HETERYLADAMANTANES: 
SYNTHETIC INVESTIGATIONS 
OF RECENT YEARS, BIOLOGICAL 
ACTIVITY, AND OTHER ASPECTS 
OF PRACTICAL APPLICATION. (REVIEW)*

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Published data of the last five years on methods for the synthesis of adamantyl-substituted heterocycles were analyzed. Data on the biological activity and other practical applications of heteryladamantanes are reviewed for the first time.

Keywords: heteryladamantanes, biological activity.

The chemistry of adamantane and its derivatives is a comparatively young department of organic chemistry. (About 70 years have elapsed since the discovery of adamantane in petroleum [1].) At the same time a constant growth has been observed in the number of investigations in this region, particularly beginning with the seventies of the twentieth century. This is due not only to the unique structure of the adamantane molecule, resulting in a series of unique features in its physical and chemical characteristics, but also to the prospects for practical application of its derivatives – from heat-resistant polymers, lubricants, plasticizers, jet fuels, and explosives to components of artificial leather (perfluorinated adamantane) and medicines with a wide range of activity. (Currently about 20 effective medicinal products based on adamantane derivatives are being produced.) The introduction of the adamantyl fragment into organic compounds modifies their biological activity, changing and often intensifying it. This is due to change in the stereochemical structure, hydrophobicity, and lipophilicity of the compounds and the more favorable conditions of their transport through biological membranes. Investigators have paid particular attention to heteryladamantanes as shown, in particular, in the reviews [2-13], which include papers on methods for their synthesis and study of their structure and reactivity. Although some of these reviews give fragmentary data on the biological activity of individual derivatives of heteryladamantanes, an analysis of the present state of the problem has not been made.

The present review gives data from the last five years on methods for the synthesis of heteryladamantanes (saturated and aromatic) and classifies and analyzes for the first time data on the biological activity of this promising class of organic compound. The methods of synthesis are grouped on the basis of the size of the heterocyclic fragment, and the biological activity is arranged according to type.

* Dedicated to Academician M. G. Voronkov on his eightieth birthday.

Three-membered Heteryladamantanes

Over the last five years several reports have been published on adamantyl-substituted thiiranes and diaziridines. Thus, the reaction of biadamantylidene (1) with triphenylmethanesulfonyl chloride (2) in an atmosphere of nitrogen gave biadamantylidenethiirane (3) with a 93% yield. Treatment of the latter with \( m \)-chloroperbenzoic acid (\( m \)-CPBA) in dichloromethane at \(-78^\circ C\) under nitrogen led to biadamantylidenethiirane 1-oxide. Compound 4 decomposes when heated [14], and with 2,3-dimethyl-1,3-butadiene (5) (boiling in toluene, 12 h) it gives a mixture of biadamantylidene (1) and 2,5-dihydro-3,4-dimethylthiophene 1-oxide (6) [15].

The synthesis of mono- and diadamantyl-substituted diaziridines has been described. Thus, the reaction of 1-aminoadamantane (7) with CH\(_2\)O in H\(_2\)NSO\(_3\)H in the presence of potassium carbonate gave the previously unknown 1-(1-adamantyl)diaziridine (8) (4%) and (1-adamantyl)aminoacetonitrile (9) (13%) [16]. Earlier 1,2-di(1-adamantyl)diaziridine (10) had been obtained with a yield of 9.8% by the analogous reaction of the amine 7 with CH\(_2\)O and \( t \)-BuOCl [17].

As a result of the photoirradiation of (2-adamantyl)-2,3'-[3H]diaziridine in isooctane at room temperature 2-diazoadamantane and biadamantylidene (1) were obtained as the primary products [18].