Syntheses and metabolism of selected general & local anesthetics

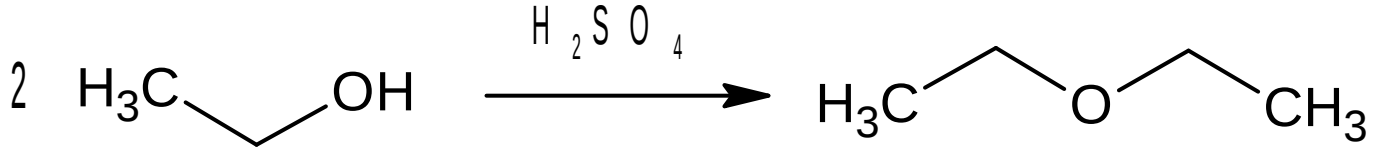
General anesthetics

Syntheses of some inhalation general anesthetics

Preparation of nitrous oxide: heating of ammonium nitrate to 180 – 250°C:

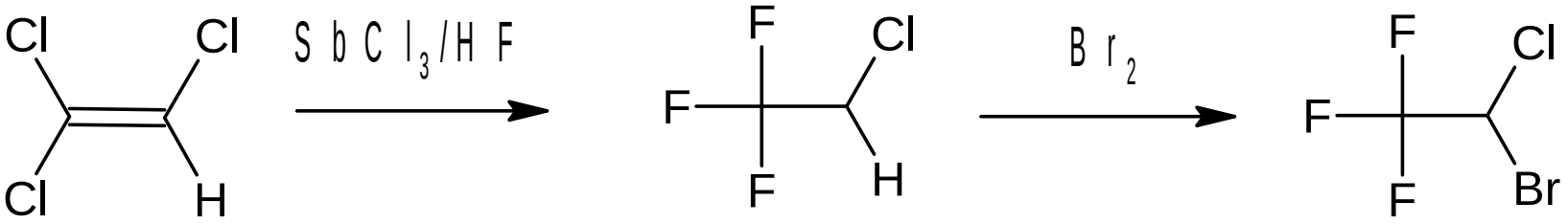
$NH_4NO_3 \rightarrow N_2O + H_2O$

Synthesis of diethyl ether

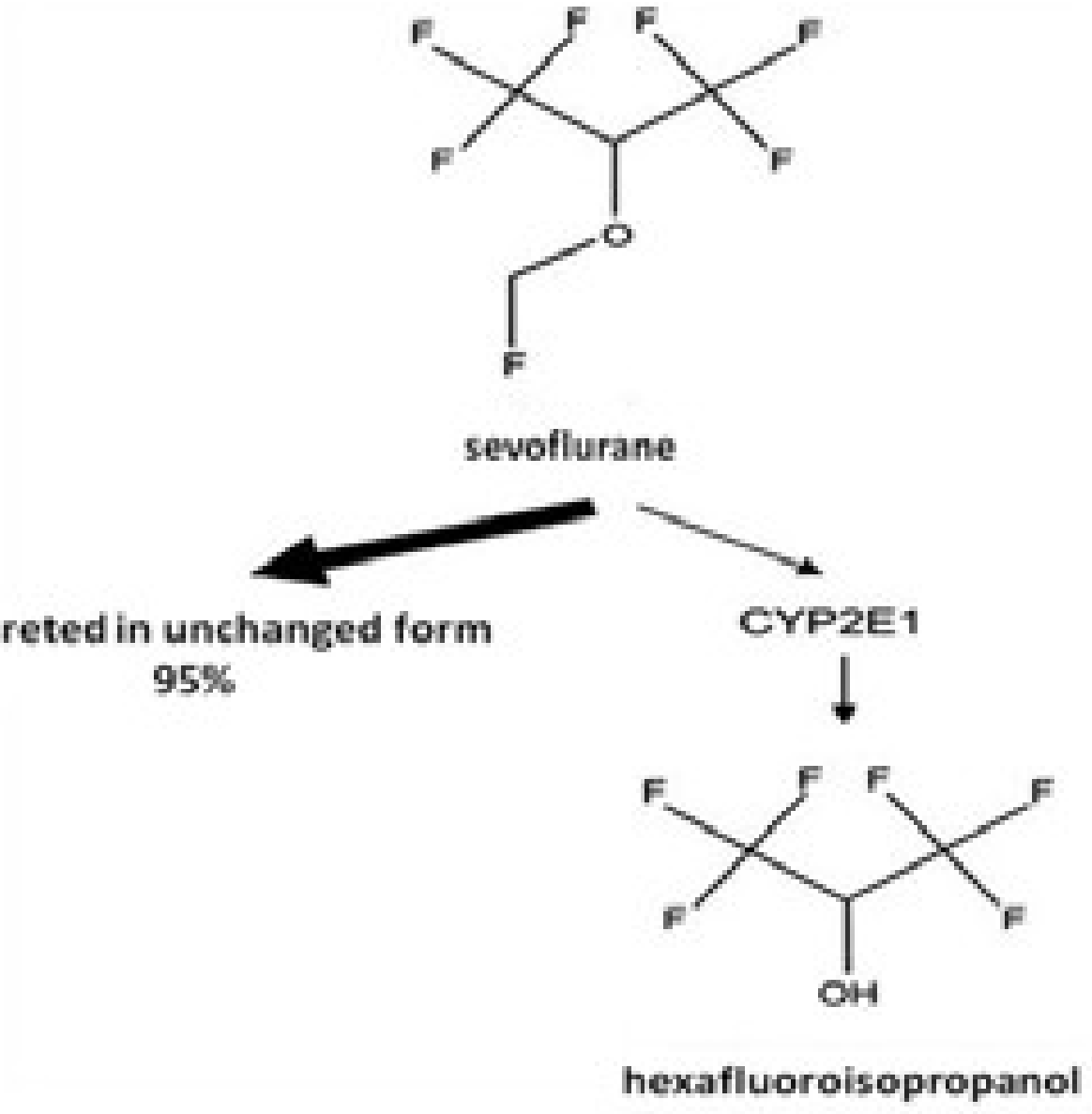


- known since 10th -11th century: Abu al-Khasim al-Zahravi Ibn Zuhr, an Arab alchemist

