

Propargylation of aromatic compounds using Ce(OTf)₃ as catalyst

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INTRODUCTION

The propargylation of aromatic compounds from propargylic alcohols by Friedel-Crafts reactions provide key intermediates for the synthesis of pharmaceuticals and natural products.¹ In recent years, propargylation of aromatic compounds has been studied using Brønsted acids,² Lewis acids,³ and complexes involving metals such as rhenium,⁴ ruthenium,⁵ and gold.⁶

Lanthanide salts are often employed as catalysts in organic synthesis. These salts have attracted scientific interest due to their low toxicity, low cost, stability, and ease of handling.⁷

In view of our interest in developing new methods for reactions catalyzed by salts of cerium (III),⁸ we decided to study the direct alkylation reaction of aromatic compounds with propargylic alcohols using Ce(OTf)₃.

RESULTS AND DISCUSSION

Indole (1.0mmol) and 2,4-diphenylbut-3-yn-2-ol (1.1mmol) were used as starting materials to establish the best conditions. At first, the effect of solvent on the reaction was tested using MeNO₂, glicerol, DMAc, CH₃CN and *i*-propanol. The results revealed that the reaction was influenced by the solvent and the best yield being obtained in MeNO₂. The catalyst amount also was tested using 0.1 to 0.5 mmol, the best result was obtained using 0.3 mmol of Ce(OTf)₃ (Table 1).

Table 1. Effect of the solvent and catalyst amount on the reaction.^a

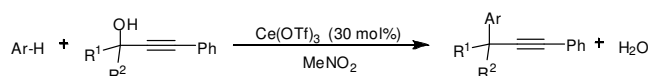
Entry	Solvent	Ce(OTf) ₃ (mmol)	Time (h)	Yield (%) ^c
1	CH ₃ CN	0,3	3.0	15
2	MeNO ₂	0,3	1.5	83
3	Glicerol	0,3	3.0	- ^b
4	DMAc	0,3	3.0	- ^b
5	Isopropanol	0,3	3.0	49
6	MeNO ₂	0,1	3.0	23
7	MeNO ₂	0,2	3.0	55
8	MeNO ₂	0,5	1.5	84

^a Reaction performed with indole (1 mmol) and 2,4-diphenylbut-3-yn-2-ol (1,1 mmol) at 100 °C.

^b No reaction.

^c Determined by GC-MS.

Scheme 1.



R¹, R² = H, Me, Ph
Ar = indole, phenol, anisole, *o*-cresol, furan.

With these optimized conditions in hand, we next extended the transformation to other examples in order to find out the scope and limitations of the present method, as described in Table 2, Scheme 1.

Table 2. Synthesis of aromatic propargylation.

Entry	Ar	R ¹ , R ²	Time (h)	Yield (%) ^a
1	Indole	Ph, H	1.50	83 ^c
2	Indole	Ph, Me	1.50	53 ^c
3	Furan	Ph, H	1.50	77 ^b
4	Phenol	Ph, H	0.50	92 ^b
5	<i>o</i> -cresol	Ph, H	0.25	93 ^b
6	Anisole	Ph, H	0.50	95 ^b

^a Isolated yields.

^b Reaction performed at rt.

^c Reaction performed at 100 °C.

CONCLUSION

To conclude, we have developed a very simple and efficient method using Ce(OTf)₃ as catalyst for the propargylation of a variety aromatic compounds. The products were obtained regioselectively, in good yields, and in short reaction times.

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