Supporting Information

Selective Synthesis of 4-Hydroxyisophorone and 4-Ketoisophorone by Fungal Peroxygenases

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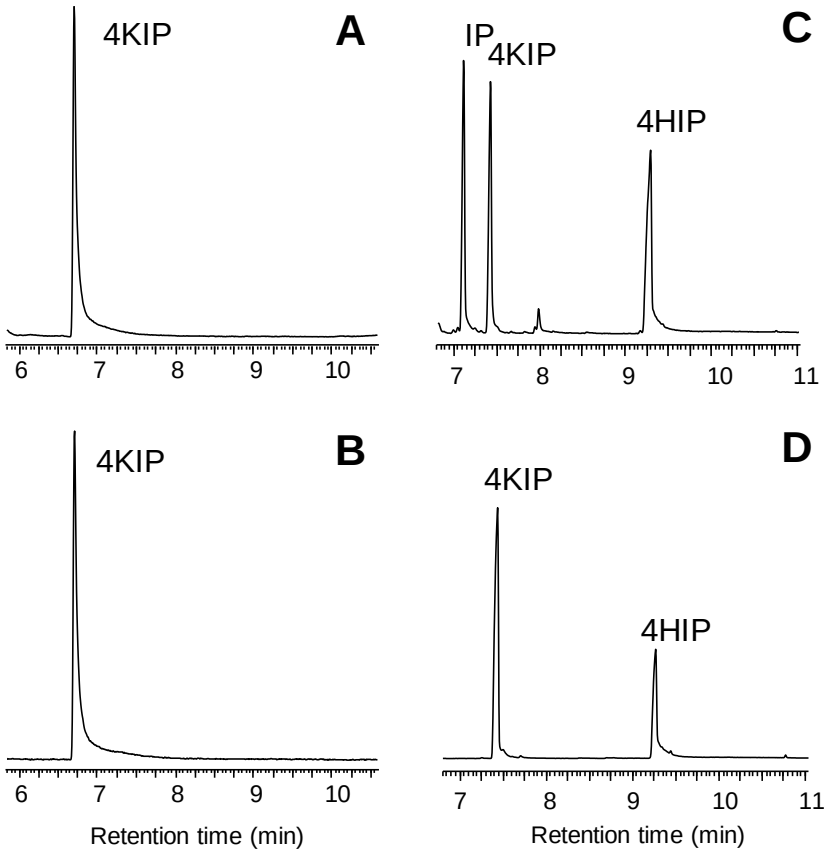

Figure S1. Comparison of GC-MS retention times of the products from isophorone (IP) reaction with *Cgl*UPO (**A**) and r*Hin*UPO (**C**), compared with the corresponding 4KIP and 4HIP (from 4KIP chemical reduction) authentic standards (**B** and **D**).

