

K₅CoW₁₂O₄₀.3H₂O: Highly Efficient Heterogeneous Catalyst for the Synthesis of α -Aminonitriles

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Abstract: One-pot three-component condensation of aldehydes or ketones, amines and trimethylsilyl cyanide was accomplished in the presence of a catalytic amount of K₅CoW₁₂O₄₀.3H₂O as an efficient and reusable catalyst.

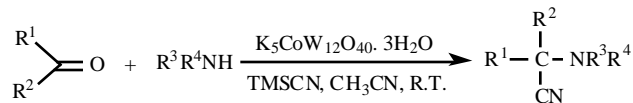
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1. INTRODUCTION

Polyoxometalates (POM's) have become a subject of general interest because of their potential applications in fields as diverse as catalysis, biochemical analysis, medicinal chemistry, and materials science. Some of the most relevant properties for technological applications rely on solubility, acidity and redox potentials [1, 2]. Heteropoly compounds with Keggin structure are the most studied class within POM's, and those containing tungsten as addenda atoms exhibit a strong acidity, high thermal stability and low oxidation potential [3] which allow them to be used as catalysts in various reactions at moderate temperatures.

Bifunctional α -aminonitriles are not only versatile intermediates for the synthesis of α -aminoacids [4-7] and various nitrogen containing heterocycles [8, 9] such as imidazoles and thiadiazoles but also exhibit a valuable dual reactivity, which has been utilized in a broad range of synthetic applications [10]. Additionally, the α -aminonitrile moiety has been found to occur in saframycin A, a natural product with anti-tumour activity, and phtalascidin, a synthetic analogue, which exhibits even greater potency [11]. The Strecker reaction [12] provides one of the most important methods for the Synthesis of α -aminonitriles. Numerous modifications have been made to the original Strecker reaction, using a variety of cyanating agents such as hydrogen cyanide, sodium or potassium cyanide, Bu₃SnCN, bis(dialkylamino)cyanoboranes, diethylphosphorocyanidate, and trimethylsilyl cyanide (TMSCN) [12-17]. TMSCN is a safer, more effective, and more easily handled anion source compared to others [18-24]. The efficiency of the reaction has been increased by the use of catalysts [12-29]. Although these methods are valuable, they suffer from one or more of certain deficiencies, including the tedious isolation of pure α -aminonitriles from the reaction mixtures, strongly acidic conditions, extended reaction times, leading to the generation of a large amount of toxic waste, and use of stoichiometric or relatively expensive reagents. Furthermore,

many of these protocols are limited to aldehydes only, and many of the used catalysts are deactivated or sometimes decomposed by amines. Therefore, there is further room to explore milder, safer and more efficient protocols for synthesis of α -aminonitriles. In continuation of our work to investigation of activity of POM's for developing new synthetic methodologies, [30-33] an excellent modification of Strecker synthesis has been reported here by using K₅CoW₁₂O₄₀.3H₂O as a non-toxic and reusable catalyst (Scheme 1).



Scheme 1.

2. EXPERIMENTAL

2.1. Preparation of the Catalyst

The synthesis of potassium dodecatungstocobaltate trihydrate (K₅CoW₁₂O₄₀.3H₂O) starts with the preparation of sodium tungstodicobalt(II)ate from cobaltous acetate (2.5 g, 0.01 mol) and sodium tungstates (19.8 g, 0.06 mol) in acetic acid and water at pH 6.5-7.5. The sodium salt is then converted to the potassium salt by treatment with potassium chloride (13 g).

Finally the cobalt(II) complex is oxidized to the cobalt(III) complex by potassium persulfate (10 g) in 40 mL of 2M H₂SO₄. The crystal of K₅CoW₁₂O₄₀.3H₂O were dried at 200 °C, after recrystallization with methanol, potassium dodecatungstocobaltate trihydrate (K₅CoW₁₂O₄₀.3H₂O) was obtained and fully characterized [8, 34, 35].

