Answers to reviewers' comments

We thanks both reviewers for all the comments that helped us to improve this manuscript. We've corrected the manuscript following the several points mentioned here, and answered point by point to your questions to provide as much context as possible.

Reviewer 2

Comments and Suggestions for Authors

A manuscript by F. Descamps *et al*. describes the synthesis and in vitro and in silico studies of a series of compounds with a structure similar to that of the known drug losartan. The structure of the new compounds was rationally designed with the hope of achieving biological activity similar to or better than that of the reference compound. This was not entirely successful, although the synthesis of many new substances with confirmed purity and structure is valuable.

It's a pity that the m/z values in the LRMS are expressed to the nearest whole number; it would be helpful to know at least one decimal place. However, it's good that HRMS was performed for the new compounds and the number of decimal places (four) is correct. In the first LRMS spectrum shown in the Supplementary Materials, the accuracy is to one decimal place; for all others, it is rounded to whole numbers. Therefore, this may be due to the instrument's settings rather than its low resolution. Please check whether the instrument allows for accuracy to one decimal place. If so, please enter the corrected values into the characteristics.

Unfortunately, our device for LRMS only allow us to provide unit values while final compounds were systematically analyzed in HRMS to have proper number of decimal values.

The word "novel" has a much stronger connotation than the word "new". I do not agree that the substances obtained deserve such a strong term. They are not particularly unexpected or "exotic", so please use the word "new" instead in the body of the manuscript. Furthermore, in article titles, it is recommended to use strong words sparingly and only when justified. In my opinion, the use of either "new" or "novel" in the title is not justified. Please remove the word 'novel' from the title and do not even include "new".

We understand that such a nuance may exist in english, so we modified the title and text accordingly.

As soon as a figure, table, scheme, etc., is first mentioned in the text, it should appear as close as possible to that reference. In line 72 (page 2), there is a reference to Table 1, whereas Table 1 does not appear until page 7. In addition, other figures and schemes appear before Table 1.

We moved the table 1 accordingly, while it may be moved again during the editorial process.

In papers, when there are many compounds or they have complicated names, they are designated by numbers or alphanumeric symbols, both of which are written in bold. Since these abbreviations identify the substances on their own, it is unnecessary to precede them with the word “compound”. Instead of using, for example, the term “compound 6”, it is sufficient to use only “6”; this is truly sufficient, as it is clearer and less tiresome to read. Furthermore, in the experimental section, before the synthesis, although the systematic names were provided, the authors failed to write these abbreviations in bold.

We tried to removing the many occurrences of “compound” and add the bold into the experimental section.

Substituents are denoted by the symbol R. If there are several such substituents, we add the numbers 1, 2, and so on. It is better to write the numbers next to the R symbol as superscripts rather than subscripts. A subscript could be confused with the number of such substituents. Furthermore, labeling a tetrazole derivative (in terms of a substituent) as CN_4 (Scheme 1) or CN_4H (Table 1) is not ideal; it is probably better to represent it with a structural formula rather than a molecular formula, as this is ambiguous and may cause confusion regarding the nature of the substituent.

We modified the CN_4 with full letter tetrazole as it was indeed quite confusing.

It is recommended to use consistent abbreviations or symbols throughout a single article. In the body of the article, the authors refer to methylene chloride as DCM, while in Scheme 3 they use the molecular formula, CH_2Cl_2.

The notations were harmonized here and corrected in the text.

The common names of drugs are written with a lowercase letter. Brand names of drugs, on the other hand, are written with an uppercase letter. Generally, the name “losartan” is written with a lowercase letter, although it is sometimes written with an uppercase letter (Table 1 and line 242).

Lower case was harmonized in the text.

In the experimental section, line 280 reads “NH4OH”. This is incorrect. Ammonium hydroxide does not exist. It is better to write “NH_3(aq)”.

It is now corrected

Although 9 was crystallized from ethanol, the formula for acetonitrile was incorrectly listed after the melting point.

We corrected the typo here.

At Publishing House MDPI, we use the term Supplementary Materials rather than Supporting Information.

We changed it for supplementary Materials.