Date	March 25, 2016	Court	Intellectual Property High Court, Special Division
Case number	2015 (Ne) 10014		

– A case in which, with regard to a manufacturing process of a preparation, etc., the court upheld a claim for an injunction against the import and sale of the preparation, etc. and other claims based on a patent right on the grounds that said process is equivalent to a patented invention.

– A case in which the court ruled as follows: The essential part of a patented invention in the first requirement of the doctrine of equivalents means a characteristic part, which constitutes a unique technical idea that is not seen in prior art, in the statements in the scope of claims of the patented invention, and the essential part should be found based on the statements in the scope of claims and the description, in particular, the comparison with prior art stated in the description and the degree of contribution.

– A case in which the court ruled as follows: The fact that the applicant did not state another structure, which a person ordinarily skilled in the art can easily conceive of as of the filing date as one that is substantially identical with the structure stated in the scope of claims, in the scope of claims only because of the existence of such other structure cannot be considered to fall under the "special circumstances" in the fifth requirement of the doctrine of equivalents; however, if the applicant is objectively and externally recognized as having recognized another structure that is outside the scope of claims as a replacement for a different part in the structure stated in the scope of claims as of the filing date, the applicant's failure to state said other structure in the scope of claims can be considered to fall under the "special circumstances" in the fifth requirement of the doctrine of equivalents.

Reference: Article 100, paragraphs (1) and (2), Article 70, paragraph (1), and Article 29, paragraph (2) of the Patent Act

Number of related rights, etc.: Patent No. 3310301 (the "Patent"), Invalidation Trial No. 2013-800080

Summary of the judgment

1. Background

The appellee (plaintiff in the first instance), who holds the patent right in question (the "Patent Right") for an invention titled "intermediates for the synthesis of vitamin D and steroid derivatives and process for preparation thereof," alleged that the manufacturing process (the "Appellant's Process") of the maxacalcitol preparations, etc. (the "Appellants' Products") imported and sold by the appellants (defendants in the first instance) is equivalent to the invention claimed in Claim 13 of the Patent (the

"Corrected Invention") and that the sale, etc. of the Appellants' Products constitutes infringement of the Patent Right. Based on this allegation, the appellee filed this action against the appellants to seek an injunction against the import, assignment, etc. of the Appellants' Products and disposal thereof.

Briefly speaking, the Corrected Invention is a process for preparing a compound wherein an intermediate is prepared by having the starting material react with a specific reagent and the objective substance is prepared by treating the intermediate with a reducing agent. The Appellant's Process fulfills the constituent features pertaining to the reagent and objective substance of the Corrected Invention (Constituent Features [A], [B-2], [D], and [E]), but does not fulfill the constituent features pertaining to the starting material and intermediate of the Corrected Invention (Constituent Features [B-1], [B-3], and [C]) in that the carbon skeletons of the starting material and the intermediate do not have cis-form vitamin D structures but have trans-form vitamin D structures that are the geometric isomers thereof.

In relation to the doctrine of equivalents, the five requirements for applying the doctrine of equivalents are indicated in the judgment of the Third Petty Bench of the Supreme Court of February 24, 1998, 1994 (O) 1083 ("Ball spline bearing" case). In this case, the parties disputed whether the doctrine of equivalents is established through specific application of the five requirements. In addition, the appellants alleged that the Patent should be invalidated by a trial for patent invalidation.

The court of prior instance recognized that the Appellant's Process is equivalent to the Corrected Invention and determined that the patent for the Corrected Invention is not recognized as one that should be invalidated by a trial for patent invalidation. Based thereon, the court of prior instance upheld all of the appellee's claims. Therefore, dissatisfied with this, the appellants filed an appeal (the "Appeal").

2. Content of this judgment

In this judgment, the court ruled as summarized below, and recognized that the Appellant's Process is equivalent to the Corrected Invention. The court also determined that there is no reason for all of the grounds for invalidation alleged by the appellants. Based thereon, the court upheld the judgment in prior instance and dismissed the Appeal.

(1) Regarding the burden of proving the fulfillment of the five requirements for the doctrine of equivalents

"Regarding the burden of alleging and proving the fulfillment of the first to fifth requirements, it is reasonable to understand as follows, taking into account that the doctrine of equivalents should be applied within the scope of those that are found to be

easily conceived of by a person ordinarily skilled in the art as one that is substantially identical with the statements in the scope of claims beyond the scope of the literal interpretation of said statements: a person who alleges that the subject product, etc. is equivalent to a patented invention should be considered to have the burden of allegation and proof for the first to third requirements, which are the facts required for the subject product, etc. to be recognized as falling within said scope, while a person who denies the application of the doctrine of equivalents in relation to the subject product, etc. has the burden of allegation and proof for the fourth and fifth requirements, which are related to the cases where the application of the doctrine of equivalents should be eliminated, even if the subject product, etc. is within the aforementioned scope."

(2) Regarding the first requirement of the doctrine of equivalents (non-essential part)

The first requirement of the doctrine of equivalents in the Supreme Court judgment on the "Ball spline bearing" case is that even if the structure stated in the scope of claims contains any part that is different from that of the product manufactured, etc. by the other party or the process used thereby, said part is not the essential part of the patented invention.

A. "The substantial value of an invention which the Patent Act intends to protect exists in the disclosure, with a specific structure, to society of a means for solving a technical problem that could not have been solved by prior art, which is based on a unique technical idea that is not seen in prior art. Therefore, the essential part of a patented invention should be understood as the characteristic part which constitutes a unique technical idea that is not seen in prior art in the statements in the scope of claims of the patented invention.

The aforementioned essential part should be found by first understanding the problem to be solved and means for solving the problem of the patented invention … and its effects … based on the statements in the scope of claims and the description and then determining the characteristic part that constitutes a unique technical idea that is not seen in prior art in the statements in the scope of claims of the patented invention. That is, taking into account that the substantial value of a patented invention is defined depending on the degree of contribution in comparison with prior art in the relevant technical field, the essential part of a patented invention should be found based on the statements in the scope of claims and the description, in particular, through comparison with prior art stated in the description. [i] If the degree of contribution of the patented invention is considered to be more than that of prior art, the patented invention is found as a generic concept in relation to part of the statements in the scope of claims …. [ii] If the degree of contribution of the patented invention is evaluated as not much more than

prior art, the patented invention is found to have almost the same meaning as stated in the scope of claims.

However, if the statement of the problem, which is described as one that prior art could not solve, in the description is objectively insufficient in light of prior art as of the filing date …, a characteristic part which constitutes a unique technical idea of the patented invention that is not seen in prior art should be found also in consideration of prior art that is not stated in the description. In such cases, the essential part of the patented invention is closer to the statements in the scope of claims compared to the cases where it is found only based on the statements in the scope of claims and the description, and the scope of application of the doctrine of equivalents is considered to be narrower.

In addition, in determining the fulfillment of the first requirement, that is, whether a difference from the subject product, etc. is a non-essential part, it is not appropriate to first divide the constituent features stated in the scope of claims into essential parts and non-essential parts and then consider that the doctrine of equivalents is not applicable to all of the constituent features that fall under essential parts, but it is necessary to first determine whether the subject product, etc. commonly has the essential part of the patented invention determined as mentioned above and then consider a difference not to be an essential part if the subject product, etc. is recognized as having said essential part. Even if the subject product, etc. has a difference other than the characteristic part that constitutes a unique technical idea that is not seen in prior art, this fact does not become a reason for denying the fulfillment of the first requirement."

B. "The Corrected Invention makes it possible to prepare its objective substance through a new preparation route that is not available in prior art, and its degree of contribution to prior art is large. … The Corrected Invention made it possible to industrially produce maxacalcitol for the first time. …

In light of the problem to be solved and means for solving the problem of the Corrected Invention and its effects as mentioned above, the essential part of the Corrected Invention … is recognized as existing in finding that a side chain having an epoxy group by an ether bond can be introduced through one step by having an alcohol compound at position 20 of a vitamin D structure or steroid ring structure react with an epoxy hydrocarbon compound of Constituent Feature [B-2] which has an eliminating group at its end and in making it possible to introduce a maxacalcitol side chain into an alcohol compound at position 20 of a vitamin D structure or steroid ring structure through a new route of first going through an intermediate that is a vitamin D structure or steroid ring structure into which a side chain having an epoxy group by an ether bond

is introduced through such one step and then opening the ring of the epoxy group of the side chain. …

The Appellant's Process … is considered to have the characteristic part that constitutes a unique technical idea that is not seen in prior art in the statements in the scope of claims of the Corrected Invention.

On the other hand, in the Appellant's Process, the point that a vitamin D structure that corresponds to "Z" of the starting material and the intermediate, which is a difference from the Corrected Invention, is not a cis form but a trans form … is not the essential part of the Corrected Invention.

Therefore, the Appellant's Process is recognized as fulfilling the first requirement of the doctrine of equivalents."

(3) Regarding the second requirement of the doctrine of equivalents (replaceability)

"In … Starting Material A and Intermediate C in the Appellant's Process, the carbon skeleton that corresponds to Z of the Corrected Invention is a trans-form vitamin D structure, and the Appellant's Process differs from the Corrected Invention in that the carbon skeleton of Z of the starting material … and intermediate … in the Corrected Invention is a cis-form vitamin D structure. However, the starting materials and intermediates in both the Appellant's Process and the Corrected Invention have the same function and effect of being able to prepare maxacalcitol by a process of going through an intermediate that is a vitamin D structure into which a side chain having an epoxy group by an ether bond through one step by having an alcohol compound at position 20 of a vitamin D structure react with the same epoxy hydrocarbon compound. It is recognized that the same purpose as that of the Corrected Invention can be achieved and the same function and effect are produced even if the aforementioned starting material and intermediate having a cis-form vitamin D structure in the Corrected Invention are replaced with the aforementioned starting material and intermediate having a trans-form vitamin D structure in the Appellant's Process. … Therefore, the Appellant's Process is recognized as fulfilling the second requirement of the doctrine of equivalents."

(4) Regarding the third requirement of the doctrine of equivalents (easiness of replacement)

In this judgment, the court determined that the Appellant's Process is one that a person ordinarily skilled in the art could have easily conceived of based on the Corrected Invention as of the time of infringement of the Patent Right and found that the Appellant's Process fulfills the third requirement of the doctrine of equivalents.

(5) Regarding the fourth requirement of the doctrine of equivalents (whether the subject

process can be easily presumptively conceived of)

In this judgment, regarding the fourth requirement of the doctrine of equivalents, the court cited the judgment in prior instance and determined that the Appellant's Process is not recognized as one that can be easily presumptively conceived of.

(6) Regarding the fifth requirement of the doctrine of equivalents (special circumstances)

The fifth requirement of the doctrine of equivalents mentioned in the Supreme Court judgment on the "Ball spline bearing" case is that there are no special circumstances, such as the fact that the subject product, etc. falls under those that are intentionally excluded from the scope of claims in the patent application procedures for the patented invention.

A. "The substantial value of a patented invention extends to the art which a person ordinarily skilled in the art can easily conceive of based on the structure stated in the scope of claims as one that is substantially identical with said structure, and third parties should expect this. Therefore, if the subject product, etc. is identical with a patented invention in the essential part, purpose, and function and effect, and is one that a person ordinarily skilled in the art can easily conceive of based on the patented invention, the subject product, etc. can be in principle considered to be equivalent to the patented invention. However, with regard to a structure which was once approved by the patentee as not falling under the technical scope of the patented invention (for example, in the case where the applicant intentionally excluded it from the scope of claims in the patent application procedures) or for which the patentee has taken action that is externally considered as such approval, the patentee is not permitted to subsequently make an allegation that goes against said approval or action in light of the doctrine of estoppel. Therefore, if there are such special circumstances, the application of the doctrine of equivalents is exceptionally denied (see the aforementioned Supreme Court judgment on the "Ball spline bearing" case).

(A) In this regard, even if there is another structure that is outside the scope of claims, which a person ordinarily skilled in the art can easily conceive of as of the filing date as one that is substantially identical with the structure stated in the scope of claims and the applicant could thus have also easily conceived of said another structure as of the filing date, this fact alone cannot serve as a reason for alleging that the applicant's failure to state said another structure in the scope of claims falls under the "special circumstances" in the fifth requirement of the doctrine of equivalents.

This is because of the following reasons. [i] As mentioned above, the substantial value of a patented invention extends to the art that a person ordinarily skilled in the

art can easily conceive of as one that is substantially identical with the structure stated in the scope of claims based on said structure even if it is a structure other than the structure stated in the scope of claims. This principle does not change at all in relation to any art that a person ordinarily skilled in the art can easily conceive of as of the filing date. If it is not at all permitted to allege the doctrine of equivalents only for the reason that a structure could have been easily conceived of by a person ordinarily skilled in the art as of the filing date, the scope to which the substantial value of a patented invention extends will differ from the aforementioned scope. [ii] In addition, taking into account that an applicant should first disclose his/her invention to the public by stating it in the description and then clearly specify the scope of the exclusive right in the scope of claims, the applicant should state the scope of claims in just proportion within the scope of the invention disclosed in the description while fulfilling the requirements, such as the support requirements under Article 36, paragraph (5) of the Patent Act and paragraph (6), item (i) of said Article and the clarity requirements under item (ii) of said paragraph. However, in some cases, it is considered to be harsh to require the applicant to prepare the scope of claims that contains all the expected infringing embodiments and the description supporting such scope of claims within a limited period of time, taking into account the fact that, under the first-to-file system, applicants are generally required to prepare the scope of claims and the description and file applications within a limited period of time. On the other hand, in many cases, a third party who has received the disclosure of an invention as described in the description pertaining to a patent application can easily conceive of one which has the essential part of the patented invention but part of which is not included in the literal interpretation of the scope of claims, based on the statements in the scope of claims and the description, etc., during the duration of the patent. The doctrine of equivalents is applicable because if any third party can easily escape from the exercise of rights by the patentee, including an injunction, through replacement of the non-essential part of the patented invention, incentive to invent in society in general will be diminished, which not only goes against the purpose of the Patent Act, that is, contributing to the development of industry through protection and encouragement of inventions, but also goes against social justice and results in running counter to the principle of equity. In light of the aforementioned situation, etc., even if a person ordinarily skilled in the art could have easily conceived of another structure that is outside the scope of claims as of the filing date, it is not reasonable to exclude said another structure from the application of the doctrine of equivalents only for the reason of such fact without exception.

(B) However, even in such a case, if the applicant is objectively and externally

recognized as having recognized another structure that is outside the scope of claims as a replacement for a different part in the structure stated in the scope of claims as of the filing date (for example, where the applicant can be considered to have stated the invention based on said another structure in the description or where the applicant stated the invention based on another structure that is outside the scope of claims in a paper, etc. which he/she published as of the filing date), the applicant's failure to state said another structure in the scope of claims is considered to fall under the "special circumstances" in the fifth requirement.

The reason therefor is as follows. In the aforementioned cases, it can be understood that the patentee intentionally excluded said another structure from the scope of claims when stating the scope of claims, that is, the patentee approved that said another structure does not fall under the technical scope of the patented invention or took action that is externally understood as such approval, and the trust of a third party who understands as such should be protected. Therefore, the patentee is not permitted to subsequently allege the application of the doctrine of equivalents in relation to the subject product, etc. that is based on said another structure in contradiction to such protection in light of the doctrine of estoppel."

B. In this judgment, the court specifically considered the statements, etc. in the corrected description, which the appellants allege as the "special circumstances" in the fifth requirement, and determined as follows: The corrected description does not include any statement that can be considered to be stating an invention wherein the starting material of the Corrected Invention has a trans-form vitamin D structure, and there is no other evidence sufficient to objectively and externally recognize that the applicant recognized a trans-form vitamin D structure as a replacement for a cis-form vitamin D structure as the starting material of the Corrected Invention as of the filing date of the application for the Patent; therefore, the special circumstances in the fifth requirement of the doctrine of equivalents cannot be recognized.

(6) Regarding the existence or absence of grounds for invalidation of the Corrected Invention

In this judgment, the court determined that all of the grounds for invalidation alleged by the appellants are unacceptable.

Judgment rendered on March 25, 2016
2015 (Ne) 10014 Appeal Case of Seeking Injunction against Patent Right Infringement
(the court of prior instance: Tokyo District Court, 2013 (Wa) 4040)
Date of conclusion of oral argument: February 19, 2016

Judgment

Appellant: DKSH Japan K.K.
(Hereinafter referred to as "Appellant DKSH")
Appellant: Iwaki Seiyaku Co., Ltd.
(Hereinafter referred to as "Appellant Iwaki Seiyaku")
Appellant: Takata Pharmaceutical Co., Ltd.
(Hereinafter referred to as "Appellant Takata Pharmaceutical")
Appellant: Pola Pharma Inc.
(Hereinafter referred to as "Appellant Pola Pharma")
Counsel attorney for the aforementioned four appellants: SHINBO Katsuyoshi
Same as above: TAKASAKI Jin
Same as above: HORA Takashi
Same as above: INOUE Akira
Same as above: SAKO Teiyu
Counsel patent attorney for the aforementioned four appellants: MAMURA Masazumi
Same as above: WATANABE Shiho
Counsel patent attorney as an assistant in court for the aforementioned four appellants: MUROFUSHI Yoshinobu
Same as above: INOUE Kaori
Appellee: Chugai Pharmaceutical Co., Ltd.
Counsel attorney: OZAKI Hideo
Same as above: HINO Eiichiro
Same as above: EGURO Sayaka

Main text

1. All of the appeals in question shall be dismissed.
2. The appellants shall bear the cost of the appeal.

Facts and reasons

No. 1 Object of the appeal

1. The judgment in prior instance shall be revoked.
2. All of the appellee's claims shall be dismissed.
No. 2 Outline of the case
1. In this case, the appellee is one of the joint owners of the patent right for an invention titled "intermediates for the synthesis of vitamin D and steroid derivatives and process for preparation thereof" (Patent No. 3310301; hereinafter, said patent right is referred to as the "Patent Right"; the patent pertaining to the Patent Right is referred to as the "Patent"). The appellee alleges that the process described in the Process List attached to this judgment (hereinafter referred to as the "Appellant's Process"), which is the process for the preparation of the maxacalcitol active pharmaceutical ingredient described in Item List 1 attached to the judgment in prior instance (hereinafter referred to as "Appellant's Product 1"), which is imported and sold by Appellant DKSH, and the maxacalcitol preparations described in (1) to (3) in Item List 2 attached to the judgment in prior instance, which are sold by Appellant Iwaki Seiyaku, Appellant Takata Pharmaceutical, and Appellant Pola Pharma, respectively (hereinafter, each of said maxacalcitol preparations is independently referred to as "Appellant's Product 2(1)," etc., and are collectively referred to as "Appellants' Products 2"; these preparations and Appellant's Product 1 are collectively referred to as "Appellants' Products"; incidentally, Appellant's Product 1 is identified as having been prepared by the Appellant's Process in Item List 1 attached to the judgment in prior instance, and Appellants' Products 2 are identified as maxacalcitol preparations prepared by the Appellant's Process in Item List 2 attached to the judgment in prior instance), are equivalent to and fall under the technical scope of the invention claimed in Claim 13 (hereinafter referred to as the "Invention") in the scope of claims in the description pertaining to the Patent (the description as of the registration of establishment of the Patent Right; hereinafter, referred to as the "Description"; incidentally, as the Patent pertains to an application filed before June 30, 2003, the Description includes the scope of claims [Article 1, item (ii) and Article 3, paragraph (1) of the Supplementary Provisions of Act No. 24 of 2002 and Cabinet Order No. 214 of 2003]). Based on this allegation, the appellee demands that [i] Appellant DKSH suspend the import and assignment of Appellant's Product 1 until September 3, 2017 and dispose of it, and that [ii] all the other appellants suspend the assignment and offer for assignment of Appellants' Products 2(1) to (3), respectively, until the same date and dispose of them, under Article 100, paragraphs (1) and (2) of the Patent Act. Incidentally, the appellee corrected Claim 13 in the scope of claims by a written request for correction dated September 25, 2013 in a trial for patent invalidation for the Patent after filing this action.

The court of prior instance recognized that the Appellant's Process is equivalent to the Invention and the invention claimed in Claim 13 in the scope of claims after the aforementioned correction (hereinafter referred to as the "Corrected Invention"), and also determined that the patent pertaining to the Invention is not recognized as one that should be invalidated by a trial for patent invalidation. Based thereon, the court of prior instance upheld all of the appellee's claims. Therefore, dissatisfied with the judgment in prior instance, the appellants (defendants in prior instance) filed this appeal.

In the proceedings in this instance, a JPO decision accepting the aforementioned correction became final and binding.

2. Facts on which the decision is premised (facts undisputed by the parties or facts that can be easily found by the evidence described in the text and the entire import of argument)

(1) Parties

A. The appellee is a stock company engaging in the business of research, development, preparation, sale, and import and export, etc. of medicines.

B. Appellant DKSH is a stock company engaging in the business of import, sale, etc. of medicines.

C. Each of Appellant Iwaki Seiyaku, Appellant Takata Pharmaceutical, and Appellant Pola Pharma is a stock company engaging in the business of sale, etc. of medicines, respectively.

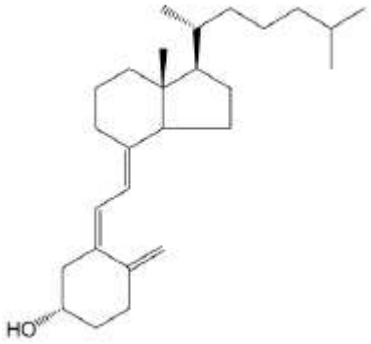
(2) Maxacalcitol

A. The appellee prepares and sells products named "Oxarol Ointment" and "Oxarol Lotion," respectively, which are cures for keratoma and whose active ingredient is maxacalcitol, an activated vitamin D_3 derivative.

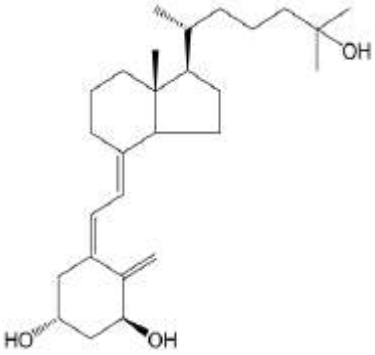
B. For many years, calcium metabolism-controlling activity has been known as a physiological activity of activated vitamin D_3. A broad range of new activities, including growth-inhibiting activity and differentiation-inducing activity on cells, were discovered, and activated vitamin D_3 has become expected to serve as a cure for dyskeratosis. However, activated vitamin D_3 has a problem of a side effect, that is, an increase in the blood calcium level.

