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Synthesis of Nitriles from Aerobic Oxidation of Amines Catalyzed by Ruthenium Supported on Activated Carbon

Baoqiang Niu, Fei Lu, Hong-Yu Zhang, Yuecheng Zhang, and Jiquan Zhao*
School of Chemical Engineering and Technology, Hebei University of Technology, Tianjin 300130, P. R. China

(E-mail: zhaojq@hebut.edu.cn)

Nitriles were synthesized from the aerobic oxidation of amines over commercially available catalysts, which were activated carbon-supported ruthenium catalysts (Ru/AC). The 5%Ru/AC catalyst can tolerate a wide range of substrates, such as aromatic, aliphatic, and heterocyclic amines, and afford the target nitriles in good-to-excellent yields. The 5%Ru/AC catalyst was easily recovered and no ruthenium leaking took place in the catalytic run.

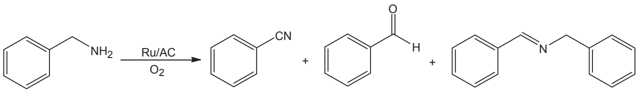
Keywords: Aerobic oxidation | Nitrile | Ruthenium

Nitriles are important intermediates for the synthesis of dyes, agricultural chemicals, fine chemicals, and polymers.[1] Additionally, compounds containing a cyano group are used as pharmaceuticals and functional materials.[2] Nitriles are generally prepared by nucleophilic reaction of substrates with appropriate leaving groups such as organic halide, aryl sulfonates, alcohols, diazonium salts, and nitro or amino compounds with various metal cyanides.[3] However, these methods need stoichiometric or excessive amounts of polluting or toxic reagents, harsh reaction conditions, and produce large amount of by-products. Due to the important role of nitriles in organic synthesis, exploring new environmentally friendly methods to synthesize nitriles is still an important subject.

In recent reports, many novel protocols have been explored to prepare nitriles, such as the dehydration of primary amides,[4] oxidative dehydrogenation of benzylic alcohols in the presence of various nitrogen source,[5] and using NH_3, DMF, or TMSCN as the CN source for C–H cyanidation of arenes.[6] Compared with these methods, the catalytic oxidation of primary amines by molecular oxygen is a more desirable route for the synthesis of nitriles. In this respect, homogeneous catalytic systems, such as the cyclometalated ruthenium(III) complex,[7] has been reported. However, this catalytic system is only active in the oxidation of aromatic amines to the corresponding nitriles, meanwhile, requires the presence of a base in the reaction. Though an amide-derived NNN-Ru(II) hydride complex,[8] a ruthenium-terpyridyl complex,[9] and an iron Schiff base complex[10] have been found efficient in the oxidation of amines to nitriles under mild conditions, the complicated ligands are hard to synthesize, which makes them less attractive for practical purposes. Heterogeneous catalytic systems, mainly copper-, iron-, and ruthenium-based catalyst systems, have been described. Stahl et al. reported a Cu/nitroxyl system[11] that enabled selective formation of nitriles from diverse primary amines under room temperature. However, it needs ligand, nitroxyl, and DMAP as a base to coexist to realize the catalytic process. Red copper in the presence of NH_4Br as the cocatalyst[4c] and Fe_2O_3/NGr@C catalyst[12] are also found effective in the synthesis of nitriles from amines. However, generally, many additives are required to facilitate the reaction. It has been reported that several ruthenium-based heterogeneous catalysts, such as Ru/hydroxyapatite,[13] Ru/Al_2O_3,[14] $Ru(OH)_3/Al_2O_3$,[15] $Ru(OH)_3/Fe_3O_4$,[4a] $RuO_2{\cdot}xH_2O/Co_3O_4$,[16] Ru/$TiO_2$,[17] and Co_3O_4/NGr@C[18] are effective in the aerobic oxidation of amines to nitriles without requiring the presence of any additives. The simple heterogeneous catalysts make purification of the products easy. Inspired by the excellent performance of the ruthenium-based catalysts, we evaluated some commercially available activated carbon-supported ruthenium catalysts (Ru/AC) in the aerobic oxidation of amines to nitriles without the presence of any additives. It was found the Ru/AC catalysts showed high activity in the reaction, and can tolerate a wide range of substrates, including aromatic, aliphatic, and heterocyclic amines.

