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(54) Title: PHOTOCHEMICAL PROCESS FOR THE PREPARATION OF A PREVITAMIN D

(57) Abstract: The invention is directed to a photochemical process for the preparation of a previtamin D or a derivative thereof from a 7-dehydrosterol or a corresponding derivative thereof which process comprises irradiating the 7-dehydrosterol or the derivative thereof with UV LED(s).

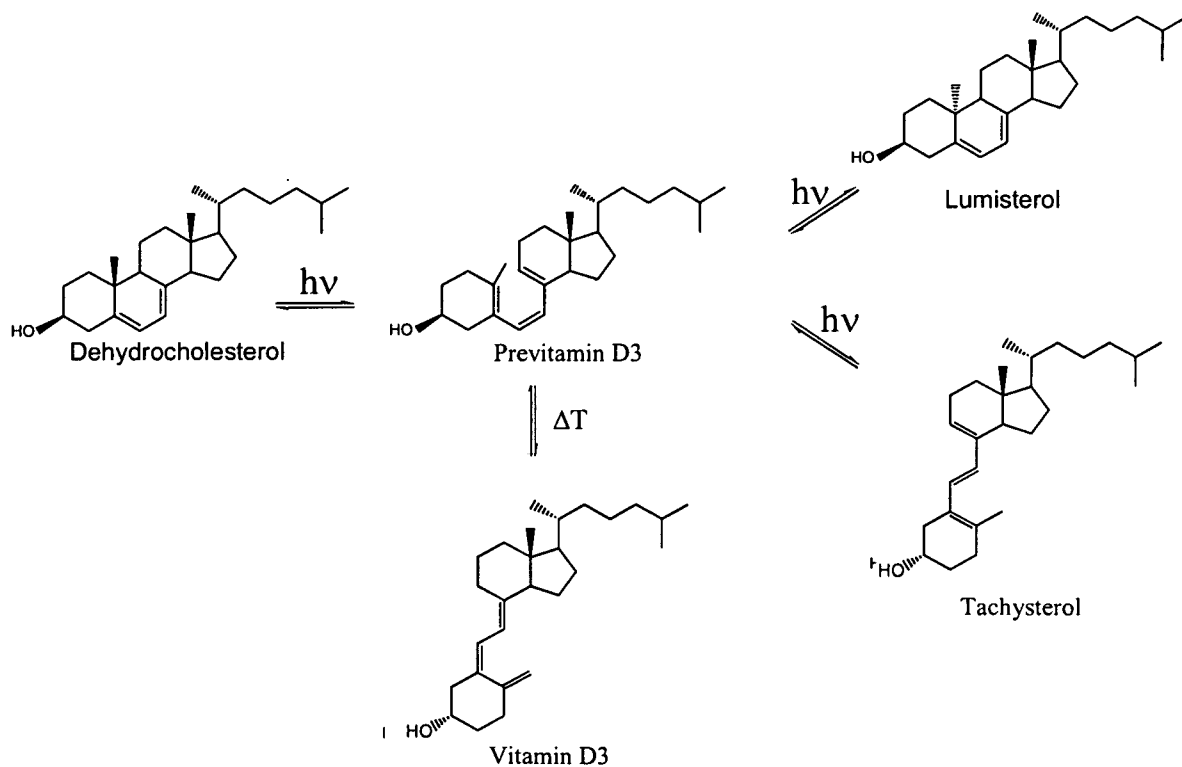
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PHOTOCHEMICAL PROCESS FOR THE PREPARATION OF A PREVITAMIN D

- 5 The present invention relates to a photochemical process for the preparation of a previtamin D or a derivative thereof from a 7-dehydrosterol using UV LED(s) as UV radiation source.

It is known that previtamin D₃ may be obtained from 7-dehydrocholesterol (7-DHC, provitamin D₃) by irradiation with UV light. In this photochemical step the 9,10-bond of 7-DHC is cleaved to give the (Z)-triene previtamin D₃. This previtamin may be converted by thermal rearrangement into vitamin D₃ which is thermally more stable. Unfortunately, previtamin D₃ can also absorb photons and convert to unwanted byproducts such as lumisterol and tachysterol (see Scheme 1).

15



Scheme 1

The quantum yields of all these photoreactions are wavelength-dependent.

Conventional photochemical synthesis of previtamin D₃ on an industrial scale reportedly has been effected by irradiation of 7-DHC using mercury medium-pressure lamps.

- 5 Because the starting material (7-DHC), the primary product (previtamin D₃) as well as byproducts, absorb with different efficiency in the same wavelength range, polychromatic radiation of the kind supplied by these lamps favors the formation of photochemical byproducts which are inactive and in some cases toxic. Therefore, with the present state of the art, it is necessary to interrupt the irradiation after relatively low conversion of the 7-
10 DHC to previtamin to D₃. The unconverted 7-DHC is recycled while the primary product (previtamin D₃) must be purified in an expensive working up procedure.

- Filter effects are a further consequence of substrates and products which absorb in the same wavelength range. For example, when the absorption spectrum of previtamin D₃
15 overlaps completely with that of 7-DHC, the previtamin absorbs a continuously increasing proportion of the light as the conversion proceeds.

- Another reason for interrupting the conventional reaction after a relatively low conversion (10-20%) of 7-DHC to previtamin D₃ is the fact that the quantum yield (i.e., the
20 efficiency) of the subsequent photochemical reaction of previtamin D₃ to, e.g. tachysterol, is greater than the quantum yield of the formation of the desired product (previtamin D₃). Thus, in conventional reactions, the efficiency of the reaction is decreased while the cost of production of the end product is increased.

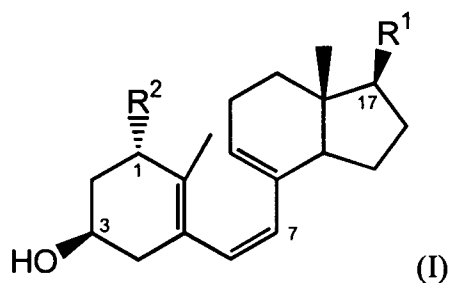
- 25 Another significant problem during conventional production of previtamin D₃ is the poor correlation between the emission spectrum of mercury medium-pressure lamps and the absorption spectrum of 7-DHC. Thus, in conventional processes using mercury medium-pressure lamps only about 1% of the radiation radiating therefrom is in the desired range, i.e., between about 280 and about 300 nm. Moreover, because the radiation spectrum
30 produced by a conventional mercury medium-pressure lamp is not optimized for the 280-300 nm wavelength, a large amount of undesired byproducts are produced by irradiation outside this optimum wavelength region.