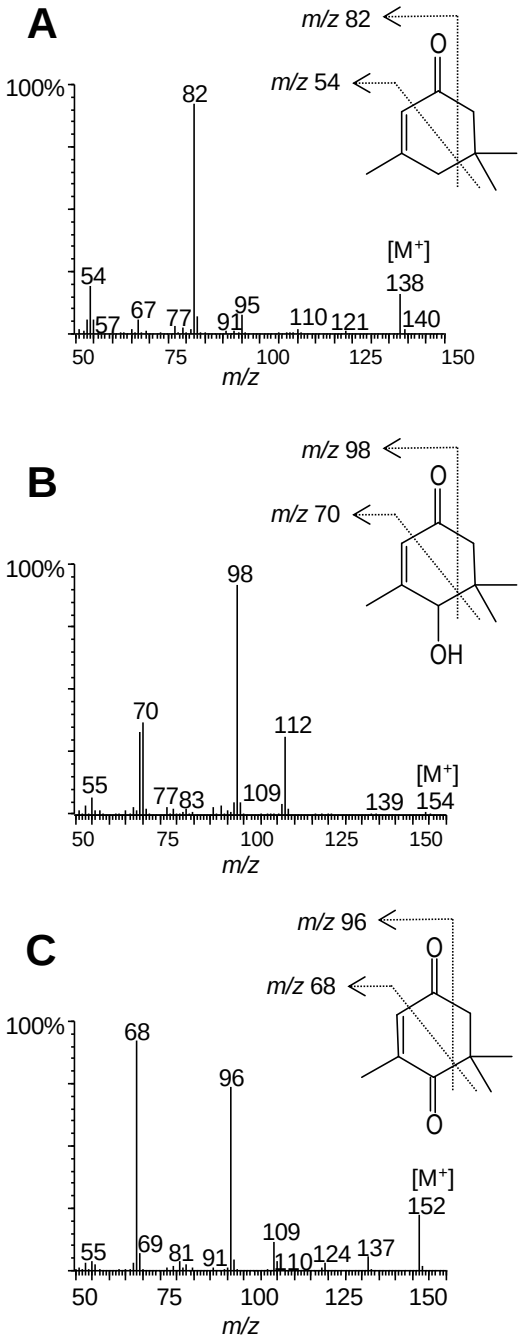

Figure S2. Mass spectra of isophorone (**A**) and the products from the enzymatic reaction with *Cgl*UPO, 4HIP (**B**) and 4KIP (**C**).

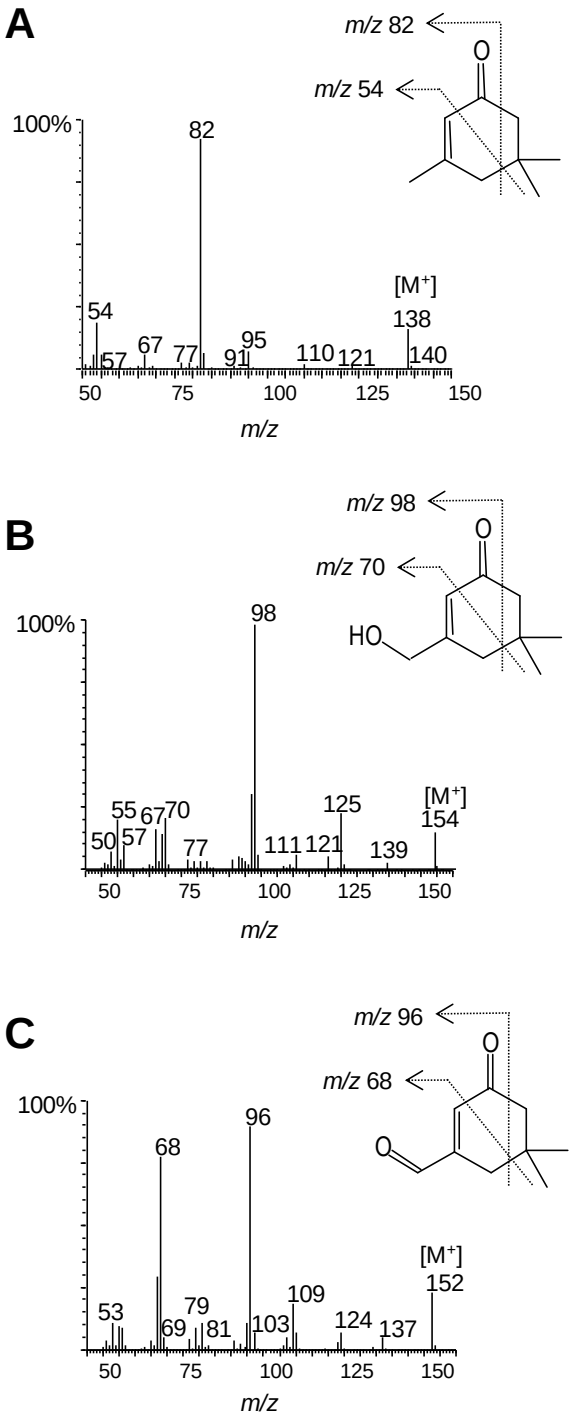

Figure S3. Mass spectra of isophorone (**A**) and the products from enzymatic reaction 7HIP (**B**) and 7FIP (**C**).

