Supporting Information
for

C-H functionalization of quinoline N-oxides catalyzed by Pd(II) complexes: a computational study

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Table S1. Experimental results considered for the computational work:[1,2] reactions of QO with benzaldehyde in dichloroethane.

Catalyst	Oxidant	Additive	T / °C	yield (%)	
				P1	**P2**
PdCl$_2$	TBHP[a]	-	100	52	45
	K$_2$S$_2$O$_8$	-	100	nd	48
	AgOAc	-	100	nd	nd
	BQ	-	100	nd	nd
	DTBP	-	100	nd	48
	TBHP[b]	-	100	nd	80
	TBHP[b]	H$_2$O	100	76	nd
	TBHP[b]	H$_2$O	80	70	nd
	TBHP[b]	H$_2$O	120	80	nd
	TBHP[b]	H$_2$O	140	90	nd
Pd(OAc)$_2$	*TBHP[a]*	-	*100*	*traces*	*30*
		[a] 70 aq.% [b] 5-6M in decane			

1   (a) X. Chen, X. Cui and Y. Wu, *Org. Lett.* 2016, **18**, 2411–2414. (b) Chen, X.; Cui, X.; Wu, Y. *Org. Lett. 2016*, **18**, 3722-3725.

2   J. Wu, X. Cui, L. Chen L., G. Jiang, Y. Wu, *J. Am. Chem. Soc.* 2009, **131**, 13888-13889.
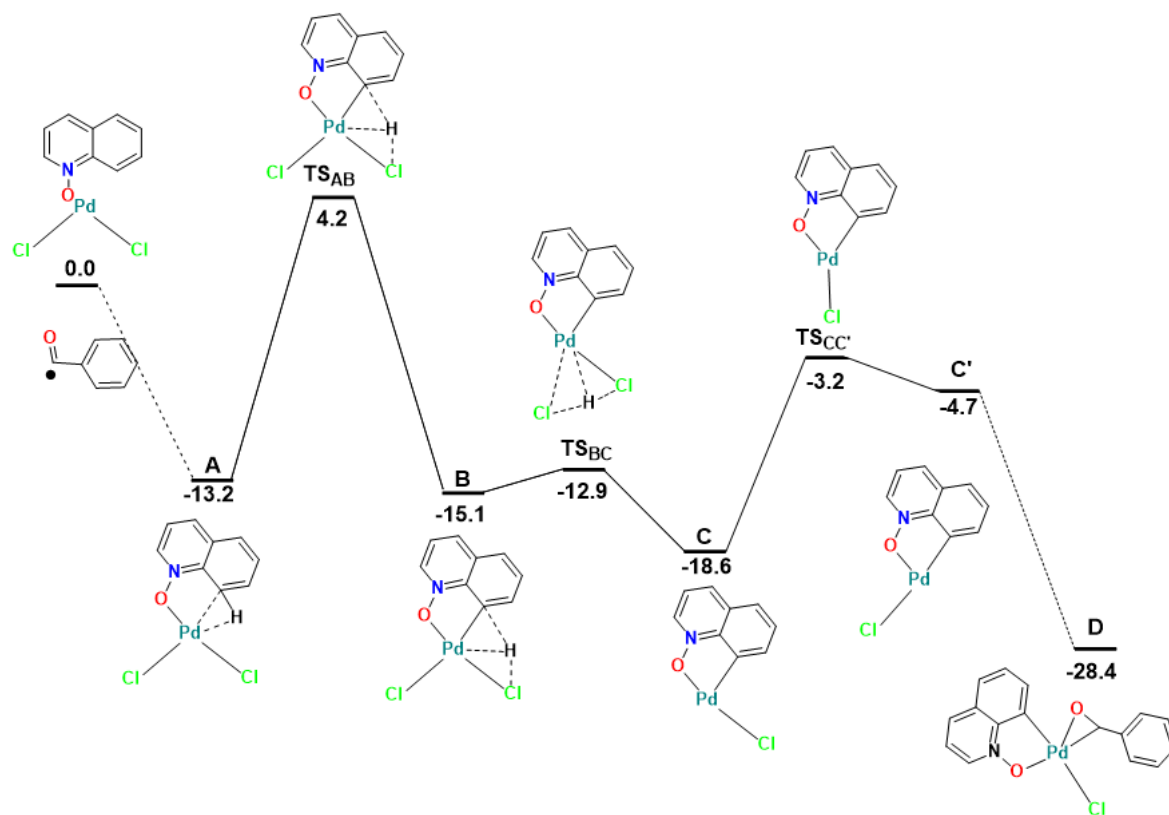
Figure S1. Energy profile for the initiating steps of the functionalization of QO at C8 (relative Gibbs energies in kcal mol^{-1} in dichloroethane).
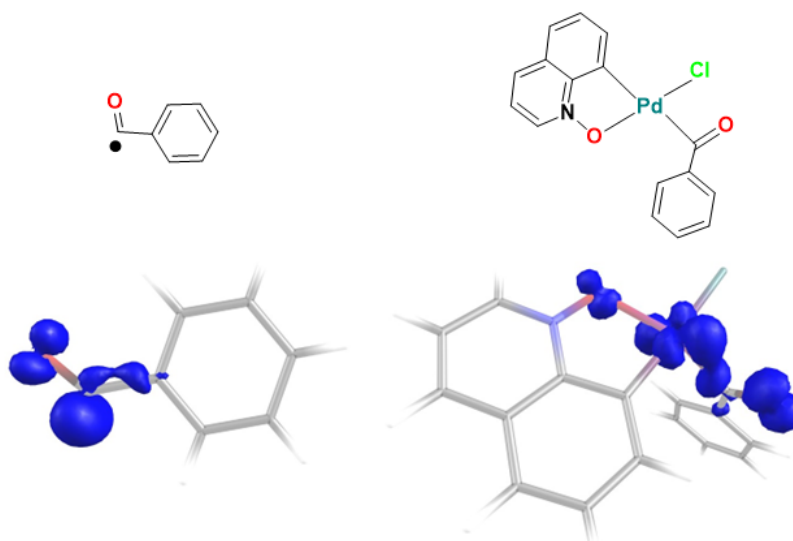
Scheme S1. Spin density of the benzaldehyde radical (•COPh, left) and the radical intermediate **D** (right).
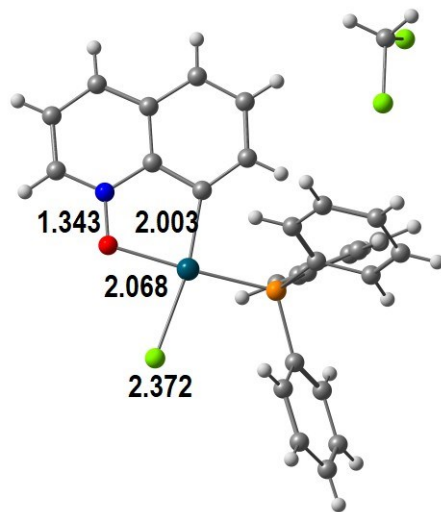
Figure S2. Single crystal X-ray diffraction structure (REFCODE INOZOC[1]) of the complex resulting from the reaction of the unsaturated intermediate **C'**, [PdCl(QO)], with PPh$_3$ (distances in Å).[2]

