Catalytic Hydration of Nitriles to Amides with Manganese Dioxide on Silica Gel

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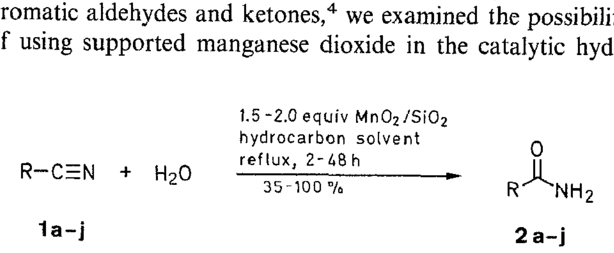
Dedicated to Professor Edward C. Taylor on the occasion of his 65th birthday.

Hydration of representative nitriles with silica gel supported manganese dioxide at the reflux temperature of hydrocarbon solvents gives the corresponding amides in good to excellent yield. Phenylacetonitrile, however, was partially oxidized to benzoylformamide. Other manganese catalyst systems were also evaluated.

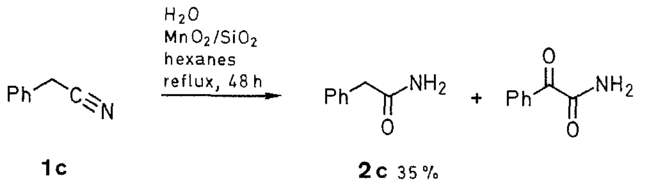
Active manganese dioxide has long been a useful oxidizing agent in organic preparations.[1,2] It can also be employed as an effective catalyst for the hydration of nitriles to amides.[3] In this procedure, large quantities of manganese dioxide (5–10 fold by weight) and long reaction times (18–96 hours) are necessary.[3] Moreover, certain nitriles, such as pyridinecarbonitriles,[1] were unreactive toward this reagent. Since manganese dioxide on inorganic support was found to be superior to active manganese dioxide in the oxidation of substituted benzyl alcohols to aromatic aldehydes and ketones,[4] we examined the possibility of using supported manganese dioxide in the catalytic hydration of nitriles to amides. Once again, the superiority of manganese dioxide on silica gel (MnO_2/SiO_2) over active manganese dioxide was realized.



The selective hydration of nitriles to amides can be accomplished under a variety of conditions,[5,6] and continously receives attention due to new developments.[7] Supported manganese dioxide is made by treating potassium permanganate on an inorganic support with aqueous solution of manganese(II) sulfate as previously described.[4] Preliminary studies on the hydration of benzonitrile revealed that among a number of inorganic supports the readily available chromatographic grade silica gel (Merck) was the best one for this purpose. Nonpolar solvents were better than the polar ones, and saturated hydrocarbons, such as hexanes, isooctane and cyclohexane, were always the choice, unless the nitrile was only sparingly soluble. The use of 1.5 equivalents of manganese dioxide at reflux in the appropriate solvent with gentle stirring results in complete conversion in a reasonable time. For less reactive nitriles, a higher boiling solvent and/or larger quantity of MnO_2/SiO_2 accelerate the reaction. The amount of manganese dioxide and the water content on the catalyst were found to be crucial. The MnO_2/SiO_2 containing 0.83 mmole of manganese dioxide and 1.5 mg of 'extra' water per gram of catalyst (*vide infra*) gave the most satisfactory result. A number of representative aliphatic, alicyclic, aromatic, and heteroaromatic nitriles have been studied under these conditions (Table 1).

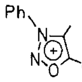
The reaction is easy to conduct, and the yield is in general higher than the hydration using active manganese dioxide[3] or under other conditions. For examples, the hydration of acrylonitrile with potassium fluoride on alumina gave only 10% yield of acrylamide,[8] and the phase-transfer-catalyzed hydration of benzonitrile with pentacarbonylmanganese bromide yielded the corresponding amide of not higher than 58 %.[7] Furthermore, in the present study the conversion of 3-pyridinecarbonitrile to nicotinamide was found to be nearly quantitative in contrast to "no reaction" as had been reported.[1] Even with the less effective benzene as solvent, the yield (94%) of the amide from 3-phenylsydnone-4-carbonitrile (**1e**), which was insoluble in saturated hydrocarbons, was still better than that observed under acid-catalyzed conditions (81%).[9] After the reaction, the amount of manganese dioxide on the catalyst was found essentially unchanged. After careful washing and drying, the recovered MnO_2/SiO_2 could be reused at least once without losing its activity.

