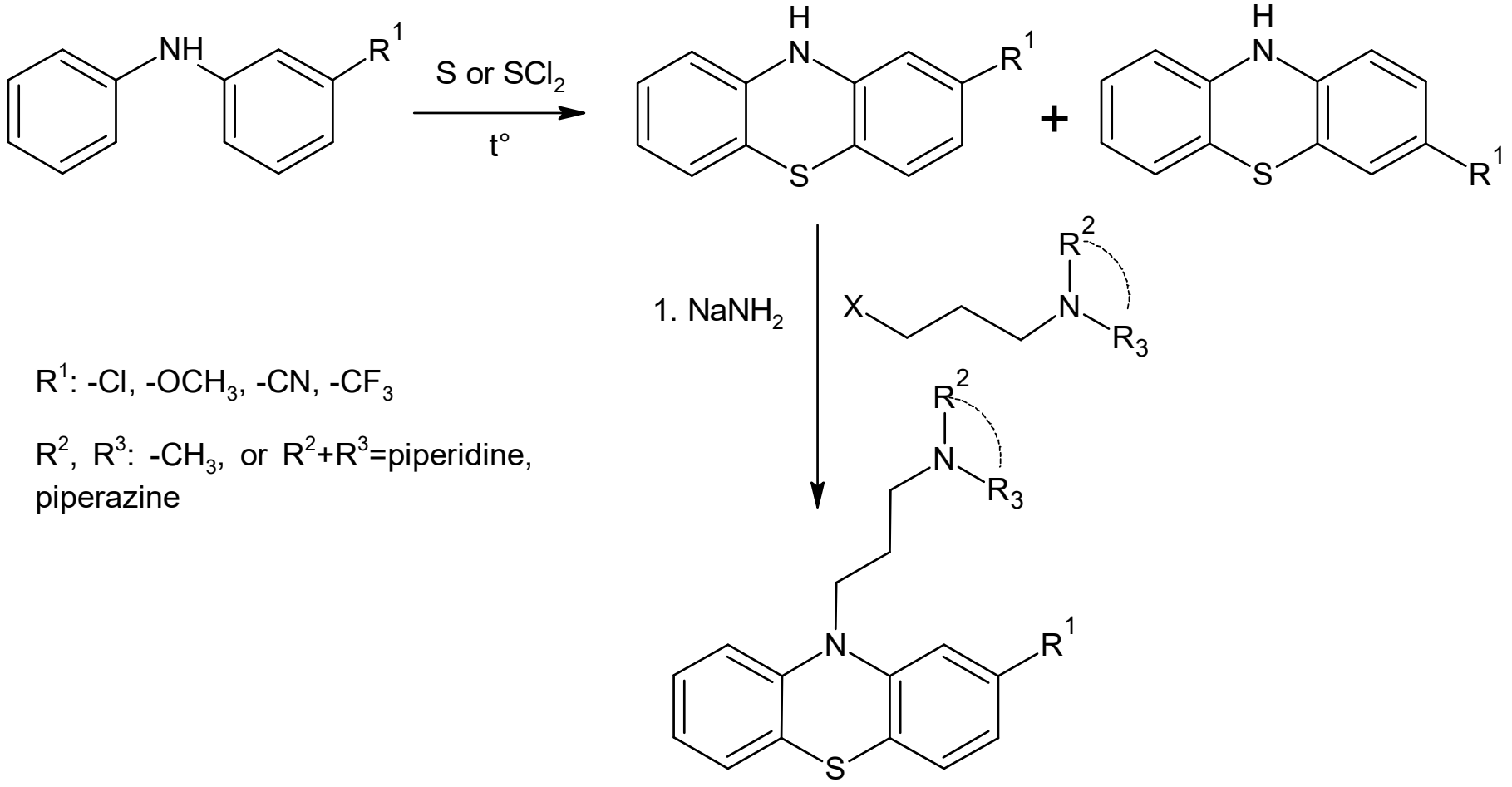
Syntheses and metabolism of selected antipsychotics

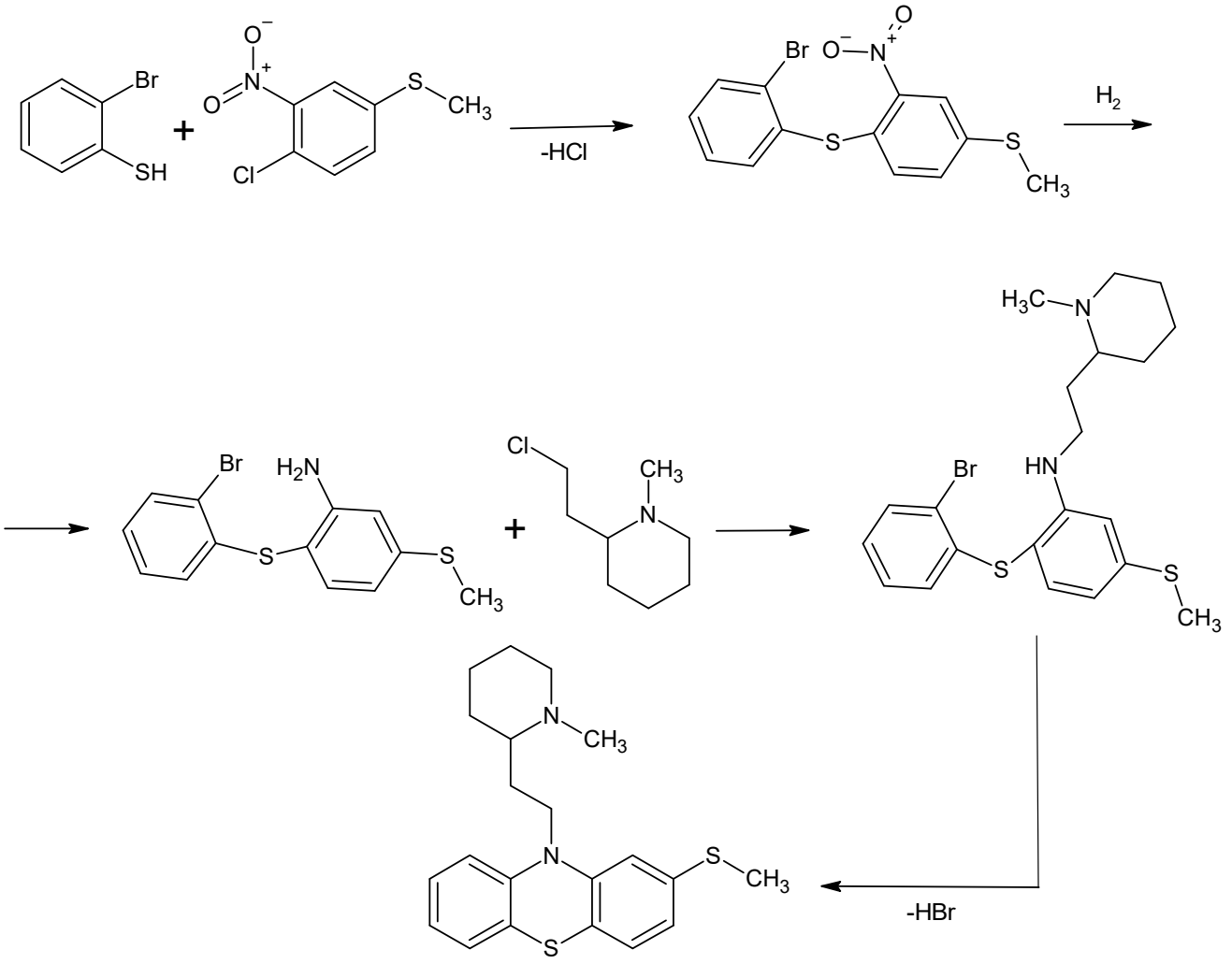
General synthesis of phenothiazine neuroleptics



