



Catalyzed cascade reaction of α -keto nitriles with 3-oxo-1,2,4-triazole



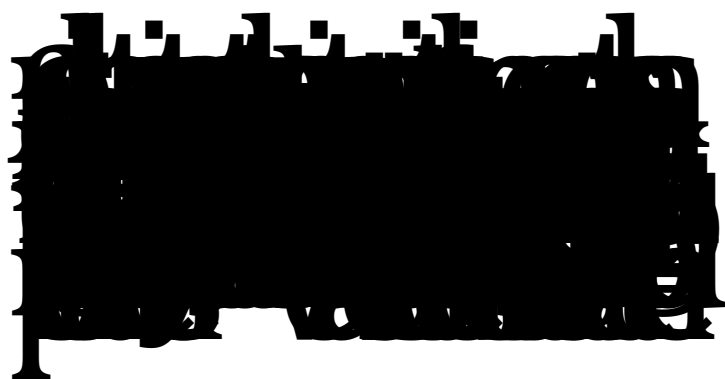
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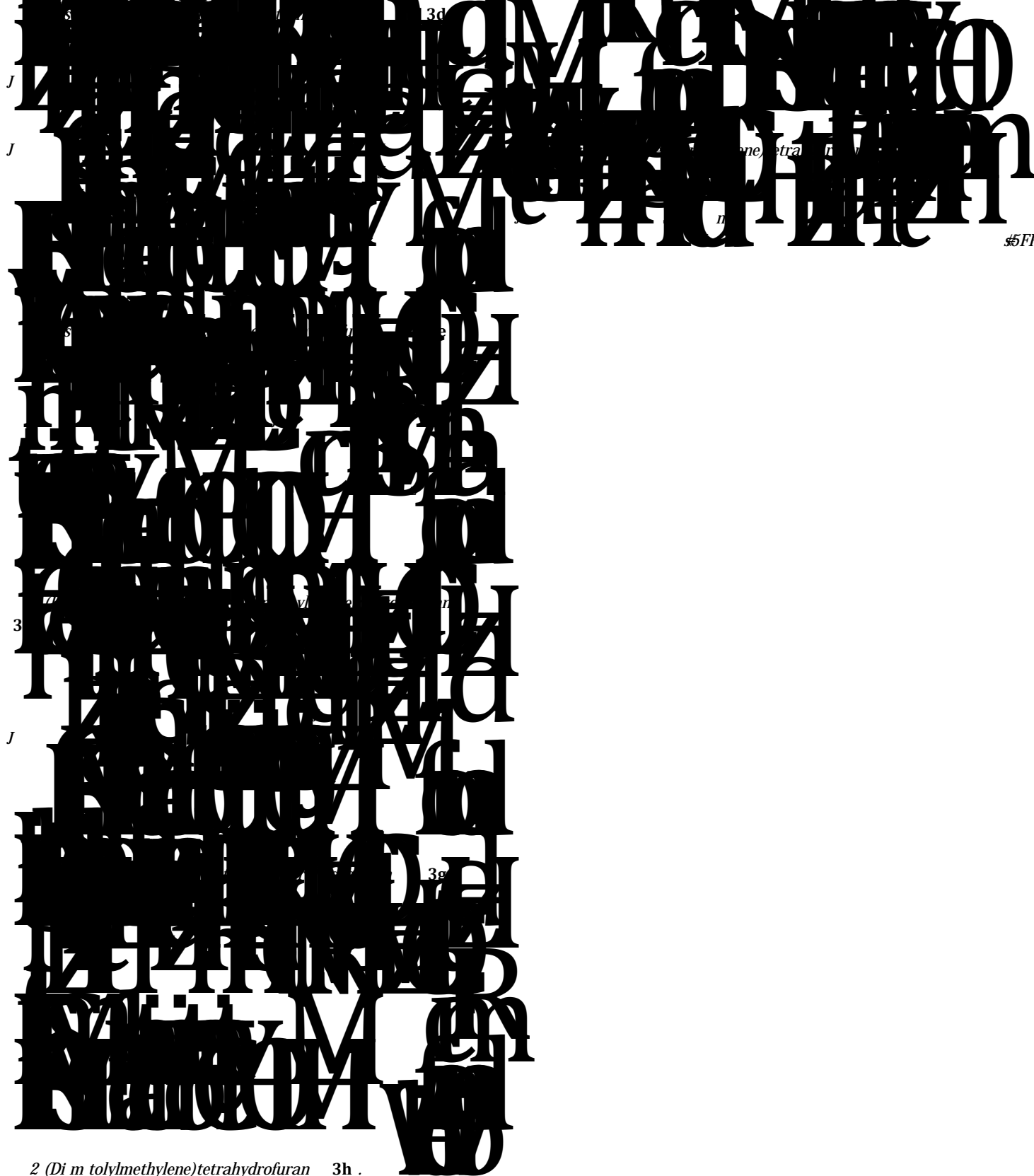
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1. Introduction

