

Synthesis and properties of diverse pyrazolines based on flow-generated diazomethanes

D. Volochnyuk, V. Pendiukh, S. Shuvakin, A. Pashenko, S. Ivonin, A. Rozhenko, S. Ryabukhin

Pyrazoline synthesis and structure elucidation

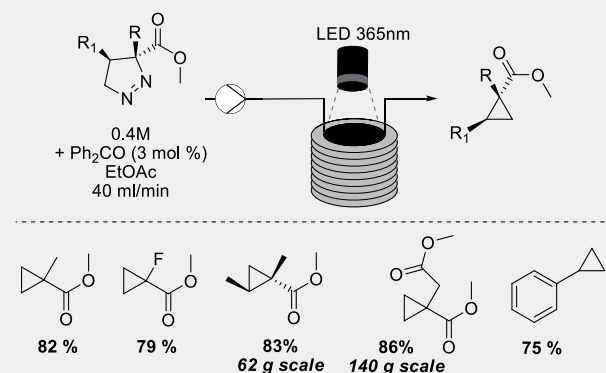
Reactions of CH_2N_2 are known for more than 90 years, but preparative applications of diazomethane were limited due to its toxicity and explosivity. We elaborated continuous-flow procedure that enables safe and reproducible generation of diazomethane to afford up to 200 g of a cycloaddition product.

Activated alkenes, mainly acrylic acid derivatives were used as substrates. The initial cyclization products, namely 1-pyrazolines **1**, are hard to isolate due to isomerization into more stable 2-pyrazolines (**2a** or **2b**) and subsequent oxidation to pyrazoles. We investigated the alkene behavior under the reaction conditions. Stability of the pyrazoline formed depends on the substrate structure:

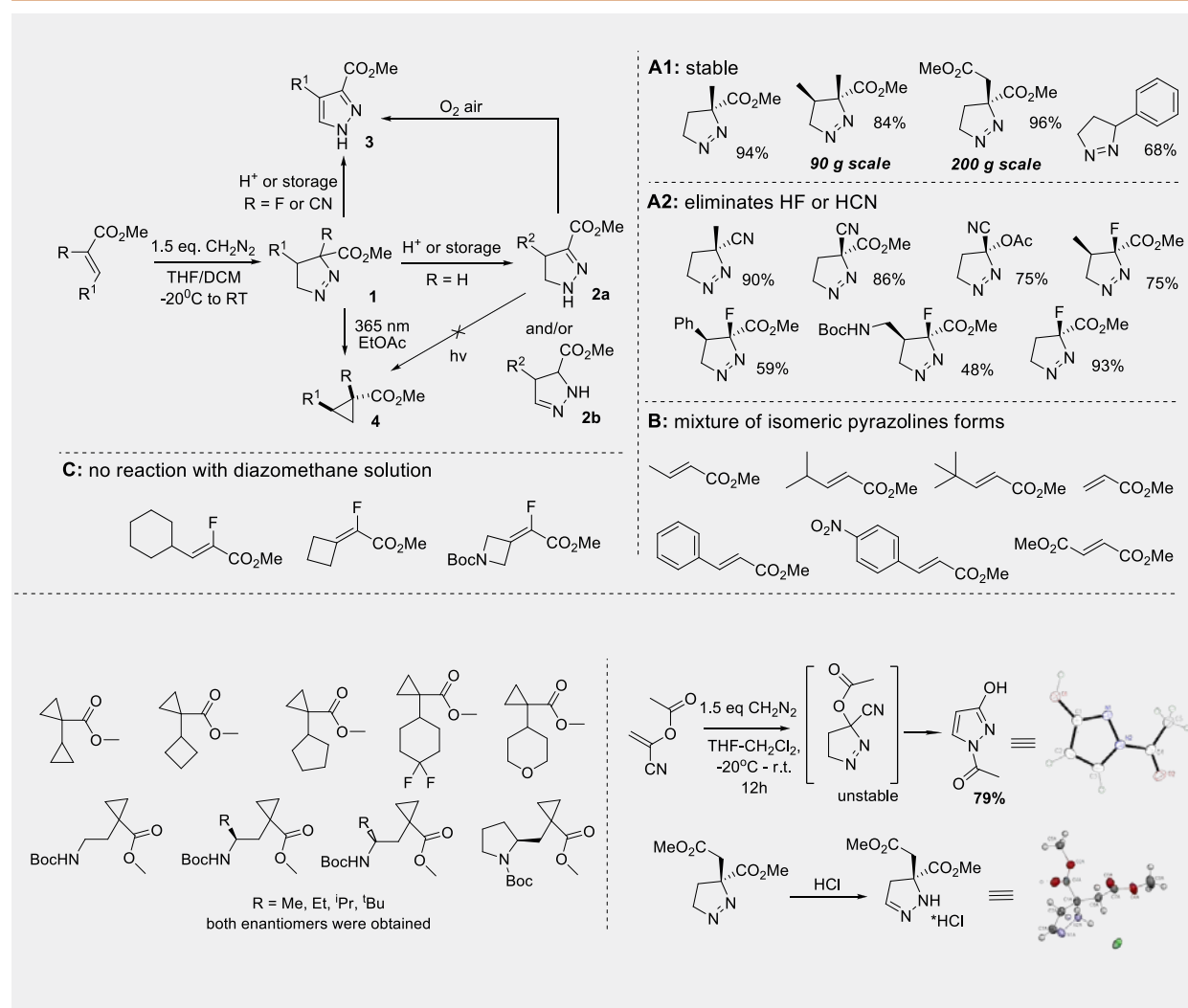
- 1-pyrazolines bearing a quaternary carbon atom or an aryl substituent in the third position are relatively stable, and were obtained as individual compounds (up to 200 g scale). Exact structure was proven by 2D NMR experiments (**A1**).
- In case of a leaving group (e.g. F, CN) in the third position of a pyrazoline, corresponding pyrazoles are formed under storage or acidic conditions (**A2**).
- 1-pyrazolines without a quaternary carbon atom or an aryl substituent in the third position haven't been isolated due to their fast isomerization. Mixtures of isomers formed (**B**).
- Some three- and tetrasubstituted alkenes were inert towards CH_2N_2 solution (**C**).

1-Pyrazolines were converted to cyclopropanes **4** under 365 nm irradiation, while 2-pyrazolines didn't under go the transformation.

Cyclopropane synthesis



Scope and limitations



Contact

Sergey V. Ryabukhin, Prof. Dr. Sci.;
Dmitriy M. Volochnyuk, Prof. Dr. Sci.
s.v.ryabukhin@gmail.com, d.volochnyuk@gmail.com