The appellee discovered that maxacalcitol, which is a substance that is made by modifying the chemical structure of calcitriol, which is activated vitamin D_3, has weak blood calcium level increasing activity while it has growth-inhibiting activity and differentiation-inducing activity on cells. That is, the drawing below to the left indicates vitamin D_3 (inactive), and the drawing below in the middle indicates calcitriol wherein the 1α- and 25-positions of vitamin D_3 are hydroxylated and activated (1α,25-dihydroxy

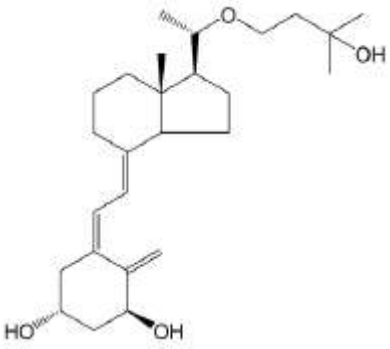
vitamin D_3). The appellee discovered that it is possible to obtain a substance, whose growth-inhibiting activity is better than calcitriol by 10 to 100 times and whose blood calcium and phosphorus level increasing activity (a side effect) is significantly weaker than calcitriol, by replacing the methylene group at the 22-position of calcitriol with the oxygen atom (entire import of argument). This substance is maxacalcitol (the drawing below to the right).



Vitamin D_3



Calcitriol (1α,25-dihydroxy vitamin D_3)



Maxacalcitol

C. On December 26, 1985 (priority claim: December 28, 1984 (priority date)), the appellee filed a patent application (Exhibit Ko 1) for 9,10-seco-5,7,10(19)-pregnatriene derivative, which contained maxacalcitol that was a novel substance. The appellee obtained the registration of establishment of a patent right therefor (Patent No. 1705002) in October 1992. The duration of said patent right expired on December 26, 2010 after going through the registration of extension of the duration.

The Corrected Invention is related to a process for the preparation of a compound containing this maxacalcitol.

(3) Patent Right

The appellee jointly owns the following patent right (the "Patent Right") fifty-fifty with the Trustees of Columbia University in the City of New York (hereinafter referred to as "Columbia University").

A. Patent number: Patent No. 3310301

B. Title of the invention: Intermediates for the synthesis of vitamin D and steroid derivatives and process for preparation thereof

C. Filing date: September 3, 1997

D. Application number: Patent Application No. 1998-512795

E. Priority date: September 3, 1996 (a priority claim based on US60/025,361; hereinafter referred to as the "Priority Date")

F. Registration date: May 24, 2002

G. Extension of the duration: On March 31, 2010, the extension of the duration of the Patent Right was registered with the following content under Article 67, paragraph (2) of the Patent Act (incidentally, the effect of the aforementioned registration of extension does not become a problem in this case because the appellee seeks an injunction for the period until the last day of the duration before the registration of extension).

(A) Disposition which serves as a reason for the extension of the duration of the Patent Right

Approval set forth in Article 14, paragraph (9) of the Pharmaceutical Affairs Act (the Act prior to the change of the title of the law by Act No. 84 of 2013) pertaining to a medicine as provided for in said paragraph

(B) Number to specify the disposition

Approval No. 21800AMX10386000

(C) Article subject to the disposition

Maxacalcitol (generic name)

(D) Usage specified in relation to the article subject to the disposition

Palmoplantar pustulosis

(E) Period of the extension

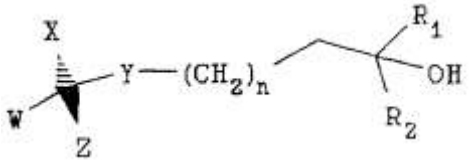
Five years

(4) Invention

The statement of Claim 13 in the scope of claims in the Description is as follows.

"[Claim 13]

A process for preparing a compound having the following structure:



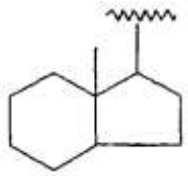
(in the formula, n is an integer from 1 to 5;

each of R_1 and R_2 independently is optionally substituted C1-C6 alkyl;

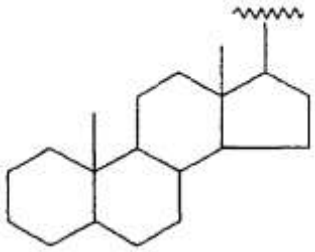
each of W and X is independently hydrogen or C1-C6 alkyl;

Y is O, S or NR_3 where R_3 is hydrogen, C1-C6 alkyl or a protective group; and

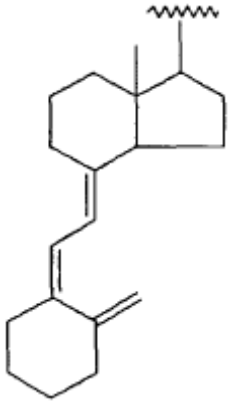
Z is a CD ring structure of the formula:



a steroid ring structure of the formula:



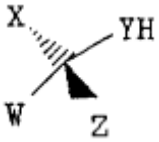
or a vitamin D structure of the formula:



wherein each of the structures of Z may optionally have one or more protected or unprotected substituents and/or one or more protective groups, and wherein any ring of the structure of Z may optionally have one or more unsaturated bonds);

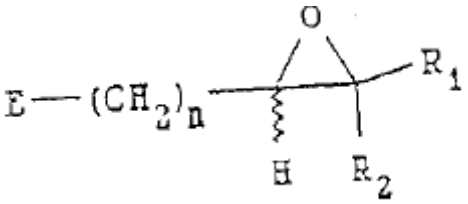
which comprises:

[a] the step of reacting a compound having the following structure:

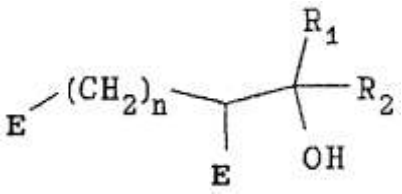


(in the formula, W, X, Y and Z are as defined above)

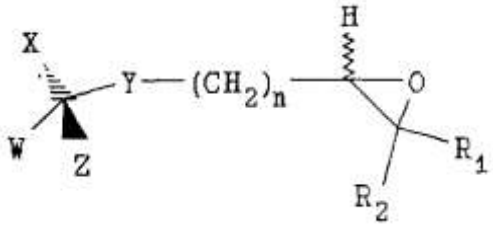
in the presence of a base, with a compound having the following structure:



or



(in the formula, n, R_1, and R_2 are as defined above, and E is an eliminating group)
to produce an epoxide compound having the following structure:



[b] the step of treating the epoxide compound with a reducing agent to produce the compound; and

[c] the step of recovering the compound so produced."

(5) Request for a trial for patent invalidation and request for correction

On May 2, 2013, Cerbios-Pharma SA (hereinafter referred to as "Cerbios") filed a request for a trial for patent invalidation (Invalidation Trial No. 2013-800080) in relation to the Patent (patent pertaining to Claims 1 to 30) (Exhibit Ko 28).

The appellee and Columbia University submitted a written request for correction dated September 25, 2013 (Exhibit Ko 15) to request the correction of the Description (the number of claims after the correction is 28; hereinafter, said correction is referred to as the "Correction," and the description after the Correction is referred to as the "Corrected Description"; incidentally, only the scope of claims in the Description was corrected by the Correction) for the purpose of restriction of the scope of claims. On July 25, 2014, the JPO rendered a decision to the effect that "The correction shall be accepted as requested. The request for a trial in question shall be dismissed" (Exhibit Ko 28).

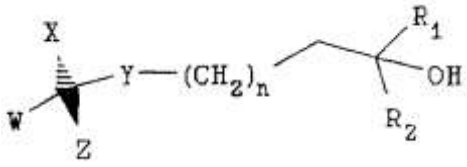
Cerbios instituted an action to seek the rescission of said JPO decision (2014 (Gyo-Ke) 10263) with the Intellectual Property High Court. However, on December 24,

2015, said court rendered a judgment that dismissed Cerbios's claim, and said judgment became final and binding (Exhibits Ko 33 and 34).

(6) Corrected Invention

A. The statement of Claim 13 after the Correction is as stated in [Claim 13] in the scope of claims in the Corrected Description attached to the judgment in prior instance, and the invention pertaining to said claim (Corrected Invention; hereinafter, in the Patent, the patent pertaining to said claim is referred to as the "Patent Pertaining to the Corrected Invention") is segmented into the following constituent features (underlined parts are corrected parts; Constituent Features [A-1] and [A-2] to [A-6] are collectively referred to as "Constituent Feature [A]," and Constituent Features [B-1] to [B-3] are collectively referred to as "Constituent Feature [B]").

[A-1] A process for preparing a compound having the following structure:



[A-2] (in the formula, n is 1;

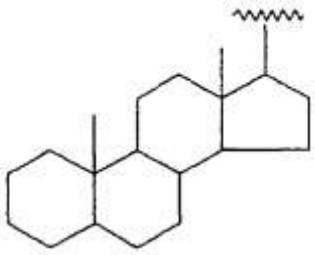
[A-3] R_1 and R_2 are methyl;

[A-4] each of W and X is independently hydrogen or methyl;

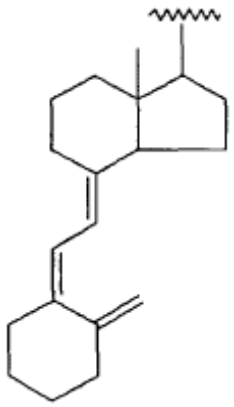
[A-5] Y is O; and

[A-6] Z is

a steroid ring structure of the formula:



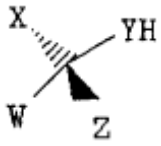
or a vitamin D structure of the formula:



wherein each of the structures of Z may optionally have one or more protected or unprotected substituents and/or one or more protective groups, and wherein any ring of the structure of Z may optionally have one or more unsaturated bonds);

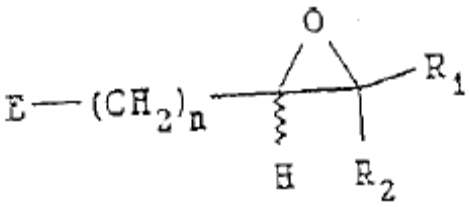
[E] which comprises:

[B-1] [a] the step of reacting a compound having the following structure:

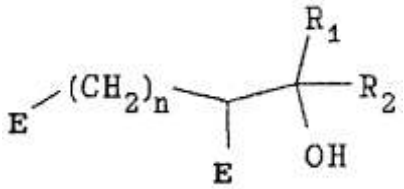


(in the formula, W, X, Y and Z are as defined above)

[B-2] in the presence of a base, with a compound having the following structure:

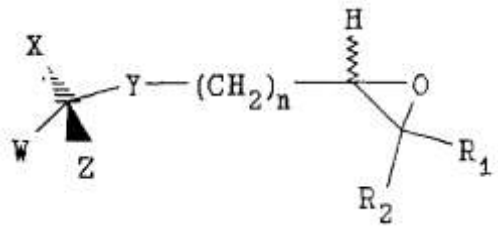


or



(in the formula, n, R_1, and R_2 are as defined above, and E is an eliminating group)

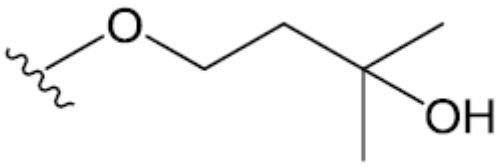
[B-3] to produce an epoxide compound having the following structure:



[C] [b] the step of treating the epoxide compound with a reducing agent to produce the compound; and

[D] [c] the step of recovering the compound so produced."

B. The Correction is intended to limit "Z" of the objective substance and the starting material of the Invention to those having a "steroid ring structure" or a "vitamin D structure" and also to limit a side chain to be introduced to those having the following structure (3-hydroxy-3-methylbutoxy group; hereinafter referred to as a "Maxacalcitol Side Chain"). The Correction restricts the scope of claims (incidentally, among such objective substances, a substance in which "Z" has a "vitamin D structure" and which has two hydroxy groups [OH] in "Z" as substituents is maxacalcitol).



The Appellant's Process does not fall under the part that was excluded from the Invention by the Correction (the parties do not dispute this point).

(7) Appellants' acts

A. Appellant DKSH imports Appellant's Product 1, which was prepared by Cerbios, a Swiss drug manufacturer, by the Appellant's Process, as a business and sells it at least to Defendant Takata Pharmaceutical and Defendant Pola Pharma.

B. On August 15, 2012, Appellant Iwaki Seiyaku, Appellant Takata Pharmaceutical, and Appellant Pola Pharma obtained the approval of the Minister of Health, Labour and Welfare in relation to the preparation and sale of Appellants' Products 2(1) to (3), respectively. These products were listed in the National Health Insurance Drug Price Standard on December 14 of the same year.

Any maxacalcitol that is contained in Appellants' Products 2 as an active pharmaceutical ingredient (active ingredient) was prepared by the Appellant's Process.

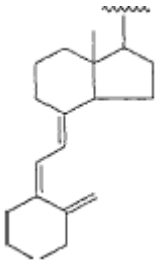
C. The Appellant's Process is as stated in the Process List attached to this judgment, and

it is in short a process for preparing maxacalcitol which comprises [i] the step of reacting Starting Material A with Reagent B (1-bromo-3-methyl-2,3-epoxybutane; it is also referred to as "4-bromo-2,3-epoxy-2-methylbutane"; hereinafter referred to as the "Reagent" in some cases) in the presence of a base to synthesize Intermediate C of an epoxide compound (Step I), [ii] the step of opening the ring of the epoxy group by treating Intermediate C with a reducing agent to obtain Substance D (trans form of maxacalcitol) (Step II), [iii] the step of converting Substance D to a cis form and removing protective groups to obtain maxacalcitol, which is the objective substance (Step III), and [iv] the step of recovering maxacalcitol (Step IV).

D. The Appellant's Process fulfills Constituent Features [A], [B-2], [D], and [E] of the Corrected Invention.

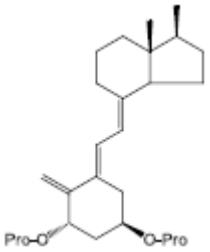
The Appellant's Process does not fulfill Constituent Feature [B-1] of the Corrected Invention in that the carbon skeleton of Starting Material A in Step I is not a "cis-form vitamin D structure" (cis (5Z) secosteroid structure) which "has one or more protected … substituents" and has two protected substituents among "Z" of Constituent Feature [A-6] cited in Constituent Feature [B-1] of the Corrected Invention" but is a trans-form vitamin D structure (trans (5E) secosteroid structure), which is a geometric isomer of said cis-form vitamin D structure.

(Vitamin D structure of Z in the Corrected Invention)



(Z may have one or more protected substituents.)

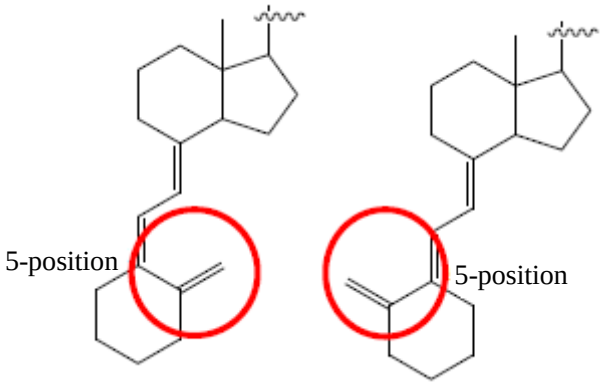
(Carbon skeleton of Starting Material A for the Appellant's Process)



In addition, the Appellant's Process does not fulfill Constituent Features [B-3] and [C] of the Corrected Invention in that the carbon skeleton of Intermediate C in Steps I and II is not a cis-form vitamin D structure but a trans-form vitamin D structure in the same manner as the above.

Incidentally, the basic skeleton of vitamin D group includes three double bonds connected from the upper two rings (triene; double bonds are indicated by double lines

in the following figures). In vitamin D group, there are two geometric isomers that derive from this triene structure. A vitamin D having the left-hand triene sequence in the following figures is called "cis form," and a vitamin D having the right-hand triene sequence is called "trans form."



Cis form Trans form

3. Issues

The issues of this case are [i] whether the Appellant's Process falls under the technical scope of the Corrected Invention as an equivalent thereto and [ii] whether the Patent Pertaining to the Corrected Invention is recognized as one that should be invalidated by a trial for patent invalidation (existence or absence of the grounds for invalidation mentioned in (2)A. to C. below).

(1) Whether the Appellant's Process is equivalent to the Corrected Invention

(2) Whether there are grounds for invalidation in relation to the Corrected Invention

A. Lack of an inventive step by citing Exhibit Otsu 14 Document as the primarily cited document (Ground for Invalidation A)

B. Lack of an inventive step by citing Exhibit Ko 12 Document as the primarily cited document (Ground for Invalidation B)

C. Lack of an inventive step by citing Exhibit Otsu 4 Document as the primarily cited document (Ground for Invalidation C)

Incidentally, in prior instance, the appellants alleged Grounds for Invalidation 1, 2, and 4 to 6 (Ground for Invalidation 3 is a vacant number) as briefly indicated in No. 2, 3. in "Facts and reasons" in the judgment in prior instance. However, in this instance, the appellants backed off their allegations of Grounds for Invalidation 1, 5, and 6 as briefly indicated in No. 2, 3. in "Facts and reasons" in the judgment in prior instance, and alleged the lack of an inventive step by citing Exhibit Ko 12 Document as the primarily cited document (the aforementioned Ground for Invalidation B) as a new ground for

invalidation. Therefore, the grounds for invalidation to be examined in this instance are only the aforementioned Grounds for Invalidation A to C.

No.3 Allegations of the parties

1. Regarding whether the Appellant's Process is equivalent to the Corrected Invention

The allegations of the parties concerning the fulfillment of the first to fifth requirements of the doctrine of equivalents are supplemented as follows by the allegations of the parties in this instance, and are also as briefly indicated in No. 3, 1. to 5. in "Facts and reasons" in the judgment in prior instance. Therefore, the relevant part is cited (however, in the judgment in prior instance pertaining to the citation, the terms "plaintiff," "defendant," "Defendant's Process," and "Constituent Feature [A-6']" are deemed to be replaced with "appellee," "appellant," "Appellant's Process," and "Constituent Feature [A-6]," respectively [hereinafter the same shall apply in the case of citation]; the phrase "hereinafter referred to as the 'Reagent'" in line 21 of page 16 of the judgment in prior instance and "Exhibit Otsu 4-2" in line 14 of page 19 are revised to the "Reagent" and "Publication of Japanese Translation of PCT International Application No. 1992-504573 (hereinafter referred to as Exhibit Otsu 4 Document)," respectively).

(Supplementary allegations of the parties in this instance)

(1) Regarding the first requirement of the doctrine of equivalents

(Appellants)

A.(A) In the case of using a starting material having a cis-form vitamin D structure, the starting material and the intermediate are candy-like and unstable. Therefore, there are difficulties in handling and using such starting material. In addition, as such starting material is not crystal, it needs to be purified by column chromatography using silica, which is an oxidation catalyst, as filler. Therefore, there is a loss at the time of purification as vitamin D is easily degraded by oxidation.

On the other hand, in the Appellant's Process, all of Starting Material A (trans form), Intermediate C (trans form) obtained by reaction with Reagent B, and Substance D (trans-form maxacalcitol) obtained by opening the ring of Intermediate C are crystal and highly stable, and they can be extracted and preserved as crystal in the middle of a synthesis route. Moreover, as they can be purified by recrystallization, the number of kinds of analogues and the amount thereof can be reduced.

In this manner, the Appellant's Process has a technical significance that the Corrected Invention does not have, as a manufacturing process, in that it increases the stability of steps and easiness of purification. On the other hand, it differs from the Corrected Invention in terms of the number of steps. That is, the Corrected Invention

comprises two steps while the Appellant's Process comprises three steps.

(B) Originally, processes using a starting material having a cis-form vitamin D structure, those using a starting material having a trans-form vitamin D structure, and those using a starting material having a steroid ring structure have been understood as different general processes for the synthesis of vitamin D_3 derivatives by persons ordinarily skilled in the art.

In addition, the Corrected Description includes the following statement: "Some of the compounds which are used as the starting compound in the aforementioned process according to the present invention are publicly known compounds. For example, … the 9,10-seco-5,7,10(19)-pregnatriene-1α,3β,20β-triol optionally with the hydroxyl group being protected described in … International Patent Publications WO/1990/09991 (September 7, 1990) and WO/1990/09992 (September 7, 1990)." In the publications corresponding to these two international patent publications (Exhibits Otsu 3-2 and 4-2), trans form and cis form are distinctively described. It is described in the latter publication that an additional step is required for conversion from a trans form to a cis form and that cis-form maxacalcitol is prepared from a trans-form starting material. The case of using a cis-form starting material and the case of using a trans-form starting material are distinguished from each other.

In the end, the Corrected Invention using a cis-form starting material is established as a separate process from a process using a trans-form starting material.

(C) In the technical field of processes for the preparation of a compound, reactivity differs in some cases depending on a difference in the structure of a compound or a slight difference in the reaction conditions. All the steps before obtaining the objective substance from the starting material are organically linked, and this organic linkage itself is a technical idea for solving a problem. Therefore, a change in the constituent elements or combination of the steps leads to a different technical idea.

As mentioned in (A) above, the Appellant's Process differs from the Corrected Invention in terms of the starting material, the intermediate, and the necessity of a step of isomerization from the intermediate. In addition, it also differs in terms of the stability of steps and easiness of purification.

The starting material just falls under an essential part in terms of where the starting point of a series of steps to obtain the objective substance is placed. As mentioned in (B) above, processes using a starting material having a cis-form vitamin D structure and those using a starting material having a trans-form vitamin D structure are understood as separate processes. The intermediate also falls under an essential part in terms of where the pass point in a series of steps to obtain the objective substance is placed. As

mentioned in (A) above, a choice between stable steps and reduced number of steps depends on whether the process goes through trans-form maxacalcitol. Therefore, the intermediate just falls under the essential part of a manufacturing process.

There is no other choice but to say that it is erroneous to extract part of a manufacturing process in disregard of such differences in the stating material and the intermediate, which are the important constituent elements of the manufacturing process, as well as differences in stability and the number of steps. The essence of the Corrected Invention exists not in its part but in the entire manufacturing process, and the Appellant's Process, which differs from the Corrected Invention in the starting material and the total number of steps, cannot be considered to be essentially identical with the Corrected Invention.

B.(A) In addition, a cis-form vitamin D structure and a trans-form vitamin D structure differ in that the former has low oxidation resistance while the latter has high oxidation resistance. The conventional manufacturing process described in Publication of Unexamined Patent Application No. 1994-256300 (hereinafter referred to as "Exhibit Otsu 46 Publication") wherein the starting material is an alcohol compound at the 20-position of a steroid ring structure is difficult to apply because it has the following problem: In the case of using a starting material having a cis-form vitamin D structure, the starting material has low oxidation resistance, and thus, protection of the triene structure is indispensable for the selective introduction of an epoxy group into a side chain; therefore, introduction of a side chain cannot be efficiently conducted. For the purpose of solving said problem, in the Corrected Invention, a cis-form vitamin D structure is chosen as the starting material, and the order of introduction of an ether bond and an epoxy group conformable to such structure is found. Consequently, the essence of the Corrected Invention exists in that it solved a problem (oxidation resistance) that arises in the case of using a starting material having a cis-form vitamin D structure while enjoying the advantage of the reduced number of steps by using such starting material. The point that the starting material has a cis-form vitamin D structure is an indispensable essential element.