The development of new catalytic systems for the synthesis of complex molecules is a major challenge in organic chemistry. In this context, the discovery of new catalysts and reaction conditions for the synthesis of α -keto nitriles is of great interest. In this paper, we report a new catalytic system for the synthesis of α -keto nitriles from 3-oxo-1,2,4-triazole and α -keto nitriles. The reaction proceeds via a cascade reaction involving the formation of a 3-oxo-1,2,4-triazole intermediate, followed by the reaction with α -keto nitriles to form the final product. The reaction is catalyzed by a new catalyst system consisting of a metal complex and a ligand. The reaction conditions are mild and the catalyst is reusable. The reaction is highly regioselective and yields high yields of the final product. The reaction is also highly tolerant of various functional groups. The reaction is a valuable tool for the synthesis of complex molecules.





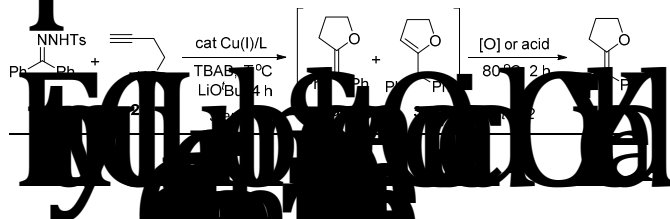
1. **Reaction of 1a with 2a**
A solution of 1a (0.5 mmol) and 2a (0.5 mmol) in CH₂Cl₂ (10 mL) was stirred at room temperature for 24 h. The mixture was concentrated under reduced pressure to give a solid residue. Purification by silica gel chromatography (hexane/EtOAc = 1/1) gave 3a (0.1 mmol, 20% yield) as a white solid. mp 105–106 °C. ¹H NMR (CDCl₃) δ: 7.2–7.4 (m, 4H), 6.8–7.0 (m, 4H), 6.5–6.7 (m, 4H), 6.2–6.4 (m, 4H), 5.8–6.0 (m, 4H), 5.5–5.7 (m, 4H), 5.2–5.4 (m, 4H), 4.8–5.0 (m, 4H), 4.5–4.7 (m, 4H), 4.2–4.4 (m, 4H), 3.8–4.0 (m, 4H), 3.5–3.7 (m, 4H), 3.2–3.4 (m, 4H), 2.8–3.0 (m, 4H), 2.5–2.7 (m, 4H), 2.2–2.4 (m, 4H), 1.8–2.0 (m, 4H), 1.5–1.7 (m, 4H), 1.2–1.4 (m, 4H), 0.8–1.0 (m, 4H), 0.5–0.7 (m, 4H), 0.2–0.4 (m, 4H), 0.0–0.2 (m, 4H).

