Access to Tricyclic Heteroarenes by an Iodine-promoted Cyclization Reaction

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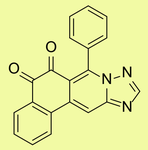
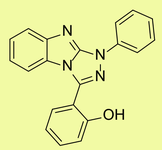
Introduction

Heterocycles have been an essential part of organic synthesis for many years because of their usefulness in creating pharmaceuticals and agrochemicals.



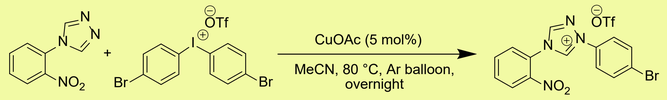
Anticancer



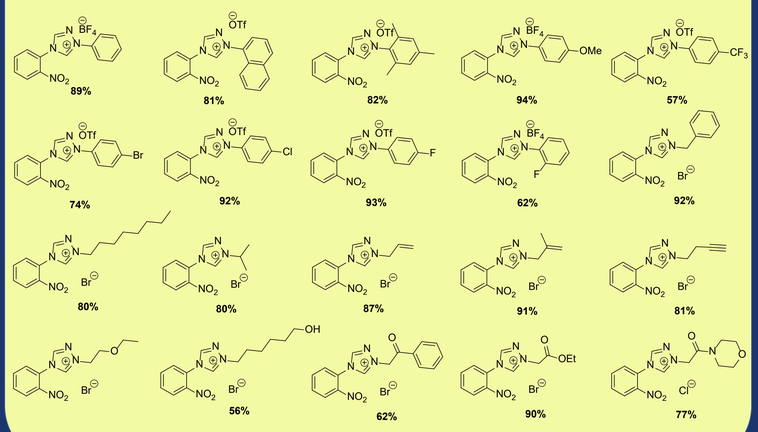
Antibacterial

Our research examines ways to optimize and expand on past methods from the Bolliger lab with the goal of increasing the yield of the desired product and minimizing the formation of unwanted by-products. For our arylation reactions, we will be using diaryliodonium salts and a metal catalyst, copper(I) acetate, to promote the catalytic *N*-arylation of the compound. This ability to transfer an aryl group is just one reason why diaryliodonium salts are being used for this research. Diaryliodonium salts also have low toxicity, making them safe to work with, as well as having high reactivity and good selectivity. The *N*-alkylation products are formed using a simple substitution reaction. The nitro groups of these *N*-substituted compounds are then reduced to the amino substituent. The amino analogues produced are then used to complete the cyclization reaction, which results in several important heterocycles.