In contrast to this, in the case of using a starting material having a trans-form vitamin D structure, an isomerization step is by necessity required to obtain the objective substance. Therefore, it is impossible to enjoy the advantage of the reduced number of steps in the entire manufacturing process, which can be achieved in the case of using a starting material having a cis-form vitamin D structure. On the other hand, unlike a cis-form vitamin D structure, a trans-form vitamin D structure has high oxidation resistance. Therefore, it is possible to efficiently introduce an epoxy group

into a side chain by using a conventional oxidation process. Consequently, there is no problem relating to oxidation resistance, and it is thus not necessary to use the principle whereby the problem is solved. Next, a trans-form vitamin D structure has many advantages, such as the capacity of stocking epoxy intermediate and recovery of target compounds by recrystallization, as it is crystalline and excellent in stability. Furthermore, in the case of using a vitamin D structure as the starting material, it is necessary to introduce a hydroxyl group at the 1-position at any of the steps. In this case, it is more favorable to adopt a trans-form vitamin D structure.

(B) The only effect stated in the Corrected Description is the reduction of the number of steps, and the effect of the Corrected Invention exists in the reduction of the number of steps compared to prior art. There has been no manufacturing process, as prior art, whereby a Maxacalcitol Side Chain can be introduced in two steps in the case of using a starting material having a steroid ring structure or a cis-form vitamin D structure, like the Corrected Invention. However, in the case of using a starting material having a trans-form vitamin D structure, a Maxacalcitol Side Chain can be introduced through one step by a process described in Publication of Japanese Translation of PCT International Application No. 1992-504573 (Exhibit Otsu 4 Document), which is introduced as prior art in the Corrected Description. Therefore, it is impossible to allege the effect of reducing the number of steps compared to prior art.

C. As mentioned above, the effect of the Corrected Invention as a manufacturing process completely differs depending on whether the starting material has a cis-form vitamin D structure or a trans-form vitamin D structure, and the Corrected Invention can be established as separate inventions accordingly. In the latter case, the Corrected Invention does not have the effect of reducing the number of steps compared to prior art. Therefore, the Appellant's Process cannot be considered to be identical with the Corrected Invention in the essential part, and does not fulfill the first requirement of the doctrine of equivalents.

(Appellee)

A.(A) The issue of the essential part of an invention in the doctrine of equivalents is not the question of whether there are differences between the subject product, etc. and the patented invention but is the question of whether differences between them are related to the essential part of the patented invention. Even if there are differences between them, if those differences are not in the essential part of the patented invention and are in the matters which a person ordinarily skilled in the art can choose as appropriate, and the subject product, etc. and the patented invention are identical with each other in the essential part, the first requirement of the doctrine of equivalents is fulfilled.

Differences in stability and easiness of purification between a cis form and a trans form as alleged by the appellants are not related to the process for introducing a Maxacalcitol Side Chain, which is the essential part of the Corrected Invention. Even if the Corrected Invention is considered to be a different process depending on the starting material, this does not serve as a reason for denying that the Corrected Invention and the Appellant's Process are substantially identical with each other.

(B) The reduction of the number of steps compared to prior art is not the only function and effect of the Corrected Invention. As the Corrected Invention is a specific chemical reaction for the introduction of a Maxacalcitol Side Chain, it should be compared to all the other publicly known processes for the introduction of a Maxacalcitol Side Chain in order to express its effect most accurately. The processes whereby a Maxacalcitol Side Chain could be introduced prior to the filing of the application for the Patent were only the following three: [i] the first process for the synthesis of maxacalcitol, which was developed by the appellee (Exhibit Ko 12; this process is very inefficient in consideration of industrial production for such reasons as that it produces a large amount of by-products and also requires sensitivity to safety in the context of use of oxygen); [ii] the synthesis process called Michael process as of the time of the clinical test, which was developed by the appellee as an improved process of the said first process (Figure 6 in Exhibit Otsu 14; this process is difficult to use for mass production as it uses a large amount of cerium chloride, which needs to be treated as metallic waste); and [iii] the process using prenyl bromide as the reagent, which was carried out by the inventors of the Corrected Invention (this process cannot be used for industrial production as it requires a mercury compound to selectively introduce a hydroxyl group at the 25-position, which is the end of the side chain). None of these processes was suited for industrial production. The Corrected Invention is the first process for the introduction of a Maxacalcitol Side Chain which is industrially practicable, and its effect exists in a difference in the process for the introduction of a Maxacalcitol Side Chain from the aforementioned conventional processes for the introduction of a Maxacalcitol Side Chain.

Therefore, the essential feature of the Corrected Invention exists in the novel process for the introduction of a Maxacalcitol Side Chain, which made it possible to mass produce maxacalcitol for the first time, by way of the reaction between an alcohol compound at the 20-position and the reagent of Constituent Feature [B-2], wherein the double bond of prenyl bromide is oxidized into an epoxy substance in advance. The Appellant's Process has this essential feature in common with the Corrected Invention.

B. As the side chain introduction process of the Corrected Invention does not include

oxidation reaction, difference in oxidation resistance between a cis form and a trans form does not affect the introduction of a Maxacalcitol Side Chain of the Corrected Invention. In addition, as the reaction of the Corrected Invention is carried out in a solvent, the fact that a trans-form vitamin D structure is crystalline and excellent in stability has no relation in the process of the Corrected Invention. Furthermore, the fact that it is favorable to adopt a trans form in terms of the introduction of an hydroxyl group at the 1-position is nothing more than the advantage of a trans form in relation to the obtainment of the starting material because the starting material has a hydroxyl group at the 1-position, irrespective of whether it is a cis form or a trans form. Incidentally, there is no ground for the appellants' allegation that a Maxacalcitol Side Chain could be introduced through one step by prior art in the case of using a starting material having a trans-form vitamin D structure.

C. Therefore, the difference between the Corrected Invention and the Appellant's Process is not the essential part of the Corrected Invention, and the Appellant's Process thus fulfills the first requirement of the doctrine of equivalents.

(2) Regarding the second requirement of the doctrine of equivalents

(Appellants)

A. As the appellants' allegation in B. in (1) above, the effect of the Corrected Invention exists in the reduction of the number of steps compared to prior art. In the case of a process wherein the starting material has a trans-form vitamin D structure, it has been possible to introduce a Maxacalcitol Side Chain through one step for some time now. Therefore, it is impossible to allege the effect of reducing the number of steps compared to prior art.

B. In addition, the efficiency of the effect of the Corrected Invention of reducing the number of steps should be decided based on the total number of steps in the manufacturing process. Looking at the total number of steps in the manufacturing process, the number of steps increases in the Appellant's Process because of the necessity of a step of isomerization from a trans form to a cis form, and three steps are substantially required to obtain the objective compound. Therefore, the Appellant's Process does not have the same function and effect as the Corrected Invention, and it cannot be considered to be a "replacement" at all.

C. Other than these, as the appellants' allegation in A.(A) in (1) above, the Appellant's Process has a technical significance that the Corrected Invention does not have, and the actual yield is not the same as that in the case of using a cis-form starting material. Therefore, the Appellant's Process is considered to be different processes in the case of using a cis-form starting material and in the case of using a trans-form starting material.

Consequently, the Appellant's Process differs from the Corrected Invention, and it is not considered to be possible to "replace" them.

D. Therefore, the Appellant's Process does not fulfill the second requirement of the doctrine of equivalents.

(Appellee)

The fact that the number of steps was reduced compared to prior art cannot be considered to be the only function and effect of the Corrected Invention, as the appellee's allegation in A.(B) in (1) above.

Even if the reduction of the number of steps is the function and effect of the Corrected Invention, said effect is obtained by using the Reagent and omitting the oxidation step after reaction with a reagent that was carried out in prior art. Consequently, even if the starting material is replaced with one having a trans-form vitamin D structure, the same function and effect as those of the Corrected Invention can be produced.

(3) Regarding the third requirement of the doctrine of equivalents

(Appellants)

A. As the appellants' allegation in A.(B) in (1) above, processes using a starting material having a cis-form vitamin D structure, those using a starting material having a trans-form vitamin D structure, and those using a starting material having a steroid ring structure are understood as different processes for the synthesis of vitamin D derivatives. A person ordinarily skilled in the art cannot easily conceive of the fact that the same effect of reducing the number of steps, which is expected to be achieved by the Corrected Invention, can also be achieved even if the starting material having a cis-form vitamin D structure is changed to a starting material having a trans-form vitamin D structure.

B. The Corrected Description does not contain any working example wherein the starting material has a cis-form vitamin D structure. Therefore, whether or not reaction proceeds in the case of using a starting material having a cis-form vitamin D structure is originally unclear for a person ordinarily skilled in the art who sees the Corrected Description. Furthermore, it is totally unclear whether or not reaction proceeds in the case of the process using a starting material having a trans-form vitamin D structure, which is recognized as a process that is different from the process using a starting material having a cis-form vitamin D structure, and this is not considered to be as clear as if stated in the scope of claims. Therefore, it cannot be said that a person ordinarily skilled in the art can easily replace a cis-form with a trans-form.

C. Consequently, the Appellant's Process also does not fulfill the third requirement of

the doctrine of equivalents.

(Appellee)

A reaction experiment using a starting material having a cis-form vitamin D structure under the experiment conditions of the working example of the Corrected Description immediately reveals that the reaction can be carried out. In the field of vitamin D, the mutual converse relationship between a trans form and a cis form is well-known among persons ordinarily skilled in the art. Therefore, an experiment immediately reveals that the reaction can also be carried out in the case of using a starting material having a trans-form vitamin D structure.

Therefore, the Appellant's Process fulfills the third requirement of the doctrine of equivalents.

(4) Regarding the fifth requirement of the doctrine of equivalents

(Appellants)

A. Regarding inventions in the chemical field for which the subject of the invention is objectively and easily defined under certain rules by using chemical formulas and names of compounds, there naturally arises the third-party trust that a right will never be expanded from its clear scope based on the objective and clear statements in the scope of claims that are indicated by chemical formulas. It is extremely difficult for a third party to foresee expansion of the scope of a right beyond the statements in the scope of claims. The level of the third-party trust in the statements in the scope of claims totally differs between inventions in the chemical field for which the clear provision of the scope of rights is required and inventions in the fields for which functional expressions are permitted. It is indicated in the judgment of the Supreme Court of December 14, 1972 (Phenothiazine Derivative Manufacturing Process case) that the third-party trust in the statements in the scope of claims should be protected in relation to chemical inventions. In the judgment of the Supreme Court of June 5, 2015 (Product-by-Process Claim case), the court also indicates the necessity of weighing the applicant's burden of clearly stating the scope of the exclusive right which he/she alleges and the third party's burden of predicting the scope to which the right extends based on the statements in the scope of claims, in relation to the interpretation of claims in the field of medicine like this case.

For the Corrected Invention for which the scope of claims is stated by chemical formulas, it is safe to say that the applicant bears little burden to include a trans-form starting material in the scope of claims at the time of filing the application. On the other hand, there naturally arises the third-party trust that the right will never be expanded from the scope of claims specified by objective and clear expressions, as mentioned

above. In weighing the applicant's burden and the third-party trust, the third-party trust should be protected more in light of the principle of "fairness," which is the principle of equivalents.

In the first place, in the judgment of the Third Petty Bench of the Supreme Court of February 24, 1998, Minshu, Vol. 52, No. 1, at 113 (hereinafter referred to as the "Supreme Court Judgment on the "Ball spline bearing" Case"), the court first indicates that it is a principle to comply with the provisions of Article 70, paragraph (1) of the Patent Act, which is a statute law. The court then indicates that the doctrine of equivalents is applicable only within the scope that does not inhibit the development of industry, which is the purpose of the Patent Act. Thereby, the court only approves the doctrine of equivalents on the premise of the existence of a reason for protecting the patentee even in contradiction to the principle of the Patent Act. Approving the establishment of equivalence in this case leads to approving an argument that ignores the aforementioned principle of the Patent Act to the effect that the applicant may prepare claims on the premise of the expansion of a right by application of the doctrine of equivalents, which will cause extensive damage to third parties who believe in the public notice function of the patent system.

B. In addition, in this case, the reason for the applicant to describe the starting material having a cis-form vitamin D structure alone is not a difficulty or a mistake at the time of filing the application, according to the circumstances mentioned below. There is no circumstance where the applicant forgot to state a trans-form vitamin D structure when defining the starting material. In stating the scope of claims, the applicant decided the starting material, being clearly and objectively conscious of not including a trans-form vitamin D structure in the scope of claims. The applicant thus intentionally chose to actively exclude a trans-form vitamin D structure.

(A) It is a well-known matter that there are two kinds of geometric isomers, cis form and trans form, as the basic skeletons of vitamin D and that there are only these two kinds of basic skeletons in the natural world. In addition, as of the Priority Date, a route for the synthesis of a vitamin D derivative using a starting material having a trans-form vitamin D structure was widely known among persons ordinarily skilled in the art. The inventors of the Patent who study vitamin D derivatives should have known these facts very well. Therefore, the applicant was never erroneously ignorant of the existence of a synthesis route using a starting material having a trans-form vitamin D structure as of the Priority Date.

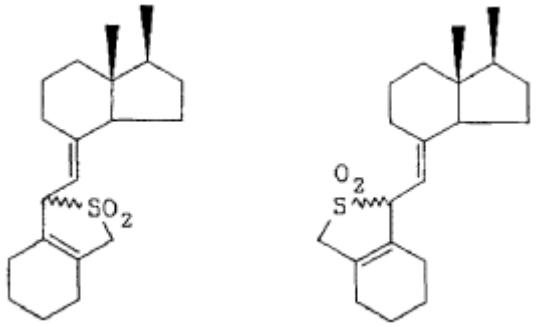
Moreover, as the appellants' allegation in A.(B) in (1) above, processes using a starting material having a trans-form vitamin D structure and those using a starting

material having a cis-form vitamin D structure were understood as different processes in relation to the synthesis of vitamin D derivatives.

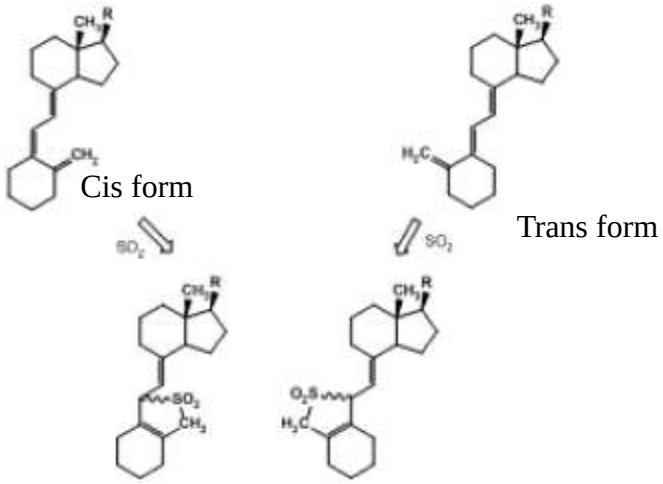
(B) In Claim 13 in the scope of claims in the Corrected Description, a chemical bond is described by a wavy line, "〜H," in the structural formula of Constituent Feature [B-3] of the Corrected Invention, and it is thereby clearly specified that the steric structure at the root of H includes both R-stereoisomer and S-stereoisomer. However, the geometric isomer of a vitamin D structure is described as being limited to a cis form. The applicant can immediately understand that a trans form is not included in the scope of claims and a third party also understand as such if the applicant describes only a cis form in the scope of claims in relation to geometric isomer while clearly specifying that both of said stereoisomers are included. Therefore, in the Corrected Description, the applicant clearly and objectively states that a trans form is not included in the scope of claims.

(C) Moreover, as the appellants' allegation in A.(B) in (1) above, the detailed explanation of the invention (in lines 32 to 48 in column 41) in the Corrected Description describes two international publications describing a starting material having a trans-form vitamin D structure, in addition to a patent gazette describing a starting material having a cis-form vitamin D structure. Despite that, it is stated in the Corrected Description (in lines 10 to 12 in column 37) that "each of the CD ring structure, steroid structure, and vitamin D structure for the present invention particularly means a structure as described below … (omitted)." The chemical structural formula of a cis-form vitamin D structure is then chosen and described. As a result of this choice, a cis-form vitamin D structure alone is stated in the scope of claims. In this manner, the starting material is "particularly" limited to a cis form out of the two kinds of the existing basic skeletons. Therefore, in the Corrected Description, the applicant clearly and objectively states that a trans form is not included in the scope of claims. Consequently, a trans-form vitamin D structure is intentionally excluded from the scope of claims.

(D) Furthermore, the following figures are stated in the detailed explanation of the invention (line 1 and thereafter in the right-hand column on page 20) in the Corrected Description as examples of vitamin D structures protected by addition of SO_2.



The left and right figures indicate the same compound, and it is sufficient to draw the left figure to indicate an "example of vitamin D structures protected (by addition of SO_2)." Despite that, the aforementioned two structural formulas are presented in the Corrected Description, which can only be interpreted as meaning that each of these structural formulas expresses a structural formula immediately after addition of SO_2 to a cis-form starting material (structural formula on the left side) and a structural formula immediately after addition of SO_2 to a trans-form starting material (structural formula on the right side), respectively, as indicated in the following figures.



In addition, it is common general technical knowledge as of the Priority Date that if a vitamin D derivative to which SO_2 is added as a protective group is used as a starting material, it necessarily becomes a trans form in alkylation reaction (Exhibit Otsu 1).

Despite the existence of such a statement that is based on the assumption of a trans-form starting material in the "detailed explanation of the invention" section in the Corrected Description, the starting material is limited to a cis-form starting material in the scope of claims. Therefore, an intentional limitation is also clear in this regard.

(E) Although the Corrected Description includes only working examples using a starting

material having a steroid ring structure, the Corrected Invention is enlarged to include the cases where the partial structure corresponding to "Z" is a cis-form vitamin D structure. The applicant also knew that if the applicant specifies the starting material as a cis form when adding a vitamin D structure to the scope of right as enlargement from working examples, this leads to setting the limits of enlargement and such statement defines the scope to which the right can be claimed against third parties. In addition, if a specifically stated invention has already been generalized and a third party sees the description wherein the invention is stated in the scope of claims as the scope of exclusive right alleged by the applicant him/herself, the third party naturally recognizes as follows: The scope to which the right extends was determined after consideration of the partial structure corresponding to "Z", and at the same time, a vitamin D structure that was not stated in the scope of claims was excluded from the scope to which the right extends.

(F) As it was not required to state a specific working example for each starting material in the examination practice at the time of the filing of the patent application in question, the starting material the applicant chose was totally voluntary. The applicant could choose any of a cis-form vitamin D structure, a trans-form vitamin D structure, a steroid ring structure, and a CD ring, etc. as the partial structure corresponding to "Z" of the starting material, and there was no difficulty in including a trans form.

(G) It can be understood that the applicant limited starting materials having a vitamin D structure to those having a cis-form vitamin D structure, in consideration of the involvement of an inventive step of the invention. That is, as the appellants' allegation in (2) above, the only function and effect stated in relation to the Corrected Invention in the Corrected Description is "reduction of the number of steps," but said function and effect cannot be alleged in the case of using a trans-form starting material because an additional step of converting a trans form to a cis form is required. Moreover, in the case of using a starting material having a trans-form vitamin D structure, the effect of reducing the number of steps compared to prior art cannot be achieved because there are publicly known arts (Exhibits Otsu 4-2 and 50) whereby a side chain is introduced through one step. Therefore, the applicant limited the starting material to cis-form starting materials because it was highly likely to be unable to receive an examiner's decision to grant a patent based on the allegation of the effect of reducing the number of steps if it included a starting material having a trans-form vitamin D structure in the subject of the invention.

(H) As mentioned above, in the Corrected Invention, there are the "special circumstances, such as the fact that the subject item falls under what is intentionally

excluded from the scope of claims," as mentioned in the Supreme Court Judgment on the "Ball spline bearing" Case, in relation to a trans-form vitamin D structure, but there is no circumstance where the patentee should be specially protected, which is indicated in said judgment as a ground for the application of the doctrine of equivalents, specifically, the fact that "it is extremely difficult to foresee all kinds of infringements … and state the scope of claims in the description." Then, the Corrected Description does not disclose any invention using a trans-form starting material, and there is absolutely no circumstance where it is against social justice unless the right is to be expanded to include trans-form starting materials. On the other hand, a third party who sees the Corrected Description can only understand that the right of the Corrected Invention does not extend to a manufacturing process using a starting material having a trans-form vitamin D structure.

C. In addition to the above, when the appellants adjusted earlier and later patents in preparation for commercialization of the preparations, the appellee sent a document to Appellant DKSH, and thereby alleged not only that the Appellant's Process constitutes infringement under the doctrine of equivalents in relation to a cis-form vitamin D structure but also that the Appellant's Process constitutes literal infringement in relation to a CD ring structure on the premise that a CD ring structure having an optional substituent falls under those that form a trans-form vitamin D structure. In the Corrected Description, a trans-form substituent-bonded vitamin D structure is not excluded in relation to a CD ring structure, but only a cis-form vitamin D structure is stated in the scope of claims. Taking this fact into account, it is further clear that a trans form is intentionally excluded from the scope of claims in the case of a vitamin D structure. The aforementioned appellee's document is intended to have the appellants reconfirm the content stated in the Corrected Description to the effect that the starting material is limited to a cis form in the case of using a starting material having a vitamin D structure. This is an indication made by the patentee before the appellants started preparing and selling their preparations, and it should be considered to be an intentional limitation.

Moreover, the appellee only alleged equivalence in this lawsuit, and subsequently deleted a CD ring from the options for "Z" by the Correction. Regarding the statements concerning different constituent features, i.e. literal infringement in the case of a CD ring and infringement under the doctrine of equivalents in the case of a cis-form vitamin D structure, literal infringement can be alleged in relation to only one (CD ring) of them. This fact indicates that a trans-form vitamin D structure is excluded from the statements of the constituent features in relation to the other one (cis-form vitamin D structure). Accepting the allegation of infringement under the doctrine of equivalents in place of

the allegation of literal infringement in such a case goes against the principle of fairness that underlies the doctrine of equivalents, i.e. protection of third parties.

