expected effect on biochemical assay:

free in H2O solution (pH 7.4)

add -R

$\Delta LogD = +1$
$\Delta LogK_i = +1$
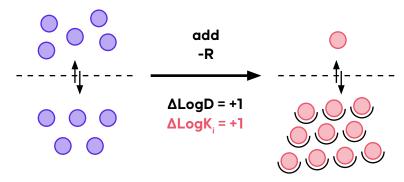
bound to lipophilic pockets in target

expected effect on off-target (e.g. hERG):

free in H_2O solution (pH 7.4)

add -R

$\Delta LogD = +1$
$\Delta LogK_i = +1$
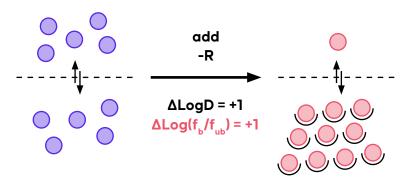
bound to lipophilic pockets in off-target

expected effect on serum protein binding:

free in H_2O solution (pH 7.4) (f_{ub})

add -R

$\Delta LogD = +1$
$\Delta Log(f_b/f_{ub}) = +1$

bound to lip. pockets in serum proteins (f_b)

net expected effects of $\Delta LogD = +1$:

10x increase in biochemical activity BUT:

No change in selectivity:

$\Delta LogK_{i\text{-target}} = +1$
$\Delta LogK_{i\text{-off-target}} = +1$
$\Delta Log(selectivity) = 0$

No change in protein-binding adjusted K_i

$\Delta LogK_{i\text{-target}} = +1$
$\Delta Log(f_b/f_{ub}) = +1$
$\Delta LogK_{i\text{-target}} - \Delta Log(f_b/f_{ub}) = 0$

drug hunter