The Ru/AC catalysts were evaluated for the aerobic oxidation of amines to nitriles with benzylamine as a model substrate. Four catalysts with different ruthenium contents supported on AC were compared under the same reaction conditions. As shown in Table 1, all the catalysts showed high activity in view of the conversion of benzylamine (higher than 99.9%), but the selectivity towards benzonitrile changed with the ruthenium content of the catalysts. In the case of a ruthenium content of 3% (Table 1, Entry 1), the selectivity towards benzonitrile was 81.7% with benzaldehyde as the only by-product. When the content was increased from 3% to 5%, the selectivity of benzonitrile was maintained constant (Table 1, Entries 1 and 2). Further increasing the ruthenium content led to the decrease in the selectivity of benzonitrile. When the ruthenium content was 7%, the selectivity towards benzonitrile decreased to 79.7% due to the increase in the selectivity towards benzaldehyde (Table 1, Entry 3). In the case of the ruthenium content of 10%, a small amount of *N*-(benzyl)benzylimine derived from the homocoupling of benzylamine was detected, and the selectivity of benzonitrile was 77.6% (Table 1, Entry 4). The 5%Ru/AC catalyst was then thoroughly investigated in the subsequent experiments.

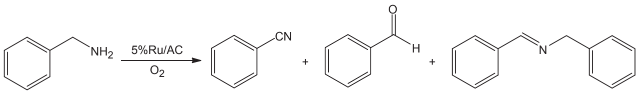
Table 1. Evaluation of the catalysts[a]



Entry	Catalyst	Conversion[b] /%	Selectivity/%[b]		
			Nitrile	Aldehyde	Imine
1	3%Ru/AC	99.9	81.7	18.3	—
2	5%Ru/AC	99.9	81.7	18.2	—
3	7%Ru/AC	99.9	79.7	20.2	—
4	10%Ru/AC	99.9	77.6	20.7	1.7

[a]Conditions: benzylamine 1 mmol, Ru/AC 5 mol %, toluene 5 mL, reaction temperature 150 °C, 0.5 MPa O_2, reaction time 4 h. [b]Determined by GC, anisole as internal standard.

Table 2. Optimization of the reaction conditions[a]



Entry	Catalyst /mol %	Solvent	Temperature /°C	P_{O_2} /MPa	Conversion /%[b]	Selectivity/%[b]		
						Nitrile	Aldehyde	Imine
1	5	toluene	130	0.5	99.9	72.4	27.6	—
2	5	toluene	140	0.5	99.9	72.7	27.2	—
3	5	toluene	150	0.5	99.9	81.7	18.2	—
4	5	toluene	160	0.5	99.9	79.7	20.2	—
5	5	toluene	170	0.5	99.9	78.8	21.1	—
6	5	acetonitrile	150	0.5	99.9	65.1	34.8	—
7	5	1,4-dioxane	150	0.5	99.9	49.2	50.8	—
8	5	trifluorotoluene	150	0.5	99.9	73.4	26.5	—
9	5	DMF	150	0.5	99.9	67.0	33.0	—
10	5	toluene	150	0.4	99.9	77.3	20.0	2.6
11	5	toluene	150	0.6	99.9	81.7	18.2	—
12	5	toluene	150	0.7	99.9	81.7	18.3	—
13	—	toluene	150	0.5	14.7	—	2.1	97.9
14	2	toluene	150	0.5	99.9	79.5	16.4	4.0
15	3	toluene	150	0.5	99.9	81.5	18.3	—
16	4	toluene	150	0.5	99.9	81.6	18.3	—
17[c]	3	toluene	150	0.5	99.9	81.6	18.2	—
18[d]	3	toluene	150	0.5	99.9	80.8	18.4	0.6
19[e]	3	toluene	150	0.5	99.9	81.5	18.5	—
20[f]	3	toluene	150	0.5	99.9	81.4	18.5	—
21[g]	3	toluene	150	0.5	99.9	47.2	9.6	43.2

[a] Conditions: benzylamine 1 mmol, 5%Ru/AC as catalyst, solvent 5 mL, oxygen pressure 0.5 MPa O_2, reaction time 4 h. [b] Determined by GC, anisole as internal standard. [c] 0.1 g molecular sieve powder was added. [d] Reaction time 3 h. [e] Reaction time 5 h. [f] Reaction time 6 h. [g] Recycle results.

