3.18	0.57	2.015	1.616	2.7	-82.4
-SO ₃ H	16	0.88	-0.39	3.18	0.55	2.032	1.617	3.1	-81.9
-NO ₂	16	0.88	-0.39	3.18	0.57	2.015	1.616	2.9	-82.2
CH ₃ •									-135.0

Table S5. Spin densities ρ and charges q on the tetravalent Fe, on the oxygen of the ferryl group O_{oxo} and on the central oxygen of the node Oc for all the **up-AB** clusters as obtained at the UM06-L/def2-TZVP level in their ground spin state. The distance of the tetravalent iron center from them are also reported, $d(Fe-O_{oxo})$ and $d(Fe-Oc)$ (in Å). $d(HB)$ is the hydrogen bond length involving the O_{oxo} (in Å). Torsional angle $\theta(Fe-O_{axial})$ as defined in Scheme S1 is reported in degrees. Spin densities are expressed as the difference between the α and β electron densities. The hydrogen affinity E_H of the clusters (in kJ mol^{-1}) expressed as in Eq. 1 is also reported.

up-AB	2S + 1	$q(Fe)$	$q(O_{oxo})$	$\rho(Fe)$	$\rho(O_{oxo})$	$d(Fe-Oc)$	$d(Fe-O_{oxo})$	$\theta(Fe-O_{axial})$	$d(HB)$	E_H
-H	16	0.88	-0.40	3.18	0.56	2.019	1.617	2.5	3.921	-81.8
-NH ₂	16	0.88	-0.41	3.18	0.54	1.999	1.622	2.9	2.758	-82.9
-OH	16	0.88	-0.40	3.18	0.56	2.003	1.619	2.2	2.928	-81.0
-Br	16	0.88	-0.39	3.17	0.56	2.013	1.617	3.3	—	-87.4
-F	16	0.88	-0.39	3.18	0.57	2.016	1.616	2.8	—	-87.2
-COOH	16	0.89	-0.40	3.19	0.53	2.019	1.626	4.8	2.273	-96.3
-CF ₃	16	0.88	-0.38	3.17	0.57	2.017	1.615	4.2	—	-89.6
-SO ₃ H	16	0.90	-0.40	3.22	0.48	2.009	1.630	3.1	1.842	-91.3
-NO ₂	16	0.88	-0.38	3.17	0.57	2.020	1.615	2.8	—	-94.5

Table S6. Spin densities ρ and charges q on the tetravalent Fe, on the oxygen of the ferryl group O_{oxo} and on the central oxygen of the node Oc for all the **hb-AB** clusters as obtained at the UM06-L/def2-TZVP level in their ground spin state. The distance of the tetravalent iron center from them are also reported, $d(\text{Fe-O}_{\text{oxo}})$ and $d(\text{Fe-Oc})$ (in Å). $d(\text{HB})$ is the hydrogen bond length involving the Ooxo (in Å). Torsional angle $\theta(\text{Fe-O}_{\text{axial}})$ as defined in Scheme S1 is reported in degrees. Spin densities are expressed as the difference between the α and β electron densities. The hydrogen affinity E_{H} of the clusters (in kJ mol⁻¹) expressed as in Eq. 1 is also reported.

hb-AB	$2S+1$	$q(\text{Fe})$	$q(\text{Ooxo})$	$\rho(\text{Fe})$	$\rho(\text{O}_{\text{oxo}})$	$d(\text{Fe-Oc})$	$d(\text{Fe-O}_{\text{oxo}})$	$\theta(\text{Fe-O}_{\text{axial}})$	$d(\text{HB})$	E_{H}
-SO ₂ NH ₂	16	0.89	-0.54	3.20	0.55	2.002	1.626	2.5	1.968	-89.1
-CH ₂ NH ₂	16	0.88	0.55	3.18	-0.39	2.012	1.620	2.6	2.472	-89.4
-CH ₂ CH ₂ NH ₂	16	0.89	-0.39	3.19	0.53	2.007	1.624	3.2	2.092	-85.7
-CONH ₂	16	0.88	-0.41	3.19	0.54	2.010	1.623	3.0	2.663	-85.8
-CONHOH	16	0.89	-0.39	3.21	0.51	2.000	1.630	1.8	1.833	-98.6
-NH ₂	16	0.88	-0.41	3.18	0.54	2.005	1.622	2.3	2.742	-82.1
-NHSO ₃ H	16	0.89	-0.40	3.22	0.49	1.990	1.636	2.4	1.740	-104.2
-NHCH ₃	16	0.88	-0.42	3.18	0.54	2.002	1.623	2.4	2.738	-82.3
-NHNH ₂	16	0.87	-0.42	3.18	0.53	2.001	1.624	2.3	2.718	-82.2
-NHOH	16	0.88	-0.41	3.18	0.54	2.005	1.621	2.2	2.753	-82.8
-NHCOOH	16	0.89	-0.41	3.21	0.51	1.996	1.633	2.6	2.155	-98.4
-NHCOCH ₂ NH ₂	16	0.88	-0.40	3.18	0.54	1.994	1.621	1.4	2.282	-85.3
-NHCOCOOH	16	0.88	-0.54	3.18	0.56	2.013	1.617	2.9	2.878	-80.9
-NHCONH ₂	16	0.46	-0.41	3.20	0.52	1.997	1.630	2.7	2.220	-91.1
-NHCOSO ₃ H	16	0.90	-0.40	3.23	0.47	1.978	1.635	1.0	1.632	-103.4

S2. Additional data on TS1

In Table S7, electronic, geometrical and energetic parameters for the structures of **TS1** relevant for the discussion in the main text are reported.

In the Table S7, Y_{TS1} ($Y = E, H$, and G) are defined as:

$$\Delta Y_{\text{TS1}} = Y_{\text{TS1}} - Y_{\text{AO}} \quad (2)$$

Table S7. Spin densities ρ on the Fe in interaction with N_2O and on the N_2O molecule for all the *meta*-**TS1** structures as obtained at the UM06-L/def2-TZVP level in their ground spin state. Spin densities are expressed as the difference between the α and β electron densities. Relevant geometrical parameters are also reported as the distance of the reacting iron from the O of the N_2O molecule $d(\text{Fe}-\text{ON}_2\text{O})$ and from the central O of the *meta*-cluster $d(\text{Fe}-\text{O}_c)$ and the N-N and N-O distance in N_2O (in Å). The energy ΔE_{TS1}^c , enthalpy $\Delta H_{\text{TS1}}^{0c}$ and Gibbs free energy $\Delta G_{\text{TS1}}^{0c}$ barriers defined as in Eq. 2 are also reported (in kJ mol^{-1}). The imaginary mode associated with the reaction coordinate is shown in cm^{-1} ($\tilde{\nu}_{\text{im}}$). For reference the calculated geometrical parameters of N_2O in the gas phase are: $d(\text{N}-\text{ON}_2\text{O}) = 1.175$ Å and $d(\text{N}-\text{N}) = 1.128$ Å.

<i>meta</i> - TS1	$2S+1$	$\rho(\text{Fe})$	$\rho(\text{N}_2\text{O})$	$d(\text{Fe}-\text{ON}_2\text{O})$	$d(\text{N}-\text{ON}_2\text{O})$	$d(\text{N}-\text{N})$	$d(\text{Fe}-\text{O}_c)$	ΔE_{TS1}^c	$\Delta H_{\text{TS1}}^{0c}$	$\Delta G_{\text{TS1}}^{0c}$	$\tilde{\nu}_{\text{im}}$
-H	15	4.01	-0.43	1.849	1.520	1.129	2.086	145.8	134.2	132.4	700i
-NH ₂	15	4.06	-0.52	1.866	1.525	1.143	2.084	147.0	135.7	138.8	650i
-OH	15	4.06	-0.50	1.860	1.510	1.131	2.079	148.7	137.4	136.5	664i
-Br	15	4.06	-0.50	1.861	1.515	1.129	2.089	148.3	137.0	135.1	655i
-F	15	4.04	-0.40	1.860	1.430	1.134	2.059	144.2	132.4	132.5	676i
-COOH	15	4.00	-0.41	1.857	1.530	1.127	2.094	148.7	136.8	137.7	720i
-CF ₃	15	4.01	-0.42	1.846	1.521	1.128	2.080	145.8	134.5	132.8	699i
-SO ₃ H	15	4.00	-0.40	1.855	1.533	1.126	2.097	151.4	139.5	140.1	731i
-NO ₂	15	4.00	-0.42	1.846	1.521	1.128	2.081	146.9	135.3	133.9	701i

Table S8. Spin densities ρ on the Fe in interaction with N₂O and on the N₂O molecule for all the **up-TS1** structures as obtained at the UM06-L/def2-TZVP level in their ground spin state. Spin densities are expressed as the difference between the α and β electron densities. Relevant geometrical parameters are also reported as the distance of the reacting iron from the O of the N₂O molecule $d(\text{Fe}-\text{O}_{\text{N}_2\text{O}})$ and from the central O of the **up**-cluster $d(\text{Fe}-\text{O}_c)$ and the N-N and N-O distance in N₂O (in Å). The energy ΔE_{TS1}^c , enthalpy $\Delta H_{\text{TS1}}^{\text{oc}}$ and Gibbs free energy $\Delta G_{\text{TS1}}^{\text{oc}}$ barriers defined as in Eq. 2 are also reported (in kJ mol⁻¹). The imaginary mode associated with the reaction coordinate is shown in cm⁻¹ ($\tilde{\nu}_{\text{im}}$). For reference the calculated geometrical parameters of N₂O in the gas phase are: $d(\text{N}-\text{O}_{\text{N}_2\text{O}}) = 1.175$ Å and $d(\text{N}-\text{N}) = 1.128$ Å.

up-TS1	$2S+1$	$\rho(\text{Fe})$	$\rho(\text{N}_2\text{O})$	$d(\text{Fe}-\text{O}_{\text{N}_2\text{O}})$	$d(\text{N}-\text{O}_{\text{N}_2\text{O}})$	$d(\text{N}-\text{N})$	$d(\text{Fe}-\text{O}_c)$	ΔE_{TS1}^c	$\Delta H_{\text{TS1}}^{\text{oc}}$	$\Delta G_{\text{TS1}}^{\text{oc}}$	$\tilde{\nu}_{\text{im}}$
-H	15	4.01	-0.43	1.848	1.521	1.128	2.086	146.0	134.5	132.9	698i
-NH ₂	15	4.06	-0.52	1.873	1.514	1.129	2.066	134.4	122.3	120.5	653i
-OH	15	4.05	-0.49	1.867	1.521	1.126	2.074	143.1	131.5	129.8	682i
-Br	15	4.00	-0.41	1.843	1.529	1.126	2.085	145.8	134.2	133.9	691i
-F	15	4.05	-0.48	1.857	1.525	1.126	2.094	150.0	138.4	136.0	690i
-COOH	15	4.02	-0.47	1.892	1.518	1.128	2.084	134.6	122.2	123.9	684i
-CF ₃	15	4.04	-0.45	1.850	1.531	1.124	2.094	153.2	142.2	140.7	711i
-SO ₃ H	15	4.03	-0.51	1.893	1.496	1.130	2.071	146.5	132.9	132.2	654i
-NO ₂	15	4.03	-0.43	1.851	1.535	1.122	2.096	156.1	144.9	143.8	728i

Table S9. Spin densities ρ on the Fe in interaction with N₂O and on the N₂O molecule for all the **up-TS1** structures as obtained at the UM06-L/def2-TZVP level in their ground spin state. Spin densities are expressed as the difference between the α and β electron densities. Relevant geometrical parameters are also reported as the distance of the reacting iron from the O of the N₂O molecule $d(\text{Fe-O}_{\text{N}_2\text{O}})$ and from the central O of the **hb**-cluster $d(\text{Fe-O}_c)$ and the N-N and N-O distance in N₂O (in Å). The energy ΔE_{TS1}^c , enthalpy $\Delta H_{\text{TS1}}^{\text{oc}}$ and Gibbs free energy $\Delta G_{\text{TS1}}^{\text{oc}}$ barriers defined as in Eq. 2 are also reported (in kJ mol⁻¹). The imaginary mode associated with the reaction coordinate is shown in cm⁻¹ ($\tilde{\nu}_{\text{im}}$). For reference the calculated geometrical parameters of N₂O in the gas phase are: $d(\text{N-O}_{\text{N}_2\text{O}}) = 1.175$ Å and $d(\text{N-N}) = 1.128$ Å.

hb-TS1	$2S+1$	$\rho(\text{Fe})$	$\rho(\text{N}_2\text{O})$	$d(\text{Fe-O}_{\text{N}_2\text{O}})$	$d(\text{N-O}_{\text{N}_2\text{O}})$	$d(\text{N-N})$	$d(\text{Fe-O}_c)$	$d(\text{HB})$	ΔE_{TS1}^c	$\Delta H_{\text{TS1}}^{\text{oc}}$	$\Delta G_{\text{TS1}}^{\text{oc}}$	$\tilde{\nu}_{\text{im}}$
-SO ₂ NH ₂	15	4.02	-0.46	1.880	1.508	1.129	2.057		148.4	134.7	132.3	677i
-CH ₂ NH ₂	15	4.05	-0.49	1.871	1.522	1.125	2.087	2.446	150.5	138.6	137.3	697i
-CH ₂ CH ₂ NH ₂	15	4.07	-0.53	1.883	1.500	1.131	2.082	2.106	152.6	139.6	138.9	635i
-CONH ₂	15	4.07	-0.53	1.882	1.502	1.131	2.087	2.472	144.4	135.0	128.0	626i
-CONHOH	15	4.01	-0.41	1.889	1.518	1.124	2.062	1.870	139.1	127.0	127.8	722i
-NH ₂	15	4.06	-0.52	1.874	1.513	1.129	2.075	2.663	137.6	125.8	124.1	652i
-NHSO ₃ H	15	4.05	-0.54	1.914	1.487	1.133	2.054	1.754	144.1	132.4	136.3	596i
-NHCH ₃	15	4.07	-0.54	1.883	1.511	1.130	2.070	2.683	136.2	124.9	124.2	645i
-NHNH ₂	15	4.07	-0.55	1.883	1.501	1.132	2.070	2.711	137.9	126.1	123.9	608i
-NHOH	15	4.01	-0.46	1.865	1.511	1.130	2.068	2.672	140.3	128.2	126.7	668i
-NHCOOH	15	4.04	-0.54	2.054	1.491	1.133	2.054	1.970	119.9	108.2	112.7	600i
-NHCOCH ₂ NH ₂	15	3.99	-0.40	1.867	1.517	1.126	2.061	2.416	139.2	127.9	129.6	723i
-NHCOCOOH	15	4.01	-0.43	1.849	1.520	1.128	2.083	2.901	160.6	148.7	145.4	698i
-NHCONH ₂	15	4.08	-0.55	1.904	1.491	1.132	2.064	2.150	129.0	117.4	118.1	615i
-NHCOSO ₃ H	15	4.04	-0.51	1.901	1.478	1.131	2.030	1.639	122.3	110.3	113.3	611i

S3. Additional data on TS2

In Table S11 electronic, geometrical and energetic parameters are reported for the structures of **TS2** in the methane cycle.

