# United States Patent [19]

**Rakoutz**

[11] **3,755,101**

[45] **Aug. 28, 1973**

[54] **PROCESS FOR THE PREPARATION OF SALIGENOL**

[75] Inventor: **Michel Rakoutz,** Lyon, France

[73] Assignee: **Rhone-Poulenc S.A.,** Paris, France

[22] Filed: **Nov. 18, 1971**

[21] Appl. No.: **200,050**

[30] **Foreign Application Priority Data**

Nov. 19, 1970 France .............................. 7041498

[52] **U.S. Cl.** .................................................. **204/75**
[51] **Int. Cl.** ........................ **C07b 29/06,** C07c 29/00
[58] **Field of Search** ....................................... 204/75

[56] **References Cited**

UNITED STATES PATENTS

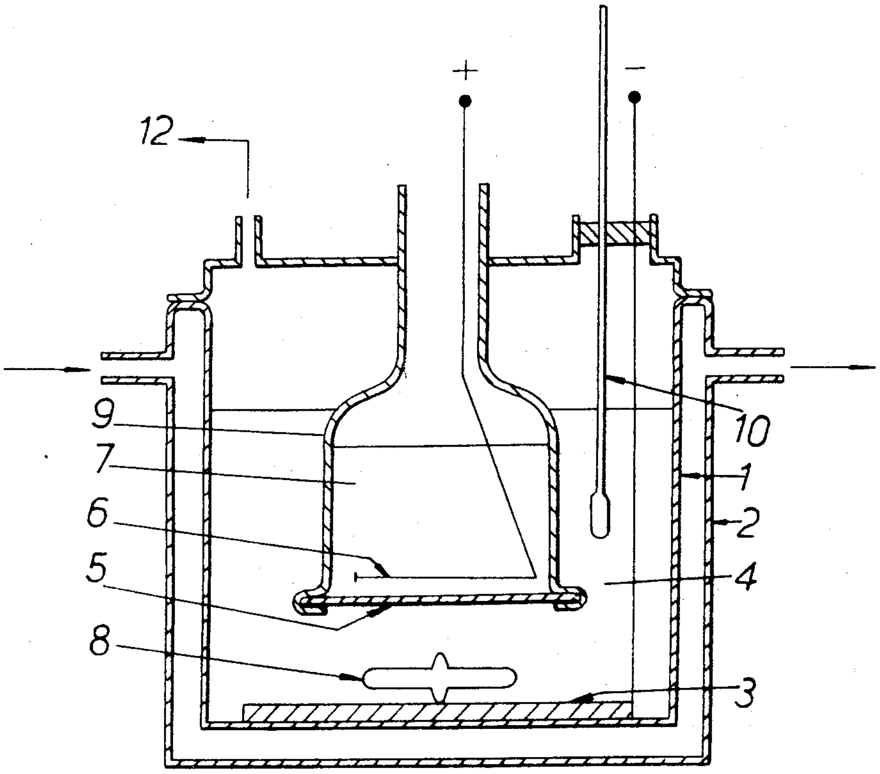
| | | | |
|---|---|---|---|
| R12,654 | 5/1907 | Mettler | 204/75 |
| 815,193 | 3/1906 | Mettler | 204/75 |
| 3,193,480 | 7/1965 | Baizer | 204/73 A |

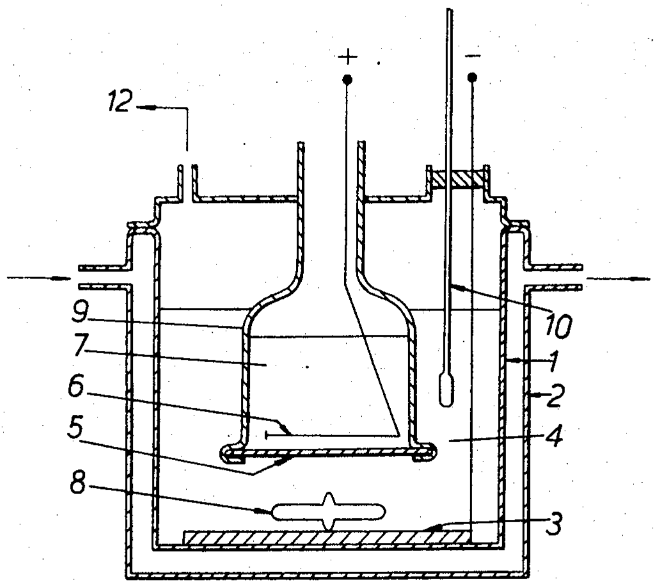
*Primary Examiner*—F. C. Edmundson
*Attorney*—Ellsworth H. Mosher et al.

