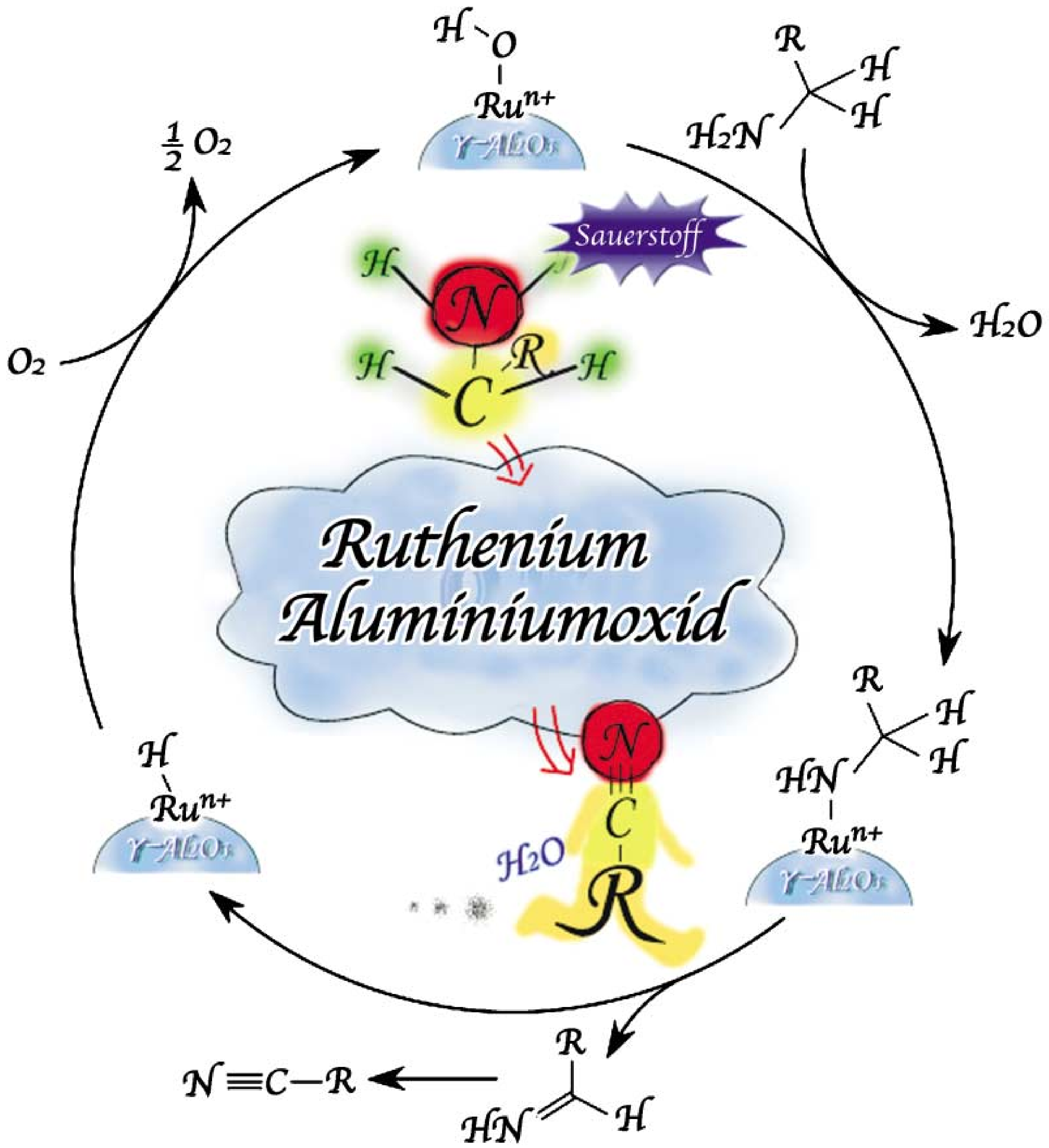
Zuschriften



Ein heterogener aluminiumgeträgerter Rutheniumkatalysator, der einfach herzustellen, billig und wiederverwendbar ist, vermittelt die Oxidation von primären und sekundären Aminen zu den entsprechenden Nitrilen und Iminen in guten Ausbeuten. Details finden Sie in der Zuschrift von N. Mizuno und K. Yamaguchi auf den folgenden Seiten.