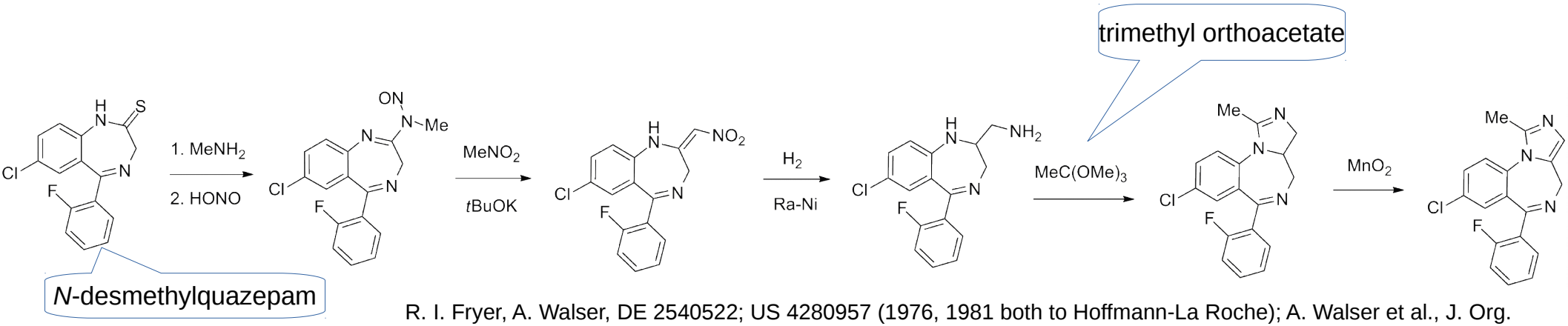
Synthesis of halothan



Metabolism of sevoflurane

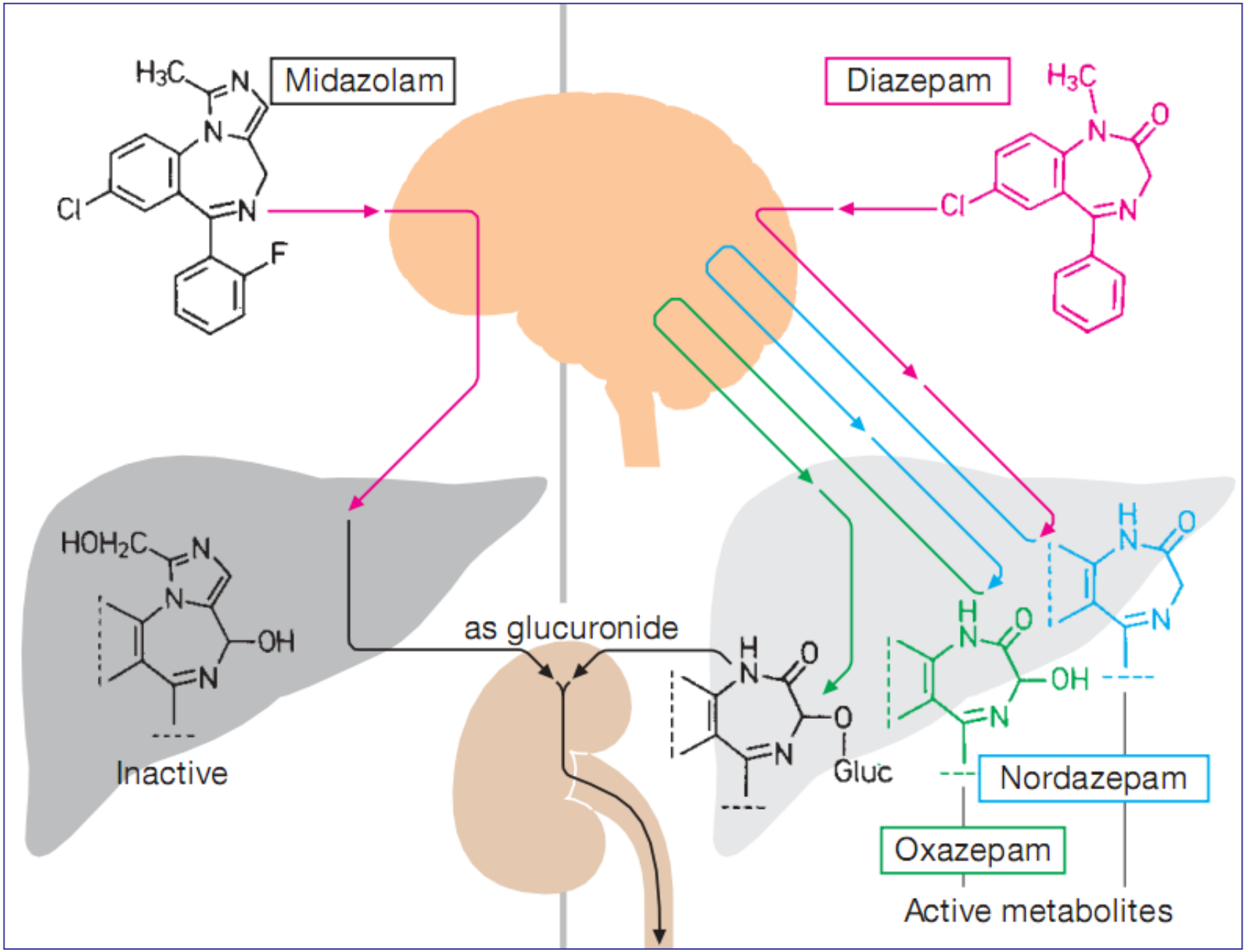


Synthesis of midazolam

