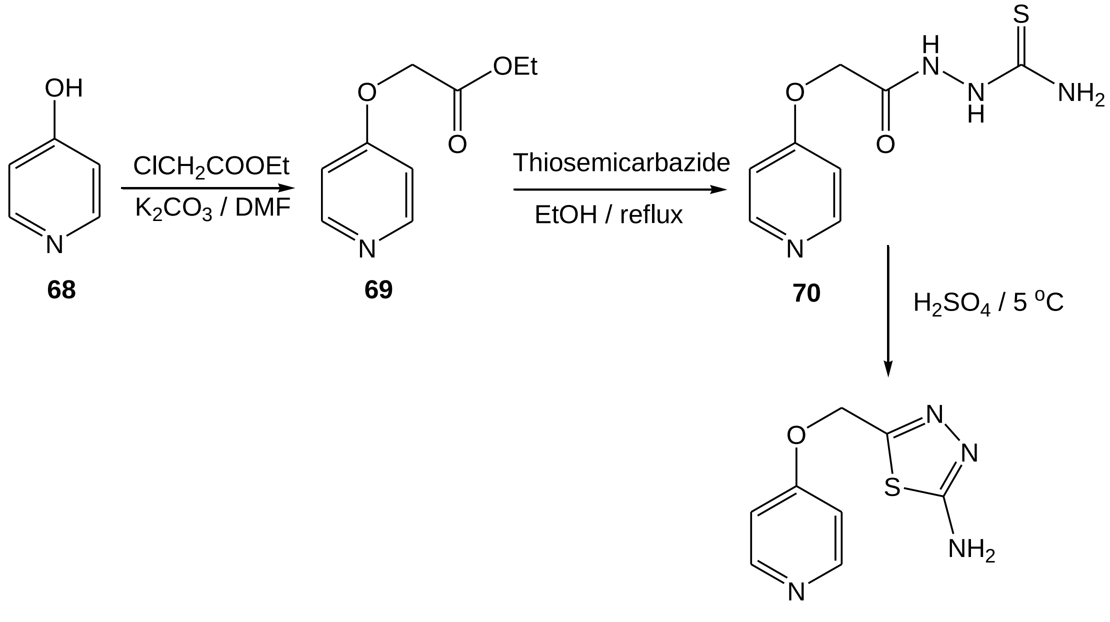
Summary

The thesis reports the synthesis and antimicrobial activity of new disubstituted 1,3,4-thiadiazole derivatives, their derived pyrazoles, sugar hydrazones as well as derived *C*-nucleoside analogs. The newly synthesized compounds were characterized by their spectral and analytical data; IR, ^{1}H NMR and elemental analysis.

The synthesized compounds were studied for their antimicrobial activity against a number of bacteria and fungi some of the tested compounds showed high activities and others showed moderate to low inhibition activities.

Reaction of the starting compound 4-hydroxypyridine with ethyl chloroacetate gave the ethyl ester derivative **69** in 70% yield. Reaction of the latter ester **69** with thiosemicarbazide at reflux temperature afforded the substituted thiosemicarbazide derivative **70.**

Heterocyclization of the resulting acylthiosemicarbazide derivative in sulfuric acid at low temperature afforded after neutralization the 2-amino-1,3,4-thiadiazole derivative 71 (Scheme 20).



Scheme 20

Acetylation of the 2,5-disubstituted thiadiazole derivative **71** with acetyl chloride in benzene produced the *N*-acetylamino-1,3,4-thiadiazole derivative **72** in 63% yield. When the latter *N*-acetyl derivative was allowed to react with 2,6-dimethylbenzaldehyde it afforded the substituted acrylamide derivative **73**.

Heterocylization of substituted enone derivative **73** by reaction with hydrazine hydrate resulted in the formation of the substituted pyrazole derivative **74** (Scheme 21).

