NALSAR PROXIMATE EDUCATION
NALSAR UNIVERSITY OF LAW, HYDERABAD
P.G.DIPLOMA IN PATENTS LAW

2014-15
Supplementary Exams (November, 2015)

Paper II – Practical

(Exploitation of Patents – Drafting, Specification & Patent Writing)

Time: 2 ½ hours. **TOTAL MARKS: 90**

INSTRUCTIONS TO CANDIDATES

1. **The questions to be interpreted as given and no clarification can be sought from the invigilator.**
2. **Do not draw or attach figures**
3. **The claim drafting will carry 30 marks**
4. **The rest of the specification will carry 60 marks**
5. **Attempt only one choice – either A or B**

Draft a Patent based on the information given by the inventor as below:

Option A

"I have been thinking about how to make it easier for disabled people in wheel chairs to operate light switches. These are frequently located on walls at a height, which cannot be reached by someone in a wheel chair. Of course, it is possible to re-locate a light switch at a different position on a wall but that usually requires the services of an electrician and is expensive.

What I propose is something that can be fitted to existing light switches by anyone. My invention takes two slightly different forms in order to be compatible with two different kinds of light switches, the so called toggle type and the rocker type. These two types are illustrated in the attached sheet 1 of drawings. It should be understood that the positions 'off' and 'on' are used for convenience since it is possible that, due to wiring, the switch may turn on a light when in the position illustrated as 'off' and turn off a light when the position illustrated as 'on'. Furthermore it should be remembered that switches such as those illustrated could be used to control other electrical appliances and not just lights.

I have sketched the invention to be applied to a rocker switch on Sheet 2 attached. When the rod is pulled, the rocker switch is turned on. Then when the rod is pushed up, the rocker switch is turned off. The switch can still be accessed through the slot for people not requiring assistance. The pin engaging the ends of the slot limits movement of the actuator. If more limited movement is required, stops (not illustrated) can be provided inside the cover.

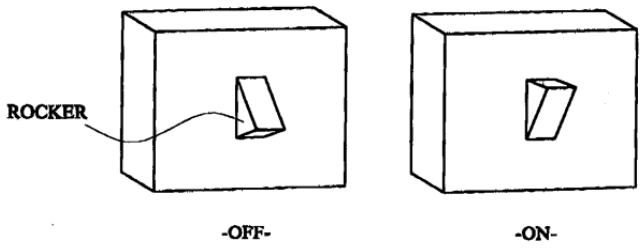
The rod can be adjustable in length so as to make the invention suitable for switches at any height from floor level. A handle can be provided at its free end. Sheet 3 shows the invention applied to a toggle switch. The assembly is very much the same as that for a rocker switch except that an aperture is formed in the actuator, which is fitted over the toggle component of the switch. Thus when the actuator is moved down from the position illustrated the toggle is moved from the 'off' position to the 'on' position. And moving the actuator up returns the toggle to the 'off' position. A pin can still be provided in the arrangement shown in Sheet 3, so that the switch can be operated manually by moving the pin along the slot.

Please can you prepare a patent specification and claims for my invention?

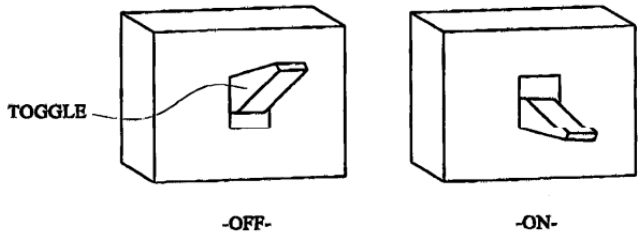
By the way I am enclosing an extract from US Patent No.5782342 which shows a device which is a bit like my invention but not so good!"