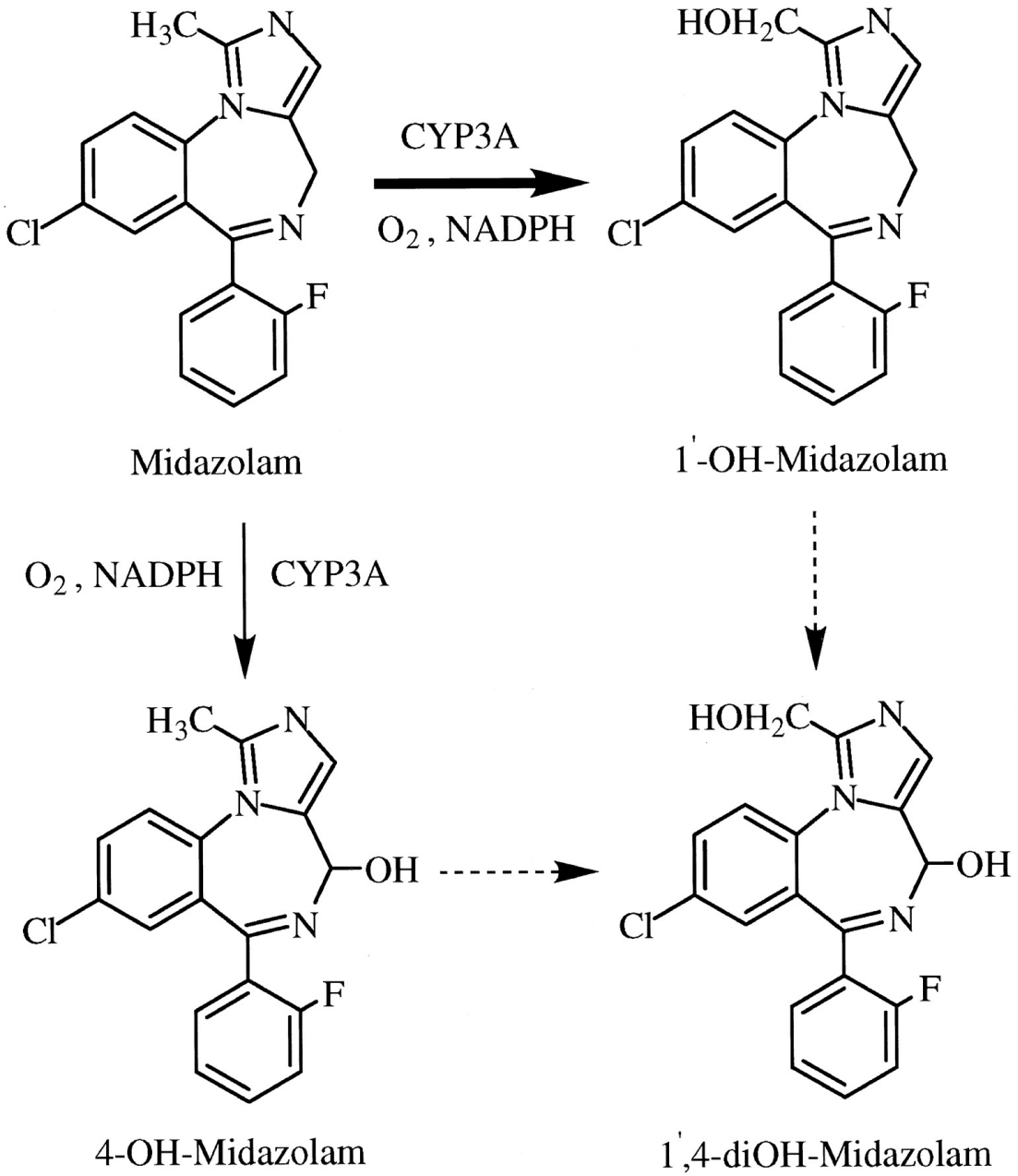


R. I. Fryer, A. Walser, DE 2540522; US 4280957 (1976, 1981 both to Hoffmann-La Roche); A. Walser et al., J. Org. Chem. 43, 936 (1978).

