MECHANOCHEMICAL SYNTHESIS OF QUATERNARY SALTS *N*-ACYLHYDRAZONE DERIVATIVES OF PYRIDOXAL HYDROCHLORIDE

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INTRODUCTION

Because of its important biological effects, vitamin B6 has been intensively researched for many years. In addition to being one of the vitamins from the vitamin B-complex group, which are necessary for the normal functioning of the nervous system, vitamin B6 is necessary for the normal functioning of the metabolism of lipids, glucose and amino acids, and is also important in numerous enzymatic activities. In the context of the importance of vitamin B6, chemists have focused their efforts on the synthesis of various structurally modified derivatives of vitamin B6 and testing their biological activity. Special attention is focused on the synthesis of new hydrazone and *N*-acylhydrazone derivatives of pyridoxal hydrochloride that show antituberculosis activity as well as the ability to chelate iron.

The aim of the work was to synthesize new quaternary salts of *N*-acylhydrazone derivatives of pyridoxal hydrochloride. Earlier studies have shown that the target quaternary salts can hardly be prepared by conventional synthesis, synthesis in acetone at reflux temperature. It was assumed that the groups present on the pyridine ring draw electron density with their negative inductive effect and thus reduce the nucleophilicity of nitrogen and make the reaction with phenacyl bromides more difficult (***Figure 1***).

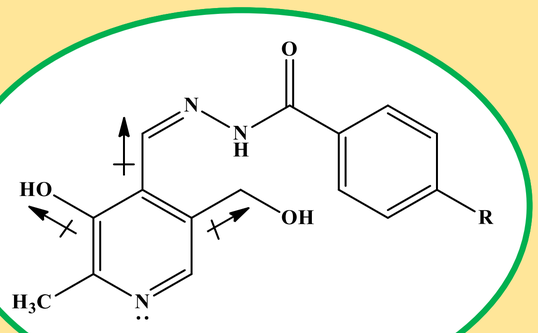


Figure 1.

Mechanochemistry is a branch of chemistry that studies the chemical and physical-chemical transformations of substances in all aggregation states created under the influence of mechanical energy. It is a green chemistry method based on mechanical grinding of the reactant and inducing chemical reactivity by applying mechanical force.

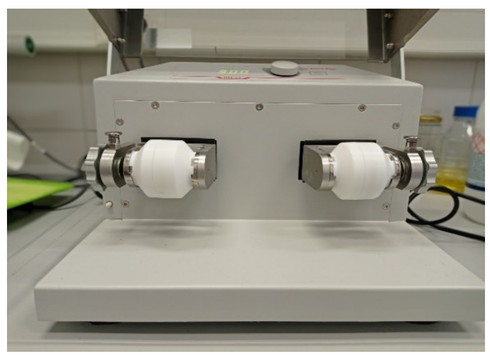
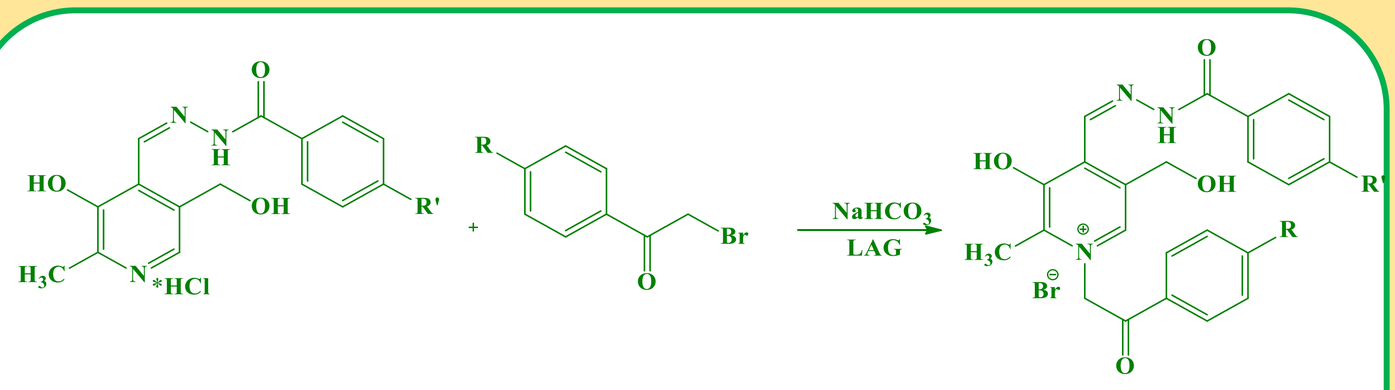