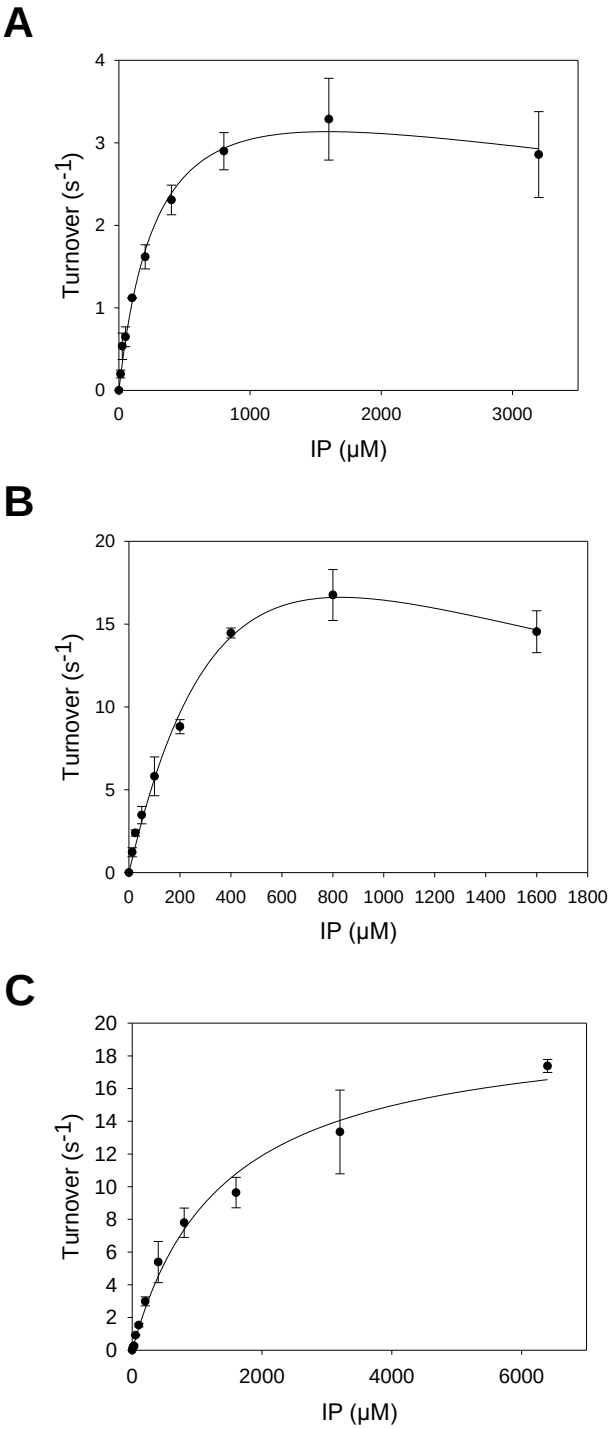

Figure S4. Kinetic curves of enzymatic hydroxylation of isophorone (IP) by *Cgl*UPO (**A**), r*Hin*UPO (**B**) and *Aae*UPO (**C**) from GC-MS estimation of 4HIP/4KIP formation (initial rates), adjusted as described in Experimental.