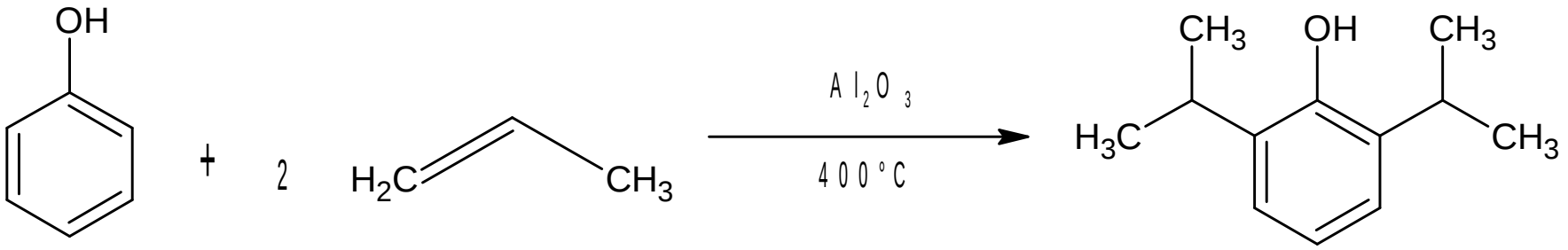
Metabolism of benzodiazepins, especially midazolam



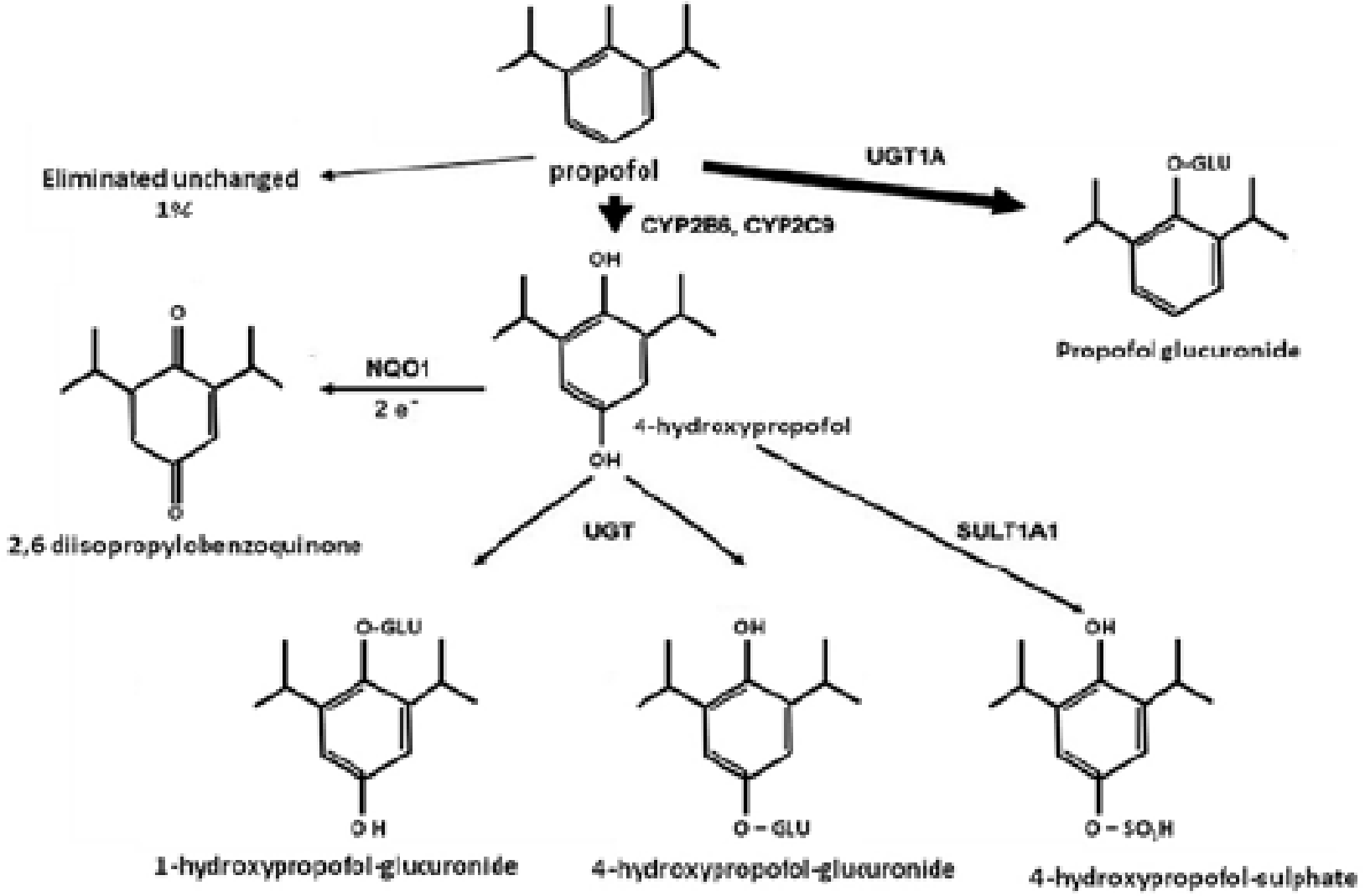
A detail of midazolam oxidative metabolism



