Studies Towards a Novel Synthesis of Indoles with Concurrent Group Migration

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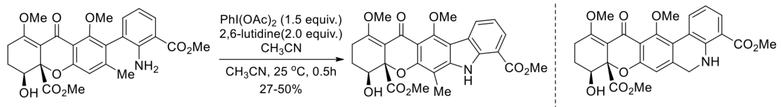
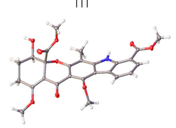
Abstract

Parnafungins are biologically active compounds which display activity against a variety of fungal pathogens. Previous work on the synthesis of tetrahydroxanthones in order to facilitate parnafungin synthesis led to the unexpected formation of a carbazole product with methyl shift. Much of the work of Driver et al. investigates similar migration reactions; while those reactions utilize aryl azides, the observed carbazole formation involved an aniline. Investigations were thus carried out in order to determine if the chemistry of aniline substrates is comparable to those of aryl azides, especially with respect to the formation of indoles.

PIDA Oxidation of 2-Aniline-Tetrahydroxanthone

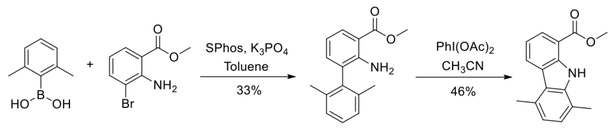




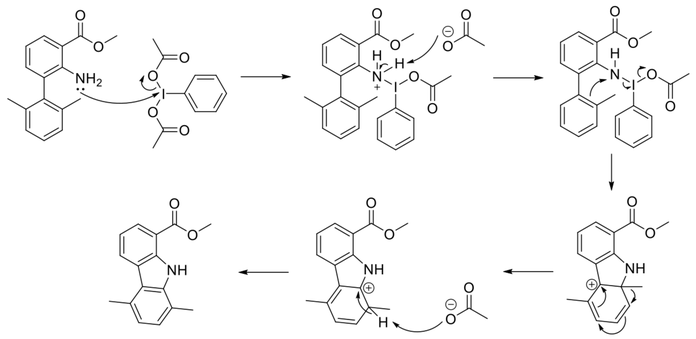
X-ray crystal structure

Wu, X. Unpublished work, 2016.