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Supported Ru Catalysis of Amines

Efficient Heterogeneous Aerobic Oxidation of Amines by a Supported Ruthenium Catalyst**

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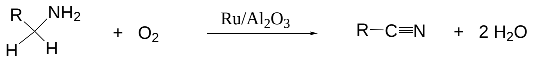
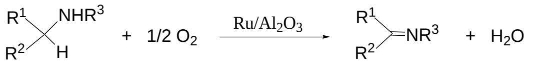
Oxidative functional transformations of organic compounds are important in industry and synthetic chemistry.[1–3] Stoichiometric amounts of metal oxidants such as dichromate ions, permanganate ions, manganese dioxide, silver oxide, and lead tetraacetate are often still used for the transformations.[1–3] The stoichiometric use and disposal of such oxidants is undesirable from both economical and environmental points of view. Therefore, much attention has been paid to the use of transition-metal catalysts to achieve effective oxidation, with dioxygen and hydrogen peroxide as oxidants.[4,5]

Nitriles and imines are used as versatile synthetic intermediates. Although several oxidation procedures that use stoichiometric reagents for the synthesis of nitriles and imines from amines are known,[6–9] only a few catalytic procedures have been reported.[10–16] A number of ruthenium complexes have been used for the oxidation of amines with dioxygen,[11–14] iodosylbenzene,[15] and persulfate ions[16] as oxidants. However, these systems are not generally useful because of their low turnover numbers and frequencies, the formation of significant amounts of by-products, severe deactivation of the catalysts, and narrow applicability to a limited number of amines.[10–16]

Very recently we reported the effective aerobic heterogeneous oxidation of both activated and nonactivated alcohols containing sulfur, nitrogen, and carbon–carbon double bonds with dioxygen or in air, catalyzed by ruthenium supported on alumina (Ru/Al_2O_3).[17] During the course of our investigation of Ru/Al_2O_3-catalyzed aerobic alcohol oxidation we found that this system could be effective for the oxidation of various amines to the corresponding nitriles or imines [Eqs. (1) and (2)]. To the best of our knowledge, the procedure reported in this paper is an efficient and widely applicable method for the aerobic oxidation of various amines.



(1)



(2)

The catalytic activity and selectivity for the oxidation of 4-methylbenzylamine with O_2 (1 atm) at 373 K were compared for a variety of ruthenium catalysts; the results are shown in Table 1. Oxidation did not occur in the absence of the catalyst or in the presence of γ-Al_2O_3. Among the various ruthenium catalysts tested, Ru/Al_2O_3 showed the highest catalytic activity (93 % yield after 1 h) for the oxidation of 4-methylbenzylamine to 4-methylbenzonitrile under the experimental conditions. The reaction rate for the oxidation of 4-methylbenzylamine was 6.25×10^{-3} M min^{-1}, approximately 40 times higher than that for the active heterogeneous catalyst [$(RuCl)_2Ca_8(PO_4)_6(OH)_2$] ($1.60\times10^{-4}$ M min^{-1}; Table 1, entry 2),[11] and higher than for homogeneous ruthenium catalysts, such as [$n$$Pr_4NRuO_4$], $RuCl_3$, [$RuCl_2(PPh_3)_3$], [$RuCl_2(dmso)_4$], [{$RuCl_2$(p-cymene)}$_2$], and [$RuCl_2(bpy)_2$] (bpy = 2,2′-bipyridyl).