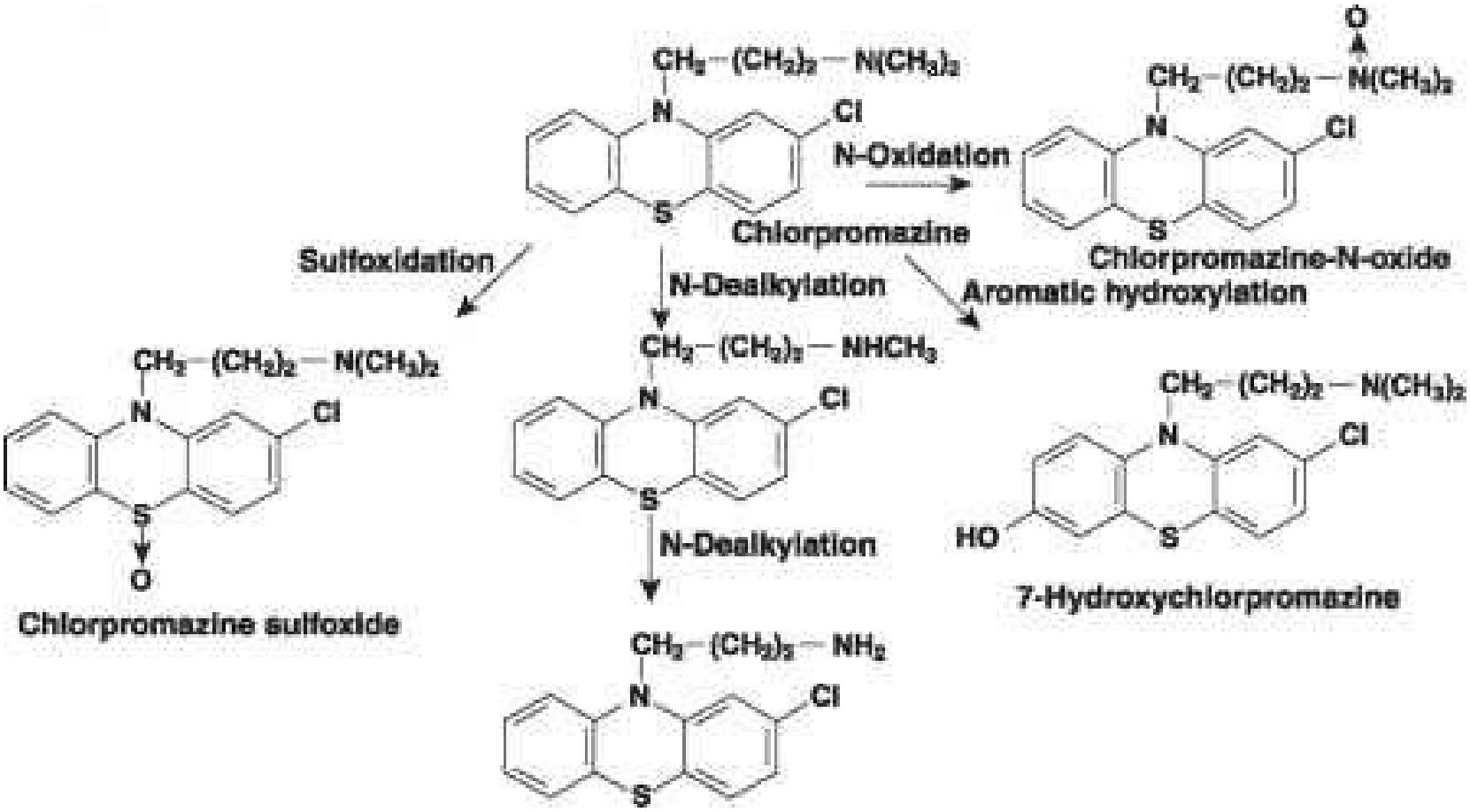
R^1: -Cl, -OCH_3, -CN, -CF_3

R^2, R^3: -CH_3, or R^2+R^3=piperidine, piperazine

Other approach to phenothiazine skeleton: synthesis of thioridazine

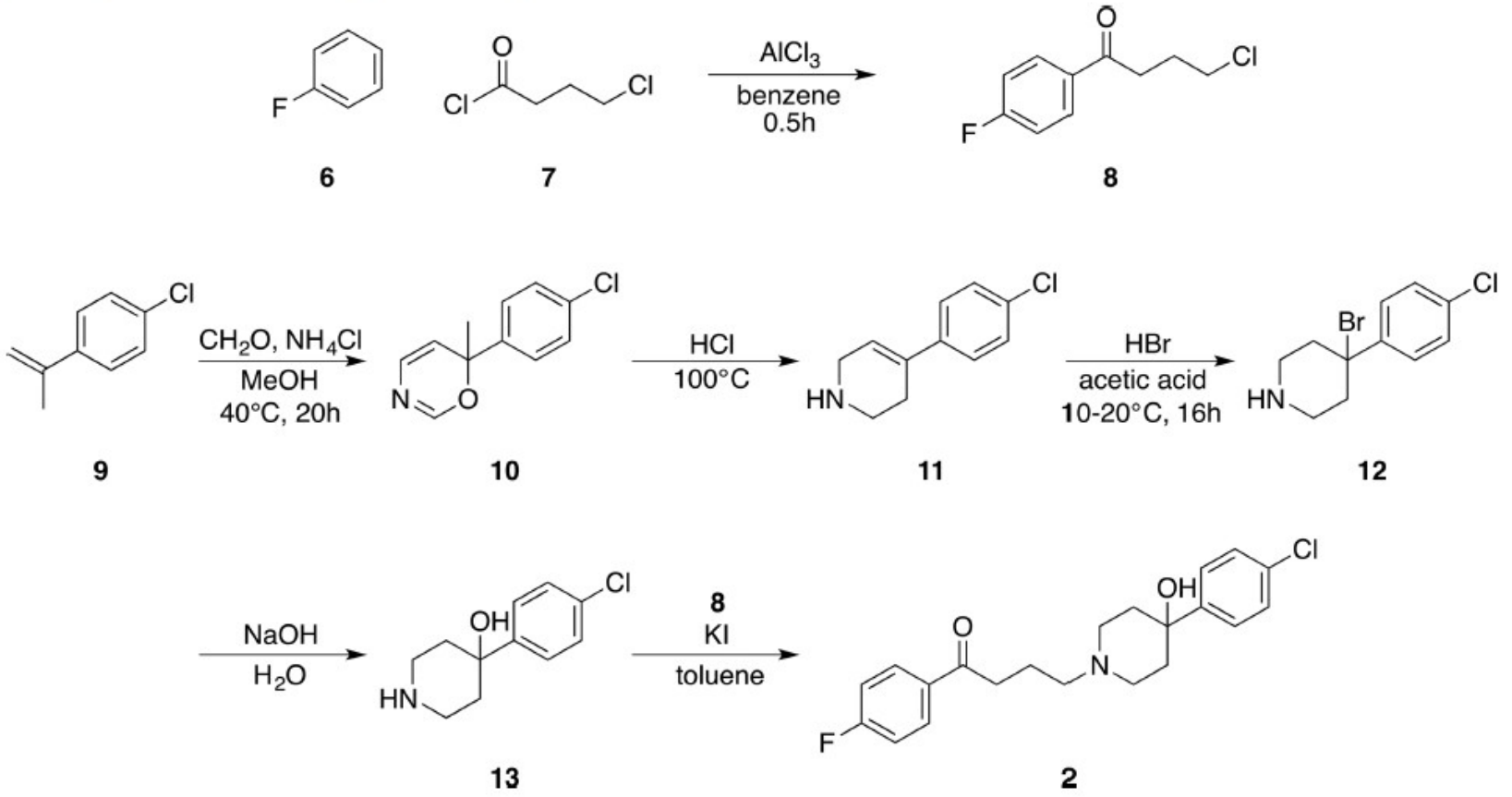


Metabolism of chlorpromazine



Original synthesis of haloperidol

Scheme 1. Original Synthesis of Haloperidol by Janssen Pharmaceutica in 1958



Metabolism of haloperidol

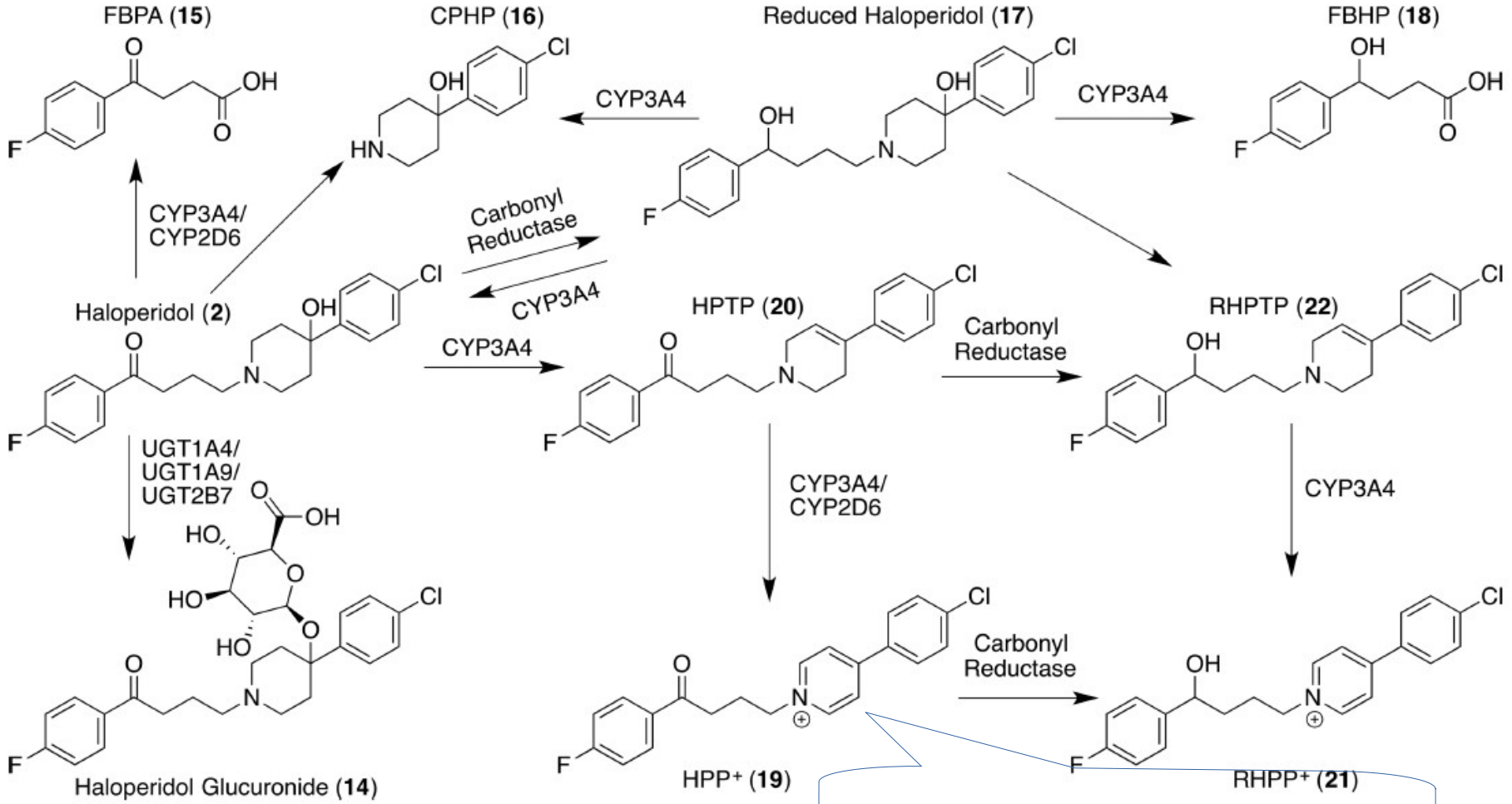
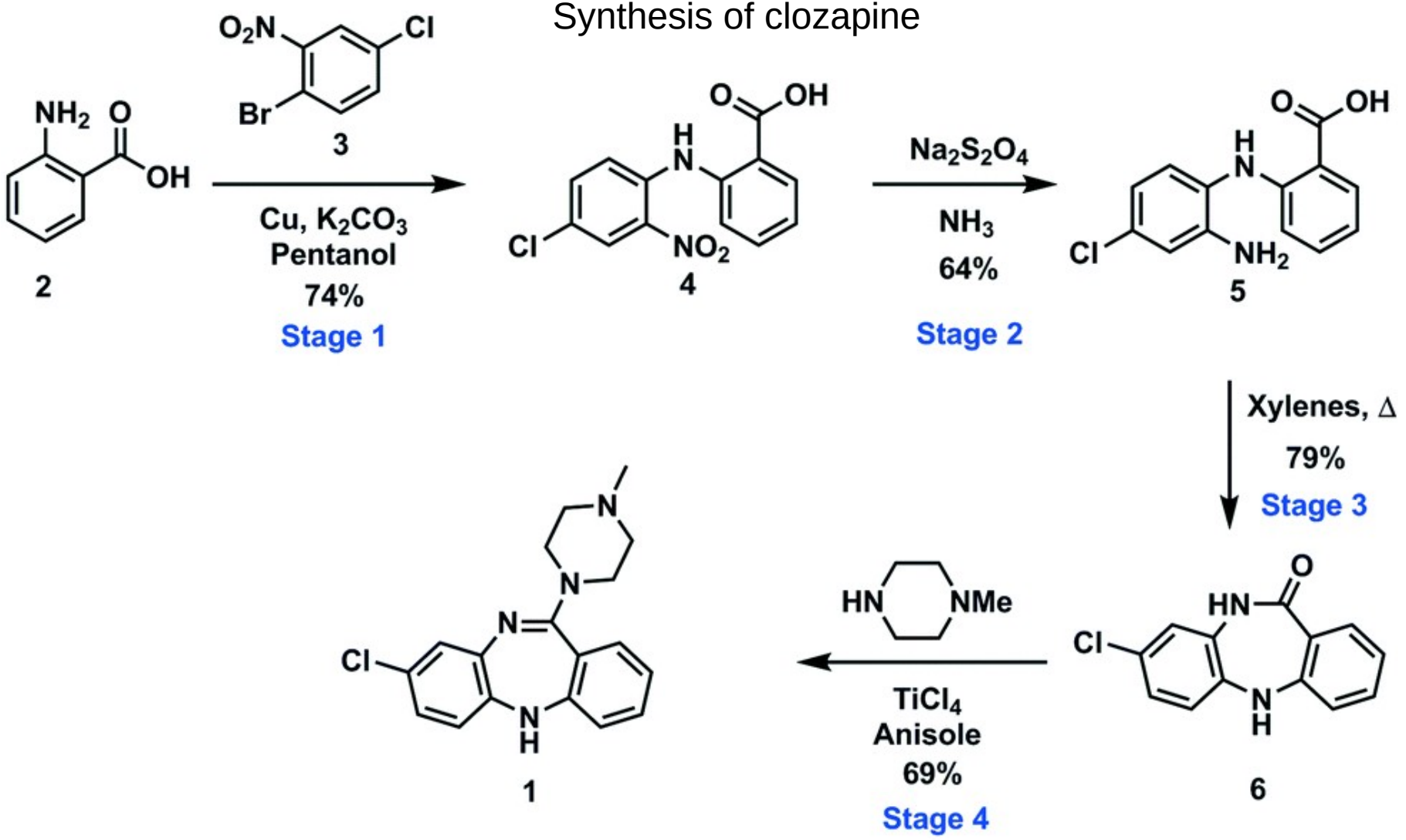
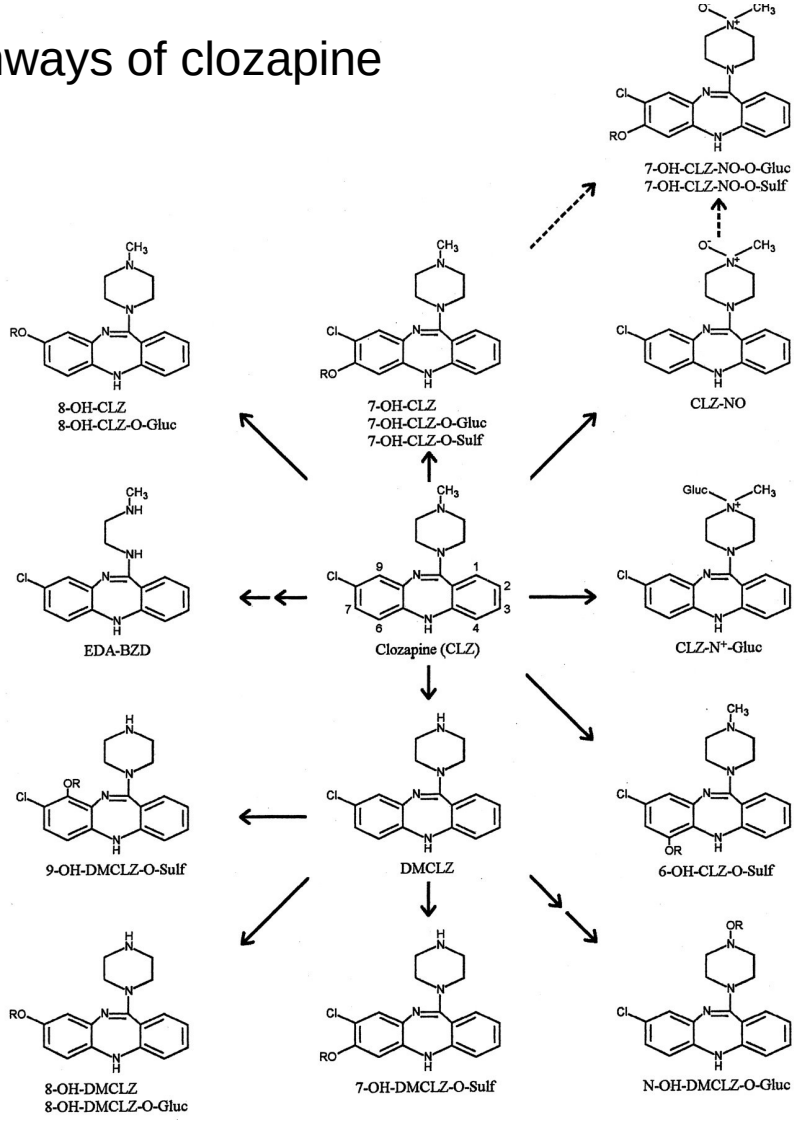