[57] **ABSTRACT**

Saligenol is obtained by electrochemical reduction of salicylic acid in a cell in which the anolyte and catholyte are separated from each other by a cation exchange membrane and in which the catholyte initially consists of water, a cosolvent, salicylic acid and a quaternary ammonium salt.

**8 Claims, 1 Drawing Figure**




+
−
12
9
7
6
5
8
10
1
2
4
3

# PROCESS FOR THE PREPARATION OF SALIGENOL

The present invention relates to a process for the preparation of saligenol (2-hydroxy-benzyl alcohol) by electro-chemical reduction of salicylic acid (2-hydroxy-benzoic acid).

It is known that some juxtanuclear aromatic acids can be reduced to the corresponding alcohols by electro-chemical reduction [C. METTLER Ber 38, 1745–1753 (1905) : Ber 39, 2933–2942 (1906) ; German Pat. Specification No. 177,490 and Friedlander 8,148–150]. The techniques described in these various documents essentially involved carrying out an electrolysis [illegible] a catholyte which was a mixture of ethyl alcohol, sulphuric acid and the carboxylic acid to be reduced.

When such methods were used for the preparation of saligenol by electro-chemical reduction of salicylic acid, METTLER indicates (Ber 38, 1748) that the reaction lacks speed and (Ber 39,2935) that it presents difficulties. These facts are confirmed by F. SOMLO [Zeitsch. Elektrochem 35 (10) 773 (1929) ] who, under the general conditions described by METTLER, only obtained saligenol in electrical yields of less than 6.3 percent, these yields even falling to zero in certain cases (in which case the electro-chemical reduction stops).

According to the present invention, a new process is provided for the preparation of saligenol by electro-chemical reduction of salicylic acid which does not suffer from the disadvantages of the known processes.

The process according to the invention consists of carrying out the electrolysis in a cell having an anode compartment and a cathode compartment separated from one another by a cation exchange membrane, and the catholyte, initially consisting essentially of salicylic acid, water, a cosolvent and a quarternary ammonium salt. Once the electrolysis has commenced, part of the salicylic acid will be converted to saligenol and the catholyte will then, of course, contain saligenol in addition to the other components mentioned previously.

The nature of the cation exchange membrane, which separates the catholyte from the anolyte is not critical to the invention. It is possible to use any known cation exchange membrane and, in particular, homogeneous-type membranes or heterogeneous-type membranes which if desired, can be reinforced by a screen. In order to be able to carry out electrolysis operations of long duration, it is preferred to use membranes which do not swell and are stable under the influence of the various constituents of the catholyte and of the anolyte, especially the cosolvent. Membranes which can be used, include those described in the following patent specifications:

U.S. Pat. No. 2,681,320.

France Pat. Nos. 1,568,994, 1,575,782, 1,578,019, 1,583,089, 1,584,187 and 2,040,950.

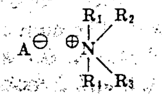
The catholyte can contain one or two liquid phases. If it contains two liquid phases, it is preferred to carry out the process in such a way that the catholyte is in the form of an emulsion, for example by stirring or by circulating the liquid.

