Interrupted Barton-Zard/Friedel-Crafts Alkylation Telescoped Reaction for the Synthesis of Pyrrolo[3,4-*b*]indole Cores Bearing Multiple Aryl Substituents

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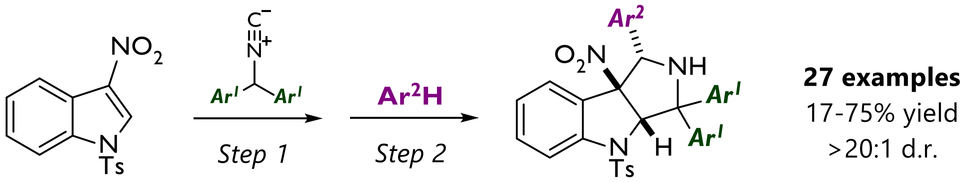
The Barton–Zard reaction is a direct route to 2-carboxyl-3,4-disubstituted pyrroles from electron-deficient alkenes/nitroarenes/nitroindoles and α-isocyanoacetates under basic conditions.[1] By employing α-substituted isocyanoacetates, the interrupted Barton-Zard reaction occurs, where the rearomatization step is prevented and polycyclic skeletons are generated instead of substituted pyrroles.[2] Herein, we report a dearomatization reaction between electron-deficient indoles and α,α-diaryl-substituted methyleneisocyanides (interrupted Barton-Zard reaction), followed by the *in situ* Friedel-Crafts alkylation. In a telescoped reaction mediated by the Brønsted base in the first step and by the Brønsted acid in the second step, aryl-substituted pyrrolo[3,4-*b*]-indole cores are generally obtained in moderate to good yields and in high diastereoselectivities (Scheme 1).[3] The reaction is tolerant of various 3-nitroindoles and aryl nucleophiles, however, the substrate scope of isocyanide derivatives has limitations. The developed methodology offers a modular approach for the synthesis of target multi-substituted polycyclic cores.



Scheme 1. Interrupted Barton-Zard/Friedel-Crafts alkylation telescoped reaction.

[1] D. H. R. Barton, S. Z. Zard, *J. Chem. Soc., Chem. Commun.* **1985**, 1098.
[2] Q. Wan, J. H. Xie, C. Zheng, Y. F. Yuan, S. L. You, *Angew. Chem. Int. Ed.* **2021**, *60*, 19730.
[3] J. Rešetar, K. Remar, A. Mikleušević, J. Suć Sajko, I. Bašić and M. Gredičak, **2025**, *submitted*