SHEET 1

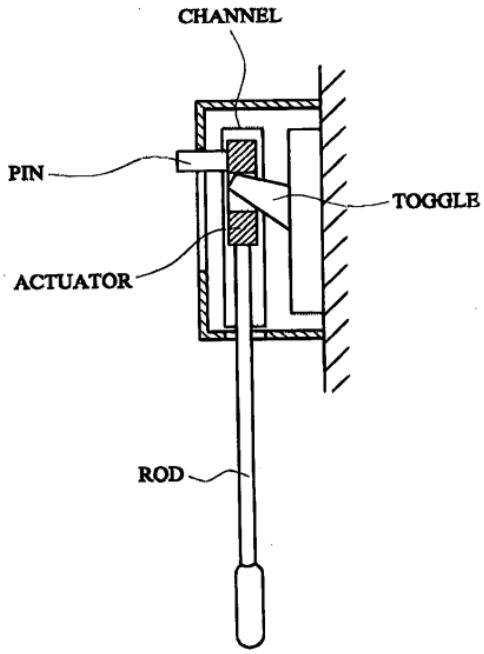
ROCKER TYPE SWITCH



TOGGLE TYPE SWITCH

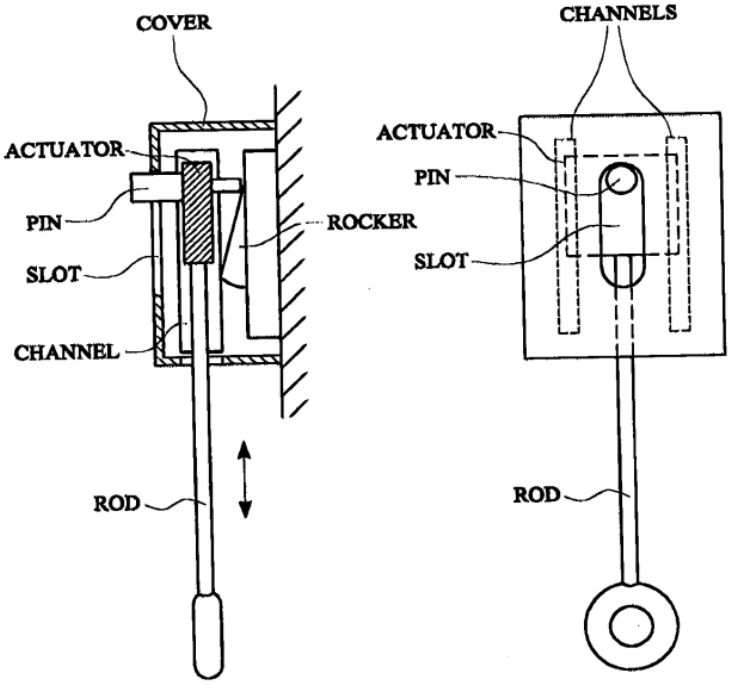


SHEET 3



SIDE ELEVATION PARTLY IN SECTION

SHEET 2



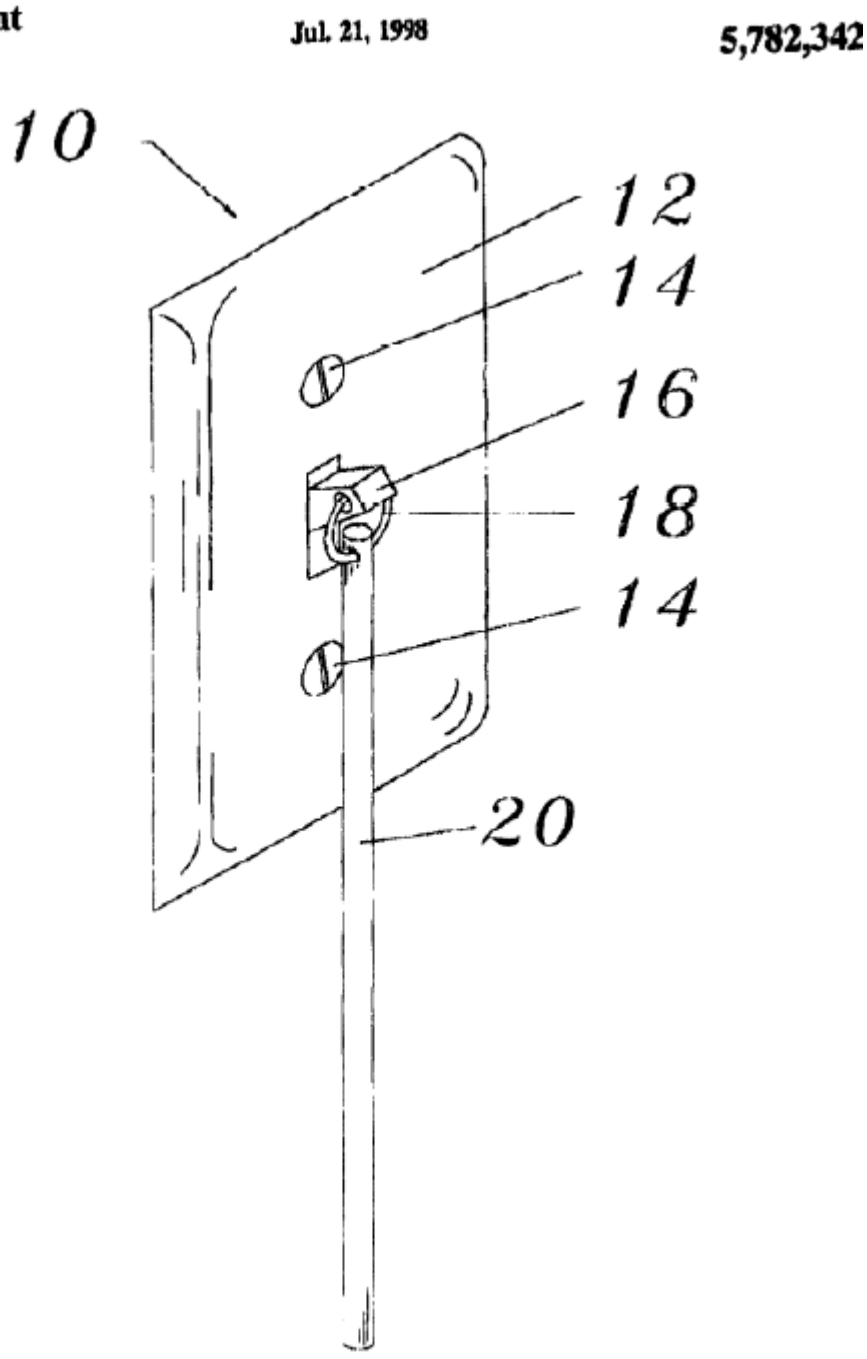
SIDE ELEVATION PARTLY IN SECTION

FRONT ELEVATION

US PATENT No. 5,782,342 (EXTRACT)

The drawing shows a light switch assembly 10 comprising a rod 20 having an aperture through one of its ends and a ring 18 connected through the aperture. The ring is connected through a hole in a light switch lever 16. Screws 14 are used to secure the switch to a wall surface.

As rod 20 is raised to lift ring 18, light switch lever 16 is also lifted to turn on an associated light. When rod 20 is lowered to bring down ring 18, switch lever 16 is also lowered to turn off an associated light.



Option B

The present invention generally relates to metal mesoporphyrin halide compounds and processes for their preparation. More specifically, it relates to processes for making novel intermediate compounds which can be converted to such mesoporphyrin halide compounds.

Tin (IV) mesoporphyrin IX dichloride or stannsoporfin is a chemical compound having the structure indicated in FIG. 1. It has been proposed for use, for example, as medicament in the treatment of various diseases including, for example, psoriasis (U.S. Pat. No. 4,782,049 to Kappas et al.) and infant jaundice (for example, in U.S. Pat. Nos. 4,684,637, 4,657,902 and 4,692,440). Stannsoporfin is also known to inhibit heme metabolism in mammals, to control the rate of tryptophan metabolism in mammals, and to increase the rate at which heme is excreted by mammals (U.S. Pat. Nos. 4,657,902 and 4,692,400 both to Kappas et al.).