The cosolvent contained in the catholyte is a solvent for salicylic acid, which is preferably chemically inert towards salicylic acid under the reaction conditions, is electro-chemically inert at potentials between 0 and −2.5 volts relative to the saturated calomel electrode, and has a dielectric constant of less than 50. Cosolvents which can be used include alcohols, ethers, nitriles, aliphatic amides and aliphatic esters. The cosolvent preferably contains one to 10 carbon atoms. Cosolvents which can be used in a one liquid phase catholyte, include methanol, ethanol, n-propanol, isopropanol, acetonitrile, 1-methoxy-ethanol-2, 1,2-dimethoxy-ethane, glycol, 1-ethoxy-ethanol-2, 1,2-diethoxy-ethane, tetrahydrofurane, dioxane, 1,2-ethanediol diacetate and dimethylformamide.

The proportion of cosolvent in the water-cosolvent mixture present in the catholyte depends on the ability of the cosolvent to dissolve salicylic acid. The proportion is usually between 10 and 90 percent by weight, preferably between 45 and 80 percent by weight.

The concentration of salicylic acid in the catholyte is advantageously above 35 g/litre and below the saturation value in the water/cosolvent/quarternary ammonium salt mixture in question ; these limiting values apply to the initial acid concentration in discontinuous processes, and to the instantaneous acid concentration in continuous processes.

The quarternary ammonium salts used in the catholyte are essentially salts of the general formula:



$$A^{\ominus}\ {}^{\oplus}N(R_1)(R_2)(R_3)(R_4) \qquad (I)$$

in which each of $R_1$, $R_2$, $R_3$ and $R_4$ represent identical or different hydrocarbon radicals, each having from 1 to 20 carbon atoms in their chain, or in which two of the R radicals together form a single divalent radical and together with the nitrogen atom to which they are attached, form a heterocyclic ring.

The radicals $R_1$, $R_2$, $R_3$, $R_4$ can represent linear or branched alkyl radicals, such as methyl, ethyl, propyl, isopropyl, butyl, pentyl, hexyl, heptyl, octyl, 2-ethyl-hexyl or dodecyl, cycloalkyl or alkyl-cycloalkyl radicals such as cyclohexyl, or aryl radicals such as phenyl, tolyl or xylyl.

Examples of cations which may be derived from salts of formula (I) are tetramethylammonium, trimethylethylammonium, methyltriethyl-ammonium, tetraethylammonium, tetra(n-propyl)ammonium, tetra(n-butyl)ammonium, tetra(n-pentyl)ammonium, triethylbutylammonium, triethylhexylammonium, triethyl(2-ethyl-hexyl)ammonium triethyl(n-octyl)ammonium, triethyl(n-dodecyl)ammonium, and tributyl(n-dodecyl)ammonium ions.

The nature of the anion $A^-$ of the salts of the formula (I) is not critical since the anion cannot be reduced electrochemically under the reaction conditions. Preferably, anions are used such that the acid AH has a pK less than or equal to the pK of the aromatic carboxylic acid to be reduced ; anions $A^-$ such that AH has a pK above the pK of salicylic acid can also be used, especially if the amount of ammonium salt is such that there still remains salicylic acid in the undissociated acid form.

The anion $A^-$ can be such that AH is an inorganic acid or an organic acid. Examples of such inorganic acids AH include sulphuric, phosphoric, pyrophosphoric, hydrochloric, hydrobromic, hydriodic, perchloric, boric and fluoboric acids. Examples of such organic acids AH include formic, malonic, methanesulphonic, ethanesulphonic, benzene-sulphonic, toluenesulphonic, methylsulphuric, ethylsulphuric acid, and salicylic acid.

Specific quarternary ammonium salts of formula (I) which may be used are tetramethylammonium, tetraethylammonium, tetra(n-butyl)ammonium, tetra(n-pentyl)ammonium, triethyl(n-hexyl)ammonium, triethyl(n-octyl)ammonium, triethyl(2-ethylhexyl) ammonium, and triethyl(n-dodecyl)-ammonium sulphates, phosphates and halides.

Apart from the various constituents of the catholyte which have been specified above, the catholyte can contain other products, especially products which are inert under the operating conditions and by-products of the electrochemical reduction.

The cathode in the cell utilised in the process of the invention can be a metal, especially mercury or a solid amalgam of mercury.

