4. Summary

The objective of the present thesis was the synthesis of a large variety of bicyclic azidothiosugars with thiolane or thietane structure, starting from simple carbohydrates such as D-ribose and D-xylose. These bicyclic thiosugars should be oxidized to the corresponding diastereomeric sulfoxides and sulfones, enabling the possibility of stereoselective coupling with electrophiles after deprotonation at the α-position of the oxidized sulfur.
In addition, the bicyclic thiosugars are of interest from a pharmacological point of view, especially after coupling of azido- and aminoderivatives with nucleobases to nucleosides.

Twelve different bicyclic azidothiocompounds were obtained: the thioethers **14a**, **14b** and **93a**, the sulfoxides **105a**, **108a**, **108b** and **109b**, the sulfones **110a** and **110b** and the nucleosides **96a** and **97a**.
Because the 3-position in furanosides is much more reactive as compared with the 2-position, most of the mentioned target-molecules are 3-azidoderivatives. For this reason and because of it is all-cis-configuration the β-anomeric **93b** could not be synthesized at all with the methods used in this thesis.
Beside the classical route via the epoxides, which give good overall yields but need many reaction steps to be synthesized, more effective syntheses could be developed. The use of cyclic sulfites, dimesylates and tosylates made possible the synthesis of some target bicyclic azidothiosugars in seven instead of eleven reaction steps with satisfying yields.

For the introduction of sulfur, a thio-variant of the Mitsunobu reaction is well-established to give good yields combined with a high stereo- and regioselectivity.
Simple bicyclic thiosugars (without azido groups) can be synthesized much easier in only four steps from the starting compounds because of the selectivity of the Mitsunobu reaction. These products were prepared to make sufficient quantities available for testing purposes for the large number of the following synthesis steps.
Among others, the 2-desoxybicyclic compounds **92a**, **92b**, **107a**, **107b**, **101a**, **101b**, **87a** and **87b** were obtained in only four steps starting from 2-desoxy-D-ribose.

The anomers of all bicyclic products were separated. No mixtures of any isomers were used for any reaction of a bicyclic compound.

The oxidation-step was carried out by two standard procedures. The less powerful hydrogen peroxide was used when only sulfoxides were desired. With m-chloroperbencoic acid also the sulfones could be synthesized quickly and in good yields. The ratio of the two diastereomeric sulfoxides and the sulfone can be controlled by the molecular amount of oxidation agent.

Further reactions were carried out with the bicyclic thiosugars. Bicyclic aminothiosugars **104a**, **123a** and **124a** were synthesized by chemoselective reduction of the azido group. This reduction with triphenylphosphine did not influence the sulfoxide group.

Some nucleosides were synthesized with the nucleobase thymine. It´s silylated derivative was added to the azide **14a** resulting in **96a** and to the desoxysugar **92a** to give both anomers **120a** and **120b**.
The 3'-Azidonucleoside **96a** was oxidized to give the sulfoxide **97a**.

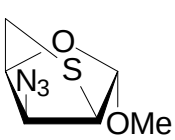
The deprotonation reactions of the bicyclic target molecules were not successful. Under the influence of the strong bases, which has to be used, the thietanes were decomposed spontaneously because of the pronounced strain in the four-membered ring system. Besides decomposition some eliminations have been observed, identified by the resulting double bond between C-2 and C-3.
Also the more stable five-membered thiolane systems tend to decomposition and elimination, especially because of the neighbouring reactive acetalgroup at 1-position.

These side-reactions should be prevented by using 2-desoxybicyclic thiosugars. The used carbanion of sulfone **87b** showed an increased stability but still did not react with the added electrophiles.

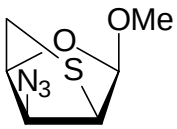
The synthesized bicyclic compounds seem to be not suitable for deprotonation reaction and subsequent coupling with an electrophile. One advantage of the carbohydrates, which was one of the reasons why these molecules were chosen from the chiral pool, is the high functionalization which makes a variety of follow-up reaction steps possible. Unfortunately, this follow-up chemistry takes place a little too early.

The structures of the target-molecules were investigated by X-ray structural analyses, if suitable crystals were obtained. In addition, the structures of all synthesized bicyclic products were calculated and compared with the results of the X-ray spectroscopy.
If the fact is considered that in the X-ray structures the molecules are under the influence of intermolecular interactions whereas in calculations only single, isolated molecules are treated, the results are in good conformity.
As expected, the bicyclic thiolanes exhibit stable conformations, resulting in a C3-exo-conformation for the furane-ring in all investigated thiolanes.
On the other hand, at least four different conformations were found for the bicyclic thietanes.