Figure 3. Structures of metabolites of haloperidol (2).

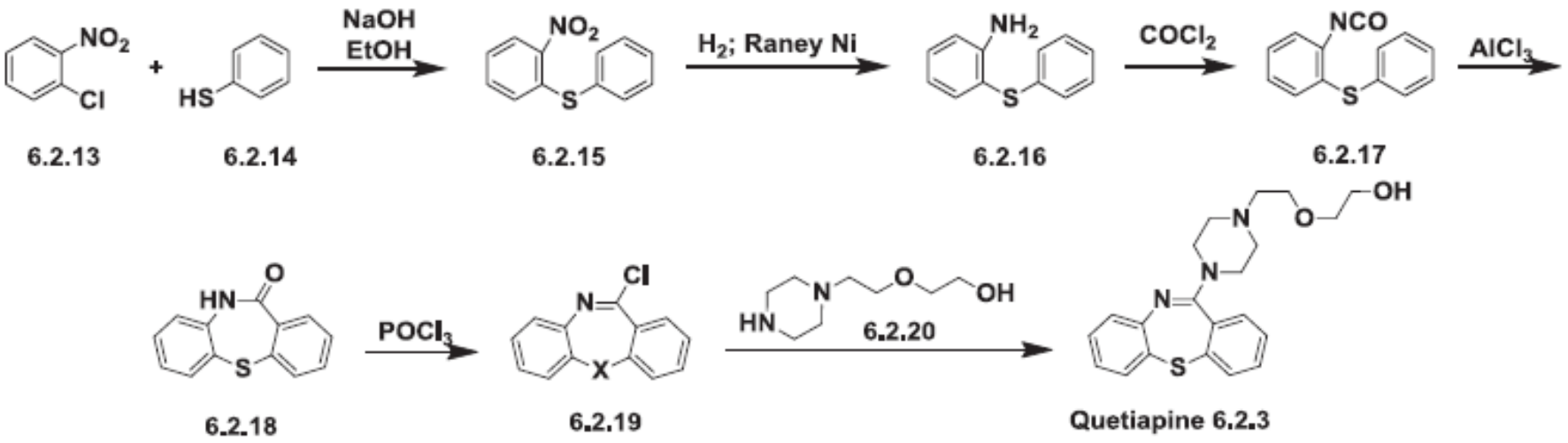
Synthesis of clozapine



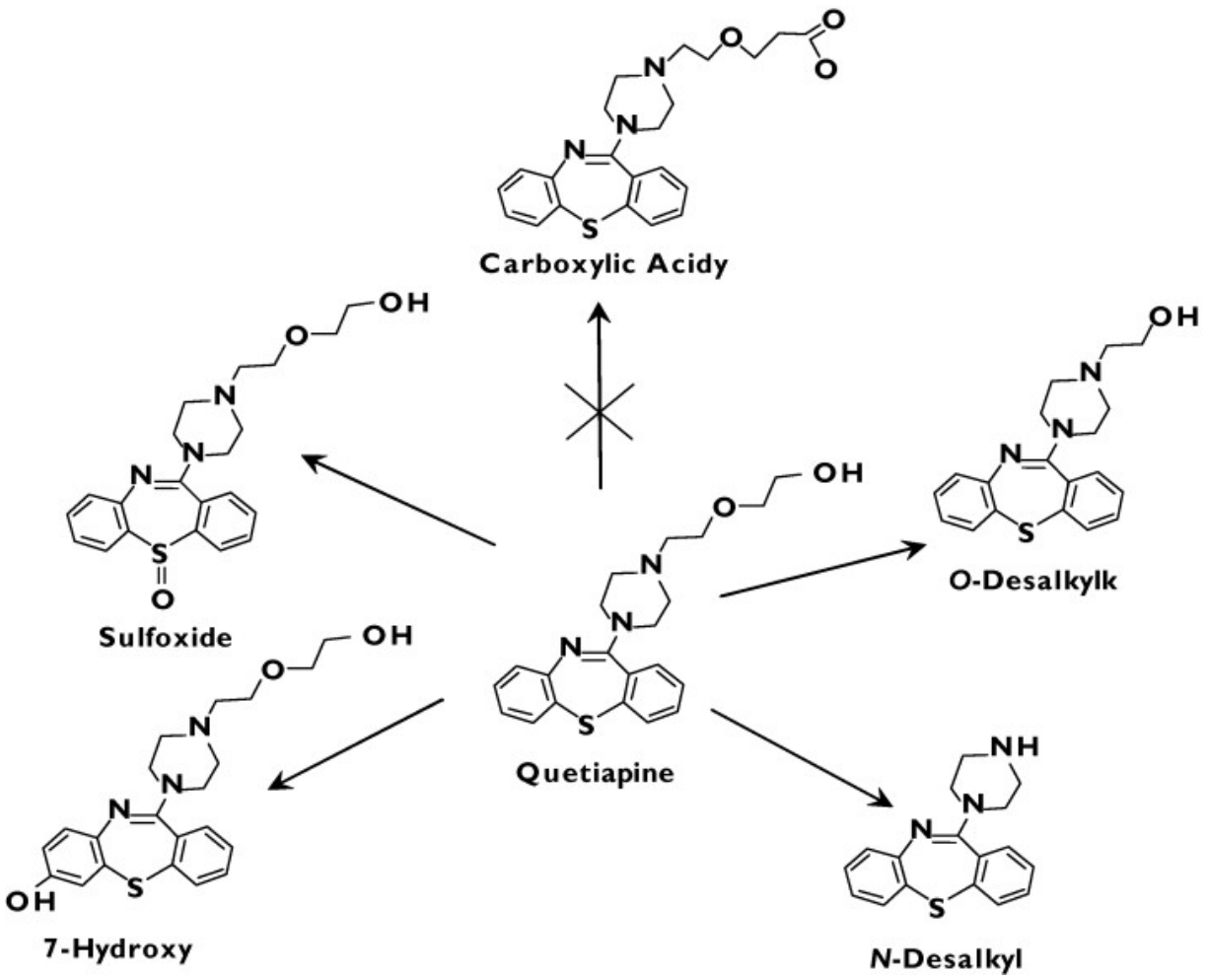
Main metabolic pathways of clozapine



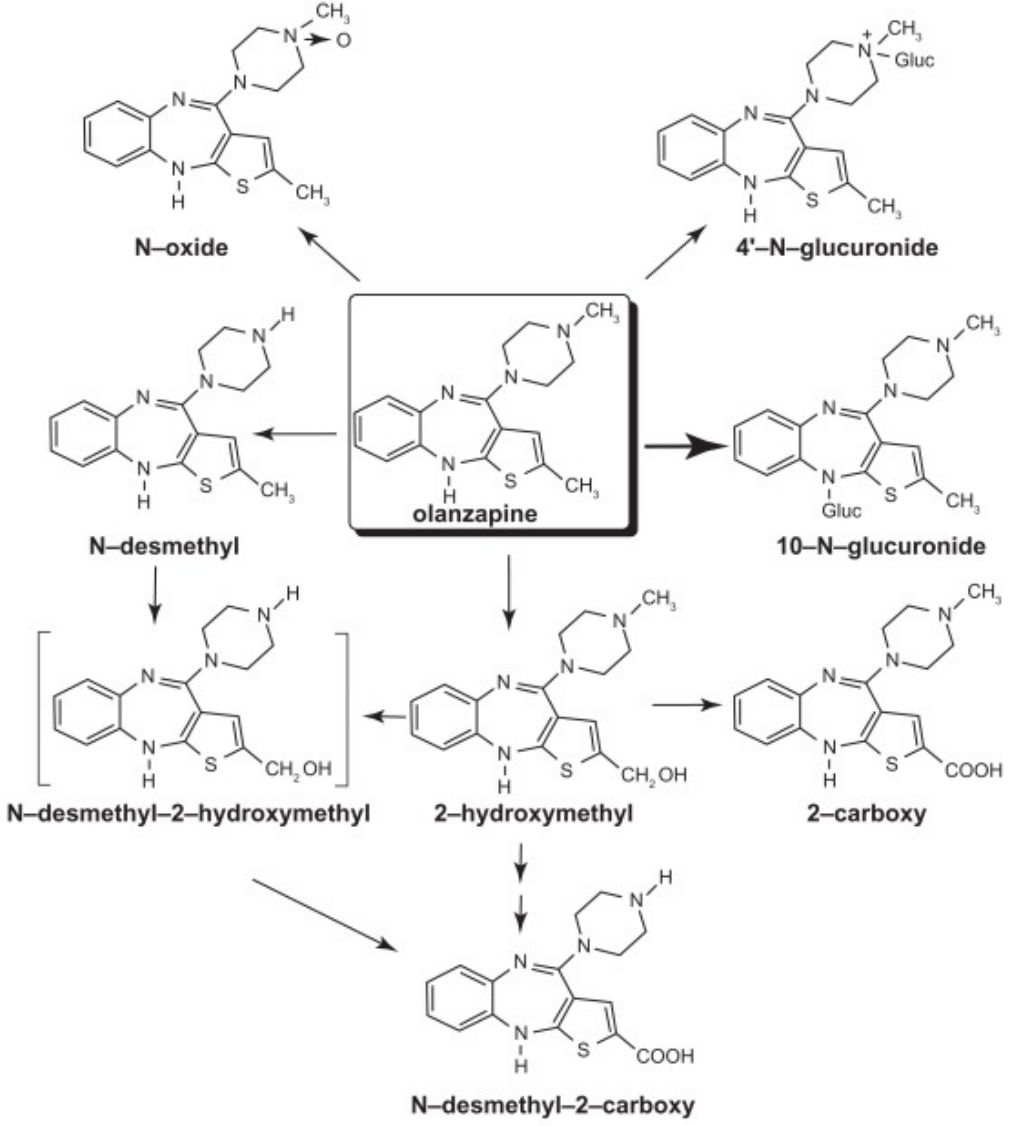