Synthesis of propofol

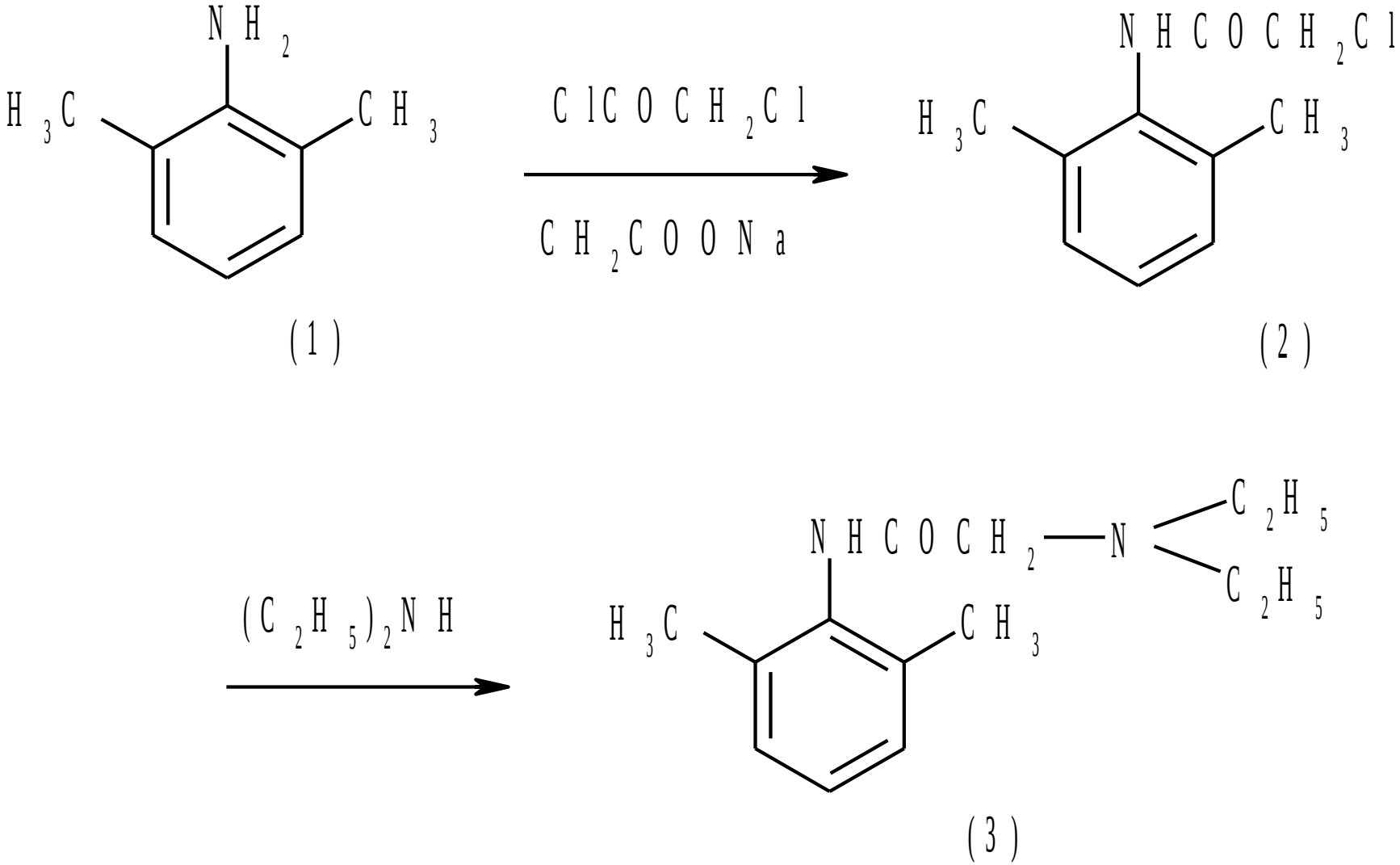


Metabolism of propofol

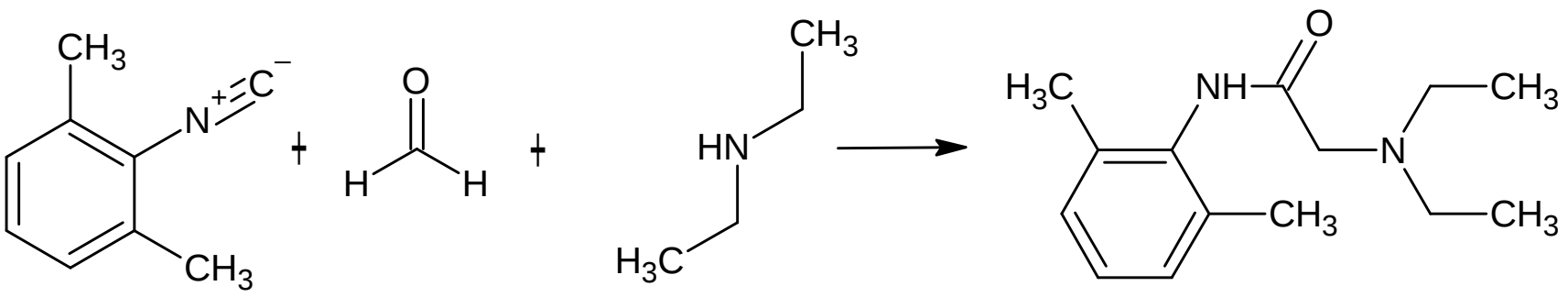