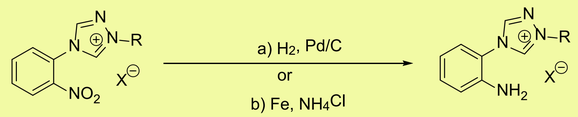
Example of an *N*- Arylation Reaction



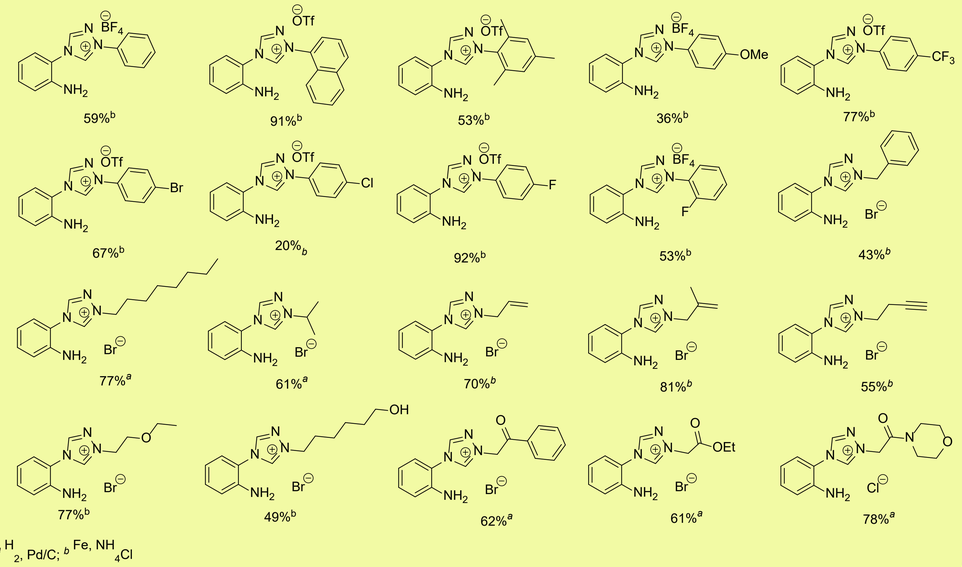
N-Arylation and N-Alkylation Products



Reduction Reactions

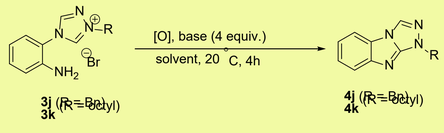


Reduction Products



a H2, Pd/C; b Fe, NH4Cl

Optimization of Cyclization Reaction

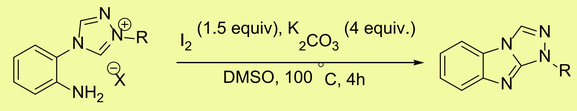


3j (R = Bn)
3k (R = octyl)

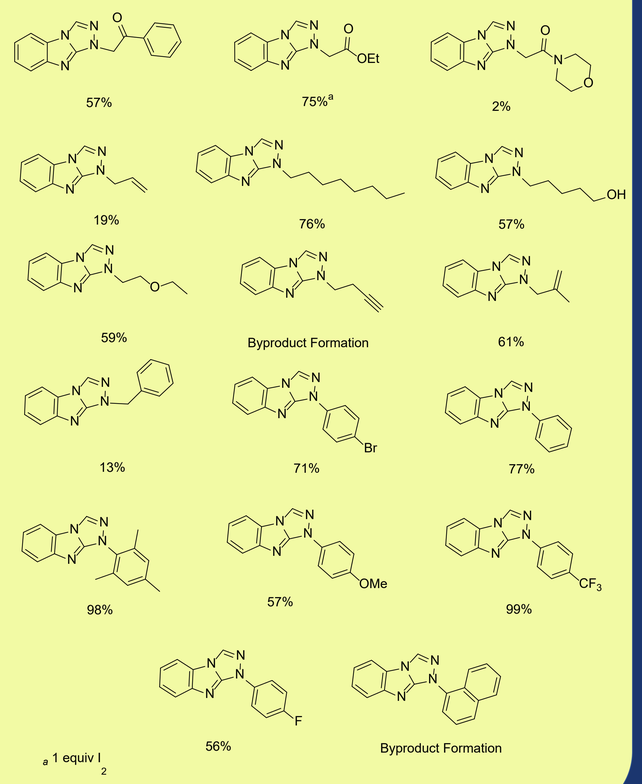
4j (R = Bn)
4k (R = octyl)

Entry	Aniline	Solvent	[O]	Base	Conversion
1	3j	CH_2Cl_2	*m*-CPBA (1.5 equiv)	K_2CO_3	0%
2	3j	EtOH/H_2O (1:1)	H_2O_2 (5 equiv)	None	0%
3	3j	DMSO	I_2 (2 equiv)	None	0%
4	3k	DMSO	I_2 (2 equiv)	K_2CO_3	95%
5	3k	DMSO	I_2 (2 equiv)	K_2CO_3	81%
6	3k	DMSO	I_2 (2 equiv)	K_3PO_4	64%
7	3k	DMSO	I_2 (2 equiv)	NEt_3	<5%
8	3k	DMSO	I_2 (2 equiv)	$NEtiPr_2$	<5%
9	3k	DMSO	I_2 (2 equiv)	DBU	>99%
10	3k	DMSO	I_2 (2 equiv)	KOtBu	<5%, messy
11	3k	CH_2Cl_2	I_2 (2 equiv)	DBU	>99%
12	3k	EtOH	I_2 (2 equiv)	DBU	<10%, messy
13	3k	MeCN	I_2 (2 equiv)	DBU	<50%, messy
14	3k	EtOAc	I_2 (2 equiv)	DBU	<5%, messy
15	3k	DMSO	None	DBU	0%
16	3k	DMSO	I_2 (1 equiv)	DBU	> 95%
17	3k	DMSO	I_2 (1.5 equiv)	DBU	> 99%

Cyclization Reaction



Cyclization Products



a 1 equiv I2

Acknowledgments

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Works Cited

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