Immobilization of $CuSO_4$ on alginate for synthesis of α-triazoloketones

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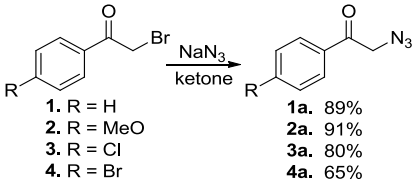
INTRODUCTION

1,2,3-Triazole derivatives have gained attention as an attractive heterocyclic compound with antifungal, antibacterial, anti-HIV, anticonvulsants and anti-allergic activities.[1] The copper-catalyzed azide-alkyne cycloaddition reaction (CuAAC) is an example of click reaction, since is a simple method for synthesized triazoles with an wide scope, high yields in mild conditions. Combining with concept of green chemistry, the CuAAC click reaction has been improved by immobilization of copper species onto various supports.[2] In this work, it was studied the recovery and reuse of copper in CuAAC reaction by immobilizing it in alginate spheres (Alg-$CuSO_4$).

RESULTS AND DISCUSSION

It was studied the optimization method for the synthesis of α-triazoloketones using the Alg-$CuSO_4$ spheres as catalysts. Syntheses and yields of α-ketoazides from α-haloketones (**1**-**4**) and sodium azide are showed in Scheme 1.

Scheme 1. Syntheses of α-ketoazides.



1. R = H
2. R = MeO
3. R = Cl
4. R = Br

1a. 89%
2a. 91%
3a. 80%
4a. 65%

*Reaction conditions: haloketone (5,0 mmol), sodium azide (15,0 mmol), ketone (20 ml), rt, 16h, magnetic stirring. Isolated yield.

Optimization method was performed for azide **1a** to obtain triazole **5**. Reactions in r.t. and T = 50ºC were made in three cycles, in 24 h. In presence of ascorbic acid was made one cycle (rt, 5h).

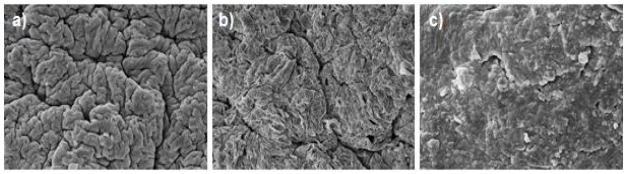
Table 1. Optimization method to synthesize triazole **5**.[a]

	Yield		
Number of Cycles	**Room temperature**	**50ºC**	**Ascorbic acid**
1	69%	93%	95%
2	60%	74%	-
3	53%	65%	-

[a] ketoazide (0,25 mmol), alkyne (0,30 mmol), 4 spheres of Alg-$CuSO_4$, H_2O (2 ml), rt, magnetic stirring. Isolated yield.

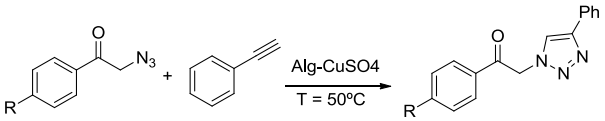
After reaction with ascorbic acid Alg-$CuSO_4$ turned from blue to yellow, showing faster utilization of copper. Figure 1 shows the microscopy micrograph of Alg-$CuSO_4$ spheres. Despite the shorter reaction time with ascorbic acid (5 h), there was a greater surface detrition of spheres indicating larger use of copper ion, hindering the reuse of spheres.

Figure 1. Scanning electron microscopy micrographs of $CuSO_4$ immobilized on alginate. a) no use, b) reaction in 50ºC (24 h) and c) reaction with ascorbic acid (rt, 5h).



The best results were obtained at 50ºC, which enable at least three cycles showing good yields. However, after the third cycle the Alg-$CuSO_4$ spheres were complete destroyed into the reaction. This method was applied in the synthesis of triazoles **6**-**8**.

Schme 2. Syntheses of triazoles by optimized method.



1a. R = H
2a. R = MeO
3a. R = Cl
4a. R = Br

5. 93%
6. 93%
7. 87%
8. 85%

*ketoazide (0,25 mmol), alkyne (0,30 mmol), 4 spheres of Alg-$CuSO_4$, H_2O (2 ml), rt, magnetic stirring. Isolated yield.

CONCLUSION

The copper (II) immobilized on alginate enable synthesis of α-triazoloketones in good yields, allowing the catalyst to be reused. Another reactions will be performed with different azides and alkynes by optimized method.

ACKNOWLEDGEMENTS

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REFERENCES

[1] Kamalraj, V. R.; Senthil, S.; Kannan, P. *J. Mol. Struct.* **2008,** *892*, 210.
[2] Sharghi, H.; Sarvari, M. H.; Moeini, F. Khalife, R.; Beni, A. S. *Helv. Chim. Acta.* **2010**, *93*, 435.