



# Calixarene Catalyze Cascade Povarov–Hydrogen-Transfer Reaction in Synthesis of Quinolines

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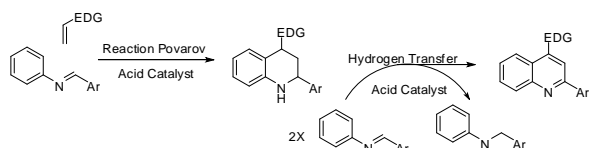
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## INTRODUCTION

Quinoline nucleus is a common heterocyclic ring found in natural and unnatural compounds endowed with biological properties.<sup>1</sup> Tetrahydroquinolines are easily obtained from Povarov reaction which correspond to the reaction of arylimines with electron-rich olefins. Further, the obtained tetrahydroquinolines may be further transformed into quinolines by oxidation.<sup>2</sup> Indeed, Povarov reaction followed by an oxidative aromatization, in a cascade process, was reported using excess of arylimine as oxidant (Fig. 1).<sup>2</sup>



**Figure 1** – Cascade process catalysis in the synthesis of quinoline.

The *p*-sulfonic acid calix[4]arene (CX4SO<sub>3</sub>H) has been employed as catalysts in Povarov reaction for synthesis of julolidines.<sup>3</sup> Here we employ CX4SO<sub>3</sub>H as a catalyst for synthesis of substituted quinolines.

## RESULTS AND DISCUSSION

In order to evaluate the effect of CX4SO<sub>3</sub>H as a catalyst, we used the 4-bromoaniline **1a**, benzaldehyde **2** and styrene **3**, as substrates for Povarov reaction (Tab. 1).

**Table 1.** Optimization of Reaction Conditions<sup>a</sup>

Solvents	Time (h)	Catalyst (mol %)	Yield (%) <sup>b</sup>	
			4a	4b
CH <sub>3</sub> CN	4	CX4SO <sub>3</sub> H (25)	54	-
THF	4	CX4SO <sub>3</sub> H (25)	-	-
CHCl <sub>3</sub>	4	CX4SO <sub>3</sub> H (25)	-	8
Without solvent	4	CX4SO <sub>3</sub> H (25)	20	5
CH <sub>3</sub> CN	12	CX4SO <sub>3</sub> H (1.0)	65	-
CH <sub>3</sub> CN	12	PHA (4.0)	12	-
CH <sub>3</sub> CN	12	CF <sub>3</sub> COOH (4.0)	64	-
CH <sub>3</sub> CN	12	CH <sub>3</sub> COOH (4.0)	-	-
CH <sub>3</sub> CN	12	Lactic acid (4.0)	39	Trace
CH <sub>3</sub> CN	12	Oxalic acid (2.0)	43	-
CH <sub>3</sub> CN	12	H <sub>2</sub> SO <sub>4</sub> (2.0)	-	-

<sup>a</sup> The reaction of **1a** (1 mmol), **2** (1.2 mmol) and **3** (1.5 mmol) was carried sob temperature 80 °C <sup>b</sup> Isolated Yield. <sup>c</sup> The concentration of H<sup>+</sup> was kept constant.

The results for the optimization reactions conditions using CX4SO<sub>3</sub>H as a catalyst and also the results employing other acids are show in Tab. 1.

Our results suggest that not only the imine is acting as an oxidant since some yields obtained in these reactions were higher than 50%. O<sub>2</sub> (air) or other receptor hydride, such as acetonitrile, may also act as a possible oxidants. The CF<sub>3</sub>COOH presented similar performance as CX4SO<sub>3</sub>H, however the use of CX4SO<sub>3</sub>H is advantageous since it is a reusable catalyst.<sup>3</sup> Additional examples of CX4SO<sub>3</sub>H-catalyzed Povarov-hydrogen-transfer reaction is presented in Table 2.

**Table 2.** CX4SO<sub>3</sub>H-catalyzed Povarov-hydrogen-transfer reaction for different anilines<sup>a</sup>

R	4	Yield <sup>b</sup> 4 (%)	5	Yield <sup>b</sup> 5 (%)
4-Br	4a	65	5a	-
4-F	4f	60	5f	-
4-OCH <sub>3</sub>	4c	60	5c	-
4-SCH <sub>3</sub>	4d	64	5d	-
4-t-butyl	4e	62	5e	-
4-OH	4b	71	5b	-
4-NO <sub>2</sub>	4g	45	5g	29
4-CN	4h	40	5h	21
3,4,5-OCH <sub>3</sub>	4i	49	5i	-

<sup>a</sup> The reaction of **1a** (1 mmol), **2** (1.2 mmol) and **3** (1.5 mmol) was carried sob 80 °C <sup>b</sup> Isolated Yield.

In general, anilines bearing electron-donor groups furnished quinoline in high yields.

## CONCLUSION

We have uncovered a cascade Povarov-hydrogen-transfer process that can be employed to produce substituted quinolones in good yields.

## ACKNOWLEDGEMENTS

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## REFERENCES

- Michael, J. P. *Nat. Prod. Rep.* **2007**, 24, 223.
- Shindoh, N.; Tokuyama, H.; Takemoto, Y.; Takasu, K. J. *Org. Chem.* **2008**, 73, 7451.
- Simões, J.B.; de Fátima, A.; Sabino, A.A.; de Aquino, F.J.T.; da Silva, D.L.; Barbosa, L.C.A. and Fernandes, S.A. *Org. Biomol. Chem.*, **2013**, 11, 5069.