United States Patent Office 3,192,258 Patented June 29, 1965

3,192,258

PROCESS FOR OXIDIZING A PRIMARY ALCOHOL

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No Drawing. Filed Aug. 23, 1962, Ser. No. 218,824
Claims priority, application Japan, Aug. 25, 1961, 36/30,818
6 Claims. (Cl. 260—523)

The present invention relates to a process for oxidizing an organic compound, and particularly to a process for oxidizing a primary alcohol to the corresponding carboxylic acid. More particularly, it relates to the use of nickel peroxide for the oxidation of the primary alcohol having a group represented by the formula: —CH_2—OH in the molecule to the corresponding carboxylic acid having a group represented by the formula: —COOH in the molecule.

In the present specification, the term "nickel peroxide" is expediently applied to designate the black, hydrous, higher oxides of nickel which are formed by reaction between a strong oxidizing agent, such as alkali hypohalites or alkali persulfates, and freshly precipitated nickelous hydroxide in an aqueous alkaline medium.

With respect to the use of nickel peroxide as an oxidizing agent in the field of organic chemistry, there has been heretofore known only one literature reference, i.e. German Patent 127,388, in which toluene was oxidized with nickel peroxide in water or no solvent at 90 to 100° C. to give benzaldehyde as a main product and benzoic acid as a by-product. However, it has been now discovered that primary alcohols are oxidized with nickel peroxide to give carboxylic acids in excellent yields, when the oxidation is performed in an aqueous alkaline medium. Furthermore, the process of the German patent was carried out at a relatively high temperature (90 to 100° C.), while that of the present invention can be performed at a lower temperature. Thus, the process of the present invention may be applied for the oxidation of relatively unstable primary alcohols.

Accordingly, a primary object of the present invention is to embody a process for oxidizing a primary alcohol to the corresponding carboxylic acid. Another object is to embody a utilization method of nickel peroxide as an oxidizing agent suitable for the economical conversion of primary alcohols into carboxylic acids. A further object is to embody a process for oxidizing relatively unstable primary alcohols to carboxylic acids. These and other objects will be apparent to those skilled in the art to which the present invention pertains from the subsequent description.

The process of the present invention comprises treating the primary alcohol having a group represented by the formula: —CH_2OH in the molecule with nickel peroxide in an aqueous alkaline medium for several hours at a temperature from 0 to 60° C. (cf. illustrative examples infra) to give the corresponding carboxylic acid having a group represented by the formula: —COOH in the molecule.

The nickel peroxide possessing a high oxidizing activity may be prepared by treating a nickel salt (e.g. nickel chloride, nickel sulfate, nickel carbonate, nickel nitrate) with a strong oxidizing agent such as alkali hypohalites (e.g. sodium hypochlorite, potassium hypochlorite, sodium hypobromite) or alkali persulfates (e.g. sodium persulfate, potassium persulfate) in an aqueous alkaline medium. Alternatively, nickel peroxide may be prepared by treating the oxides of nickel with an alkali hypohalite in an aqueous alkaline medium, the

said oxides being obtained by any conventional methods, e.g.

(a) The oxide prepared by treating $NiSO_4$ with aqueous NaOH and drying the precipitated $Ni(OH)_2$ for 1.5 hours at 500° C.,

(b) The oxide prepared by drying $NiCO_3.2Ni(OH)_2.4H_2O$ for 2 hours at 500° C.,

(c) The oxide prepared by drying $Ni(NO_3)_2.6H_2O$ for 2 hours at 500° C.,

(d) The commercially available oxide having the formula: Ni_2O_3.

However, the nickel peroxides obtained in the latter methods are usually much inferior to that prepared by the former method in oxidizing activity. One of the presently-preferred procedures for obtaining the highly active nickel peroxide is set forth as follows:

To a solution of nickel sulfate hydrate ($NiSO_4.6H_2O$) (130 mg.) in water (300 ml.), there is added dropwise a solution of sodium hydroxide (42 g.) in 6% sodium hypochlorite (300 ml.), while stirring, and the resultant mixture is stirred for about 30 minutes at a temperature between 10 and 25° C. The black precipitate is collected by filtration, washed with water to remove active chlorine and, after crushing the cake to powder, dried over anhydrous calcium chloride under reduced pressure.