5a
(E) 2
1. **Reaction of 1a with 2b**
A solution of 1a (0.5 mmol) and 2b (0.5 mmol) in CH₂Cl₂ (10 mL) was stirred at room temperature for 24 h. The mixture was concentrated under reduced pressure to give a solid residue. Purification by silica gel chromatography (hexane/EtOAc = 1/1) gave 3b (0.1 mmol, 20% yield) as a white solid. mp 105–106 °C. ¹H NMR (CDCl₃) δ: 7.2–7.4 (m, 4H), 6.8–7.0 (m, 4H), 6.5–6.7 (m, 4H), 6.2–6.4 (m, 4H), 5.8–6.0 (m, 4H), 5.5–5.7 (m, 4H), 5.2–5.4 (m, 4H), 4.8–5.0 (m, 4H), 4.5–4.7 (m, 4H), 4.2–4.4 (m, 4H), 3.8–4.0 (m, 4H), 3.5–3.7 (m, 4H), 3.2–3.4 (m, 4H), 2.8–3.0 (m, 4H), 2.5–2.7 (m, 4H), 2.2–2.4 (m, 4H), 1.8–2.0 (m, 4H), 1.5–1.7 (m, 4H), 1.2–1.4 (m, 4H), 0.8–1.0 (m, 4H), 0.5–0.7 (m, 4H), 0.2–0.4 (m, 4H), 0.0–0.2 (m, 4H).

5b
(E) 2
1. **Reaction of 1a with 2c**
A solution of 1a (0.5 mmol) and 2c (0.5 mmol) in CH₂Cl₂ (10 mL) was stirred at room temperature for 24 h. The mixture was concentrated under reduced pressure to give a solid residue. Purification by silica gel chromatography (hexane/EtOAc = 1/1) gave 3c (0.1 mmol, 20% yield) as a white solid. mp 105–106 °C. ¹H NMR (CDCl₃) δ: 7.2–7.4 (m, 4H), 6.8–7.0 (m, 4H), 6.5–6.7 (m, 4H), 6.2–6.4 (m, 4H), 5.8–6.0 (m, 4H), 5.5–5.7 (m, 4H), 5.2–5.4 (m, 4H), 4.8–5.0 (m, 4H), 4.5–4.7 (m, 4H), 4.2–4.4 (m, 4H), 3.8–4.0 (m, 4H), 3.5–3.7 (m, 4H), 3.2–3.4 (m, 4H), 2.8–3.0 (m, 4H), 2.5–2.7 (m, 4H), 2.2–2.4 (m, 4H), 1.8–2.0 (m, 4H), 1.5–1.7 (m, 4H), 1.2–1.4 (m, 4H), 0.8–1.0 (m, 4H), 0.5–0.7 (m, 4H), 0.2–0.4 (m, 4H), 0.0–0.2 (m, 4H).

5c
(E) 2
1. **Reaction of 1a with 2d**
A solution of 1a (0.5 mmol) and 2d (0.5 mmol) in CH₂Cl₂ (10 mL) was stirred at room temperature for 24 h. The mixture was concentrated under reduced pressure to give a solid residue. Purification by silica gel chromatography (hexane/EtOAc = 1/1) gave 3d (0.1 mmol, 20% yield) as a white solid. mp 105–106 °C. ¹H NMR (CDCl₃) δ: 7.2–7.4 (m, 4H), 6.8–7.0 (m, 4H), 6.5–6.7 (m, 4H), 6.2–6.4 (m, 4H), 5.8–6.0 (m, 4H), 5.5–5.7 (m, 4H), 5.2–5.4 (m, 4H), 4.8–5.0 (m, 4H), 4.5–4.7 (m, 4H), 4.2–4.4 (m, 4H), 3.8–4.0 (m, 4H), 3.5–3.7 (m, 4H), 3.2–3.4 (m, 4H), 2.8–3.0 (m, 4H), 2.5–2.7 (m, 4H), 2.2–2.4 (m, 4H), 1.8–2.0 (m, 4H), 1.5–1.7 (m, 4H), 1.2–1.4 (m, 4H), 0.8–1.0 (m, 4H), 0.5–0.7 (m, 4H), 0.2–0.4 (m, 4H), 0.0–0.2 (m, 4H).