The effect of the reaction temperature on the catalysis of the 5%Ru/AC catalyst was screened in the temperature range of 130–170 °C under 0.5 MPa oxygen. The results indicated that the conversion of benzylamine was close to 100% in the investigated temperature range (Table 2, Entries 1–5). The selectivity of benzonitrile increased with the temperature increase from 130 to 150 °C, and reached its maximum of 81.7% at 150 °C (Table 2, Entries 1–3). Above this temperature, the selectivity towards benzonitrile decreased with a further increase in the temperature (Table 2, Entries 4 and 5).

The catalysis of the 5%Ru/AC catalyst was also evaluated in other solvents including acetonitrile, 1,4-dioxane, trifluorotoluene, and DMF. It was found that the selectivity towards benzonitrile was low in acetonitriles, 1,4-dioxane, and DMF due to the formation of large amounts of benzaldehyde (Table 2, Entries 6, 7, 9). The selectivity towards benzonitrile obtained in trifluorotoluene was slightly lower than that in toluene (Table 2, Entries 3 and 8).

The influence of oxygen pressure on the catalytic performance of the catalyst was also investigated. The conversion of benzylamine was always close to 100% in the oxygen pressure range of 0.4 to 0.7 MPa. However, the selectivity towards benzonitrile increased with the increase in the oxygen pressure from 0.4 to 0.5 MPa, and reached its maximum of 81.7% under 0.5 MPa (Table 2, Entries 3 and 10). Then, the selectivity was maintained at this value with a further increase in the oxygen pressure (Table 2, Entries 11 and 12).

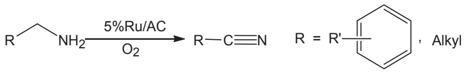
A control experiment was carried out to evaluate the necessity of the catalyst in the aerobic oxidation of benzylamine to benzonitrile, indicating that the use of the catalyst is necessary. Only 14.7% of benzylamine was converted, and no benzonitrile was formed after 4 h in the absence of the catalyst (Table 2, Entry 13). In the presence of 2 mol % catalyst, the reaction proceeded smoothly, and the conversion reached nearly 100% with a selectivity of 79.5% towards benzonitrile (Table 2, Entry 14). Besides the by-product benzaldehyde, 4% of the homocoupling imine was formed in this case. With increasing catalyst loading to 3 mol % or higher than 3 mol %, the selectivity towards benzonitrile was improved and reached about 81.5%, and no imine as the by-product was detected (Table 2, Entries 15 and 16).

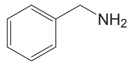
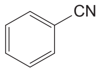
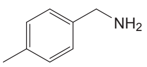
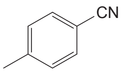
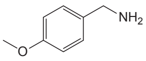
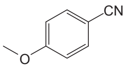
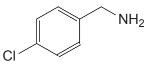
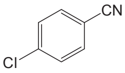
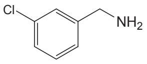
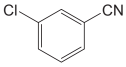
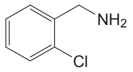
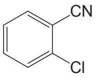
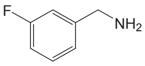
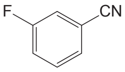
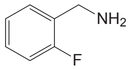
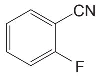
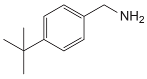
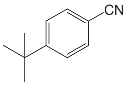
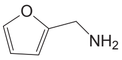
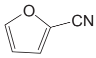
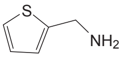
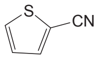
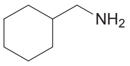
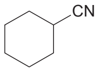
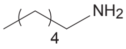
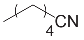
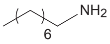
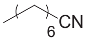
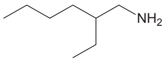
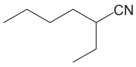
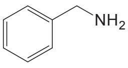
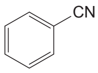
Molecular sieve powder as a dehydrating agent was added into the reaction mixture to improve the selectivity of benzonitrile, but no improvement was obtained (Table 2, Entry 17).

