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Synthesis of atropoisomeric pyridines via cobalt-catalyzed cocyclotrimerization of diynes with benzonitrile

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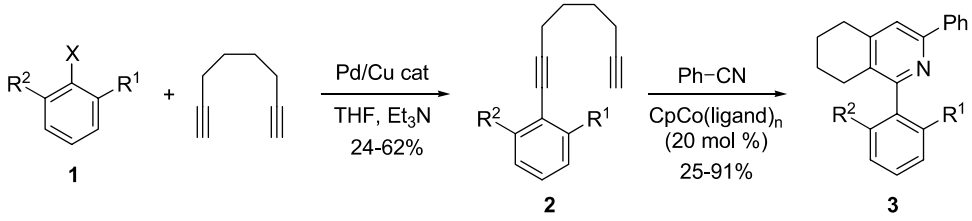
Abstract—Arylpyridines (precursors for potential organocatalysts) are easily accesible by cobalt-catalyzed cocyclotrimerization of *ortho*-substituted 1-aryl-1,7-octadiynes with benzonitrile. The scope of the reaction with respect to the *ortho* substituents (OMe, Me, COOMe, NHCOMe, F, etc.) was investigated. Three potentially atropoisomeric arylpyridines were prepared and one of them was converted into the corresponding *N*-oxide and resolved into its enantiomers. The absolute configuration of the *N*-oxide was established by X-ray crystal structure analysis. Preliminary results of its application in asymmetric organocatalysis are presented.

1. Introduction

The interest in the field of organocatalysis (acceleration of a reaction by a catalytic amount of an organic compound) has increased in the last few years. In particular, organocatalysis is gaining importance in asymmetric synthesis, complementing bio- and metal-catalysis.[1] Out of several concepts of organocatalysis, a significant role is played by activation of a Lewis acid by a Lewis base. One type of the typical Lewis base organocatalysts are pyridine *N*-oxides with a biaryl framework.[2–5] Since pyridine *N*-oxides are easily accessible from pyridines, there is general interest in the development of new synthetic methods for pyridine preparation. One of them is based on [2+2+2] cocyclotrimerization of two C–C-triple bonds with a nitrile.[6] The use of the most widely and generally utilized cobalt catalysts was pioneered by Wakatsuki,[7] Vollhardt,[8] and Bönnemann.[9] Over the years a number of other transition metal compounds such as Ti,[10] Zr,[11] Fe,[12] Ta,[13] and Rh[14] were shown to catalyze or mediate the cyclotrimerization. Recently, a Ru-based catalyst has been shown to be suitable for cyclotrimerization of diynes with electron-deficient nitriles.[15,16] Cocyclotrimerization has also been used for preparation of oligopyridines (namely bipyridines) either by cocyclotrimerization of diynes with dinitriles,[17] or alkynylnitriles with diynes,[18] or cyanopyridines with alkynes.[19] The synthesis of chiral pyridines is based either on cyclotrimerization with chiral nitriles[20] or enantioselective cyclotrimerization by treatment with chiral cyclopentadienyl cobalt complexes.[21] Herein, we report on the cobalt-catalyzed cyclotrimerization of substituted aryldiynes with nitriles to potentially atropoisomeric pyridines, conversion



Scheme 1. Preparation of diynes **2** and their cocyclotrimerization with nitriles to arylpyridines **3** under Co-catalysis.

Keywords: Pyridine; Cocyclotrimerization; Cobalt; Catalysis; Organocatalysis.
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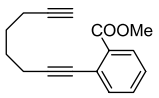
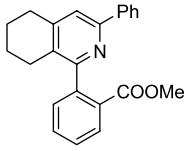
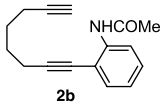
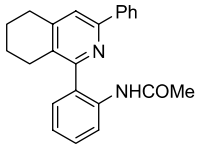
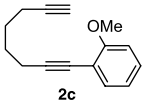
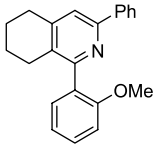
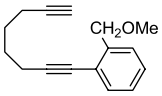
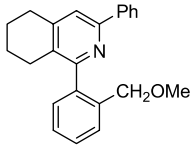
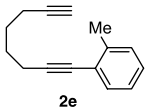
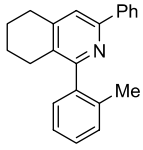
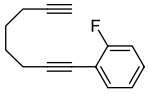
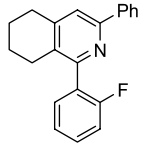
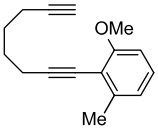
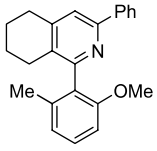
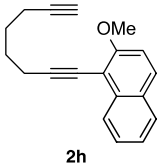
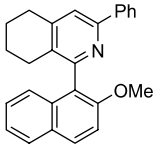
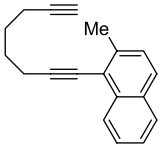
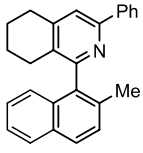
Table 1. Cobalt-catalyzed cocyclotrimerization of diynes **2** with benzonitrile to arylpyridines **3**

Entry	Diyne **2a**	Product **3**	Conditions[a]	Yield %[b]
1	 **2a**	 **3a**	A	54
2	 **2b**	 **3b**	A	35
3	 **2c**	 **3c**	A	76
4	 **2d**	 **3d**	A	33
5	 **2e**	 **3e**	A	91
6	 **2f**	 **3f**	A	46
7	 **2g**	 **3g**	A, B, C	30, 25, 62
8	 **2h**	 **3h**	A, B, C	75 (54)[c], 67, 0
9	 **2i**	 **3i**	A, B, C	30, 69, 48

[a] Conditions: A=$CpCo(CO)_2$ (20 mol%), PPh_3 (40 mol%), 140 °C, 48 h; B=CpCo(COD) (20 mol%), 140 °C, 48 h; C=$CpCo(CH_2{=}CH_2)_2$ (10 mol%), 20 °C, 30 min.
[b] Isolated yields.
[c] $CpCo(CO)_2$ (10 mol%), 140 °C, 48 h.