



**Figure S3. Bond types shared in the overall reactions of functional analogs.** Enzymes were clustered according to similarities of overall reactions into three groups as defined in Table 1 (group 1 consisted only of EC sub-subclasses with similar overall reactions, group 2 consisted of EC sub-subclasses with both similar and non-similar reactions, and group 3 consisted only of EC sub-subclasses with non-similar reactions). Only bond types conserved in all members of a sub-subclass were considered, displayed from most common (left) to least common (right). These ten bond types correspond, from left to right, to the 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>, 4<sup>th</sup>, 5<sup>th</sup>, 6<sup>th</sup>, 7<sup>th</sup>, 8<sup>th</sup>, 10<sup>th</sup> and 37<sup>th</sup> most common bond types involved in enzyme catalyzed reactions according to Figure 10 in reference [47].