Supporting Information

Scheme 1: DYNAFIT Reaction Mechanism and Differential Equations

REACTION MECHANISM[a]

E + S <===> ES : k1 k-1
ES —> FS : k2
FS + O2 <===> FSO2 : k3 k-3
FSO2 —> GSO2 : k4
GSO2 —> HSO : k5
HSO —> EP : k6
EP <===> E + P : k7 k-7
GSO2 —> E + S + H2O2 : k8
HSO —> E + S + H2O : k9

[a] E = ferric P450, S = *p*-alkoxyacylanilide substrate, F = ferrous P450, O2 = O_2, GSO2 = $(FeO_2)^+S$ complex, HSO = $(FeO)^{3+}$ S complex or an alternate complex capable of oxygenation, P = product (phenol or acetol), H2O2 = H_2O_2, H2O = H_2O. All rates are in min^{-1} (first-order) or min^{-1} M^{-1} (second-order).

DIFFERENTIAL EQUATIONS

d[E]/dt = -k1[S]+k-1[ES]+k7[EP]-k-7[E][P]+k8[GSO2]+k9[HSO]
d[S]/dt = -k1[E][S]+k-1[ES]+k8[GSO2]+k9[HSO]
d[ES]/dt = +k1[E][S]-k-1[ES]-k2[ES]
d[FS]/dt = +k2[ES]-k3[FS][O2]+k-3[FSO2]
d[O2]/dt = -k3[FS][O2]+k-3[FSO2]
d[FSO2]/dt = +k3[FS][O2]-k-3[FSO2]-k4[FSO2]
d[GSO2]/dt = +k4[FSO2]-k5[GSO2]-k8[GSO2]
d[HSO]/dt = +k5[GSO2]-k6[HSO]-k9[HSO]
d[EP]/dt = +k6[HSO]-k7[EP]+k-7[E][P]
d[P]/dt = +k7[EP]-k-7[E][P]
d[H2O2]/dt = +k8[GSO2]
d[H2O]/dt = +k9[HSO]

Supporting Information

Scheme 2: Sample DYNAFIT Operating File Used for Fitting d_3 Compound 4 *O*-Demethylation *v* vs. *S* Data (E225I) (Figure 5 of paper, "basic system")

```
;DYNAFIT script file      ./test/
;Basic mechanism for P450 1A2
; all units in uM, min
;Trial 105
[task]
data = velocities
task = fit
[mechanism]
E    +    S    <==> ES    :    k1    k-1
ES   —>   FS   :    k2
FS + O2   <==> FSO2 :    k3    k-3
FSO2 —>   GSO2 :    k4
GSO2 ->   HSO  :    k5
HSO  —>   EP   :    k6
EP   <==> E    +    P    :    k7    k-7
GSO2 —> E + S + H2O2    :    k8
HSO  —> E + S + H2O     :    k9
[constants]
k1 = 6000, k-1 = 132000
k2 = 700
k3 = 6000, k-3 = 6
k4 = 700
k5 = 110
k6 = 33
k7 = 660, k-7 = 6000
k8 = 50
k9 = 50
[sweep]
[velocity]
      variable S = from 2 to 120 step 2
      file    ./scripts/WTIVd3short.txt
[concentrations]
      E = 0.4
      O2 = 180
[responses]
      P = 1
[progress]
      delay = 0.01
[output]
  directory ./projects/P450/output/run105

[end]
```