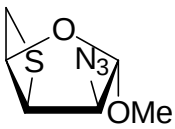
Compounds mentioned in this summary:



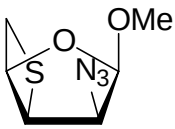
14a



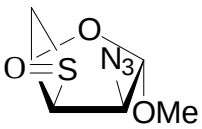
14b



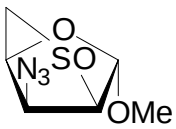
93a



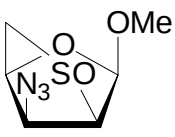
93b



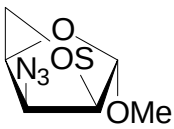
105a



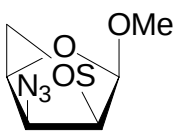
108a



108b



109a



109b

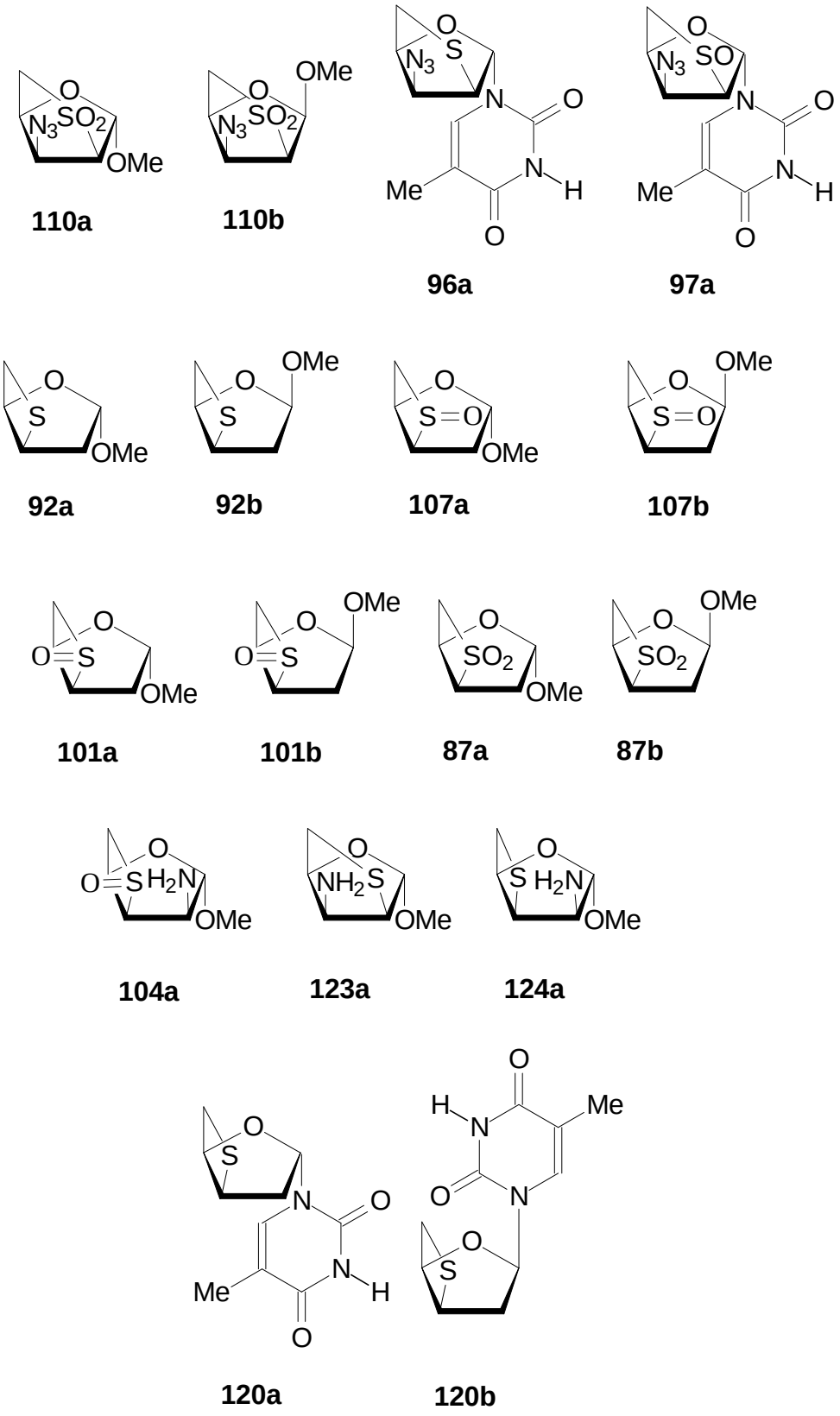


Abbildung 68: Compounds mentioned in the summary