

# SYNTHESIS OF SUBSTITUTED PYRROLO[3,4-B]INDOLE CORES VIA AN INTERRUPTED BARTON-ZARD REACTION/FRIEDEL-CRAFTS ALKYLATION CASCADE

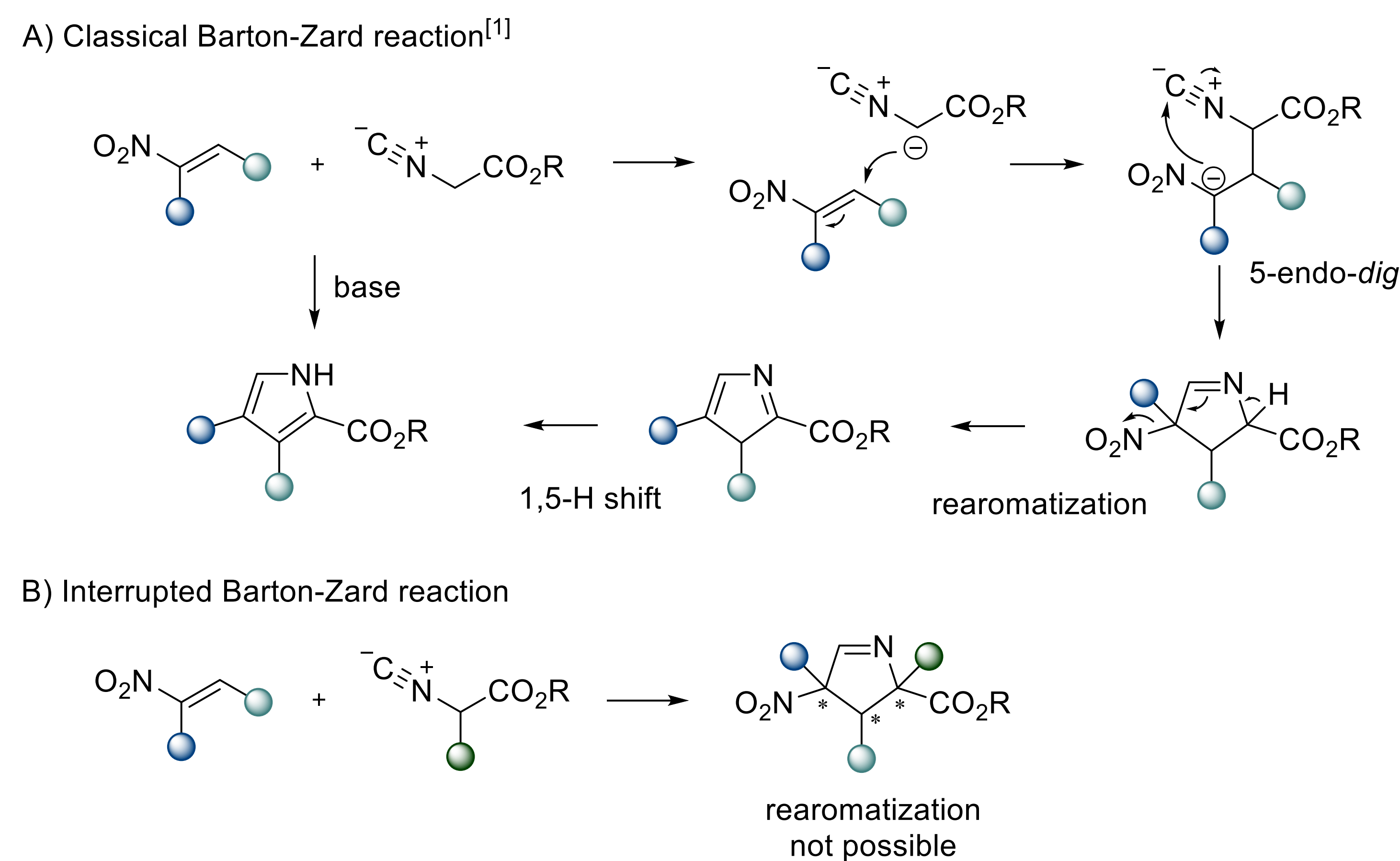
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## INTRODUCTION