In the Table S11, Y_{TS2} ($Y = E, H$, and G) are defined as:

$$\Delta Y_{\text{TS2}} = Y_{\text{TS2}} - Y_{\text{C}} \quad (3)$$

Table S10. Spin densities ρ on the Fe(IV), on the O of the oxoferryl and on the C of the methane molecule for all the *meta*-**TS2** structures as obtained at the UM06-L/def2-TZVP level in their ground spin state. Spin densities are expressed as the difference between the α and β electron densities. Relevant geometrical parameters are also reported: the bond length of the oxoferryl group $d(\text{Fe-O}_{\text{oxo}})$, the bond length of the activated C-H bond $d(\text{C-H})$ and the distance between the O_{oxo} and the H atom in the activated C-H bond $d(\text{H-O}_{\text{oxo}})$ (in Å). The energy $\Delta E_{\text{TS2}}^{\text{c}}$, enthalpy $\Delta H_{\text{TS2}}^{\text{0c}}$ and Gibbs free energy $\Delta G_{\text{TS2}}^{\text{0c}}$ defined as in Eq. 3 are also reported (in kJ mol⁻¹). The imaginary mode associated with the reaction coordinate is shown in cm⁻¹ ($\tilde{\nu}_{\text{im}}$). For reference, the calculated C-H bond distance in the methane molecule in the gas phase is $d(\text{C-H}) = 1.086$ Å.

<i>meta</i> - TS2	2S+1	$\rho(\text{Fe})$	$\rho(\text{O}_{\text{oxo}})$	$\rho(\text{C})$	$d(\text{Fe-O}_{\text{oxo}})$	$d(\text{H-O}_{\text{oxo}})$	$d(\text{C-H})$	$\Delta E_{\text{TS2}}^{\text{c}}$	$\Delta H_{\text{TS2}}^{\text{0c}}$	$\Delta G_{\text{TS2}}^{\text{0c}}$	$\tilde{\nu}_{\text{im}}$
-H	15	3.98	0.09	-0.47	1.762	1.178	1.330	85.9	63.0	69.3	1824i
-NH ₂	15	3.99	0.09	-0.40	1.765	1.172	1.341	85.2	62.6	69.4	1774i
-OH	15	3.97	0.07	-0.36	1.761	1.177	1.295	84.7	62.7	69.7	1754i
-Br	15	4.01	0.08	-0.41	1.771	1.160	1.334	84.2	61.2	70.5	1635i
-F	15	3.99	0.08	-0.40	1.770	1.167	1.320	84.0	61.3	67.9	1690i
-COOH	15	4.00	0.02	-0.36	1.778	1.191	1.283	90.8	68.6	74.1	1758i
-CF ₃	15	3.97	0.10	-0.39	1.758	1.180	1.330	83.9	61.5	67.5	1825i
-SO ₃ H	15	4.00	0.03	-0.36	1.775	1.193	1.281	88.7	66.3	70.8	1744i
-NO ₂	15	3.97	0.11	-0.39	1.756	1.180	1.330	83.6	61.2	67.0	1817i

Table S11. Spin densities ρ on the Fe(IV), on the O of the oxoferryl and on the C of the methane molecule for all the **up-TS2** structures as obtained at the UM06-L/def2-TZVP level in their ground spin state. Spin densities are expressed as the difference between the α and β electron densities. Relevant geometrical parameters are also reported: the bond length of the oxoferryl group $d(\text{Fe-O}_{\text{oxo}})$, the bond length of the activated C-H bond $d(\text{C-H})$ and the distance between the O_{oxo} and the H atom in the activated C-H bond $d(\text{H-O}_{\text{oxo}})$ (in Å). $d(\text{HB})$ is the length of the hydrogen bond involving O_{oxo} (in Å). The energy $\Delta E_{\text{TS2}}^{\text{c}}$, enthalpy $\Delta H_{\text{TS2}}^{\text{0c}}$ and Gibbs free energy $\Delta G_{\text{TS2}}^{\text{0c}}$ defined as in Eq. 3 are also reported (in kJ mol⁻¹). The imaginary mode associated with the reaction coordinate is shown in cm⁻¹ ($\tilde{\nu}_{\text{im}}$). For reference, the calculated C-H bond distance in the methane molecule in the gas phase is $d(\text{C-H}) = 1.086$ Å.

up-TS2	2S + 1	$\rho(\text{Fe})$	$\rho(\text{O}_{\text{oxo}})$	$\rho(\text{C})$	$d(\text{Fe-O}_{\text{oxo}})$	$d(\text{H-O}_{\text{oxo}})$	$d(\text{C-H})$	$d(\text{HB})$	$\Delta E_{\text{TS2}}^{\text{c}}$	$\Delta H_{\text{TS2}}^{\text{0c}}$	$\Delta G_{\text{TS2}}^{\text{0c}}$	$\tilde{\nu}_{\text{im}}$
-H	15	3.97	0.07	-0.36	1.762	1.178	1.295	3.930	86.0	63.3	69.9	1748i
-NH ₂	15	4.02	-0.02	-0.36	1.788	1.196	1.280	2.706	85.2	63.4	69.6	1783i
-OH	15	3.93	0.13	-0.38	1.748	1.163	1.319	2.947	83.7	62.0	70.2	1705i
-Br	15	3.99	0.04	-0.35	1.770	1.199	1.276	3.502	80.8	59.1	66.3	1722i
-F	15	3.99	0.04	-0.35	1.769	1.196	1.278	3.434	80.5	58.3	64.0	1715i
-COOH	15	4.02	-0.05	-0.35	1.801	1.217	1.264	1.923	72.8	50.6	60.9	1647i
-CF ₃	15	3.94	0.12	-0.36	1.748	1.180	1.297	3.042	76.9	54.5	60.0	1727i
-SO ₃ H	15	4.01	-0.04	-0.35	1.797	1.206	1.272	1.703	73.9	51.4	56.4	1704i
-NO ₂	15	3.94	0.11	-0.35	1.748	1.196	1.281	3.563	72.3	49.9	55.0	1671i

Table S12. Spin densities ρ on the Fe(IV), on the O of the oxoferryl and on the C of the methane molecule for all the **hb-TS2** structures as obtained at the UM06-L/def2-TZVP level in their ground spin state. Spin densities are expressed as the difference between the α and β electron densities. Relevant geometrical parameters are also reported: the bond length of the oxoferryl group $d(\text{Fe-O}_{\text{oxo}})$, the bond length of the activated C-H bond $d(\text{C-H})$ and the distance between the O_{oxo} and the H atom in the activated C-H bond $d(\text{H-O}_{\text{oxo}})$ (in Å). $d(\text{HB})$ is the length of the hydrogen bond involving O_{oxo} (in Å). The energy $\Delta E_{\text{TS2}}^{\text{c}}$, enthalpy $\Delta H_{\text{TS2}}^{\text{0c}}$ and Gibbs free energy $\Delta G_{\text{TS2}}^{\text{0c}}$ defined as in Eq. 3 are also reported (in kJ mol⁻¹). The imaginary mode associated with the reaction coordinate is shown in cm⁻¹ ($\tilde{\nu}_{\text{im}}$). For reference, the calculated C-H bond distance in the methane molecule in the gas phase is $d(\text{C-H}) = 1.086$ Å.

hb-TS2	2S+1	$\rho(\text{Fe})$	$\rho(\text{O}_{\text{oxo}})$	$\rho(\text{C})$	$d(\text{Fe-O}_{\text{oxo}})$	$d(\text{H-O}_{\text{oxo}})$	$d(\text{C-H})$	$d(\text{HB})$	$\Delta E_{\text{TS2}}^{\text{c}}$	$\Delta H_{\text{TS2}}^{\text{0c}}$	$\Delta G_{\text{TS2}}^{\text{0c}}$	$\tilde{\nu}_{\text{im}}$
-SO ₂ NH ₂	15	4.00	-0.01	-0.35	1.783	1.208	1.274	1.882	79.7	58.1	65.2	1717i
-CH ₂ NH ₂	15	3.98	0.04	-0.35	1.770	1.201	1.275	2.395	82.9	60.8	66.2	1696i
-CH ₂ CH ₂ NH ₂	15	3.99	0.01	-0.36	1.780	1.189	1.285	2.053	82.7	61.2	69.4	1766i
-CONH ₂	15	4.01	-0.01	-0.36	1.790	1.194	1.282	2.270	81.0	57.9	63.7	1589i
-CONHOH	15	4.02	-0.04	-0.34	1.792	1.234	1.254	1.775	75.3	53.5	58.2	1491i
-NH ₂	15	4.01	0.00	-0.36	1.786	1.194	1.283	2.693	92.4	70.0	72.7	1779i
-NHSO ₃ H	15	4.08	-0.14	-0.36	1.838	1.227	1.263	1.676	77.6	56.1	62.0	1698i
-NHCH ₃	15	4.06	0.03	-0.44	1.805	1.160	1.361	2.676	90.5	67.8	73.8	1573i
-NHNH ₂	15	4.02	-0.02	-0.36	1.793	1.193	1.283	2.639	86.7	64.2	71.1	1780i
-NHOH	15	3.98	0.04	-0.36	1.772	1.183	1.290	2.663	86.0	64.0	71.3	1765i
-NHCOOH	15	4.10	0.00	-0.49	1.826	1.217	1.268	1.917	77.4	55.2	60.3	1738i
-NHCOCH ₂ NH ₂	15	4.02	-0.03	-0.35	1.789	1.215	1.266	2.283	82.5	62.2	67.4	1676i
-NHCOCOOH	15	4.01	0.00	-0.35	1.778	1.215	1.263	2.716	76.9	55.1	63.3	1633i
-NHCONH ₂	15	4.06	-0.09	-0.36	1.819	1.210	1.274	2.060	85.7	64.2	69.7	1798i
-NHCOSO ₃ H	15	4.07	-0.14	-0.35	1.824	1.251	1.247	1.539	73.8	51.3	54.8	1449i

S4. Additional data on D

In Table S14, electronic, geometrical and energetic parameters are reported for the structures of **D** in the methane cycle, respectively.

In the Table S14, ΔH_{methyl} is defined as:

$$\Delta H_{\text{methyl}} = H_{\text{D}} - H_{\text{methyl}} - H_{\text{AD}} \quad (4)$$

where AD is the cluster optimized in its hydroxylated form (formula: $\text{Fe}_2(\text{III})\text{Fe}(\text{III})(\text{OH})(\mu_3\text{-O})(\text{C}_6\text{H}_4\text{MCOO})_6$, where M = -H or a functional group, depending on the cluster) The corresponding Gibbs free energies are defined in a similar way.

Table S13. Spin densities ρ on the Fe involved in the reaction, on the O of the hydroxy group and on the C of the methane molecule for all the *meta-D* structures as obtained at the UM06-L/def2-TZVP level in their ground spin state. Spin densities are expressed as the difference between the α and β electron densities. Relevant geometrical parameters are also reported: the bond length $d(\text{Fe-O}_{\text{OH}})$, the hydroxy bond length $d(\text{H-O}_{\text{OH}})$, the distance between the C and H of the activated C-H bond $d(\text{C-H})$ (in Å). The enthalpy of adsorption of the methyl radical is also reported defined as in Eq. 4 (in kJ mol^{-1}).

<i>meta-D</i>	$2S+1$	$\rho(\text{Fe})$	$\rho(\text{O}_{\text{OH}})$	$\rho(\text{C})$	$d(\text{Fe-O}_{\text{OH}})$	$d(\text{H-O}_{\text{OH}})$	$d(\text{C-H})$	$\Delta H_{\text{methyl}}^{\text{c}}$	$\Delta G_{\text{methyl}}^{\text{c}}$
-H	15	4.15	0.35	-0.79	1.829	0.967	2.273	-6.3	29.8
-NH ₂	15	4.15	0.35	-0.79	1.829	0.967	2.285	-7.5	29.2
-OH	15	4.15	0.35	-0.79	1.829	0.967	2.285	-6.7	31.7
-Br	15	4.15	0.35	-0.79	1.826	0.967	2.263	-7.3	29.3
-F	15	4.15	0.35	-0.79	1.827	0.967	2.276	-7.6	30.3
-COOH	15	4.15	0.35	-0.80	1.835	0.966	2.431	-12.5	28.4
-CF ₃	15	4.15	0.35	-0.79	1.825	0.967	2.254	-7.3	29.6
-SO ₃ H	15	4.14	0.35	-0.80	1.833	0.966	2.444	-12.5	27.4
-NO ₂	15	4.15	0.36	-0.79	1.824	0.967	2.265	-7.8	30.4

Table S14. Spin densities ρ on the Fe involved in the reaction, on the O of the hydroxy group and on the C of the methane molecule for all the **up-D** structures as obtained at the UM06-L/def2-TZVP level in their ground spin state. Spin densities are expressed as the difference between the α and β electron densities. Relevant geometrical parameters are also reported: the bond length $d(\text{Fe-O}_{\text{OH}})$, the hydroxy bond length $d(\text{H-O}_{\text{OH}})$, the distance between the C and H of the activated C-H bond $d(\text{C-H})$ (in Å). $d(\text{HB})$ is the hydrogen bond length involving the O_{OH} (in Å). The enthalpy of adsorption of the methyl radical is also reported defined as in Eq. 4 (in kJ mol^{-1}).

up-D	$2S+1$	$\rho(\text{Fe})$	$\rho(\text{O}_{\text{OH}})$	$\rho(\text{C})$	$d(\text{Fe-O}_{\text{OH}})$	$d(\text{H-O}_{\text{OH}})$	$d(\text{C-H})$	$d(\text{HB})$	$\Delta H_{\text{methyl}}^{\text{c}}$	$\Delta G_{\text{methyl}}^{\text{c}}$
-H	15	4.15	0.35	-0.79	1.829	0.967	2.291	3.989	-7.7	31.6
-NH ₂	15	4.15	0.32	-0.80	1.843	0.966	2.422	2.667	-5.6	32.2
-OH	15	4.15	0.34	-0.79	1.828	0.967	2.291	2.937	-9.0	29.8
-Br	15	4.15	0.36	-0.80	1.832	0.966	2.813	2.776	-13.1	27.0
-F	15	4.15	0.37	-0.81	1.835	0.963	3.923	2.912	-7.4	32.9
-COOH	15	4.16	0.27	-0.78	1.865	0.970	2.260	1.848	-12.7	26.1
-CF ₃	15	4.14	0.37	-0.79	1.821	0.967	2.343	2.451	-6.8	34.1
-SO ₃ H	15	4.17	0.25	-0.79	1.868	0.968	2.334	1.656	-9.7	31.2
-NO ₂	15	4.14	0.38	-0.79	1.819	0.969	2.332	2.691	-9.8	26.2

