Synthese en chemie van 4-azahomoadamantan-5-on

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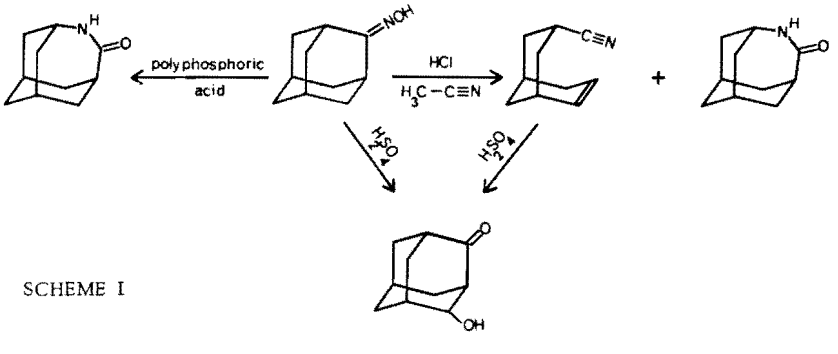
SUMMARY

This thesis deals with the synthesis of 4-azatricyclo-[4.3.1.1^{3,8}]undecan-5-one (4-azahomoadamantan-5-one) and derivatives thereof. Moreover a new and convenient synthesis of 4-hydroxyadamantan-2-one is described.

After an introductory chapter, a review of the literature on variations of the adamantane skeleton and on the pharmacological and anti-viral properties of adamantane derivatives is given in chapter two.

The synthesis of 4-azahomoadamantan-5-one is the subject of chapter three. The Beckmann rearrangement of adamantanone oxime was shown to be a very complicated reaction, the product composition depending on the catalyst employed. With polyphosphoric acid the expected 4-azatricyclo[4.3.1.1^{3,8}]undecan-5-one was mainly obtained. With hydrogen chloride in acetonitrile adamantanone oxime also underwent rearrangement to the lactam, but in addition a fragmentation known as the "Beckmann fission" was observed. In this way bicyclo[3.3.1]non-6-ene-3-carbonitrile was obtained. Surprisingly a Ritter reaction of this unsaturated nitrile in concentrated sulfuric acid yielded 4-hydroxyadamantan-2-one as the main product. Isomerisation of the secondary hydroxy compound in the strongly acidic medium did not occur. A still more convenient synthesis of 4-hydroxyadamantan-2-one was possible by treating adamantanone oxime itself with concentrated sulfuric acid. The main reactions are shown in scheme I.

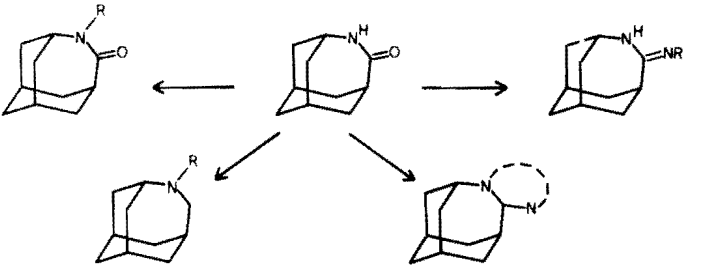


SCHEME I

In chapter four the synthesis of derivatives of 4-azahomoadamantan-5-one is described. Four types of products were prepared as is shown in scheme II:

1. alkylated or acylated 4-azahomoadamantan-5-ones.
2. substituted 5-imino-4-azahomoadamantanes.
3. alkylated 4-azahomoadamantanes.
4. heterocycles fused with 4-azahomoadamantane.

SCHEME II



Furthermore the first synthesis of a diazadihomoadamantane was achieved by a Beckmann rearrangement of 4-azahomoadamantan-5-one oxime.

Finally the results of an investigation about the pharmacological and anti-viral properties of the synthesized compounds are given in chapter five. It was found that some of the compounds showed anti-viral and/or hypotensive activities.