A New Approach for the Synthesis of N-Arylamides Starting from Benzonitriles

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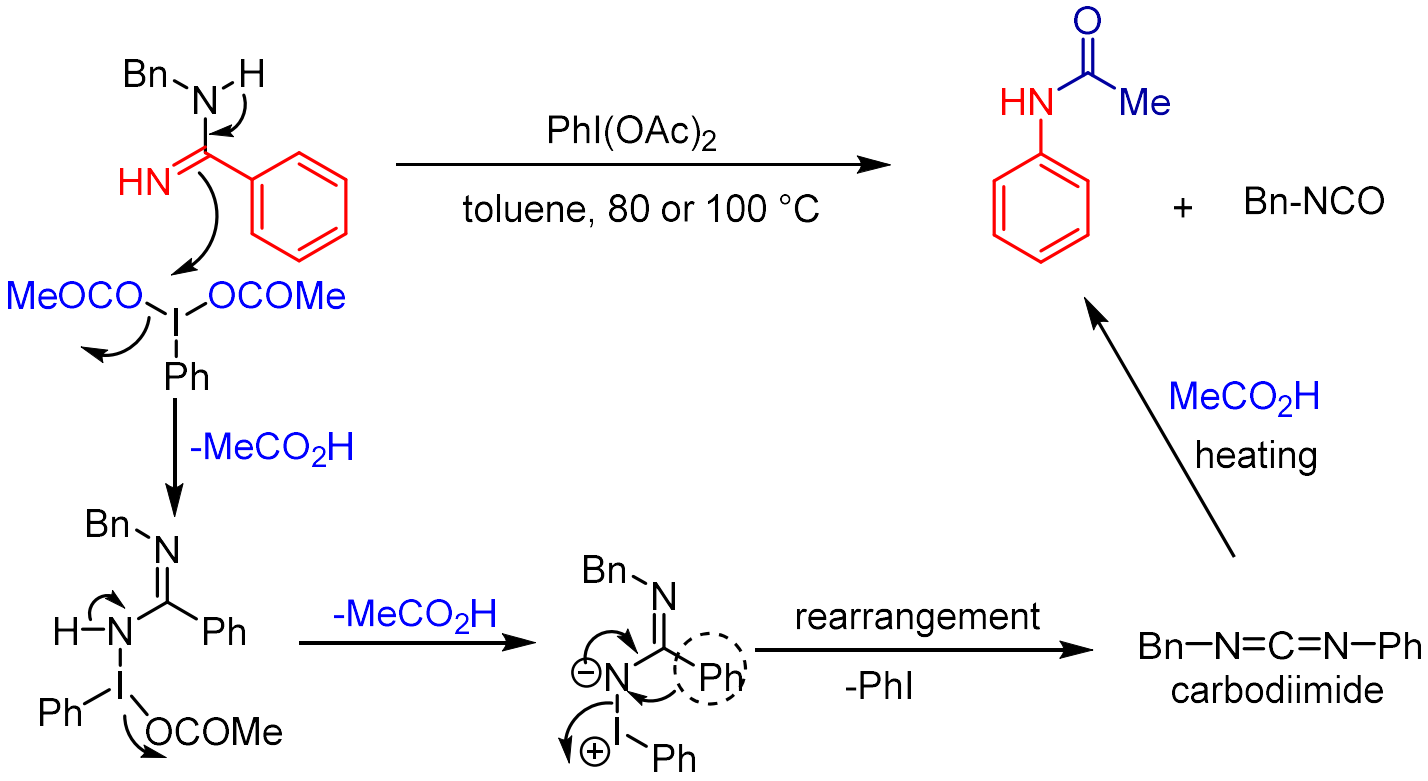
Abstract and Keywords