Figure 2. Anton Paar ball mill

Figure 3. Grinding jar



Scheme 1. Reaction scheme for the preparation of quaternary salts of *N*-acylhydrazone derivatives

The target compounds **1-16** were prepared by mechanochemical synthesis. Starting raw materials *N*-acylhydrazone derivatives of pyridoxal hydrochloride, phenacyl bromide or substituted phenacyl bromides (R= F, -Cl, -Br, $-NO_2$, $-CH_3$, $-OCH_3$, -Ph), sodium bicarbonate and acetone were placed in Teflon containers (**Figure 3**) in to which 10 mL of acetone was then added and ten grinding balls. The contents were mixed on a ball mill Anton Paar (***Figure 2***) for 4 hours at a frequency 30 Hz. After 4 hours, 50 mL of acetone was added to the container and poured into a beaker to separate the steel balls. The obtained product was separated by vacuum filtration, washed with methanol and then dried.

Table 1. Yields of quaternization rections in vibrating mill Anton Parr at a frequency 30 Hz

Compound	M / $gmol^{-1}$	M ($-Br^-$) / $gmol^{-1}$	Yield / %
1	518,79	438,88	13,6
2	536,78	456,87	17.5
3	553,23	473,33	21,8
4	597,68	517,78	19,4
5	563,97	438,88	14,1
6	532,81	452,91	2,7
7	548,81	468,91	29,8
8	594,88	514,98	23,9
9	483,34	404,44	17,4
10	502,33	422,43	10,3
11	518,79	438,88	20,6
12	563,24	483,33	14,8
13	529,34	449,44	10,8
14	498,37	418,46	22,6
15	516,38	434,46	12,65
16	560,44	480,53	2

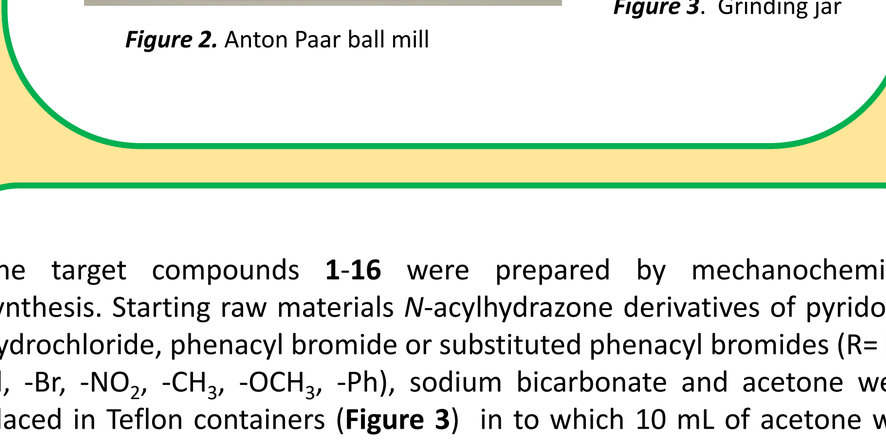


Figure 4. MS spectrum of compound 1-(2-([1,1'-biphenyl]-4-yl)-2-oxoethyl)-4-((2-benzoylhydrazono)methyl)-3-hydroxy-5-(hydroxymethyl) -2-methylpyridinium bromide **(16)**

- new quaternary salts of *N*-acylhydrazone derivatives of pyridoxal hydrochloride were synthesized for the first time by mechanochemical synthesis
- conventional synthesis of the target compounds has not been successful
- the advantage of mechanochemical synthesis is the short reaction time, the formation of the product after only 4 hour
- reactions take place with the addition of a minimum amount of solvent, LAG method
- the structures of the newly synthesized compounds were confirmed by recording mass spectra and ^1H and ^{13}C NMR

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