Synthesis of quetiapine



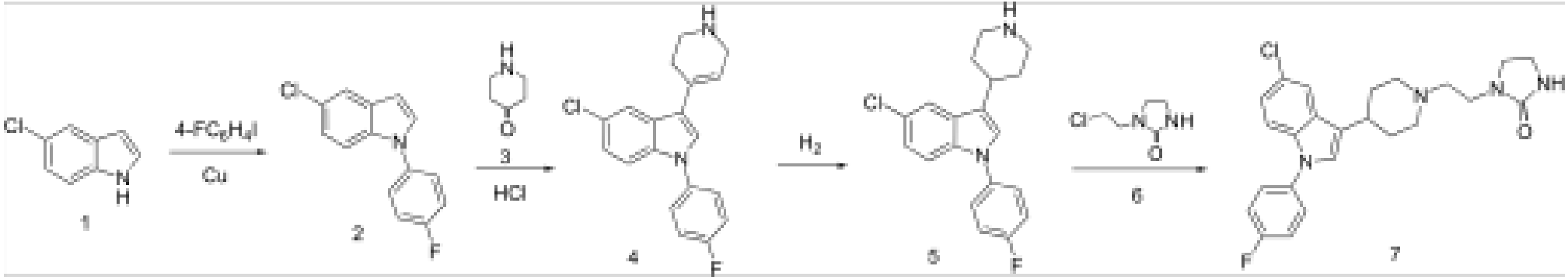
Quetiapine metabolism



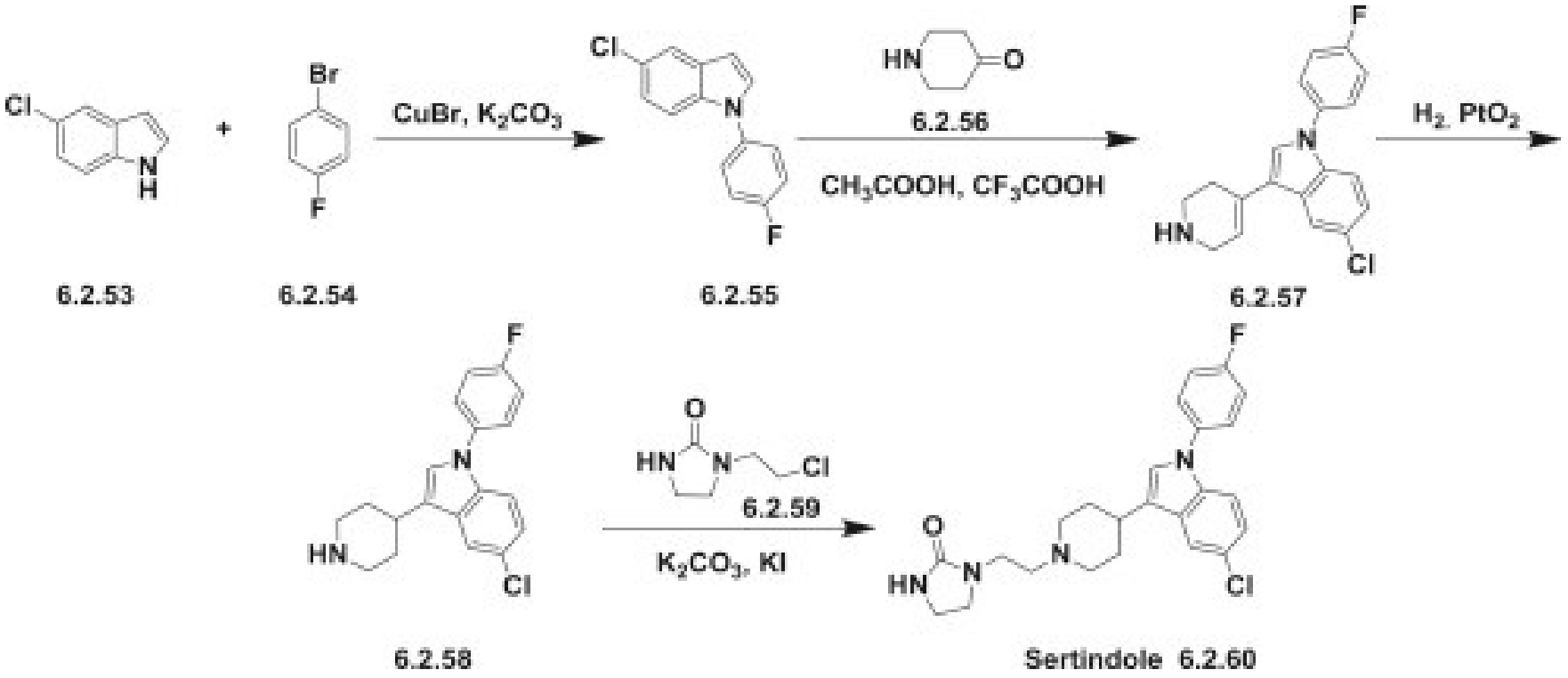
Olanzapine metabolism



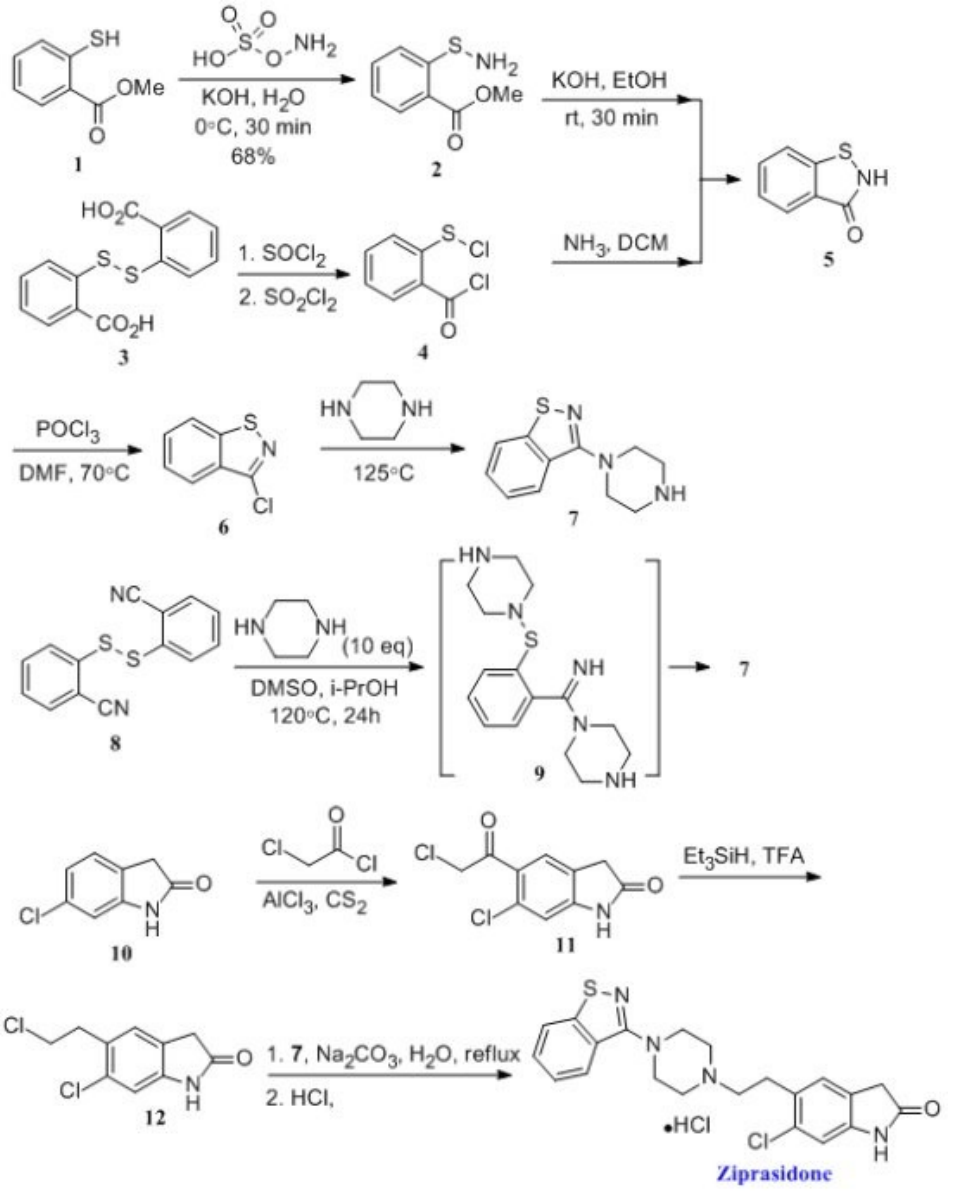
Sertindole synthesis