Similar problems exist with respect to the production of other previtamins of the vitamin D group, e.g. previtamin D₂, by photolysis.

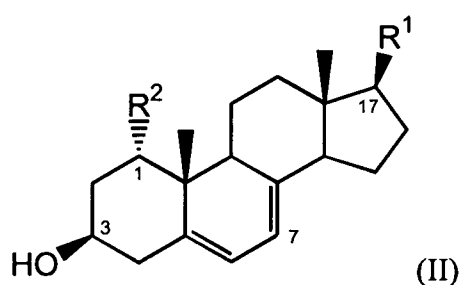
- 5 Various other sources of UV irradiation have been considered to drive the 7-DHC to previtamin D₃ reaction. For example, the process of forming photons from excimer or exciplex reactions is known from laser technology. The use of excimer or exciplex lasers for the photolytic conversion of 7-DHC to previtamin D₃ is described in US-A-4 388 242, EP-A-0 118 903, and Reza Kagaku Kenkyu 11, 24 - 7 (1989)/Chem. Abs. 114, No. 9,
10 82251 (1991). Laser photon sources, however, are not suitable for photochemical synthesis of previtamin D₃ on an industrial scale because of their high technical complexity and the fact that their radiation geometry has little suitability for preparative photochemistry and the associated radiation density is insufficient over a large area.
- 15 EP-A-0 967 202 discloses a photochemical process for the production of previtamin D₃ wherein the UV radiation source is an excimer or exciplex emitter which emits quasi-monochromatically in the UV range according to the "corona discharge" mechanism. Although the use of an incoherent excimer/exciplex light source seemed to be promising for the production of previtamin D₃ the reliability of presently available excimer/exciplex
20 light sources is insufficient for industrial application. For example, the UV power output of a XeBr lamp decreases steadily during continuous use.

- Accordingly, the object of the present invention is to provide a new photolytic process for the preparation of a previtamin D, especially previtamin D₃, from a 7-dehydrosterol, which
25 process avoids the drawbacks of the prior-art procedures. The new photolytic process should be suitable for the industrial production of previtamin D₃, other previtamins D and derivatives thereof on large scale.

- The object is met by a photochemical process for the preparation of a previtamin D
30 according to formula (I)

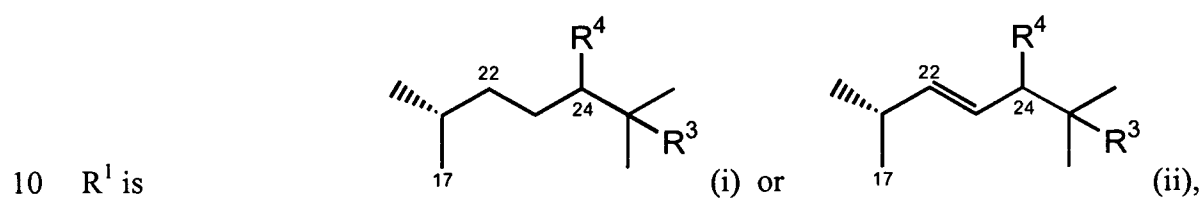


or a derivative thereof from a 7-dehydrosteroid according to formula (II)



or a corresponding derivative thereof,

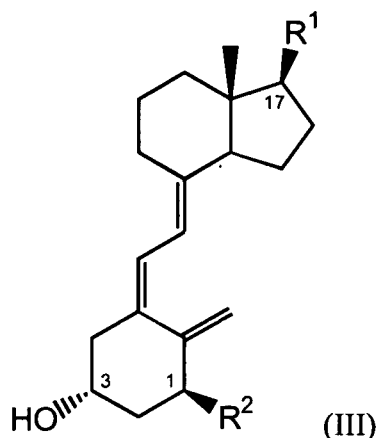
wherein in formulae (I) and (II)



R^2 is H; R^3 is H; and R^4 is H, CH_3 or C_2H_5 ,

15 comprising irradiating the 7-dehydrosteroid or the derivative thereof with UV light emitting diode(s) (UV LED(s)).

The present invention is further directed to a process for the preparation of a vitamin D according to formula (III)



or a derivative thereof from a 7-dehydrosterol according to formula (II) or a corresponding derivative thereof comprising preparing the previtamin D according to formula (I) or the
5 corresponding derivative thereof as described above and further explained in detail below and converting the previtamin D or the derivative thereof to the vitamin D or the derivative thereof by thermal rearrangement.

Fig. 1 and Fig. 2 show the effect of wavelength on reaction course
10 (DHC = 7-DHC, P = previtamin D₃, T = tachysterol, and L = lumisterol).

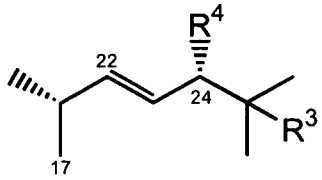
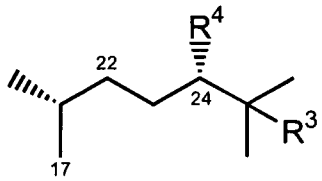
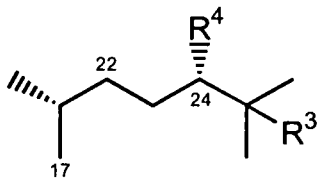
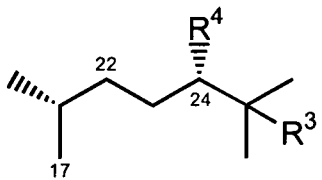
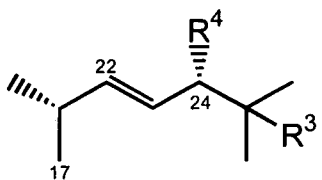
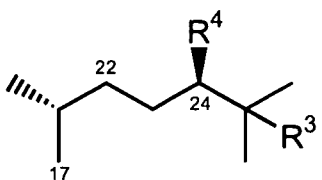
Fig. 3 shows the microreactor used in the examples.

Fig. 4 shows the experimental setup used in the examples.
15

In the present invention, significantly improved levels of previtamin D production from a 7-dehydrosterol are achieved by using as the radiation source UV light emitting diode(s) (UV LED(s)). The present process is not restricted to the preparation of previtamin D₃ but can be used to prepare various compounds of the vitamin D group as defined above,
20 including derivatives, because all their provitamins (the 7-dehydrosterols) have the same 4-ring steroid skeleton with two double bonds in the 5- and 7-position (steroidal 5,7-dienes), the 5,7 diene structure being responsible for the photochemical behavior of these compounds.