Table S15. Spin densities ρ on the Fe involved in the reaction, on the O of the hydroxy group and on the C of the methane molecule for all the **hb-D** structures as obtained at the UM06-L/def2-TZVP level in their ground spin state. Spin densities are expressed as the difference between the α and β electron densities. Relevant geometrical parameters are also reported: the bond length $d(\text{Fe-O}_{\text{OH}})$, the hydroxy bond length $d(\text{H-O}_{\text{OH}})$, the distance between the C and H of the activated C-H bond $d(\text{C-H})$ (in Å). $d(\text{HB})$ is the hydrogen bond length involving the O_{OH} (in Å). The enthalpy of adsorption of the methyl radical is also reported defined as in Eq. 4 (in kJ mol^{-1}).

hb-D	$2S+1$	$\rho(\text{Fe})$	$\rho(\text{O}_{\text{OH}})$	$\rho(\text{C})$	$d(\text{Fe-O}_{\text{OH}})$	$d(\text{H-O}_{\text{OH}})$	$d(\text{C-H})$	$d(\text{HB})$	$\Delta H_{\text{methyl}}^{\text{c}}$	$\Delta G_{\text{methyl}}^{\text{c}}$
-SO ₂ NH ₂	15	4.16	0.29	-0.78	1.853	0.969	2.336	1.842	-15.2	22.5
-CH ₂ NH ₂	15	4.14	0.38	-0.81	1.830	0.971	3.985	2.189	-13.6	24.1
-CH ₂ CH ₂ NH ₂	15	4.15	0.31	-0.79	1.843	0.968	2.250	2.051	-7.5	30.2
-CONH ₂	15	4.16	0.31	-0.79	1.847	0.968	2.262	2.219	-7.3	31.4
-CONHOH	15	4.16	0.30	-0.80	1.862	0.969	3.660	1.760	-18.3	22.0
-NH ₂	15	4.15	0.33	-0.80	1.847	0.965	2.598	2.632	-13.2	26.9
-NHSO ₃ H	15	4.17	0.23	-0.79	1.885	0.967	2.401	1.611	-9.6	28.4
-NHCH ₃	15	4.15	0.32	-0.80	1.849	0.966	2.488	2.603	-13.6	27.3
-NHNH ₂	15	4.15	0.30	-0.79	1.848	0.966	2.218	2.533	-8.0	31.7
-NHOH	15	4.15	0.31	-0.79	1.842	0.966	2.221	2.560	-8.1	30.5
-NHCOOH	15	4.16	0.26	-0.79	1.881	0.967	2.497	1.852	-15.6	23.5
-NHCOCH ₂ NH ₂	15	4.15	0.30	-0.78	1.842	0.968	2.250	2.243	-17.2	23.4
-NHCOCOOH	15	4.13	0.37	-0.79	1.825	0.967	2.614	2.909	-27.4	13.0
-NHCONH ₂	15	4.16	0.28	-0.79	1.866	0.968	2.400	2.012	-10.5	29.6
-NHCOSO ₃ H	15	4.17	0.24	-0.79	1.875	0.967	2.604	1.501	-18.9	20.5

S5. Reaction energies for all the clusters for the ferryl formation and the C-H bond scission

In the following tables, the electronic, enthalpy and Gibbs free energy for the **AO** \rightarrow **B** reaction and the **C** \rightarrow **D** reaction are reported for all the systems.

Table S16. Reaction electronic energy, enthalpy and Gibbs free energy for the **AO** \rightarrow **B** step and the **C** \rightarrow **D** step for all the *meta* clusters as obtained at the UM06-L/def2-TZVP level in their ground spin state. All the values are in kJ mol⁻¹ and have been corrected for the BSSE.

<i>meta</i>	2S+1	$\Delta E_{\text{AO} \rightarrow \text{B}}^{\text{c}}$	$\Delta H_{\text{AO} \rightarrow \text{B}}^{\text{c}}$	$\Delta G_{\text{AO} \rightarrow \text{B}}^{\text{c}}$	$\Delta E_{\text{C} \rightarrow \text{D}}^{\text{c}}$	$\Delta H_{\text{C} \rightarrow \text{D}}^{\text{c}}$	$\Delta G_{\text{C} \rightarrow \text{D}}^{\text{c}}$
-H	15	3.2	-1.8	-9.3	48.1	36.1	29.7
-NH ₂	15	0.8	-3.8	-12.1	47.3	35.4	28.9
-OH	15	-0.4	-4.8	-12.1	48.2	36.7	32.1
-Br	15	3.0	-1.8	-9.7	47.2	35.3	29.4
-F	15	3.5	-2.1	-10.3	47.1	35.2	29.9
-COOH	15	0.9	-4.2	-10.1	47.9	36.7	32.8
-CF ₃	15	2.8	-1.9	-10.2	47.0	35.4	29.7
-SO ₃ H	15	3.7	-1.2	-5.6	47.2	35.6	30.3
-NO ₂	15	3.8	-1.2	-8.9	46.9	35.1	30.0

Table S17. Reaction electronic energy, enthalpy and Gibbs free energy for the **AO** \rightarrow **B** step and the **C** \rightarrow **D** step for all the **up** clusters as obtained at the UM06-L/def2-TZVP level in their ground spin state. All the values are in kJ mol⁻¹ and have been corrected for the BSSE.

up	2S +1	$\Delta E_{AO \rightarrow B}^c$	$\Delta H_{AO \rightarrow B}^c$	$\Delta G_{AO \rightarrow B}^c$	$\Delta E_{C \rightarrow D}^c$	$\Delta H_{C \rightarrow D}^c$	$\Delta G_{C \rightarrow D}^c$
-H	15	3.2	-1.8	-9.6	46.9	35.0	31.3
-NH ₂	15	-14.4	-19.9	-27.4	49.8	38.1	32.4
-OH	15	-3.9	-9.0	-12.3	45.4	33.5	29.8
-Br	15	0.6	-4.6	-12.0	36.6	25.6	23.9
-F	15	6.3	0.6	-7.3	41.1	28.7	24.8
-COOH	15	-7.8	-13.7	-21.3	29.6	17.6	19.2
-CF ₃	15	9.7	4.9	-0.6	39.7	28.3	24.9
-SO ₃ H	15	2.2	-4.8	-13.6	34.2	21.8	18.3
-NO ₂	15	15.1	10.1	2.8	33.9	21.5	14.6

Table S18. Reaction electronic energy, enthalpy and Gibbs free energy for the **AO** \rightarrow **B** step and the **C** \rightarrow **D** step for all the **hb** clusters as obtained at the UM06-L/def2-TZVP level in their ground spin state. All the values are in kJ mol⁻¹ and have been corrected for the BSSE.

hb	2S +1	$\Delta E_{AO \rightarrow B}^c$	$\Delta H_{AO \rightarrow B}^c$	$\Delta G_{AO \rightarrow B}^c$	$\Delta E_{C \rightarrow D}^c$	$\Delta H_{C \rightarrow D}^c$	$\Delta G_{C \rightarrow D}^c$
-SO ₂ NH ₂	15	-2.0	-9.3	-19.5	36.0	24.4	20.3
-CH ₂ NH ₂	15	1.9	-3.9	-11.9	39.8	29.5	27.4
-CH ₂ CH ₂ NH ₂	15	5.3	-1.7	-9.5	43.6	32.7	29.8
-CONH ₂	15	-1.6	-6.7	-12.9	40.8	28.8	24.3
-CONHOH	15	-9.8	-15.9	-22.7	28.2	16.8	12.7
-NH ₂	15	-16.1	-21.5	-28.3	47.6	35.8	28.9
-NHSO ₃ H	15	-7.0	-13.1	-17.4	29.5	17.9	15.2
-NHCH ₃	15	-18.3	-23.2	-31.1	46.8	35.3	31.4
-NHNH ₂	15	-11.3	-16.7	-24.1	46.8	34.6	30.8
-NHOH	15	-4.5	-10.1	-17.5	46.4	34.3	30.5
-NHCOOH	15	-25.6	-30.7	-35.5	29.1	17.6	12.8
-NHCOCH ₂ NH ₂	15	-19.6	-26.2	-33.7	40.8	30.8	24.9
-NHCOCOOH	15	15.6	10.1	0.7	27.7	16.7	14.6
-NHCONH ₂	15	-26.5	-31.4	-37.0	40.3	29.0	24.3
-NHCOSO ₃ H	15	-30.8	-37.2	-43.2	21.2	9.0	5.5

S6. Energetic parameters of all the *meta*-clusters

In the following tables, the electronic, enthalpy and Gibbs free energy for all the intermediates and transition states along the reaction cycle for methane to methyl radical conversion are provided for all the *meta*-systems.

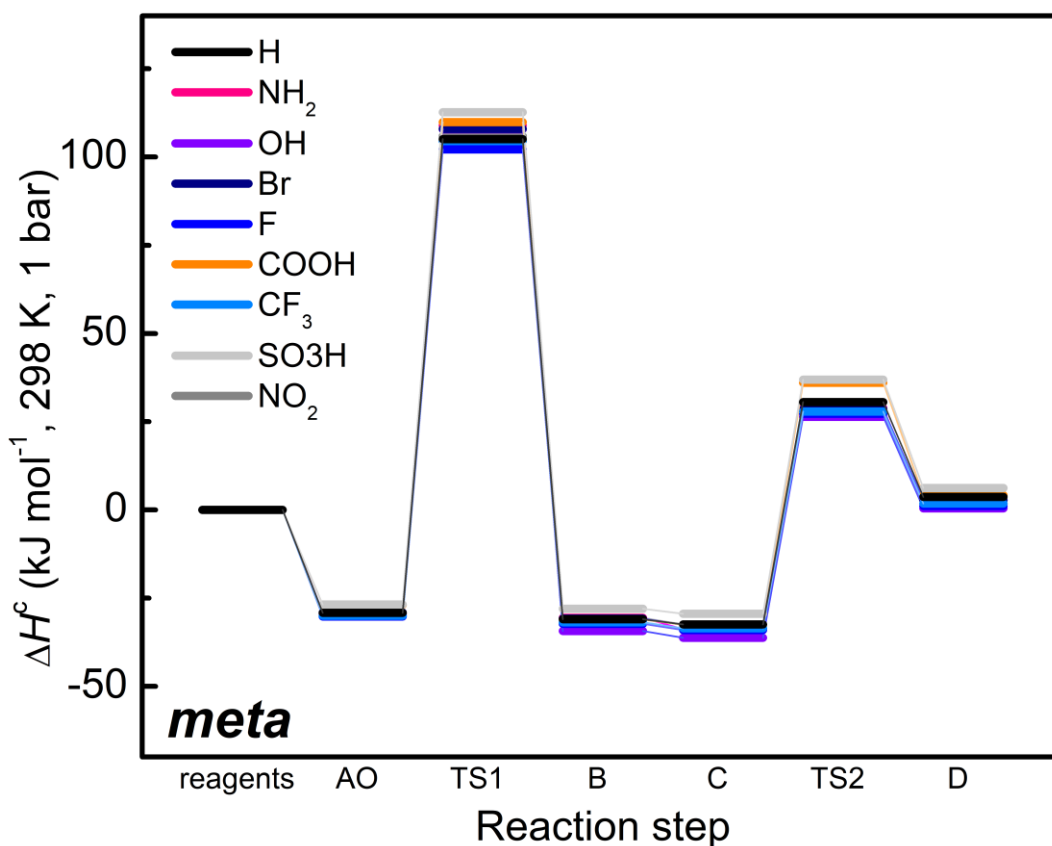


Figure S1. Reaction enthalpies for the oxidation of methane to methyl radical as computed at the UM06-L/def2-TZVP level following the cycle reported in Figure 2 on the pentadectet spin energy surface for the *meta*-clusters taking separated reactants as zero of the enthalpy (data in Tables S19-S27).

Table S19. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by *meta*-H ($2S+1 = 15$) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (E , H^0 , G^0 , in hartree) or referenced to the energies of the separated reagents A, N₂O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol⁻¹; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). H^0 and G^0 have been calculated at 1 atm and 25 °C.

<i>meta</i> -H	E	H^0	G^0	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-6388.73288916	-6388.265381	-6388.349256	–	–	–	–
AB	-6463.91837424	-6463.446759	-6463.532621	–	–	–	–
AO	-6573.48085077	-6572.996847	-6573.090592	-36.2	-32.9	-29.2	10.2
TS1	-6573.42520178	-6572.945614	-6573.040047	109.9	112.9	105.0	142.6
B	-6573.47889127	-6572.996808	-6573.093414	-31.1	-29.7	-31.0	0.9
C	-6504.44697840	-6503.924425	-6504.021303	-33.6	-32.2	-32.5	3.3
TS2	-6504.41462442	-6503.900776	-6503.995262	51.3	53.6	30.5	72.5
D	-6504.42871364	-6503.910720	-6504.010055	14.3	15.9	3.7	32.9

Table S20. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by *meta*-NH₂ ($2S+1 = 15$) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (E , H^0 , G^0 , in hartree) or referenced to the energies of the separated reagents A, N₂O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol⁻¹; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). H^0 and G^0 have been calculated at 1 atm and 25 °C.

<i>meta</i> -NH ₂	E	H^0	G^0	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-6720.96441555	-6720.391682	-6720.492016	–	–	–	–
AB	-6796.14981735	-6795.572646	-6795.674962	–	–	–	–
AO	-6905.71154503	-6905.122255	-6905.232223	-34.0	-30.7	-26.8	13.2
TS1	-6905.65545303	-6905.070462	-6905.179245	113.2	116.3	108.9	152.1
B	-6905.71051236	-6905.122996	-6905.236113	-31.3	-29.9	-30.6	1.1
C	-6836.67901944	-6836.051239	-6836.164518	-35.0	-33.6	-33.8	2.1
TS2	-6836.64689920	-6836.027727	-6836.138424	49.3	51.7	28.8	71.5
D	-6836.66107008	-6836.037797	-6836.153568	12.1	13.7	1.6	30.9

Table S21. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by *meta*-OH ($2S+1 = 15$) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (E , H^0 , G^0 , in hartree) or referenced to the energies of the separated reagents **A**, N_2O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol^{-1} ; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). H^0 and G^0 have been calculated at 1 atm and 25 °C.

