

4. Phenytoin

Systematic name: 5,5-diphenylimidazolidine-2,4-dione; 5,5-diphenylhydantoin

Chemicals:

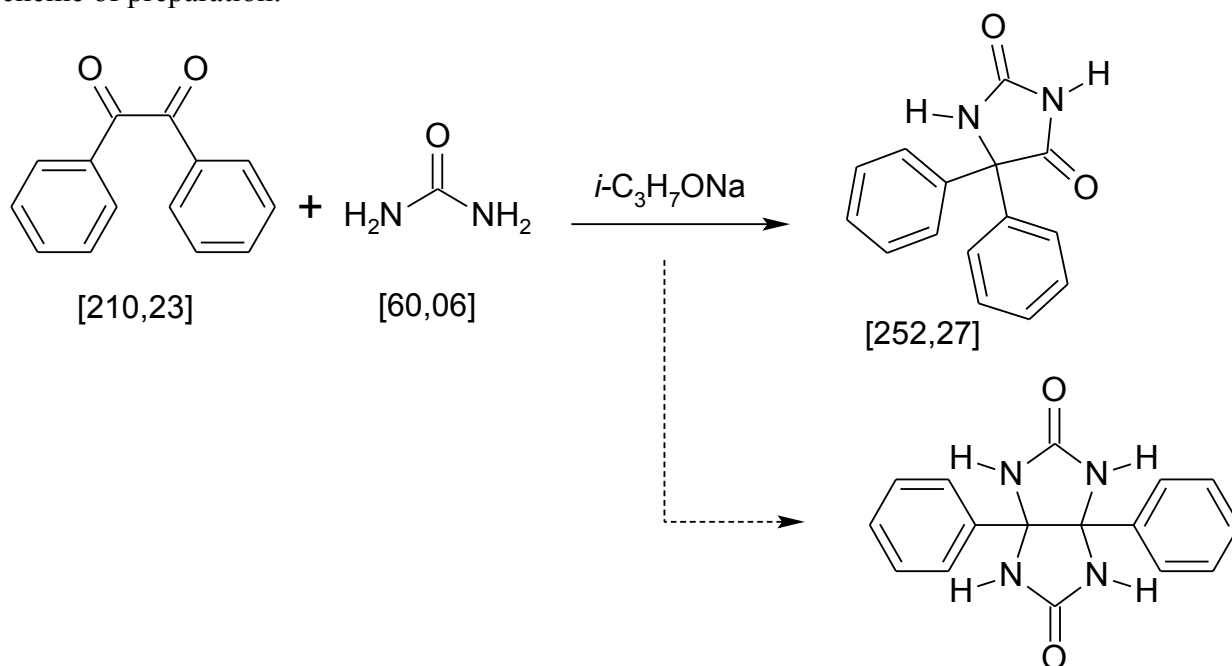
benzil (1,2-diphenyl-1,2-dione) 2.3g (0.011 mol)

urea 1 g (0.017 mol)

sodium 0.7 g (0.03 mol)

propan-2-ol 50 ml

Scheme of preparation:



Procedure:

Sodium (is supplied by the laboratory technician cut into small pieces) is gradually added into propan-2-ol placed in a well dried round-bottom flask equipped with a condenser with a humidity-absorbing closure. After its dissolution by the stirring on a magnetic stirrer (forming of alcoholate), urea is added and finally 2.3 g benzil (well dried). The reaction mixture is then refluxed under stirring on a magnetic stirrer for 30 minutes. Once a precipitate begins to form water is added until the precipitate is dissolved (8 – 16 ml). Then approx. 25 ml of the solvent is distilled off on a rotary vacuum evaporator. The mixture is then poured into 170 ml of cold water and let stand. The formed precipitate of the side product is then filtered off. The filtrate which contains sodium salt of phenytoin is carefully acidulated with concentrated hydrochloric acid to the pH ~3. The micro-crystalline precipitate of phenytoin is then formed. It is isolated by suction, washed with water on the filter and dried. It can be recrystallized from boiling water with usage of active carbon. Its purity, especially the absence of starting benzil, is then tested by TLC with benzil as the comparison compound. The identity is then confirmed by ¹H- and ¹³C-nuclear magnetic resonance (NMR) spectroscopy: place approx. 20 mg of the dried substance into a plastic tube with a lid and consult your lecturer.

Yield 65-70% of theory.

Properties:

Phenytoin is a colourless micro-crystalline compound of m.p. 293-296°C, insoluble in water, benzene and chloroform. (The side reaction product 1,5-diphenyl-2,4,6,8-tetraazabicyclo[3,3,0]octan-3,7-dione or 3a,6a-diphenyltetrahydroimidazo[4,5-*d*]imidazole-2,5-(1*H*,3*H*)-dione has m.p. 390 – 394°C. Both melting temperatures are, unfortunately, not measurable

on a common capillary melting point apparatus.) Phenytoin dissolves in alkaline hydroxides solutions forming salts. It was first prepared by Biltz and Rimpel as early as in 1908. It is still used as an antiepileptic (Epilan D Gerot[®]).