



Research Article

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Efficient, one-pot synthesis of α -aminonitriles via Strecker reaction: New recyclable catalysts

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ABSTRACT

Pyridine dicarboxylic acid guanidine-cobalt complex ((GH)₂[Co(H₂O)₆][Co(pydc)₂]₂) and uranyl acetate (UO₂(CH₃COO)₂·2H₂O) catalyze one-pot, three-component coupling of aldehydes, amines, and potassium cyanide to afford the corresponding α -aminonitriles. The significant features of this method are simple work-up procedure, shorter reaction times and excellent product yields. Also, these two catalysts were recyclable for four consecutive runs.

Keywords: α -Aminonitriles, Strecker Reaction, Cobalt Complex, Uranylacetate

INTRODUCTION

The German chemist Adolph Strecker [1, 2], reacted potassium cyanide, ammonium chloride and an aldehyde to afford α -amino nitriles, which is subsequently hydrolyzed to produce the α -amino acid. α -Amino nitriles are remarkably important intermediates for the synthesis of a wide variety of amino acids [3, 4], also they are very useful synthons for the synthesis of heterocyclic compounds such as imidazoles [5], thiadiazoles [6], 1,2-aminoalcohols [7], 1,2-diamines [8] and other biologically important molecules [9].

Due to this importance, academic investigations were very fast, and virtually every major journal was flooded with papers on the Strecker α -amino nitriles using a variety of primary, secondary amines and ketones [10], viewed in terms of economic viability, operational simplicity, and greater selectivity (such as utilizing asymmetric auxiliaries [11] or asymmetric catalysts [12]). Although, different methods for such products based on the use of Lewis acids and bases such as Sc(OTf)₃ [13], KSF clay [14], InCl₃ [15], Cd(II)-salt [16], K₂PdCl₄ [17], Pt-salt [18], BiCl₃ [19], Yb(OTf)₃-pybox [20], bisformamides [21], nanocrystal-MgO [22], Ga(OTf)₃ [23], Fe(Cp)₂PF₆ [24], Jacobsen's thiourea catalyst [25], BINOL-phosphoric acid [26, 27], N-heterocyclic carbene (NHC)-mediated palladium (II) complex [28], N,N-dimethylcyclohexylamine [11], superparamagnetic iron oxide [29] and varieties of other conditions such as ionic liquid [30] media have been reported in the literature.

In continuation of my investigations on modification of organic synthesis by catalyst [31, 32], here in, I report the efficient new catalysts (**PD-Co** [33]; Fig. 1 and **UA**) for the synthesis of α -amino nitriles (ANs) via Strecker protocol.

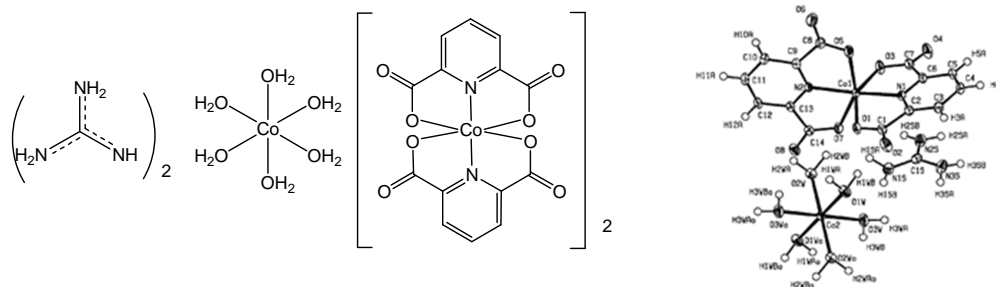


Fig. 1 Pyridine dicarboxylic acid guanidine-cobalt complex (PD-Co; $(\text{GH})_2[\text{Co}(\text{H}_2\text{O})_6][\text{Co}(\text{pydc})_2]_2$); and the ORTEP diagram