An aqueous acid solution is preferably used as the anolyte. The precise nature of this anolyte is not critical because the anolyte merely serves the purpose of completing the electrically conducting pathway between the two electrodes. Usually, aqueous solutions of sulphuric, phosphoric, nitric, hydrochloric, boric or fluoboric acid are used. The concentration of these solutions is generally between 0.1 and 5 mols/litre and preferably between 0.5 and 2 mols/litre.

The anode of the cell used in the practice of the invention may be any material which conducts electricity and is electrochemically stable in the anolyte under the working conditions in question. Suitable materials include metals and metalloids such as lead and its alloys, platinum, platinised titanium and graphite.

The current density at the cathode is generally 1 to 25 A/dm$^2$, preferably 5 to 15 A/dm$^2$.

The temperature at which the electrolysis is carried out is generally 5° to 60° C and preferably 25° to 45° C.

At the end of the electrolysis (when operated discontinuously) or during electrolysis (if operated continuously), the saligenol is isolated from the catholyte by any of the known methods, for example by solvent extraction. According to a preferred procedure, the cosolvent is first removed, for example by distillation, which causes precipitation of any unreduced salicylic acid which may be present ; this acid is filtered off and the filtrate is then extracted with ether or with another saligenol solvent which is immiscible with water ; on evaporating the latter solvent, saligenol is obtained. Where the precipitation of the salicylic acid during the removal of the cosolvent has only been partial, the residual salicylic acid in solution can be converted into a salt which prevents it being extracted with the saligenol.

To avoid deformations of the cation exchange membrane and to avoid contact of this membrane with the electrodes, spacers can be used, placed between the membrane and the electrodes. These spacers, which are well known in electro-chemistry, generally consist of interlaced or crossed plastic filaments, or of apertured or grooved sheets.

The electrical cell in which the process of the invention is carried out can be grouped in series in accordance with any known techniques, for example, in devices such as filter-press systems.

The process according to the invention can be carried out continuously or discontinuously. The process allows saligenol to be obtained in good electrical yields and chemical yields in a process where the electrodes, especially the cathode, are not chemically degraged by the electrolyte.

Saligenol is a starting material used in the synthesis of coumarine.

## EXAMPLE 1

The electrical cell used is that shown in the FIGURE of the accompanying drawing. The cell comprises a main trough 1 having an outer jacket 2 through which liquid at a controlled predetermined temperature may be circulated. Main trough 1 is divided up into a cathode compartment containing catholyte 4 and cathode 3 and an anode compartment containing anolyte 7 and anode 6. Catholyte 4 and anolyte 7 are separated from one another by cation exchange membrane 5 and internal cell divider 9. The cathode compartment is provided with a magnetic stirrer 8, thermometer 10 and a gas outlet 12 to remove gas evolved from the cathode compartment. Outlet 12 leads to a gas flow rate measuring device (not shown).

The electrolysis conditions are as follows:

Cathode : lead amalgam disc of surface area 0.6 dm$^2$ (prepared by immersing a disc of lead in a bath of mercury for 10 hours)

Catholyte : initially a mixture consisting of
250 cm$^3$ of isopropanol
80 cm$^3$ of water
45 g of salicylic acid and
30 g of tetraethylammonium bromide.

Cathode - cation exchange membrane distance : 2 cm.

Cation exchange membrane : heterogeneous-type membrane having a matrix of polyvinylidene fluoride ; the cation exchange resin is a sulphonic resin based on polystyrene crosslinked with divinylbenzene ; the exchange capacity of the membrane is 1.05 meg/g ; its substitution resistance is 9.6 Ω cm$^2$ in an 0.1 N aqueous solution of NaCl and 4.8 Ω cm$^2$ in a normal aqueous solution of NaCl ; the permeation selectivity of the membrane, measured between two aqueous NaCl solutions which are respectively normal and half-normal, is 96.2 percent.

Anolyte: 10% by weight aqueous solution of sulphuric acid.