1 C. R. Groom, I. J. Bruno, M. P. Lightfoot, S. C. Ward, The Cambridge Structural Database, *Acta Cryst*. 2016, **B72**, 171-179.
2 X. Chen, X. Cui and Y. Wu, *Org. Lett.* 2016, **18**, 2411–2414.
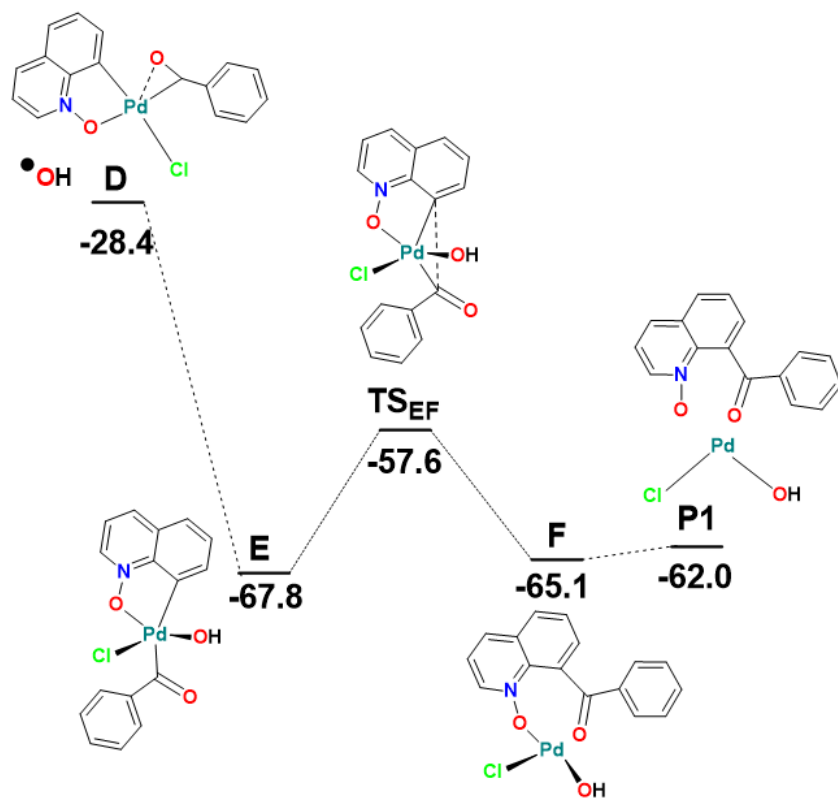
Figure S3. Energy profile for the second part of the functionalization of QO at C8 in the absence of water (relative Gibbs energies in kcal mol^{-1} in dichloroethane).
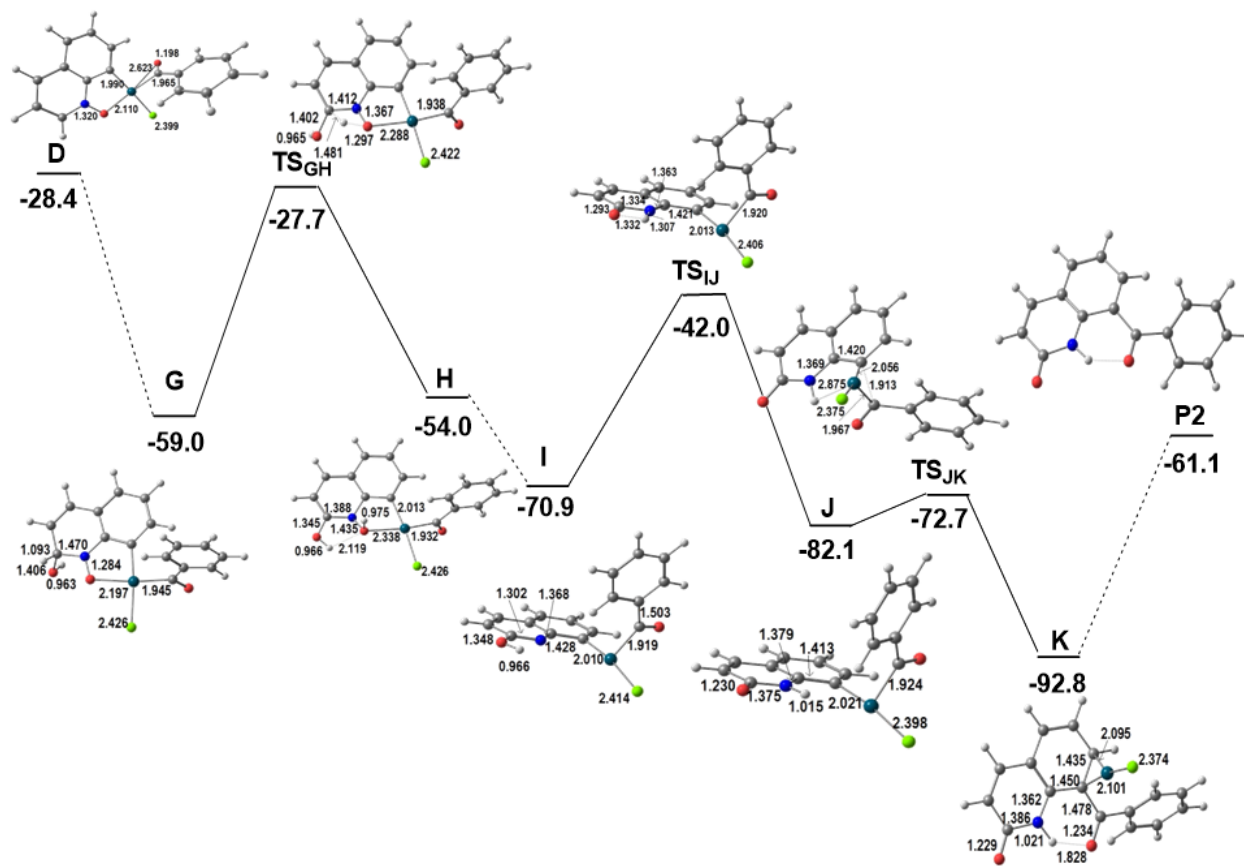