The nickel peroxide is a black fine powder containing a considerable amount of water. The results of the quantitative analysis make it possible to give the molecular formula: $Ni_2O_3.3H_2O$ or $Ni(OH)_3$ to the oxidant, but the structure has not yet been confirmed. The nickel peroxide possesses usually about $0.3\sim0.4\times10^{-2}$ g.-atom of available oxygen per gram (measured by titrating the iodine, produced from the reaction between the nickel peroxide and potassium iodide in acetic acid, with sodium thiosulfate), of which a considerable portion is lost gradually when heated, but remains for a long time when stored at room temperature under protection against atmospheric moisture. Since it has a remarkably broad surface compared with its weight, the available oxygen can be used effectively in the oxidation reaction. Owing to this character of the reagent, the present oxidation can advantageously be completed in a short time normally with one to two equivalent amounts of the oxidant.

The optimum reaction conditions such as reaction medium, reaction temperature, reaction time and amount of the oxidant are more or less associated with the kind of the starting primary alcohols. Therefore, the preferable conditions are selected in each case. Generally speaking, the presence of enough excess of alkali for neutralizing the produced carboxylic acids affords good results. The extent and rapidity of oxidation can be suitably controlled by the adjustment of alkalinity. When the oxidation is not accompanied with a side-reaction, the reaction time may be reduced by the use of excess of the oxidizing agent. However, when unstable carboxylic acids are produced, it is preferred to carry out the oxidation in a large amount of medium at a low temperature using a theoretical amount or less of the oxidizing agent. The oxidation of straight chain primary alkanols proceeds more rapidly than that of the branched isomers and, therefore, the former reaction may be performed at a lower temperature than the latter. The alcohols having an unsaturated bond at the position adjacent to the carbon atom in the hydroxymethyl radical such as benzyl alcohol and propargyl alcohol are oxidized more rapidly than the said straight chain primary alkanols and, therefore, the oxidation reaction is preferably executed under milder conditions. Generally, an aromatic ring, a double bond conjugated therewith and a triple bond are

stable against the oxidation, but a double bond is relatively unstable. In some cases, the simultaneous oxidation of the methyl radical on an aromatic ring may proceed, but it can be avoided by the use of a proper amount of nickel peroxide. Although active methylene is apt to be oxidized, its oxidation can be also avoided by carrying out the reaction at a low temperature. Heterocyclic compounds are oxidized with nickel peroxide as well as isocyclic compounds.

From the illustration made hereinabove some advantages which the present invention possesses will be obvious to those skilled in the art. Comparing with the heretofore known oxidation procedures, some other advantages may be also noted. Thus, the present oxidation using nickel peroxide generally proceeds more mildly than the known acidic oxidation using potassium permanganate and more severely than the known alkaline oxidation using silver oxide or manganese dioxide. Accordingly, the present oxidation is applicable to the oxidation of the primary alcohols having a structure readily affected by the acidic oxidation. For instance, it has been reported that the oxidation of α-furfuryl alcohol with acidic oxidants results in the opening of the ring, and in the case of oxidation with potassium permanganate, the resulting α-furoic acid is so contaminated that it is hardly purified [J. Volhard, Ann., 261, 379 (1911)]. However, according to the process of the present invention, α-furoic acid is readily obtainable in a good yield with a high purity. Further, it is advantageous that the separation of the oxidizing agent from the reaction mixture can be accomplished by an easy operation, i.e., filtration. Furthermore, it is also advantageous that the employed oxidizing agent can be readily renewed by a simple procedure, i.e. the treatment with a strong oxidizing agent such as alkali hypohalites or alkali persulfates. A typical renewal procedure is herein set forth as follows:

After the oxidation reaction, the nickel peroxide is collected by filtration, washed with water, stirred with 6% sodium hypochlorite (about ten times the quantity of nickel peroxide) in an aqueous alkaline medium for 20 minutes, filtered, washed with water and dried.

The following examples set forth illustratively presently-preferred embodiments of the present invention.

g. of sodium hydroxide in 100 ml. of water, nickel peroxide (1.5 times the theoretical amount) is added while stirring with a magnetic stirrer, and the heterogeneous mixture is allowed to react for the given times at various temperatures. The solid is then separated from the reaction by suction filtration and washed with water. The combined filtrate is acidified with dilute sulfuric acid and a portion accurately weighed out from the solution is steam distilled. The volatile carboxylic acid in the distillate is titrated with 0.1 N sodium hydroxide solution. Reaction rates calculated on the basis of the obtained value are shown in Table I.

