Table S1. Parameters resulting from the QM/MM studies. The distances (d, in angstroms), angles (∠, in degrees) and Mulliken charges (q) are associated with the optimized structures of the superoxo intermediate, peroxo transition state and ferryl intermediate shown in Figs. 6A and S4a, in their singlet spin states. E_a and ΔE (in kcal/mol) are the activation energies and total reaction energies associated with the superoxo + L-Trp → ferryl + indole 2-3-epoxide reaction along the singlet reaction coordinate; those associated with the triplet reaction are included in parentheses as comparisons. The subscripts "p" and "t" on the oxygen atoms refer to the proximal and terminal atom, respectively. $C_{2,Trp}$ and H_{Trp} stand for the C_2 atom and the indoleamine H atom, respectively, of the substrate; $N\varepsilon,_{H55}$ stands for the Nε atom of the H55 residue of xcTDO.

	hIDO			xcTDO		
	Superoxo	Peroxo	Ferryl	Superoxo	Peroxo	Ferryl
d Fe-O_p	1.858	1.876	1.668	1.772	1.810	1.667
d O_p-O_t	1.312	1.416	2.834	1.313	1.476	2.738
∠ Fe-O_p-O_t	121.0	122.6	150.6	124.1	121.5	149.7
q O_2	-0.377	-0.563	-	-0.371	-0.541	-
q Trp-O_t[a]	-	0.112	0.064	-	-0.033	-0.060
q Fe-O_p[b]	-	-0.114	-0.068	-	0.035	0.058
d $N\varepsilon,_{H55}$–H_{Trp}	-	-	-	1.673	1.697	1.642
d $C_{2,Trp}$-O_t	2.848	1.755	1.486	2.685	1.636	1.484
E_a		15.5 (13.8)			11.2 (8.1)	
ΔE		-9.2 (-16.2)			-12.1 (-21.7)	

a. The total Mulliken charge including Trp and O_t; for TDO the Mulliken charge on H55 is also included.

b. The total Mulliken charge including Fe, O_p, porphyrin and proximal histidine heme ligand.