Processes for obtaining stannsoporfin are known in the art. Protoporphyrin IX iron (III) chloride or hemin, of the structural formula indicated in FIG. 2, is commonly used as starting material. The hemin is generally hydrogenated to form an intermediate mesoporphyrin IX dihydrochloride, which is subsequently subjected to tin insertion, yielding stannsoporfin.

One prior method for the preparation of the intermediate mesoporphyrin IX dihydrochloride has involved catalytic hydrogenation of hemin over Pd(0) in formic acid at elevated temperature. Column chromatography of the resulting intermediate obtained by such a method yields an intermediate mesoporphyrin IX dihydrochloride product that reportedly contains about 15% of an unidentified impurity. Another preparation method for this intermediate has been typically performed at lower temperatures with heating hemin in formic acid in the presence of palladium catalyst. This process is reported to reduce the amount of the unidentified impurity; however, the reaction is difficult to drive to completion without decomposition of the intermediate product.

The above referenced methods for the preparation of the mesoporphyrin IX intermediate are used to produce only small, gram scale quantities of the product, and the product further requires subsequent isolation and purification, generally by preparative or column chromatography. Additionally, those methods in which hydrogenation is carried out at lower temperatures yield incomplete reactions, and when higher temperatures are used, degradation of the intermediate product is observed. Consequently, the crude intermediate product requires purification. Furthermore, the above referenced procedures require exceedingly high solvent volumes, thus making the process unsuitable for industrial scale up, since isolation of mesoporphyrin IX dihydrochloride or its free base is performed using a filtration process. Such filtrations and subsequent washings of the products are time-consuming, making the large-scale isolations costly and difficult. Additionally, the limited stability of mesoporphyrin IX in hydrochloric acid at the elevated temperatures required to form the dihydrochloride also complicates the industrial scale up of this process.

The insertion of various metals into porphyrin rings, including the insertion of tin into mesoporphyrin IX, has been described by Fischer and Neumann (Ann. Chem. (1932), 494, 225). The reaction for the insertion of tin is performed in an acid, typically acetic acid, and further typically under reflux, using Sn (II) in the presence of an oxidant. A modified process is also described by Fuhrhop and Smith, as reported in "Porphyrins and Metalloporphyrins" p. 757, Elsvier, Amsterdam, 1975, to include sodium acetate, which buffers the solution and enhances deprotonation of the porphyrin. In most cases, the metal mesoporphyrin halide product crystallizes directly from the reaction mixture on cooling. Such crystallization may be enhanced by the addition of water or methanol.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 illustrates the chemical structure of tin mesoporphyrin chloride (tin (IV) mesoporphyrin IX dichloride) or stannsoporfin.

FIG. 2 illustrates the chemical structure of protoporphyrin IX iron (III) chloride or hemin,

FIG. 3 illustrates the chemical structure of mesoporphyrin IX formate, a novel chemical compound,

which constitutes a novel product of the present invention.

FIG. 4 illustrates the conversion of protoporphyrin IX iron (III) chloride (ferriporphyrin chloride or hemin) to mesoporphyrin IX formate, in accordance with an embodiment of the first aspect of the invention; and

FIG. 5 illustrates the conversion of mesoporphyrin IX formate to tin mesoporphyrin chloride (tin (IV) mesoporphyrin IX dichloride) or stannsoporfin, in accordance with an embodiment of the second aspect of the invention.

DETAILED DESCRIPTION

In the first aspect of an example of the invention, illustrated in accompanying FIG. 4, hemin is hydrogenated in formic acid, over an appropriate metal catalyst such as, for example, palladium, platinum or nickel, among others, under a hydrogen atmosphere, at elevated temperatures. Preferred embodiments of the invention involve the use of palladium on carbon as metal catalyst. In the first stage of hydrogenation, the temperature of hydrogenation is held at about 85-95.degree. C. for a period of about 1-3 hours. Most preferred conditions are a temperature of about 90.degree. C. and a time of about 1 hour.