D. Therefore, the Appellant's Process does not fulfill the fifth requirement.

(Appellee)

A. Whether or not the scope of claims is clearly stated has no relationship to the necessity of applying the doctrine of equivalents or the principle of the doctrine of equivalents. An invention is required to be clearly stated in the scope of claims, and it is possible only in the case of an invention thus clearly defined to make an evaluation as to whether the relevant product is equivalent to the invention.

As long as the doctrine of equivalents is acknowledged by the Supreme Court Judgment on the "Ball spline bearing" Case, an applicant can file a patent application on the premise of said doctrine. In addition, a third party is required to evaluate a patent on the premise of said doctrine. Therefore, a choice of a certain literal structure in the scope of claims does not necessarily become an indication of an intention to give up alleging the right for structures other than the literal structure. The same applies even if "structures other than the literal structure" are widely known.

B. The appellants allege that the applicant should state all equivalent arts, which can be easily known as of the filing date, in the description in a manner that they are included in the scope of claims and that if the applicant fails to do so, he/she is not permitted to allege the applicability of the doctrine of equivalents. However, such obligation is not provided for in any part of the Patent Act, and there is no ground therefor in the current patent practice where the doctrine of equivalents has already been established.

According to the appellants' allegation, if the applicant makes an invention of a "cis form," he/she must also study an invention of a "trans form" for filing a patent application. Furthermore, the applicant also needs consideration at the time of filing an application so as to prevent the occurrence of other "intentional exclusion." The more matters to be considered to avoid "intentional exclusion," the longer study time is required. Therefore, more time, labor, and costs are required for filing a patent application. On the other hand, an infringer will be able to seek an equivalent to an invention without worrying about infringement under the doctrine of equivalents by considering another person's patent and deeming that the doctrine of equivalents does not extend to an equivalent unless the equivalent is stated in the scope of claims. This situation is unjustifiable.

(A) The appellants allege that if the applicant states "cis form" in the scope of claims when only two kinds, cis form and trans form, exist, it means a "particular" limitation to cis form. However, there is no reason for understanding that the statement of one of the

two kinds is an active indication of the intention to "particularly" limit the invention.
(B) The following is stated in column 37 in the Corrected Description, as pointed out by the appellants, in the course of the explanation of the structural formulas of the starting material of the Corrected Invention: "Each of the CD ring structure, steroid ring structure, and vitamin D structure for the present invention particularly means a structure as described below." The three kinds of structural formulas of Z, which are stated in the scope of claims, are thus only stated. On the other hand, documents are cited in column 41 in the Corrected Description in relation to part of the starting materials of the Corrected Invention that falls under the category of publicly known compounds.

The appellants purposefully link these separate statements and thereby allege that the patent applicant intentionally excluded a trans-form vitamin D structure from the technical scope of the invention at the time of filing of the application. This allegation is excessively arbitrary.
(C) The appellants allege that the limitation was made intentionally based on the existence of statements concerning vitamin D structures protected by addition of SO_2 in the Corrected Description.

A protective group for SO_2 is to protect a vitamin D structure from oxidation reaction. However, the reaction of the Corrected Invention does not include any reaction that possesses oxidizing properties. Therefore, said protective group is not a protective group used in the reaction of the Corrected Invention but is an example of protective groups used for vitamin D structures in general. The two figures of protective groups stated in the Corrected Description have the same structure, and it is thus sufficient to state one of these figures. However, both of these figures are stated. Therefore, the appellants' allegation that these figures indicate the applicant's intentional exclusion of a trans form is hard to understand.
(D) It is general in the patent practice that the technical scope of an invention stated in the scope of claims is broader than specific embodiments stated in working examples, and even in such cases, it is not said that the scope of claims is "enlarged" from the working examples. The appellants' allegation as if there were the "first-phase enlargement" between the working examples and the scope of claims and the finding of equivalence were the "second-phase enlargement" is not based on the correct understanding of the Patent Act.
C. The appellants make allegations based on the statements in the document which the appellee sent to the appellants before the filing of this action. However, in said document, the appellee alleges that a trans-form vitamin D structure is equivalent to the

claims of a cis-form vitamin D structure, as well as a literal infringement of the claims of a CD ring structure. Therefore, the allegation that such act falls under an intentional exclusion is not understandable. Moreover, said document is nothing more than a written counterargument of a lawyer against Cerbios's opinion. An expression of an opinion made in such discussions does not fall under the special circumstances in the fifth requirement of the doctrine of equivalents.

D. The appellants allege that the acknowledgement of equivalence in this case goes against the ideas of fairness. However, this case is a case where protection under the doctrine of equivalents should be granted based on the principle of fairness. The appellee invented maxacalcitol in 1985 and conducted its clinical tests with considerable investment, and thereby developed a new business for medicine. However, as in the appellee's allegation in A.(B) in (1) above, conventional manufacturing processes could not realize mass production or could only supply a small amount as an expensive medicine even if the clinical tests were successful. The Corrected Invention, which was discovered after a period of about 10 years, made it possible to supply maxacalcitol to society as a medicine at a sufficiently reasonable price. The appellants entered the market as generic medicine manufacturers in December of 2012 after the duration of the substance patent expired and the extended duration of the invention of the use of maxacalcitol for the treatment of psoriasis expired in September 2012. This market entry was possible because Cerbios supplied the active pharmaceutical ingredient of maxacalcitol at a price affordable for the appellants. Cerbios did not uniquely develop the Appellant's Process but came to know the Corrected Invention from the technical information of the appellee and supplied the appellants with the active pharmaceutical ingredient of maxacalcitol that it prepared by the Appellant's Process on the assumption that it is possible to avoid infringement of the Patent by changing cis form to trans form. Cerbios obtained the most important information, i.e. the use of the Reagent, from the technical information of the appellee. This fact is obvious from the fact that Cerbios did not submit a document that corresponds to a paper titled "Reactions of 1-halo-3-methyl-2,3-epoxybutane with alcohols" wherein the Reagent was stated (placed in a book titled "CHEMISTRY OF HETEROCYCLIC COMPOUNDS" that was distributed in 1982; hereinafter referred to as "Exhibit Otsu 9 Document") in a request for a trial for patent invalidation (Invalidation Trial No. 2013-800080), which Cerbios filed in relation to the Patent.

If it is possible, in this case, to avoid infringement of the Patent Pertaining to the Corrected Invention concerning an efficient industrial production process for maxacalcitol, which the researchers of the appellee had discovered through efforts over

10 years, only by changing cis form to trans form, the infringers can enjoy the effect of the efficient production achieved by the Corrected Invention and enter the market with inexpensive generic medicines. This is not reasonable in light of the purpose of Article 1 of the Patent Act.

E. Therefore, the Appellant's Process fulfills the fifth requirement.

2. Regarding whether there are grounds for invalidation in relation to the Corrected Invention

(1) Regarding the lack of an inventive step by citing Exhibit Otsu 14 Document as the primarily cited document (Ground for Invalidation A)

(Appellants)

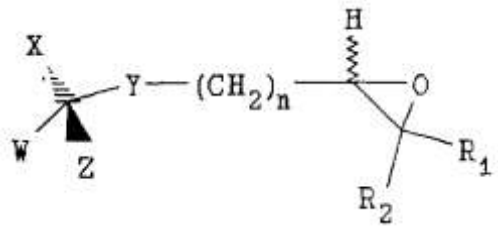
A. Figure 9 in a paper written by Noboru Kubodera, which is titled "Active Vitamin D Analogs - Important and Various Roles by Medicinal Chemists during the Course of Development of Promising Candidates as Useful Medicines" (Journal of Synthetic Organic Chemistry, Japan, Vol. 54, No. 2; Exhibit Otsu 14; hereinafter referred to as "Exhibit Otsu 14 Document") describes a process for the synthesis of Anticipated Metabolites of Maxacalcitol 12 and 13, which comprises the step of reacting the same starting material as that of the Corrected Invention with 4-bromo-2-methyl-tetrahydropyranyloxy-2-butene to produce a steroid compound having a prenyl group, the step of subsequently producing Epoxide Compounds 18 and 19 by using the Katsuki-Sharpless reaction, and the step of light illumination and thermal isomerization by using DIBAH (diisobutylaluminum hydride) thereon (hereinafter referred to as "Exhibit Otsu 14 Invention").

The Corrected Invention and Exhibit Otsu 14 Invention differ in the following points but are identical with each other in all the other points.

(Difference 1) Regarding a side chain, which is the objective substance, the side chain of the Corrected Invention is a Maxacalcitol Side Chain whose group at the end is a methyl group, while the side chain of Exhibit Otsu 14 Invention is one whose group at the end is a hydroxymethyl group and is not a Maxacalcitol Side Chain.

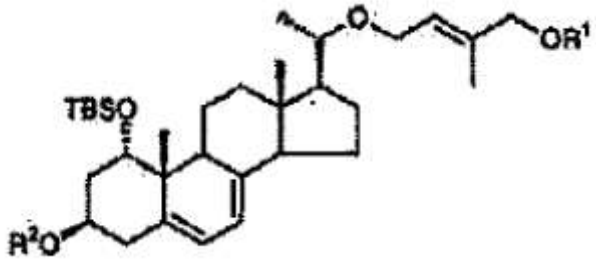
(Difference 2) In the Corrected Invention, the reagent used for alkylation reaction is "4-bromo-2,3-epoxy-2-methylbutane" (the Reagent). On the other hand, in Exhibit Otsu 14 Invention, it is "4-bromo-2-methyl-tetrahydropyranyloxy-2-butene."

(Difference 3) In the Corrected Invention, an epoxide compound having the following structure is obtained by reacting the starting material, in the presence of a base, with the Reagent:

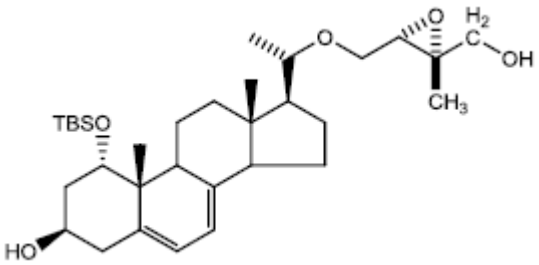


n=1, R_1, and R_2 = methyl.

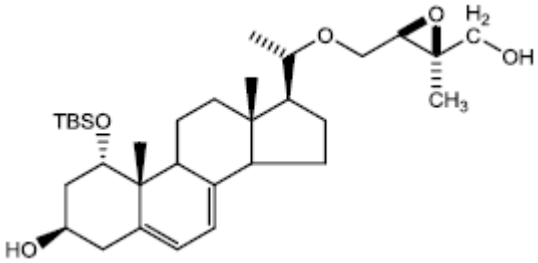
On the other hand, in Exhibit Otsu 14 Invention, a compound having the following structure is produced by reacting the starting material with a reagent that differs from the Reagent:



and then, epoxide compounds having the following structures are produced by using the Katsuki-Sharpless reaction:



Compound 18



Compound 19

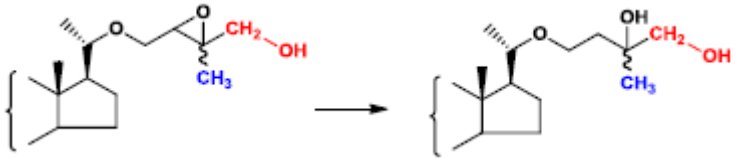
However, Difference 3 is a difference that naturally arises from Difference 2, and it is not separate from and independent of Difference 2. Therefore, the only substantial difference is Difference 2.

B. The aforementioned differences can be easily overcome as follows.

(A) Exhibit Otsu 14 Document is a document that considers a process for the synthesis of maxacalcitol as a whole, and it clearly specifies that a process for the industrially efficient preparation of maxacalcitol is a technical problem.

(B) In addition, as indicated in Figure 1 below, Figure 9 in Exhibit Otsu 14 Document describes a reaction of opening the ring of an epoxy group by reduction from an epoxide compound, and also describes that the anticipated metabolite of maxacalcitol was obtained in a good yield.

(Figure 1)



Reduction (ring-opening reaction)

(Epoxide compound) (Anticipated metabolite)

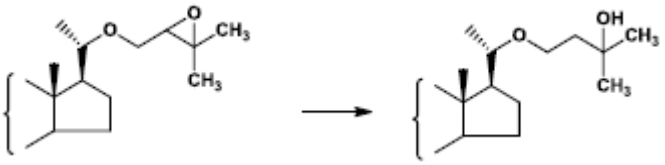
The side chain of this anticipated metabolite was synthetized on the assumption of the possibility that one of the methyl groups at the end of a Maxacalcitol Side Chain will change to a hydroxymethyl group "on the assumption of the part that is easily subject to metabolism in view of the structure" of maxacalcitol. It differs from a Maxacalcitol Side Chain only in that one of the methyl groups at the end (CH_3; the blue-colored part in Figure 1 above) is a hydroxymethyl group (CH_2-OH; the red-colored part in Figure 1 above).

(C) In the study of organic synthesis, it is normal to obtain ideas from a process for the synthesis of a compound having a similar structure. When seeing the statements in Figure 9 in Exhibit Otsu 14 Document, a person ordinarily skilled in the art, who intends to obtain the process for the efficient preparation of maxacalcitol described in Exhibit Otsu 14 Document as a solution for the problem, can be motivated to apply the synthesis process of Exhibit Otsu 14 Invention to the synthesis of maxacalcitol and change the hydroxymethyl group in the epoxide compound to a methyl group by focusing attention on the fact that the structures of the side chain of a vitamin D derivative, which is the anticipated metabolite of Exhibit Otsu 14 Invention, and its precursor, i.e. steroid compound, and the structure of a Maxacalcitol Side Chain are very similar to each other as mentioned above.

In the ring-opening reaction indicated in Figure 1 above, the hydroxymethyl group and methyl group at the end of the epoxide compound are preserved in the anticipated metabolite as they are. Therefore, a person ordinarily skilled in the art can easily understand and conceive of the fact that even if the hydroxymethyl group in the epoxide compound of Exhibit Otsu 14 Invention is replaced with a methyl group, both of the

methyl groups are preserved as indicated in Figure 2 below, and maxacalcitol can be synthesized by the ring-opening reaction of the epoxy group.

(Figure 2)

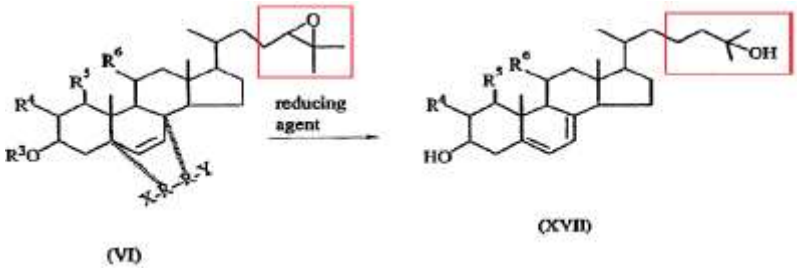


Epoxide compound　　Steroid compound having the same side chain as that of maxacalcitol

The fact that the hydroxymethyl group and the methyl group are preserved as they are even after the opening of the ring of the epoxy group is consistent with the common general technical knowledge of persons ordinarily skilled in the art (Exhibit Otsu 10).

Moreover, a process for forming a side chain wherein two methyl groups are bonded at the end in the same manner as maxacalcitol by opening the ring of the epoxy group of the epoxide compound having a steroid ring structure with a reducing agent had been known by persons ordinarily skilled in the art prior to the Priority Date, as indicated in Figure 3 below (Exhibit Otsu 19; however, the side chain indicated in Figure 3 differs from a Maxacalcitol Side Chain in that the atom at the 22-position is not an oxygen atom but a carbon atom).

(Figure 3)



(VI)　　(XVII)

The inventors of the Corrected Invention themselves conceived of maxacalcitol by replacing the carbon atom at the 22-position of a calcitriol side chain with an oxygen atom (Exhibit Otsu 14). However, it is described in International Publication No. 1993/21204 (Exhibit Otsu 19; hereinafter referred to as "Exhibit Otsu 19 Document") that an epoxide compound is used when forming the same side chain as said calcitriol side chain. A person ordinarily skilled in the art can immediately understand that the process for forming a Maxacalcitol Side Chain described in Figure 9 in Exhibit Otsu 14 Document is very similar to the process for forming a side chain of Exhibit Otsu 19

Document. A person ordinarily skilled in the art who has technical knowledge similar to that which is described in Exhibit Otsu 19 Document has no difficulty in conceiving of the synthesis of a maxacalcitol precursor (epoxide compound) from the epoxide compound indicated in Figure 9 in Exhibit Otsu 14 Document.

Therefore, based on Figure 9 in Exhibit Otsu 14 Document, a person ordinarily skilled in the art who recognizes the problem mentioned in (A) above can easily conceive of using and is motivated to use an epoxide compound in which the hydromethyl group of the epoxide compound indicated in Figure 9 is replaced with a methyl group as the precursor of maxacalcitol for the purpose of synthesizing maxacalcitol.

(D) Then, as mentioned below, it is easy to conceive of the alcohol compound at the 20-position of the steroid ring structure as the reagent and starting material of the Corrected Invention based on the epoxide compound indicated in Figure 2 above.

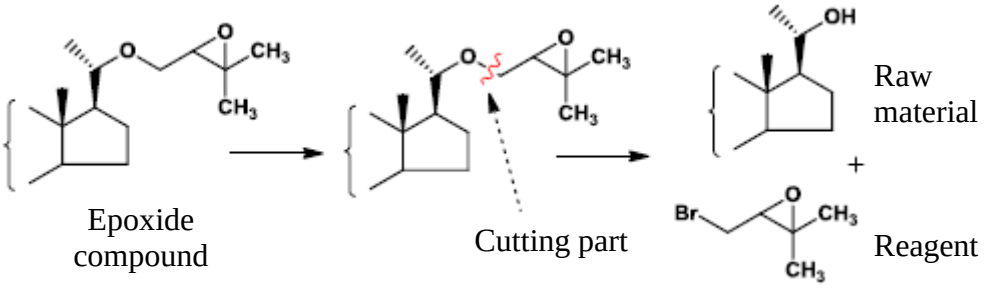
a. In considering the routes for the synthesis of known substances, "retrosynthesis" is common practice used by researchers in the field of organic synthesis (Exhibits Otsu 37 and 38). In retrosynthesis, researchers consider synthesis processes by starting from the objective substance and retrograding required reactions. As of the Priority Date, retrosynthesis was a synthesis process which any person engaging in synthetic organic chemistry has necessarily learned. It is natural for a person ordinarily skilled in the art to use retrosynthesis to solve the problem of efficiently producing a known substance, maxacalcitol.

Retrosynthesis is applied to synthesize an epoxide compound that serves as a precursor for the synthesis of maxacalcitol as efficiently as possible, and the matter that is first considered is whether it is possible to synthesize such epoxide compound by one-step reaction.

Looking at the epoxide compound indicated in Figure 2 above, it can be cut between the oxygen atom of the ether bond and the carbon atom on its right side, as indicated in Figure 4 below, and such cut is also reasonable from the perspective of organic synthesis (Exhibit Otsu 39A Written Opinion).

(Figure 4)

Cutting into the starting material and the reagent by retrosynthesis analysis



In the case of cutting as indicated above, the oxygen atom in the ether bond part is electronically negatively charged. Therefore, a hydrogen atom that has low electronegativity is added to cancel the negative charge. On the other hand, the carbon atom, which is in the other part of the cutting, is electronically positively charged. Therefore, Br or another halogen atom that has high electronegativity is added to cancel the positive charge. This is common general technical knowledge. In fact, the relationship between the starting material and the reagent is also the same in Exhibit Otsu 14 Invention, and a substance obtained by making the 22-position of the steroid ring structure after this cutting be a hydroxyl group is the very starting material of Exhibit Otsu 14 Invention.

b. Cutting at the aforementioned part is also consistent with the common general technical knowledge of persons ordinarily skilled in the art. That is, a method of alkylating the hydroxyl group at the 22-position of the starting material with alkyl bromide is art which was well-known and common among persons ordinarily skilled in the art as of the Priority Date (Exhibit Ko 1). In addition, it was also well-known as of the Priority Date that a glycidyl ether compound can be synthesized by reacting a compound having an epoxy group, such as epibromohydrin, with alcohol when alkylating a certain compound (Exhibits Otsu 6 to 8 and 29 to 31; Exhibit Otsu 31 in relation to secondary alcohol that is bonded to a sterically complex three-membered ring skeleton; Exhibits Otsu 41 and 42 in relation to sterically complex steroid alcohol).

c. Based on the above, a person ordinarily skilled in the art who considers an efficient manufacturing process for maxacalcitol can conceive, through application of retrosynthesis, of applying the Reagent (compound indicated at the bottom right of Figure 4 above; its structure is the same as that of the epoxy reagent of Corrected Invention 1) which is obtained by first cutting an epoxide compound at the part indicated in said figure and then adding Br on the side of the carbon atom to the starting material of Exhibit Otsu 14 Invention (compound indicated at the top right of Figure 4; the carbon skeleton of the starting material of the Corrected Invention is the same as

that of a steroid ring structure; hereinafter referred to as the "Steroid Starting Material") which is obtained by adding a hydrogen atom on the side of the oxygen atom.

In addition, in Exhibit Otsu 14 Invention, two steps, specifically, introduction of prenyl and the Katsuki-Sharpless reaction, are required to introduce an epoxy group into a side chain. However, a person ordinarily skilled in the art can easily understand that it is possible to reduce the number of steps because an epoxy group can be introduced into a side chain through one step by using the Reagent.

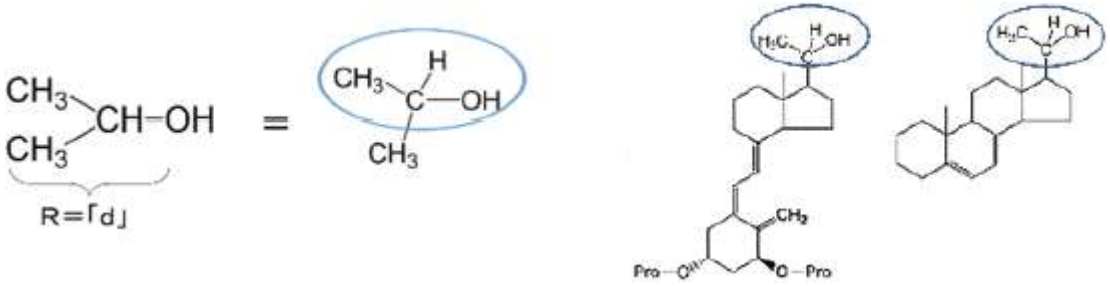
d. A person ordinarily skilled in the art who has conceived of the Reagent as above can discover Exhibit Otsu 9 Document, in which the Reagent is described, as a result of document search.

Exhibit Otsu 9 Document reports that the Reagent reacts with 10 kinds of alcohols that have different structures. Said document describes that among these alcohols, isopropanol reacts with the Reagent in a good yield of about 50% despite the conditions not being optimized.