<i>meta</i> -OH	E	H^0	G^0	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-6840.19707822	-6839.701213	-6839.799101	–	–	–	–
AB	-6915.38384219	-6914.883652	-6914.983508	–	–	–	–
AO	-7024.94523605	-7024.432850	-7024.540487	-36.7	-33.4	-29.6	10.1
TS1	-7024.88846841	-7024.380379	-7024.488374	112.3	115.3	107.9	146.6
B	-7024.94463311	-7024.433912	-7024.544353	-35.1	-33.8	-34.4	-2.0
C	-6955.91259643	-6955.361717	-6955.472446	-37.4	-35.9	-36.3	-0.1
TS2	-6955.88064480	-6955.338168	-6955.446212	46.5	48.8	26.4	69.6
D	-6955.89426437	-6955.347776	-6955.460259	10.7	12.3	0.4	32.0

Table S22. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by *meta*-Br ($2S+1 = 15$) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (E , H^0 , G^0 , in hartree) or referenced to the energies of the separated reagents **A**, N_2O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol^{-1} ; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). H^0 and G^0 have been calculated at 1 atm and 25 °C.

<i>meta</i> -Br	E	H^0	G^0	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-21829.50469660	-21829.090137	-21829.203155	–	–	–	–
AB	-21904.69027040	-21904.271298	-21904.386155	–	–	–	–
AO	-22014.25282210	-22013.821577	-22013.944244	-36.6	-33.3	-29.1	10.9
TS1	-22014.19620920	-22013.769259	-22013.892661	112.0	115.0	108.0	146.0
B	-22014.25091850	-22013.821499	-22013.947172	-31.6	-30.3	-30.9	1.2
C	-21945.21897880	-21944.749230	-21944.874973	-34.1	-32.7	-32.6	3.9
TS2	-21945.18725750	-21944.726297	-21944.848493	49.1	51.5	28.6	74.4
D	-21945.20105540	-21944.735808	-21944.863815	12.9	14.5	2.8	33.3

Table S23. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by *meta*-F ($2S + 1 = 15$) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (E , H^0 , G^0 , in hartree) or referenced to the energies of the separated reagents **A**, N_2O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol^{-1} ; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). H^0 and G^0 have been calculated at 1 atm and 25 °C.

<i>meta</i> -F	E	H^0	G^0	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-6984.33941492	-6983.920071	-6984.015283	–	–	–	–
AB	-7059.52542779	-7059.101742	-7059.198887	–	–	–	–
AO	-7169.08792107	-7168.651943	-7168.756964	-37.6	-34.3	-30.2	9.4
TS1	-7169.03293745	-7168.601472	-7168.706461	106.7	109.9	102.2	141.8
B	-7169.08588985	-7168.652045	-7168.760184	-32.3	-30.9	-32.3	-1.0
C	-7100.05417131	-7099.579717	-7099.687732	-35.4	-34.0	-34.1	2.2
TS2	-7100.02254285	-7099.556740	-7099.662257	47.7	50.0	27.2	70.0
D	-7100.03626583	-7099.566366	-7099.676372	11.6	13.1	1.1	32.1

Table S24. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by *meta*-COOH ($2S + 1 = 15$) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (E , H^0 , G^0 , in hartree) or referenced to the energies of the separated reagents **A**, N_2O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol^{-1} ; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). H^0 and G^0 have been calculated at 1 atm and 25 °C.

<i>meta</i> -COOH	E	H^0	G^0	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-7520.53397598	-7519.963616	-7520.090790	–	–	–	–
AB	-7595.71721443	-7595.142664	-7595.271718	–	–	–	–
AO	-7705.28114131	-7704.694218	-7704.831195	-34.1	-30.9	-26.9	12.7
TS1	-7705.22443831	-7704.642049	-7704.778677	114.8	117.8	109.9	150.4
B	-7705.28004614	-7704.695045	-7704.834268	-31.2	-30.0	-31.1	2.6
C	-7636.24806481	-7635.622675	-7635.761868	-33.6	-32.3	-32.6	5.7
TS2	-7636.21418557	-7635.597228	-7635.734340	55.3	58.5	36.1	79.8
D	-7636.22988028	-7635.608745	-7635.749421	14.1	15.6	4.1	38.5

Table S25. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by *meta*-CF₃ ($2S + 1 = 15$) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (E , H^0 , G^0 , in hartree) or referenced to the energies of the separated reagents **A**, N₂O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol⁻¹; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). H^0 and G^0 have been calculated at 1 atm and 25 °C.

<i>meta</i> -CF ₃	E	H^0	G^0	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-8411.59039428	-8411.078566	-8411.216352	–	–	–	–
AB	-8486.77623161	-8486.260021	-8486.399668	–	–	–	–
AO	-8596.33871609	-8595.810372	-8595.957830	-37.2	-33.8	-30.0	9.9
TS1	-8596.28311816	-8595.759076	-8595.907184	108.8	112.0	104.5	142.7
B	-8596.33687655	-8595.810311	-8595.960948	-32.3	-31.0	-31.9	-0.3
C	-8527.30493344	-8526.738056	-8526.888732	-34.8	-33.4	-33.6	2.4
TS2	-8527.27329408	-8526.714933	-8526.863331	48.3	50.5	27.9	69.9
D	-8527.28707334	-8526.724612	-8526.877445	12.1	13.6	1.8	32.1

Table S26. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by *meta*-SO₃H ($2S + 1 = 15$) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (E , H^0 , G^0 , in hartree) or referenced to the energies of the separated reagents **A**, N₂O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol⁻¹; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). H^0 and G^0 have been calculated at 1 atm and 25 °C.

<i>meta</i> -SO ₃ H	E	H^0	G^0	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-10132.34222850	-10131.790593	-10131.914993	–	–	–	–
AB	-10207.52451120	-10206.968570	-10207.094830	–	–	–	–
AO	-10317.08947790	-10316.521181	-10316.655482	-34.3	-31.1	-26.8	12.5
TS1	-10317.03175750	-10316.467982	-10316.602062	117.2	120.3	112.7	152.6
B	-10317.08730770	-10316.520889	-10316.656853	-28.6	-27.3	-28.0	6.9
C	-10248.05533270	-10247.448456	-10247.584702	-31.0	-29.7	-29.4	9.3
TS2	-10248.02193300	-10247.423567	-10247.558113	56.6	59.0	36.9	80.1
D	-10248.03739220	-10247.434933	-10247.573231	16.1	17.5	6.2	39.6

Table S27. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by *meta*-NO₂ (2*S* +1 = 15) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (*E*, *H*⁰, *G*⁰, in hartree) or referenced to the energies of the separated reagents A, N₂O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol⁻¹; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). *H*⁰ and *G*⁰ have been calculated at 1 atm and 25 °C.

<i>meta</i> -NO ₂	<i>E</i>	<i>H</i> ⁰	<i>G</i> ⁰	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-7616.14950703	-7615.655776	-7615.780294	–	–	–	–
AB	-7691.33479656	-7690.836773	-7690.963213	–	–	–	–
AO	-7800.89766890	-7800.387329	-7800.521543	-36.7	-33.5	-29.4	10.5
TS1	-7800.84164865	-7800.335728	-7800.470489	110.3	113.5	105.9	144.4
B	-7800.89549458	-7800.387076	-7800.524205	-31.0	-29.6	-30.6	1.6
C	-7731.86356295	-7731.314819	-7731.452083	-33.5	-32.1	-32.5	3.9
TS2	-7731.83204303	-7731.291825	-7731.426885	49.2	51.4	28.7	70.9
D	-7731.84569981	-7731.301441	-7731.440672	13.4	14.8	2.7	33.9

S7. Energetic parameters of all the *up*-clusters

In the following tables, the electronic, enthalpy and Gibbs free energy for all the intermediates and transition states along the reaction cycle for methane to methyl radical conversion are provided for all the *up*-systems.

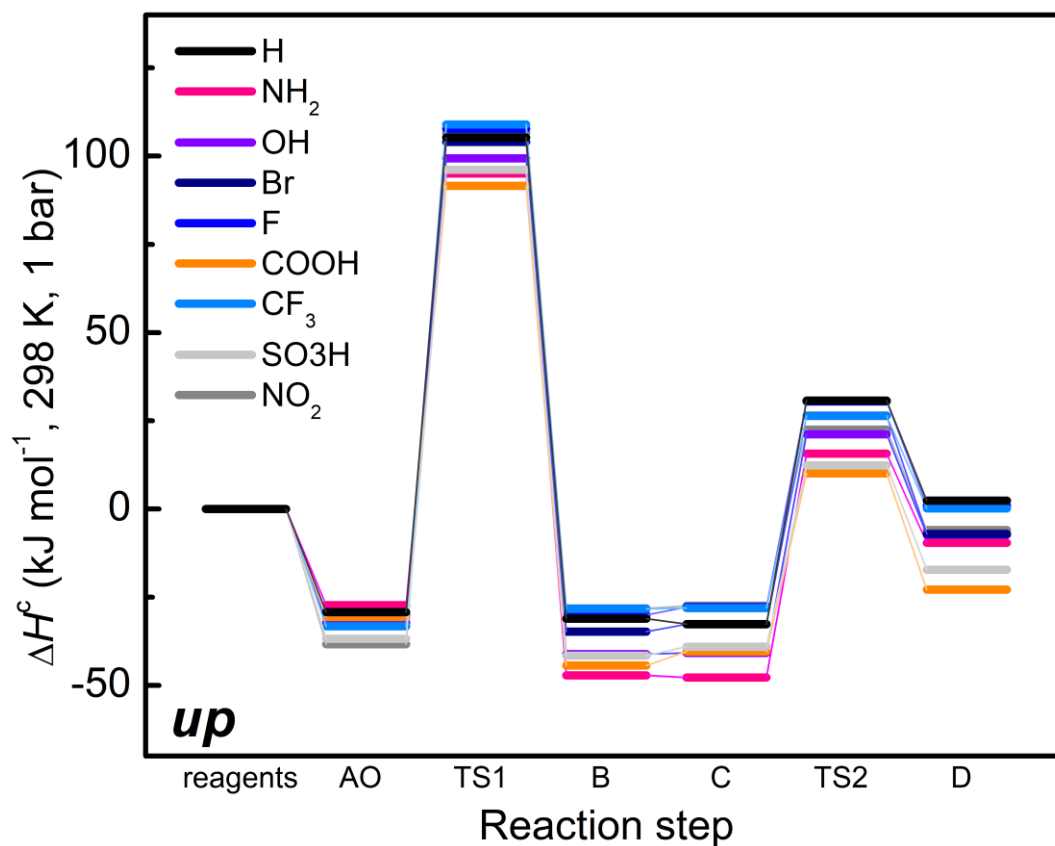


Figure S2. Reaction enthalpies for the oxidation of methane to methyl radical as computed at the UM06-L/def2-TZVP level following the cycle reported in Figure 2 on the pentadectet spin energy surface for the *up*-clusters taking separated reactants as zero of the enthalpy (data in Tables S28-S51).

Table S28. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by **up-H** ($2S+1 = 15$) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (E , H^0 , G^0 , in hartree) or referenced to the energies of the separated reagents **A**, N_2O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol^{-1} ; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). H^0 and G^0 have been calculated at 1 atm and 25 °C.

up-H	E	H^0	G^0	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-6388.73288995	-6388.239902	-6388.328195	–	–	–	–
AB	-6463.91840848	-6463.421286	-6463.511549	–	–	–	–
AO	-6573.48086367	-6572.971400	-6573.069570	-36.2	-33.0	-29.2	10.1
TS1	-6573.42518188	-6572.920097	-6573.018868	109.9	113.0	105.3	143.1
B	-6573.47890785	-6572.971364	-6573.072504	-31.1	-29.8	-31.1	0.5
C	-6504.44702987	-6503.898977	-6504.000143	-33.8	-32.4	-32.6	3.4
TS2	-6504.41505812	-6503.875646	-6503.974309	50.2	53.6	30.7	73.3
D	-6504.42923250	-6503.885705	-6503.988283	13.0	14.4	2.4	34.7

Table S29. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by **up-NH₂** ($2S+1 = 15$) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (E , H^0 , G^0 , in hartree) or referenced to the energies of the separated reagents **A**, N_2O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol^{-1} ; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). H^0 and G^0 have been calculated at 1 atm and 25 °C.

up-NH₂	E	H^0	G^0	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-6720.97085820	-6720.372083	-6720.476344	–	–	–	–
AB	-6796.16142802	-6795.558423	-6795.664972	–	–	–	–
AO	-6905.71831342	-6905.102796	-6905.216890	-34.9	-31.7	-27.2	12.3
TS1	-6905.66699382	-6905.056078	-6905.170881	99.9	102.7	95.1	132.7
B	-6905.72295887	-6905.109535	-6905.226491	-47.1	-46.0	-47.1	-15.1
C	-6836.69058464	-6836.036809	-6836.153721	-48.4	-47.3	-47.7	-11.1
TS2	-6836.65892785	-6836.013461	-6836.128009	34.7	37.8	15.7	58.5
D	-6836.67175265	-6836.022448	-6836.141516	1.0	2.5	-9.6	21.4

Table S30. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by **up-OH** ($2S+1 = 15$) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (E , H^0 , G^0 , in hartree) or referenced to the energies of the separated reagents **A**, N_2O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol^{-1} ; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). H^0 and G^0 have been calculated at 1 atm and 25 °C.

up-OH	E	H^0	G^0	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-6840.20942516	-6839.687004	-6839.788339	–	–	–	–
AB	-6915.39849430	-6914.871777	-6914.974948	–	–	–	–
AO	-7024.95844340	-7024.419582	-7024.530707	-39.0	-35.8	-32.2	7.4
TS1	-7024.90382184	-7024.369386	-7024.481160	104.4	107.3	99.3	137.2
B	-7024.95909396	-7024.422160	-7024.534572	-40.7	-39.7	-41.1	-4.9
C	-6955.92644934	-6955.349062	-6955.463225	-41.3	-40.4	-40.8	-4.6
TS2	-6955.89547148	-6955.326344	-6955.437366	40.0	43.3	21.2	65.6
D	-6955.90935827	-6955.336477	-6955.452072	3.5	5.0	-7.3	25.1

Table S31. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by **up-Br** ($2S+1 = 15$) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (E , H^0 , G^0 , in hartree) or referenced to the energies of the separated reagents **A**, N_2O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol^{-1} ; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). H^0 and G^0 have been calculated at 1 atm and 25 °C.

up-Br	E	H^0	G^0	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-21829.49789210	-21829.057825	-21829.174234	–	–	–	–
AB	-21904.68296770	-21904.238762	-21904.357173	–	–	–	–
AO	-22014.24643540	-22013.789640	-22013.915399	-37.7	-34.5	-30.2	10.6
TS1	-22014.19089110	-22013.738544	-22013.864413	108.1	111.3	104.0	144.5
B	-22014.24562140	-22013.790837	-22013.919416	-35.6	-33.9	-34.8	-1.4
C	-21945.21210840	-21944.716893	-21944.845721	-34.0	-32.7	-32.7	4.6
TS2	-21945.18214780	-21944.695196	-21944.821283	44.7	48.1	26.4	70.9
D	-21945.19834840	-21944.707322	-21944.836801	2.2	3.9	-7.1	28.5