Table 1: The oxidation of 4-methylbenzylamine with dioxygen using various catalysts.[a]

Entry	Catalyst	Rate $\times10^3$ [M^{-1} min^{-1}]	Conversion of amine [%]	Selectivity to nitrile [%]
1	Ru/Al_2O_3	6.25	>99	93
2[b]	[$(RuCl)_2Ca_8(PO_4)_6(OH)_2$]	0.16	5	97
3	$Ru(OH)_3\cdot n\,H_2O$	0.07	2	95
4	RuO_2	–	no reaction	–
5	[$n$$Pr_4NRuO_4$]	2.24	46	88
6	$RuCl_3\cdot n\,H_2O$	0.94	24	81
7	[Ru(acac)$_3$]	–	no reaction	–
8	[$RuCl_2(PPh_3)_3$]	0.98	25	94
9	[$RuCl_2(DMSO)_4$]	0.72	22	75
10	[{$RuCl_2$(p-cymene)}$_2$]	0.19	6	96
11	[$RuCl_2(bpy)_2$]	0.09	3	97
12[c]	Al_2O_3	–	no reaction	–
13	no catalyst	–	no reaction	–

[a] Reaction conditions: 4-Methylbenzylamine (1 mmol), Ru catalyst (Ru: 2.8 mol%), $PhCF_3$ (5 mL), 373 K, O_2 (1 atm), 1 h. Conversion and selectivity were determined by GC using diphenyl as an internal standard. The main by-product was *N*-(4-methylbenzylidene)-4-methylbenzylamine. [b] Prepared according to the literature procedure.[11] [c] Al_2O_3 (0.2 g).

After oxidation, the Ru/Al_2O_3 catalyst could be easily separated by filtration; induced coupled plasma (ICP) analysis confirmed that no Ru was present in the filtrate. In addition, the oxidation process was terminated by the removal of Ru/Al_2O_3 from the reaction solution. These results indicate that any Ru species that had leached into the reaction solution were not catalytically active and that the observed catalysis is truly heterogeneous.[18] The Ru/Al_2O_3 catalyst could be reused, and both the catalytic activity and selectivity towards oxidation reactions were retained (entry 11 in Table 2).

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Table 2: The oxidation of various amines with dioxygen, catalyzed by Ru/Al_2O_3.[a]

Entry	Substrate	Time [h]	Conversion [%]	Product	Selectivity [%]
1	benzylamine	1	> 99	benzonitrile	82
2	2-methoxybenzylamine	1	> 99	2-methoxybenzonitrile	97
3	3-methoxybenzylamine	1	94	3-methoxybenzonitrile	93
4	4-methylbenzylamine	1	> 99	4-methylbenzonitrile	93
5	geranylamine	10	98	geranylnitrile	90
6	*n*-octylamine	2	> 99	*n*-octanenitrile	96
7	*n*-dodecylamine	3	84	*n*-dodecanenitrile	90
8	*N*-benzylaniline	15	85	*N*-benzylideneaniline	94
9[b]	dibenzylamine	16	85	*N*-benzylidenebenzylamine	84[c]
10	indoline	2	> 99	indole	> 99
11[d]	indoline	2	> 99	indole	> 99
12	1,2,3,4-tetrahydroquinoline	7	95	quinoline	> 99

[a] Reaction conditions: Amine (1 mmol), Ru/Al_2O_3 (Ru: 2.8 mol%), $PhCF_3$ (5 mL), 373 K, O_2 (1 atm). Conversion and selectivity were determined by GC using naphthalene or diphenyl as an internal standard. The main by-products were *N*-alkylimines. [b] *p*-Xylene (5 mL) was used as a solvent, and the reaction was carried out at 403 K. [c] Benzonitrile (7% selectivity) and benzaldehyde (6% selectivity) were formed as by-products. [d] This experiment used a recycled catalyst; the reaction conditions were the same as those in entry 10, except that the recovered Ru/Al_2O_3 catalyst was used.