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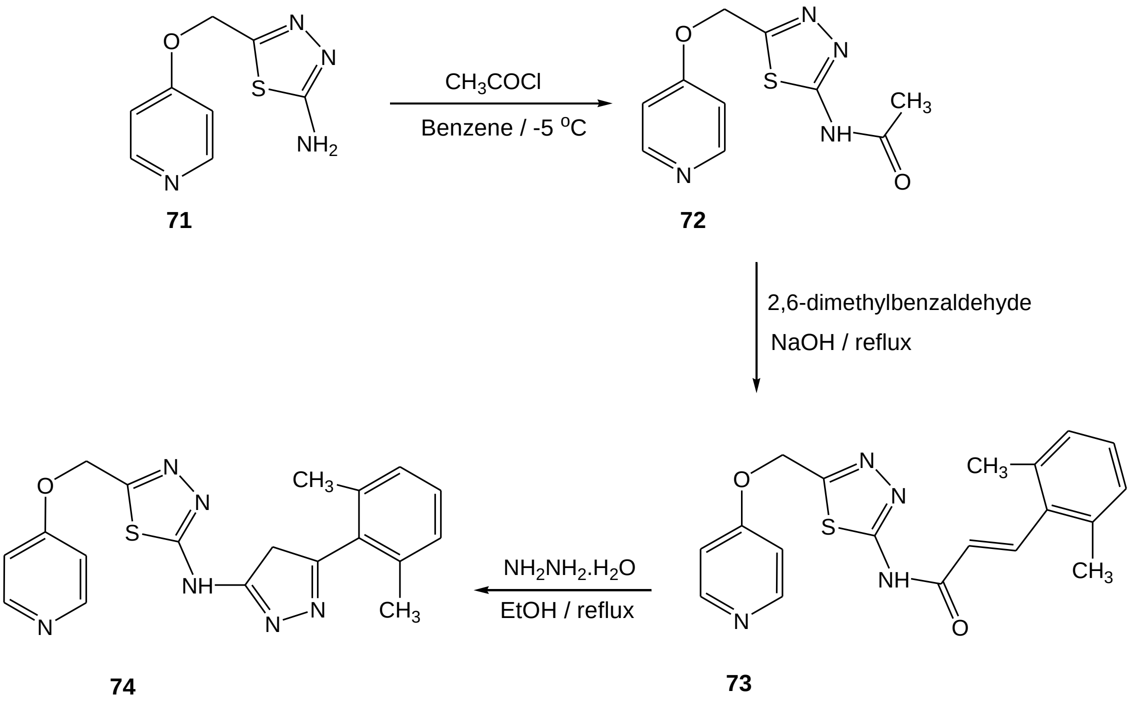
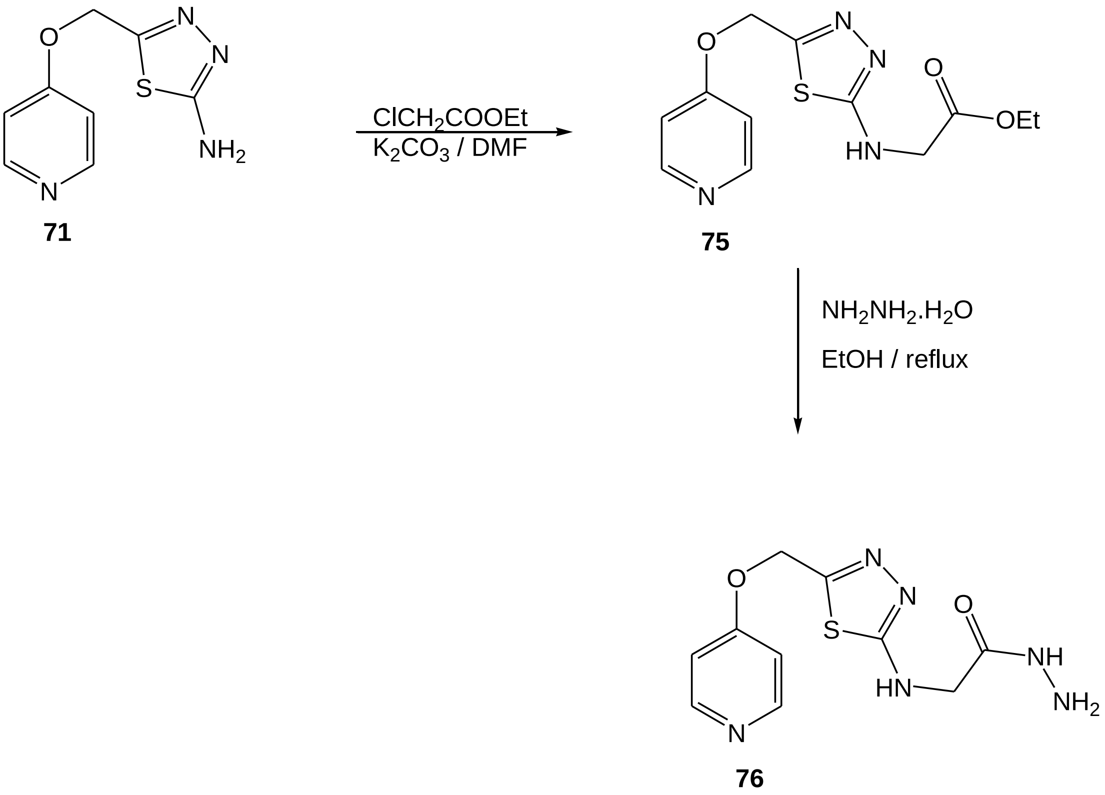


Scheme 21

Reaction of the aminothiadiazole **71** with ethyl chloroacetate in presence of potassium carbonate at room temperature gave the ethyl N-substituted acetyl ester **75**.

Hydrazinolysis of the latter ester with hydrazine hydrate afforded the corresponding acid hydrazide derivative **76** in73% yield (Scheme 22).



