Category

Synthesis of Heterocycles

Key words

tricyanomethane
thermolysis
ring enlargement
epoxides
aziridines
push–pull alkenes

Synfact of the Month

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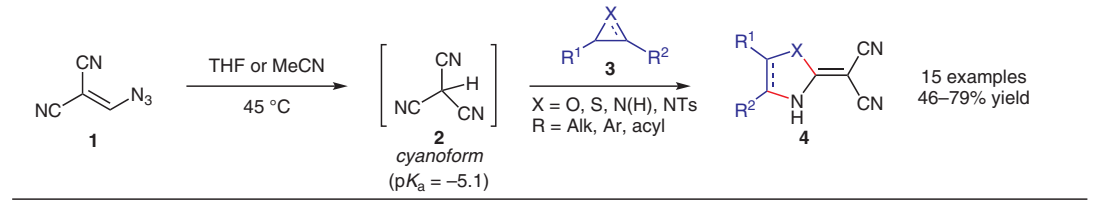
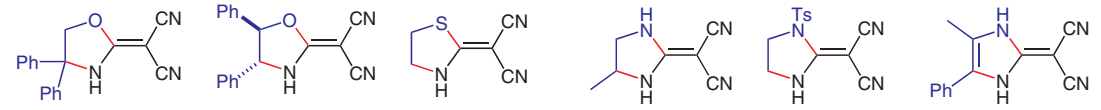
Ring Enlargement of Three-Membered Heterocycles by Treatment with In Situ Formed Tricyanomethane
Chem. Eur. J. **2020**, *26*, 6158–6164.

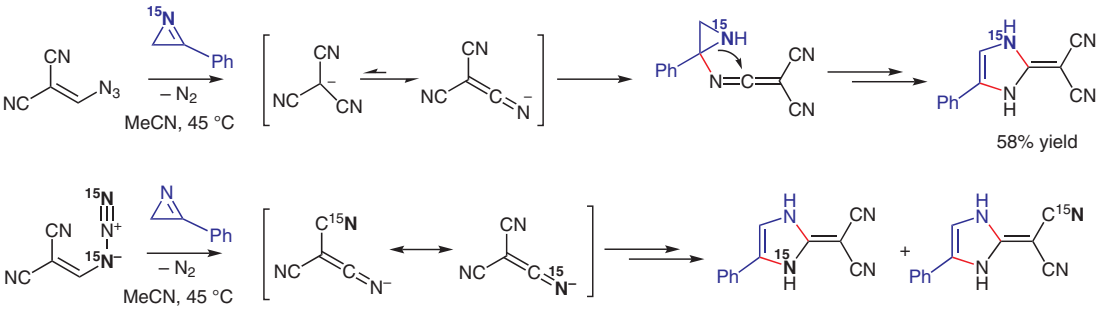
Reactions of Epoxides, Thiiranes, Aziridines and Azirines with Cyanoform



Selected examples:



Plausible reaction pathway:



Significance: Vinyl azide **1** can be prepared on a gram scale, is safe to handle at room temperature, and can be stored in the solid state at –25 °C. Oxazolidines, thiazolidines, and imidazolidines are useful pharmacophores (S. Sasho et al. *Chem. Pharm. Bull.* **2009**, *57*, 288; M. Takagi T. Nishibe, K. Ishimitsu WO 2003000668, **2003**) and have been prepared by other methods (L. G. Chanu, O. M. Singh, S. H. Jang, S. G. Lee *Bull. Korean Chem. Soc.* **2010**, *31*, 859; A. Samzadeh-Kermani *Monatsh. Chem.* **2016**, *147*, 761). However, previous preparations are limited by lack of commercial availability of reagents. The present method increases the scope of accessible derivatives of these heterocycles; electrophiles can be prepared using well-known procedures such as epoxidation or aziridination.

Comment: The regio- and stereochemical outcome of the reaction is consistent with the conventional acid-catalyzed epoxide ring-opening process. Under similar conditions, the reaction of cyanoform (**2**) or tricyanomethanide salts with other electrophiles (alkyl halides, ketones, Michael acceptors) results in C-alkylation (K. Rakus, S. P. Verevkin, H.-D. Beckhaus, C. Rüchardt *Chem. Ber.* **1994**, *127*, 2225; K. Banert et. al. *Angew. Chem. Int. Ed.* **2017**, *56*, 9582). The observed N-alkylation reported here suggests a ketenimine intermediate in this transformation. The proposed mechanism is supported by ^{15}N-labelling of the electrophile (azirine) or nucleophile (**1**) to confirm the regiochemistry of the nucleophile addition as shown.

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