Some specific provitamins, previtamins and vitamins herein involved are shown in the Table 1 below:

Table 1

7-dehydrosterol (provitamin D)	previtamin D	vitamin D	R ¹ in formulae (I), (II), (III)	R ⁴
ergosterol	previtamin D ₂	vitamin D ₂ (ergocalciferol)		CH ₃
7-dehydro- cholesterol (7-DHC)	previtamin D ₃	vitamin D ₃ (cholecalciferol)		H
22,23-dihydro- ergosterol	previtamin D ₄	vitamin D ₄		CH ₃
7-dehydro- β-sitosterol	previtamin D ₅	vitamin D ₅		C ₂ H ₅
7-dehydro- stigmasterol	previtamin D ₆	vitamin D ₆		C ₂ H ₅
7-dehydro- campesterol	previtamin D ₇	vitamin D ₇		CH ₃

5 R² in formula (I) and R³ = H

The preferred provitamins and vitamins are previtamin D₂/vitamin D₂ and previtamin D₃/vitamin D₃; previtamin D₃/vitamin D₃ being most preferred.

A light emitting diode (LED) is a semiconductor device that emits incoherent narrow-spectrum, quasi-monochromatic light when electrically biased in the forward direction (electroluminescence). A LED is a unique type of semiconductor diode. Like a normal diode, it consists of a chip of semiconducting material impregnated, or doped, with
5 impurities to create a p-n junction. As in other diodes, current flows easily from the p-side, or anode, to the n-side, or cathode, but not in the reverse direction. Charge-carriers - electrons and electron holes - flow into the junction from electrodes with different voltages. When an electron meets a hole, it falls into a lower energy level, and releases energy in the form of a photon.

10 The wavelength of the light emitted, and therefore its color, depends on the band gap energy of the materials forming the p-n junction. In "ordinary" silicon or germanium diodes, the electrons and holes recombine by a non-radiative transition which produces no optical emission, because these are indirect bandgap materials. The materials used for an LED have a direct band gap with energies corresponding to near-infrared, visible or near-
15 ultraviolet light. Typically, UV LEDs are based on (AlGaIn)N built on a sapphire substrate. However, the actual material of the UV LED is not critical for the present invention. UV LEDs suitable for the present process are, for example, commercially available from SENSOR ELECTRONIC TECHNOLOGY, INC., South Carolina, U.S.A. under the trade mark UV TOP®.

20

In the present process a single UV LED or a plurality of UV LEDs, for example several individual UV LEDs that are clustered into a bigger system, may be used.

It is evident from the molar absorbance spectrum of the 7-dehydrosterols, e.g. 7-DHC, that
25 the preferred wavelength for effecting the photolysis reaction lies between 270 and 300 nm. The UV spectrum of 7-DHC shows a first dominant peak at about 282 nm and a second dominant peak at about 296 nm, those wavelengths representing the optimum wavelengths for the irradiation of 7-DHC. As all the 7-dehydrosterols have the same chromophor (the 5,7-diene system) their UV spectra are very similar. Thus, the UV LEDs
30 for use in the present process preferably emit UV light having a wavelength between 250 and 320 nm, more preferably between 270 and 300 nm. In one embodiment of the present invention the UV LEDs emit UV light having a wavelength of $280 \text{ nm} \pm 10 \text{ nm}$.

Typically, the 7-dehydrosterol to be irradiated is dissolved in a suitable solvent. Any solvent, preferably organic solvent, that does not absorb or has low absorbency for UV radiation above 240 nm and sufficiently dissolves the 7-dehydrosterol or the derivative of interest can be used. Examples include lower alcohols such as methanol, ethanol and 1-propanol; simple ethers, such as diethylether; cyclic ethers, such as tetrahydrofuran and 1,4-dioxane; unsymmetrical ethers, such as tert-butyl methyl ether; alkanes, such as n-hexane, and mixtures thereof. The preferred solvent used to convert the 7-dehydrosterol, especially 7-DHC, to the previtamin D is 1-propanol or a mixture of methanol and n-hexane. Typically, the concentration of the 7-dehydrosterol, e.g. 7-DHC, in the solvent is within the range of from 1 to 10 % by weight, preferably from 5 to 10 % by weight.

The irradiation temperature does not effect the photochemical reaction. Generally, the temperature is selected to provide solubility of the 7-dehydrosterol in the solvent employed. Depending on the type of solvent and specific 7-dehydrosterol employed, the irradiation is typically performed at a temperature within the range of from -20 to 60°C, preferably from 0 to 50°C, more preferably from 10 to 45°C, and most preferably from 25 to 45°C. An irradiation temperature within the preferred ranges is typically used in combination with the preferred solvents mentioned above.

20

The irradiation may be performed in the presence of a free radical scavenger, e.g. tert-butyl hydroxy anisole (BHA), to minimize degradation of previtamin D.

The present photochemical process may be conducted in any reactor suitable for photoreactions. The reactor design is not critical for the present invention. For example, the 7-dehydrosterol may be irradiated in a falling-film reactor, especially suitable for production of previtamin D on an industrial scale. However, it is also possible to irradiate very small amounts of the 7-dehydrosterol in a microreactor. The use of a microreactor in combination with a small UV LED enables production of small quantities of previtamin D.

30

For example in the case of previtamin D₃ preparation, 7-DHC, previtamin D₃ and the unwanted byproducts lumisterol and tachysterol form a photochemical equilibrium.

Theoretical calculations based on a simplified kinetic model for this system and using literature data concerning the wavelength dependency of the quantum yield and the molar absorption coefficients of the components involved lead to a graph of the concentration of each component versus reaction time. Fig. 1 shows the effect of a wavelength of 254 nm on the reaction course and is representative for radiating with a mercury medium-pressure lamp emitting a line spectrum with an intensive line at 254 nm (effect of the other emission lines omitted). Fig. 2 shows the effect of a wavelength of 282 nm on the reaction course and is representative for radiating with UV LED(s). A similar graph is obtained in case of irradiation at a wavelength of about 296 nm which corresponds to the second dominant peak in the absorption spectrum of 7-DHC. It is evident that even at high conversion of 7-DHC the theoretical selectivity for previtamin D₃ is still relatively high (> 50 %) at a wavelength of 282 nm whereas tachysterol will become the main product at high conversion of 7-DHC at a wavelength of 254 nm. It is thus a significant advantage of the present process that a UV LED having the matching wavelength to favor the production of previtamin D₃, even at high conversion, can be employed. Nevertheless, it may be preferred to conduct the present process at very low conversion of 7-DHC, e.g. not more than 5 %, in order to obtain a very high selectivity for previtamin D₃, e.g. at least 96 %. Of course, slightly higher conversions will result in slightly lower, though still high selectivities for previtamin D₃, e.g. a 7-DHC conversion of not more than 6 % results in a previtamin D₃ selectivity of at least 95 % and a 7-DHC conversion of not more than 7 % results in a previtamin D₃ selectivity of at least 94 %. It is within the ordinary skill of the expert involved to decide whether the process should be conducted at high or low conversion. He will weigh the advantage of very high selectivity against the disadvantage of higher costs to recycle the unreacted 7-DHC at lower conversion.