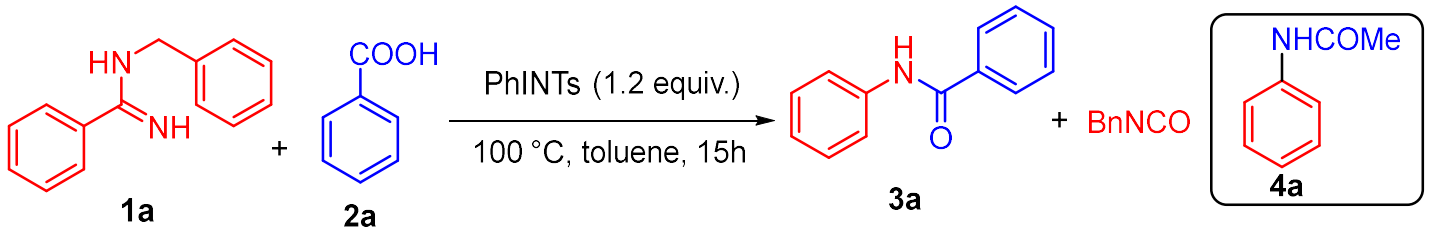
Abstract: *N*-Arylamides are a ubiquitous component of a broad range of natural products and biologically active compounds. In this paper, a new synthetic protocol for the preparation of *N*-arylamides has been developed *via* hypervalent iodine mediated *aza*-Hofmann type rearrangement of amidines. The reaction proceeds smoothly at 100 °C in the presence of PhINTs in toluene solvent. The requisite amidine substrates were prepared from amines and nitriles by applying Pinner reaction approach. Considering the easy access of amidines from nitriles, the overall process is the conversion of nitriles to acetanilide and *N*-arylamides. As an application of the protocol, the preparation of paracetamol from 4-cyanophenol has been also described.

Keywords: *N*-Arylamides, nitriles, amidines, paracetamol

Synthesis of secondary amides *via* $PhI(OAc)_2$-mediated oxidative rearrangement of *N*-substituted amidines (Previous method)

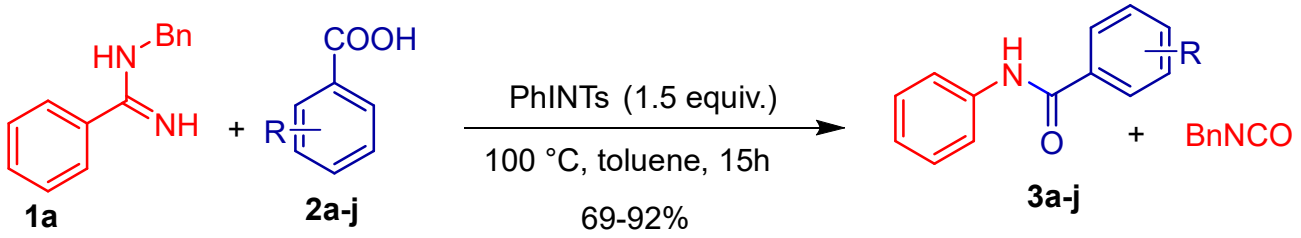


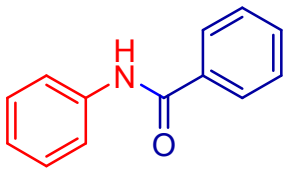
Optimization reactions for the preparation of benzanilide from *N*-benzylbenzamidine



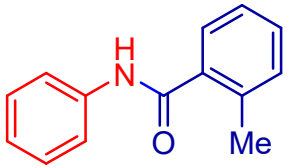
Entry	Oxidant (1.5 eq)	Solvent (1 mL)	Additives (1.1 eq)	Yield (%) 3a/4a
1	$PhI(OAc)_2$	toluene	-	48/40
2	$PhI(OCOCF_3)$	toluene	-	0/0
3	PhINTs	toluene	-	86/0
4	PhINTs	THF	-	74/0
5	PhINTs	DMF	-	35/0
6	PhINTs	o-xylene	-	68/0
7	PhINTs	toluene	Et_3N	77/0
8	PhINTs	toluene	AcOK	58/34
9	PhINTs	toluene	Cs_2CO_3	42/0
10	PhINTs	toluene	Pyridine	58/0