Local anesthetics

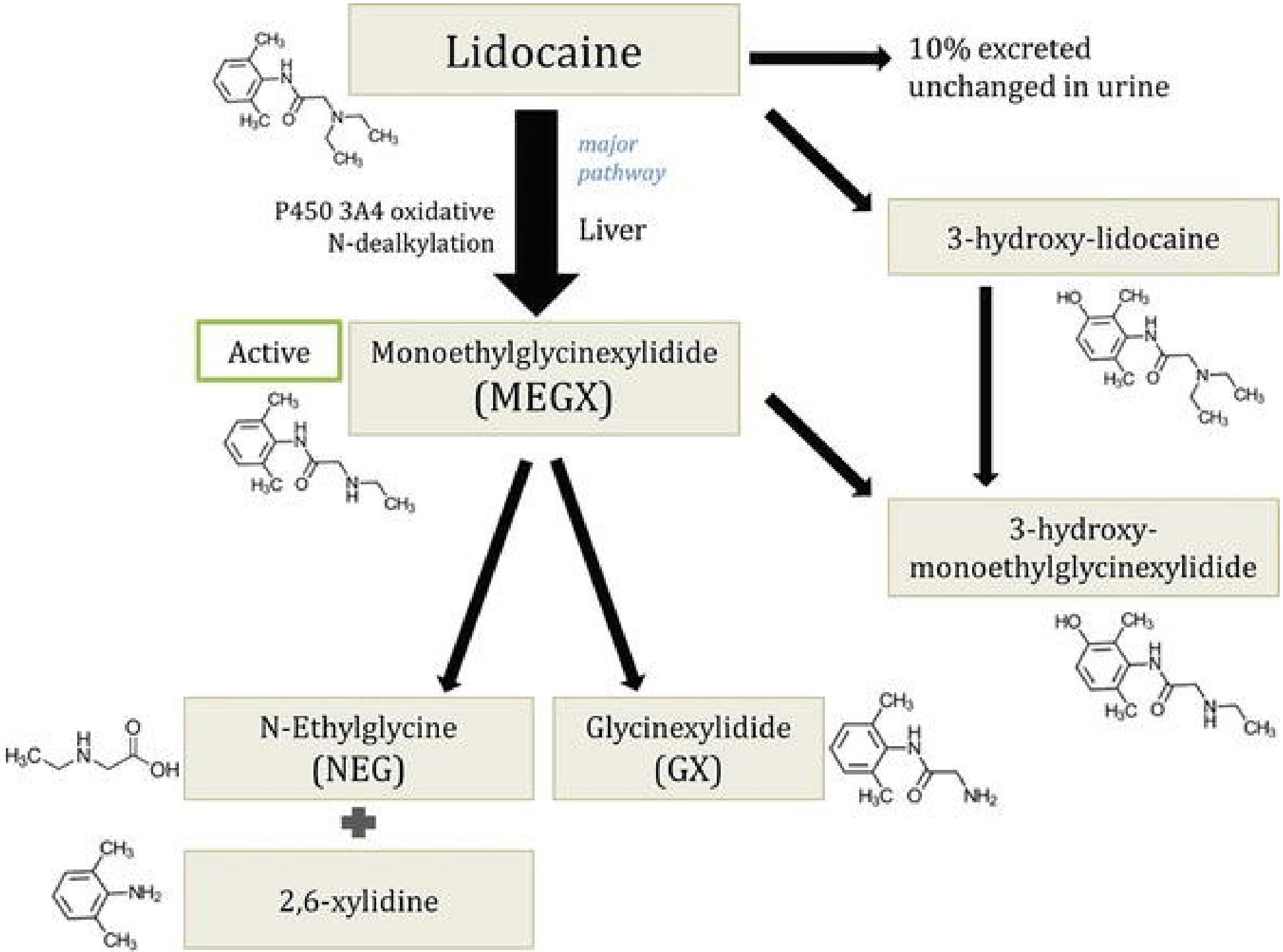
Classical sythesis of lidocaine