25

Presently available UV LEDs typically have a low UV output, e.g. about 10 mW per individual LED. The small size of an individual UV LED allows clustering into bigger systems thereby providing enough UV energy density for a commercial scale production. The still relatively low UV output of the UV LED clusters results in relatively long irradiation times that are typically used in the present process. However, it is expected that UV LEDs having a higher UV output will be available in the future, thus allowing shorter irradiation times.

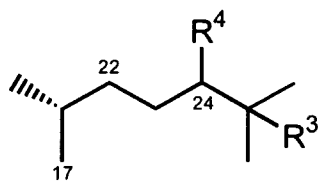
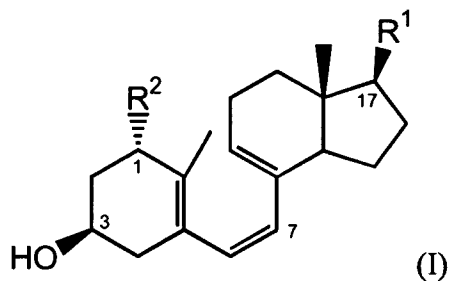
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In one embodiment of the present invention the process further comprises recovering the previtamin D. Suitable methods to recover the previtamin D are known to the person skilled in the art and include commonly used separation procedures, such as for example
5 crystallization of the unreacted 7-dehydrosterol, e.g. 7-DHC, and subsequent solid/liquid separation; chemical conversion of byproducts, e.g. tachysterol; and industrial chromatography. It is a matter of fact that the purification of the previtamin D is much easier if it is obtained with high selectivity as it is possible by employing the present process.

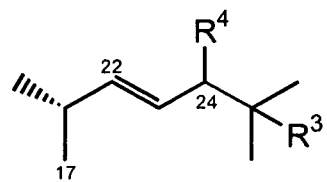
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The present invention is also directed to the preparation of a vitamin D or a derivative thereof by thermal rearrangement of the previtamin D or the corresponding derivative thereof. The thermal conversion to the vitamin D is a sigmatropic 1,7-hydrogen shift from C-19 to C-9 and is done at a suitable point in the process after the photochemical reaction;
15 for example, the thermal conversion may be performed before or after the separation of the 7-dehydrosterol. The thermal rearrangement of the previtamin D during photolysis should be avoided because the vitamin D itself (or its derivatives) can also undergo photoconversion which results in further unwanted byproducts.

20 The process in accordance with the present invention also includes the preparation of vitamin D derivatives and previtamin D derivatives by irradiating the corresponding derivatives of the 7-dehydrosterols. Derivatives of 7-dehydrosterol include all analogous compounds having the 4-ring steroid nucleus as shown in formula (II) wherein the 9,10-bond can be cleaved photochemically to give the corresponding (Z)-triene. Such
25 analogous compounds may have any additional substituents thereon, provided the substituents do not interfere in the photochemical conversion. All statements made within this application equally apply to the derivatives of vitamins D, previtamins D and 7-dehydrosterols. Typically, the derivatives include but are not limited to hydroxylated and ester derivatives. More specifically the derivative of a previtamin D is an ester derivative
30 or a derivative according to formula (I)



(i) or



(ii),

wherein R^1 is

R^2 is H, a hydroxy or acyloxy group;

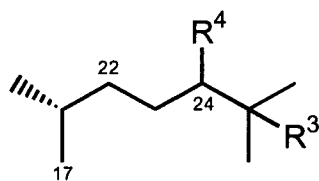
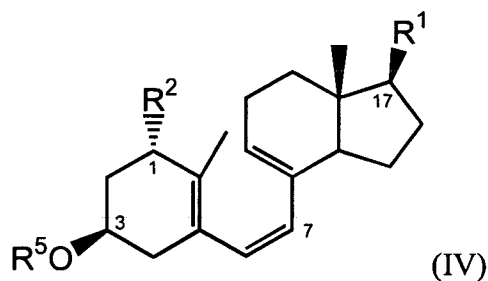
5 R^3 is H, a hydroxy or acyloxy group; and

R^4 is H, CH_3 , C_2H_5 , a hydroxy or acyloxy group;

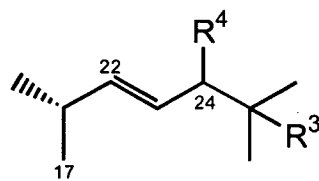
provided that least one of R^2 , R^3 and R^4 is a hydroxy or acyloxy (ester) group.

The term "ester derivatives" or "esters" means derivatives wherein the 3-OH group is

10 esterified with an organic acid and includes (a) previtamin D esters according to formula (IV)



(i) or



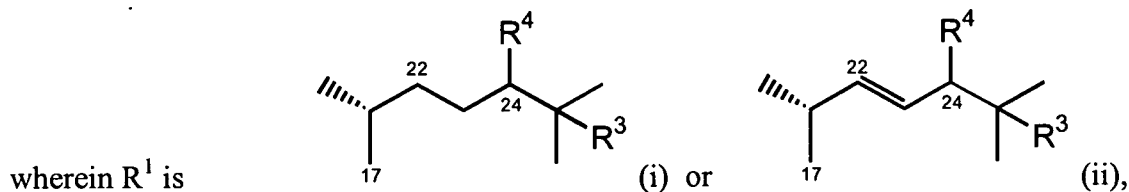
(ii),

15 wherein R^1 is

R^2 is H; R^3 is H; R^4 is H, CH_3 or C_2H_5 , and

R^5 is an acyl group, preferably having 1 to 10 carbon atoms, e.g. acetyl and benzoyl;

as well as (b) esters of previtamin D derivatives, the esters being represented by formula (IV) above



R² is H, a hydroxy or acyloxy group;

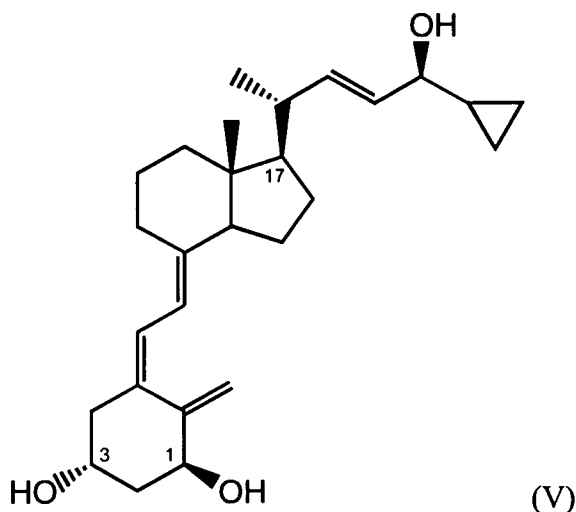
5 R³ is H, a hydroxy or acyloxy group;

R⁴ is H, CH₃, C₂H₅, a hydroxy or acyloxy group; and

R⁵ is an acyl group, preferably having 1 to 10 carbon atoms, e.g. acetyl and benzoyl; provided that least one of R², R³ and R⁴ is a hydroxy or acyloxy (ester) group.