Other modification of sertindole synthesis



Synthesis of ziprasidone



Main metabolites of ziprasidone

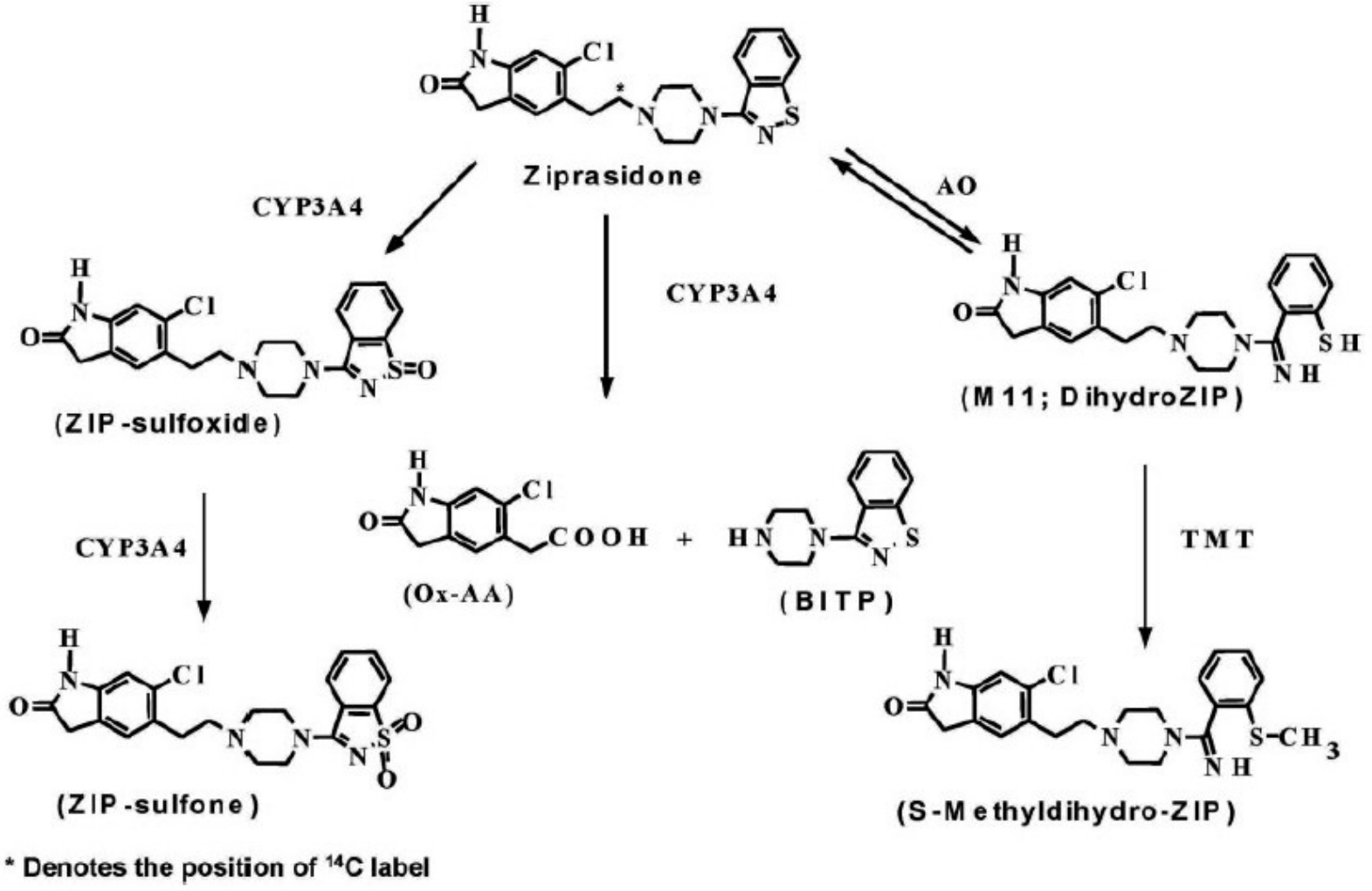
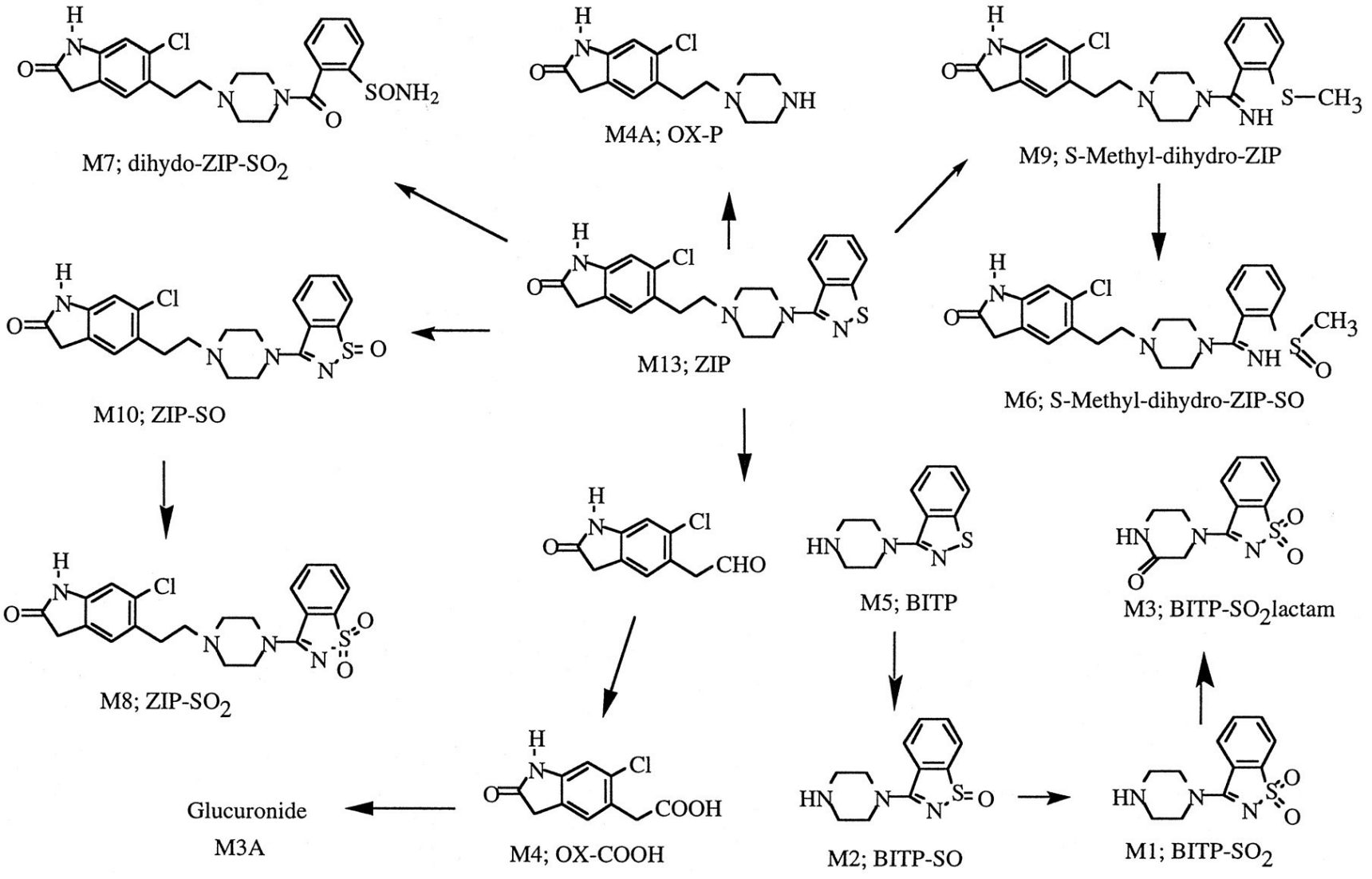
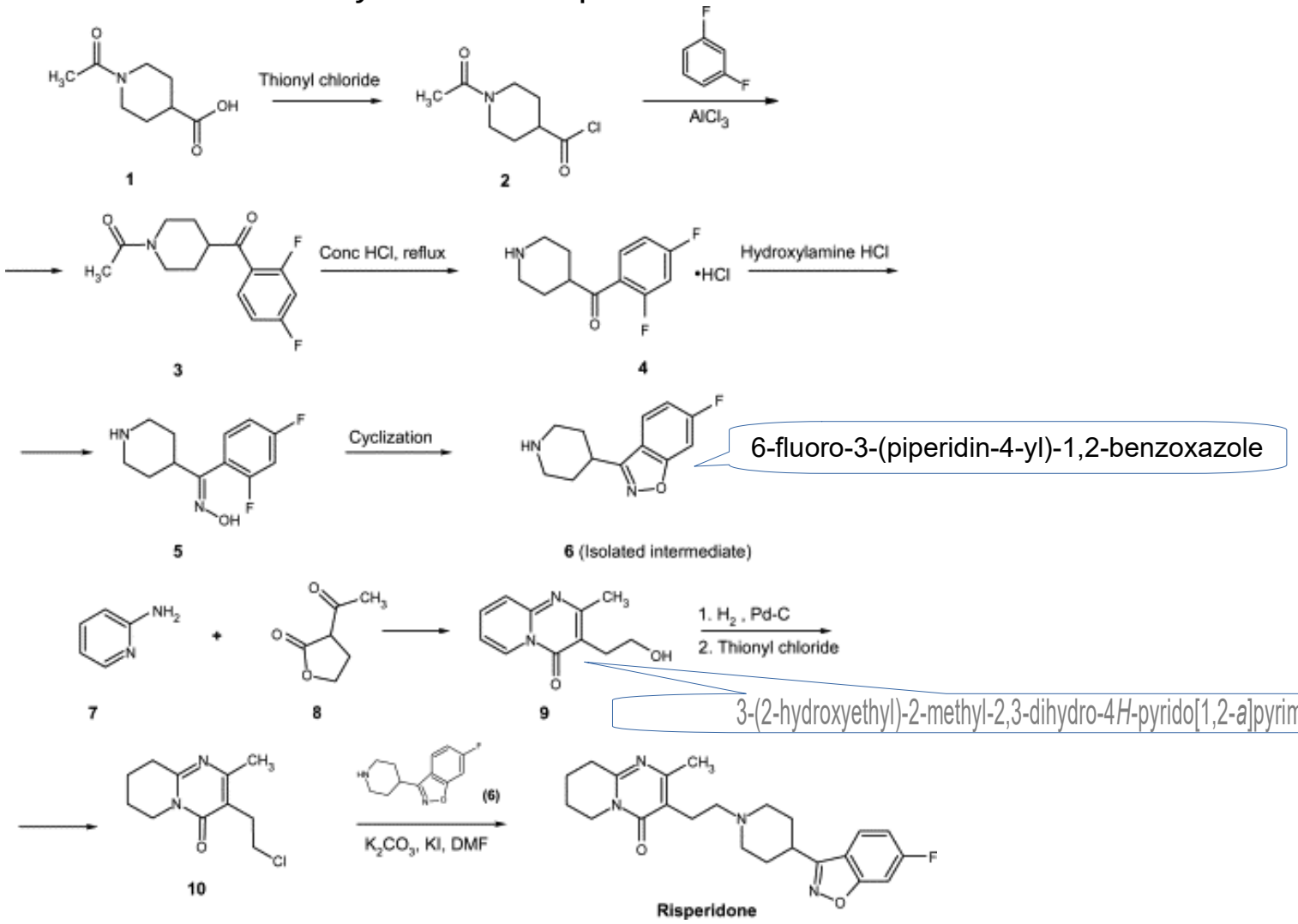


