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THE TRANSFORMATION OF NITRILES INTO AMIDES USING SODIUM PERCARBONATE

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Abstract: The usefulness of sodium percarbonate, an inexpensive, safe and easily handled reagent for the transformation of nitriles into amides was investigated. Aromatic nitriles lacking ortho-substituents and heteroaromatic nitriles were efficiently transformed into amides; while ortho-substituted aromatic nitriles and aliphatic nitriles gave moderate yields of the corresponding amides.

The hydrolysis of nitriles is one of the most effective methods for preparing amides.[1] The hydration can be induced by a variety of reagents: basic hydrogen peroxide (Radziszewski reaction),[2-6] mineral acids,[7] titanium tetrachloride in acetic acid,[8] chloropentaammineruthenium(III) chloride,[9] potassium hydroxide in tert-butyl alcohol,[10] sodium superoxide in dimethyl sulfoxide,[11] hydrogen peroxide under phase-transfer conditions,[12] potassium fluoride on alumina,[13] hydroxylamine derivatives[14] such as 4-benzyloxy-1-hydroxy-2,2,6,6-tetramethylpiperidine and diethylhydroxylamine, pentacarbonylmanganese bromide in basic ethanol in the presence of phase-transfer catalyst,[15] manganese

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dioxide on silica gel,[16] sodium perborate in aqueous methanol,[17] and basic hydrogen peroxide in dimethyl sulfoxide.[18] Of the various methods available, the treatment of a nitrile with a base and hydrogen peroxide is the simplest.[19,20]

Sodium percarbonate is an inexpensive, stable, and easily handled reagent that has an excellent shelf life. It is extensively used in the detergent industry as a bleaching agent.[21] The reagent is an addition compound of hydrogen peroxide and sodium carbonate and its molecular formula is written as $Na_2CO_3 \cdot 3/2H_2O_2$.[22,23] The crystal structure has also been reported;[24] the carbonate ions are hydrogen-bonded to the peroxide molecules. On dissolution in water, one equivalent of sodium percarbonate releases one and one-half equivalents of hydrogen peroxide.[23] The usefulness of sodium percarbonate as a safe source of hydrogen peroxide in organic synthesis has not yet been fully explored. It has only been used for the oxidation of sulfides,[25] amines[25,26] and organoboranes,[27,28] and in the epoxidation reactions of alkenes.[25] We now wish to report the use of sodium percarbonate for the hydration of nitriles to amides.

$$\text{R-CN} \xrightarrow[50^\circ\text{C}]{Na_2CO_3 \cdot 3/H_2O_2/CH_3COCH_3:H_2O} \text{R-CONH}_2$$

A variety of nitriles, which included aryl, heteroaryl, aralkyl and aliphatic nitriles, were treated with sodium percarbonate at 50°C in a mixture of acetone and water. The reaction conditions utilized and the results obtained are listed in

Table: The Transformation of Nitriles into Amides Using Sodium Percarbonate[a]

Entry	Substrate	Time, h	Product[b]	Isolation Procedure[c]	Yield, %[d]
1.	C_6H_5CN	1	$C_6H_5CONH_2$	A	94
2.	m-$CH_3C_6H_4CN$	1.7	m-$CH_3C_6H_4CONH_2$	B	90
3.	p-$CH_3C_6H_4CN$	1.5	p-$CH_3C_6H_4CONH_2$	B	92
4.	m-$NO_2C_6H_4CN$	0.75	m-$NO_2C_6H_4CONH_2$	B	90
5.	p-$NO_2C_6H_4CN$	1	p-$NO_2C_6H_4CONH_2$	B	95
6.	p-ClC_6H_4CN	1	p-$ClC_6H_4CONH_2$	B	96
7.	p-CNC_6H_4CN	1[e]	p-$H_2NOCC_6H_4CONH_2$	B	95
8.	o-CNC_5H_4N	6	o-$H_2NOCC_5H_4N$	B	87
9.	m-CNC_5H_4N	6	m-$H_2NOCC_5H_4N$	A	90
10.	p-CNC_5H_4N	3	p-$H_2NOCC_5H_4N$	A	92
11.	$C_6H_5CH_2CN$	1	$C_6H_5CH_2CONH_2$	B	95
12.	o-$CH_3C_6H_4CN$	6	o-$CH_3C_6H_4CONH_2$	C	20(75)
13.	o-ClC_6H_4CN	6	o-$ClC_6H_4CONH_2$	C	20(74)
14.	o-$NO_2C_6H_4CN$	6	o-$NO_2C_6H_4CONH_2$	C	30(64)
15.	$CH_3(CH_2)_3CN$	6	$CH_3(CH_2)_3CONH_2$	C	50(42)
16.	$CH_3(CH_2)_8CN$	6	$CH_3(CH_2)_8CONH_2$	C	50(46)

