

Thematic course: *gem*-Dichlorocyclopropylmethyl substituted nitrogen containing heterocycles. Part 3.

## Synthesis and properties of 3-[(1-methyl-2,2-dichlorocyclopropyl)methyl]hydantoins

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### Abstract

Hydantoin derivatives containing aromatic or heterocyclic substituents attract attention as drugs and antibacterial agents. Introduction of *gem*-dichlorocyclopropyl group to their composition causes the considerable interest because three-membered carbocyclic group is a nutrient and also has high reactivity. Therefore, an actual task is the development of methods of synthesis of *gem*-dichlorocyclopropylhydantoins.

In this report are given results on studying of reactions 1-methyl-1-chloromethyl-2,2-dichlorocyclopropan (**1**) with 5,5-dimethyl- (**2a**), 5,5-diphenyl- (**2b**) and 1-phenylhydantoins (**2c**) in the environment of dimethylformamide in the presence of sodium hydroxide. Effective use of cheap sodium hydroxide was confirmed by the example of 5,5-dimethylhydantoin alkylation chloride (**1**).

Carrying out these reactions, it was necessary to take into account that the alkylating reagent **1** comprises a different activity on halogen atoms, and hydantoins (**2a-c**) – imide group. This does not exclude the possibility of leakage in the presence of sodium hydroxide in a polar solvent competing reactions. We have found that when an equimolar ratio of the reactants and temperature of 120-125 °C in high yields the products are formed exclusively by *gem*-dichlorocyclopropyl in position "3" hydantoin cycle – 1-*R*-5,5-*R*<sup>1</sup>-3-[(1-methyl-2,2-dichlorocyclopropyl)methyl]hydantoins [**3a-c**, R = H, R<sup>1</sup> = CH<sub>3</sub> (**a**), Ph (**b**); R = Ph, R<sup>1</sup> = H (**c**)].

Obviously, in the above conditions initially hydantoins corresponding sodium salts (**2a-c**) are formed which are further alkylated by cyclopropane **1** according to halogenomethyl group without exposing cyclopropane ring.

Structure of compounds **3a-c** was confirmed by nuclear magnetic resonances methods <sup>1</sup>H NMR and IR spectroscopy. The IR spectrum contains signals characterizing carbonyl group, and *gem*-dichlorocyclopropyl and benzene rings. In the analysis of <sup>1</sup>H NMR spectra we established magnetic nonequivalence methylene protons of the cyclopropane ring and CH<sub>2</sub>N-group.

Thus, reaction of 1-methyl-1-chloromethyl-2,2-dichlorocyclopropane 5-phenyl-, 5,5-diphenyl- and 5,5-dimethylhydantoins in the presence of sodium hydroxide in dimethylformamide medium at equimolar ratio of reagents are received corresponding 3-[(*gem*-dichlorocyclopropyl)methyl]substituted hydantoins. We studied their physical and chemical properties. Synthesized 3-substituted hydantoins can potentially have biological activity.