Annulation reactions of hetero-aromatic compounds. A new synthetic route to benzo[b]thiophene, benzo[c]thiophene and quinoline derivatives
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Document Version
Publisher's PDF, also known as Version of record

Publication date:
1982

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):

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In this thesis the annulation reactions of ortho-disubstituted hetero-aromatic compounds with Michael acceptors are described.

In Chapter I a general introduction is given to annulation reactions. The choice of the hetero-aromatic compounds that we used for our annulations, i.e. thiophenes and pyridines, is elucidated. Furthermore, properties of thiophenes and pyridines with respect to their substitution and annulation reactions are discussed. Existing annulation routes to benzo[b]thiophenes, benzo[α]thiophenes and quinolines, and substitution reactions of these groups of compounds, also get attention in Chapter I.

Chapter II describes the synthesis of the starting materials for the annulation reactions, that is:

\[
\begin{align*}
&\text{E} = \text{COOMe, CN of CHO} \\
&\text{R}_1 = 4, 5, \text{di}-
\end{align*}
\]

The general requirements, i.e. a nucleophilic and an electrophilic centre, both a to the heterocycle and in ortho-positions, and the specific choice of substituents for our starting materials are discussed. These compounds are all new compounds. Comments are given on the problems encountered in the synthesis of 3,4-disubstituted pyridines. We have been unable to solve these problems.

The annulation reactions of 2,3-disubstituted thiophenes to benzo[b]-thiophenes and 4,5-dihydrobenzo[b]thiophenes are described in Chapter III.

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\begin{align*}
&\text{E} = \text{COOMe, CN of CHO} \\
&\text{R}_1 = 4, 5, \text{di}-
\end{align*}
\]

Various reaction conditions for these annulation reactions were investigated. In this chapter X-ray proof of the (dihydro)benzo[b]thiophene struc-

\[
\begin{align*}
&\text{E} = \text{COOMe, CN of CHO} \\
&\text{R}_1 = 4, 5, \text{di}-
\end{align*}
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of the stereochemistry of the annulation products is given, as well as \(^1\)H and \(^{13}\)C NMR data of these products. The mechanism of the annulation reactions is also discussed in Chapter III. Further, reactions are described to convert 4,5-dihydrobenzo[\(\ell\)]thiophene products into benzo[\(\ell\)]thiophenes.

Chapter IV discusses annulation reactions of 3,4-disubstituted thiophenes with Michael acceptors. These reactions lead to benzo[\(a\)]thiophene derivatives.

In the last Chapter, V, reactions are discussed of 2,3-disubstituted pyridines with Michael acceptors, leading to quinolines and 7,8-dihydroquinolines.

\(^1\)H and \(^{13}\)C NMR data supported the quinoline structure of the products. A comparison of the annulation reactions described in Chapter III, IV, and V showed the following reactivity order towards Michael acceptors: 2,3-disubstituted pyridines > 2,3-disubstituted thiophenes > 3,4-disubstituted thiophenes.