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THE MILD SELECTIVE CONVERSION OF NITRILES TO AMIDES

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Although numerous methods have been reported for the hydrolysis of nitriles to amides, many require extreme reaction conditions and the yields for aliphatic nitriles in particular are often low.[1] Several of the more recent methods involve metal catalysis.[2-6] This communication describes a mild and selective means for effecting this transformation in near neutral media at room temperature using chloropentaammineruthenium(III) chloride $[(NH_3)_5RuCl]Cl_2$ in which the resulting amides require no further purification.

In a typical experiment $[(NH_3)_5RuCl]Cl_2$ (0.82 mmoles), easily prepared in one step from commercially available materials,[7] is dissolved in a solution of silver oxide (0.75 mmoles) in trifluoroacetic acid[8] to a final solution volume of approximately 15 ml. (4:1 in H_2O-ethanol, pH ~ 3). The solution is stirred under argon and several pieces of zinc amalgam[9] are added. A stoichiometric amount of nitrile is added and the reaction mixture stirred for approximately 6 - 8 hours at room temperature (heating to 40-50° C. for shorter periods is adequate). The resulting solution is filtered to remove the zinc amalgam and then oxidized using silver oxide (0.89 mmoles) in trifluoroacetic acid (pH ~ 3) overnight with stirring.[10] Oxygen (pH ~ 7) has been used for this oxidation also, but it should be noted that side reactions (e.g., disproportionation) are promoted at higher pH's. Filtration is followed by reduction using zinc amalgam for one hour to liberate the amide. Subsequent filtration and extraction of the aqueous medium with CH_2Cl_2 yields the amide as the exclusive product. In no case was recrystallization of the amides necessary. The starting ruthenium complex can be recovered by acidification of the aqueous phase with concentrated HCl, oxidation using O_2, and concentration of the solution if necessary.

Some representative results of hydrolyses are shown in Table 1. As the data indicate, this method is compatible with a wide variety of functional groups and the yields as determined by glpc are good. (The isolated yields in some cases are low due to the extreme water solubility of the resulting amides.) It should be noted that no attempt was made to optimize the yields reported. Furthermore, the method is successful for the conversion of α,β-unsaturated nitriles to conjugated amides with retention of stereochemical integrity in contrast to several of the methods referred to earlier.[2]

Table 1

Ruthenium(III) Ammine Promoted Hydrolysis of Nitriles to Amides

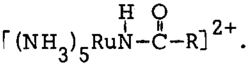
Nitrile	Amide[d]	Yield
$PhC{\equiv}N$	$PhCONH_2$	93[b]
$CH_3CH_2O_2CC{\equiv}N$	$CH_3CH_2O_2CCONH_2$	75[a]
$CH_3(CH_2)_5C{\equiv}N$	$CH_3(CH_2)_5CONH_2$	89[b] 75[a]
$CH_3C{\equiv}N$	CH_3CONH_2	99[c]
$PhCH{=}CHC{\equiv}N$	$PhCH{=}CHCONH_2$	92[b] 75[a]
$ClCH_2(CH_2)_3C{\equiv}N$	$ClCH_2(CH_2)_3CONH_2$	64[a]

a Yields determined by isolation

b Yields determined by glpc

c Yield determined spectrophotometrically based upon formation of $[(NH_3)_5RuH_2O]^{2+}$ after second reduction

d Amides characterized by m.p., i.r. and mass spectral data

The mechanism of this reaction[11] involves initial coordination of the nitrile forming $[(NH_3)_5RuN{\equiv}C{-}R]^{2+}$. The ability of ruthenium(II) for back donation stabilizes the nitrile complex, making coordindation very favorable. It is for this reason that the method is successful for nitriles in which water solubility is a severe problem. One-electron oxidation of the ruthenium(II) nitrile complex produces the ruthenium(III) nitrile complex which is not so stabilized and the nitrile is therefore activated towards nucleophilic attack by water, forming the ruthenium(III) amide  $[(NH_3)_5Ru\overset{\overset{H}{|}}{N}-\overset{\overset{O}{\|}}{C}-R]^{2+}$. Subsequent one-electron reduction of this species results in the unstable ruthenium(II) amide complex which spontaneously liberates the amide regenerating aquopentaammineruthenium(II) $[(NH_3)_5RuH_2O]^{2+}$. (This is the ruthenium species produced by the reduction of the starting material $[(NH_3)_5RuCl]Cl_2$.) Studies of the kinetics of the hydrolysis reaction reveal it to be independent of acid (10^{-2}M to 10^{-3}M). The half-time for benzonitrile is approximately 270 minutes.

Based on this mechanism an electrochemical system was constructed which employs cyclical electrolytic oxidation and reduction. Preliminary results show that the system is catalytic, but reliable turnover numbers are not yet available.

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8. The Ag_2O is dissolved in hot H_2O by dropwise addition of trifluoroacetic acid and the Ru complex is added. After stirring for 10 minutes the silver chloride is removed by filtration.
9. The zinc amalgam is prepared from mossy zinc by first washing with 1 M HCl (3-5 min.) followed by amalgamation using a slightly acidic solution of saturated mercuric chloride (3-5 min.).
10. For activated nitriles 25° C. was adequate; however, non-activated substrates required heating to 40° C. for convenient reaction times.
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