In the second stage of hydrogenation, the reaction mixture is cooled to about 45-50 .degree. C. and hydrogenated for a further period of time of about 3-6 hours, in order to convert substantially all hemin (protoporphyrin IX iron (III) chloride) to mesoporphyrin IX formate. This second stage is also conducted in formic acid. The same catalyst may be used as in the first aspect above, so that the two stages of the process may be conducted in the same reactor. Optionally, a further charge of hydrogen may be supplied to the reactor prior to commencing the second stage. The second hydrogenation stage increases the yield of the mesoporphyrin IX formate, while reducing the amount of impurities in the final metal mesoporphyrin halide.

In contrast to previously described methods, the mesoporphyrin IX intermediate compound in the present invention is not isolated as a dihydrochloride, but rather as a formate salt.

The mesoporphyrin IX formate may be isolated from the formic acid solution by the addition of a solvent such as an ether or other organic solvent, leading directly to the mesoporphyrin IX formate intermediate, which is further subjected to drying. Ethers such as, for example, methyl tert-butyl ether, diethyl ether or di-isopropyl ether, among others, may be used. Preferred embodiments of the invention involve methyl tert-butyl ether.

The amounts of solvent used in the process according to the invention are much lower than those used in the referenced processes; such smaller volumes allow for less filter time. Ratios of amount of hemin to amount of solvent of about 1:10 to about 1:20 may be used. In addition, the filtration and washings of the mesoporphyrin IX formate are rapid. After drying, the crude intermediate formate is obtained, in high yields (about 80-95%) and its purity, established by HPLC, is about or above 97%. The intermediate formate obtained in accordance with the process of the invention is of quality equal to or better than that of the intermediate mesoporphyrin IX dihydrochloride produced in the process described in the art, after purification by preparative chromatography.

The insertion of metal into mesoporphyrin IX formate to obtain metal mesoporphyrin halide is described below with specific reference to tin, to prepare stannsoporfin, a known pharmaceutical and a specific preferred embodiment of the invention. It is not intended that the scope of the invention should be limited thereto, but is generally applicable to preparation of mesoporphyrin halides, for example, but not limited to, mesoporphyrin chlorides, of other metals such as, for example, iron, zinc, chromium, manganese, copper, nickel, magnesium, cobalt, platinum, gold, silver, arsenic, antimony, cadmium, gallium, germanium and palladium, among others.

Preparation of mesoporphrin halides of these other metals simply entails a substitution of a halide such as chloride, bromide or iodide of the chosen metal in place of stannous chloride in the process described, in substantially equivalent amounts.

The second stage of the process according to the invention is illustrated in FIG. 5. Mesoporphyrin IX

formate is subjected to heating with a tin (II) carrier in acetic acid, buffered with an acetate ion, in the presence of an oxidant, at reflux. Tin (II) carriers such as tin (II) halides or tin (II) acetate can be used. Suitable acetate counter ions include ammonium, sodium or potassium ions. Oxidants such as oxygen from air or in pure form as well as hydrogen peroxide can also be used. In one exemplary embodiment of this second stage, mesoporphyrin IX formate is subjected to heating with tin (II) chloride in acetic acid, buffered with ammonium acetate, and the reaction is conducted in the presence of air, at reflux. Tin mesoporphyrin chloride is isolated from the reaction mixture by the addition of water, followed by filtration. Prior to drying at about 90-100.degree. C., the cake is triturated into hot, dilute hydrochloric acid, preferably of concentration of about 0.1N-6N, at an elevated temperature, of about 90-100.degree. C. The crude, substantially pure tin mesoporphyrin chloride (crude tin (IV) mesoporphyrin IX dichloride) is obtained with a yield of about 75-95% and a purity of about 95%, as judged by HPLC analysis.