2.4. **General procedure for the Cu(I)-catalyzed reaction of N-alkyl-2-oxo-1,2-dihydro-1H-benz[e][1,2,4]triazole-3-carboxamides with 1a**
A solution of 1a (0.5 mmol) and N-alkyl-2-oxo-1,2-dihydro-1H-benz[e][1,2,4]triazole-3-carboxamide (0.5 mmol) in CH₂Cl₂ (10 mL) was stirred at room temperature for 24 h. The mixture was concentrated under reduced pressure to give a solid residue. Purification by silica gel chromatography (hexane/EtOAc = 1/1) gave the product as a white solid.



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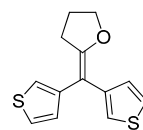
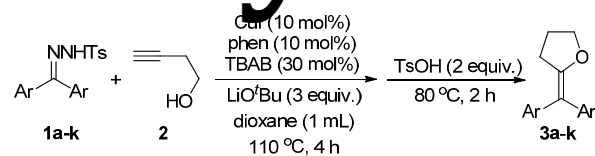
3a 3a'

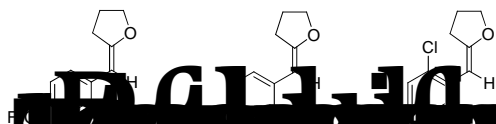
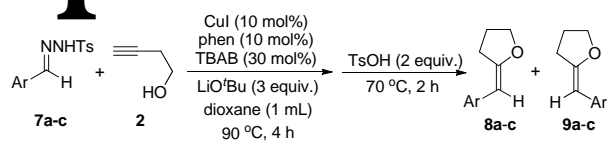
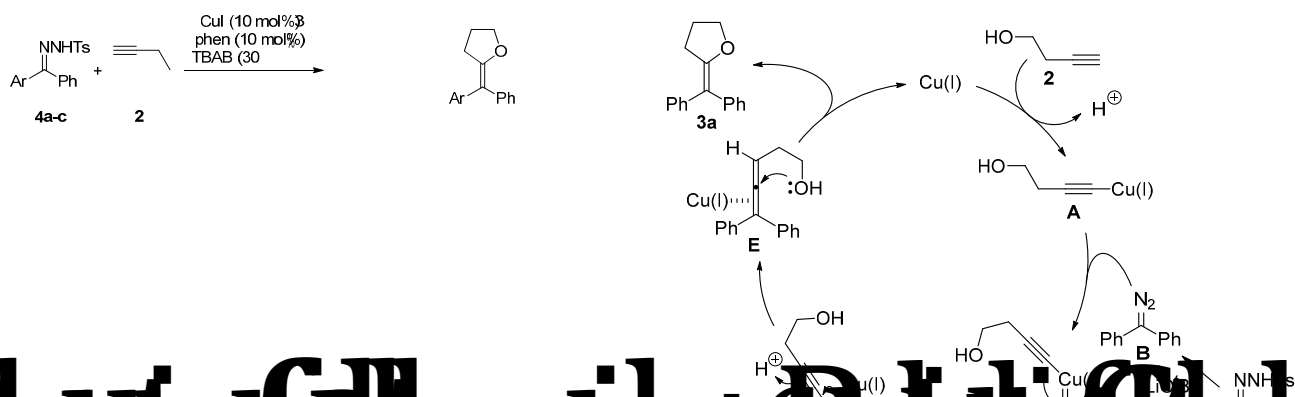
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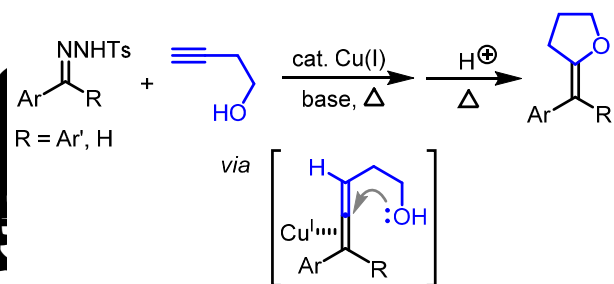
3a 3a'





References

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