Table I.—Reaction rates of oxidation for saturated aliphatic primary alcohols (percent)

Starting alcohol	Reaction temperature (° C.)	Reaction time (hour) 0.5	1.0	3.0	5.0	Produced carboxylic acid
Ethanol	30±2	------	96.6	97.3	99.4	Acetic acid.
n-Propanol	30±2	------	74.9	93.0	96.6	Propionic acid.
n-Butanol	30±2	------	81.6	94.1	96.9	n-Butyric acid.
iso-Butanol	0±2	19.6	20.1	29.0	40.3	iso-Butyric acid.
	30±2	47.3	59.1	72.7	84.9	
	80±2	------	60.1	64.9	65.1	
n-pentanol	30±2	------	------	83.2	96.8	n-Valeric acid.
	60±2	------	------	81.0	81.0	
iso-Pentanol	30±2	------	------	69.7	77.5	iso-Valeric acid.
n-Octanol	30±2	------	------	------	58.5	n-Caprylic acid.

EXAMPLE 2

Oxidation of aromatic primary alcohols.—To a solution of 0.02 mole of the starting alcohol and 1 g. of sodium hydroxide in 50 ml. of water, the given amount of nickel peroxide is added while stirring with a magnetic stirrer, and the heterogeneous mixture is allowed to react for the given times at various temperatures. The solid is then separated from the reaction solution by suction filtration and washed with water. The combined filtrate is acidified with dilute sulfuric acid and shaken with a suitable water-immiscible solvent. Removing the solvent from the solvent phase, there is obtained the carboxylic acid. Reaction rates calculated on the basis of the amount of the obtained carboxylic acid are shown in Table II.

Table II.—Reaction rates of oxidation for aromatic primary alcohols (percent)

Starting alcohol	Nickel peroxide [1]	Reaction temperature (° C.)	Reaction time (hour)	Produced carboxylic acid	Yield (Percent)
Benzyl alcohol	1.5	30	3	Benzoic acid	96.7
Phenethyl alcohol	0.5	0	2	do	26.2
				Phenylacetic acid	16.9
	1.5	30	10	Benzoic acid	63.5
				Phenylacetic acid	9.2
	2.0	60	5	Benzoic acid	60.0
				Phenylacetic acid	0.5
3-phenyl-1-propanol	1.5	0	7	Benzoic acid	1.6
				Benzylacetic acid	37.0
	1.5	0	30	Benzoic acid	7.5
				Benzylacetic acid	70.5
	1.5	30	10	Benzoic acid	17.6
				Benzylacetic acid	56.7
2-methylbenzyl alcohol	1.5	30	3	2-methylbenzoic acid	97.0
3-methylbenzyl alcohol	1.0	30	4	3-methylbenzoic acid	40.2
				Isophthalic acid	5.9
4-methylbenzyl alcohol	1.0	30	3	4-methylbenzoic acid	78.5
				Terephthalic acid	0
	1.5	30	3	4-methylbenzoic acid	62.5
				Terephthelic acid	12.0

[1] Ratio of nickel peroxide to primary alcohol based on the available oxygen.

In the examples, the abbreviations have the following significances: g., gram(s); ml., millilitre(s); Anal. Calcd., analysis calculated; and ° C., degrees centigrade. Other abbreviations have conventional significances.

EXAMPLE 1

Oxidation of saturated aliphatic primary alcohols:—To a solution of 0.04 mole of the starting alcohol and 2

EXAMPLE 3

Oxidation of propargyl alcohol.—To a solution of 5.6 g. of propargyl alcohol and 5 g. of sodium hydroxide in 250 ml. of water, 71 g. of nickel peroxide (1.1 times the theoretical amount) are added with stirring while ice-cooling in 10 minutes, and the heterogeneous mixture is stirred for 30 minutes. The solid is then separated from the reaction solution by suction filtration and washed

with water. The combined filtrate is acidified with dilute sulfuric acid and shaken with 800 ml. of ether. The ether phase is dried and fractionally distilled to give 3.9 g. of propiolic acid (purity, 98%) as a fraction boiling at 53 to 56° C./15 mm. Hg.