Figure S4. Energy profile for the second part of the alternative functionalization at C8 and functionalization at C2 of QO in the presence of water (relative Gibbs energies in kcal mol^{-1} in dichloroethane; distances in Å).
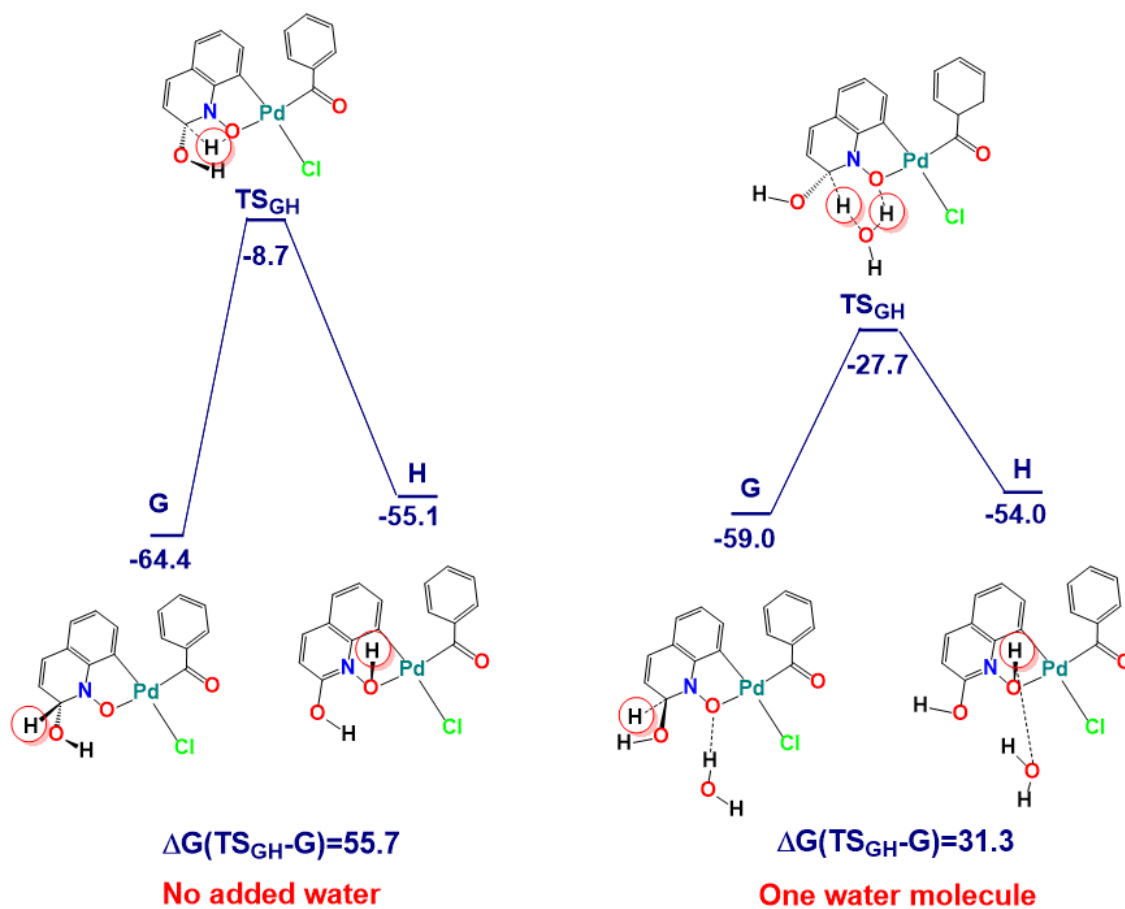
Scheme S2. Hydrogen migration from the C2 position to the oxygen atom of QO (left) and the same migration assisted by a water molecule (right, relative Gibbs energy in dichloroethane, kcal mol^{-1}).