The reaction between isopropanol and the Reagent is S_N2 reaction. The issues that arise in relation to the predictability of the obtainment of the objective product by S_N2 reaction are similarity in the structure of the functional group, which becomes the reaction site, and, for alcohols, similarity in the environment in the immediate vicinity of the reaction point, such as what grade of alcohol is the structure of the reaction point. The molecular weight of the entire compound provided for reaction and the molecular structure of the sites that are distant from the reaction site and are not related to reaction do not become issues (Exhibit Otsu 39A Written Opinion and Exhibit Otsu 64).

Then, isopropanol is the secondary alcohol like the starting material of the Corrected Invention, and isopropanol and the starting material of the Corrected Invention are very similar to each other in the partial structure of the reaction site (the parts circled in blue in Figure 5 below). Therefore, a person ordinarily skilled in the art can understand that S_N2 reaction between the starting material of the Corrected Invention and the Reagent also proceeds well.

(Figure 5)



(Isopropanol) (Starting material of the Corrected Invention)

Looking at a molecule model, which is common practice used by persons ordinarily skilled in the art when considering reaction, the Reagent has a large space in the path of a nucleophilic agent (substance subjected to reaction). Therefore, it is clear that reaction with the Steroid Starting Material easily proceeds and that the steroid ring structure does not become a steric obstruction to reaction with the Reagent at all.

e. Then, Exhibit Otsu 9 Document also describes the step of opening the ring of an epoxy group of an epoxy ether compound obtained by reaction of butanol and the Reagent in an intended direction with a reducing agent. It also describes that a side chain that is identical with a Maxacalcitol Side Chain is formed if said ring is opened. It is obvious that the side chain formed by using isopropanol in place of butanol will have the same structure (Maxacalcitol Side Chain) if the ring of the epoxy group is opened.

Therefore, a person ordinarily skilled in the art should be considered to be motivated to synthesize the epoxide compound of the Corrected Invention based on the idea that epoxy alkylation reaction between the Reagent and the Steroid Starting Material is highly likely to proceed with high degree of probability (Exhibit Otsu 39A Written Opinion).

C. Regarding the allegation of the appellee

(A) Regarding whether a person ordinarily skilled in the art can easily conceive of the idea of using an epoxide compound wherein the hydroxymethyl group of the epoxide compound indicated in Figure 9 in Exhibit Otsu 14 Document is replaced with a methyl group

The appellee alleges that there is no reason for focusing attention only on the reduction reaction of the epoxy substance of Exhibit Otsu 14 Invention because the Katsuki-Sharpless reaction is used due to the existence of two kinds of different steric configurations for the vitamin D derivatives that are the objective substances of Exhibit Otsu 14 Invention. However, both of these vitamin D derivatives are very similar to a Maxacalcitol Side Chain in terms of their structure, and are obtained in a good yield by the opening of the ring of the epoxy group. Therefore, a person ordinarily skilled in the art can conceive of application to the synthesis of maxacalcitol by focusing on either of these derivatives. In addition, a person ordinarily skilled in the art can easily understand the purpose of using the Katsuki-Sharpless reaction in Exhibit Otsu 14 Document, and he/she can understand that the issue in terms of steric configuration does not arise in relation to maxacalcitol and that it is possible to efficiently prepare maxacalcitol by using only one kind of precursor epoxide compound. Therefore, the existence of two

kinds of isomers in Figure 9 does not reduce the easiness of conceiving of the idea alleged by the appellants.

In addition, the appellee alleges that it is straightforward to replace the reagent with prenyl bromide in the case of applying Exhibit Otsu 14 Invention to the synthesis of maxacalcitol. However, retrosynthesis is applied in order to synthesize an epoxide compound, which is a precursor, as efficiently as possible, and a person ordinarily skilled in the art would not bother to adopt a roundabout synthesis process which comprises a larger number of steps. Therefore, the appellee's allegation is unreasonable.

(B) Regarding the predictability of reaction between the Reagent and the Steroid Starting Material

The appellee alleges that a person ordinarily skilled in the art cannot predict the progress of reaction between the Reagent and the Steroid Starting Material, and cites the following as grounds for the allegation: [i] The Reagent can cause a side reaction as it has three candidates for the reaction point; [ii] The ring of the epoxy group of the Reagent can be opened; [iii] It is not possible to predict that reaction proceeds at Reaction Point 1 mentioned later based on the charge distribution of the Reagent; [iv] It is not possible to predict that reaction proceeds by direct replacement reaction based on knowledge about the reactivity of epihalohydrin; [v] The reaction of the Steroid Starting Material is affected by the solid of the Reagent.

However, regarding [i] and [ii] above, it is clear from Exhibit Otsu 9 Document itself that reaction proceeds at Reaction Point 1 by direct replacement reaction without the ring of the epoxy group being opened.

In addition, regarding [iii] above, the appellee's allegation that in the Reagent, both the carbon atom at the reaction point and a carbon atom next to it are positively charged is erroneous.

Regarding [iv] above, it is known that in Williamson reaction, epihalohydrin also reacts at Reaction Point 1 (Exhibit Otsu 58).

Furthermore, regarding [v] above, said fact is nothing more than the knowledge which the researchers of the appellee personally had, and is not common general technical knowledge. It was well-known as of the Priority Date that the hydroxyl group of the Steroid Starting Material easily yields S_N2 reaction with a variety of alkyl halide reagents that have molecular weight equivalent to that of the Reagent or have a structure similar to that of the Reagent (Exhibits Ko 12 and 20 and Exhibits Otsu 18 and 41).

D. As mentioned above, a person ordinarily skilled in the art who intends to find an efficient manufacturing process for maxacalcitol can easily conceive of all of the following matters: [i] changing the hydroxymethyl group at the end to a methyl group to

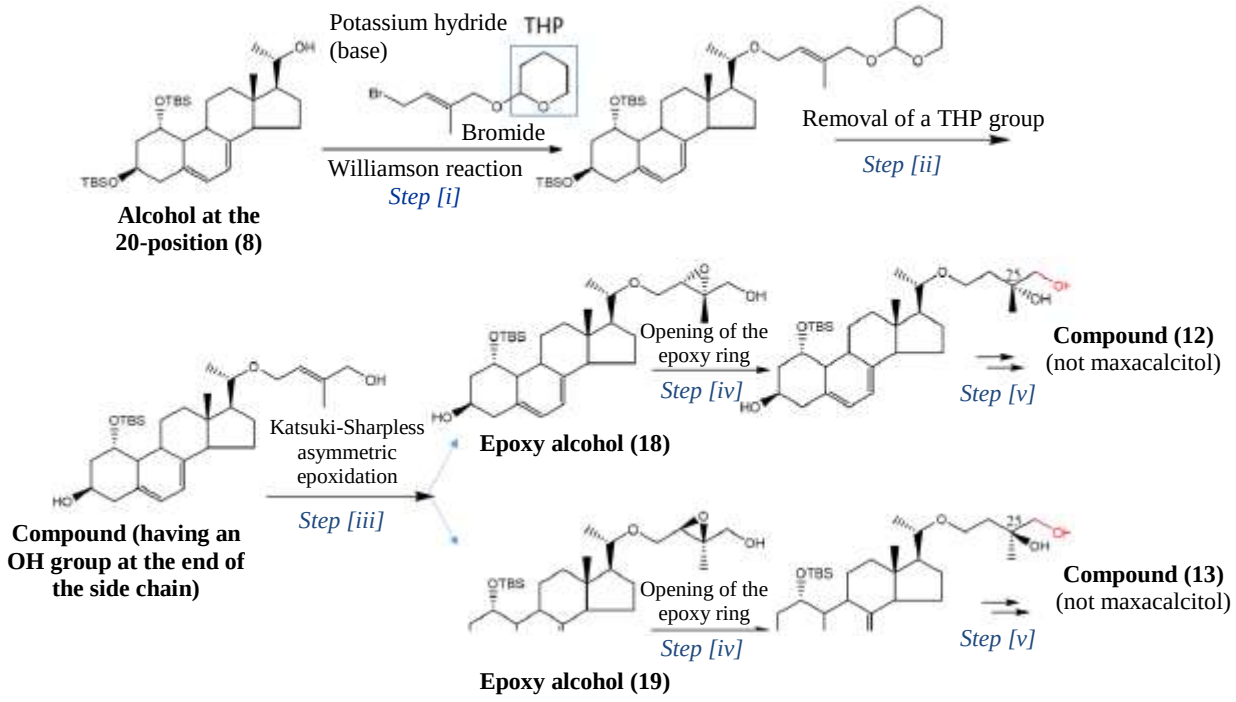
make the anticipated metabolite of maxacalcitol of Exhibit Otsu 14 Invention be maxacalcitol (Difference 1), [ii] applying the Reagent to the Steroid Starting Material in place of the reagent of Exhibit Otsu 14 Invention (Difference 2), and [iii] obtaining the epoxide compound of the Corrected Invention by applying the Reagent to the Steroid Starting Material (Difference 3).

Then, the existence of Exhibit Otsu 9 Document that describes the Reagent builds further confidence in the possibility of the aforementioned application. The fact that Exhibit Otsu 9 Document neither describes nor suggests use of the Reagent in place of the reagent of Exhibit Otsu 14 Invention does not affect said easiness. In fact, the inventors of the Corrected Invention say that they thought that maxacalcitol could be synthesized by using the Reagent after seeing the reaction of isopropanol of Exhibit Otsu 9 Document (Exhibit Ko 13 and Exhibit Otsu 24).

Therefore, the Corrected Invention can be easily conceived of by a person ordinarily skilled in the art based on Exhibit Otsu 14 Invention and the technical matters described in Exhibit Otsu 9 Document.

(Appellee)

A. The reaction steps of Exhibit Otsu 14 Invention are as indicated in the following figures.

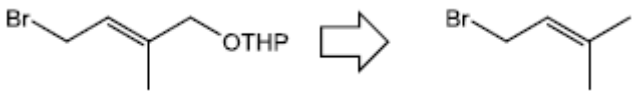


Common features and differences between the Corrected Invention and Exhibit Otsu 14 Invention are as alleged by the appellants, and the inventions differ in the structure of the end of the side chain subject to introduction and also differ in the reagent used for reaction.

B. The appellants allege that it is easy to use substances obtained by replacing the hydromethyl group of each of Epoxide Compounds (18) and (19) with a methyl group as the precursor for maxacalcitol, focusing attention on the point that Anticipated Metabolites (12) and (13), which are the final objective substances, are obtained by the opening of the ring of the epoxy groups of Epoxide Compounds (18) and (19) in the reaction steps of Exhibit Otsu 14 Invention.

However, the reaction of Epoxide Compounds (18) and (19) is used in the reaction steps of Exhibit Otsu 14 Invention because special reaction steps, including the Katsuki-Sharpless reaction, are adopted to make it possible to selectively produce the steric configurations of the end of the side chain of the Final Objective Substances (12) and (13). That is, whether the final objective substance is (12) or (13) depends on whether the epoxide compound used is (18) or (19). The reaction does not require a step involving an epoxide compound without the objective of controlling the steric structure. On the other hand, as there is no different steric configuration for the end of a Maxacalcitol Side Chain, there is no reason for focusing attention only on the reduction reaction of an epoxy substance in the reaction steps of Exhibit Otsu 14 Invention when developing a process for preparing maxacalcitol. The appellants focus attention only on the reduction reaction of an epoxy substance of Exhibit Otsu 14 Invention based on the afterthought which arose after seeing the Corrected Invention.

Supposing the case of applying Exhibit Otsu 14 Invention to the synthesis of maxacalcitol while focusing attention on the similarity between the structure of the anticipated metabolites of Exhibit Otsu 14 Invention and that of maxacalcitol, it is natural not to replace the hydroxymethyl group bonded to the epoxy group with a methyl group but to change the reagent to be reacted with the starting material (8) in Exhibit Otsu 14 Invention to bromide having the structure indicated in the lower right figure (prenyl bromide) (Exhibit Otsu 13).



Reagent of Exhibit Otsu 14 Prenyl bromide

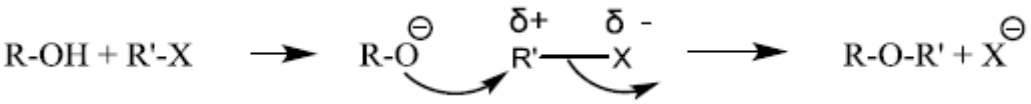
The reagent in the right figure reacts with the starting material, but it does not produce an epoxide compound. If the end of the side chain of the objective substance becomes a Maxacalcitol Side Chain, there is no reason for producing an epoxy substance by using the Katsuki-Sharpless reaction.

Exhibit Otsu 14 Document does not suggest that an epoxy reagent is used in the Williamson reaction with the alcohol compound at the 20-position, and it does not contain any statement suggesting that the ring-opening reaction of an epoxy substance is used in the introduction of a Maxacalcitol Side Chain. The allegation that the Reagent can be derived from Exhibit Otsu 14 Invention ignores the technical significance of the reaction steps of Exhibit Otsu 14 Invention.

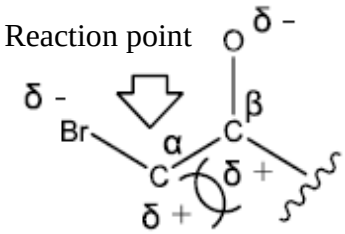
C. Moreover, the reaction between the Reagent and the alcohol compound at the 20-position, like the starting material of the Corrected Invention, had been predicted to be difficult based on the common general technical knowledge of organic chemistry, as mentioned below.

(A) Difficulty in prediction on the side of the Reagent

a. The higher the degree of positive charge (**δ**+) of the reaction point on the R'-X side of alkyl halide is or the more stable the positive charge is, the more easily the Williamson reaction, which is the reaction of the Corrected Invention, proceeds (Exhibit Otsu 56).

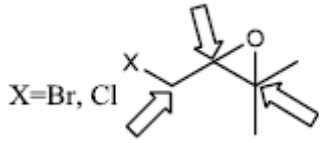


In terms of the common sense of organic chemistry, when considering the structure of the reagent of the Corrected Invention, both the α carbon atom, which is the reaction point, and the β carbon atom next to it are supposed to be positively charged because each is bonded to a negative atom, specifically, Br atom and oxygen atom, respectively, as indicated in the figure below. However, both of those neighboring carbon atoms are positively charged and thus repel each other. Therefore, the positive charge of the carbon atom at the reaction point is difficult to stabilize, and Williamson reaction is also predicted to be difficult to progress.



b. In addition, as the Reagent has three candidates for the reaction point, the possibility of causing a side effect is predicted.

Reaction Point 2



Reaction Point 1 Reaction Point 3

c. Furthermore, an epoxide compound having an epoxy group in its molecule is generally rich in reactivity, and its ring is easy to open. Therefore, the opening of the ring by reaction is predicted.

d. According to many studies concerning epihalohydrin, whose structure is similar to that of the Reagent, epihalohydrin causes the opening of the ring of an epoxy group by reaction with a nucleophilic reagent in many cases (direct replacement reaction occurs in few cases). The conditions and route of such reaction (whether or not direct replacement reaction occurs) are difficult to predict (Exhibit Ko 31). It is impossible to predict the direct replacement reaction of the Reagent from the knowledge of epihalohydrin.

(B) Difficulty in prediction on the side of the alcohol compound at the 20-position

On the other hand, the alcohol compound at the 20-position is sensitive to the effect of the solid (bulkiness of the position of the ring of the reagent, etc.) of the reagent which is the reaction partner. It is not possible to directly introduce a Maxacalcitol Side Chain into the alcohol compound at the 20-position, and reaction between the alcohol compound at the 20-position and Compound 9 of Exhibit Ko 13 or Reagent 1 of Exhibit Ko 12 mentioned later does not proceed at all. The alcohol compound at the 20-position is presumed to have a steric hindrance that hinders its reaction with the Williamson reaction reagent that has a structure into which a Maxacalcitol Side Chain can be introduced.

D. Exhibit Otsu 9 Document describes the consequence that the prediction based on the common general technical knowledge of organic chemistry mentioned in C. above is not applicable to reaction between the Reagent and a low-molecular-weight alcohol, such as isopropanol. However, the reason why reaction between the starting material and reagent of Exhibit Otsu 9 Document proceeds has not been clarified, and Exhibit Otsu 9 Document does not include any statement that explains the reason in an understandable manner. Moreover, the reaction yield (40.6 to 76.4%) and reaction conditions (requiring a heated reflux at 40 to 80°C for eight to 10 hours) of Exhibit Otsu

9 Document suggest that the Reagent has a steric hindrance. In that case, the Reagent has a reason for having people predict the difficulty of reaction in general. On the other hand, Exhibit Otsu 9 Document also suggests the existence of an action that promotes reaction, which goes beyond an action that makes reaction difficult, in reaction with low-molecular-weight alcohol, though the reason therefor is unknown.

However, Exhibit Otsu 9 Document does not have people predict reactivity in relation to reaction with the alcohol compound at the 20-position, whose structure significantly differs from that of low-molecular-weight alcohol. Therefore, it is reasonable to predict that reaction with the Reagent is also difficult, or to consider that whether or not the alcohol compound at the 20-position reacts with the Reagent is unknown without conducting experiments. In addition, there is no knowledge that serves as the basis for the predictability of the reactivity of the Reagent other than Exhibit Otsu 9 Document, and it is also difficult to predict the reaction of the Corrected Invention from the perspective of the Reagent.

In the Corrected Invention, actual experiments revealed that a combination of the alcohol compound at the 20-position causes reaction in a very good yield, despite the aforementioned prediction based on the common general technical knowledge. In consideration of the purpose of the patent system, a reaction that is not known to proceed without experiments should be evaluated as an invention involving an inventive step only if it is found to be reactive by actual experiments.

(2) Regarding the lack of an inventive step by citing Exhibit Ko 12 Document as the primarily cited document (Ground for Invalidation B)

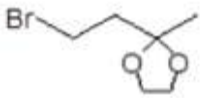
(Appellants)

A. In a paper written by Noboru Kubodera and four other authors titled "Synthetic studies of vitamin D3 analogues VIII" (Chem. Pharm. Bull., 1986, 34 (10), 4410; Exhibit Ko 12; hereinafter referred to as "Exhibit Ko 12 Document"), it is stated that alkylation reaction did not occur though Compound 9, which is the same starting material as that of the Corrected Invention (Steroid Starting Material), and "1-bromo-3,3-ethylenedioxybutane" (hereinafter referred to as "Exhibit Ko 12 Reagent 1") as a reagent were used for the purpose of the synthesis of maxacalcitol.

The aforementioned process for preparing maxacalcitol described in Exhibit Ko 12 Document (hereinafter referred to as "Exhibit Ko 12 Invention") and the Corrected Invention are identical with each other in the requirements for the objective substance, the starting material, and recovery, but differ in the reagent (Difference 1) and also differ in the intermediate and the reduction treatment to ring opening step (Difference 2).

B. The aforementioned Difference 1 can be easily overcome as mentioned below.
(A) As the appellants' allegation in (1) above, obtaining an efficient process for preparing maxacalcitol was naturally a technical problem facing a person ordinarily skilled in the art as of the Priority Date (Exhibit Ko 12 and Exhibit Otsu 14).

In addition, alkylation of the hydroxyl group at the 22-position of the Steroid Starting Material by an alkylation reagent in preparing maxacalcitol was the art that had already been commonly used as of the Priority Date (Exhibit Ko 12 and Exhibits Otsu 18 and 14). As of the Priority Date, a person ordinarily skilled in the art who was engaged in studies of the aforementioned technical problem only had to find an alkylation reagent that could alkylate the hydroxyl group at the 22-position of the steroid compound in a good yield.
(B) In Note 10 in Exhibit Ko 12 Document, the following is stated as a reason for a failure in synthesis using Exhibit Ko 12 Reagent 1: "It may be due to the bulkiness of 1-halo-3,3-ethylenedioxybutane." This statement suggests that among Exhibit Ko 12 Regent 1 (figure below), one wherein five-membered ring cyclic ether is less bulky can be expected to cause the progress of alkylation reaction with the Steroid Starting Material (Compound 9).



(C) On the other hand, a Maxacalcitol Side Chain has a structure wherein four-carbon straight alkyl is bonded to an ether group. Therefore, the reagent used for introducing a Maxacalcitol Side Chain is also required to be one whose straight chain structure has four carbons.

Then, Exhibit Ko 12 Document describes that maxacalcitol was obtained at the yield of 9% by reaction between the Steroid Starting Material and "4-bromo-1-butene" (hereinafter referred to as "Exhibit Ko 12 Reagent 2") indicated in the figure below.

In that case, a person ordinarily skilled in the art can conceive of using and is motivated to use a compound which has a cyclic structure but is not bulky while maintaining a four carbon straight alkyl structure, specifically, a compound whose number of elements that constitute the ring of the cyclic part is reduced to reduce the five-membered ring cyclic ether part, as the reagent.

Then, it is possible to find Exhibit Ko 9 Document, which places the Reagent as a compound that meets the aforementioned conditions, by examining compounds that

were publicly known at that time.
(D) The content described in Exhibit Otsu 9 Document is as the appellants' allegation in B.(D)d. in (1) above. The alkylation reaction described in Exhibit Ko 12 Document and the reaction between the Reagent and alcohol in the presence of alkali metal, alkoxide, as described in Exhibit Otsu 9 Document have commonality in that they are arts relating to S_N2 reaction. Therefore, the Reagent is predicted to react well with the Steroid Starting Material.

