

The thesis submitted by Lucie Řehová presents interesting investigation on the mechanism of metalation of alkyl aryl sulfones with the idea to employ their alpha-deprotonated form in the synthesis of cyclopentanoid monoterpenes using Julia olefination as the key step. The preliminary studies showed unusual course of deprotonation of  $\gamma$ -branched alkyl phenyl sulfones with *n*-butyllithium at -78 °C which started by *ortho*-metalation followed upon warming by transmetalation to form originally expected  $\alpha$ -deprotonated sulfones. This unexpected observation stimulated author to investigate phenomena of branched sulfones metalation in detail and this study became the important part of the thesis. This approach needs to be appreciated as the investigation led to many important conclusions useful for planning Julia olefination with branched sulfones.

Mechanistic investigation was done with the regard to the structure of alkyl phenyl sulfones with a special attention to their branching in  $\gamma$ -position. Author applied kinetic measurements, deuterium labelling, measurement of kinetic isotope effect as well as crossover experiments to map the mechanism of the observed metalation/transmetalation procedure. Having *ortho*-lithium phenyl sulfone in hand, she studied its reactivity with various electrophiles, aromatic and aliphatic aldehydes and ketones as well as with trimethyl silyl chloride and iodine. Analogously, the reactivity of  $\alpha$ -deprotonated sulfones with electrophiles was studied. Finally, major role of steric hindrance in regioselectivity of metalation as well as intermolecular character of transmetalation were concluded on the bases of experimental data. In the second part of the thesis, branched disilylated alkyl phenyl sulfone **1-2a** was used in total synthesis of racemic dihydronepetalactone and dolicholactone. Julia olefination and tandem alkoxyacylation/oxidative radical cyclization were the most important steps in this synthesis. Conditions for Julia olefination were suggested based on the results obtained in the first part of the thesis thus demonstrating usefulness of the work. The desired dihydronepetalactone and dolicholactone were obtained in 10 steps in 18% and 20% yields, respectively.

The thesis are well written, I appreciate clear presentation of mechanistic studies. The thesis starts with a short introduction where cyclopentanoid monoterpenes, reactivity of sulfones and sulfoxides towards bases as well as Julia olefination are reviewed. Motivation to the work is clearly formulated in the last part of introduction and in the chapter Aims of the work. Main part of the thesis (results and discussion) is complemented with conclusions, experimental part and list of references. It should be noted that all experimental procedures are well described; compounds are characterized by NMR, IR and MS techniques. All references important to the area are cited within the thesis. Style of the presentation is on high level. Schemes, Figures and other illustrations meet standard criteria of publishing in the area of organic chemistry. The results were published in two full papers in European Journal of Organic Chemistry thus supporting their importance and originality. There are only few comments and recommendations which should be addressed within the defense:

- In the scheme for Table 1.8 (p.31), products 1-36, 1-37 and 1-38 should be given with deuterated hydroxy group.
- Low regioselectivity was observed for the reactivity of dilithiated intermediate **1- $\sigma$ , $\alpha$ -45** with aldehydes (p.44). Probably the reaction with less electrophilic ketones or Eschenmoser salt could be more regioselective. Did author try to test an another type of electrophiles for these regioselectivity studies?
- Is there any difference in yields of  $\beta$ -benzoyloxysulfones **4-13a,c** prepared by methods A and B? What about the amount of the side product **4-14** observed when using A or B?
- "Osmylation" used on p. 80 is unusual and misleading term.
- Some nomenclature problems should be addressed: 4,4-dimethylpent-1-en-2-yl phenyl sulfone is recommended for **1-8**, compounds **2-7** are expected to be named as alkenes and not as benzene derivatives; configuration is missing in the case of **2-10a-d** (p. 142-145).
- In all experiments, *n*-butyllithium was used as a base for lithiation. Did author try to apply methyllithium, isopropyllithium or *tert*-butyllithium? Can author at least comment their use especially taking into account (i) the fact that steric hindrance is the major factor responsible for regioselectivity of branched phenyl alkyl sulfone metalation and (ii) higher basicity of isopropyllithium and *tert*-butyllithium compared to *n*-butyllithium.

**Evaluation:**

I would like to conclude that the work is at a high level and fulfils all criteria for PhD. thesis in the branch of Organic Chemistry. Thus, I strongly recommend **PhD. thesis to be accepted** and doctoral degree to be awarded to author after successful defence.

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