Figure S5. Energy profile for isomerization between **P1** and **P2** (relative Gibbs energies in kcal mol^{-1} in dichloroethane; distances in Å).

Figure S6. Energy profile for the functionalization of QO at C2 (relative Gibbs energies in kcal mol^{-1} in dichloroethane; distances in Å).

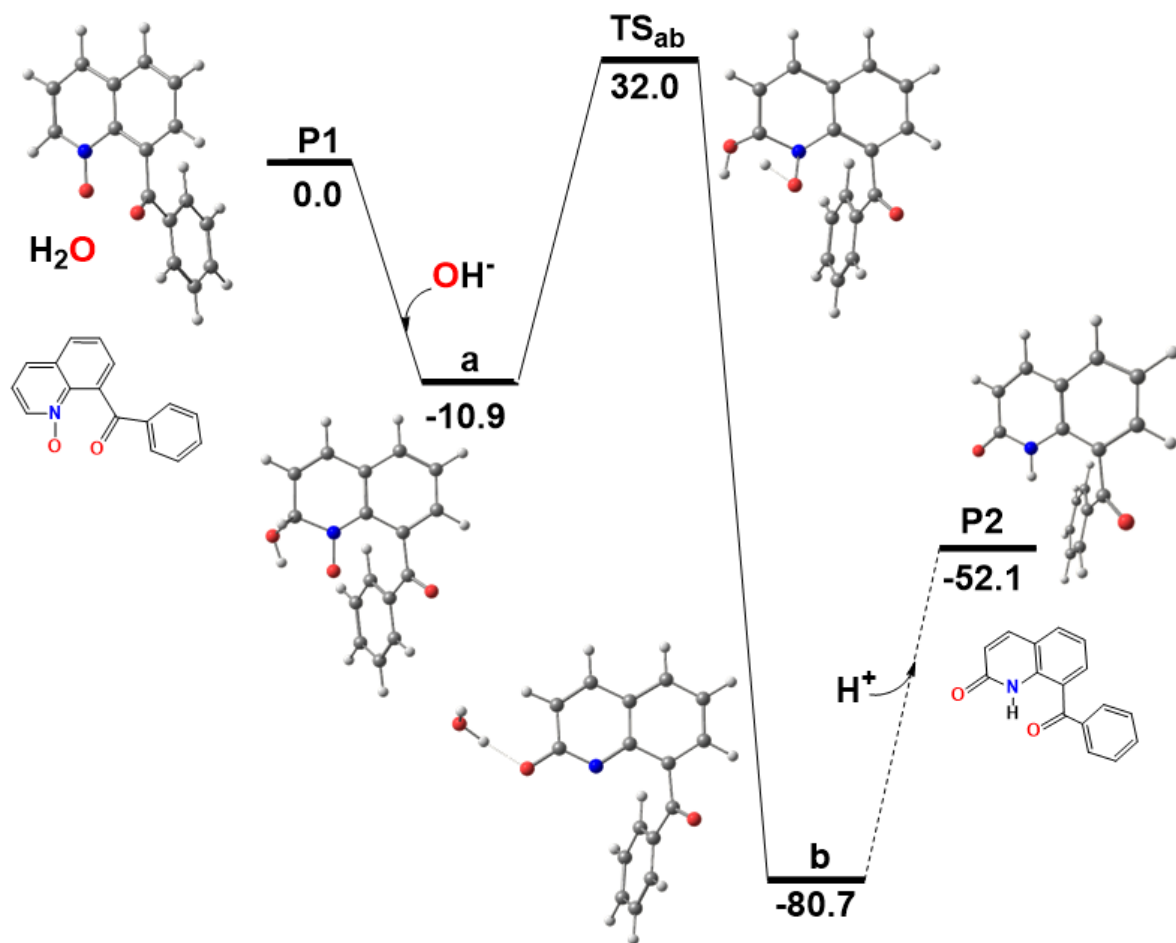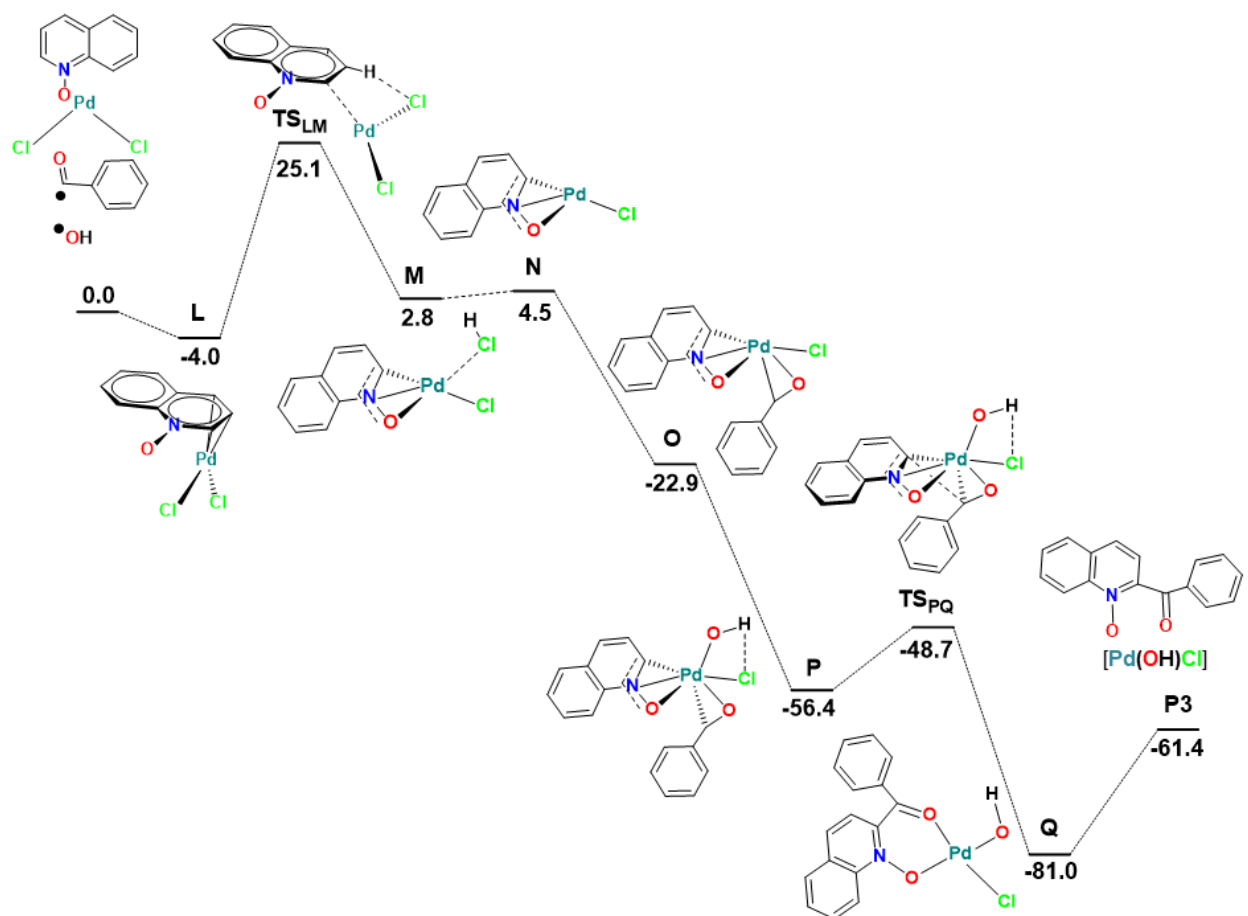**Table S2**. Energy Decomposition Analysis (EDA, kcal mol^{-1}) addressing the interaction between QO with PdCl$_2$ in intermediates **A** (σ bonding) and **L** (π bonding).