The reaction time was also examined. The selectivity towards benzonitrile increased with the extension of the reaction time from 3 to 4 h, and reached its maximum of 81.5% after 4 h (Table 2, Entries 15 and 18). Then, the selectivity towards benzonitrile was maintained at this value with further extension of the reaction time (Table 2, Entries 19 and 20).

From the experimental results, we concluded the optimal conditions for the aerobic oxidation of benzylamine to benzonitrile catalyzed by the catalyst 5%Ru/AC in toluene: they are benzylamine 1 mmol, catalyst loading 3 mol %, reaction temperature 150 °C, and oxygen pressure 0.5 MPa.

Table 3. Synthesis of nitriles via aerobic oxidation of primary amines catalyzed by 5%Ru/AC[a]



Entry	Substrate	Product	Conversion /%[b]	Selectivity /%[b]	Yield /%[c]
1			99.9	81.6	71.0
2			99.9	76.9	64.0
3			99.9	82.1	70.6
4			99.9	78.0	60.4
5			99.9	84.8	73.4
6			99.9	83.1	61.5
7			99.9	77.2	54.2
8			99.9	80.7	59.2
9			99.9	85.4	69.1
10			99.9	82.5	70.3
11			99.9	81.6	67.9
12			99.9	92.4	81.6
13			99.9	91.2	81.9
14			99.9	90.2	79.6
15			99.9	89.7	77.8
16[d]			99.9	80.5	—

[a] Condition: benzylamine 1 mmol, 5%Ru/AC 3 mol %, 5 mL toluene as solvent, 150 °C, 0.5 MPa O_2, 4 h. [b] Determined by GC based on area%. [c] Isolated yields. [d] Benzylamine 20 mmol, 5%Ru/AC 3 mol %, 100 mL toluene.

It should be noted that the catalyst was easily recovered by filtration. The recovered catalyst was subjected to ICP analysis, and the results indicated that no ruthenium leaking took place during the catalytic run. However, the recycle test results were depressing. Though benzylamine was almost converted, the selectivity towards benzonitrile was only 47.2%, and as high as 43.2% of the homocoupling product (imine) was obtained (Table 2, Entry 21). The poor results could be ascribed to the aggregation of Ru nanoparticles during the catalytic run (Figure S1).

To demonstrate the versatility of the 5%Ru/AC catalyst, the aerobic oxidation of various amines to the corresponding nitriles was explored under the optimized reaction conditions obtained above, and the results are shown in Table 3. As summarized in Table 3, primary benzylic amines with both electron-donating and electron-withdrawing substituents were converted to the corresponding nitriles in good to excellent yields (Table 3, Entries 1–9). The results indicated that the reaction was not affected by the electronic properties of the substituents. It seemed that the substrates with an *ortho*-substituent gave high yields compared to their *para*-counterparts (Table 3, Entries 4–8). These results may be ascribed to the steric hindrance of the *ortho*-substituent that prevents the homocoupling of the substrate to the imine. The generated imine was transformed to the corresponding aldehyde and substrate in situ. The 5%Ru/AC catalyst also showed good tolerance for the heterocyclic substrates, and good yields of the corresponding nitriles were obtained in the oxidation of 2-furylamine and 2-thiophenemethylamine (Table 3, Entries 10 and 11). The oxidation of non-activated aliphatic amines also proceeded efficiently over the 5%Ru/AC catalyst (Table 3, Entries 12–15). The yields higher than 90% (GC) were received in the cases of *n*-hexylamine, 1-cyclohexylmethanamine, and octylamine as substrates (Table 3, Entries 11–14), which were better than those of benzylic amines and heterocyclic amines as substrates. A multigram-scale reaction was carried out with benzylamine as the substrate to demonstrate the practicality of this methodology. Similar results were received when the loading amount of ethylbenzene was increased to 20 mmol. In this case, the selectivity of benzonitrile was 80.5% (Table 3, Entry 16).

In conclusion, a commercial 5%Ru/AC catalyst performed excellently in the aerobic oxidation of amines to the corresponding nitriles. The catalyst can tolerate a wide range of substrates. The catalyst was easily recovered, and no ruthenium leaking was found in the catalytic run.

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