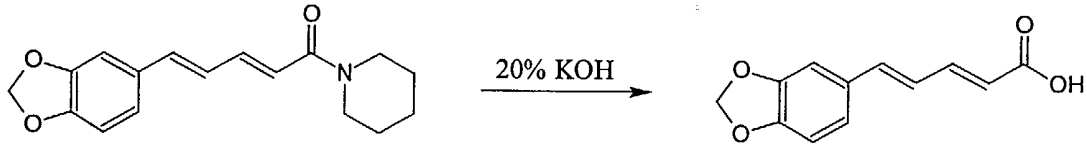
2. Synthesis of amide derivatives of piperinic acid

2.1 Preparation of piperinic acid (RV-A00)

To piperine (1) (2g, 0.7mmol, 1eq), 20% of methanolic KOH (100ml) was added and refluxed for 2days. After completion of the hydrolysis, methanol was removed under reduced pressure and a yellow coloured oily solid was obtained. This residue was dissolved in water (50ml) and acidified with 6N HCl to pH <1 yielding a yellowish precipitate of piperinic acid. Recrystallization from methanol gave yellow needles (0.9g, 60% yield). m.p. 206^0-208^0C (Lit m.p. 217^0-218^0C)[1]



Piperine (1) Piperinic acid

2.2 Synthesis of piperlonguminine (RV-A06)

A mixture of piperinic acid (350mg, 0.0016mole, 1eq) and triethylamine (0.4ml, 0.0032mole, 2eq) in dichloromethane (50ml) was stirred for 15min at 0^0C. To this mixture methanesulfonyl chloride (0.18ml, 0.0024mole, 1.5eq) was added and stirred for further 30 min at 0^0C. Isobutylamine (0.23ml, 0.0024mole, 1.5eq) was added to the mixture and stirred for 1h at 0^0C and 2h at room temperature. Dichloromethane (50ml) was added to the mixture which was then washed with 5% HCl (3x100ml), saturated aqueous $NaHCO_3$ (3x100ml) and water (3x100ml). The organic fraction was dried over anhydrous sodium sulphate, filtered and rotary evaporated to yield a yellowish solid residue. Recrystallisation from methanol yielded colourless needles of piperlonguminine (120mg, 32% yield)[2]. The reaction is presumed to proceed through a mesylate ester intermediate.