Table S32. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by **up-F** ($2S + 1 = 15$) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (E , H^0 , G^0 , in hartree) or referenced to the energies of the separated reagents **A**, N_2O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol^{-1} ; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). H^0 and G^0 have been calculated at 1 atm and 25 °C.

up-F	E	H^0	G^0	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-6984.33560657	-6983.889955	-6983.989387	–	–	–	–
AB	-7059.51983408	-7059.070086	-7059.171591	–	–	–	–
AO	-7169.08431260	-7168.622045	-7168.730642	-38.2	-34.8	-30.7	10.6
TS1	-7169.02702592	-7168.569168	-7168.678686	112.2	115.2	107.8	146.6
B	-7169.08118783	-7168.621090	-7168.732717	-30.0	-28.5	-30.1	3.2
C	-7100.04800031	-7099.547113	-7099.658615	-29.2	-28.0	-27.8	10.4
TS2	-7100.01825926	-7099.525822	-7099.635137	48.9	52.4	30.5	74.4
D	-7100.03264511	-7099.536469	-7099.649475	11.1	13.1	0.9	35.2

Table S33. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by **up-COOH** ($2S + 1 = 15$) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (E , H^0 , G^0 , in hartree) or referenced to the energies of the separated reagents **A**, N_2O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol^{-1} ; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). H^0 and G^0 have been calculated at 1 atm and 25 °C.

up-COOH	E	H^0	G^0	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-7520.52532164	-7519.929047	-7520.059662	–	–	–	–
AB	-7595.71306559	-7595.112924	-7595.245261	–	–	–	–
AO	-7705.27382867	-7704.661185	-7704.801101	-37.6	-34.1	-30.6	10.3
TS1	-7705.22243485	-7704.614496	-7704.753785	97.3	100.5	91.6	134.1
B	-7705.27600838	-7704.665621	-7704.808428	-43.4	-41.9	-44.4	-11.1
C	-7636.24203941	-7635.591087	-7635.734083	-40.5	-39.2	-40.4	-3.1
TS2	-7636.21504912	-7635.572575	-7635.711617	30.3	33.6	10.1	57.8
D	-7636.23083178	-7635.584469	-7635.726838	-11.1	-9.6	-22.9	16.1

Table S34. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by **up**-CF₃ ($2S+1 = 15$) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (E , H^0 , G^0 , in hartree) or referenced to the energies of the separated reagents **A**, N₂O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol⁻¹; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). H^0 and G^0 have been calculated at 1 atm and 25 °C.

up -CF ₃	E	H^0	G^0	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-8411.58416633	-8411.046218	-8411.186676	–	–	–	–
AB	-8486.76806690	-8486.225606	-8486.367812	–	–	–	–
AO	-8596.33398082	-8595.779300	-8595.929017	-41.1	-37.6	-33.2	7.8
TS1	-8596.27556853	-8595.725102	-8595.875378	112.3	115.6	108.9	148.5
B	-8596.32953915	-8595.776674	-8595.928505	-29.4	-27.9	-28.3	7.2
C	-8527.29685962	-8526.703516	-8526.855632	-30.0	-28.8	-28.1	11.1
TS2	-8527.26844404	-8526.683649	-8526.833655	44.6	48.1	26.4	71.2
D	-8527.28194269	-8526.692936	-8526.846351	9.2	10.9	0.2	36.0

Table S35. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by **up**-SO₃H ($2S+1 = 15$) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (E , H^0 , G^0 , in hartree) or referenced to the energies of the separated reagents **A**, N₂O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol⁻¹; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). H^0 and G^0 have been calculated at 1 atm and 25 °C.

up -SO ₃ H	E	H^0	G^0	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-10132.34708630	-10131.764017	-10131.893718	–	–	–	–
AB	-10207.53500270	-10206.948446	-10207.080007	–	–	–	–
AO	-10317.09833390	-10316.498599	-10316.637241	-44.8	-41.0	-36.8	5.0
TS1	-10317.04245180	-10316.447901	-10316.586836	101.9	105.5	96.1	137.2
B	-10317.09660870	-10316.499524	-10316.641528	-40.3	-38.8	-41.6	-8.6
C	-10248.06304650	-10247.425474	-10247.566948	-38.5	-37.4	-39.0	-0.1
TS2	-10248.03558800	-10247.406594	-10247.546145	33.5	36.5	12.3	56.3
D	-10248.05008210	-10247.417232	-10247.560044	-4.5	-3.2	-17.2	18.2

Table S36. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by *up*-NO₂ ($2S+1 = 15$) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (E , H^0 , G^0 , in hartree) or referenced to the energies of the separated reagents **A**, N₂O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol⁻¹; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). H^0 and G^0 have been calculated at 1 atm and 25 °C.

<i>up</i> -NO ₂	E	H^0	G^0	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-7616.14296197	-7615.623449	-7615.751635	–	–	–	–
AB	-7691.32650467	-7690.802735	-7690.932599	–	–	–	–
AO	-7800.89454338	-7800.358388	-7800.495705	-45.7	-42.5	-38.3	3.0
TS1	-7800.83508800	-7800.303209	-7800.440940	110.4	113.6	106.5	146.8
B	-7800.88801407	-7800.353746	-7800.493864	-28.6	-27.4	-28.2	5.8
C	-7731.85542636	-7731.280519	-7731.420335	-29.4	-28.1	-27.4	11.9
TS2	-7731.82843505	-7731.262049	-7731.399939	41.5	44.2	22.5	66.9
D	-7731.84263298	-7731.272472	-7731.414894	4.2	5.8	-6.0	26.5

S8. Energetic parameters of all the *hb*-clusters

In the following tables, the electronic, enthalpy and Gibbs free energy for all the intermediates and transition states along the reaction cycle for methane to methyl radical conversion are provided for all the *hb*-systems.

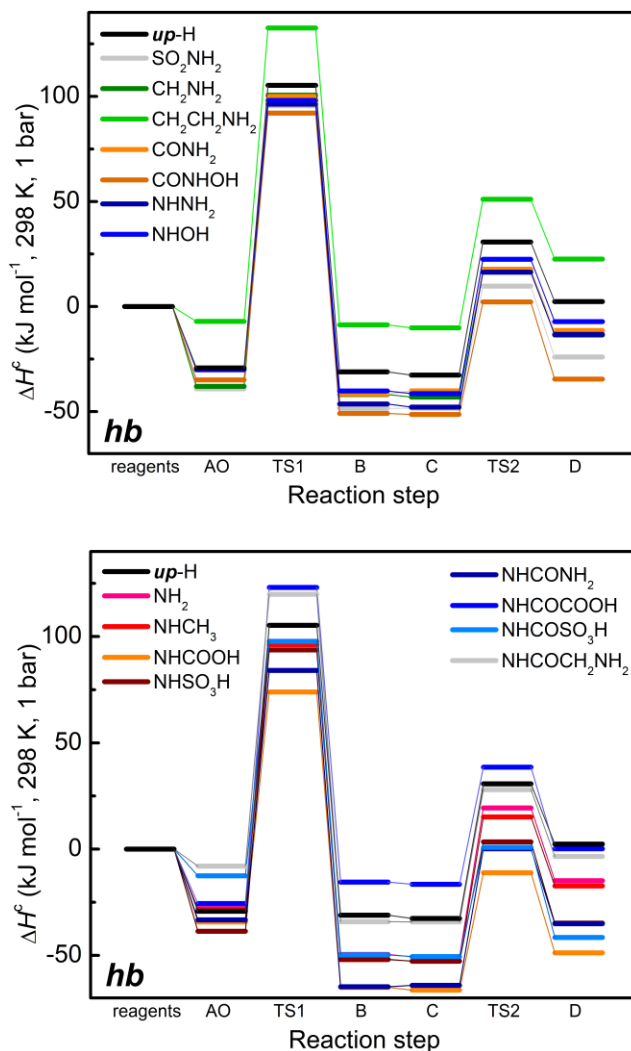


Figure S3. Reaction enthalpies for the oxidation of methane to methyl radical as computed at the UM06-L/def2-TZVP level following the cycle reported in Figure 2 on the $2S+1=15$ spin energy surface for the *hb*-clusters taking separated reactants as zero of the enthalpy (data in Tables S37-S51). The reaction profiles are split on the two plots only for the sake of clarity. The *up*-H profile is also reported in both plots to evidence the effect of the functional group on the Fe reactivity.

Table S37. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by **hb**-SO₂NH₂ (2*S* + 1 = 15) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (*E*, *H*⁰, *G*⁰, in hartree) or referenced to the energies of the separated reagents **A**, N₂O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol⁻¹; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). *H*⁰ and *G*⁰ have been calculated at 1 atm and 25 °C.

hb -SO ₂ NH ₂	<i>E</i>	<i>H</i> ⁰	<i>G</i> ⁰	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-6992.78699595	-6992.261659	-6992.358360	–	–	–	–
AB	-7067.97687097	-7067.447870	-7067.546231	–	–	–	–
AO	-7177.53919819	-7176.997143	-7177.102571	-47.3	-43.5	-39.2	3.2
TS1	-7177.48248267	-7176.945656	-7177.052025	101.6	104.9	95.6	135.5
B	-7177.53907374	-7176.999788	-7177.109090	-47.0	-45.6	-48.5	-16.2
C	-7108.50672755	-7107.926800	-7108.035314	-48.4	-47.0	-48.4	-9.6
TS2	-7108.47711691	-7107.905435	-7108.011256	29.3	32.8	9.7	55.6
D	-7108.49314802	-7107.917664	-7108.027729	-12.8	-10.9	-24.0	10.7

Table S38. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by **hb**-CH₂NH₂ (2*S* + 1 = 15) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (*E*, *H*⁰, *G*⁰, in hartree) or referenced to the energies of the separated reagents **A**, N₂O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol⁻¹; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). *H*⁰ and *G*⁰ have been calculated at 1 atm and 25 °C.

hb CH ₂ NH ₂	<i>E</i>	<i>H</i> ⁰	<i>G</i> ⁰	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-6483.41669511	-6482.874870	-6482.967837	–	–	–	–
AB	-6558.60379195	-6558.058128	-6558.153271	–	–	–	–
AO	-6668.16812979	-6667.609774	-6667.712184	-45.3	-41.9	-38.0	2.5
TS1	-6668.11063285	-6667.556816	-6667.659742	105.6	108.6	100.6	139.8
B	-6668.16674743	-6667.610602	-6667.716077	-41.7	-40.0	-41.9	-9.5
C	-6599.13462857	-6598.538049	-6598.643298	-43.7	-42.1	-43.1	-5.5
TS2	-6599.10373236	-6598.515573	-6598.618748	37.4	40.7	17.6	60.7
D	-6599.11956361	-6598.526897	-6598.632946	-4.2	-2.3	-13.6	21.9

Table S39. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by **hb-CH₂CH₂NH₂** (2S +1 = 15) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (E , H^0 , G^0 , in hartree) or referenced to the energies of the separated reagents **A**, N₂O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol⁻¹; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). H^0 and G^0 have been calculated at 1 atm and 25 °C.

hb-CH₂CH₂NH₂	E	H^0	G^0	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-6522.75089240	-6522.178817	-6522.273414	–	–	–	–
AB	-6597.92698856	-6597.351466	-6597.449343	–	–	–	–
AO	-6707.48981462	-6706.901202	-6707.006749	-12.5	-10.9	-7.0	29.5
TS1	-6707.43231502	-6706.848646	-6706.954483	138.5	141.7	132.6	168.4
B	-6707.48774265	-6706.901778	-6707.010313	-7.0	-5.7	-8.7	20.0
C	-6638.45580498	-6637.829371	-6637.937856	-9.5	-8.1	-10.1	23.2
TS2	-6638.42502728	-6637.806778	-6637.912126	71.3	74.6	51.1	92.7
D	-6638.43923223	-6637.816954	-6637.926545	34.0	35.5	22.6	53.1

Table S40. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by **hb-CONH₂** (2S +1 = 15) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (E , H^0 , G^0 , in hartree) or referenced to the energies of the separated reagents **A**, N₂O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol⁻¹; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). H^0 and G^0 have been calculated at 1 atm and 25 °C.

hb-CONH₂	E	H^0	G^0	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-6557.48125522	-6556.958226	-6557.053645	–	–	–	–
AB	-6632.67075347	-6632.143404	-6632.240322	–	–	–	–
AO	-6742.23155447	-6741.691962	-6741.797119	-42.4	-38.9	-34.9	4.8
TS1	-6742.17642916	-6741.640418	-6741.748214	102.4	105.5	100.0	132.8
B	-6742.23131492	-6741.693685	-6741.801187	-41.7	-40.5	-41.7	-8.1
C	-6673.19838550	-6672.620071	-6672.727333	-41.6	-40.6	-40.2	-1.4
TS2	-6673.16842580	-6672.598889	-6672.703942	37.0	40.4	17.8	62.3
D	-6673.18305455	-6672.609324	-6672.718300	-1.4	0.3	-11.4	22.9

Table S41. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by **hb**-CONHOH ($2S+1 = 15$) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (E , H^0 , G^0 , in hartree) or referenced to the energies of the separated reagents **A**, N_2O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol^{-1} ; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). H^0 and G^0 have been calculated at 1 atm and 25 °C.

hb -CONHOH	E	H^0	G^0	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-6632.66802789	-6632.139748	-6632.236685	–	–	–	–
AB	-6707.85713951	-6707.325270	-6707.423617	–	–	–	–
AO	-6817.41824427	-6816.873597	-6816.979284	-42.1	-38.4	-34.9	7.4
TS1	-6817.36524080	-6816.825191	-6816.930562	97.0	100.7	92.1	135.2
B	-6817.42134207	-6816.879023	-6816.987302	-50.3	-48.2	-50.9	-15.3
C	-6748.38909279	-6747.806151	-6747.913237	-51.9	-50.1	-51.3	-8.1
TS2	-6748.36094053	-6747.786282	-6747.891588	22.0	25.2	2.2	50.1
D	-6748.37841581	-6747.799815	-6747.908461	-23.9	-21.9	-34.6	4.5

Table S42. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by **hb**-NH₂ ($2S+1 = 15$) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (E , H^0 , G^0 , in hartree) or referenced to the energies of the separated reagents **A**, N_2O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol^{-1} ; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). H^0 and G^0 have been calculated at 1 atm and 25 °C.