EXPERIMENTAL SECTION

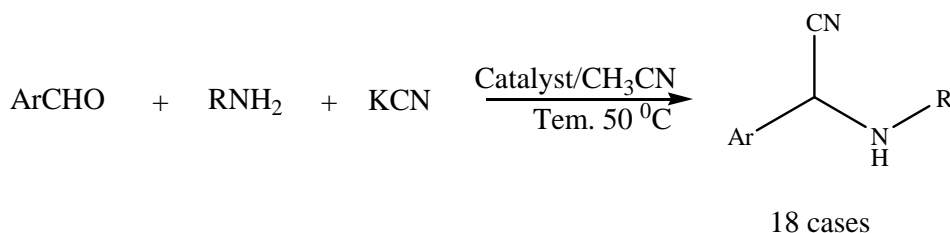
All reactions were carried out in an efficient hood. The starting materials were purchased from Merck and Fluka chemical companies. Melting points were determined with a Branstead Electrothermal model 9200 apparatus and are uncorrected. IR spectra were recorded on a Perkin Elmer RX1 Fourier transform infrared spectrometer. The ^1H and ^{13}C NMR spectra were recorded in DMSO-d_6 and CDCl_3 on Bruker Advance 300 MHz spectrometers. Elemental analyses were carried out by a Perkin Elmer 2400 series II CHN/O analyzer.

Synthesis of PD-Co: It was synthesized according to method specified in ref. 33.

Synthesis of AN_1 (2-(N-Anilino)-2-phenylacetonitrile) as general procedure: A mixture of benzaldehyde (1 mmol), aniline (1 mmol), KCN (1.5 mmol) and (3 mol%) PD-Co (3 mol%) or UA (5 mol%) was stirred on oil-bath at 50°C for 3 hour (Tables 1 and 2). Then the reaction mixture was poured in ice water and the precipitated solid was collected by filtration, washed with distilled water and dried. The crude product was purified by silica gel column chromatography (EtOAc-n-hexane; 1: 3) to afford the pure AN_1 . mp $74\text{--}76^\circ\text{C}$, IR (KBr): 3341, 30045, 2242, 1611, 1530, 1275, 750 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 4.09 (br, s, 1H), 5.48 (s, 1H), 6.82 (d, $J = 7.7$ Hz, 2H), 6.95 (t, $J = 7.7$ Hz, 1H), 7.28 (t, $J = 7.7$ Hz, 2H), 7.44-7.55 (m, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 51.5, 115.5, 119.3, 121.0, 128.6, 130.3, 131.6, 131.9, 134.9, 136.1; Anal. Calcd for $\text{C}_{14}\text{H}_{12}\text{N}_2$: C, 80.77; H, 5.77; N, 13.46; Found: C, 80.64; H, 5.64; N, 13.64.

RESULTS AND DISCUSSION

To best of my knowledge, my first finding was that the reaction of benzaldehyde and aniline with KCN in the presence of 20 mol% PD-Co or UA catalyst, afforded the desired AN_1 respectively in 93% and 90% yields at 50°C in acetonitrile (Scheme 1, Table 3). The reaction was performed in various solvents (CH_3CN , THF, EtOH, toluene, MeOH, CH_2Cl_2 , DMSO, EtOH/ H_2O (1:1)) using PD-Co or UA as the catalyst to identify the best condition (Table 1).



Scheme 1 Strecker reaction

Table 1 Strecker reaction (effect of solvent): benzaldehyde (1 mmol), aniline (1 mmol) and KCN (1.5 mmol) in the presence of catalyst (20 mol %)

Entry	Solvent	Product yield % (with PD-Co)	Product yield % (with UA)
1	CH_3CN	93	90
2	THF	52	51
3	Ethanol	81	83
4	Toluene	63	60
5	Methanol	75	76
5	CH_2Cl_2	60	65
6	DMSO	79	76
8	Ethanol/ H_2O (1:1)	68	61

Then, i optimized the reaction conditions by conducting the reaction in different temperatures, times, and amount of catalyst, as typical sample. The results are summarized in Table 2, whereby the better yields were obtained when the temperature was at 50 °C with 3 hours reaction time and 3mol% of PD-Coor5mol% of UA.