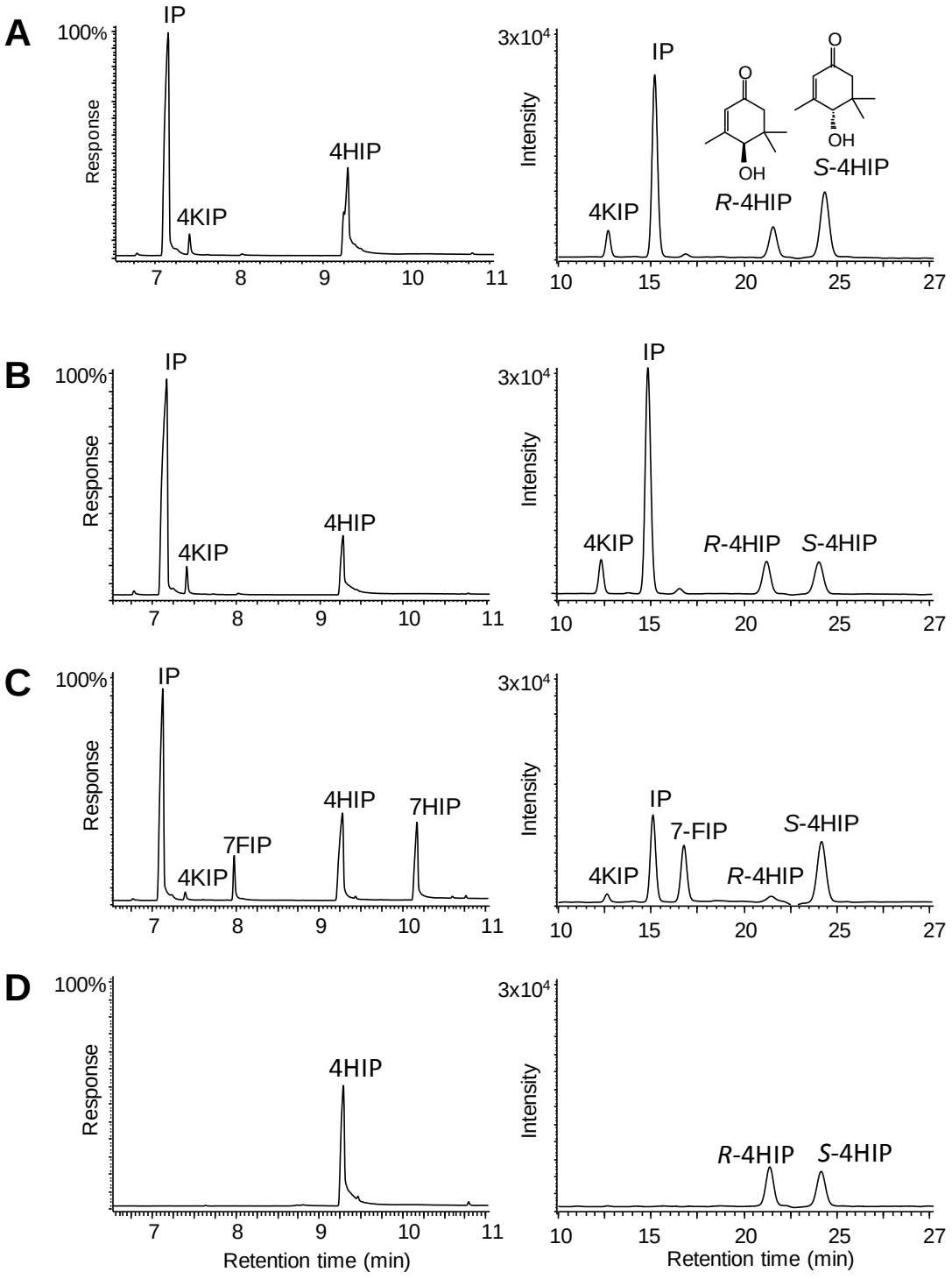

Figure S5. GC-MS (*left*) and chiral HPLC (*right*) analyses of isophorone (IP) hydroxylation by *Cgl*UPO (**A**), r*Hin*UPO (**B**) and *Aae*UPO (**C**) and the chemical reduction of 4KIP (**D**), showing the *R*-4HIP, *S*-4HIP, 4KIP and 7FIP products.