Perhaps the only drawback of using MnO_2/SiO_2 is the concurrent oxidation at the benzylic position due to the enhanced oxidative power of the supported manganese dioxide.[4] Thus, benzoylformamide has been isolated from the product mixture of hydration of phenylacetonitrile (**1c**). Furthermore, in this case the recovered catalyst contained less manganese dioxide than the freshly prepared one.



Incidentally, nitriles containing other functional groups labile to active manganese dioxide[1] will not be suitable for hydration with this modified reagent. However, allylic functions and cyclopropyl rings are stable to the reaction conditions.

Table 1. Hydration of Nitriles **1** to Amides **2**

Product	R	Mole Ratio, MnO_2/nitrile	Solvent	Time (h)	Yield[a]	mp (°C) found	Lit.
2a	Ph	1.5:1	cyclohexane	3	100	126-7	127-8[15]
			hexanes	3	98		
			isooctane	2	100		
			benzene	3	82		
2b	PhCH=CH	1.5:1	cyclohexane	4	77	146-7	147[16]
2c	$PhCH_2$	1.5:1	hexanes	48	35[b]	158-9	158-9[17]
2d	3-pyridyl	1.5:1	hexanes	8	100	128-9	129[18]
2e		1.5:1	benzene	8	94	235-7	236-8[9]
2f	*n*-Pr	1.5:1	hexanes	16	100	114-5	114-5[19]
2g	*n*-$C_6H_{13}CH(CH_3)$	1.5:1	isooctane	24	97	79-80	80.8[20]
2h	*t*-Bu	2:1	isooctane	48	93	155-6	155-7[21]
2i	CH_2=CH	2:1	hexanes	16	85	83-4	83.6[22]
2j	*c*-C_3H_5	2:1	hexanes	5	90	123-4	125[23]

[a] Isolation.

[b] Accompanied with benzoylformamide and unreacted nitrile.

Table 2. Effect of Different Catalysts for Hydration of Benzonitrile (**1c**)

Catalyst	Catalyst/ Nitrile[a] (mole ratio)	Time (h)	Yield of Benzamide (**2c**)[b] (%)
SiO_2	1.5:1	15	0
MnO_2/SiO_2	1.5:1	4	100
$MnSO_4/SiO_2$	1.5:1	15	3
MnO/SiO_2[c]	1.5:1	15	3
$KMnO_4/SiO_2$[d]	1.5:1	15	16
Active MnO_2	1.5:1	4	30
Active $MnO_2 + SiO_2$	1.5:1	4	90

[a] Gram of SiO_2/mmol of nitrile.

[b] Determined with GC on OV-17 column.

[c] Containing 30% MnO_2 in MnO.

[d] Containing 25% MnO_2 in $KMnO_4$.

The catalytic property of the supported manganese dioxide can be further ascertained by comparative studies. Table 2 showed that neither Mn(VII) nor Mn(II) species was able to promote the hydration of benzonitrile. Silica gel alone was unable to induce the hydration, either. A mixture of silica gel and active manganese dioxide was more effective than active manganese dioxide, but was less effective than MnO_2/SiO_2. Evidently, the manganese dioxide catalyzed transformation of nitriles to amides is facilitated by the appropriate inorganic support.[10]

Under the optimum conditions, for each millimole of nitrile the amount of water on the catalyst (1.81 g of MnO_2/SiO_2) is 2.7 mg more than that on the same amount of support. Although this amount of 'extra' water (0.15 mol) is not sufficient to hydrate 1 mmole of nitrile, it does help to effect the hydration. We have found that the presence of a smaller amount of this 'extra' water will slow down the reaction. On the other hand, larger amount of water or manganese dioxide retard the hydration. Nitriles with a sterically hindered cyano group were found to be less reactive.