Scheme 22

When the hydrazide **76** was allowed to react with D-galactose, D-mannose or D-xylose in an aqueous ethanolic solution and a catalytic amount of acetic acid, the corresponding sugar acetyl hydrazones **77-79** were obtained respectively.

Acetylation of the sugar hydrazones **77-79** with acetic anhydride in pyridine at room temperature afforded the corresponding per-O-acetylated hydrazone derivatives **80-82**, respectively.

When the reaction was carried out with acetic anhydride at the reflux temperature gave 1,3,4-thiadiazolidine acyclic nucleoside analoges **83-85** respectively (Scheme 23).

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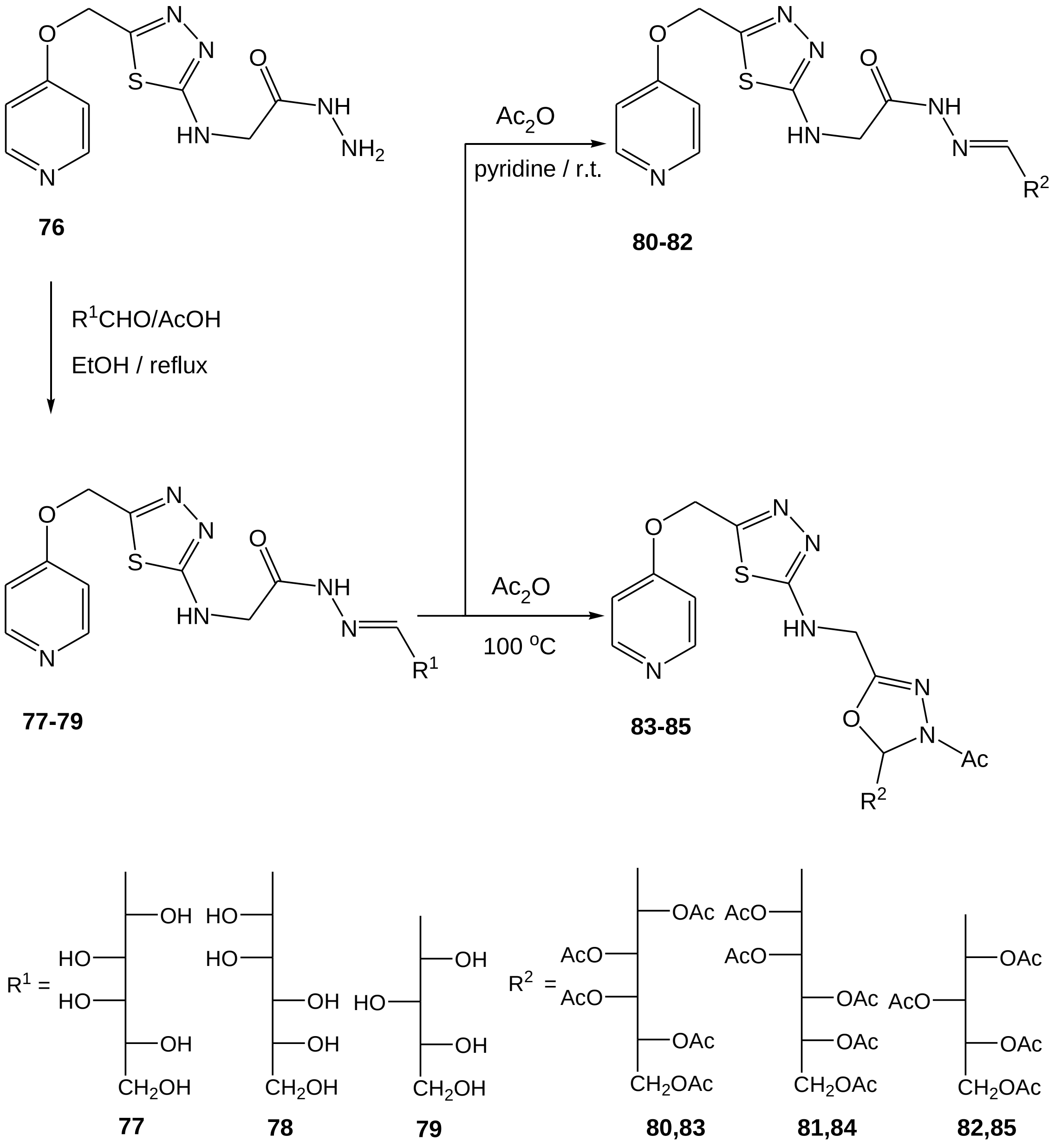
76
R¹CHO/AcOH
EtOH / reflux
77-79
Ac₂O
pyridine / r.t.
80-82
Ac₂O
100 °C
83-85
R¹ =
77
78
79
R² =
80,83
81,84
82,85

Scheme 23