Anode: lead disc of surface area 0.125 dm$^2$

Anode/cation exchange membrane distance : 1 cm

Temperature: between 30° and 35° C, which ensures that the medium is homogeneous.

Current density at the cathode: 6.66 A/dm$^2$ until 61,910 coulombs have been passed ; thereafter 7.5 A/dm$^2$.

The electrolysis is stopped after 80,000 coulombs have passed. 3350 cm$^3$ of hydrogen (measured at 0° C under a pressure of 760 mm Hg) are collected from outlet (12).

The catholyte is distilled under a reduced pressure of 20 mm of mercury, which allows the isopropanol to be removed and causes a precipitate to form. The precipitate is filtered off and washed with water, and the filtrate and the wash waters are combined and neutralised (pH = 7) with sodium bicarbonate. The mixture is extracted with ether, the ether phase dried by means of sodium sulphate and concentrated to dryness ; 14.8 g of saligenol are obtained.

The yield of saligenol based on the acid converted is 66.6 percent while the electrical yield is 57.6 percent.

## EXAMPLE 2

Example 1 is repeated, replacing the isopropanol by methanol and using a constant current density of 6.66 A/dm$^2$. at the cathode. After passing 84,500 coulombs and treating the catholyte as described in Example 1, 11.1 g of saligenol are obtained.

This corresponds to a yield based on acid converted of 48.7 percent and an electrical yield of 41 percent.

## EXAMPLE 3

Example 1 is repeated with the following modifications:

Composition of the catholyte:

250 cm$^3$ of water

250 cm$^3$ is isopropanol

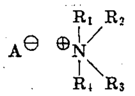
45 g of salicylic acid

40 g of tetraethylammonium bromide.

The current density at the cathode is constant and equal to 10 A/dm$^2$, After passing 49,720 coulombs and treating the catholyte as described in Example 1, 7.2 g of saligenol are obtained. This corresponds to a yield based on acid converted of 79 percent and an electrical yield of 45 percent.

I claim:

**1.** Process for the preparation of saligenol by electrochemical reduction of salicyclic acid in an electrolysis cell having a cathode compartment and an anode compartment, separated from one another by a cation exchange membrane and a catholyte initially consisting essentially of salicylic acid, water, a cosolvent and a quaternary ammonium salt of the general formula:



$$A^{\ominus}\ \overset{R_1\ R_2}{\oplus N}\underset{R_4\ R_3}{} \qquad (I)$$

in which each of $R_1$, $R_2$, $R_3$ and $R_4$ represent identical or different hydrocarbon radicals, each having from 1 to 20 carbon atoms in their chain, or in which two of the R radicals together form a single divalent radiacal and together with the nitrogen atom to which they are attached, form a heterocyclic ring and $A^-$ represents an anion.

**2.** Process according to claim **1**, wherein the cosolvent is present in proportions by weight of 10 to 90 percent in the water-cosolvent mixture contained in the catholyte.

**3.** Process according to claim **1**, wherein the cosolvent is chemically inert under the reaction conditions towards the acid to be reduced, which is electrochemically inert at potentials of between 0 and −2.5 volts relative to the saturated calomel electrode, and which has a dielectric constant of less than 50.

**4.** Process according to claim **3**, wherein the cosolvent is selected from the group consisting of an alcohol, an ether, a nitrile and an aliphatic acid.

**5.** Process according to claim **1**, wherein the current density at the cathode is 1 to 25 A/dm$^2$.

**6.** Process according to claim **1**, wherein the anolyte consists essentially of an aqueous acid solution.

**7.** Process according to claim **1**, wherein the quaternary ammonium salt is a tetra-alkylammonium sulphate, phosphate or halide in which each alkyl group contains 1–20 carbon atoms.

**8.** Process according to claim **1**, wherein the anolyte is aqueous sulphuric acid, the catholyte initially consists essentially tetra-alkyl-ammonium salicylic acid, water, methanol or isopropanol and a tetra-alkalyammonium bromide and electrolysis is carried out at a current density at the cathode of 5–15 A/dm$^2$.

* * * * *