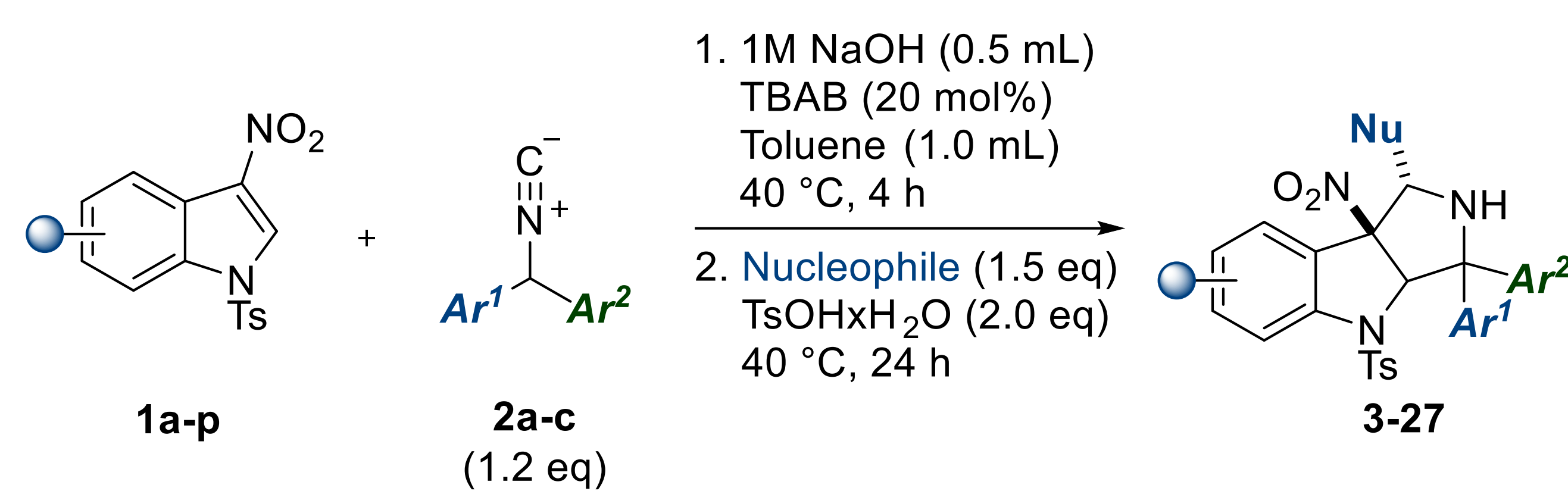
The Barton–Zard reaction is a direct route to aromatic 2-carboxyl-3,4-disubstituted pyrroles from electron-deficient alkenes/nitroarenes/nitroindoles and  $\alpha$ -isocyanoacetates under basic conditions.<sup>1</sup> Introduction of  $\alpha$ -substitution on isocyanoacetates nucleophiles prevents the rearomatization step and generates non-aromatic polycyclic products, also known as the interrupted Barton-Zard reaction.<sup>2</sup>

## RESULTS AND DISCUSSION

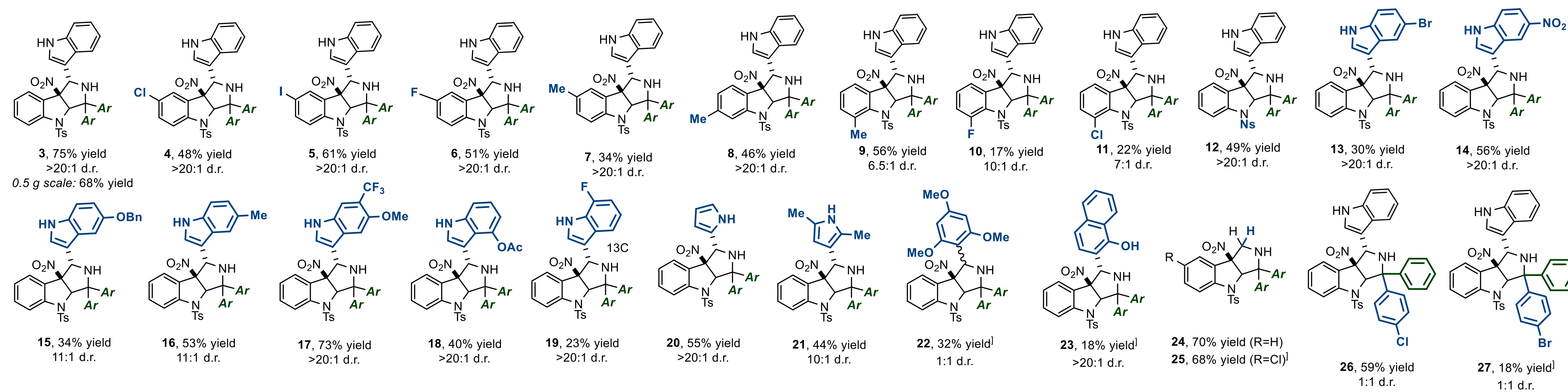
To the best of our knowledge, there is only one example of the synthesis of 3,3-diaryl-substituted hexahydropyrrolo[3,4-*b*]indole polycyclic skeleton, as a postmodification reaction.<sup>3</sup> Herein, we report an interrupted Barton-Zard reaction/Friedel-Crafts alkylation cascade for the synthesis of hexahydropyrrolo[3,4-*b*]indole cores bearing multiple aryl substituents. Mediated by a Brønsted base under phase-transfer conditions, an interrupted Barton-Zard reaction between 3-nitroindoles (**1a-p**) and benzophenone-derived isocyanides (**2a-c**) leads to the formation of pyrrolo[3,4-*b*]indole cores, which are *in situ* alkylated with heteroaromatic and aromatic nucleophiles under acidic conditions (**3-27**).



**Scheme 1.** Classical vs. Interrupted Barton-Zard reaction



**Scheme 2.** Developed cascade reaction for the synthesis of polycyclic pyrrolo[3,4-*b*] indole cores



## CONCLUSION

In the reaction between 3-nitroindoles and  $\alpha,\alpha$ -diaryl-substituted methyleneisocyanides followed by the *in situ* addition of an aryl nucleophile, target products were generally obtained in moderate to good yields as single diastereomers.<sup>4</sup> Although tolerant of most electron-deficient indoles and nucleophiles, the reaction is highly dependent on the structure of isocyanide derivatives, where the dearomatization step proved to be the limiting step of the cascade. The reaction was preliminarily tested under asymmetric conditions, but the products were obtained in low yields as racemates, so further studies on this issue are ongoing in our group.