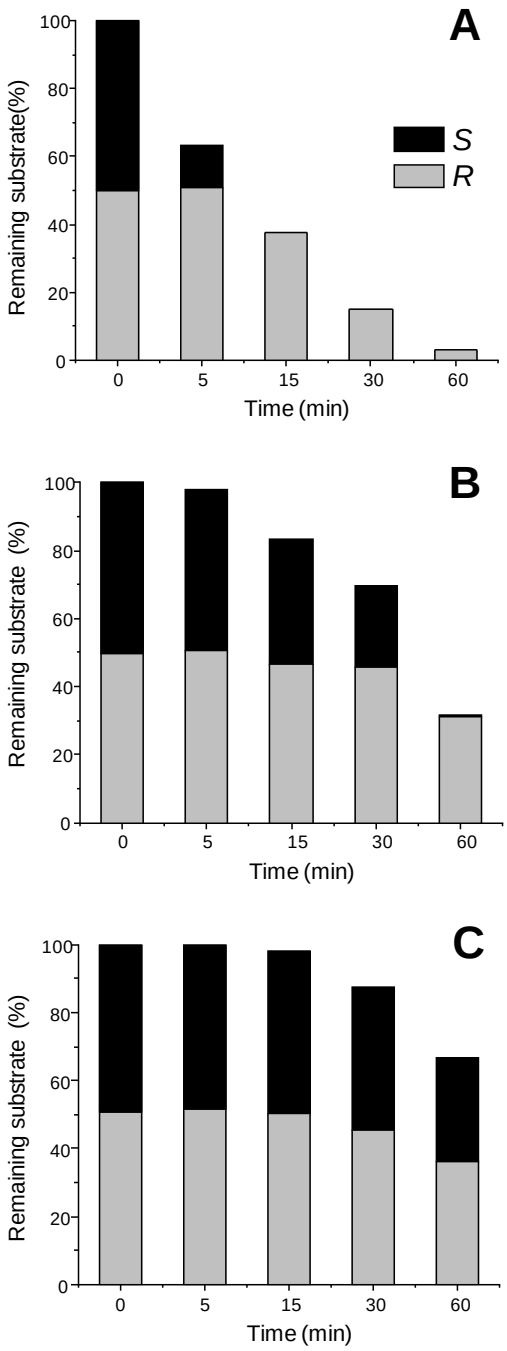

Figure S6. *R*-4HIP and *S*-4HIP enantiomers during reaction of 4-hydroxyisophorone (4-HIP) racemate with r*Hin*UPO (**A**), *Cgl*UPO (**B**) and *Aae*UPO (**C**), in percentage (%) of the initial chiral substrate.