[a]The reactions were carried out at 50°C using nitrile (10 mmol) and sodium percarbonate (20 mmol, equivalent to 30 mmol of hydrogen peroxide).

[b]All the products were characterized by comparison of their spectral and physical properties with those of authentic samples.

[c]See experimental part.

[d]The yields reported are of pure isolated products. The number in parenthesis indicates % recovery of the starting material.

[e]Sodium percarbonate (40 mmol, equivalent to 60 mmol of hydrogen peroxide) was used.

the Table. The progress of the reaction was followed by TLC. The results showed that the aromatic nitriles lacking ortho-substituents, heteroaromatic nitriles and aralkyl nitrile were all efficiently transformed into the corresponding amides in excellent yields. Under our experimental conditions, ortho-substituted aromatic nitriles (entries 12-14) were only partially converted to the corresponding amides (20-30% yield). This was not entirely unexpected because it has been noted previously that the higher concentration ($\geq$30%) of hydrogen peroxide is required for the efficient hydration of ortho-substituted aromatic nitriles.[3] The yields of amides from ortho-substituted aromatic nitriles could not be improved even by using large excess of sodium percarbonate (e.g. four equivalents, corresponding to six equivalents of hydrogen peroxide) and prolonged reaction time (12 h). Aliphatic nitriles (entries 15 and 16) gave the corresponding amides in moderate yields (50%).

In conclusion, sodium percarbonate is a useful reagent for the transformation of heteroaromatic nitriles and aromatic nitriles lacking ortho-substituents into the corresponding amides. It appears that this reagent, which is inexpensive and easy to handle, will find applications as a convenient source of hydrogen peroxide.

EXPERIMENTAL

All the nitriles are commercially available and were used without further purification. Sodium percarbonate (practical grade) was purchased from Fluka. The active oxygen content of the sample was determined by titration with potassium permanganate and found to be 13%.

General Procedure for the Conversion of Nitriles to Amides.

Sodium percarbonate (3.69 g, equivalent to 30 mmol of hydrogen peroxide) was added to a solution of nitrile (10 mmol) in a mixture of acetone (in most cases about 30 mL) and water (20 mL). The reaction mixture was heated to 50°C and kept at that temperature for the indicated time (Table). After cooling to room temperature, the acetone was removed using a rotary evaporator. Depending on the solubility characteristics of amides, one of the following isolation procedures was adopted.

Method A: For water soluble amides, the residue was extracted with dichloromethane (entries 1 and 9) or ethyl acetate (entry 10). The organic layer was dried ($MgSO_4$), filtered, and concentrated. Recrystallization afforded the pure amide.

Method B: For water-insoluble amides (entries 2-8 and 11), water (50 mL) was added to the residue and the mixture filtered. The solid was washed with water (2x10 mL), dried, and recrystallized to give the pure amide.

Method C: For the reactions which were incomplete (entries 12-16) the residue was extracted with dichloromethane. The dichloromethane layer was dried ($MgSO_4$), filtered, and concentrated under reduced pressure. From the mixture of product amide and starting nitrile, the product was separated either by column chromatography or by taking advantage of the differential solubility of the amide and nitrile.

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