To avoid undesirable oxidation caused by the supported manganese dioxide, we have also carried out preliminary studies to find other supported metal oxides that are also able to catalyze the hydration of nitriles, but will not oxidize the benzylic carbon. Although copper on kieselgur had been used as a catalyst for the hydration of acrylonitrile to acryloamide,[11] we found that copper(II) oxide was both less reactive and less selective for the conversion of benzonitrile to benzamide. Sugiyama and coworkers have studied the heterogeneous hydration of acrylonitrile over a number of metal oxide catalysts, and have found that some of them are quite reacitve.[12] The examination on the use of different supported transition metal oxides for hydration without accompanying oxidation is in progress in this laboratory.

Capillary melting points are uncorrected. IR spectra (KBr) were recorded with a Jasco Model A-1 spectrometer and proton NMR with a Varian Model EM390 instrument. Nitriles, with the exception of 3-phenylsydnone-4-carbonitrile, which was kindly provided by Professor Mou-Yung Yeh, were reagent grade commercial chemicals or were prepared from the corresponding bromides.[13] Solvents were dried over molecular sieves. Chromatographic adsorbents and other chemicals were commercially available and used as received.

The content of water was determined using Karl-Fischer's method by Mr. C.J. Chen at Chun-Shan Institute of Technology.

Preparation of Manganese Dioxide on Silica gel:

In a 250 mL round-bottomed flask $KMnO_4$ (3.79 g) is dissolved in water (60 mL) at room temperature. Chromatographic grade silica gel (Merck, 70–230 mesh ASTM, 60 g) is added with stirring, and the flask is connected to a rotary evaporator to strip off the water at 60 °C. The purple solid is ground to fine powders, which is then added with vigorous stirring to a solution of $MnSO_4 \cdot H_2O$ (9.3 g) in water (100 mL). The resultant brown precipitate is filtered with water until no more manganese(II) ion could be detected in the wash-water by adding ammonia. The MnO_2/SiO_2 is then put into a culture dish as a layer of about 0.5 cm thick. After being dried at 100 °C for 2 h, each gram of this supported reagent is found to contain 0.83 mmol of MnO_2 (titration against sodium oxalate and $KMnO_4$)[14] and 3.1 mg of free water (Karl-Fischer's method), which was 1.5 mg, in excess of the amount absorbed on SiO_2 before treatment.

Hydration of Nitriles; General Procedure:

To a 50- mL round-bottomed flask, a stirring bar, nitrile (5 mmol), an appropriate hydrocarbon solvent (10 mL), and MnO_2/SiO_2 (9 g, 7.5 mmol MnO_2) are added successively. The reaction mixture is then magnetically stirred gently at reflux temperature for the time given in the Table. The mixture is then filtered, and the solid residue is continuously extracted (Soxhlet) with MeOH (100 mL). The MeOH solution is decolorized (charcoal), if necessary, and then evaporated to dryness *in vacuo*. The resultant solid is in general quite pure as indicated by IR and proton NMR spectra, and by the melting point as compared with the literature data.[9,15-23] In some cases one recrystallization from 95% EtOH may be necessary. The results are listed in Table 1.

Reaction of Phenylacetonitrile with MnO_2/SiO_2:
This reaction is carried out in hexanes or cyclohexane according to the general procedure. TLC indicates that the hydration is not complete even after two days, and only 34-35% of amide could be isolated in both cases. A by-product is separated by using chromatography on preparative plates of silica gel (Merck). Its spectral data and mp (89-90°C) are consistent with those found for benzoylformamide.[24]

Comparative Study on the Use of Other Manganese Compounds:
The supported catalysts containing manganese sulfate and potassium permanganate, respectively, are prepared as mentioned (*vide supra*). Treatment of MnO_2/SiO_2 with allyl alcohol at reflux temperature for two days converts the manganese(IV) oxide into the manganese(II) species. The hydration of benzonitrile by using these catalysts is carried out in the same way as the use of MnO_2/SiO_2 as the catalyst. The results are given in Table 2.

Thanks are due to the National Science Council for financial support of this work, and to Professor M.-Y Yeh for providing the sydnone derivatives.

Received: 25 January 1988; revised: 18 April 1988

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