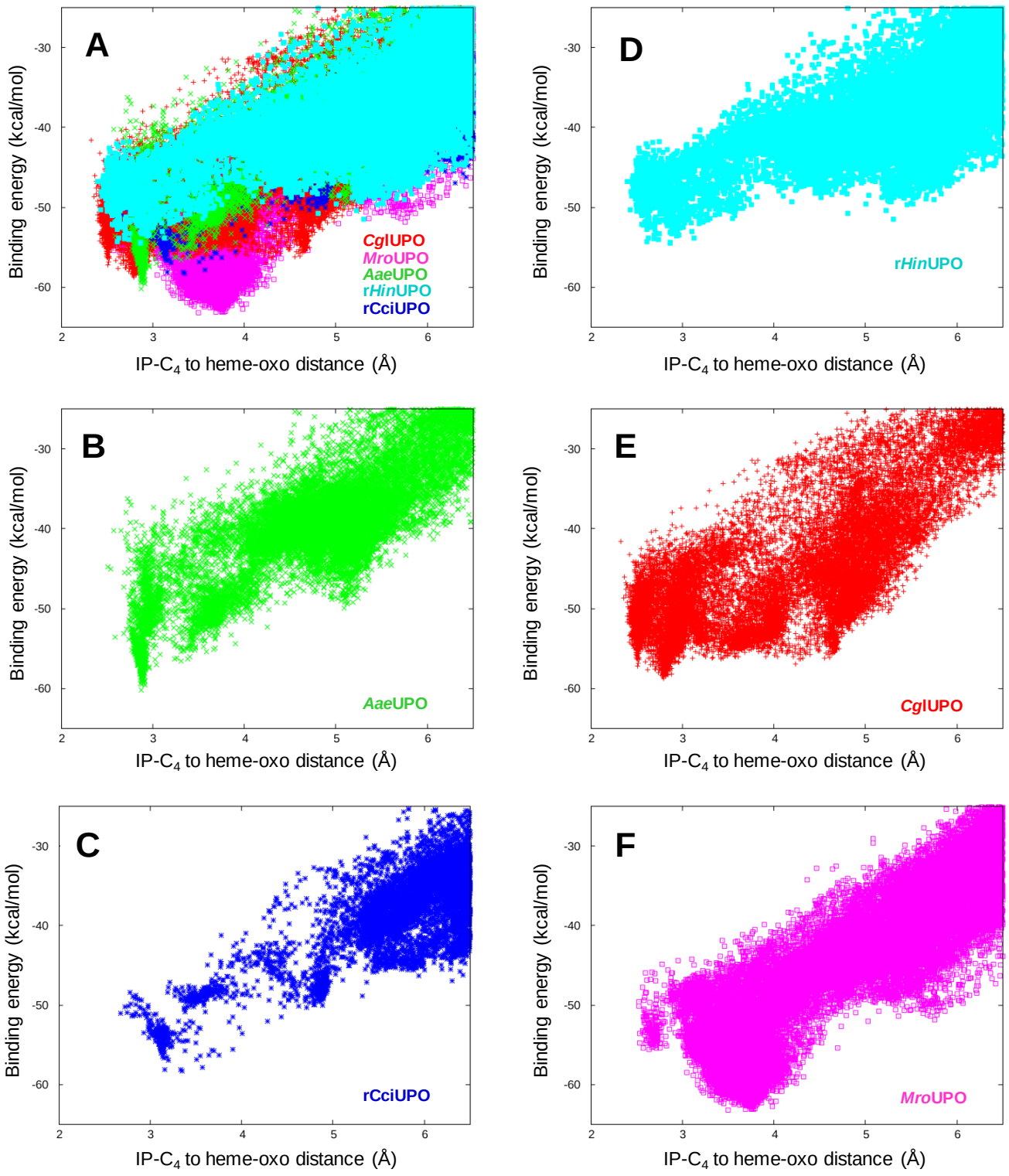

Figure S7. Individual PELE plots for isophorone (IP) diffusion in *Aae*UPO (**B**), r*Cci*UPO (**C**), r*Hin*UPO (**D**), *Cgl*UPO (**E**) and *Mro*UPO (**F**) showing the C_4-oxo distance *vs* the binding energy, compared with the overlapping plots shown in **Figure 4A** (**A**).

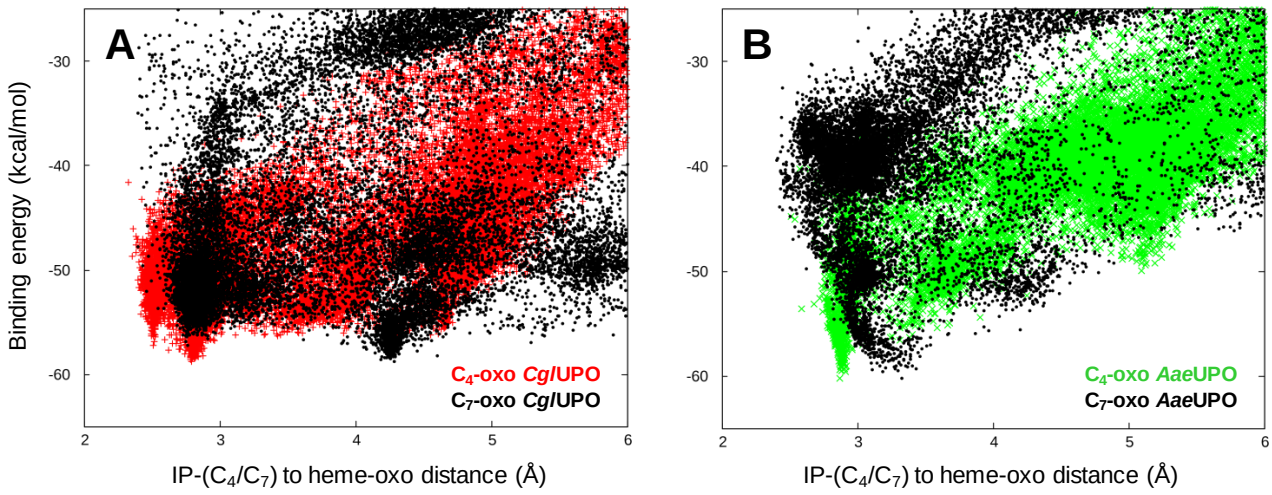

Figure S8. Comparison of C_4- and C_7-oxo distances *vs* binding energy during isophorone (IP) diffusion on *Cgl*UPO (**A**) and *Aae*UPO (**B**) using adaptive PELE.[41] For the same binding energy, the C_7 distances are always shown by black dots, while the C_4 distances for *Cgl*UPO and *Aae*UPO are shown by *red* and *green* dots, respectively.