- 10 Examples of derivatives of previtamin D/vitamin D include 1 α -hydroxy previtamin D₃/1 α -hydroxy vitamin D₃ (1 α -hydroxycholecalciferol or alfacalcidol); 1 α -hydroxy previtamin D₂/1 α -hydroxy vitamin D₂ (1 α -hydroxyergocalciferol); 25-hydroxy previtamin D₃/25-hydroxy vitamin D₃ (25-hydroxycholecalciferol or calcidiol or calcifediol or Hy-D®); 25-hydroxy previtamin D₂/25-hydroxy vitamin D₂ (25-hydroxyergocalciferol);
- 15 1 α ,25-dihydroxy previtamin D₃/1 α ,25-dihydroxy vitamin D₃ (1 α ,25-dihydroxycholecalciferol, calcitriol); 1 α ,25-dihydroxy previtamin D₂/1 α ,25-dihydroxy vitamin D₂ (1 α ,25-dihydroxyergocalciferol); 1 α ,24-dihydroxy previtamin D₃/1 α ,24-dihydroxy vitamin D₃ (1 α ,24-dihydroxycholecalciferol or tacalcitol); 24R,25-dihydroxy previtamin D₃/24R,25-dihydroxy vitamin D₃ (24R,25-dihydroxycholecalciferol or
- 20 hydroxycalcidiol); esters thereof and esters of previtamin D₂/vitamin D₂ and previtamin D₃/vitamin D₃ themselves.

Another vitamin D/previtamin D derivative of interest that can be prepared according to the present invention is calcipotriol according to formula (V)



and its corresponding previtamin. The previtamin is prepared by irradiating its corresponding provitamin.

5

It is a matter of fact that a specific previtamin D derivative is prepared by irradiating the corresponding derivative of the 7-dehydrosterol: For example 25-hydroxy previtamin D₃ is prepared by irradiating the 25-hydroxy derivative of 7-DHC (25-hydroxy provitamin D₃). Similarly, an ester of previtamin D₃ is prepared by irradiating the corresponding ester derivative of 7-DHC.

10

Using UV LEDs in accordance with the present invention it is possible to employ a radiation source which emits almost exclusively in the optimum wavelength range for the photochemical synthesis of previtamin D₃. The performance of the UV LED is comparable to the XeBr excimer type light source and it is superior to that of the presently used mercury medium-pressure lamps emitting polychromatic radiation. However, UV LEDs have a number of benefits over the XeBr excimer light source and are therefore well-suited light sources for the synthesis of previtamin D₃ on an industrial scale: They operate at low voltage and at direct current and thus there is no need for expensive high frequency power supply with necessary electromagnetic shielding as it is necessary for a XeBr excimer light source; a simple DC low voltage 5 –10 V power supply may be used for UV LEDs. This is also favorable compared to a 2-3 kV AC power supply required for a mercury medium-pressure lamp. UV LEDs have a very long lifetime, often more than 10.000, preferably more than 50.000 up to 100.000 h, with a constant UV power output

20

(compared to a XeBr excimer light source suffering a 30% power loss over 1500 h and to a mercury medium-pressure lamp having a lifetime of about 10.000 h). The energy efficiency of UV LEDs is superior to that of XeBr excimer light sources or mercury medium-pressure lamps. UV LEDs can be employed in small photochemical units with a small UV power in a small reactor, e. g. for on-site on-demand production.

The invention will now be further illustrated in the following non-limiting example.

EXAMPLES

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In the following experiments a 1 weight % solution of 7-DHC in 1-propanol is irradiated by UV TOP® 280 (available from SENSOR ELECTRONIC TECHNOLOGY, INC. South Carolina, U.S.A) comprising 8 to 10 individual UV LEDs that are clustered together in a cone and emit UV light having a wavelength of $280 \text{ nm} \pm 10 \text{ nm}$. The experiments are conducted in a microreactor available from Mikroglas Chemtech GmbH, Mainz, Germany. The microreactor is schematically depicted in Fig. 3 and consists of a quartz panel adhered to a glass panel. A small rhomboid cavity comprising an inlet and an outlet and having a height of $50 \text{ }\mu\text{m}$ and a total volume of about 19 mm^3 has been etched into the glass panel. The experimental setup is shown in Fig. 4 and contains the described microreactor (1), the LED light source (8) with the electrical DC power supply (9) and a membrane piston pump (7) with volumetric flow rate between 45-75 ml/h at 0.6 bar pressure. The cycle loop volume is measured with 45 cm^3 . If necessary heat exchanger (4) can be used to maintain the temperature. Before the pump (7) a sample can be taken out at sample point (5). (2) and (3) designate the microreactor inlet and outlet, respectively. The 7-DHC solution may be filled in through sample point (5) and drained through drain port (6).

All experiments are done in a dark room without daylight. The 7-DHC solution is circulated through the cavity and irradiated by the LED light source through the quartz panel. The UV LED has a UV power output of about 2 mW meaning a UV flux of about 5 W/m^2 at the irradiated surface. Overirradiation effects do not occur at such low UV flux. Due to the low UV flux the experiments are performed with a long irradiation time.

The equipment is rinsed with 1-propanol, filled with 36 g 7-DHC solution and the cycling loop is started with 45 – 75 ml/h, pressure of the pump equal or lower than 0.6 bar at 26-29°C. Two experiments A and B are performed and the experimental conditions thereof are shown in Table 2. Samples are taken at the times indicated in Tables 3 and 4. The typical reaction products previtamin D₃ and vitamin D₃ and the byproducts lumisterol and tachysterol were detected by HPLC analysis. The component eluting at the retention time of previtamin D₃ was positively identified as previtamin D₃ by its typical UV absorption spectrum.