hb -NH ₂	E	H^0	G^0	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-6444.11104620	-6443.600010	-6443.690688	–	–	–	–
AB	-6519.30085316	-6518.785659	-6518.878423	–	–	–	–
AO	-6628.85851407	-6628.330967	-6628.431388	-34.9	-31.9	-28.0	11.7
TS1	-6628.80607366	-6628.283016	-6628.384091	102.8	105.7	97.7	135.8
B	-6628.86415235	-6628.338650	-6628.441679	-49.7	-48.0	-49.5	-16.6
C	-6559.83217980	-6559.266050	-6559.368053	-52.1	-50.5	-50.6	-10.5
TS2	-6559.79763913	-6559.240045	-6559.341011	38.6	41.9	19.4	62.2
D	-6559.81413339	-6559.252503	-6559.357104	-4.7	-2.9	-14.9	18.4

Table S43. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by **hb**-NHSO₃H (2*S* + 1 = 15) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (*E*, *H*⁰, *G*⁰, in hartree) or referenced to the energies of the separated reagents A, N₂O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol⁻¹; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). *H*⁰ and *G*⁰ have been calculated at 1 atm and 25 °C.

hb -NHSO ₃ H	<i>E</i>	<i>H</i> ⁰	<i>G</i> ⁰	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-7068.04803978	-7067.517665	-7067.618080	–	–	–	–
AB	-7143.23875693	-7142.704328	-7142.804905	–	–	–	–
AO	-7252.79996401	-7252.252828	-7252.362208	-46.6	-43.2	-38.7	3.1
TS1	-7252.74731249	-7252.204635	-7252.312527	91.6	100.9	93.7	139.4
B	-7252.80201564	-7252.257208	-7252.368223	-52.0	-50.2	-51.8	-14.3
C	-7183.76974660	-7183.184536	-7183.295492	-53.6	-51.9	-52.7	-10.5
TS2	-7183.74071381	-7183.163690	-7183.272395	22.6	25.7	3.4	51.5
D	-7183.75853119	-7183.177742	-7183.289716	-24.2	-22.4	-34.8	4.7

Table S44. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by **hb**-NHCH₃ (2*S* + 1 = 15) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (*E*, *H*⁰, *G*⁰, in hartree) or referenced to the energies of the separated reagents A, N₂O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol⁻¹; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). *H*⁰ and *G*⁰ have been calculated at 1 atm and 25 °C.

hb -NHCH ₃	<i>E</i>	<i>H</i> ⁰	<i>G</i> ⁰	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-6483.42497450	-6482.884313	-6482.978211	–	–	–	–
AB	-6558.61572102	-6558.070696	-6558.166241	–	–	–	–
AO	-6668.17266056	-6667.615528	-6667.719278	-35.5	-32.4	-28.7	10.7
TS1	-6668.12075022	-6667.567913	-6667.671952	100.8	103.8	96.2	134.9
B	-6668.17914736	-6667.623894	-6667.730635	-52.5	-50.7	-51.9	-20.3
C	-6599.14700083	-6598.551121	-6598.656677	-54.5	-52.9	-52.6	-13.4
TS2	-6599.11315562	-6598.525917	-6598.629199	34.4	37.6	15.2	60.4
D	-6599.12924578	-6598.537743	-6598.644788	-7.9	-6.0	-17.3	18.0

Table S45. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by **hb**-NHNH₂ ($2S + 1 = 15$) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (E , H^0 , G^0 , in hartree) or referenced to the energies of the separated reagents **A**, N₂O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol⁻¹; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). H^0 and G^0 have been calculated at 1 atm and 25 °C.

hb -NHNH ₂	E	H^0	G^0	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-6499.43810477	-6498.908624	-6499.002064	–	–	–	–
AB	-6574.62916335	-6574.095615	-6574.191475	–	–	–	–
AO	-6684.18633691	-6683.640306	-6683.743719	-36.9	-33.6	-29.7	9.4
TS1	-6684.13372184	-6683.592190	-6683.696428	101.2	104.2	96.3	133.3
B	-6684.18995833	-6683.645964	-6683.752214	-46.4	-45.0	-46.4	-14.7
C	-6615.15799206	-6614.573546	-6614.680099	-48.9	-47.4	-47.9	-12.4
TS2	-6615.12574251	-6614.549860	-6614.653777	35.8	39.3	16.3	58.7
D	-6615.14030372	-6614.560531	-6614.668514	-2.4	-0.6	-13.3	18.4

Table S46. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by **hb**-NHOH ($2S + 1 = 15$) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (E , H^0 , G^0 , in hartree) or referenced to the energies of the separated reagents **A**, N₂O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol⁻¹; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). H^0 and G^0 have been calculated at 1 atm and 25 °C.

hb -NHOH	E	H^0	G^0	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-6519.29142635	-6518.775208	-6518.868081	–	–	–	–
AB	-6594.47983577	-6593.959668	-6594.054823	–	–	–	–
AO	-6704.03970364	-6703.507035	-6703.609890	-37.0	-33.8	-30.1	9.0
TS1	-6703.98623573	-6703.458187	-6703.561625	103.3	106.5	98.1	135.6
B	-6704.04066328	-6703.510145	-6703.615822	-39.6	-38.2	-40.2	-8.5
C	-6635.00862606	-6634.437701	-6634.543691	-41.8	-40.3	-41.5	-6.1
TS2	-6634.97660308	-6634.414066	-6634.517280	42.3	45.7	22.5	65.2
D	-6634.99111245	-6634.424787	-6634.532223	4.2	6.0	-7.2	24.4

Table S47. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by **hb**-NHCOOH ($2S + 1 = 15$) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (E , H^0 , G^0 , in hartree) or referenced to the energies of the separated reagents **A**, N_2O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol^{-1} ; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). H^0 and G^0 have been calculated at 1 atm and 25 °C.

hb -NHCOOH	E	H^0	G^0	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-6632.74373375	-6632.214932	-6632.311723	–	–	–	–
AB	-6707.93983394	-6707.406915	-6707.505232	–	–	–	–
AO	-6817.49397245	-6816.948400	-6817.055258	-42.2	-38.8	-34.3	4.6
TS1	-6817.44845284	-6816.907317	-6817.012480	77.3	81.1	74.0	117.3
B	-6817.50318019	-6816.959573	-6817.068260	-66.4	-64.3	-65.0	-30.9
C	-6748.47118800	-6747.886986	-6747.994202	-68.7	-67.0	-66.4	-23.9
TS2	-6748.44232506	-6747.866560	-6747.971853	7.1	10.3	-11.1	36.4
D	-6748.46017036	-6747.880340	-6747.989392	-39.8	-38.0	-48.8	-11.1

Table S48. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by **hb**-NHCOCH₂NH₂ ($2S + 1 = 15$) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (E , H^0 , G^0 , in hartree) or referenced to the energies of the separated reagents **A**, N_2O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol^{-1} ; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). H^0 and G^0 have been calculated at 1 atm and 25 °C.

hb -NHCOCH ₂ NH ₂	E	H^0	G^0	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-6652.17753799	-6651.605666	-6651.706322	–	–	–	–
AB	-6727.36032302	-6726.785021	-6726.886352	–	–	–	–
AO	-6836.91758042	-6836.329221	-6836.437728	-15.4	-11.8	-8.0	36.7
TS1	-6836.86436602	-6836.280324	-6836.388169	124.3	127.5	119.9	166.3
B	-6836.92440057	-6836.338531	-6836.449908	-33.3	-31.4	-34.2	3.0
C	-6767.89184279	-6767.265424	-6767.376359	-34.2	-32.7	-34.2	8.7
TS2	-6767.86106709	-6767.242394	-6767.351332	46.6	49.9	28.0	76.1
D	-6767.87651782	-6767.253908	-6767.367082	6.0	8.1	-3.4	33.5

Table S49. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by **hb**-NHCOCOOH ($2S + 1 = 15$) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (E , H^0 , G^0 , in hartree) or referenced to the energies of the separated reagents **A**, N_2O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol^{-1} ; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). H^0 and G^0 have been calculated at 1 atm and 25 °C.

hb -NHCOCOOH	E	H^0	G^0	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-6746.12089476	-6745.579777	-6745.680448	–	–	–	–
AB	-6821.30004599	-6820.754865	-6820.857506	–	–	–	–
AO	-6930.86772659	-6930.310035	-6930.419621	-33.2	-29.6	-25.6	16.3
TS1	-6930.80641387	-6930.253228	-6930.364065	127.7	130.9	123.1	161.7
B	-6930.86088887	-6930.305314	-6930.418492	-15.3	-14.0	-15.5	16.9
C	-6861.82883696	-6861.232767	-6861.346260	-17.5	-16.1	-16.6	19.6
TS2	-6861.80033444	-6861.212547	-6861.322926	57.3	60.8	38.5	82.9
D	-6861.81835392	-6861.226485	-6861.340771	10.0	11.7	0.2	34.3

Table S50. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by **hb**-NHCONH₂ ($2S + 1 = 15$) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (E , H^0 , G^0 , in hartree) or referenced to the energies of the separated reagents **A**, N_2O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol^{-1} ; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). H^0 and G^0 have been calculated at 1 atm and 25 °C.

hb -NHCONH ₂	E	H^0	G^0	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-6612.87196805	-6612.330489	-6612.427862	–	–	–	–
AB	-6688.06745398	-6687.521854	-6687.620833	–	–	–	–
AO	-6797.62165223	-6797.063603	-6797.170605	-40.7	-37.3	-33.3	6.7
TS1	-6797.57244546	-6797.018783	-6797.125547	88.5	91.7	84.1	124.8
B	-6797.63108200	-6797.074896	-6797.184017	-65.5	-63.8	-64.8	-30.3
C	-6728.59832430	-6728.001640	-6728.109643	-65.8	-64.3	-64.1	-22.1
TS2	-6728.56628633	-6727.977771	-6728.083702	18.3	21.4	0.1	47.5
D	-6728.58298868	-6727.990600	-6728.100397	-25.6	-24.0	-35.1	2.1

Table S51. Electronic energy, enthalpy and Gibbs free energy for all the intermediates and TS structures in the catalytic cycle related to the ethane oxidation catalyzed by **hb**-NHCOSO₃H₂ (2*S* +1 = 15) as obtained at the UM06-L/def2-TZVP level. These energies are reported as absolute values (*E*, *H*⁰, *G*⁰, in hartree) or referenced to the energies of the separated reagents **A**, N₂O and ethane and corrected for BSSE (ΔE^c , ΔH^{0c} , ΔG^{0c} , in kJ mol⁻¹; for the electronic energy, the value not corrected for BSSE is also reported for comparison, ΔE). *H*⁰ and *G*⁰ have been calculated at 1 atm and 25 °C.

hb -NHCOSO ₃ H	<i>E</i>	<i>H</i> ⁰	<i>G</i> ⁰	ΔE	ΔE^c	ΔH^{0c}	ΔG^{0c}
A	-7181.42561860	-7180.883085	-7180.985944	–	–	–	–
AB	-7256.61498998	-7256.068798	-7256.173643	–	–	–	–
AO	-7366.16732167	-7365.608296	-7365.721168	-19.8	-16.4	-12.6	26.4
TS1	-7366.12108796	-7365.566632	-7365.678366	101.6	105.9	97.7	139.7
B	-7366.17841135	-7365.621820	-7365.736987	-48.9	-47.1	-49.7	-16.7
C	-7297.14633819	-7296.549066	-7296.662957	-51.0	-49.5	-50.5	-9.6
TS2	-7297.11895093	-7296.530216	-7296.642771	20.9	24.3	0.8	45.2
D	-7297.13836117	-7296.545746	-7296.660974	-30.1	-28.3	-41.6	-4.2

S9. Energetic parameters of reagents, products and reference systems

In the following tables, the absolute electronic energy, enthalpy and Gibbs free energy for the reagent, intermediate and final products of the methane to methanol and ethane to ethanol reaction are reported. The water and dioxygen values are also reported being used for the evaluation of the hydrogen affinity of the catalyst (see Section S1.1).

Table S52. Electronic energy (E), enthalpy (H^0) and Gibbs free energy (G^0) obtained at the M06-L level for relevant molecules used in this study not reported in the other tables. All energies are reported in hartree. H^0 and G^0 have been calculated at 1 atm and 25 °C. All the energies are in hartree.

Molecule	2S+1	E	H^0	G^0
CH ₄	1	-40.525307160	-40.476398	-40.499862
CH ₃ •	2	-39.844629678	-39.811250	-39.835402
C ₂ H ₆	1	-79.844126298	-79.764451	-79.791959
C ₂ H ₅ •	2	-79.172509579	-79.108106	-79.137132
C ₂ H ₄	1	-78.602135679	-78.547104	-78.572604
H ₂	1	-1.171714054	-1.158522	-1.173318
H•	2	-0.503415617	-0.501055	-0.514070
O ₂	3	-150.369574148	-150.362511	-150.385783
N ₂ O	1	-184.734168853	-184.719113	-184.743989
N ₂	1	-109.558197047	-109.549370	-109.571106
H ₂ O	1	-76.443268469	-76.418120	-76.440195
CH ₃ OH	1	-115.748941951	-115.693261	-115.720254
C ₂ H ₅ OH	1	-155.075260400	-154.989700	-155.020258

S10. Alternative *meta*-NO₂ cluster

In order to verify if the position of the X group on the phenyl ring can influence the cluster reactivity, for *meta*-NO₂ one of the X groups was moved from the meta to the ortho position as shown in Figure S4.

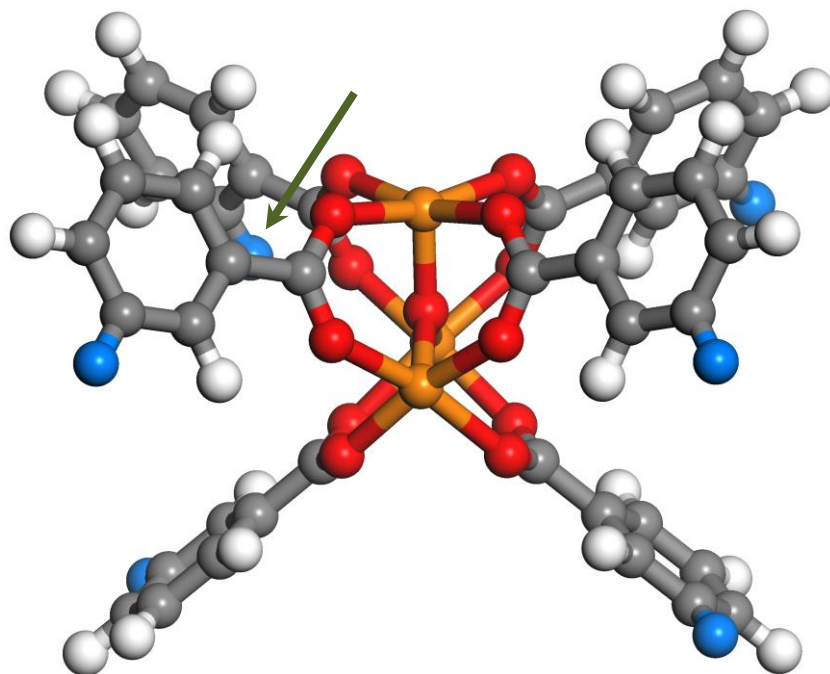


Figure S4. Alternative *meta*-NO₂ cluster. Color code as in Figure 2.