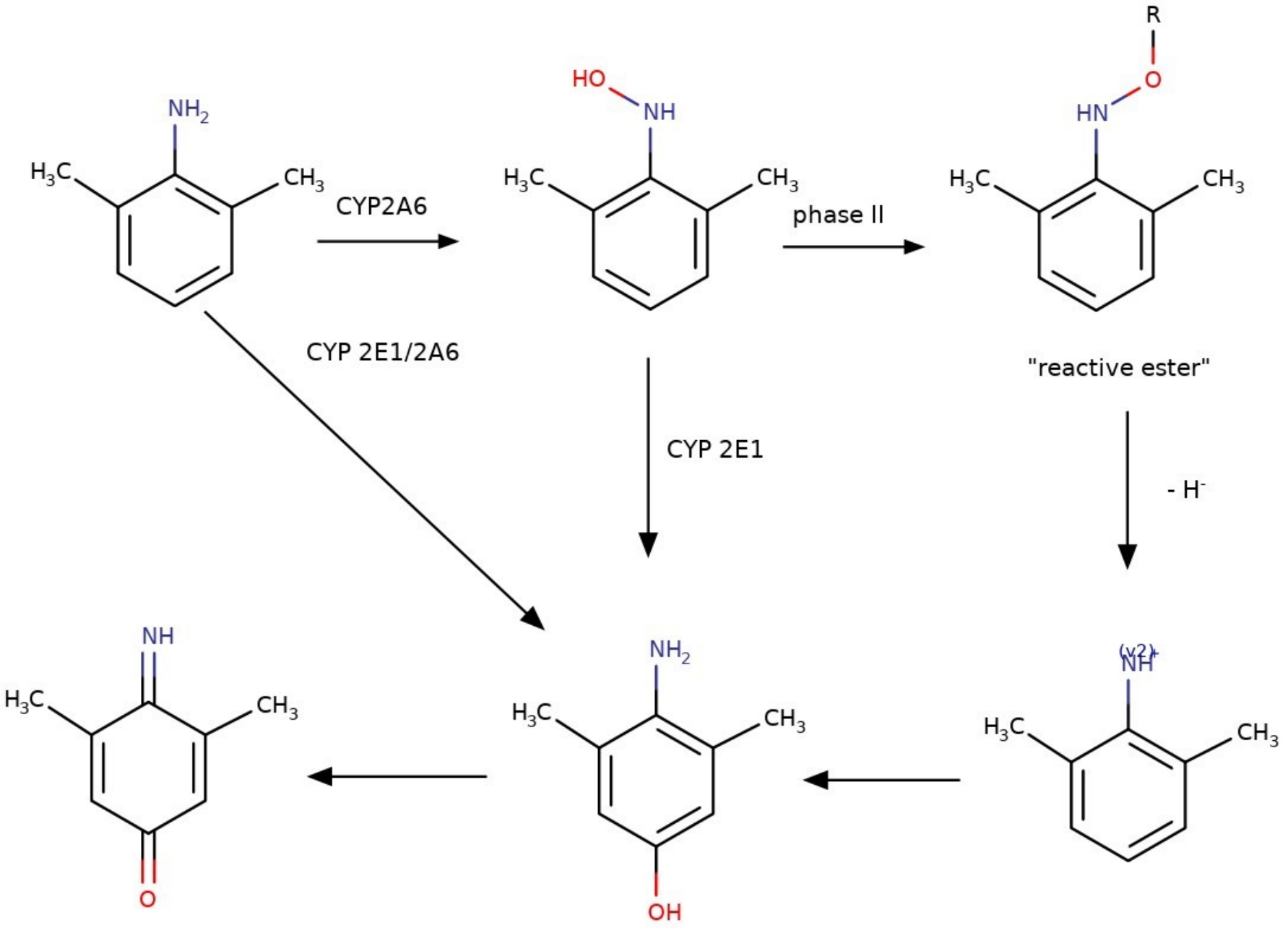
An alternative: a one-pot synthesis of lidocaine: Ugi condensation