The Ru/Al_2O_3 catalyst showed high activity for the oxidation of activated and non-activated amines with dioxygen; the results are summarized in Table 2. All primary benzylic amines with $-CH_2NH_2$ functional groups were converted into the corresponding benzonitriles in high yields (Table 2; entries 1–4). The olefinic carbon–carbon double bond did not affect oxidation under the chosen reaction conditions, and only the amino function was dehydrogenated to a nitrile, without isomerization of the double bond and intramolecular hydrogen transfer (Table 2; entry 5). Primary aliphatic amines such as *n*-octylamine and *n*-dodecylamine were effectively oxidized to the corresponding nitriles (Table 2; entries 6 and 7). Secondary and heterocyclic amines, as well as primary amines, were also selectively oxidized. In the case of the secondary amine *N*-benzylaniline, *N*-benzylideneaniline was obtained in a high yield (Table 2; entry 8). Dibenzylamine also afforded the corresponding *N*-benzylidenebenzylamine as the main product, together with benzaldehyde and benzonitrile (Table 2; entry 9). Heterocyclic amines of indoline and 1,2,3,4-tetrahydroquinoline gave indole and quinoline in greater than 99 and 95% yields, respectively (Table 2; entries 10 and 12). The oxidation of tertiary amines, such as pyridine and quinoline did not proceed at all under the chosen reaction conditions.

Small quantities of *N*-alkylimine products were observed in the oxidation of primary amines, which are formed as condensation products of the starting amines and aldehydes through imine hydrolysis. Such findings show that imines are formed as intermediate products which are rapidly dehydrogenated to nitriles. The conversion and selectivity of the oxidation of 1,2,3,4-tetrahydroquinoline was not affected by the addition of the radical scavenger 2,6-di-*tert*-butyl-4-methylphenol. In accordance with ref. [17], the skeletal isomerization of a cyclopropyl ring does not take place. This evidence shows that a radical is not involved in the present oxidation reaction. The amount of dioxygen consumed was equivalent to the quantity of 4-methylbenzylamine produced; this 1:1 relationship suggests that simple dehydrogenation does not occur. A good linear correlation between values of $\log(k_X/k_H)$ and the Brown–Okamoto constant σ^+[19] ($R^2 = 0.99$; Figure 1) was observed for the competitive oxidation of substituted benzylamines (X = *p*-Cl, *p*-H, *p*-Me, *m*-OMe, and *p*-OMe). The resulting Hammett parameter ρ was -0.154, which indicates that a carbocation-type intermediate is involved in the oxidation process.[20] When *N*-(4-methylbenzylidene)aniline (1 mmol) was treated with benzylamine (2 mL) under an argon atmosphere, *N*-phenyl-4-methylbenzylamine was obtained together with a small quantity of benzonitrile [Eq. (3)]. This fact illustrates that transfer hydrogenation from benzylamine to *N*-(4-methylbenzylidene)aniline takes place, which suggests that a ruthenium hydride species is formed.[21–24]

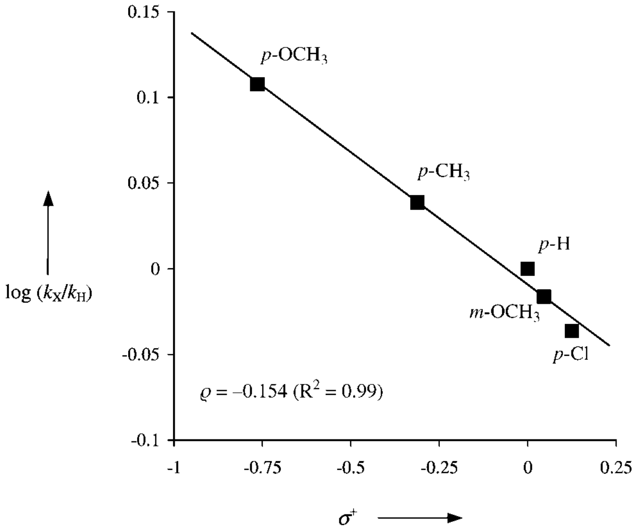
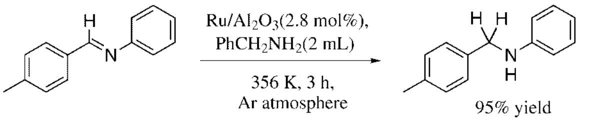
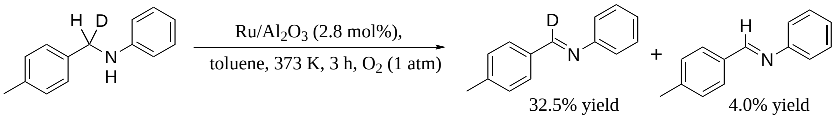


Figure 1. Hammett plots for the oxidation of substituted benzylamines with dioxygen using a Ru/Al_2O_3 catalyst; the reaction conditions are given in Table 2.