In addition, as it is obvious from a three-dimensional model, in Exhibit Ko 12 Reagent 1, the five-membered ring serves as a wall to block the path of the nucleophilic agent. Therefore, the oxygen atom of the Steroid Starting Material cannot get closer to the reagent, and S_N2 reaction does not proceed due to this steric hindrance. On the other hand, the Reagent has a large space in the path of the nucleophilic agent, and the epoxy group does not block the path of the Steroid Starting Material. Therefore, the nucleophilic agent can get closer to the back side of the carbon at the reaction point. Therefore, a person ordinarily skilled in the art who sees the statements in Note 10 in Exhibit Ko 12 Document can understand that the steric hindrance is overcome for the Reagent and is also strongly motivated to use the Reagent for the reaction in this regard.
(E) Then, as the appellants' allegation in B.(D)d. in (1) above, Exhibit Otsu 9 Document also describes that an epoxide compound obtained by reacting butanol and the Reagent was made into a Maxacalcitol Side Chain by treating the epoxy group with a reducing agent. Furthermore, it is possible to reduce the number of steps compared to Exhibit Ko 12 Invention, which goes through a step involving a ketone body, by introducing an epoxy group. Therefore, a person ordinarily skilled in the art would use the Reagent.
(F) In addition, Exhibit Ko 12 Document does not include any statement or fact that hinders the use of the Reagent in place of Exhibit Ko 12 Reagent 1.
(G) Therefore, it is natural for a person ordinarily skilled in the art who recognizes the technical problem mentioned in (A) above to try to react the Steroid Starting Material of Exhibit Ko 12 Document with the Reagent described in Exhibit Ko 9 Document based on the suggestion of Exhibit Ko 12 Document.
C. The aforementioned Difference 2 (difference in the intermediate and the reduction treatment to ring-opening step) is automatically overcome if Difference 1 (difference in the reagent) is overcome. In addition, it was widely known prior to the Priority Date that it is possible to produce the same side chain as a Maxacalcitol Side Chain by opening the ring of the epoxy group of an epoxy group-introduced steroid compound with a reducing agent. Consequently, Difference 2 can be easily overcome.
D. Therefore, the Corrected Invention is one which a person ordinarily skilled in the art

can easily conceive of based on Exhibit Ko 12 Invention and Exhibit Ko 9 Document.
(Appellee)
A. As alleged by the appellants, the Corrected Invention and Exhibit Ko 12 Invention differ in the reaction reagent (Difference 1) and also completely differ in the intermediate and the step of forming a Maxacalcitol Side Chain by opening the ring of the epoxy group (Difference 2).
B. The appellants allege that a person ordinarily skilled in the art who was engaged in studies of an efficient process for preparing maxacalcitol only had to find an alkylation reagent which can alkylate the hydroxyl group at the 22-position of a steroid compound in a good yield. However, a process which the appellee actually used for the preparation of a curative medicine in a clinical test as the improved technology of Exhibit Ko 12 Invention is not the Williamson reaction that is the same as Exhibit Ko 12 Invention, which is alkylation using an alkylation reagent, but a process called Michael process. Therefore, said allegation is based on an afterthought that arose after seeing the Corrected Invention. There are many alkylation reagents, but the Reagent is the only alkylation reagent that can be used for the industrial production of maxacalcitol.
C. The "bulkiness" referred to in Note 10 in Exhibit Ko 12 Document is mentioned in comparison with alkylation reaction between "1α,3β-bis(tetrahydropyranyloxy)-5-androstene-17β-ol" and "1-chloro-4,4-ethylenedioxypentane" (hereinafter referred to as "Exhibit Ko 12 Reagent 3"). It is presumed to be based on the degree of distance of the five-membered ring from the reaction point of the introduction of a side chain in the starting material. Originally, the aforementioned alkylation reaction differs from the reaction of Exhibit Ko 12 Invention in the structure of the reaction point on the side of alcohol, which is the starting material. Therefore, there is no reason for putting emphasis on Note 10.

Moreover, in Exhibit Ko 12 Document, the reaction using Exhibit Ko 12 Reagent 1, which is a bulky reagent having a five-membered ring, failed, and the yield of the reaction using Exhibit Ko 12 Reagent 2, which does not have any cyclic structure, as the reagent was 9%. Both of those reactions do not have satisfactory reactivity. Therefore, a person ordinarily skilled in the art who sees Exhibit Ko 12 Document normally thinks of another reagent, and the appellants' allegation that "a person ordinarily skilled in the art considers that a reaction using a compound which has a cyclic structure but is not bulky goes well" is incomprehensible.
D. It is impossible to predict from Exhibit Ko 9 Document that a reaction between the Reagent and high-molecular-weight alcohol, like the Steroid Starting Material of Exhibit Ko 12 Document, proceeds, as the appellee's allegation in D. in (1) above.

E. As mentioned above, there is no reason for the appellants' allegation that a person ordinarily skilled in the art could have easily conceived of the structure of the Corrected Invention pertaining to differences between the Corrected Invention and Exhibit Ko 12 Invention.

(3) Regarding the lack of an inventive step by citing Exhibit Otsu 4 Document as the primarily cited document (Ground for Invalidation C)

The parties' allegations concerning Ground for Invalidation C are as briefly indicated in No. 3, 7. in "Facts and reasons" in the judgment in prior instance. Therefore, the relevant part is cited (however, in the judgment in prior instance pertaining to the citation, the terms "Ground for Invalidation 2," "Exhibit Otsu 4-2," and "Exhibit Otsu 9" are deemed to be replaced with "Ground for Invalidation C," "Exhibit Otsu 4 Document," and "Exhibit Otsu 9 Document," respectively; hereinafter the same shall apply in the case of citation).

No. 4 Court decision

This court also determines that the Appellant's Process is equivalent to the Corrected Invention and that the Patent Pertaining to the Corrected Invention is not recognized as one that should be invalidated by a trial for patent invalidation. The reasons therefor are as follows.

1. Regarding whether the Appellant's Process is equivalent to the Corrected Invention

(1) Regarding the five requirements of the doctrine of equivalents and burden of proof

A patentee shall have the exclusive right to work the patented invention as a business (main clause of Article 68 of the Patent Act). The technical scope of a patented invention shall be determined based upon the statements in the scope of claims attached to the application (Article 70, paragraph (1) of said Act). An applicant for a patent shall state all matters necessary to specify the invention for which he/she requests the grant of a patent in the scope of claims (Article 36, paragraph (5) of said Act). Therefore, the statements in the scope of claims function to publicly notify third parties of the scope of the exclusive right of the patent. Consequently, the technical scope of a patented invention is in principle defined by the literal interpretation of the structure stated in the scope of claims.

However, even if, within the structure stated in the scope of claims, there is a part which is different from a product manufactured, etc. or a process used by the other party (hereinafter referred to as the "subject product, etc."), it is reasonable to understand that the subject product, etc. falls under the technical scope of the patented invention as an equivalent to the structure stated in the scope of claims if the following requirements are

fulfilled: [i] said part is not the essential part of the patented invention; [ii] even if said part is replaced with a part in the subject product, etc., the purpose of the patented invention can be achieved and the same function and effect can be obtained; [iii] a person ordinarily skilled in the art to which the invention pertains (a person ordinarily skilled in the art) could have easily conceived of the aforementioned replacement at the time of the manufacturing, etc. of the subject product, etc.; [iv] the subject product, etc. is neither identical with publicly known art at the time of the filing of the patent application for the patented invention nor is one which a person ordinarily skilled in the art could have easily presumptively conceived of at the time of said filing based on such publicly known art; and [v] there are no special circumstances, such as the fact that the subject product, etc. falls under those that were intentionally excluded from the scope of claims in the patent application procedures for the patented invention (hereinafter requirements [i] to [v] above are referred to as the "First Requirement" to the "Fifth Requirement" in order of precedence). This is because [1] it is extremely difficult to foresee all kinds of infringements which may occur in the future and formulate the scope of the claims in the description at the time of filing a patent application, and if another person is able to easily avoid injunction and other exercise of rights by the patent holder by only replacing part of the structure stated in the scope of claims by the substance or art, etc. which came to be known after the filing of the patent application, it will greatly reduce incentives for invention in society in general, which is not only against the purposes of the Patent Act, i.e. contributing to the development of industry through the protection and encouragement of inventions, but would be against social justice and the ideas of fairness. [2] Taking this into account, it is reasonable to understand that the substantive value of the patented invention extends to the art which a third party can easily conceive of as one that is substantially identical with the structure stated in the scope of claims based on said structure and that third parties should foresee this. [3] On the other hand, concerning arts which were publicly known at the time of the filing of the patent application for the patented invention or arts which a person ordinarily skilled in the art could have easily presumptively conceived of based on these arts, no one could have obtained a patent; therefore, such arts cannot be found to be within the technical scope of the patented invention. [4] Furthermore, concerning arts which the patentee had once acknowledged not to fall under the technical scope of the patented invention or arts in relation to which he/she had behaved as if he/she had objectively acknowledged so, e.g. where the applicant intentionally excluded art from the scope of claims in the patent application procedures, the patentee is not entitled to claim otherwise afterwards, since this is against the doctrine of estoppel (Supreme Court

Judgment on the "Ball spline bearing" Case).

Regarding the burden of alleging and proving the fulfillment of the First to Fifth Requirements, it is reasonable to understand as follows, taking into account that the doctrine of equivalents should be applied within the scope of those that are found to be easily conceived of by a person ordinarily skilled in the art as one that is substantially identical with the statements in the scope of claims beyond the scope of the literal interpretation of said statements: a person who alleges that the subject product, etc. is equivalent to a patented invention should be considered to have the burden of allegation and proof for the First to Third Requirements, which are the facts required for the subject product, etc. to be recognized as falling within said scope, while a person who denies the application of the doctrine of equivalents in relation to the subject product, etc. has the burden of allegation and proof for the Fourth and Fifth Requirements, which are related to the cases where the doctrine of equivalents should not be applied, even if the subject product, etc. is within the aforementioned scope.

(2) Differences between the Corrected Invention and the Appellant's Process

As mentioned in No. 2, 2.(7)(D) above, the Appellant's Process fulfills Constituent Features [A], [B-2], [D], and [E] of the Corrected Invention, but it does not fulfill Constituent Features [B-1], [B-3], and [C] of the Corrected Invention in that Starting Material A and Intermediate C in said process are not cis-form compounds having a vitamin D structure but are trans-form compounds having a vitamin D structure, which are the geometric isomers of said cis-form compounds. Therefore, the fulfillment of the requirements for the doctrine of equivalents is determined below in a sequential order to determine whether the Appellant's Process using trans-form compounds having a vitamin D structure as the starting material and the intermediate can be considered to be equivalent to the case of using cis-form compounds having a vitamin D structure as the starting material and the intermediate in the Corrected Invention.

(3) Regarding the First Requirement of the doctrine of equivalents (non-essential part)

A. Regarding the finding of the essential part

The substantial value of an invention which the Patent Act intends to protect exists in the disclosure, with a specific structure, to society of a means for solving a technical problem that could not have been solved by prior art, which is based on a unique technical idea that is not seen in prior art. Therefore, the essential part of a patented invention should be understood as the characteristic part which constitutes a unique technical idea that is not seen in prior art in the statements in the scope of claims of the patented invention.

The aforementioned essential part should be found by first understanding the

problem to be solved and means for solving the problem of the patented invention (see Article 36, paragraph (4) of the Patent Act and Article 24-2 of the Ordinance for Enforcement of the Patent Act) and its effect (purpose and structure and its effect; see Article 36, paragraph (4) of the Patent Act prior to amendment by Act No. 116 of 1994) based on the statements in the scope of claims and the description, and then determining the characteristic part which constitutes a unique technical idea that is not seen in prior art in the statements in the scope of claims of the patented invention. That is, taking into account that the substantial value of a patented invention is defined depending on the degree of contribution in comparison with prior art in the relevant technical field, the essential part of a patented invention should be found based on the statements in the scope of claims and the description, in particular, through comparison with prior art stated in the description. [i] If the degree of contribution of the patented invention is considered to be more than that of prior art, the patented invention is found as a generic concept in relation to part of the statements in the scope of claims (as mentioned later in C. and D.; the Corrected Invention is an example of such a case). [ii] If the degree of contribution of the patented invention is evaluated as not much more than prior art, the patented invention is found to have almost the same meaning as stated in the scope of claims.

However, if the statement of the problem, which is described as one that prior art could not solve, in the description is objectively insufficient in light of prior art as of the filing date (or the priority date; hereinafter the same applies in (3) in this section), a characteristic part which constitutes a unique technical idea of the patented invention that is not seen in prior art should be found also in consideration of prior art that is not stated in the description. In such cases, the essential part of the patented invention is closer to the statements in the scope of claims compared to the cases where it is found only based on the statements in the scope of claims and the description, and the scope of application of the doctrine of equivalents is considered to be narrower.

In addition, in determining the fulfillment of the First Requirement, that is, whether a difference from the subject product, etc. is a non-essential part, it is not appropriate to first divide the constituent features stated in the scope of claims into essential parts and non-essential parts and then consider that the doctrine of equivalents is not applicable to all of the constituent features that fall under essential parts, but it is necessary to first determine whether the subject product, etc. commonly has the essential part of the patented invention determined as mentioned above and then consider a difference not to be an essential part if the subject product, etc. is recognized as having said essential part. Even if the subject product, etc. has a difference other than the characteristic part which

constitutes a unique technical idea that is not seen in prior art, this fact does not become a reason for denying the fulfillment of the First Requirement.

B. Statements in the Corrected Description

The following is stated in the "detailed explanation of the invention" section in the Corrected Description (Exhibit Ko 15; incidentally, line numbers cited at the end of each sentence do not include chemical formulas as lines).

(A) "Background of the invention"

"Vitamin D and its derivatives have important physiological functions. For example, 1α,25-dihydroxy vitamin D_3 exhibits a broad range of physiological functions, such as calcium metabolism-controlling activity, growth-inhibiting activity, differentiation-inducing activity on cells, such as tumor cells, and immune-controlling activity. However, vitamin D_3 derivatives exhibit undesirable side effects, such as hypercalcemia.

Novel vitamin D derivatives have been developed to retain effectiveness in the treatment of specific diseases while reducing associated side effects.

For example, Publication of Unexamined Patent Application No. 1986-267550 (issued on November 27, 1986) discloses a 9,10-seco-5,7,10(19)-pregnatriene derivative, which exhibits an immune-controlling activity and differentiation-inducing activity on tumor cells. In addition, Publication of Unexamined Patent Application No. 1986-267550 (issued on November 27, 1986) also discloses two kinds of processes for preparing the final end product, one using pregnenolone and the other using dehydroepiandrosterone as the starting material.

1α,25-dihydroxy-22-oxavitamin D_3 (OCT), that is, the 22-oxa analog of 1α,25-dihydroxy vitamin D_3 has potent in vitro differentiation-inducing activities with low in vivo calcemic liability. OCT is being clinically investigated as a candidate for treatment of secondary hyperparathyroidism and psoriasis.

Publication of Unexamined Patent Application No. 1994-072994 (issued on March 15, 1994) discloses a 22-oxacholecalciferol derivative and a process for the preparation thereof. It discloses a process for preparing an oxacholecalciferol derivative which comprises steps of reacting a pregnene derivative having a hydroxyl group at the 20-position with a dialkylacrylamide compound to obtain an ether compound and then reacting the thus-obtained ether compound with an organometal compound to obtain the desired compound.

Publication of Unexamined Patent Application No. 1994-080626 (issued on March 22, 1994) discloses a 22-oxavitamin D derivative. It also discloses a process which comprises a step of reacting

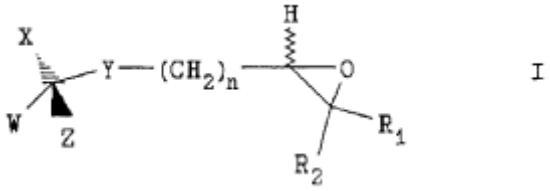
1α,3β-bis(tert-butyldimethylsilyloxy)-pregne-5,7-diene-20(S or R)-ol as a starting material with an epoxide in the presence of a base to obtain a compound having an ether bond at the 20-position.

In addition, Publication of Unexamined Patent Application No. 1994-256300 (issued on September 13, 1994) and Kubodera et al. (Bioorganic & Medicinal Chemistry Letters, 4(5): 753-756, 1994) disclose a process for stereospecifically preparing an epoxy compound which comprises steps of reacting 1α,3β-bis(tert-butyldimethylsilyloxy)-pregna-5,7-diene-20(S)-ol with 4-(tetrahydropyran-2-yloxy)-3-methyl-2-butene-1-bromide to obtain an ether compound, deprotecting it, and subjecting the deprotected ether compound to Sharpless oxidation. However, the aforementioned processes require more than one step for introducing an ether bond and an epoxy group into a side chain of a steroid group and therefore, result in low yield of the desired compound.

Furthermore, none of the aforementioned documents disclose a synthesis process in which an alcohol compound is reacted with an epoxy hydrocarbon compound having an eliminating group at its end, thereby forming an ether bond. Also, the aforementioned documents do not disclose a bicyclo [4.3.0] nonane structure (hereinafter referred to as a "CD ring structure" in this description), a steroid structure, or a vitamin D structure, each having an ether bond and an epoxy group at a side chain." (line 6 of page 15 to line 13 of page 16)

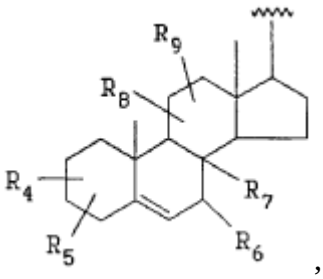
(B) "Detailed explanation of the invention"

a. "The present invention provides a process for preparing a compound having the following structure:

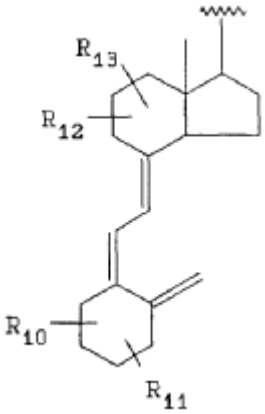


I

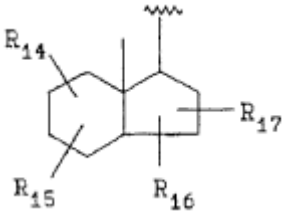
(in the formula, n is an integer from 1 to 5; each of R_1 and R_2 independently is optionally substituted C1-C6 alkyl; each of W and X is independently hydrogen or C1-C6 alkyl; Y is O, S or NR_3 where R_3 is hydrogen, C1-C6 alkyl or a protective group; and Z is:



,

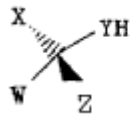


, or



where each of R_4, R_5, R_8, … and R_{17} independently is hydrogen, a substituted or unsubstituted lower alkyloxy, amino, alkyl, alkylidene, carbonyl, oxo, hydroxyl, or protected hydroxyl; and each of R_6 and R_7 independently is hydrogen, substituted or unsubstituted lower alkyloxy, amino, alkyl, alkylidene, carbonyl, oxo, hydroxyl, protected hydroxyl, or together constitute a double bond); which comprises:

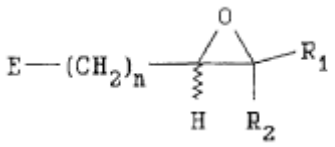
(a) the step of reacting a compound having the following structure:



IV

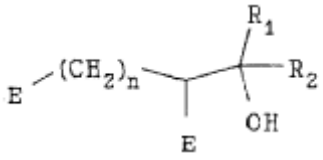
(in the formula, W, X, Y and Z are as defined above)

in the presence of a base, with a compound having the following structure:



V

or

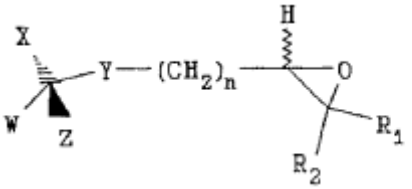


V'

(in the formula, n, R_1, and R_2 are as defined above, and E is an eliminating group) to prepare a compound; and

(b) the step of recovering the compound so prepared. …

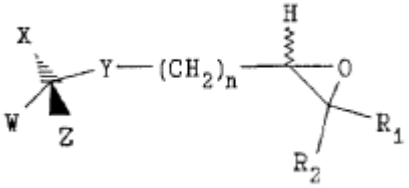
The process for preparing a compound having the following structure:



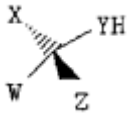
VI

is novel and is useful for the synthesis of vitamin D derivatives which can have a variety of physiological activities, such as differentiation-inducing activity and growth-inhibiting activity on cells." (line 6 of page 24 to the second line from the bottom of page 25).

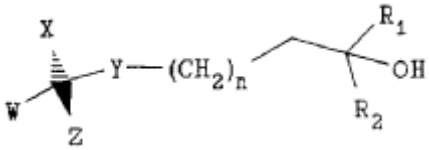
b. "The present invention also provides a compound having the following structure:



,



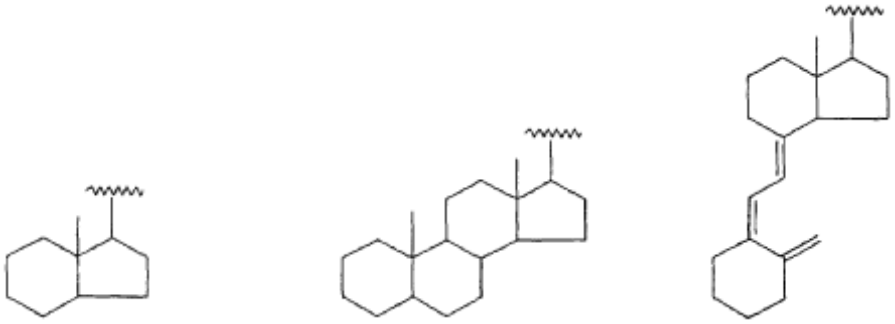
, or



(in the formula, Z represents a CD ring structure, a steroid structure or a vitamin D structure, each of which may optionally have one or more protected or unprotected

substituents and/or one or more protective groups). Each of the CD ring structure, steroid structure, and vitamin D structure for the present invention particularly means a structure as described below, any ring of which may optionally have one or more unsaturated bonds. In the steroid structure, one having one or two unsaturated bonds are preferred, and 5-ene steroid compound, 5,7-diene steroid compound, or a protected compound thereof, are particularly preferred.

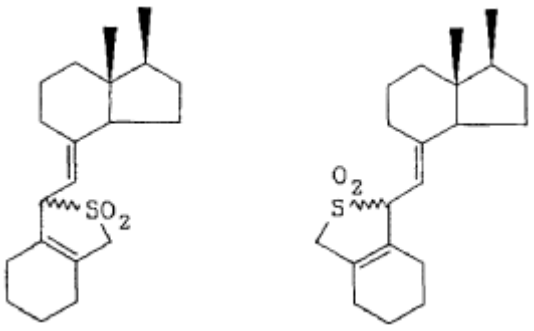
CD ring structure: Steroid structure: Vitamin D structure:



The substituents on Z, which is the CD structure, steroid structure, or vitamin D structure, are not particularly limited but may be exemplified by a hydroxyl group, a substituted or unsubstituted lower alkyloxy group, …and an oxo group (=O), with a hydroxyl group being preferred. These substituents may be protected. …

Examples of a protective group for an unsaturated bond in the steroid structure include 4-phenyl-1,2,4-triazoline-3,5-dione and diethyl maleate. An example of adducts having such protective group is the following: …

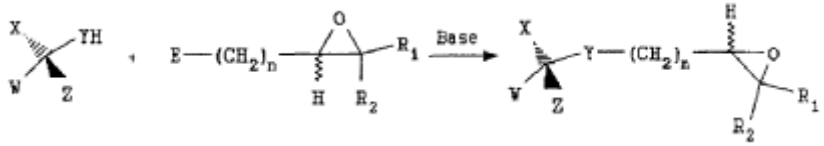
Furthermore, the vitamin D structure may be protected by addition of SO_2. Examples of such protected vitamin D structures are given below:



." (first line from the bottom of page 25 to line 2 of page 28)

c. "An outline of the reaction disclosed in this description for the preparation of the compound of Formula I is shown in the following Reaction Scheme A.