The results obtained for this cluster are fully equivalent to those obtained for *meta*-NO₂.

S11. D' structure for HB acceptors

The presence of HB acceptors on the X lowers the TS2 barrier but also facilitates the desorption of the methyl radical. In Figure S5, two structures are reported for *up*-F: (a) the structure of the intermediate more geometrically close to **TS2 (D)** with the Fe-OH in HB with the methyl, (b) a rearrangement of **D**, 6 kJ mol⁻¹ more stable (named **D'**), where the Fe-OH is involved in a direct HB with the fluorine on the X group. As a result, the reaction would proceed to the rebound mechanism only if the creation of this HB is accompanied by a rotation of the methyl to coordinate the O atom of the iron hydroxo species. Otherwise, this is expected to make more plausible dimerization reactions or other side products than what expected for HB donors functional groups.

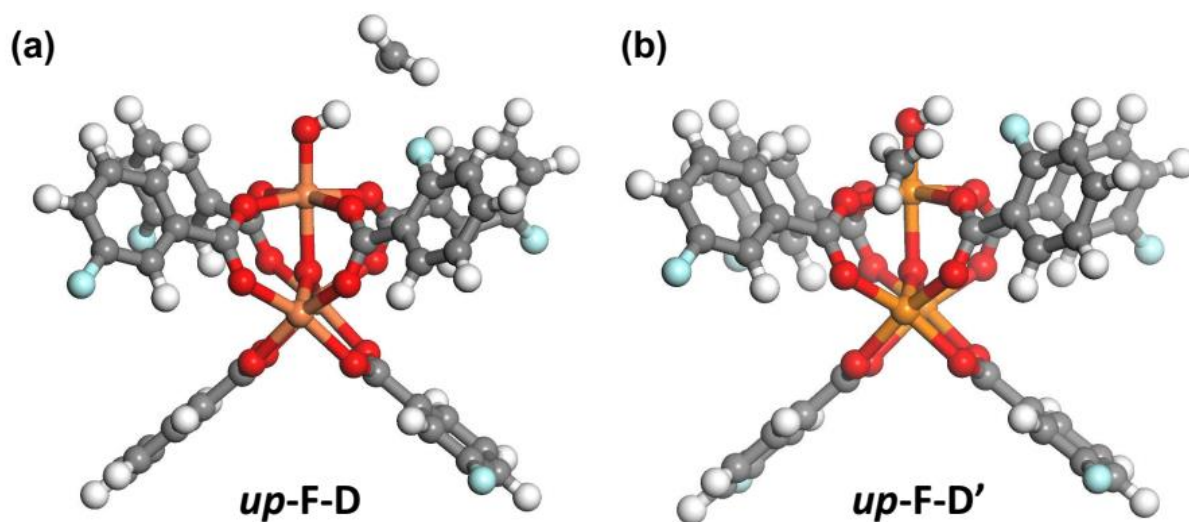


Figure S5. (a) D and (b) D' intermediates for the *up*-F cluster. Color code as in Figure 2.

S12. D' structure for groups that can be both HB donors and acceptors

Some of the groups considered can be both hydrogen donors and acceptors. -COOH is one of them. In **D**, -COOH stabilizes Fe-OH by coordinating it through the hydrogen of the -C-OH moiety (see Figure 5). -COOH can form an hydrogen bond with Fe-OH also through the -C=O moiety (**D'**, see Figure S6). Unlike for HB donor (see Figure S5b), in this case the coordination of the hydrogen of Fe-OH by the functional group does not cause the removal of the methyl from the reaction site, because it coordinates the proton of the carboxylic acid.

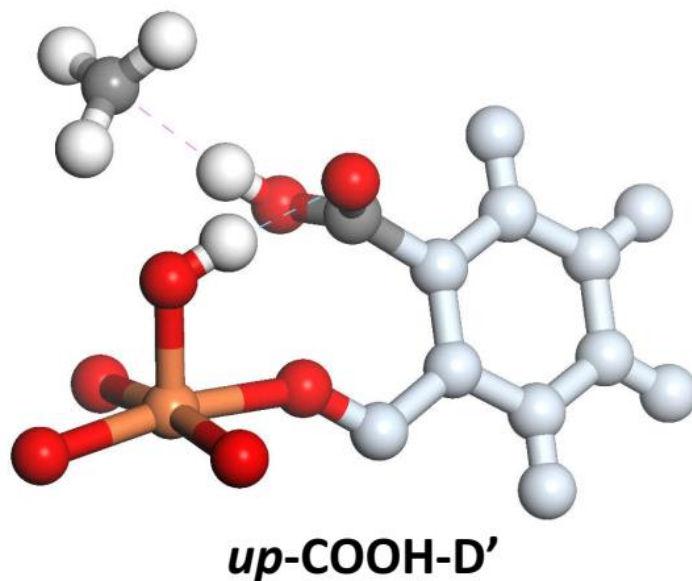


Figure S6. **D'** intermediate for the *up*-COOH cluster. Color code as in Figure 2.

S13. Hydrogen bond in *up*-SO₃H

The strong acidic character of the proton of the sulfonic group causes a decrease in the enthalpy barrier associated with the C-H bond scission step in *up*-SO₃H with respect to *up*-H. The HB involving the O_{oxo} is strong, being of only 1.841 Å in **C** (see Figure S7). The increase in the strength of the HB from the **C** to the **D** intermediate is evidenced by the decrease of the HB length of about 0.2 Å and it is associated with increased polarity of the hydroxo species with respect to the starting oxyl.

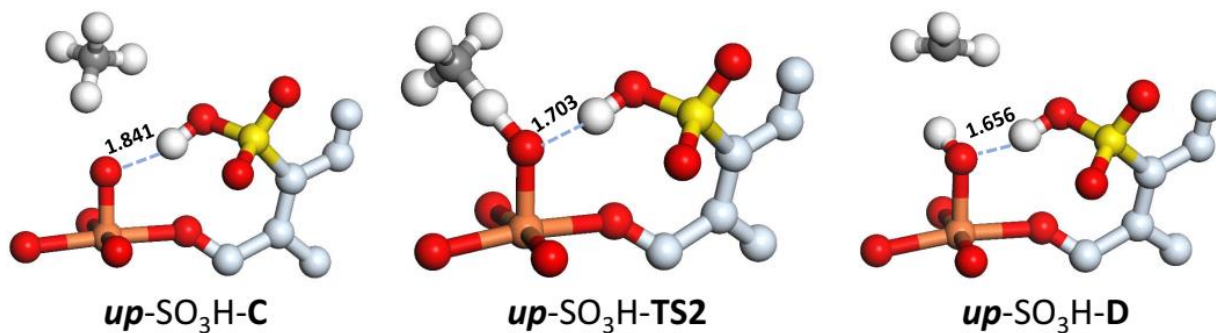


Figure S7. C, TS2, and D structures for the *up*-SO₃H cluster. Color code as in Figure 2.

S14. Other energetics plots

Linear correlations among energetic parameters associated with the reaction and geometrical and electronic parameters are valuable information because they enable the screening of large groups of catalyst candidates. Rosen et al.² have investigated if such correlations exist between the oxyl formation energy and the hydrogen affinity E_H (defined as in Section S1) and the spin density on the ferryl species or on the Fe-O_{oxo} bond length, $d(\text{Fe-O}_{\text{oxo}})$. We have investigated such correlations for the *meta* and the *up* sets and the corresponding plots are reported in Figure S8.

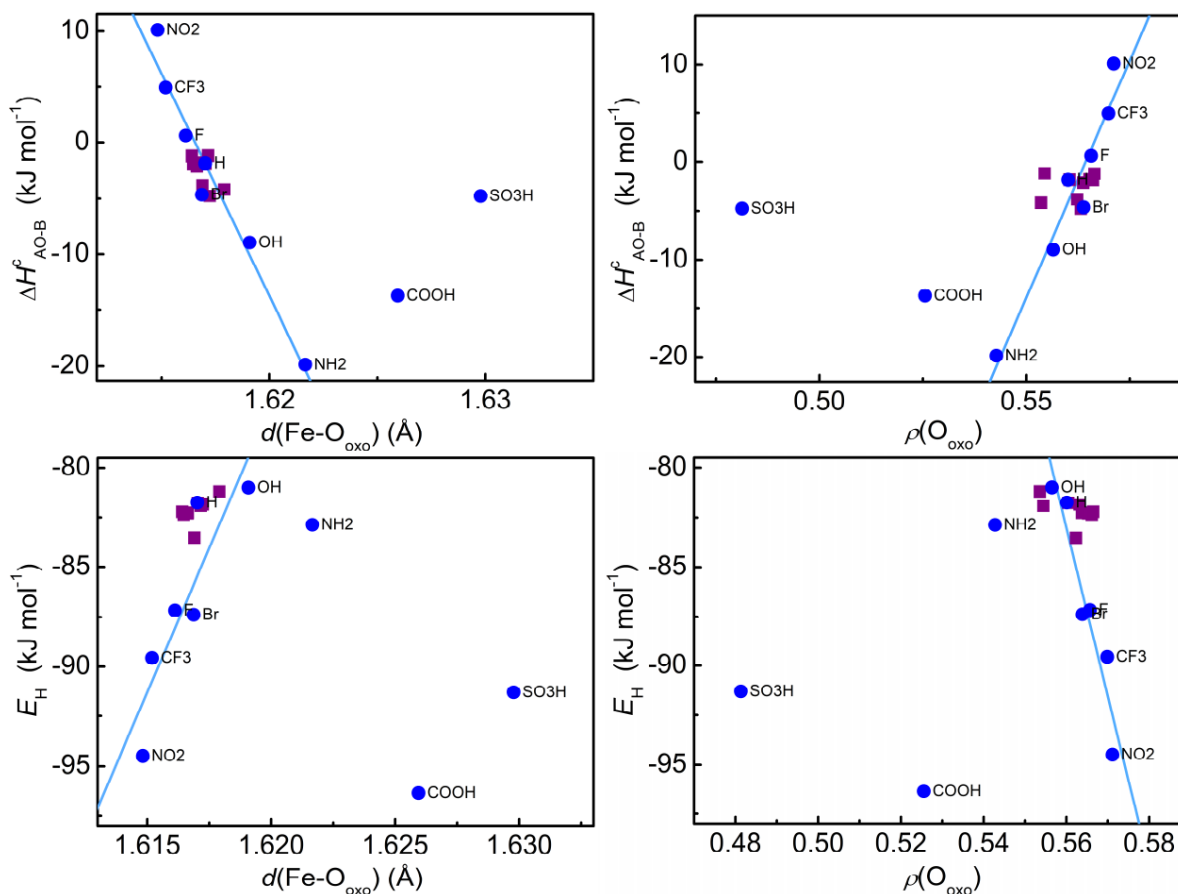


Figure S8. Reaction enthalpy for $\text{AO} \rightarrow \text{B}$, $\Delta H_{\text{AO} \rightarrow \text{B}}^\circ$, vs. the ferryl bond length, $d(\text{Fe-O}_{\text{oxo}})$, and the spin density on the oxyl, $\rho(\text{O}_{\text{oxo}})$. Hydrogen affinity of the AB cluster (defined as in Section S1), E_H , vs. the ferryl bond length, $d(\text{Fe-O}_{\text{oxo}})$, and the spin density on the oxyl, $\rho(\text{O}_{\text{oxo}})$. Values obtained at the UM06-L/def2-TZVP level. *meta* (purple squares) and the *up* sets (blue circles).

Table S53. Adjusted R-square (R^2), Residual Sum of Squares (RSS) for the linear fits reported in the plots of Figure S8. The values here reported are obtained by fitting all the data besides the outliers (*up*-COOH, *up*-SO₃H, and *up*-NH₂).

	$\Delta H_{AO \rightarrow B}$ vs. $d(\text{Fe-O}_{\text{oxo}})$	$\Delta H_{AO \rightarrow B}$ vs. $\rho(O_{\text{oxo}})$	E_{H} vs. $d(\text{Fe-O}_{\text{oxo}})$	E_{H} vs. $\rho(O_{\text{oxo}})$
R^2	0.95	0.92	0.73	0.88
RSS	24.7	38.6	27.5	11.7

It is evident that although a linear correlation can be found in all the four plots of Figure S8, systems where the hydrogen bond interaction plays an important role, do not follow this simple trend. Moreover, the range of validity of these correlations is so limited that the differences among the systems is in the limit of accuracy of the calculations.

Because of the large influence of hydrogen bonding in determining the reaction profile, we have also investigated whether a simple correlation exists between the HB length and the enthalpy barrier associate to the C-H bond scission step. The corresponding plot is reported in Figure S9. Although, as a general rule, $\Delta H_{\text{TS2}}^{\text{C}}$ is lower for shorter bond lengths, the points are too scattered to obtain a fit with using a simple function.

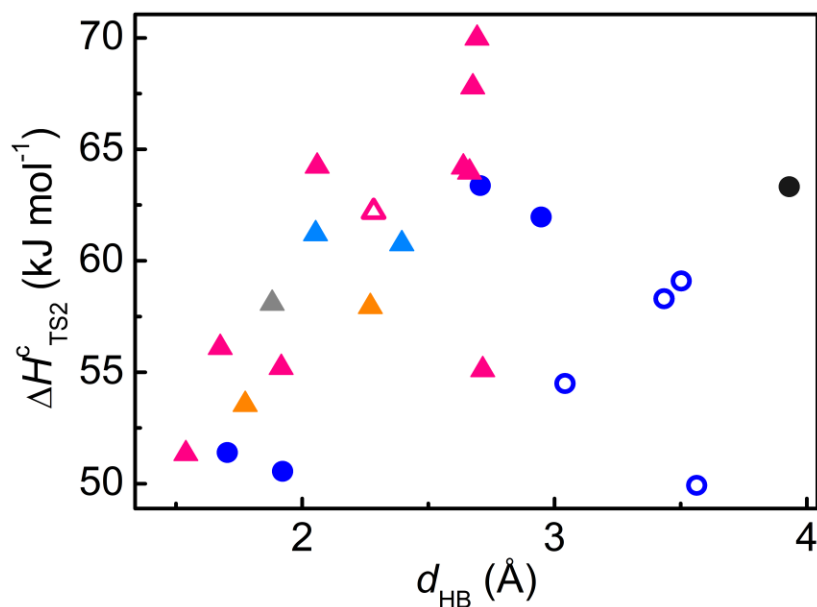


Figure S9. Enthalpy barrier for $C \rightarrow D$, ΔH_{TS2}^c , vs. the hydrogen bond length in TS2, d_{HB} , as obtained at the UM06-L/def2-TZVP level for the **meta** (squares, purple), **up** (circles, blue), and **hb** clusters (triangles: **hb-CH₂**, light blue; **hb-SO₂**, grey; **hb-CO**, orange; **hb-NH**, magenta) on the pentadectet spin surface taking separated reactants as zero of the enthalpy (data in Tables S10-S12). The scatter for **up-H** is reported in black to facilitate the comparison. The empty scatters are used for the complexes where the ring substituent acts as a hydrogen bond acceptor.