(3)

On the basis of the experimental results, a possible reaction mechanism (Figure 2) is proposed. Initially, ligand exchange between ruthenium hydroxide species and an amine takes place to form a ruthenium amide species. The ruthe-



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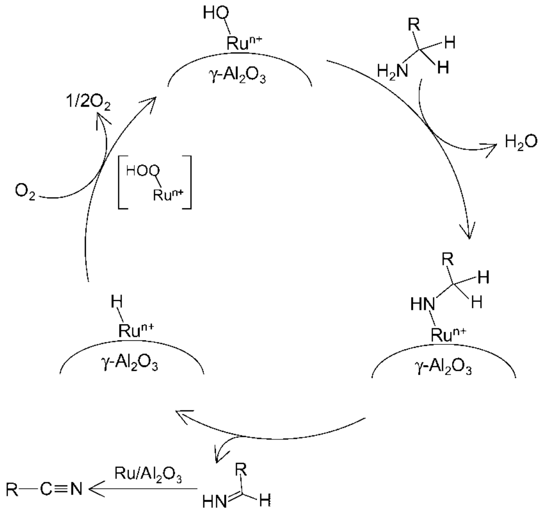

Figure 2. A possible reaction mechanism for the catalytic formation of imines and nitriles from amines.

nium amide then undergoes β-hydrogen elimination to form the corresponding imine and ruthenium hydride species, a process that has been discussed elsewhere.[25] The hydride species was then reoxidized by dioxygen,[26] and the dehydrogenation of the imine to the nitrile rapidly takes place in the same way as for the oxidation of primary amines with $-CH_2NH_2$ functions. Kinetic studies show a zero-order dependence for the reaction rate on both the partial pressure of dioxygen (P_{O2}: 0.2–2.0 atm) and the amine concentration (0.099–0.471 M), and a first-order relationship with the amount of Ru/Al_2O_3 catalyst employed (Ru: 1.4–5.6 mol%). Furthermore, the value for the kinetic isotope effect (k_H/k_D) was 8.1 ± 0.3 for the intramolecular competitive oxidation of *N*-phenyl-α-deutero-4-methylbenzylamine at 373 K [Eq. (4)]. Based on these facts, it is probable that β-hydrogen elimination of the ruthenium amide species is the rate-determining step.

In conclusion, Ru/Al_2O_3 can act as an efficient heterogeneous catalyst for the oxidation of non-activated, as well as activated amines to the corresponding nitriles or imines with 1 atm of dioxygen or air.

Experimental Section

The Ru/Al_2O_3 catalyst (1.4 wt% Ru) was prepared by a previously reported method.[17] Solvents were carefully dried and purified according to a literature procedure,[27] and substrates were also purified before use.[27] *N*-Phenyl-α-deutero-4-methylbenzylamine was synthesized by the reduction of *N*-(4-methylbenzylidene)aniline with lithium aluminum deuteride, in a modification of the procedure reported for the synthesis of deuterium-labeled toluene.[28]

The oxidation of amines was typically carried out as follows: A suspension of Ru/Al_2O_3 (Ru: 2.8 mol%) in trifluorotoluene (5 mL) was stirred for 5 min at room temperature. 4-Methylbenzylamine (1 mmol) was added and dioxygen was passed through the suspension. The resulting mixture was then heated at 373 K and water was removed azeotropically under an O_2 flow. After 1 h, 4-methylbenzonitrile was obtained in a 93% yield (by gas chromatography). The catalyst was separated by filtration, washed with acetone, and dried in vacuo prior to being recycled.

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Keywords: amines · heterogeneous catalysis · oxidation · oxygen · ruthenium

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ful as a result of the rapid decomposition of hydrogen peroxide, which is in agreement with the rapid decomposition of the Ru^{n+}–OOH species that do not contribute to the oxidation of the amines described in Figure 2.

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