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Table 2: Experiments A and B, experimental conditions

Experiment		A	B
Circulation flow	ml/h	70	45
Temperature	°C	28	28
Solvent		1-propanol	1-propanol
[7-DHC]	wt. %	1.0	1.0
[BHA]	wt. %	0.0	0.1

BHA (tert-butyl hydroxy anisole) is a free radical scavenger that is added to minimize degradation of previtamin D₃.

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The following abbreviations are used in Tables 3 and 4:

DHC: 7-DHC
 20 P: previtamin D₃
 D: vitamin D₃
 T: tachysterol
 L: lumisterol
 conv.: conversion
 25 sel.: selectivity

In both experiments a significant 7-DHC conversion is reached and the obtained selectivity towards previtamin D₃ and vitamin D is comparable to that of an XeBr excimer light source and superior to that of a mercury medium-pressure lamp (Hg MD lamp).

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Table 3: Experiment A, results

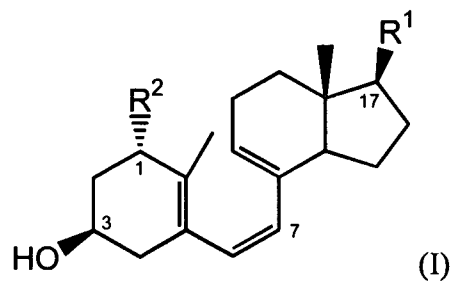
t (min)	[DHC] (wt. %)	[P] (wt. %)	[D] (wt. %)	[T] (wt. %)	[L] (wt. %)	Sum (wt. %)	Conv. %	Sel. (P+D) %
0	0.8637			0.0014		0.8651		
135	0.8471	0.0085	0.0009		0.0002	0.8567	1.12	97.92
255	0.8411	0.0187	0.0018	0.0001		0.8617	2.39	99.51
375	0.8383	0.0185	0.0023			0.8591	2.42	100.00
495	0.8279	0.0206	0.0029	0.0004		0.8518	2.81	98.33

Table 4: Experiment B, results

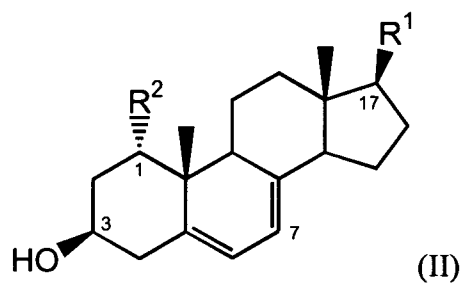
t (min)	[DHC] (wt. %)	[P] (wt. %)	[D] (wt. %)	[T] (wt. %)	[L] (wt. %)	Sum (wt. %)	Conv. %	Sel. (P+D) %
0	0.9331	0.0013		0.0015		0.9359		
170	1.0464	0.0195	0.0031	0.0002	0.0005	1.0697	2.18	97.00
290	0.8542	0.0283	0.0036	0.0003		0.8864	3.63	99.07
410	0.8330	0.0376	0.0042	0.0005		0.8753	4.83	98.82
470	0.8362	0.0416	0.0049	0.0015		0.8842	5.43	96.88

CLAIMS

1. A photochemical process for the preparation of a previtamin D according to formula (I)

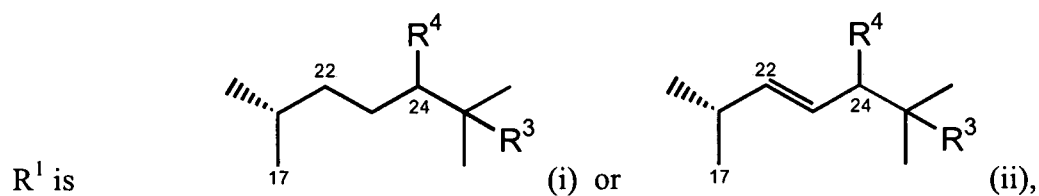


or a derivative thereof from a 7-dehydrosterol according to formula (II)



or a corresponding derivative thereof,

wherein in formulae (I) and (II)

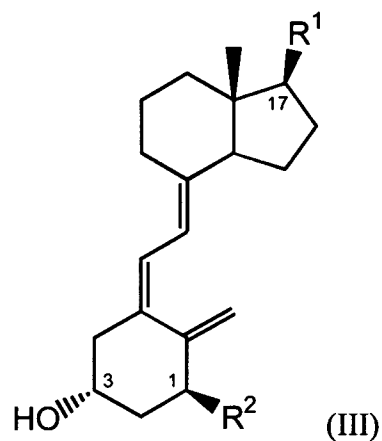


R² is H; R³ is H; and R⁴ is H, CH₃ or C₂H₅,

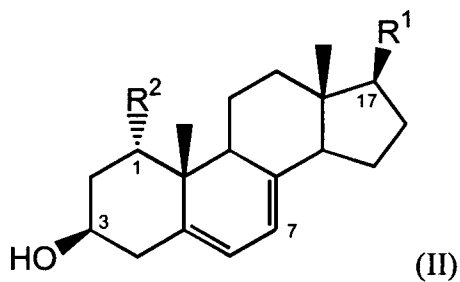
comprising irradiating the 7-dehydrosterol or the derivative thereof with UV light emitting diode(s) (UV LED(s)).

2. The process according to claim 1 wherein the 7-dehydrosterol is either ergosterol or 7-dehydrocholesterol, the ergosterol being converted to previtamin D₂ and the 7-dehydrocholesterol being converted to previtamin D₃.
3. The process according to claim 2 wherein the 7-dehydrosterol is 7-dehydrocholesterol that is converted to previtamin D₃.
4. The process according to claim 1 wherein the derivative of a previtamin D is an ester of a previtamin D or is a derivative according to formula (I) wherein R¹, R², R³ and R⁴ are defined as in claim 1 with the modification that at least one of R², R³ and R⁴ is a hydroxy or acyloxy group.
5. The process according to claim 1 wherein the derivative of a previtamin D is selected from the group consisting of previtamin of calcipotriol, 1 α -hydroxy previtamin D₃, 1 α -hydroxy previtamin D₂; 25-hydroxy previtamin D₃, 25-hydroxy previtamin D₂, 1 α ,25-dihydroxy previtamin D₃, 1 α ,25-dihydroxy previtamin D₂, 1 α ,24-dihydroxy previtamin D₃, 24R,25-dihydroxy previtamin D₃, acyloxy previtamin D₃, esters thereof and esters of previtamin D₂ and D₃.
6. The process according to claim 5 wherein the derivative of a previtamin D is 25-hydroxy previtamin D₃.
7. The process according to any of the preceding claims wherein the UV LED(s) emit UV light having a wavelength between 270 and 300 nm.
8. The process according to any of the preceding claims wherein the irradiation is performed in a falling-film reactor.
9. The process according to any of the preceding claims further comprising recovering the previtamin D or the derivative thereof.

