

Oponentský posudek na doktorskou disertační práci Mgr. Prabhakara Cherkupallyho
s názvem

Synthesis and Applications of Fluorophosphonates

The aim of the Thesis is preparation of several types of fluorophosphonates and their applications as fluoroalkylation agents in the synthesis of fluorinated compounds.

The starting Introductory part describes first in detail the properties of fluorine as the atom of high potential in organic synthesis, as well as individual variants of fluorination methods. It then continues with analogous description of the role of polyfluoroalkyl group and polyfluoroalkylations with the emphasize on potential nucleophilic substitutions with fluoranions stabilized with heteroatoms as sulfur and phosphorus. Although this part is well written and readable, it is too general and long with regard to the aims of the Thesis. I would here appreciate if the author could concentrate more on the topics related to the targets of the Thesis and probably add some applications of the given methods on the synthesis of compounds with potential applications.

In the short second part author lists individual targets of the of the Thesis. Although the two main targets are given, the third part of the Thesis aimed in dehydrofluorination of difluorophosphonates to fluorovinylphosphonates, as well as alternative synthesis based on (fluoromethylene)diphosphonate is completely missing.

The third part of the Thesis, Results and discussion, summarizes the result of the PhD student's experimental work. It is organized according to the individual targets (including those not listed in the second part, Aims of the project).

The first part of the results concentrates on the applications of new trifluoromethylating agent, diethyl (trifluoromethyl)phosphonate. This is to my opinion the most significant part of the Thesis from the scientific point of view and widens reasonably the pool of available synthetic trifluoromethylating reagents. It is a pity that the author did not concentrate more on this issue and did not try to expand the range of possible electrophiles e.g. to imines used in the last major part of the work. Although plausible mechanism of the trifluoromethylating reaction is given, author did not attempt to use analytical method for deeper insight into understanding the reaction.

The second part is concentrated on alternative stereoselective synthesis of fluoroalkenylphosphonates (erroneously named in the title of the chapter as fluorophosphonates). As these compounds are already known, I am missing here direct comparison of author's two step approach with published methods regarding the yields and stereoselectivity. The references to the first chapter are not easy to compare. Also, and this is to my opinion serious drawback of the Thesis, no more details are given about the synthetic methods (were bromides, iodides or triflates used and what were the results) used for starting difluorophosphonates **76**. The same is true about the synthesis of diethyl (trifluoromethyl)phosphonate. It is even not clear, whether the starting compounds were synthesized by the author, his coworkers or other coworking laboratory. Again, the plausible mechanism without any details is given attempting to explain the stereochemical outcome of the reaction, however, without any reasoning including for example computational results this is completely speculative.

The third part attempts in analogy to the sulfur-stabilized fluoroanions to achieve regioselective conjugate addition by modifications of previously published conditions. Here the results obtained were not as straightforward as in the previous chapters. Again, there is no information, whether the starting compound were synthesized or purchased. If the first case applies, at least brief table should be included regarding the results.

The addition of (difluoromethyl)phosphonates to imines is in the contrary highly interesting variant of the synthesis fluoroamines, which again probably deserved higher attention, especially from the point of view of subsequent manipulation with the phosphonate group (removal, transformation to trifluoro group etc.). I again would appreciate at least tabulated list of the results of the synthesis of starting imines.

The last part, especially its fragment dealing with one-electron oxidations, is again quite interesting, and probably could be extended as it allows direct difluoroalkylation of simple alkenes. Again, I would here appreciated some attempts to transform subsequently the phosphonate group.

The experimental part is written without errors and in detail. It is not clear, why for some known compounds only MS and ^{19}F NMR spectra were given, while for others complete analysis is given. Also, it is not clear, how „ ^{19}F NMR yields“ were obtained when no data are given about the mass of the product in some cases. As stated before, I am also missing information about several classes of starting compound used.

I have two questions: first, why the author did not attempt to perform the reaction of (trifluoromethyl)phosphonate with bases in the absence of electrophile to observe possible intermediates of the reaction (for example intermediate **A**)? Second, why author did not try to substitute lithium cation in difluoromethylphosphonate-based anions for other softer metals (for example zinc) with the aim to suppress 1,2-addition as can be done for example in the reduction of conjugated systems with borohydrides?

Although I feel that author did concentrate more on the list of new compounds than on the interest, how the reactions proceed and their mechanism, he performed huge amount of work and showed good knowledge of experimental and theoretical chemistry.

The results of the Thesis have been published in four original papers in journals with high impact factor. The author thus fulfilled the targets given in the Thesis aims

Although I have several small objections regarding the Thesis, **I recommend to accept** the Thesis of Mgr. Prabhakar Cherkupally as the source for defending the **Ph.D.** title.

In Prague, 1.11.2012

Doc. Ing. Jaroslav Kvíčala, CSc.