A plot similar to Figure 7 is reported in Figure S10, y-axis is the reaction enthalpy for C-H bond scission instead of the activation enthalpy as in Figure 7.

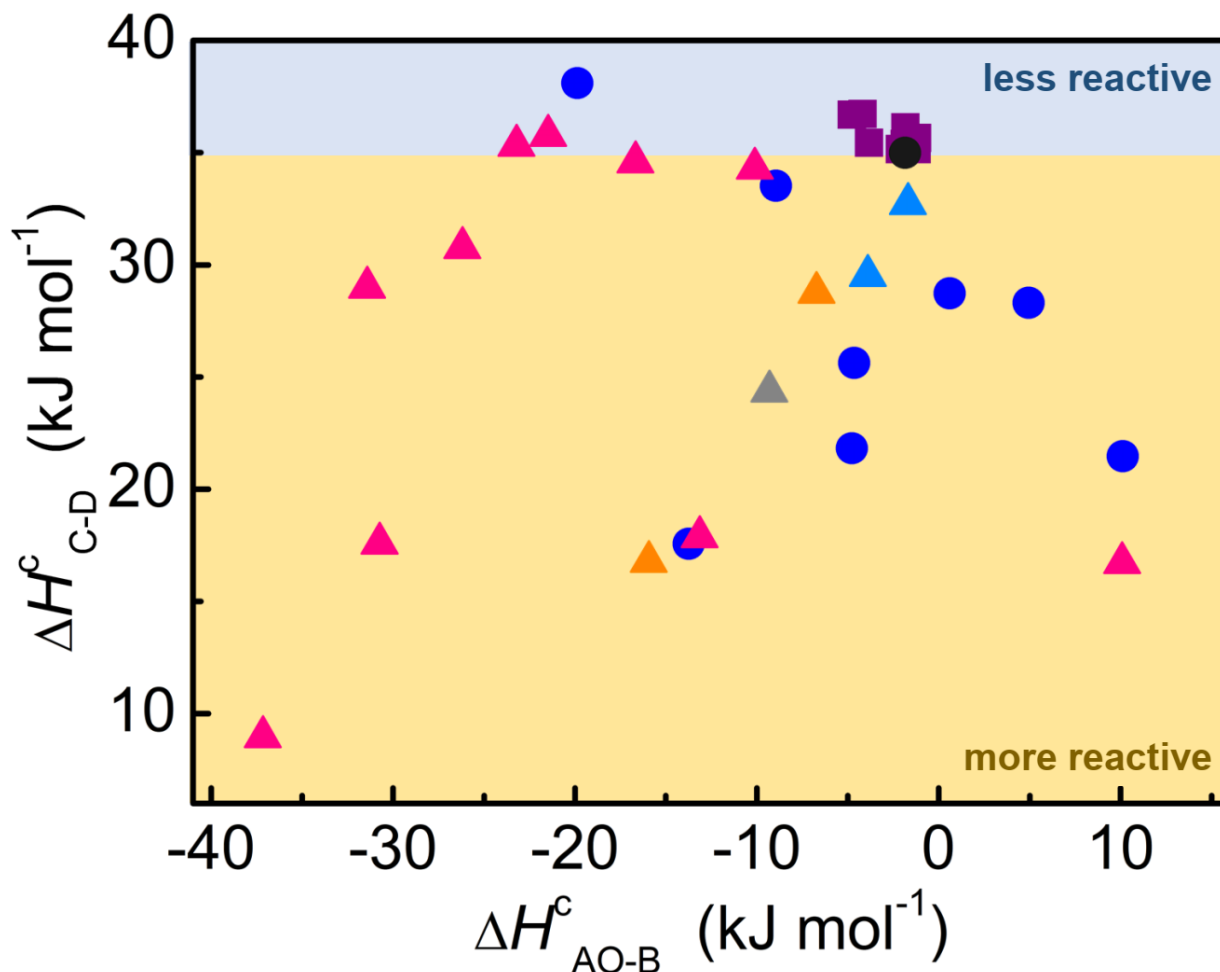


Figure S10. Reaction enthalpy for $C \rightarrow D$, $\Delta H_{C \rightarrow D}$, vs. the reaction enthalpy for $AO \rightarrow B$, $\Delta H_{AO \rightarrow B}$, at the UM06-L/def2-TZVP level following the cycle reported in Figure 1 for the *meta* (squares, purple), *up* (circles, blue), and *hb* clusters (triangles: *hb*-CH₂, light blue; *hb*-SO₂, grey; *hb*-CO, orange; *hb*-NH, magenta) on the pentadectet spin surface taking separated reactants as zero of the enthalpy (data in Tables S16-S18). The scatter for *up*-H is reported in black to facilitate the comparison. The graph is divided in two areas, dividing the ferryl more catalytically active than *up*-H (yellow background) and the less active ones (blue background). The blue line is obtained by fitting all the *up* clusters besides *up*-COOH and *up*-SO₃H.

Figure S11 shows the linear correlation between the hydrogen affinity and the $C \rightarrow D$ reaction enthalpy. The corresponding R^2 increases from 0.72 to 0.91 (and the residual sum of squares, RSS, decreases from 520.6 to 152.8) if *hb*-NHCOCOOH is excluded from the fit. Although less “perfect”, a linear relation can be evidenced also between the hydrogen affinity and the enthalpy barrier for $C \rightarrow D$ too ($R^2 = 0.52$, RSS = 407.4, see Figure S12).

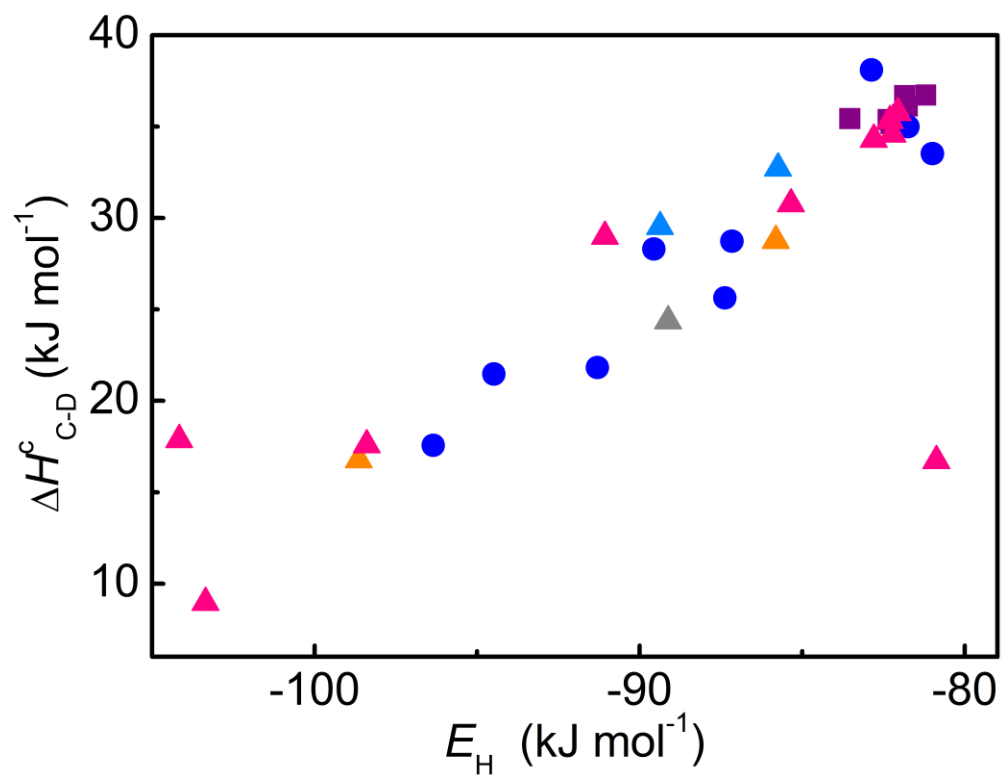


Figure S11. Reaction enthalpy for $C \rightarrow D$, $\Delta H_{C \rightarrow D}$, vs. the hydrogenation energy, E_H at the UM06-L/def2-TZVP level following the cycle reported in Figure 1 for the *meta* (squares, purple), *up* (circles, blue), and *hb* clusters (triangles: *hb*-CH₂, light blue; *hb*-SO₂, grey; *hb*-CO, orange; *hb*-NH, magenta) on the pentadectet spin surface taking separated reactants as zero of the enthalpy (data in Tables S16-S18).

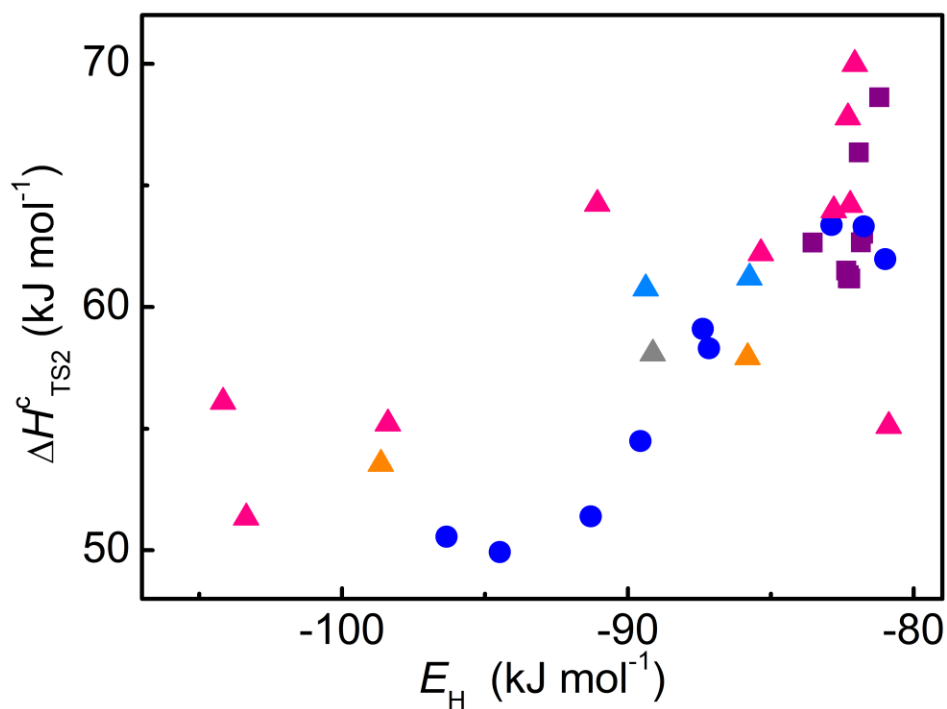


Figure S12. Enthalpy barrier for $C \rightarrow D$, ΔH^c_{TS2} , vs. the hydrogenation energy, E_H , vs. the reaction enthalpy for $C \rightarrow D$, $\Delta H_C \rightarrow D$, at the UM06-L/def2-TZVP level following the cycle reported in Figure 1 for the *meta* (squares, purple), *up* (circles, blue), and *hb* clusters (triangles: *hb*-CH₂, light blue; *hb*-SO₂, grey; *hb*-CO, orange; *hb*-NH, magenta) on the pentadectet spin surface taking separated reactants as zero of the enthalpy (data in Tables S16-S18).

S15. Electrostatic potential maps

The electrostatic potential (ESP) maps for *up*-COOH-A, *up*-H-A and *up*-NO₂-A are reported in Figure S13. It is evident that the functional group on the linkers pointing towards the iron site modifies significantly the electrostatic potential in the region around the iron site and its first coordination shell. The inductive effect of the functional group stops its effect on ESP at the C of the –COO- coordinating the iron.

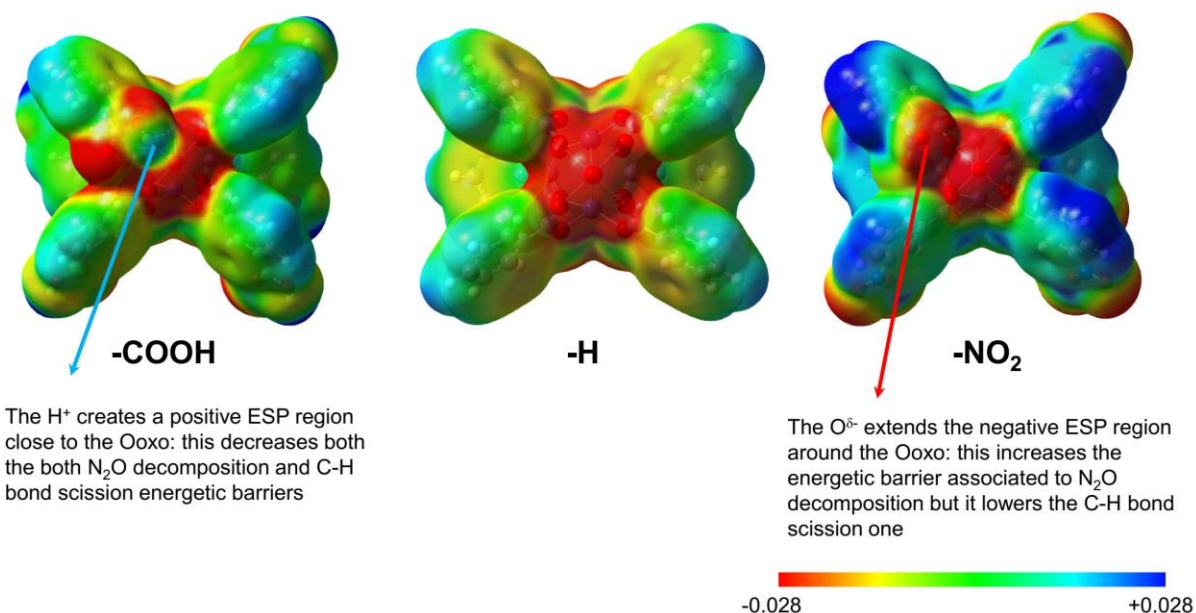


Figure S13. Electrostatic potential mapped on the 0.0004 isosurface of the total electron density for *up*-COOH-A, *up*-H-A and *up*-NO₂-A. The electrostatic potential is represented with a color scale going from red ($-2.8 \cdot 10^{-2}$ a.u.) to blue ($2.8 \cdot 10^{-2}$ a.u.).

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