The tin mesoporphyrin chloride so obtained may be further purified by dissolving the product in an aqueous inorganic base solution, preferably dilute ammonium hydroxide, followed by treatment with charcoal. The product is then re-precipitated by addition to an acid solution, such as acetic acid, hydrochloric acid or a mixture thereof. The above dissolving, charcoal treatment and re-precipitation steps may be repeated a number of times, typically about 1-3 times in order to ensure the desired purity. Prior to drying, the cake is triturated in hot, dilute hydrochloric acid of a concentration of about 0.1N-6N, at an elevated temperature of about 90-100.degree. C., in order to remove any residual ammonium salts. The tin mesoporphyrin chloride product (tin (IV) mesoporphyrin IX dichloride or stannsoporfin) is obtained in a yield of about 50-70%, with an HPLC purity of about or greater than 97%.

The invention may also be performed to produce substantially pure or pharmaceutical quality tin mesoporphyrin chloride (tin (IV) mesoporphyrin IX dichloride or stannsoporfin) in large scale quantities, such as quantities exceeding about 0.1 kg through and including multiple kilogram amounts, by slight modifications of the above procedure, such as increased reaction or drying times as appropriate based upon the increase in scale of the starting reactants. Temperature and pressure times likewise can be modified as needed within the scope of this invention. The tin mesoporphyrin chloride product (tin (IV) mesoporphyrin IX dichloride or stannsopofrin) is obtained in the large-scale production process in a yield of about 60-90%, with an HPLC purity of about 97%.

