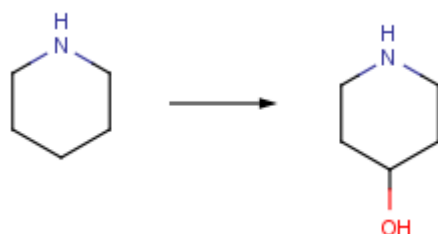
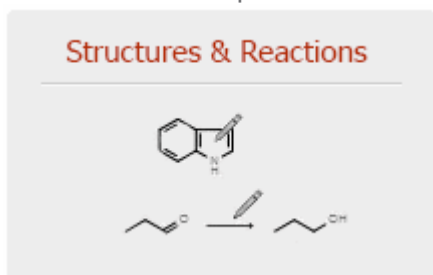


## Metabolism data: Explore the reaction details of transformations involving piperidine hydroxylation using P450

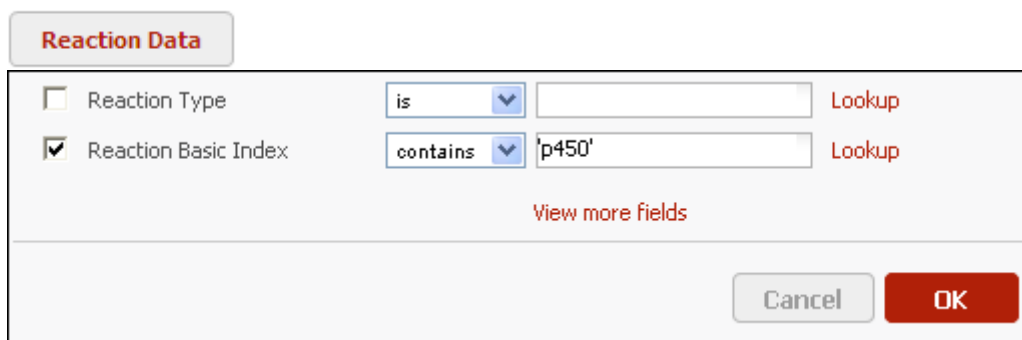


Do a substructure search for this reaction specifying that P450 is involved in the transformation.

1. Click **Structures and Reactions** from the Reaxys Start page. Click the structure box to open the structure editor (MarvinSketch is used here).



2. Draw the reaction shown above and transfer back to Reaxys. Select the **Reactions** radio button and select **Substructure on all atoms**.
3. Click to open the **Reaction Details** form. Look for the **Reaction Basic Index** field, select **Contains** from the drop-down menu, and type *p450*. (If this field does not appear in your form, click the **View more fields** link, select **Reaction Basic Index** from the list on the left, click **Add** and then click **Save** to add it to your form.)



The screenshot shows the 'Reaction Data' form. The 'Reaction Basic Index' field is checked, and the search criteria are set to 'contains' with the value 'p450'. There are 'Lookup' buttons next to the search fields. At the bottom, there are 'Cancel' and 'OK' buttons.

The final query looks like this:

Search in:  Reactions  Substances  Literature

Search as / by:  
 Product  
 Starting material  
 Reagent / Catalyst  
 Any role  
 As Drawn  
 Substructure  
 on heteroatoms  
 on all atoms  
 Similarity

Options:  
 Include tautomers  
 Ignore stereo  
 No salts  
 No mixtures  
 No isotopes  
 No charges  
 No radicals  
 No additional rings  
 Ignore Atom Mappings  
 Align results with query  
 More options

AND Reaction Basic Index contains p450

Results:

Oxydative metabolism catalyzed by CYP3A4

hydroxylation

Rx-ID: 30224878  
Find similar reactions

<p>With human cDNA-expressing cytochrome P<sub>450</sub>C<sub>3A4</sub>; Delta; -NADPH in acetonitrile        T=37°C; pH=7.4; 6-333333 h; aq. phosphate buffer        Enzymatic reaction; Kinetics; Reagent/catalyst Concentration;</p>	<p>Wang, Lifei; Zhang, Donglu; Raghavan, Nirmala; Humphreys, W. Griffith; Grossman, Scott J.; Shiang-Yuan; Goosen, Theunis C.        Drug Metabolism and Disposition, 2010, vol. 38, 4  <a href="#">Hide Title/Abstract</a> <a href="#">Full Text</a> <a href="#">View citing article</a></p>
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**In vitro assessment of metabolic drug-drug interaction potential of apixaban through cytochrome p450 phenotyping, inhibition, and**  
 Apixaban is an oral, direct, and highly selective factor Xa inhibitor in late-stage clinical development for the prevention and treatment of thromboembolic interaction potential of apixaban was evaluated in vitro. The compound did not show cytochrome P450 inhibition (IC<sub>50</sub> values >20 μM) in incubations of 11 substrates of CYP1A2, 2B6, 2C8, 2C9, 2C19, 2D6, or 3A4/5. Apixaban did not show any effect at concentrations up to 20 μM on enzyme activities or on (CYP1A2, 2B6, and 3A4/5) that are sensitive to induction in incubations with primary human hepatocytes. Apixaban showed a slow metabolic turnover in vitro with formation of O-demethylation (M2) and hydroxylation products (M4 and M7) as prominent in vitro metabolites. Experiments with human cDNA-expressing inhibitors and correlation with P450 activities in individual human liver microsomes demonstrated that the oxidative metabolism of apixaban or formation of M2 is catalyzed by CYP3A4/5 with a minor contribution of CYP1A2 and CYP2J2 for formation of M2. The contribution of CYP2C8, 2C9, and 2C19 to metabolism is minimal. In addition, a human absorption, distribution, metabolism, and excretion study showed that more than half of the dose was excreted as unchanged parent reducing the overall metabolic drug-drug interaction potential of apixaban. Together with a low clinical efficacious concentration and multiple clearance pathways, it is concluded that the metabolic drug-drug interaction potential between apixaban and coadministered drugs is low.

About 12 reactions are retrieved

Do you have an idea for a workflow example?

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