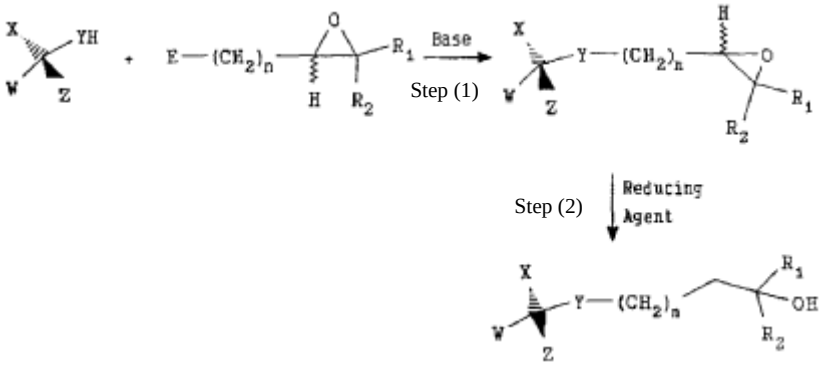
Reaction Scheme A:



Some of the compounds which are used as a starting compound in the aforementioned process according to the present invention are publicly known compounds. For example, when "Y" is O, the following can be used as the starting compounds: the lα,3β-bis(tert-butyldimethylsilyloxy)-pregna-5,7-diene-20(S)-ol as described in Publication of Unexamined Patent Application No. 1986-267550 (issued on November 27, 1986); the 9,10-seco-5,7,10(19)-pregnatriene-1α,3β,20β-triol optionally with the hydroxyl group being protected as described in Publication of Unexamined Patent Application No. 1986-267550 (issued on November 27, 1986) and International Patent Publications WO 1990/09991 (September 7, 1990) and WO 1990/09992 (September 7, 1990); the octahydro-4-(t-butyldimethylsilyloxy)-7-methyl-1H-indene-1-ol described in J. Org. Chem., 57, 3173 (1992); and the octahydro-4-(acetyloxy)-7-methyl-1H-indene-1-ol as described in J. Am. Chem. Soc., 104, 2945 (1982)." (second line from the bottom of page 29 to line 10 of page 30)

d. "The present invention relates to a process for preparing vitamin D or steroid derivatives via the novel intermediates described above in this description. An outline of this reaction is shown in the following Reaction Scheme B.

Reaction Scheme B:



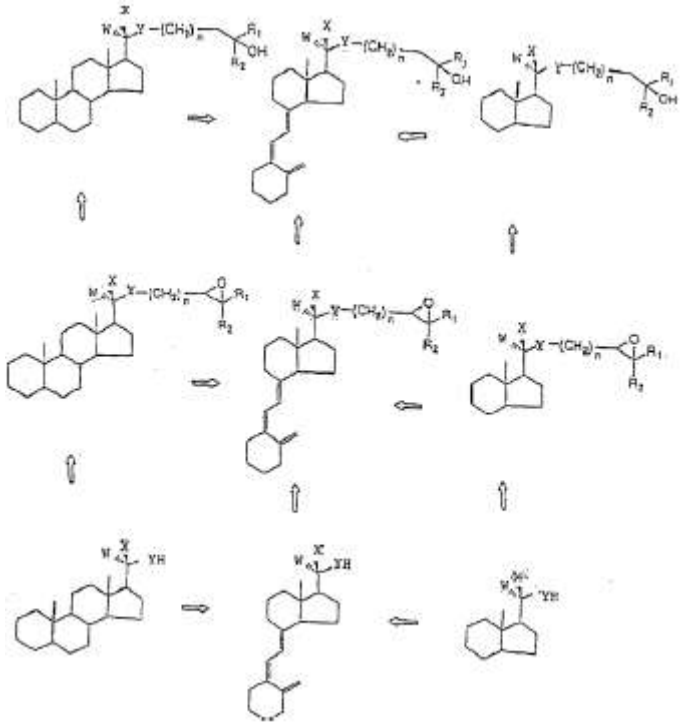
The reaction in Step (1) of the aforementioned two-step reaction according to the present invention can be carried out in the same way as in the process of Reaction Scheme A, which was already described in this description.

The reaction in Step (2) is a reaction to open the epoxy ring in the epoxide compound obtained in Step (1) and it is carried out using a reducing agent. The

reducing agent which can be used in Step (2) is such that it is capable of opening the ring of an epoxide compound obtained in Step (1) to create a hydroxyl group, preferably capable of selectively forming a tertiary alcohol." (lines 5 to 12 of page 39)

e. "The following Reaction Scheme C shows reaction routes using the compounds and processes of the present invention. Processes for the synthesis of a vitamin D compound from the corresponding steroid compound can be carried out by a conventional process such as ultraviolet irradiation and thermal isomerization. Processes for the synthesis of a vitamin D compound from the corresponding CD ring compound are also conventional. Such processes are described in, for example, E. G. Baggiolini et al., J. Am. Chem. Soc, 104, 2945-2948 (1982) and Wovkulich et al., Tetrahedron, 40, 2283 (1984). It should be understood that a part or all of the processes shown in Reaction Scheme C are embraced within the present invention.

Reaction Scheme C:



(in the formula, W, X, Y, O, R_1, and R_2 are the same as defined above, and any ring of the structure may optionally have one or two unsaturated bonds)." (line 7 of page 42 to line 3 of page 43)

C. Content of the Corrected Invention

(A) According to the statements in B. above, the following is recognized in relation to the Corrected Invention.

a. The Corrected Invention relates to a process for preparing a compound that is useful

for the synthesis of vitamin D derivatives which can have a variety of physiological activities, such as differentiation-inducing activity and growth-inhibiting activity on cells.

b. In the past, 1α,25-dihydroxy-22-oxavitamin D_3 (maxacalcitol), which is the 22-oxa analog (derivative in which the atom at the 22-position is replaced with an oxygen atom) of calcitriol (1α,25-dihydroxy vitamin D_3), etc. had been developed as novel vitamin D derivatives.

Publication of Unexamined Patent Application No. 1986-267550 (Exhibit Ko 1-2; hereinafter referred to as "Exhibit Ko 1 Publication") is a document that disclosed a 9,10-seco-5,7,10(19)-pregnatriene derivative, which contains maxacalcitol as a novel substance, and a process for preparing it. Said process is a process for preparing maxacalcitol, etc. by reacting the alcohol compound at the 20-position of a steroid ring structure with 4-bromo-1-butene as a reagent to introduce a side chain (which is not a Maxacalcitol Side Chain) at the 20-position, oxidizing it, reacting it with another reagent, an organometal compound (methylmagnesium bromide), and finally carrying out ultraviolet irradiation and thermal isomerization.

c. After the disclosure of the manufacturing process described in Exhibit Ko 1 Publication, processes for preparing a 22-oxa analog by reacting the alcohol compound at the 20-position of a steroid ring structure with a reagent to form a side chain were described in [i] Publication of Unexamined Patent Application No. 1994-72994 (Exhibit Otsu 35), [ii] Publication of Unexamined Patent Application No. 1994-80626 (Exhibit Otsu 36), and [iii] Publication of Unexamined Patent Application No. 1994-256300 (Exhibit Otsu 46 Publication; incidentally, the process described in this publication is the same as one indicated in Figure 9 of Exhibit Otsu 14 Document) (however, as mentioned below, out of these processes, the process described in [i] is the only process for preparing a compound having a Maxacalcitol Side Chain).

The process described in [i] above is a process for preparing maxacalcitol by first reacting the alcohol compound at the 20-position of a steroid ring structure with a dialkylacrylamide compound to introduce a side chain (which is not a Maxacalcitol Side Chain) at the 20-position by an ether bond and furthermore reacting it with an organometal compound to form a Maxacalcitol Side Chain.

The process described in [ii] above is a process for preparing a 22-oxavitamin D derivative (which does not have a Maxacalcitol Side Chain) by first reacting the alcohol compound at the 20-position of a steroid ring structure with an epoxide compound in the presence of a base to introduce a side chain (an epoxy group is not formed in the side chain) by an ether bond and then removing a protective group of the side chain.

The process described in [iii] above is a process for preparing a 26-hydroxy-22-oxavitamin D derivative (which differs from a Maxacalcitol Side Chain in that one of the methyl groups at the end thereof is a hydroxymethyl group), by first reacting the alcohol compound at the 20-position of a steroid ring structure with 4-(tetrahydropyran-2-yloxy)-3-methyl-2-butene-1-bromide to introduce a side chain (which is not a Maxacalcitol Side Chain) at the 20-position by an ether bond, removing the protective group of the side chain, and furthermore forming an epoxy group at the side chain by the Katsuki-Sharpless oxidation reaction to finally open the ring of the epoxy group.

However, the processes described in [i] and [ii] above are not those involving introduction of an epoxy group into a side chain having a steroid ring structure. In addition, the process described in [iii] above is not one involving a reaction with an epoxy hydrocarbon compound, and requiring more than one step for introducing an ether bond and an epoxy group into a side chain having a steroid ring structure. That is, none of the aforementioned publicly known documents, including Exhibit Ko 1 Publication, discloses either a synthesis process wherein the alcohol compound at the 20-position is reacted with an epoxy hydrocarbon compound having an eliminating group at its end to form an ether bond or a process for introducing an ether bond and an epoxy group into a side chain having a steroid ring structure or a vitamin D structure through one step, in relation to processes for preparing a 22-oxa analog (22-oxavitamin D derivative), let alone maxacalcitol.

d. The problem to be solved of the Corrected Invention is to provide a novel manufacturing process which has not been disclosed in prior art as mentioned in c. above, as a process for preparing vitamin D or steroid derivatives having a Maxacalcitol Side Chain (process for introducing a Maxacalcitol Side Chain into a compound having a vitamin D structure or a steroid ring structure). As a specific means for solving the problem, the Corrected Invention adopts a process for preparing a vitamin D or steroid derivatives having a Maxacalictol Side Chain, which comprises the step of reacting the alcohol compound at the 20-position of a vitamin D structure or a steroid ring structure (compound of Constituent Feature [B-1]), in the presence of a base, with an epoxy hydrocarbon compound having an eliminating group at its end (reagent of Constituent Feature [B-2]) to synthesize an epoxide compound having a steroid ring structure or a vitamin D structure which has an ether bond and an epoxy group at the side chain (intermediate of Constituent Feature [B-3]) and the step of treating it with a reducing agent to open the ring of the epoxy group of the side chain, thereby forming a hydroxyl group (incidentally, out of the two kinds of reagents stated in Constituent Feature [B-2],

one that does not contain an epoxy group forms the same structure as the other one that contains an epoxy group in the presence of a base).

e. Incidentally, out of the carbon skeletons of "Z" of the starting material, intermediate, and objective substance of the Corrected Invention, all of those having a vitamin D structure are cis forms. However, the carbon skeleton of Z "may optionally have one or more protected or unprotected substituents and/or one or more protective groups" (Constituent Feature [A-6]). As mentioned later in (7)B.(B)c., if SO_2 is added to a cis-form vitamin D structure as a protective group, the double bond at the 5-position of the vitamin D structure is lost and the rotational hindrance is eliminated, and the structure ceases to be a geometric isomer. The "Z" of the Corrected Invention also literally includes vitamin D structures for which cis form and trans form are no longer distinguished due to addition of such a protective group (hereinafter, the term "vitamin D structure" refers to one which is not limited to either a cis form or a trans form unless otherwise specified).

f. The Corrected Description does not specially state the effect of the Corrected Invention (see Article 36, paragraph (4) of the Patent Act and Article 24-2 of the Ordinance for Enforcement of the Patent Act). However, as mentioned above, the problem to be solved of the Corrected Invention exists in the provision of a novel process for preparing vitamin D or steroid derivatives having a Maxacalcitol Side Chain, which had not been disclosed in prior art. Taking this into account, the effect of the Corrected Invention is recognized as being capable of preparing vitamin D or steroid derivatives, such as maxacalcitol, which have a Maxacalcitol Side Chain by a novel process which had not been disclosed in prior art.

(B) As mentioned above, the Corrected Invention makes it possible to prepare its objective substance through a new preparation route that was not available in prior art, and its degree of contribution to prior art is large. Then, out of the manufacturing processes for maxacalcitol that were publicly known as of the Priority Date, the first manufacturing process for maxacalcitol described in Exhibit Ko 1 Publication had disadvantages, such as cumbersome operation, low yield of the objective substance, and difficulty in separation and purification. The manufacturing process mentioned in (A)c.[i] above, which is stated in the Corrected Description, was invented as an improvement of said process (Exhibit Otsu 35). However, the process described in [i] is also unfavorable for mass synthesis. Therefore, as of the Priority Date, further improvements were considered, and new processes for industrially manufacturing maxacalcitol were sought. The Corrected Invention made it possible for the appellee, who held a substance patent for maxacalcitol, to industrially manufacture maxacalcitol

for the first time (Exhibit Otsu 14; entire import of argument).

(C) On the other hand, the appellants allege that a process for introducing a Maxacalcitol Side Chain through one step by using a starting material having a trans-form vitamin D structure is also publicly known based on the process described in Publication of Japanese Translation of PCT International Application No. 1992-504573 (Exhibit Otsu 4 Document) as prior art as of the Priority Date. The appellants also allege that there is also a publicly known document (paper published in 1991 which is titled "22-okisabitamin D ruientai no gōsei oyobi seibutsugakuteki kassei" (Synthesis and biological activity of 22-oxavitamin D analog); Exhibit Otsu 50) which indicates, prior to the Priority Date, that it was possible to introduce a Maxacalcitol Side Chain through one step. However, the invention described in Exhibit Otsu 4 Document is a process for preparing a novel vitamin D derivative whose number of carbons of the side chain differs from that of a Maxacalcitol Side Chain. In addition, Exhibit Otsu 4 Document cannot be recognized as specifically disclosing a process for preparing a vitamin D derivative having a Maxacalcitol Side Chain through one step even in consideration of other statements therein. Moreover, regarding the "details of synthesis of an alcohol compound to o-alkylation," it is stated in the publicly known document pointed out by the appellants (Exhibit Otsu 50) that "see Reference Document 5 [note in this judgment: page 45 of International Publication No. 1990/09991]." The only process for the synthesis of a Maxacalcitol Side Chain that is specifically disclosed in International Publication No. 1990/09991 (Exhibit Otsu 3-1) is a process for forming a Maxacalcitol Side Chain by first reacting the alcohol compound at the 20-position with prenyl bromide to introduce a side chain (which is not a Maxacalcitol Side Chain) by an ether bond and then having it react with mercury acetate (Preparation Examples 11 and 12 of Exhibit Otsu 3-1). Therefore, it is reasonable to understand that the one referred to in the aforementioned publicly known document (Exhibit Ko 50) is also said process. Consequently, there is no reason for the appellants' allegation, and the statement of prior art in the Corrected Description is not recognized as being objectively insufficient.

D. Essential part of the Corrected Invention

In light of the problem to be solved and means for solving the problem of the Corrected Invention and its effect as mentioned above, the essential part of the Corrected Invention (the characteristic part which constitutes a unique technical idea that is not seen in prior art in the statements in the scope of claims) is recognized as existing in finding that a side chain having an epoxy group by an ether bond can be introduced through one step by having an alcohol compound at the 20-position of a vitamin D structure or steroid ring structure react with an epoxy hydrocarbon compound

of Constituent Feature [B-2] which has an eliminating group at its end, and in making it possible to introduce a Maxacalcitol Side Chain into an alcohol compound at the 20-position of a vitamin D structure or steroid ring structure through a new route of first going through an intermediate that is a vitamin D structure or steroid ring structure into which a side chain having an epoxy group by an ether bond is introduced through such one step and then opening the ring of the epoxy group of the side chain.

On the other hand, the fact remains that an intermediate that is obtained by introducing a side chain having an epoxy group by an ether bond into the starting material is synthesized by reacting the starting material with an epoxy hydrocarbon compound and that a Maxacalcitol Side Chain can be introduced thereafter by opening the ring of the epoxy group of the side chain, irrespective of whether the carbon skeleton (Z) of the alcohol compound at the 20-position, which is the starting material, has a cis-form or trans-form vitamin D structure. The same also applies to the cases where the carbon skeleton (Z) of the intermediate is either a cis-form or trans-form vitamin D structure. Therefore, the fact that the vitamin D structure of the carbon skeleton (Z) of the starting material or the intermediate is a cis form cannot be considered to be a characteristic part, which constitutes a unique technical idea that is not seen in prior art in the statements in the scope of claims of the Corrected Invention, and it is thus not included in the essential part of the Corrected Invention.

E. Fulfillment of the First Requirement of the Appellant's Process

The Appellant's Process is a process for introducing a Maxacalcitol Side Chain into the alcohol compound at the 20-position of a vitamin D structure by reacting the alcohol compound at the 20-position of a vitamin D structure (Starting Material A) with the same compound (Reagent B) as the epoxy hydrocarbon compound of Constituent Feature [B-2] which has an eliminating group at its end, thereby going through an intermediate (Intermediate C) that is a vitamin D structure wherein a side chain having an epoxy group is introduced by an ether bond into the starting material, and then opening the ring of the epoxy group of the side chain thereafter. Therefore, it is considered to have the characteristic part which constitutes a unique technical idea that is not seen in prior art in the statements in the scope of claims of the Corrected Invention.

On the other hand, in the Appellant's Process, the point that a vitamin D structure that corresponds to "Z" of the starting material and the intermediate is not a cis form but a trans form, which is a difference from the Corrected Invention, is not the essential part of the Corrected Invention, as mentioned in D. above.

Therefore, the Appellant's Process is recognized as fulfilling the First Requirement

of the doctrine of equivalents.

F. Regarding the appellants' allegation

(A) The appellants allege as follows: The essence of the Corrected Invention exists in solving the problem (oxidation resistance) in the case of using a cis-form starting material while enjoying the advantage of reduction of the number of steps by choosing a cis-form starting material and finding an order of introduction of an ether bond and an epoxy group that is suitable for said starting material (which does not include an oxidation step) because the conventional process described in Exhibit Ko 46 Publication includes an oxidation step and thus had a problem of not being capable of efficiently introducing a side chain in the case of using a cis-form starting material with low oxidation resistance; therefore, the point that the starting material has a cis-form vitamin D structure is an indispensable essential element; on the other hand, if the starting material has a trans-form vitamin D structure, there is no problem of low oxidation resistance, and it is not possible to enjoy the advantage of reduction of the number of steps because an isomerization step is required.

However, as mentioned above, the essential part of a patented invention should be found by determining the characteristic part which constitutes a unique technical idea that is not seen in prior art in the statements in the scope of claims of the patented invention. As mentioned above, the problem to be solved of the Corrected Invention is to provide a novel process for introducing a Maxacalcitol Side Chain which is disclosed neither in the art described in Exhibit Otsu 46 Publication nor in other prior arts described in the Corrected Description, and the Corrected Invention provides a means for solving the problem. Then, the process described in Exhibit Otsu 46 Publication has problems, such as oxidation resistance, in using a cis-form starting material, and even if such problems do not occur in the case of the Corrected Invention, there is no reason for understanding the problem solved by the Corrected Invention as being limited as such according to the findings in C. and D. above. Therefore, using a compound with low oxidation resistance as the starting material cannot be recognized as the essential part of the Corrected Invention.

Moreover, it is certainly true that using a cis-form starting material has the advantage of not requiring an isomerization step. However, Reaction Scheme C in the Corrected Description describes a route of conversion from a steroid compound to a vitamin D compound in any of the stages of the starting material, intermediate, and objective substance. As of the Priority Date, the synthesis of a vitamin D compound from a steroid compound could have been carried out by a conventional process. The Corrected Invention includes not only a compound having a cis-form vitamin D

structure but also a compound having a steroid ring structure as the starting material. In the case of choosing a steroid ring structure as "Z," a process which comprises the step of subjecting the steroid ring structure to ultraviolet irradiation and thermal isomerization under the conditions for converting it into a vitamin D structure and the step of recovering the compound thus prepared as the objective substance is also described as one of the embodiments of the Corrected Invention (B.(B)e. above). That is, in the Corrected Invention, the difference in the total number of steps that depends on the existence or absence of a conversion step cannot be considered to be the essential part of the Corrected Invention, taking into account that the total number of steps, including a conversion step, can originally vary depending on whether "Z" of the starting material is a steroid ring structure or a vitamin D structure.

In this regard, the appellants allege that the essential part of the Corrected Invention naturally differs in the case of using a compound having a steroid ring structure as the starting material compared to the case of using a compound having a vitamin D structure as the starting material. However, even if multiple options are stated in the scope of claims, the essential part of a patented invention should be found based on the entire statements in the scope of claims in light of the technical significance of permission of such options. Therefore, the appellants' allegation is unacceptable.

(B) Moreover, the appellants also allege as follows: The effect of the Corrected Invention exists in the reduction of the number of steps required to introduce a Maxacalcitol Side Chain compared to prior art; however, there has been prior art whereby a Maxacalcitol Side Chain can be introduced through one step in the case of using a trans-form starting material; therefore, the Appellant's Process cannot be considered to be identical with the Corrected Invention in the essential part. However, as mentioned in C.(C) above, it cannot be recognized that a process whereby a vitamin D derivative having a Maxacalcitol Side Chain can be prepared through one step by using a trans-form starting material has been publicly known. In addition, the function and effect of the Corrected Invention and the fact that the Appellant's Process produces the same function and effect are as mentioned later in (4)C. Therefore, there is no reason for the appellants' allegation.

(C) The appellants allege as follows: In the technical field of processes for preparing compounds, the organic linkage of all the steps itself is a technical idea for solving a problem, and a manufacturing process using a cis-form starting material and a manufacturing process using a trans-form starting material are understood as different processes by persons ordinarily skilled in the art; therefore, it is erroneous to take up only a part of a manufacturing process and consider it as the essential part thereof in

disregard of differences in the starting material and the intermediate, which are important constituent elements of the manufacturing process, and differences in stability, easiness of purification, and the total number of required steps between a cis form and a trans form.

However, as mentioned above, the essential part of a patented invention should be found by determining the characteristic part which constitutes a unique technical idea that is not seen in prior art in the statements in the scope of claims of the patented invention. The entire organic linkage of all steps cannot necessarily be considered to form the essential part even in relation to a process for preparing a compound. Therefore, existence of slight differences in the starting material and the intermediate that do not affect a reaction required to introduce a side chain does not immediately mean the existence of differences in the essential part.