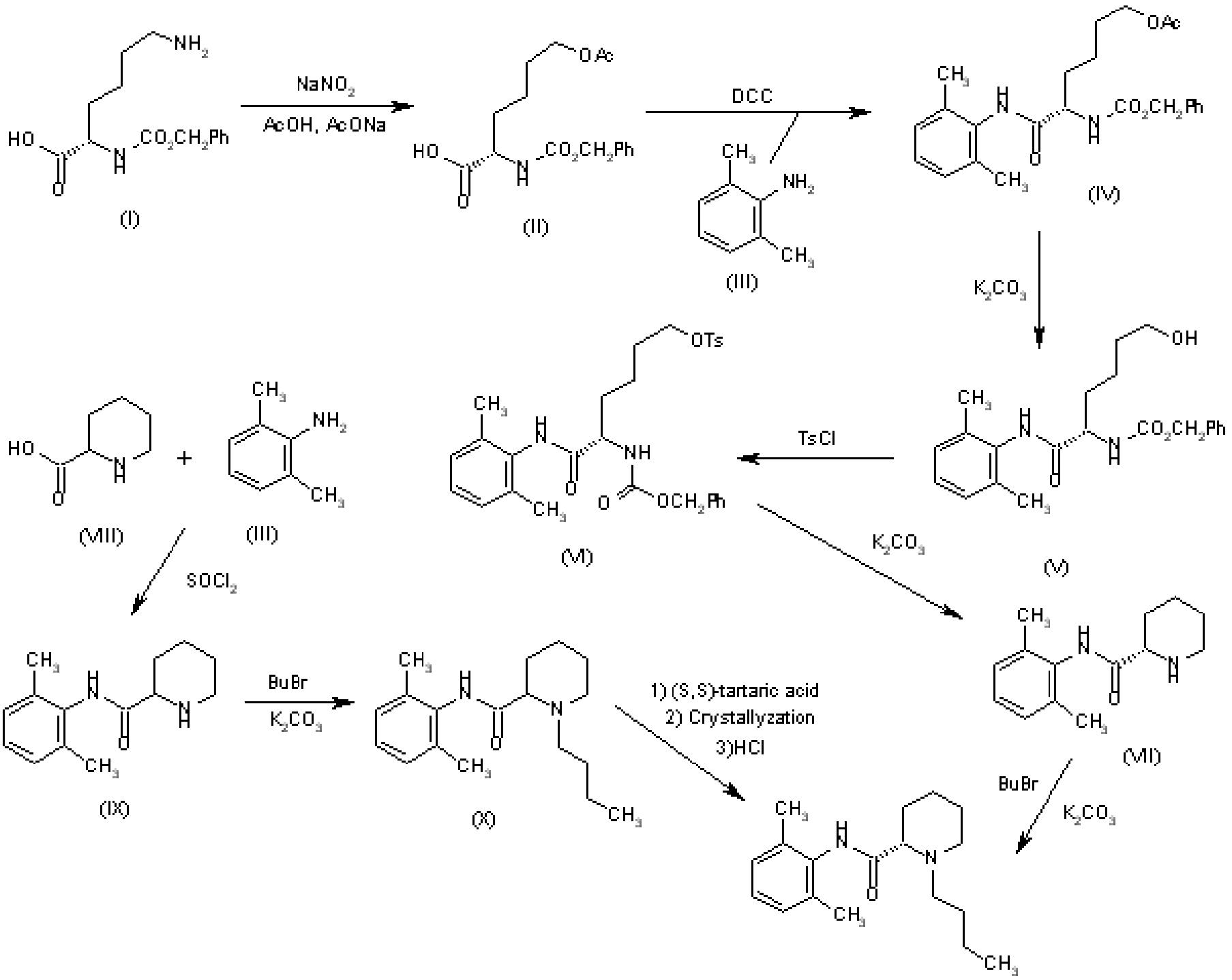
Main methabolic pathways of lidocaine



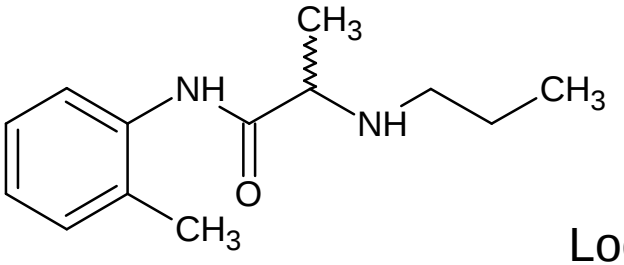
Proposed further metabolism of 2,6-xylidine



Synthesis of Levobupivacaine

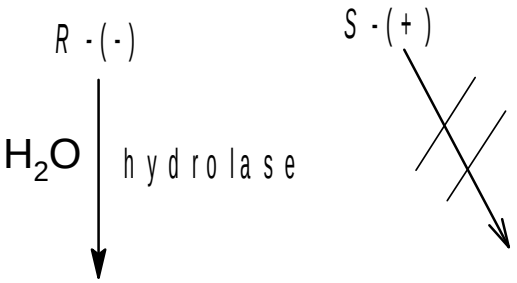


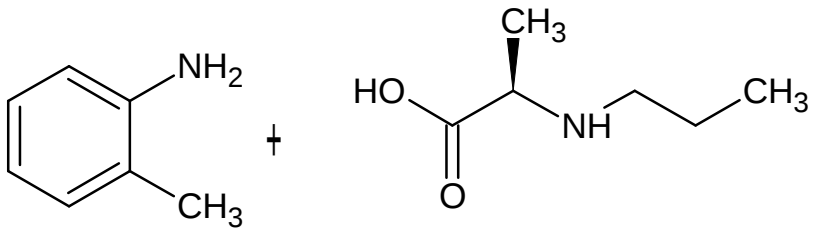
Stereoselectivity of metabolism in **prilocaine**



Local anaesthetics of anilide series: **prilocaine**

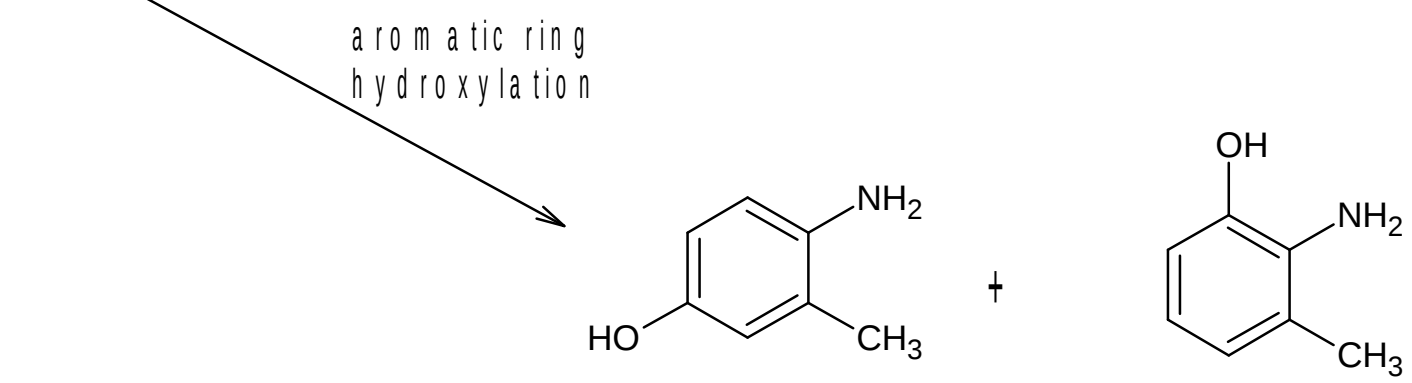
- anaesthetic activity of *R* and *S* enantiomers does not markedly differ





(2*R*)-2-(propylamino)propanoic acid

- administration of the pure *S*-(-) enantiomer can eliminate the toxicity



- toxic metabolites
- methemoglobinemia