Table 2 Synthesis of AN₁ under different conditions for optimization of reactions

Temp. °C	Time (h)	Amount of catalyst (Mol%)	Product Yield (With PD-Co%)	Product Yield (With UA %)
60	4	20	93	90
50	4	20	93	90
40	4	20	87	86
50	3	10	93	90
50	3	5	93	90
50	3	3	93	83
50	3	2	81	-
50	3	1	-	-

Aniline or benzyl amine and several activated and deactivated aldehydes including aromatic, heterocyclic aldehydes underwent the reaction to give the corresponding ANs in high to excellent yields. The experimental procedure was very simple, convenient, and had the ability to tolerate a variety of other functional groups such as methoxy, nitro, hydroxy, and halides under the reaction conditions (Table 3).

Table3 Details strecker synthesis

Entry	R-	Ar-	product	Product Yield (%) with PD-Co	Product Yield (%) with UA	mp °C
1	Ph-	Ph-	AN ₁	93	90	74-76 [34]
2	Ph-	4-Me-Ph-	AN ₂	92	89	74-76[34]
3	Ph-	4-Cl-Ph-	AN ₃	91	87	108-110[34]
4	Ph-	2-Cl-Ph-	AN ₄	86	83	66-68 [35]
5	Ph-	4-MeO-Ph-	AN ₅	87	82	92-94[34]
6	Ph-	3-MeO-Ph-	AN ₆	88	85	58-60 [36]
7	Ph-	4-HO-Ph-	AN ₇	86	83	121-123 [37]
8	Ph-	4-NO ₂ -Ph	AN ₈	95	93	90-92 [37]
9	Ph-	2-Furyl-	AN ₉	86	84	67-69 [38]
10	Ph-CH ₂ -	Ph-	AN ₁₀	95	91	30-32 [39]
11	Ph-CH ₂ -	4-Cl-Ph-	AN ₁₁	93	90	Oil [40]
12	Ph-CH ₂ -	4-MeO-Ph-	AN ₁₂	89	85	Oil[38]
13	Ph-CH ₂ -	2-MeO-Ph-	AN ₁₃	89	86	Oil [41]
14	Ph-CH ₂ -	3-MeO-Ph-	AN ₁₄	90	86	Oil[42]
15	Ph-CH ₂ -	2-HO-Ph-	AN ₁₅	90	87	Oil [43]
16	Ph-CH ₂ -	4-NO ₂ -Ph	AN ₁₆	98	95	Oil[43]
17	Ph-CH ₂ -	2-Furyl-	AN ₁₇	89	87	Oil[44]
18	Ph-CH ₂ -	4-HO-Ph-	AN ₁₈	89	86	79-80 [44]

Interestingly, both of two catalysts can be recycled for four consecutive runs without significant loss of activity (Table 4). For this purpose, after completion of the reaction, water was added. The precipitated solid was isolated by filtration; the catalyst was recovered from the filtrate by evaporation of the water, and reused for the similar reaction.

Table 4 Recycled of PD-Co and UA in the synthesis of Strecker reactions

Catalyst type	Runs				
	1	2	3	4	5
Product yield (%) with PD-Co	93	90	86	82	73
Product yield (%) with UA	90	88	85	80	72

CONCLUSION

In conclusion, I have successfully developed a quick, convenient and efficient method for the synthesis of α -acetonitrils in the presence of co-complex or uranyl acetate as catalyst. The environmental advantages include generality and simplicity of procedure, shorter reaction time, simple workup, reusable catalyst condition, and pure products in excellent yields.

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