

University of Groningen

## 2,2-digesubstitueerde adamantanen

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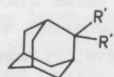
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## SUMMARY

The main goal of the research described in this thesis was to develop appropriate routes for the synthesis of 2,2-disubstituted adamantanes including adamantanespiroderivatives that might possess physiologically active properties. In addition attention was paid to the steric influence of the adamantane moiety on the course of the reactions.



Chapter I is an introductory chapter. Chapter II deals with a number of condensation reactions with 2-AdCOOCH<sub>3</sub> (8), 2,2-AdBrCOOCH<sub>3</sub>, 2-AdCHO and some addition reactions with methyleneadamantane derivatives. These reactions gave 2,2-disubstituted adamantanes in (very) poor yields while some failed entirely..

An exception was the addition of chlorosulphonylisocyanate to carbonyladamantane (49) (methanolyses of the adduct yielded 55).

In sharp contrast, the reactions of 2-AdCOOH<sub>3</sub> with lithiumdiisopropylamide followed by treatment with carbon dioxide gave the monoester of adamantane-2,2-dicarboxylic acid (33) in a nearly quantitative yield (chapter V). The latter compound served as the starting material for many other 2,2-disubstituted adamantanes. To determine the scope and limitations of this novel synthetic route to malonic acid derivatives a number of carboxylic esters were treated in the same way. The results were promising especially for the preparation of certain malonic acids which could be obtained with difficulty by classical routes.

In chapter IV the synthesis of a number of adamantanespirocyclobutane derivatives including adamantanespiro(3'-aminocyclobutane) (96) and adamantanespirocyclobutane-2',3'-dione (84) is mentioned. Adamantanespiro-2'-succinic anhydride (57) served as starting material for these compounds.

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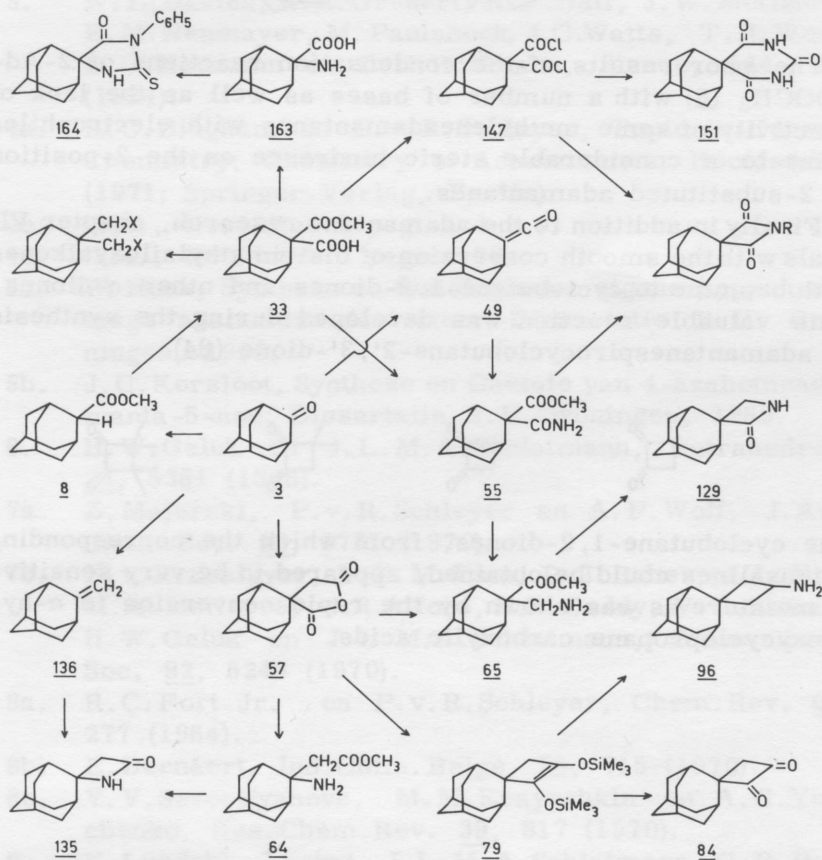
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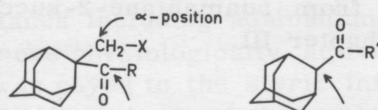
amantanespiro-  
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Chapter VI is concerned with the preparation and properties of adamantanespirocompounds with one or two nitrogen atoms (azetidines, azetidinones and malonimidic compounds). The two isomeric adamantanespiroazetidinones were prepared from the corresponding  $\beta$ -amino-esters. The amino-esters could be obtained only with great difficulty and in low yields from adamantane-2-succinic anhydride, as described in chapter III.



During this research several examples of the steric influence of the adamantyl group on the reactivity of adamantane derivatives were observed. The  $\alpha$ -carbon atoms of

2,2-disubstituted compounds strongly resemble neopentyl type atoms. In this respect the low reactivity of 2,2-di(tosylmethyl)adamantane (chapter II) and adamantane-2,2-dicarboxylic acid chloride (147; chapter VI) in nucleophilic substitution reactions is noteworthy.



The poor results of the condensation reactions of 2-Ad-COOCH<sub>3</sub> (8) with a number of bases as well as the lack of reactivity of some methyleneadamantanes with electrophiles point to a considerable steric hindrance on the 2-position of 2-substituted adamantanes.

Finally in addition to the adamantane research, chapter VII deals with the smooth conversion of bistrimethylsiloxyalkenes with bromine to cyclobutane-1,2-diones and other  $\alpha$ -diones. This valuable reaction was developed during the synthesis of adamantanespirocyclobutane-2',3'-dione (84).



The cyclobutane-1,2-diones, from which the corresponding quinoxalines could be obtained, appeared to be very sensitive to moisture as was shown by the rapid conversion to  $\alpha$ -hydroxycyclopropane carboxylic acids.