Review of the PhD. Thesis entitled „Catalytic and photochemical cycloadditions of alkynes" submitted by Mr. Alexander A. Fadeev

The structure of the Thesis is consistent with that of research papers in the field, ie. individual chapters include Introduction (State of the Art), Aims, Results and discussion, Conclusion, Experimental part and References. According to WoS data, Mr. Fadeev has contributed to two experimental publications. Specifically, he is the first author in two papers, one in *Org. Biomol. Chem.* and another in *Adv. Synth. Catal.* Since both papers report results that are clearly related to the Thesis, the conditions required by the Czech legislation as well as internal regulations of Charles University have been met.

The Thesis describes developmental synthetic efforts in two directions, united by the use of alkynes as the basic building stones. The first part deals with the use of borylated alkynes in [2+2+2] cyclotrimerizations, while the second one is focused on the investigation of the cycloaddition reactions of alkynes with quinones.

The quality and quantity of original research is, in my opinion, very good. The candidate developed the synthesis of 1,4-diborylated benzenes from ethynylpinacolborane, catalyzed by cp*Ru(cod)Cl first. Notably, for a successfull transformation, the other, disubstituted alkyne component had to bear a chelating group, capable of coordination to Ru; this was also confirmed by DFT calculations. In the next step, Mr. Fadeev explored the possibility of further transformations of the diborylated benzenes, including cross-coupling and oxidative processes. The latter reactions enabled him to access specifically substituted 1,4-benzoquinones, which were either natural products themselves (mirandamycin, violaceoid C) or could be elaborated towards natural product (alboatrin) analogs. The second part of the Thesis is no less interesting. Investigation of the conditions for [2+2] heterocycloadditions and carbocycloadditions of alkynes and 1,4-quinones revealed that, in contrast to literature reports, the reactions are governed by substitution rather than the presence of additives. I particularly appreciate the correction of a reported structure (however much unrealistic the structure is) in the literature enabled by NMR data of cyclobutene **241i**. In the last subchapter, dealing with nucleophilic additions to *p*-quinone methides, the candidate also uncovered and rationalized several erroneous conclusions from the literature. All in all, I have no doubts about the results and appropriateness of the conclusions.

The Thesis is well organized and logically guides the reader through the strategical and tactical development of the research. However, it shoud have been proofread more thoroughly, because it suffers from a number of formal mistakes and omissions, as further specified below.

The language could also have been improved, if the Thesis had been subjected to a more careful proofreading. The errors include inappropriate use of definite and indefinite articles, reverse order of subject and judgement, eg. pg. 28 „...As an example may serve the Co-catalyzed annulation reaction of triyne **121**..." should be ordered „...The Co-catalyzed annulation reaction of triyne **121** may serve as an example...". In some parts, the text is worded in a confusing fashion, eg. pg. 75, the sentence starting with „...Likewise, the additives did not improve the yield..." makes the reader think that isomers **240j** are stereoisomeric to **241j**.

Formal points:

1. In some cases, a structure has been assigned two or even more numbers throughout the Thesis. By way of example, the general structure of disubstituted alkyne is numbered **210** (Scheme 61), **203** (Scheme 55) or **9** (Scheme 6) and I am not sure if I listed all, the same is true for phenylacetylene and other compounds. In other Schemes, compound numbers are missing (eg. ketone **240f** on Scheme 82, pg. 80).
2. Pg. 26, what do you mean by the 3:1 mixture of *ortho* and *para* isomers formed from an unsymmetrical diyne **106**? Descriptors *ortho* and *para* are unambiguous only in disubstituted benzenes, and their use is no longer recommended.
3. I may have missed something, but I was unable to find or identify structures **210bc** to **210bf**, discussed in the text on pg. 55 and 56.
4. Pg. 73, line 3 from the top, you probably meant that ketone **240e** did **not** decompose.
5. Pg. 73, line 8 from the bottom, *E*/*Z* isomers **240j** (Scheme 78) are not derived from menadione, as stated on pg. 73.
6. Pg. 76, Scheme 79, some of the cyclobutenes **241** were formed as a mixture of regioisomers. In my opinion, the structures of the minor isomers should have been depicted. Similarly, adducts **241** possess 2 centers of chirality, whose relative configuration should also be indicated (however much it is beyond doubts).
7. Pg. 77, line 4 from the top, cyclobutene **240i** should be **241i**.

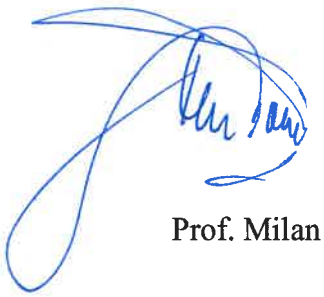
The following points might be raised in a discussion:

1. On pg. 47, you claim that stereoelectronic properties of the terminally substituted boronate **209** would allow it to selectively form a metallacycle intermediate. Since stereolectronic effects are usually about orbital alignment in the transition state, I feel that this statement should be explained in a greater detail.
2. Did you try/consider trapping of unstable methides **240** by a Diels-Alder process?

3. What is your idea of formation of naphtofurane **208** outlined in Scheme 89?

In summary, the work makes a substantial contribution to knowledge, shows a good knowledge of the most recent literature and demonstrates the ability to conceive and execute high quality chemical research. Most importantly, the candidate´s results enabled him to correct a few misleading conclusions from the literature. I just maintain that the results could have been much better communicated had the Thesis been subjected to a more careful proofreading, preferably in a printed form. Regardless of the last point, I recommend that the Thesis be unconditionally admitted to defence.

In Hradec Králové 19. 1. 2024



Prof. Milan Pour