FIG. 1. Structures of ziprasidone and its major metabolites. TMT, thiol methyltransferase.

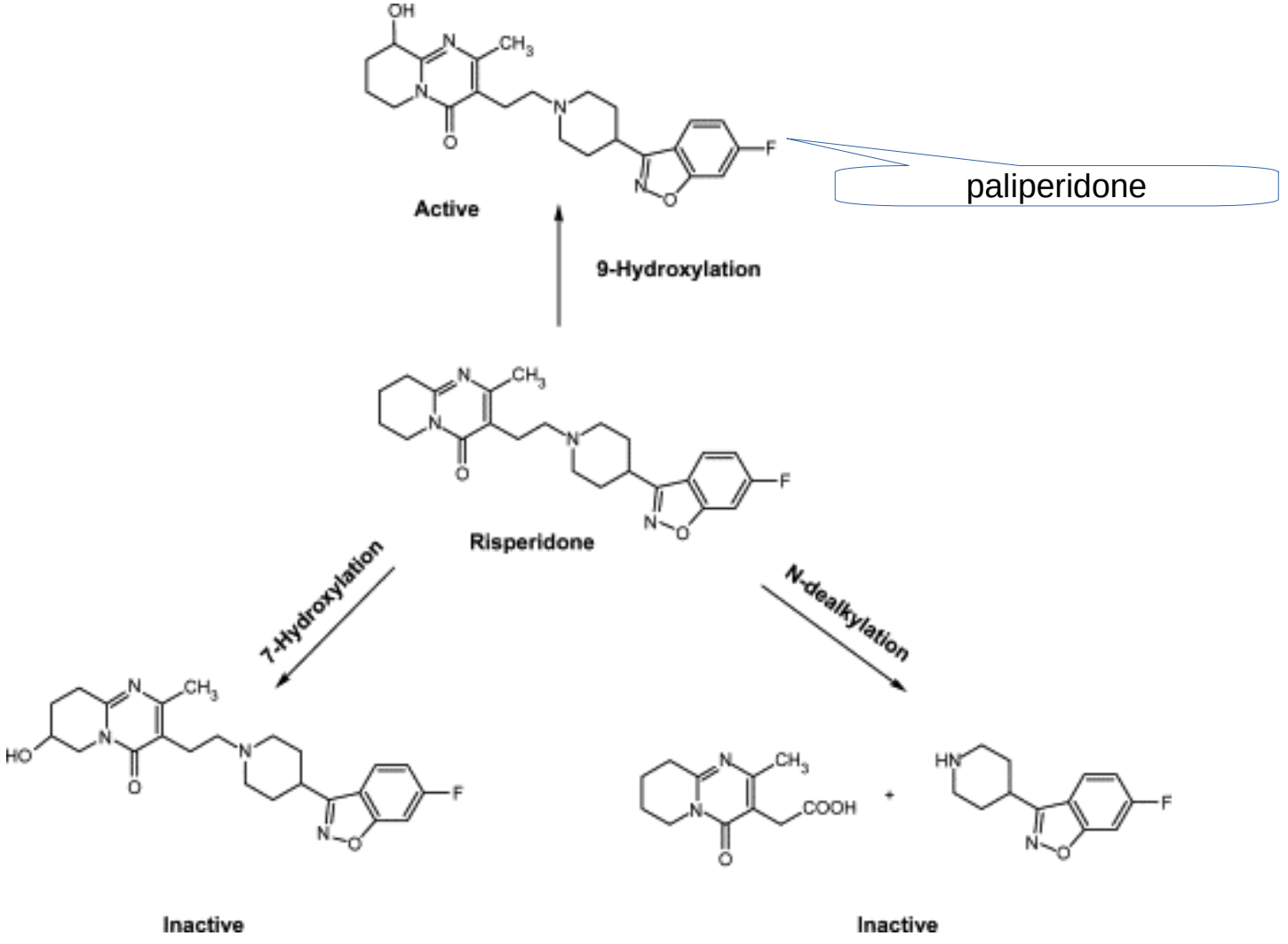
Some other metabolites of ziprasidone



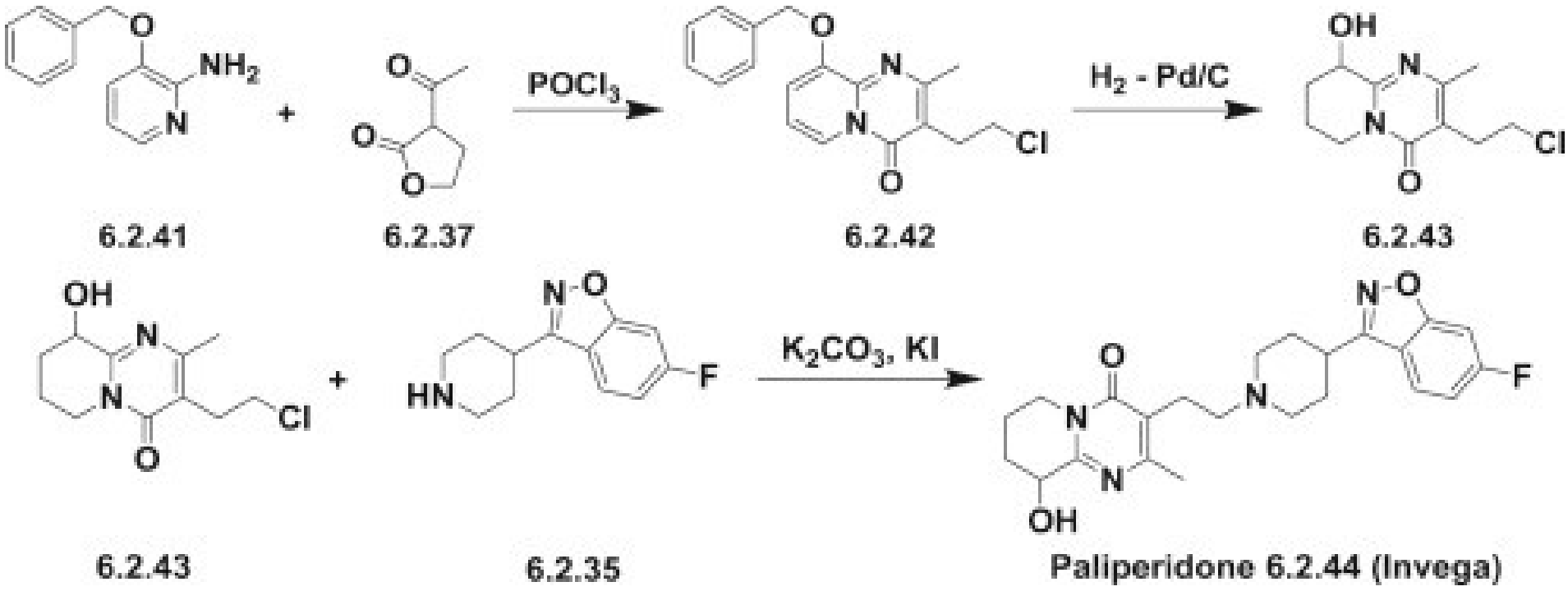
Synthesis of risperidone



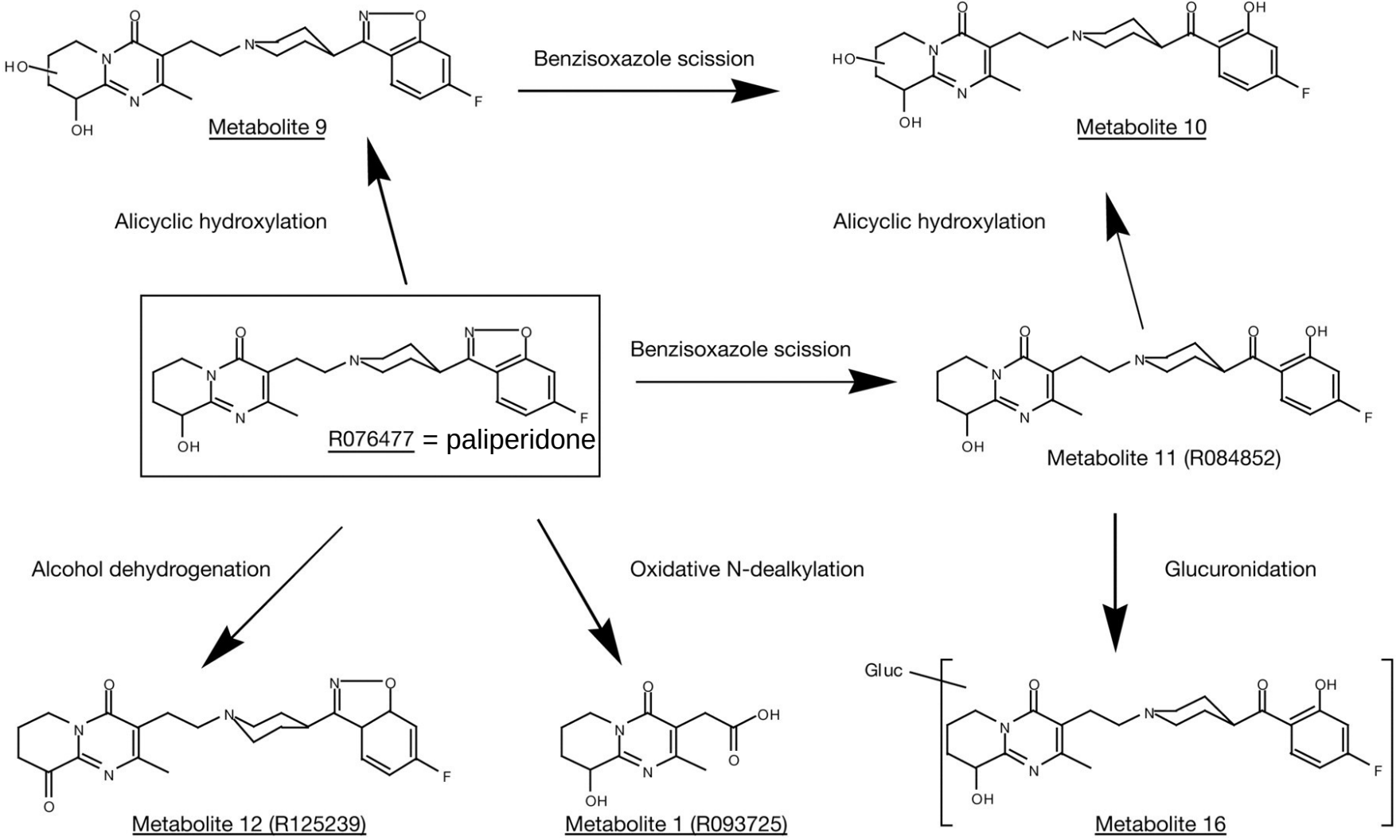
Main metabolic pathways of risperidone



Synthesis of paliperidone

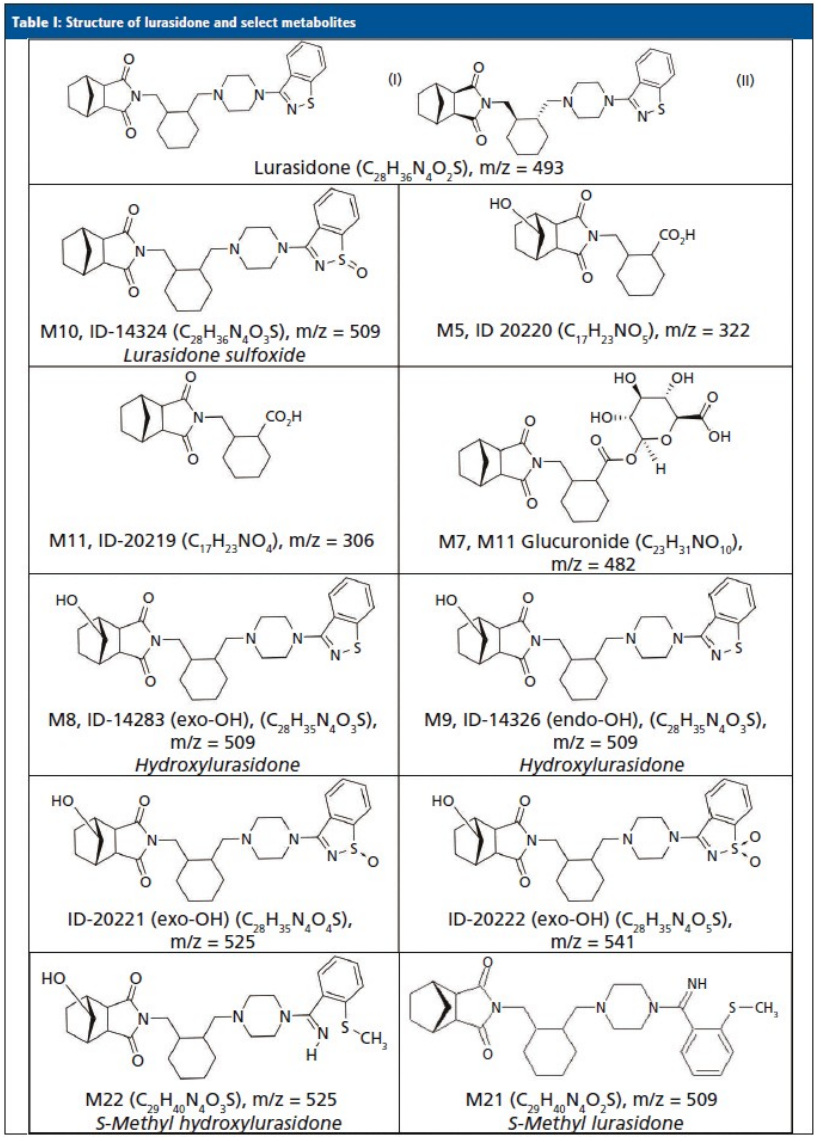


Main metabolites of paliperidone

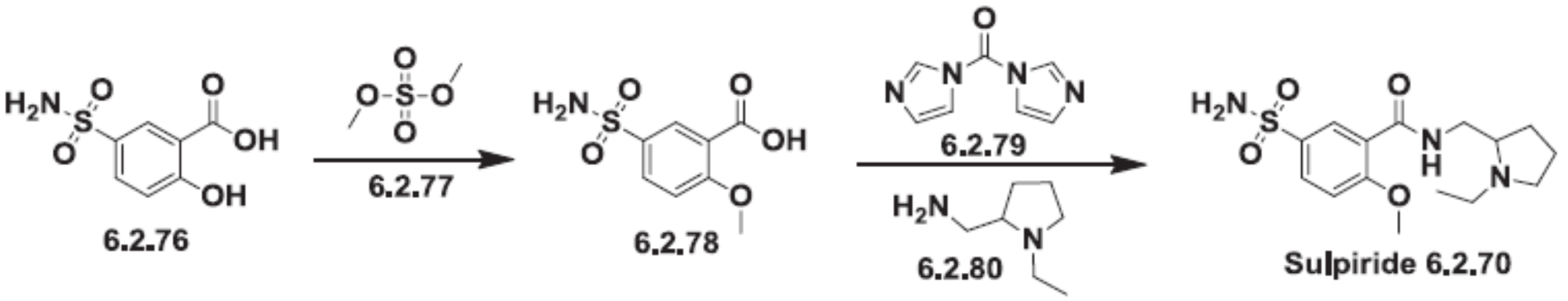


Lurasidone and its main metabolites

Table I: Structure of lurasidone and select metabolites

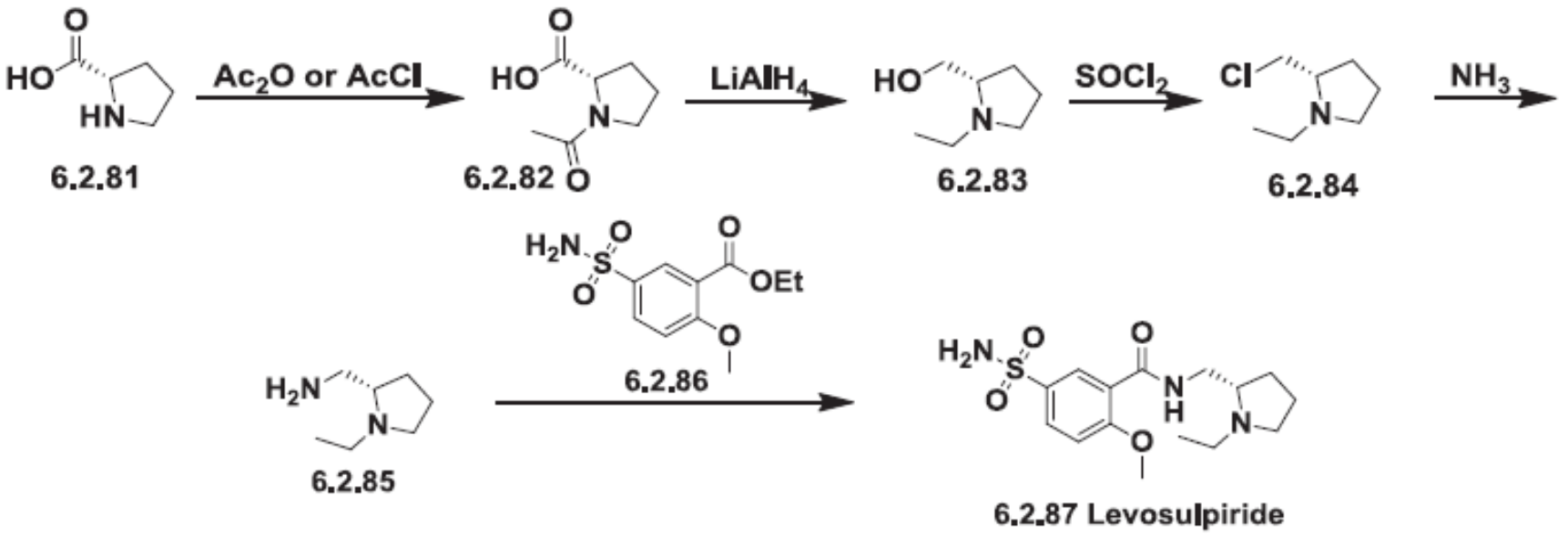


Synthesis of sulpiride



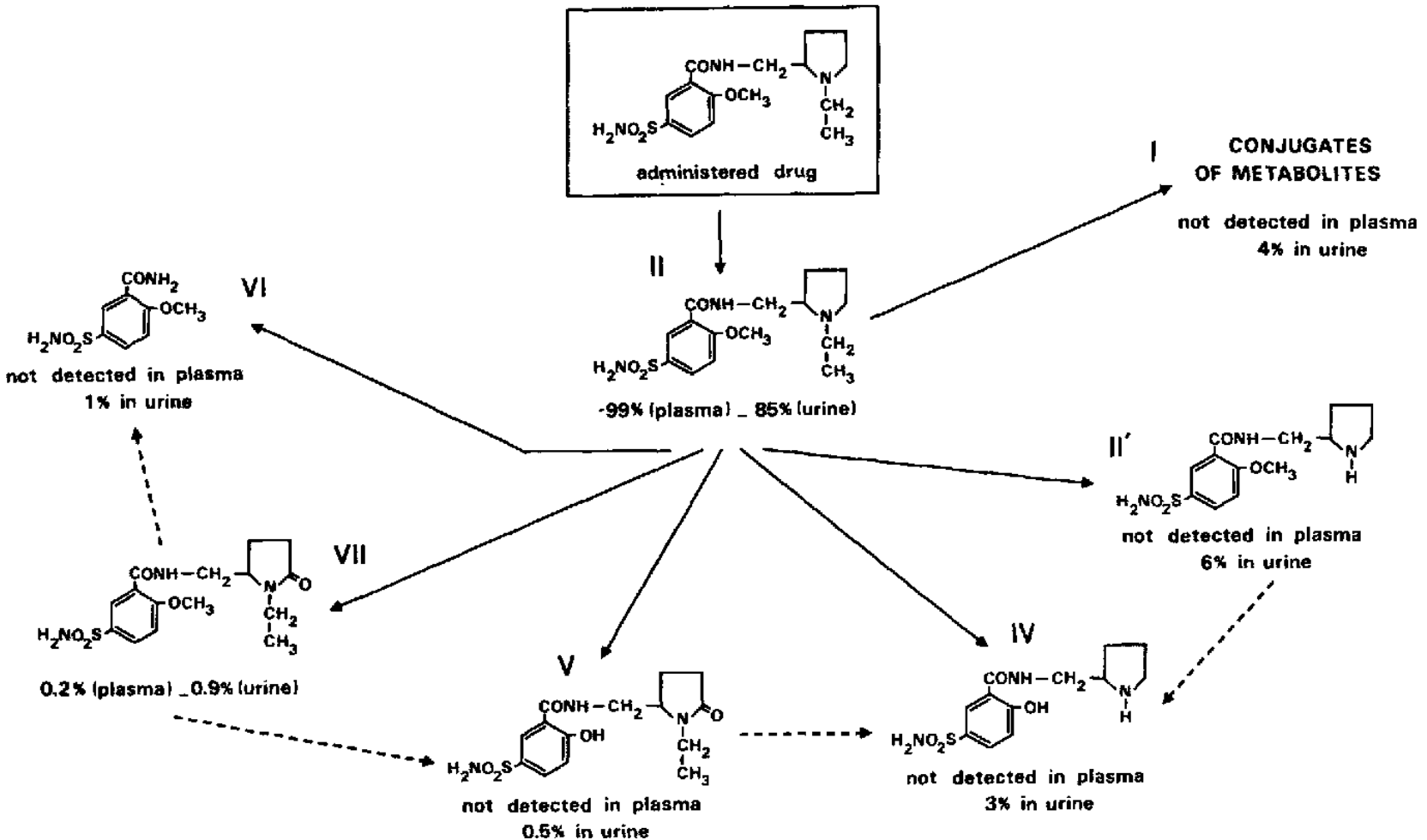
SCHEME 6.14 Synyhesis of sulpiride.

