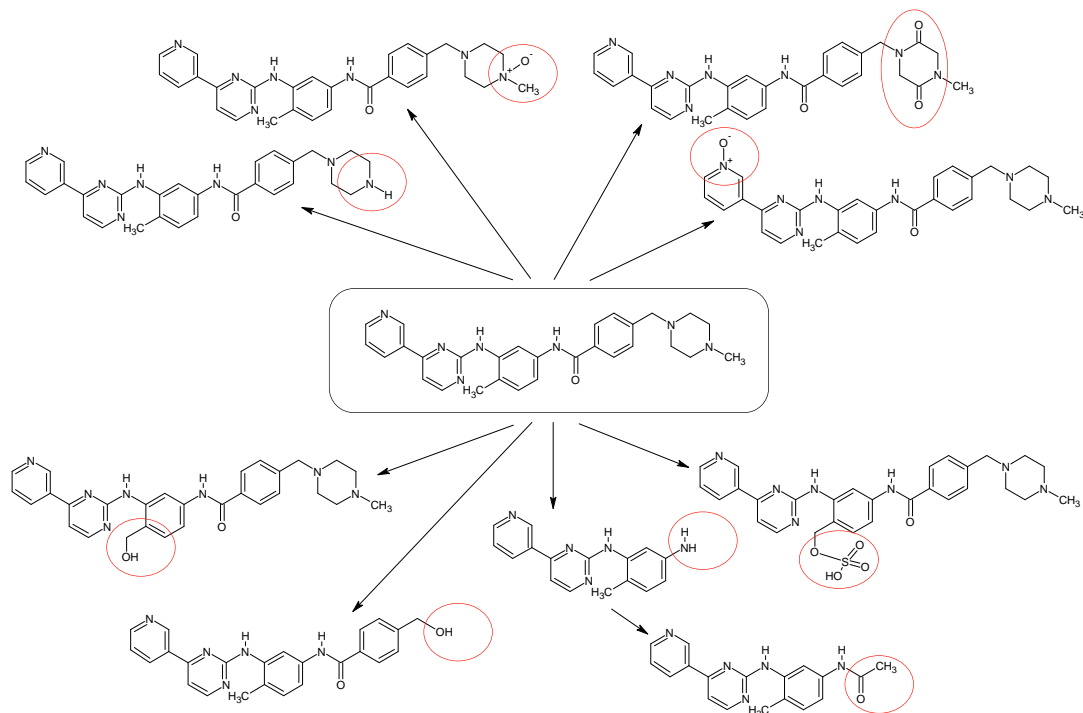


### Case study – Imatinib

Metabolism of the anticancer drug Gleevec (imatinib) proceeds primarily through *N*-demethylation of the parent, and a range of other oxidation products<sup>3</sup>.

Screening for metabolite production showed production of all reported major mammalian metabolites of imatinib, including the primary *N*-demethyl product, *N*-oxides, hydroxylations, deamination and lactam formation.

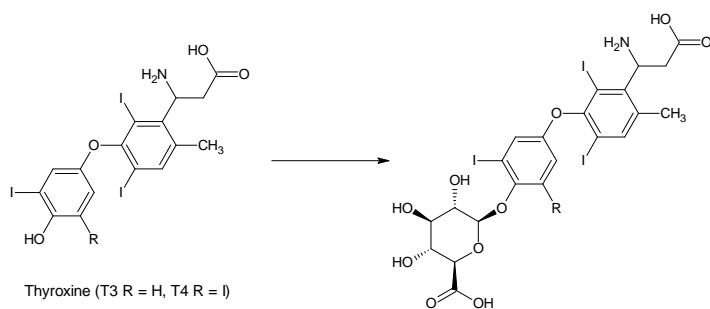
Other metabolites not seen in the study by Gschwind *et al.* were also identified.



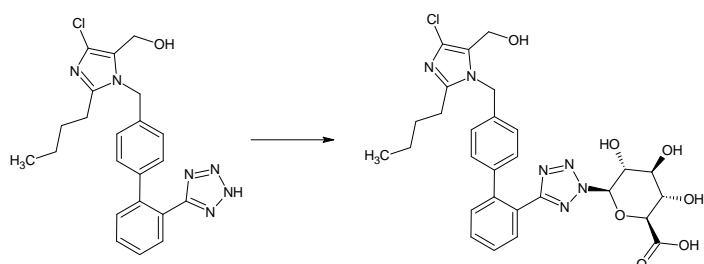
### Case study - Glucuronides

Production of glucuronides *via* synthetic chemistry can be challenging and expensive. Hypha have demonstrated the synthesis of both *O*- and *N*-glucuronides in rapid and efficient processes capable of producing large amounts of material.

#### Production of thyroxine *O*-glucuronide

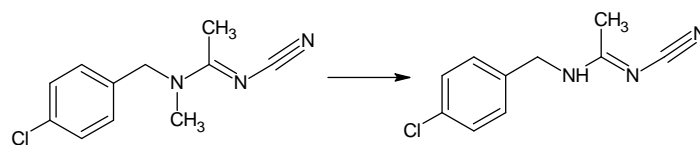


#### Production of losartan *N*-glucuronide



### Case Study - Agrochemicals

Acetamiprid is a systemic insecticide for soil and foliar application for the control of Hemiptera (esp. aphids), Thysanoptera & Lepidoptera on a wide range of crops. *N*-demethylation of the compound is the first step in its metabolism in plants & mammals and has been demonstrated at Hypha using *Streptomyces sp.*



### Our track record

<i>N</i> - and <i>O</i> -glucuronidation (+ other glycosidation)	✓
Alkyl and phenolic hydroxylation <i>N</i> -oxidation	✓
<i>N</i> - + <i>O</i> -dealkylation/ hydrogenation/ dehydrogenation	✓
Sulfation	✓
Target DMPK metabolite production rate	89%
Scale-up reproduction rate	95%

### References

Smith & Rosazza, Arch. Biochem Biophys. (1974) 161: 551-558.

Azerad, R., Adv Biochem Eng Biotechnol (1999) **63**, 169.

Gschwind, H-P., *et al.* Drug Metabolism & Distribution (2005) 33: 1503- 1512.