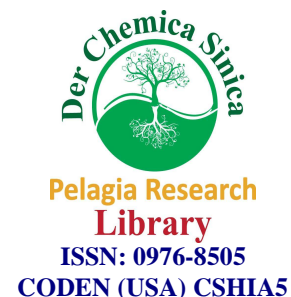




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### Synthesis of Hydantoin and Thiohydantoin

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#### ABSTRACT

*In basic media the benzil reacts with urea and thiourea to give the cyclic compounds, hydantoin and thiohydantoin respectively. The initial step in the reaction involve the attack by urea and thiourea on the carbonyl group of the benzil to give the diol, which then tends to eliminate water and gave the final products, which were characterized by physical and spectral methods*

**Key words:** Synthesis, hydantoin, thiohydantoin, benzil.

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#### INTRODUCTION

The hydantoin is also called phenytoin is used to treat various types of convulsions and seizures. Phenytoin acts on brain and nervous system in the treatment of epilepsy, its action is to damp the unwanted brain activity seen in seizure by reducing electrical conductance among brain cells by stabilizing the inactive state of voltage gated sodium channels. Phenytoin is also used to control arrhythmia (irregular heartbeat) and to treat migraine headaches and facial nerve pain [1-4]. Phenytoin (diphenyl hydantoin) was first synthesized by German physician H Biltz in 1908 [5] then it was used in 1938 for controlling seizures.

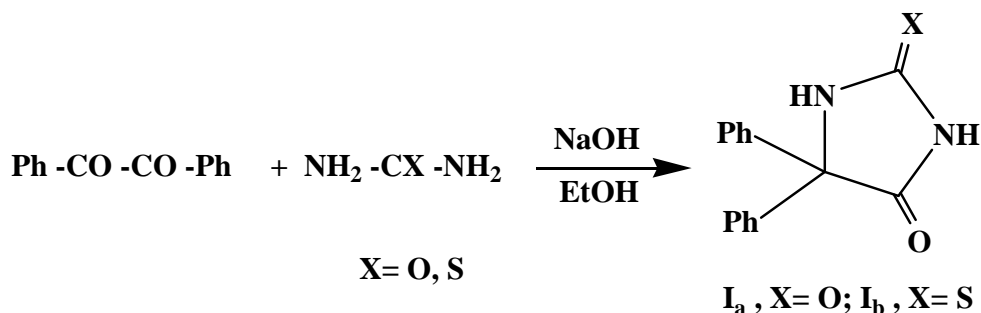
Hydantoin and its derivatives are also important intermediates in the synthesis of several amino acids, also they are the basic material of new generation of weather-proof high temperature stable epoxy resins [6]. Other hydantoin derivatives are used in numerous consumer products, such as hair spray cosmetics, once utilized medications and photographic films [7]. The synthesis and applications of optically active polymers are the newly considerable topics which have been paid more attention recently [8,9].

Due to the importance of these compounds, we have decided to synthesize the hydantoin and thiohydantoin and this paper describes the synthesis and characterization of the products.

#### MATERIALS AND METHODS

All reagents and chemicals were of analytical reagent grade, they were used without further purification. Melting points of the products were measured on Stuart apparatus and uncorrected. IR spectra were recorded on a FTIR-1615 of Perkin-Elmer spectrophotometer in KBr pellets. The <sup>1</sup>H-NMR spectra were recorded on Bruker AMX-300 spectrometer in d<sub>6</sub>-DMSO. Chemical shifts relative to TMS used as internal standard were obtained in δ unit, the spectral analysis were carried out at Cairo University, Egypt.

The hydantoin and thiohydantoin were prepared by reaction of benzil with urea and thiourea respectively, according to the scheme outlined below



### Reaction scheme

#### Preparation of hydantoin and thiohydantoin ( $\text{I}_a$ and $\text{I}_b$ ) [3,6,9]

In a round-bottomed flask equipped with a reflux condenser, a mixture of benzil (0.025 mol), urea or thiourea (0.05 mol), 15 mL of 30% aqueous sodium hydroxide solution and 75 mL of ethanol were placed. The mixture was heated under reflux for 4 hrs, after cooling to room temperature; the reaction mixture was poured into 125 mL of cold water and mixed thoroughly. The reaction mixture was allowed to stand for 15 min and it was filtered under suction. Then the filtrate was acidified with concentrated hydrochloric acid and the resulting precipitate was filtered and washed with water. The crude products were recrystallized from 95% ethanol.

#### 5,5-Diphenylhydantoin ( $\text{I}_a$ )

M.p. 292-3°C (Lit.<sup>3</sup> 288-91; Lit.<sup>6</sup> 297-8);  $\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}_2$ ; C 71.43 (70.92); H 4.78 (4.53); N 11.11 (11.46). FTIR(KBr): 3253, 3197, 1769, 1745, 1721, 1485, 1424, 1012, 780, 763, 726, 689, 651  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (300 MHz): 7.34-7.46(10H), 9.27(1H), 11.08(1H) ppm.

#### 5,5-Diphenylthiohydantoin ( $\text{I}_b$ )

M.p. 232-34°C (Lit.<sup>9</sup> 234-5);  $\text{C}_{15}\text{H}_{12}\text{N}_2\text{OS}$ ; C 67.16 (66.98); H 4.47 (4.83); N 10.44 (10.86). FTIR(KBr): 3266, 3146, 1752, 1724, 1542, 1443, 1376, 1162, 999, 841, 728, 694, 536  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (300 MHz): 7.34-7.48(10H); 7.8(1H); 8.6-9.1(1H).

## RESULTS AND DISCUSSION

An interesting and useful synthesis of hydantoin and thiohydantoin, is the condensation of  $\alpha$ -diketone with urea and thiourea respectively. The formation of these compounds ( $\text{I}_a$  and  $\text{I}_b$ ) involves a molecular rearrangement in which a phenyl group undergoes a 1,2-shift and has been cited as an example of the pinacol rearrangement [10]. It is accepted that the reaction proceeds stepwise with the formation of the intermediate 4,5-diphenyl-4,5-dihydroxy-2-imidazolone followed by a pinacol rearrangement leads to the formation of hydantoin or thiohydantoin. The reaction is carried out in aqueous ethanol and in basic media, the products were crystallizes out from the reaction mixture on cooling.

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