Simplified Model of Carbazole Synthesis

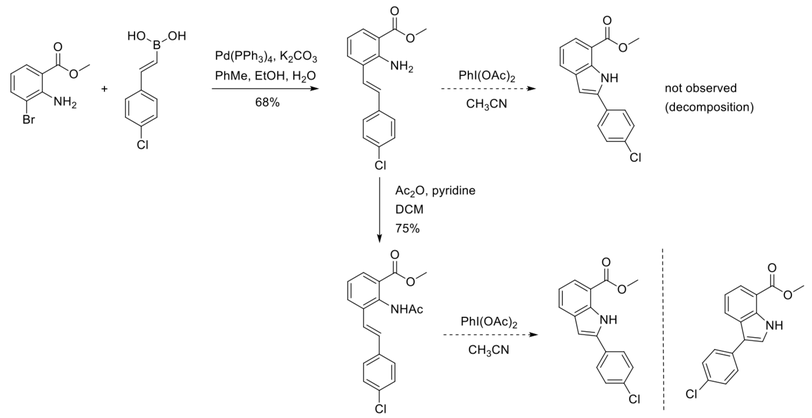


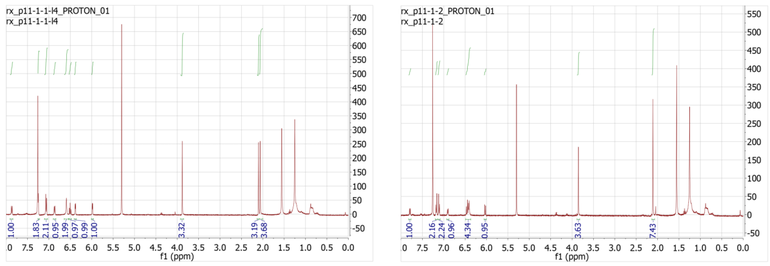
Mechanism



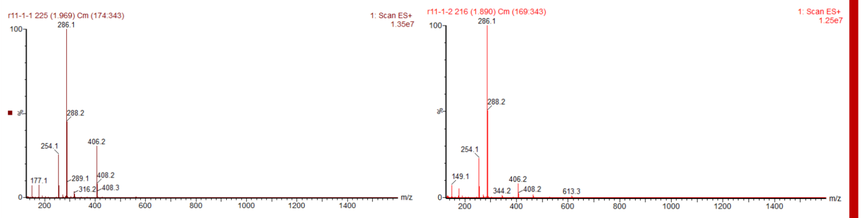
Maiti, S.; Mal, P. *Org. Lett.* **2017**, *19* (9), pp 2454-2457

Synthesis of Methyl 1H-Indole-7-Carboxylate



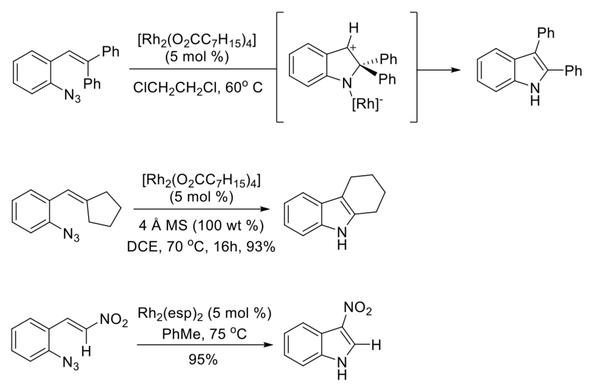


HNMR spectra show that the isolated products are isomers.



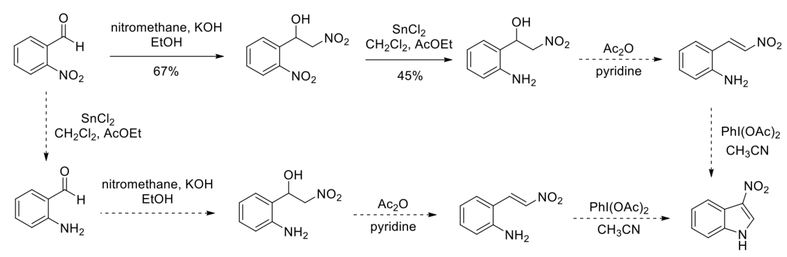
UPLC mass spectra show that the isolated products' masses match those of the desired product.

Potentially Selective 2,3-Disubstituted Indole Formation from Azides

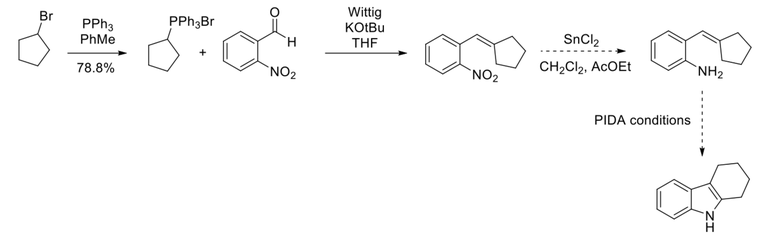


1) Stokes, B. J.; Liu, S.; Driver, T.G. *J. Am. Chem. Soc.* **2011**, *133*, pp 4702-4705
2) Sun, K.; Liu, S.; Bec, P. M.; Driver, T. G. *Angew. Chem. Int. Ed.* **2011**, *50*, pp 1702-1706

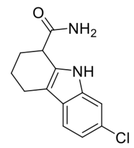
Proposed Synthesis of 2-Nitro-1H-Indene



Proposed Indole Synthesis via Wittig Olefination Reaction



Selisistat (EX 527)



Carbazole compound of interest; potent, selective deacetylase sirtin 1 (SIRT1) inhibitor; potential treatment agent for Huntington's disease

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