	A	L
ΔE_{Pauli}	154.6	146.3
ΔE_{elec}	-126.9	-91.2
ΔE_{oi}	-74.22	-90.3
ΔE_{solv}	-5.12	3.5
ΔE_{int}	**-51.6**	**-38.7**
ΔE_{prepQO}	12.4	7.3
$\Delta E_{prepPdCl_2}$	2.5	3.0
ΔE_{prep}	14.9	10.3
BE	**-36.7**	**-28.4**

In the Energy Decomposition Analysis (EDA), the interaction energy is divided in different energy terms. The interaction energy (ΔE_{int}), defined as the difference between the energy of the molecule and the sum of the energy of the two fragments (with the same geometry), is split into three terms. ΔE_{Pauli} is the repulsive contribution from the interaction between occupied orbitals, ΔE_{elec} corresponds to the classical electrostatic interaction between the charge distributions of the fragments, and ΔE_{oi} represents the charge transfer between fragments (covalent interaction). When the solvent is considered in the calculations, another term must be added (ΔE_{solv}).

$$\Delta E_{int} = \Delta E_{Pauli} + \Delta E_{elec} + \Delta E_{oi} \; (+ \; \Delta E_{solv})$$

The interaction energy can be related to the bonding energy (BE), defined for **A** (or other species) as the energy difference between the energy of the molecule and the sum of the energies of the fragments after they have relaxed to their minimum energy. The energy difference between the fragment with its geometry in the complex and after relaxation is called ΔE_{prepF}, the sum for the two fragments being $\Delta E_{prep.}$

$$BE = E_A - (E_{QO} + E_{PdCl2}) = \Delta E_{int} + \Delta E_{prep}$$

Table S3. Free energies in dichloroethane (kcal mol^{-1}) for the C-H activation step of the reaction of QO with benzaldehyde catalyzed by PdCl$_2$. The mean absolute error (MAE) relative to the CCSD(T) calculations is also given.

Method / Species	CCSD(T) /def2-tzvpp	M06-2X(D3)/ def2-tzvpp	M06-2X(D3)/ 6-311G**	PBE0 /6-311G**	PBE0(D3) /6-311G**	PBE0(D3) /def2-tzvpp
PdCl$_2$	**0.0**	0.00.0	0.0	0.0	0.0	0.0
A	**-12.51**	-6.16	-9.80	-12.60	-16.85	-13.17
TS$_{AB}$	**3.99**	14.61	12.34	6.66	1.98	4.20
B	**-18.57**	-10.86	-13.19	-13.25	-17.52	-15.07
MAE	**0**	8.2	5.48	2.6	2.5	1.5