2.2. General Procedure for the Synthesis of α -Aminonitriles

A mixture of aldehyde (1 mmol), amine (1.1mmol), TMSCN (1.5 mmol) and K₅CoW₁₂O₄₀.3H₂O (0.1 mmol) in acetonitrile (3 mL) was stirred at room temperature for an appropriate time (Table 2). After completion of the reaction, as indicated by TLC, the reaction mixture was filtered and

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washed with acetonitrile (2×10 mL). The combined organic layers were dried over anhydrous Na₂SO₄, concentrated in vacuum and purified by column chromatography on silica gel (ethyl acetate-hexane, 1:9) to afford pure α -aminonitrile.

3. RESULTS AND DISCUSSION

Initially, optimization experiments for the three component Strecker reaction involving benzaldehyde, aniline, and TMSCN in the presence of catalytic amount of K₅CoW₁₂O₄₀·3H₂O were carried out. It is remarkable to note that the reaction proceeded with a low catalyst concentration (10 mol %) at ambient conditions. There are no improvements in the reaction rates and yields by increasing the amount of the catalyst from 10 mol% to 20 mol% (Table 1, entries 1-3). In addition, acetonitrile was found to be the best solvent for the multicomponent Strecker reaction using TMSCN (Table 1, entries 3-6). Furthermore, KCN as a cyanating agent was checked (Table 1, entry 7). In comparison with other catalysts employed for the aminocyanation of benzaldehyde, K₅CoW₁₂O₄₀·3H₂O shows more catalytic reactivity than others (Table 1).

A variety of aldehydes (aliphatic, aromatic, and heterocyclic) was coupled with amines and TMSCN in a one-pot operation to produce α -aminonitriles in high to excellent yields (Table 2). The method was equally effective for aromatic, benzylic, and both primary and secondary aliphatic amines. To our knowledge, only a few reports of Strecker reactions with ketones appear in the literature [13-

16], but as evidenced in Table 2, entries 17-20, ketones gave moderate yields in this report. Furthermore, acid sensitive aldehyde such as furfuraldehyde and cinnamaldehyde worked well without any decomposition or polymerization under these reaction conditions (Table 2, entries 11-13). Enolizable aldehydes such as decanal also produced the corresponding α -aminonitrile in very short reaction time (Table 2, entry 15). This method does not require any acidic promoters or activators to promote the reaction. No cyanohydrin trimethylsilyl ethers (adduct between an aldehyde and TMSCN) were obtained as undesired side products because of the rapid formation of the imine intermediate. In view of characteristic structure of K₅CoW₁₂O₄₀ (a central ion surrounded by a spherical sheath of chemically inert oxygen atom [36]), these anions cannot significantly interact with the organic substrates, therefore reacting via an outer-sphere electron-transfer mechanism [37, 38]. In addition, this structure protects the central ion from undesired inner-sphere substitution reactions, and amines could not attached the cobalt ion and deactivate it. For this reason, electron transfer with K₅CoW₁₂O₄₀ typically leads to selective reactions and clean chemistry compare to other catalysts. The catalyst was recovered by filtration, washed with acetonitrile and recycled for use in subsequent reaction with gradual decrease in activity; for example, the reaction of benzaldehyde, aniline and TMSCN afforded α -aminonitrile in 80% yield after ten cycles.

To the best of our knowledge, this is the first report on POM's mediated for Strecker reactions. The results presented

Table 1. Effect of Different Catalysts for Condensation of Benzaldehyde, Aniline and Cyanating Agents