PhINTs-mediated synthesis of benzanilides from *N*-benzylbenzamidine

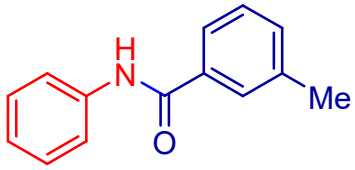




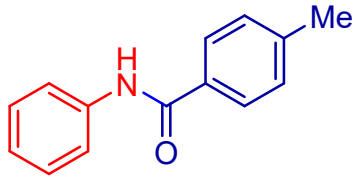
3a (86%)



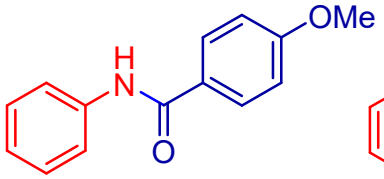
3b (80%)



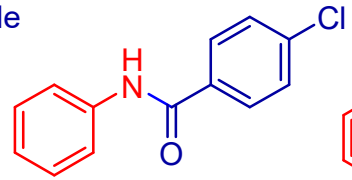
3c (82%)



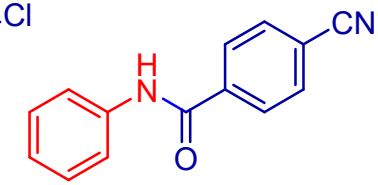
3d (87%)



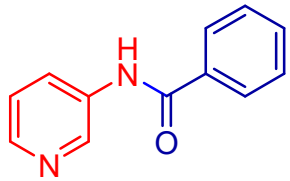
3e (92%)



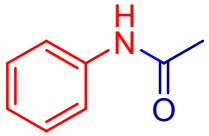
3f (75%)



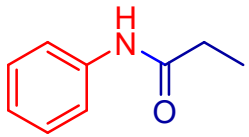
3g (70%)



3h (69%)

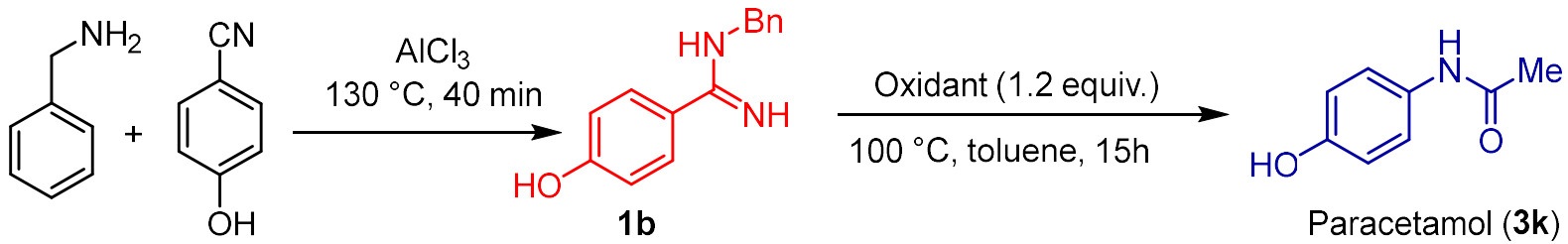


3i (86%)



3j (88%)

Synthesis of paracetamol from amidine.



Oxidant: (i) PhINTs in combination with MeCOOH (94%)
(ii) $PhI(OAc)_2$ (90%)

Conclusion

In conclusion, we have developed an efficient and sustainable protocol for the preparation of *N*-arylamides (anilides) from *N*-substituted amidines. All the reaction proceeded smoothly with PhINTs at 100 °C in toluene solvent. Various substituted *N*-arylamides were obtained in high yields under oxidative reaction conditions. As an application of this protocol we have synthesized paracetamol in high yield starting from 4-cyanophenol.