Synthesis of levosulpiride

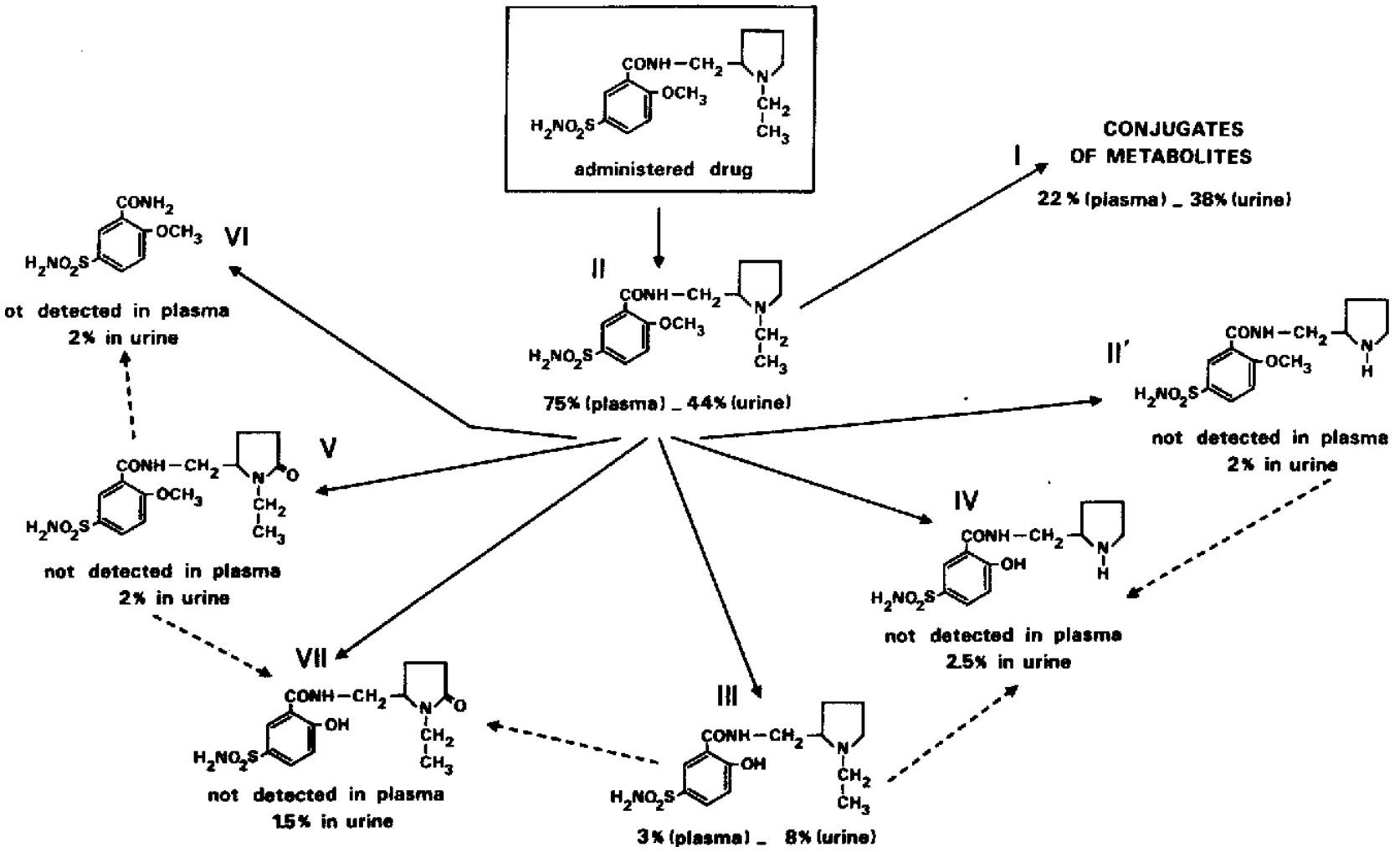


SCHEME 6.15 Synyhesis of levosulpiride.

METABOLIC PATHWAY OF SULPIRIDE IN DOG



METABOLIC PATHWAY OF SULPIRIDE IN RAT



Synthesis of amisulpride

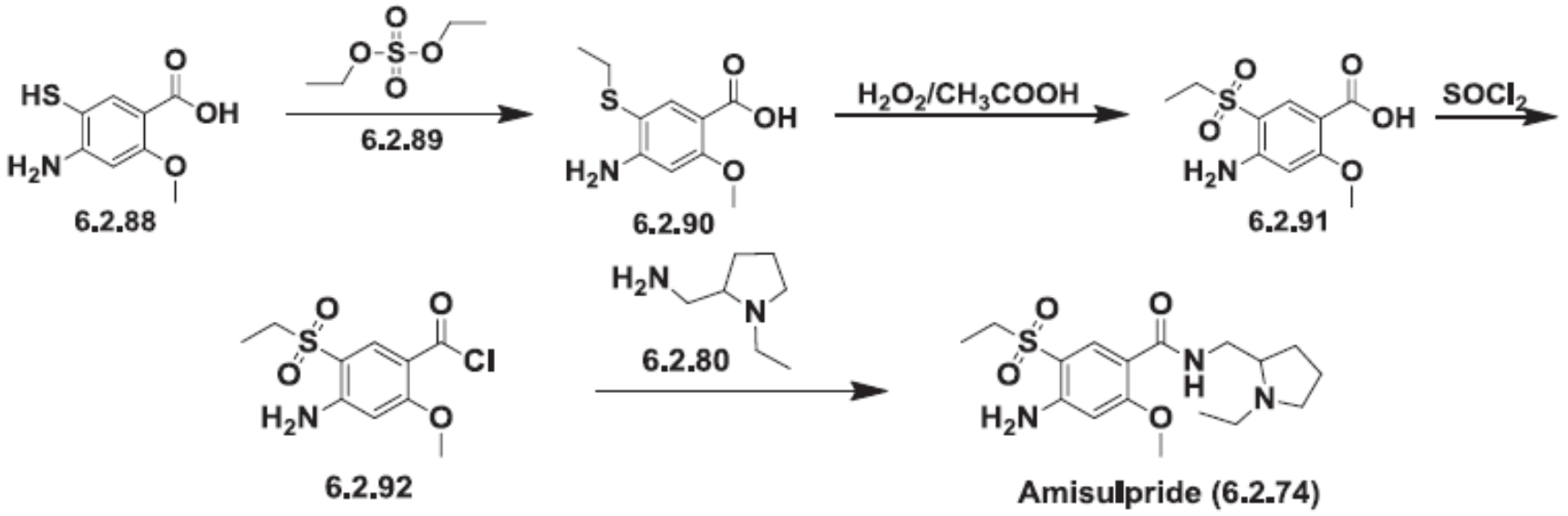
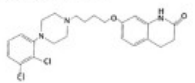
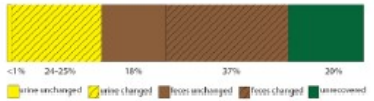
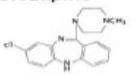
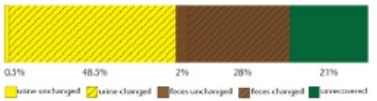
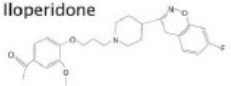
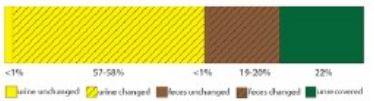
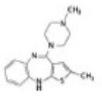
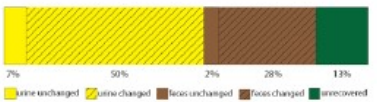
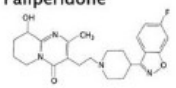
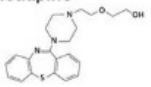
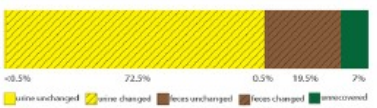
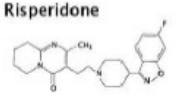
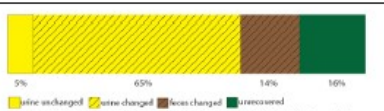
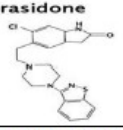
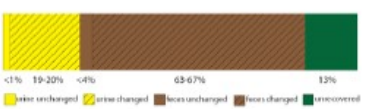


Table 1. Summary of the Chemical Structures and Excretion Profiles of the Atypical Antipsychotics

Chemical Structure	Excretion
Aripiprazole 	
Clozapine 	
Iloperidone 	
Olanzapine 	
Paliperidone 	
Quetiapine 	
Risperidone 	
Ziprasidone 	

The chemical structures of each of the 8 reviewed atypical antipsychotic agents are presented with a bar chart depicting the relationship between the excretory (i.e., urine or feces, changed or unchanged) profiles. These data highlight the magnitude of differences in the excretory profiles among the atypical antipsychotic agents.