EXAMPLE 4

Oxidation of cinnamyl alcohol.—A mixture of 2.68 g. of cinnamyl alcohol, 1.0 g. of sodium hydroxide and 23.5 g. of nickel peroxide (twice the theoretical amount) in 50 ml. of water is stirred for 6 hours at 50° C. The reaction solution is filtered, acidified, extracted with ether, and the crude product obtained (purity, 90%) is recrystallized from a mixture of ether and petroleum ether to give 2.37 g. of cinnamic acid as crystals melting at 133 to 134° C.

What is claimed is:

1. A process for oxidizing lower primary alkanol to corresponding alkanoic acid which comprises treating the said lower primary alkanol with nickel peroxide in aqueous alkaline medium at a temperature between about 0° C. and about 60° C., said medium containing sufficient alkali to neutralize the produced alkanoic acid, and recovering the latter in free form from the reaction mixture, the said nickel peroxide being the product of the treatment of a salt of nickel selected from the group consisting of nickel chloride, nickel sulfate, nickel carbonate and nickel nitrate with an oxidizing agent selected from the group consisting of alkali hypohalite and alkali persulfate in aqueous alkaline medium at a temperature between 10 and 25° C., followed by the steps of collecting, washing with water, and drying the resultant nickel peroxide precipitate.

2. A process according to claim 1 wherein the primary alkanol is selected from the group consisting of ethanol, n-propanol, n-butanol, iso-butanol, n-pentanol, iso-pentanol and n-octanol.

3. A process for oxidizing aromatic primary alcohol to corresponding aromatic carboxylic acid which comprises treating the said aromatic primary alcohol with nickel peroxide in aqueous alkaline medium at a temperature between about 0° C. and about 60° C., said medium containing sufficient alkali to neutralize the produced aromatic carboxylic acid, and recovering the latter in free form from the reaction mixture, the said nickel peroxide being the product of the treatment of a salt of nickel selected from the group consisting of nickel chloride, nickel sulfate, nickel carbonate and nickel nitrate with an oxidizing agent selected from the group consisting of alkali hypohalite and alkali persulfate in aqueous alkaline medium at a temperature between 10 and 25° C., followed by the steps of collecting, washing with water, and drying the resultant nickel peroxide precipitate, the starting aromatic primary alcohol being selected from the group consisting of benzyl alcohol, phenethyl alcohol, 3-phenyl-1-propanol, 2-methyl-benzyl alcohol, 3-methyl-benzyl alcohol and 4-methyl-benzyl alcohol.

4. A process for oxidizing propargyl alcohol to propiolic acid which comprises treating the propargyl alcohol with nickel peroxide in aqueous alkaline medium at a temperature between about 0° C. and about 60° C., said medium containing sufficient alkali to neutralize the produced propiolic acid, and recovering the latter from the reaction mixture, the said nickel peroxide being the product of the treatment of a salt of nickel selected from the group consisting of nickel chloride, nickel sulfate, nickel carbonate and nickel nitrate with an oxidizing agent selected from the group consisting of alkali hypohalite and alkali persulfate in aqueous alkaline medium at a temperature between 10 and 25° C., followed by the steps of collecting, washing with water, and drying the resultant nickel peroxide precipitate.

5. A process for oxidizing cinnamyl alcohol to cinnamic acid which comprises treating the cinnamyl alcohol with nickel peroxide in aqueous alkaline medium at a temperature between about 0° C. and about 60° C., said medium containing sufficient alkali to neutralize the produced cinnamic acid, and recovering the latter from the reaction mixture, the said nickel peroxide being the product of the treatment of a salt of nickel selected from the group consisting of nickel chloride, nickel sulfate, nickel carbonate and nickel nitrate with an oxidizing agent selected from the group consisting of alkali hypohalite and alkali persulfate in aqueous alkaline medium at a temperature between 10 and 25° C., followed by the steps of collecting, washing with water, and drying the resultant nickel peroxide precipitate.

6. A process according to claim 2, wherein the alkali hypohalite is sodium hypochlorite and is present in stoichiometric excess.

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