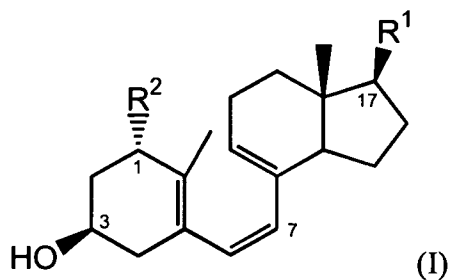
10. A process for the preparation of a vitamin D according to formula (III)



or a derivative thereof from a 7-dehydrosterol according to formula (II)

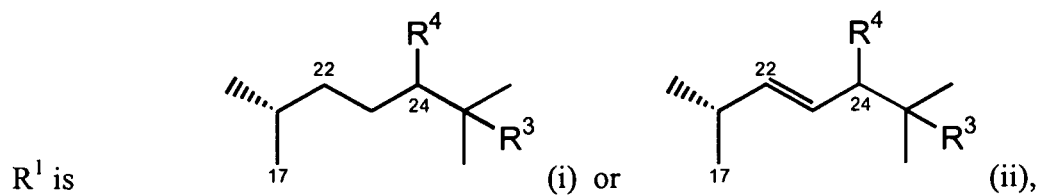


or a corresponding derivative thereof comprising preparing the previtamin D according to formula (I)



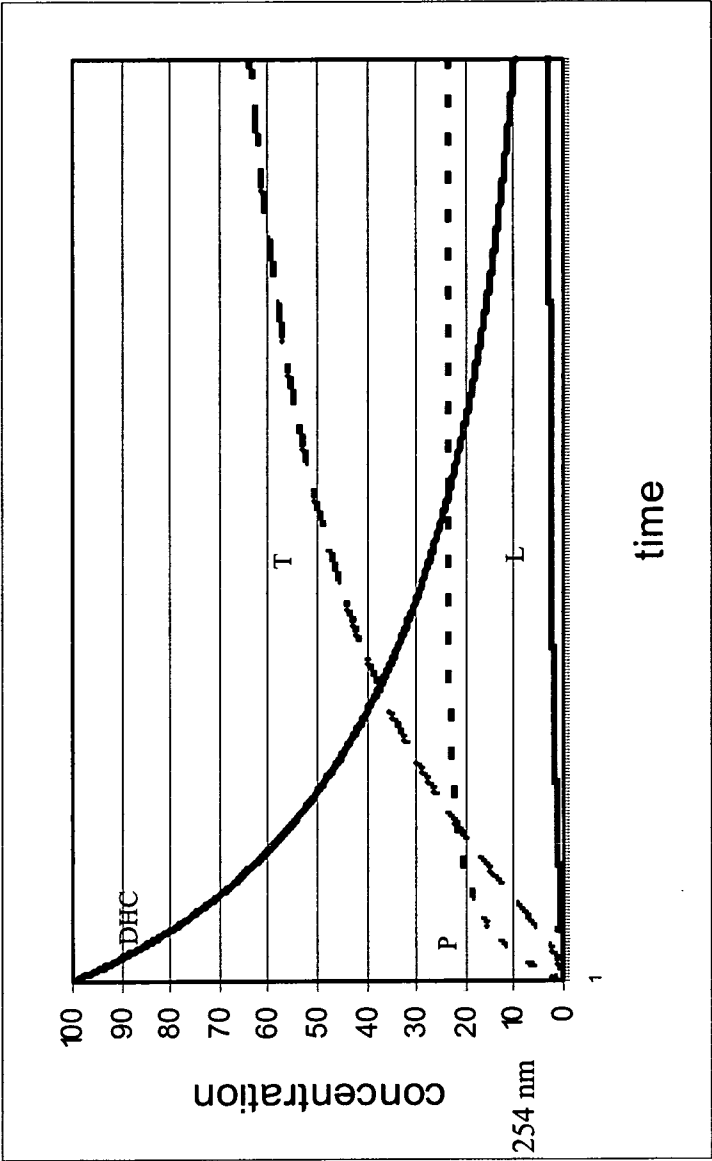
or the corresponding derivative thereof,

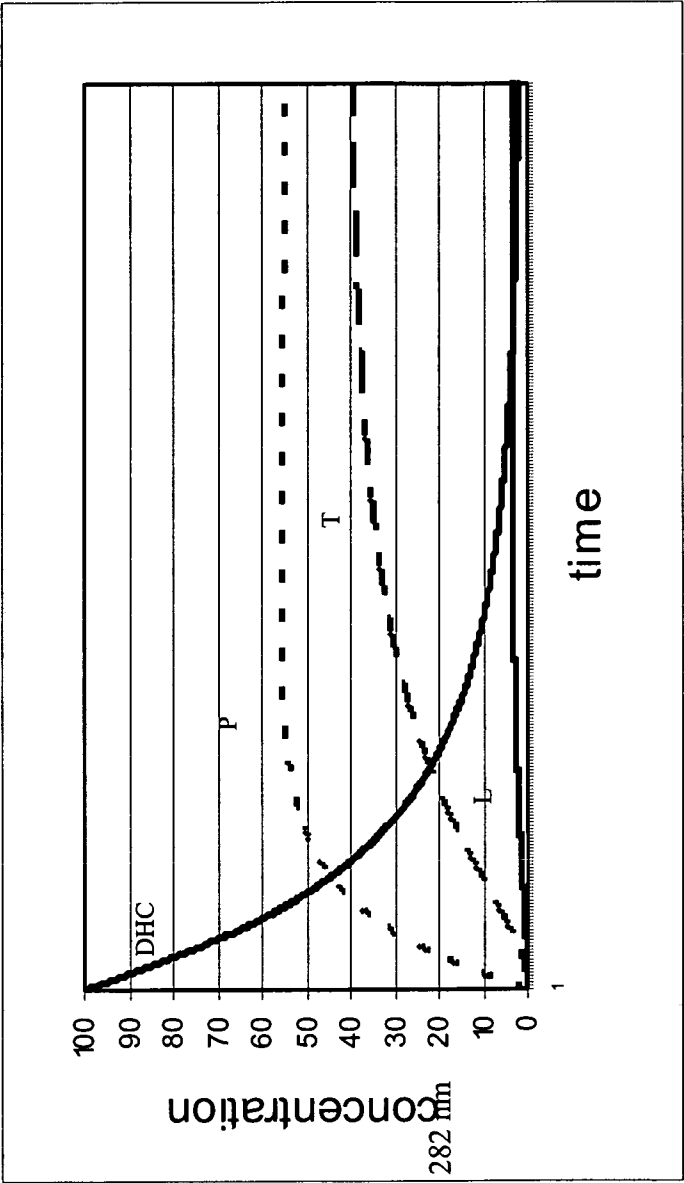
wherein in formulae (I), (II) and (III)



R² is H; R³ is H; and R⁴ is H, CH₃ or C₂H₅,

according to the process of any of claims 1 to 9 and converting the previtamin D or the derivative thereof to the vitamin D or the derivative thereof by thermal rearrangement.