FIGURES – Option B

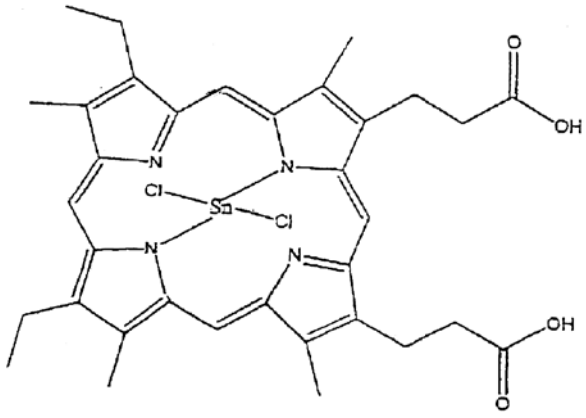


FIG.1

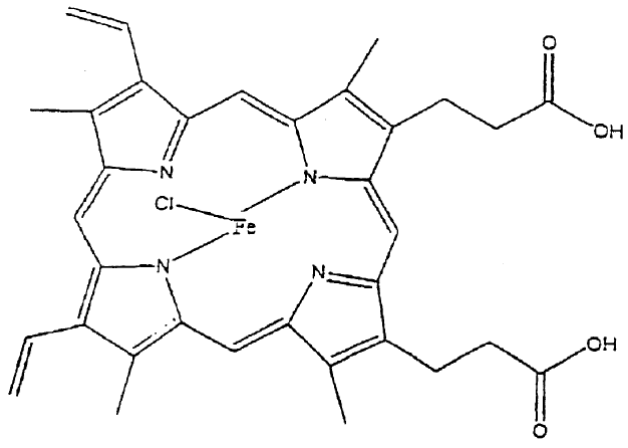


FIG.2

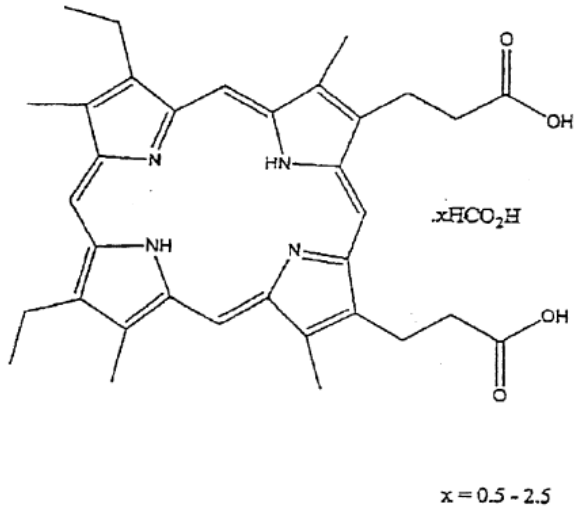


FIG.3

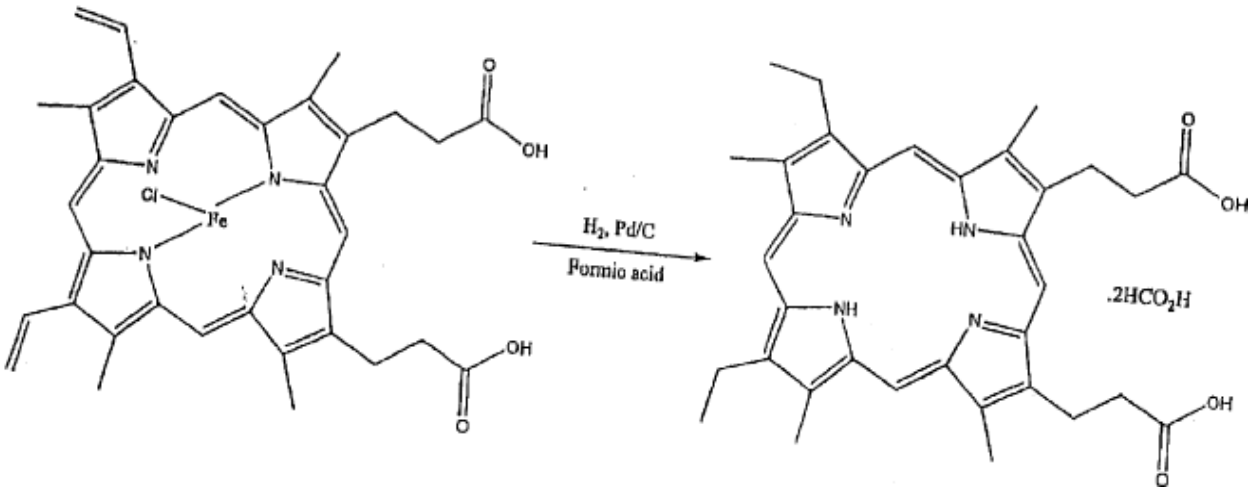


FIG.4

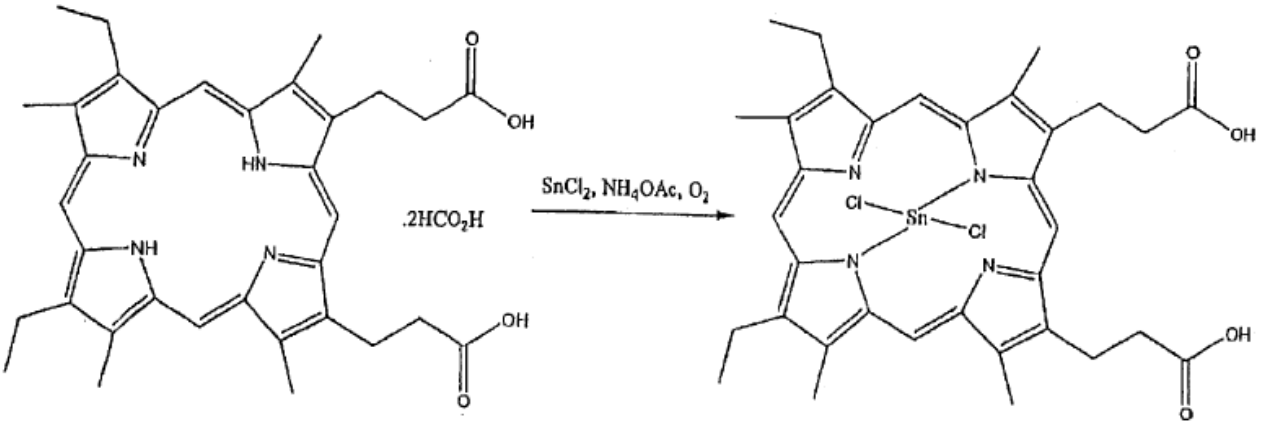


FIG.5