Entry	Catalyst	Solvent	Cyanating Agent	Time (h)	Yield (%)
1	K ₅ CoW ₁₂ O ₄₀ ·3H ₂ O (5 mol%)	CH ₃ CN	TMSCN	1	93
2	K ₅ CoW ₁₂ O ₄₀ ·3H ₂ O (20 mol%)	CH ₃ CN	TMSCN	0.2	95
3	K ₅ CoW ₁₂ O ₄₀ ·3H ₂ O (10 mol%)	CH ₃ CN	TMSCN	0.3	95
4	K ₅ CoW ₁₂ O ₄₀ ·3H ₂ O (10 mol%)	Et ₂ O	TMSCN	0.3	25
5	K ₅ CoW ₁₂ O ₄₀ ·3H ₂ O (10 mol%)	C ₆ H ₆	TMSCN	0.3	20
6	K ₅ CoW ₁₂ O ₄₀ ·3H ₂ O (10 mol%)	CH ₂ Cl ₂	TMSCN	0.3	43
7	K ₅ CoW ₁₂ O ₄₀ ·3H ₂ O (10 mol%)	CH ₃ CN	KCN	0.8	95
8	Sc(OTf) ₃ (10 mol%) ^a	H ₂ O	Bu ₃ SnCN	20	88 ¹⁷
9	RuCl ₃ (20 mol%)	CH ₃ CN	TMSCN	20	74 ²⁵
10	Pr(OTf) ₃ (10 mol%)	CH ₃ CN	TMSCN	10	89 ²⁶
11	NiCl ₂ (5 mol%)	CH ₃ CN	TMSCN	12	92 ²⁴
12	InCl ₃ (30 mol%)	THF	KCN	6	75 ¹³
13	[HP(HNCH ₂ CH ₂) ₃ N]NO (20 mol%)	CH ₃ CN	TMSCN	12	94 ¹⁹
14	I ₂ (10 mol%)	CH ₃ CN	TMSCN	1	94 ¹⁵
15	BiCl ₃ (10 mol%)	CH ₃ CN	TMSCN	10	84 ²²
16	KSF ^b	CH ₂ Cl ₂	TMSCN	3.5	90 ¹⁸
17	Yb(OTf) ₃ (5 mol%) ^a	CH ₂ Cl ₂	TMSCN	20	88 ²⁷

^aResult for benzylamine.

^b10 gr of KSF for 1 mmol of benzaldehyde.

Table 2. $K_5CoW_{12}O_{40} \cdot 3H_2O$ Catalysed Synthesis of α -Aminonitriles

Entry	Aldehyde/Ketone	Amine	Time /Min	%Yield ^a	Ref. ^b
1	benzaldehyde	aniline	20	95	[24]
2	benzaldehyde	benzylamine	30	95	[21]
3	benzaldehyde	butylamine	45	98	[24]
4	benzaldehyde	isobutylamine	50	84	[13]
5	<i>m</i> -methoxybenzaldehyde	aniline	35	95	[13]
6	<i>m</i> -methoxybenzaldehyde	benzylamine	35	80	[13]
7	<i>m</i> -methoxybenzaldehyde	butylamine	20	70	[13]
8	<i>p</i> -chlorobenzaldehyde	aniline	20	93	[24]
9	<i>p</i> -nitrobenzaldehyde	aniline	45	92	[21]
10	<i>p</i> -methylbenzaldehyde	aniline	15	98	[24]
11	furfural	aniline	15	98	[18]
12	furfural	benzylamine	15	84	[24]
13	cinamaldehyde	aniline	30	98	[24]
14	thiophene-2-carboxaldehyde	benzylamine	15	62	[21]
15	decanal	aniline	30	80	[21]
16	benzaldehyde	morpholine	15	98	[13]
17	cyclohexanone	benzylamine	200	69	[13]
18	cyclohexanone	butylamine	60	54	[13]
19	3-methyl cyclohexanone	benzylamine	100	61	[13]
20	3-methyl cyclohexanone	morpholine	200	80	[13]
21	Benzaldehyde	4-methoxyaniline	30	94	[27]

^aIsolated yield.^bProducts were characterised by comparison of their spectroscopic data with those reported in the literature.

in this paper demonstrate that $K_5CoW_{12}O_{40} \cdot 3H_2O$ can be regarded as an efficient, environmentally friendly, cheap, non-toxic, and reusable catalyst. Also the present procedure represents a clean, practical, simple, mild, and time-saving method which is applicable to a wide scope of structural types for synthesis of α -aminonitriles in short reaction times and high to excellent yields with very easy work-up.

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