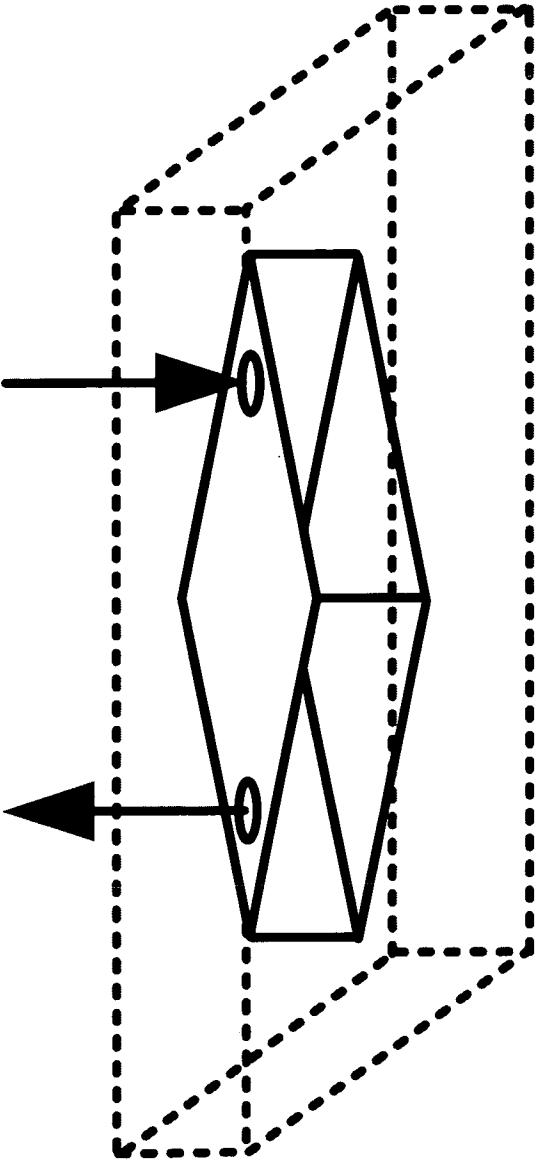


Fig. 3

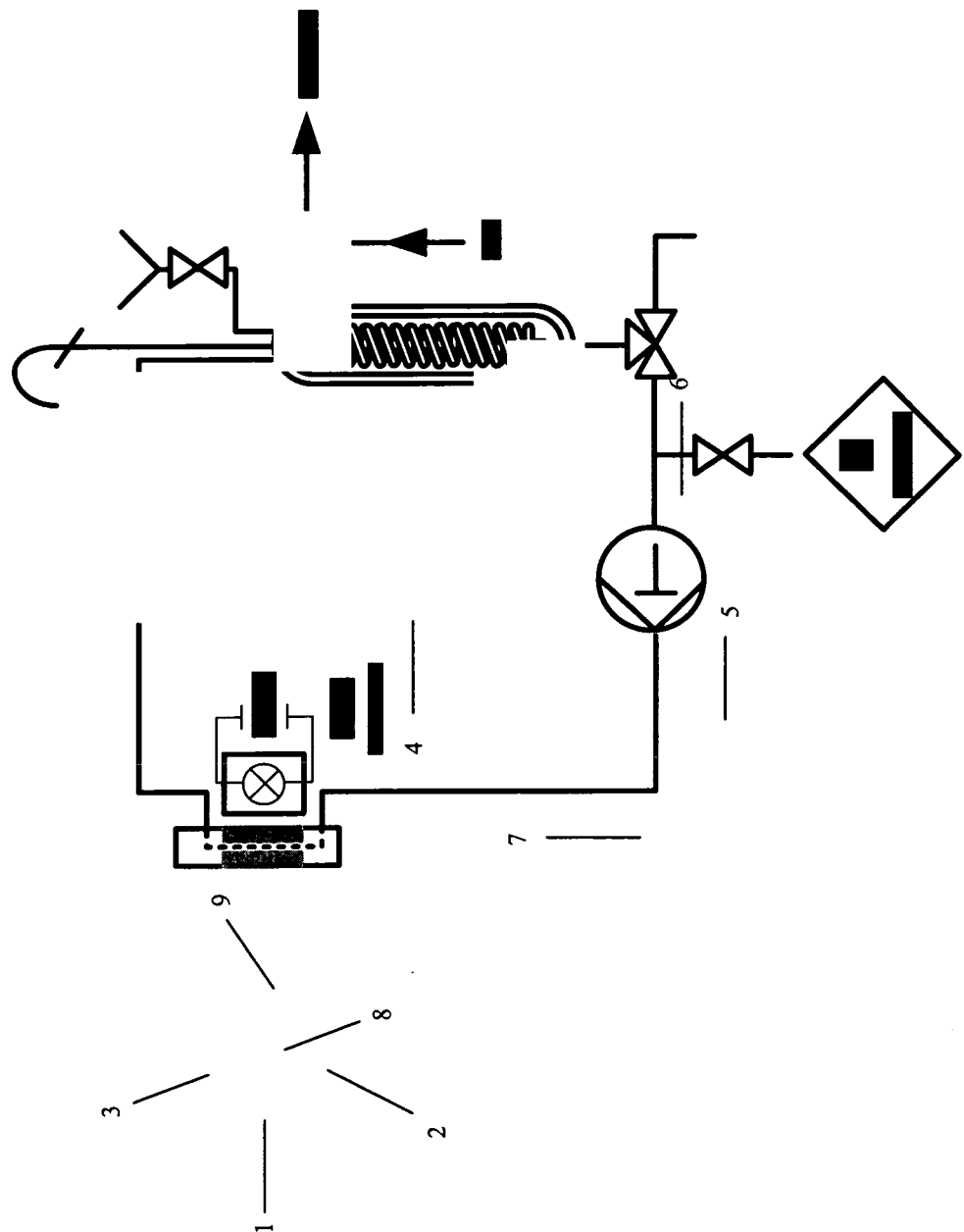


Fig. 4