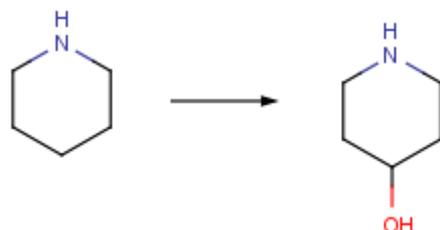


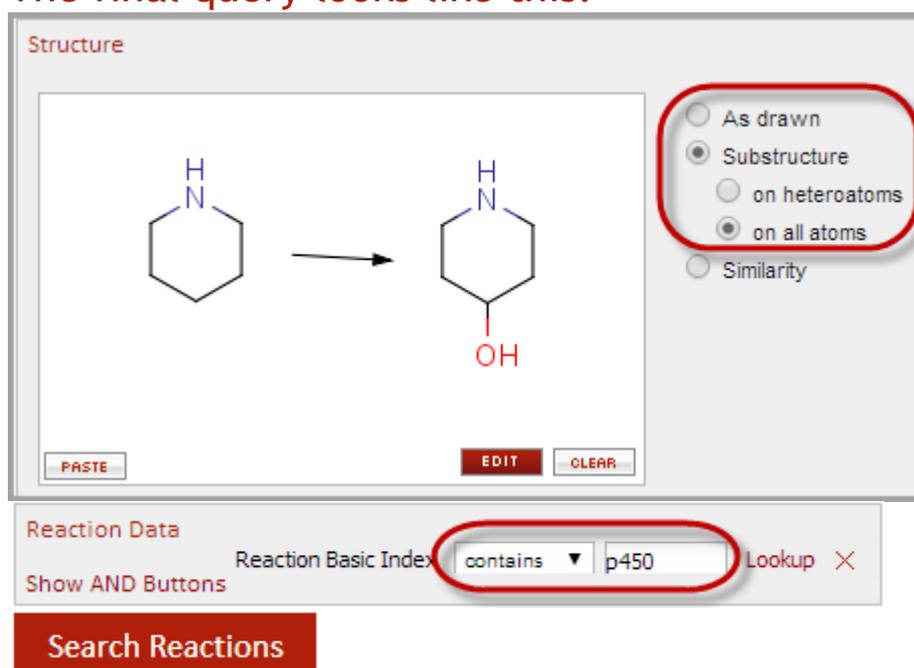
Metabolism data: Explore the reaction details of transformations involving piperidine hydroxylation using P450



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

1. Click **Reactions** theme 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 **Substructure on all atoms**.
3. The **Reaction Data** form is displayed below the structure display box. 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**, then click **Save** to add it to your form.) Click **Search Reactions**.

The final query looks like this:



Structure

As drawn
 Substructure
 on heteroatoms
 on all atoms
 Similarity

Reaction Data

Reaction Basic Index: contains p450 Lookup X

Show AND Buttons

Search Reactions

Results:

Oxydative metabolism catalyzed by CYP3A4

Rx-ID: 30224878
Find similar reactions

<p>With human cDNA-expressing cytochrome P₄₅₀3A4; beta;-NADPH in acetonitrile T=37°C; pH=7.4; 0.333333 h; aq. phosphate bufferEnzymatic reaction; Kinetics; Reagent/catalystConcentration;</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 Hide Title/Abstract Full Text View citing article</p>
<p>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 (IC50 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 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 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 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 that the metabolic drug-drug interaction potential between apixaban and coadministered drugs is low.</p>	

About 12 reactions are retrieved

Do you have an idea for a workflow example?

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