In addition, a manufacturing process using cis-form starting material and intermediate and one using trans-form starting material and intermediate are generally understood as different manufacturing processes. Moreover, even if these processes differ in stability, easiness of purification, and the total number of steps, the essential part of the Corrected Invention exists in that it made it possible to introduce a Maxacalcitol Side Chain into the alcohol compound at the 20-position of a vitamin D structure or a steroid ring structure by a novel manufacturing process that had not been disclosed in prior art as found in D. above, and said novel process for introducing a side chain does not differ depending on whether the starting material or the intermediate is a cis form or a trans form, and differences in stability, easiness of purification, and the number of steps between a cis form and a trans form are also not related to the essential part of the Corrected Invention. The existence of a difference in the function and effect other than the characteristic part which constitutes a unique technical idea that is not seen in prior art in the statements in the scope of claims of the Corrected Invention does not serve as a reason for denying that the Appellant's Process commonly has the essential part of the Corrected Invention.

Therefore, there is no reason for the appellants' allegation.

(4) Regarding the Second Requirement of the doctrine of equivalents (replaceability)

A. As mentioned above, the Appellant's Process and the Corrected Invention differ in that the carbon skeletons of Starting Material A and Intermediate C in the Appellant's Process are trans-form vitamin D structures while the carbon skeletons of the alcohol compound at the 20-position of a vitamin D structure (Constituent Feature [B-1]), which is the starting material of the Corrected Invention (in the Corrected Invention, the carbon skeletons that correspond to Z of the starting material and the intermediate are

cis-form vitamin D structures, and the protected hydroxyl group is bonded to the 1-position and the 3-position of the vitamin D structure as a substituent in the same manner as the starting material of the Appellant's Process), and the vitamin D structure into which a side chain having an epoxy group by an ether bond is introduced (Constituent Feature [B-3]), which is the intermediate of the Corrected Invention, are cis-form vitamin D structures. Then, it is considered whether it is possible to achieve the purpose of the Corrected Invention and to produce the same function and effect as those of the Corrected Invention even if the starting material and the intermediate of the Corrected Invention are replaced with those of the Appellant's Process.

B. As mentioned in (3)C.(A)d. above, the problem to be solved of the Corrected Invention is to provide a novel manufacturing process which has not been disclosed in prior art as a process for preparing a vitamin D derivative having a Maxacalcitol Side Chain. The means for solving the problem is to prepare maxacalcitol by a novel process which comprises the step of reacting the alcohol compound at the 20-position of a vitamin D structure (compound of Constituent Feature [B-1]), in the presence of a base, with the epoxy hydrocarbon compound of Constituent Feature [B-2] which has an eliminating group at its end to synthesize an epoxide compound (intermediate of Constituent Feature [B-3]), which is a vitamin D structure into which a side chain having an epoxy group is introduced by an ether bond and the step of subsequently opening the ring of the epoxy group of said side chain. In that case, the function and effect of the Corrected Invention in relation to the Second Requirement is recognized as being capable of preparing maxacalcitol by a process which comprises the step of reacting the alcohol compound at the 20-position of a vitamin D structure with an epoxy hydrocarbon compound having an eliminating group at its end and the step of going through an intermediate that is a vitamin D structure into which a side chain having an epoxy group is introduced by an ether bond through one step.

C. Then, as mentioned above, the Appellant's Process is to prepare the same maxacalcitol as that of the Corrected Invention by reacting Starting Material A (alcohol compound at the 20-position of a trans-form vitamin D structure) with Reagent B (epoxy hydrocarbon compound of Constituent Feature [B-2] of the Corrected Invention) to produce Intermediate C which is an epoxide compound, which is a trans-form vitamin D structure into which a side chain having an epoxy group is introduced by an ether bond, then opening the ring of the epoxy group of said side chain to produce Substance D having a Maxacalcitol Side Chain, and finally subjecting Substance D to light illumination to convert its carbon skeleton into a cis-form vitamin D structure.

In the aforementioned Starting Material A and Intermediate C in the Appellant's

Process, the carbon skeleton that corresponds to Z in the Corrected Invention is a trans-form vitamin D structure, and the Appellant's Process differs from the Corrected Invention in that the carbon skeleton of Z of the starting material (Constituent Feature [B-1]) and the intermediate (Constituent Feature [B-3]) of the Corrected Invention is a cis-form vitamin D structure. However, the starting materials and intermediates in both the Appellant's Process and the Corrected Invention have the same function and effect of being capable of preparing maxacalcitol by a process of going through an intermediate that is a vitamin D structure into which a side chain having an epoxy group is introduced by an ether bond through one step by having an alcohol compound at the 20-position of a vitamin D structure react with the same epoxy hydrocarbon compound. It is recognized that the same purpose as that of the Corrected Invention can be achieved and the same function and effect are produced even if the aforementioned starting material and intermediate having a cis-form vitamin D structure in the Corrected Invention are replaced with the aforementioned starting material and intermediate having a trans-form vitamin D structure in the Appellant's Process.

D. The appellants allege as follows: The only effect stated in the Corrected Description is reduction of the number of steps, and the function and effect of the Corrected Invention exist in the reduction of the number of steps for introducing a Maxacalcitol Side Chain in the case of using a cis-form starting material compared to prior art; in addition, the efficiency of the reduction of the number of steps should be determined based on the total number of manufacturing steps, and processes do not have the same function and effect if the total number of steps differ between them. However, the aforementioned appellants' allegation is unacceptable for the following reasons.

In Article 36, paragraph (4) of the Patent Act prior to amendment by Act No. 116 of 1994, the "purpose, structure, and effect of the invention" were provided for as the matters that must be stated in the detailed explanation of the invention in the description. However, through said amendment, the "problem to be solved and means for solving the problem," etc. are provided for as the matters that must be stated in said paragraph after the amendment and in Article 24-2 of the Ordinance for Enforcement of the Patent Act. The effect of the invention is no longer provided for as a matter that must be stated in the detailed explanation of the invention in the description. In the current practice, there are many descriptions that do not include any statement of the "effect of the invention" in relation to a patented invention pertaining to an international application, etc. (this is a noticeable fact in this court). The absence of the statement of the "effect of the invention" in the Corrected Description also conforms to this amendment. Then, it is not reasonable to presumptively recognize the function and effect of a patented invention,

for which the "effect of the invention" is not stated in the description, in a limited manner based only on comparison with some of prior arts.

Among prior arts, the invention described in Exhibit Otsu 46 Publication is stated as follows in the Corrected Description: "The aforementioned processes require more than one step for introducing an ether bond and an epoxy group into a side chain of a steroid group and therefore, result in low yield of the desired compound" ((3)B.(A) above). However, said statement only refers to one of the multiple inventions cited as prior art in the Corrected Description. In addition, it is a statement concerning only steps for introducing a specific side chain, specifically, steps for introducing an epoxy group by an ether bond, and is not intended to refer to the number of steps in the entire process, including these steps. Originally, the process described in Exhibit Otsu 46 Publication is not a manufacturing process wherein a Maxacalcitol Side Chain is introduced. Therefore, said statement cannot serve as a reason for saying that the reduction of the number of steps for introducing a Maxacalcitol Side Chain in the case of using a cis-form starting material compared to prior art is the function and effect of the Corrected Invention. Moreover, as mentioned in (3)F.(A) above, the Corrected Invention also includes the step of converting a steroid ring structure to a vitamin D structure, and a difference (fewer steps) in the total number of steps, including the conversion step, is not particularly recognized as a difference from prior art. Taking this into account, the function and effect of the Corrected Invention cannot be found to be the reduction of the total number of steps for preparing the objective substance, such as maxacalcitol, compared to prior art.

E. Therefore, the Appellant's Process is recognized as fulfilling the Second Requirement of the doctrine of equivalents.

(5) Regarding the Third Requirement (easiness of replacement) of the doctrine of equivalents

According to evidence (described in the text), the following facts are recognized: [i] The knowledge that a trans-form vitamin D structure can be easily converted into a cis-form vitamin D structure by light illumination was well-known art as of the Priority Date, and it was a widely-known process to obtain a cis-form vitamin D derivative by using a compound having a trans-form vitamin D structure as the starting material in preparing a desired vitamin D derivative and converting the trans-form vitamin D structure into a cis-form vitamin D structure by light illumination after introducing a side chain as appropriate (Exhibit Ko 14 and Exhibits Otsu 1, 2, and 33); [ii] It was also known that a trans-form vitamin D structure that corresponds to Starting Material A of the Appellant's Process is used for the synthesis of maxacalcitol (Exhibit Otsu 4-2); [iii]

Even in the case of using a compound having a cis-form vitamin D structure as the starting material, it was generally accepted to adopt processes wherein the compound is converted into a trans form at the time of introducing a substituent, etc. or removing a protective group in the course of preparation and is reconverted into a cis form (Exhibit Otsu 1).

Moreover, it is generally known that the steric structure near the reaction point significantly affects the progress of a chemical reaction. The hydroxyl group with which the alcohol compound at the 20-position of a vitamin D structure, which is the starting material, reacts upon the introduction of a Maxacalcitol Side Chain is far from the position of the double bond (5-position) of the vitamin D structure, which differs between a trans form and a cis form. The steric structure near the reaction point does not differ depending on whether the starting material has a trans-form vitamin D structure or a cis-form vitamin D structure. Taking this into account, it is natural for a person ordinarily skilled in the art not to consider that the reaction in the course of introduction of a Maxacalcitol Side Chain in the Corrected Invention does not differ depending on a difference between a trans form and a cis form in the position of the double bond.

In that case, it is recognized that a person ordinarily skilled in the art could have easily conceived of the Appellant's Process, which uses a trans-form vitamin D structure as "Z" of the starting material of the Corrected Invention in place of a cis-form vitamin D structure for preparing maxacalcitol that is contained in the objective substance of the Corrected Invention and comprises the step of reacting this Starting Material A with Reagent B that is the same reagent as that of the Corrected Invention to produce Intermediate C that has no difference from the intermediate of the Corrected Invention other than the point that it is a trans form, the step of opening the ring of the epoxy group of the side chain of intermediate C to obtain Substance D that is a trans form having a Maxacalcitol Side Chain, and the step of finally subjecting Substance D to light illumination to convert it into a cis form and removing the protective group of the hydroxyl group to prepare maxacalcitol that is the same as the objective substance of the Corrected Invention, based on the Corrected Invention at the time when the Appellant's Process was carried out (when the Patent Right was infringed).

Therefore, the Appellant's Process is recognized as fulfilling the Third Requirement of the doctrine of equivalents.

(6) Regarding the Fourth Requirement (whether the subject process can be easily presumptively conceived of) of the doctrine of equivalents

The appellants allege that the Appellant's Process could have been easily presumptively conceived of by a person ordinarily skilled in the art as of the Priority

Date based on Exhibit Otsu 4 Document. However, said allegation of the appellants is unacceptable as held in No. 4, 4.(1) to (6) in "Facts and reasons" in the judgment in prior instance. The relevant part is cited.

Therefore, the Appellant's Process is not recognized as having been easily presumptively conceived of by a person ordinarily skilled in the art in relation to the Fourth Requirement of the doctrine of equivalents.

(7) Regarding the Fifth Requirement (special circumstances) of the doctrine of equivalents

A. Regarding the determination standard for the Fifth Requirement

The substantive value of a patented invention extends to the art which a person ordinarily skilled in the art can easily conceive of as one that is substantially identical with the structure stated in the scope of claims based on said structure, and third parties should foresee this. Therefore, if the subject product, etc. is identical with a patented invention in the essential part, purpose, and function and effect, and is one that a person ordinarily skilled in the art can easily conceive of based on the patented invention, the subject product, etc. can be in principle considered to be equivalent to the patented invention. However, concerning art which the patentee had once acknowledged not to fall under the technical scope of the patented invention or art in relation to which he/she had behaved as if he/she had objectively acknowledged so, e.g. where the applicant intentionally excluded the art from the scope of claims in the patent application procedures, the patentee is not entitled to claim otherwise afterwards, since this is against the doctrine of estoppel. Therefore, if there are such special circumstances, the application of the doctrine of equivalents is exceptionally denied (see the aforementioned Supreme Court Judgment on the "Ball spline bearing" Case).

(A) In this regard, even if there is another structure that is outside the scope of claims, which a person ordinarily skilled in the art can easily conceive of as of the filing date as one that is substantially identical with the structure stated in the scope of claims and the applicant could thus have also easily conceived of said another structure as of the filing date, this fact alone cannot serve as a reason for alleging that the applicant's failure to state said another structure in the scope of claims falls under the "special circumstances" in the Fifth Requirement of the doctrine of equivalents.

This is because of the following reasons. [i] As mentioned above, the substantive value of a patented invention extends to the art that a person ordinarily skilled in the art can easily conceive of as one that is substantially identical with the structure stated in the scope of claims based on said structure even if it is a structure other than the structure stated in the scope of claims. This principle does not change at all in relation to

any art that a person ordinarily skilled in the art can easily conceive of as of the filing date. If it is not at all permitted to allege the doctrine of equivalents only for the reason that a structure could have been easily conceived of by a person ordinarily skilled in the art as of the filing date, the scope to which the substantial value of a patented invention extends will differ from the aforementioned scope. [ii] In addition, taking into account that an applicant should first disclose his/her invention to the public by stating it in the description and then clearly specify the scope of the exclusive right in the scope of claims, the applicant should state the scope of claims in just proportion within the scope of the invention disclosed in the description while fulfilling the requirements, such as the support requirements under Article 36, paragraph (5) of the Patent Act and paragraph (6), item (i) of said Article and the clarity requirements under item (ii) of said paragraph. However, in some cases, it is considered to be harsh to require the applicant to prepare the scope of claims that contains all the expected infringements and the description supporting such scope of claims within a limited period of time, taking into account the fact that, under the first-to-file system, applicants are generally required to prepare the scope of claims and the description and file applications within a limited period of time. On the other hand, in many cases, a third party who has received the disclosure of an invention as described in the description pertaining to a patent application can easily conceive of one which has the essential part of the patented invention but part of which is not included in the literal interpretation of the scope of claims, based on the statements in the scope of claims and the description, etc., during the duration of the patent. The doctrine of equivalents is applicable because if any third party can easily escape from the exercise of rights by the patentee, including an injunction, through replacement of the non-essential part of the patented invention, this will diminish incentives for invention in society in general, which not only goes against the purpose of the Patent Act, that is, contributing to the development of industry through protection and encouragement of inventions, but also goes against social justice and results in running counter to the principle of fairness. In light of the aforementioned situation, etc., even if a person ordinarily skilled in the art could have easily conceived of another structure that is outside the scope of claims as of the filing date, it is not reasonable to exclude said another structure from the application of the doctrine of equivalents only for the reason of such fact without exception.

(B) However, even in such a case, if the applicant is objectively and externally recognized as having recognized another structure that is outside the scope of claims as a replacement for a different part in the structure stated in the scope of claims as of the filing date (for example, where the applicant can be considered to have stated the

invention based on said another structure in the description or where the applicant stated the invention based on another structure that is outside the scope of claims in a paper, etc. which he/she published as of the filing date), the applicant's failure to state said another structure in the scope of claims is considered to fall under the "special circumstances" in the Fifth Requirement.

The reason therefor is as follows. In the aforementioned cases, it can be understood that the patentee intentionally excluded said another structure from the scope of claims when stating the scope of claims, that is, the patentee acknowledged that said another structure does not fall under the technical scope of the patented invention or behaved as if he/she had objectively acknowledged so, and the trust of a third party who understands as such should be protected. Therefore, the patentee is not permitted to subsequently allege the application of the doctrine of equivalents in relation to the subject product, etc. that is based on said another structure in contradiction to such protection in light of the doctrine of estoppel.

B. Regarding the appellants' allegations

(A) The appellants allege as follows: For an invention in the chemical field, the scope of claims is generally specified by objective and clear expressions; therefore, the third-party trust that the right will never expand from said scope naturally arises, and it should be protected. However, as mentioned above, the right under the doctrine of equivalents extends to the art which a person ordinarily skilled in the art can easily conceive of as one that is substantially identical with the structure stated in the scope of claims based on said structure even if the art is outside the scope that is literally specified in the scope of claims, and third parties should foresee this. It is not permitted to allege the doctrine of equivalents in light of the doctrine of estoppel only where there are the aforementioned special circumstances. The fact that the invention is one in the chemical field or the fact that the scope of claims is literally clear cannot serve as a reason for denying the establishment of equivalence as such "special circumstances." Therefore, there is no reason for the appellants' allegation.

(B) The appellants allege the circumstances as indicated in the appellants' allegation in B.(A) to (G) in No. 3, 1.(4) above. Then, the appellants allege as follows: In stating the scope of claims, the applicant for the Corrected Invention decided the starting material, being clearly and objectively conscious of not including a trans-form vitamin D structure in the scope of claims, and thus intentionally chose to actively exclude a trans-form vitamin D structure from the scope of claims; therefore, in this case, there are the "special circumstances, such as the fact that the products fall under those that were

intentionally excluded from the scope of claims," as mentioned in the Supreme Court Judgment on the "Ball spline bearing" Case; in addition, there is no circumstance where the patentee should be specially protected, which is indicated as a ground for the application of the doctrine of equivalents in said judgment, specifically, the fact that "it is extremely difficult to foresee all kinds of infringements … and state the scope of claims in the description."

However, as mentioned below, the Corrected Description includes no statement that can be considered to state an invention using a compound having a trans-form vitamin D structure as the starting material of the Corrected Invention (the parties agree that an invention using a starting material having a trans-form vitamin D structure is not disclosed in the Corrected Description). In addition, there is no other evidence that is sufficient to objectively and externally recognize that the applicant recognized a trans-form vitamin D structure as a replacement for a cis-form vitamin D structure as the starting material of the Corrected Invention as of the filing of the application for the Patent. Therefore, it should be said that there is no reason for the appellants' allegation.

a. The appellants allege that the applicant was never erroneously ignorant of the existence of a synthesis route using a starting material having a trans-form vitamin D structure because the existence of two kinds of geometric isomers and a synthesis route using a starting material having a trans-form vitamin D structure were well-known. However, even if the applicant of the Corrected Invention knew that a trans form generally exists as a geometric isomer of a cis form and that there is a process for the synthesis of a vitamin D derivative using a starting material having a trans-form vitamin D structure, these facts alone cannot serve as a reason for saying that the applicant is objectively and externally recognized as having recognized the use of a starting material having a trans-form vitamin D structure as a replacement for the starting material of the Corrected Invention as of the filing date. Therefore, there is no reason for the appellants' allegation.

b. The appellants allege as follows: The scope of claims of the Corrected Invention describes a chemical bond by a wavy line, "〜H" (Constituent Feature [B-3]), thereby clearly describing that the steric structure at the root of H includes the stereoisomers of both R-stereoisomer and S-stereoisomer; however, it describes only the cis-form geometric isomer of a vitamin D structure; therefore, it clearly and intentionally sets a limitation to exclude a trans form. However, RS-stereoisomerism (enantiomerism) and cis-trans stereoisomerism (geometric isomerism) differ in their properties. Even if there is a statement that is based on the premise of distinction between R-stereoisomer and S-stereoisomer in the Corrected Description, it cannot be said that the applicant is

objectively and externally recognized as having recognized a trans-form vitamin D structure as a replacement for the starting material of the Corrected Invention. Therefore, the applicant is not recognized as having intentionally limited the scope of claims. Consequently, there is no reason for the appellants' allegation.

c. The appellants allege as follows: Two structural formulas, one expressing the structure immediately after adding SO_2 to a cis-form starting material and one expressing the structure immediately after adding SO_2 to a trans-form starting material, are stated in the Corrected Description, and there is a statement on the assumption of a trans-form starting material in the Corrected Description; despite this fact, the applicant limits the starting material to a cis form in the scope of claims; therefore, in this regard, it is obvious that the applicant intentionally limited the starting material.

However, in Claim 13, "Z" of the Corrected Invention is clearly specified as one that "may optionally have one or more protected or unprotected substituents and/or one or more protective groups." Both of the two structural formulas ((3)B.(B)b. above) in the Corrected Description as pointed out by the appellants are nothing more than those that indicate a vitamin D structure to which SO_2 is added as a protective group as an example of "Z" to which such protective group is added. These structural formulas do not describe a compound before SO_2 is added. Regarding a compound wherein SO_2 is added to a vitamin D structure, the double bond of the vitamin D structure is lost and the rotational hindrance is eliminated, and the compound ceases to be a geometric isomer. Therefore, there is no line between a cis form and a trans form in relation to the aforementioned two structural formulas themselves. In that case, such statement of examples of "Z" to which a protective group is added is not sufficient to objectively and externally recognize that the applicant had recognized a trans-form vitamin D structure as a replacement for the starting material of the Corrected Invention. Therefore, it cannot be said that the applicant intentionally limited the starting material in the scope of claims. Consequently, there is no reason for the appellants' allegation.

d. The appellants allege as follows: In Column 41 in the Corrected Description, two international publications describing a trans-form vitamin D structure as the starting material in addition to a cis-form vitamin D structure are described; however, in Column 37 in the Corrected Description, the starting material is "particularly" limited to a cis form out of the two kinds of existing basic skeletons, and only a cis form is stated in the scope of claims; therefore, a trans-form vitamin D structure is intentionally excluded in the Corrected Description.

In Column 41 in the Corrected Description, the following is stated as the examples of publicly known compounds that can be used as a starting compound when preparing

a compound that falls under the intermediate of the Corrected Invention: "9,10-seco-5,7,10(19)-pregnatriene-1α,3β,20β-triol optionally with the hydroxyl group being protected as described in Publication of Unexamined Patent Application No. 1986-267550 (issued on November 27, 1986) and International Patent Publications WO/1990/09991 (September 7, 1990) and WO/1990/09992 (September 7, 1990)" ((3)B.(B)c. above). However, the statement "9,10-seco-5,7,10(19)-pregnatriene-1α,3β,20β-triol" is a general notation that does not limit the vitamin D structure to either cis form or trans form. The aforementioned statement in Column 41 does not describe an invention using a starting material having a trans-form vitamin D structure. Then, in each of the cited publications, a structural formula of a cis-form vitamin D structure or that of a trans-form vitamin D structure is described in the course of the manufacturing process pertaining to the invention described in each publication. However, in the Corrected Description, these documents are cited only as those that described a compound, "9,10-seco-5,7,10(19)-pregnatriene-1α,3β,20β-triol."

In addition, Column 37 in the Corrected Description as pointed out by the appellants specifies and describes the same content as that of the statements in the scope of claims, and it does not clearly specify a trans-form vitamin D structure as "Z" of the starting material, etc.

Then, the Corrected Description does not refer to a trans-form vitamin D structure at all. For example, it does not describe the step of converting a trans form to a cis form. There is no statement concerning an invention pertaining to a manufacturing process using a trans-form starting material in the Corrected Description.

In that case, it cannot be considered, based on each of the aforementioned statements in the Corrected Description, that an invention using a compound having a trans-form vitamin D structure as the starting material of the Corrected Invention is stated in the Corrected Description. In addition, said statements are not sufficient to objectively and externally recognize that the applicant recognized a trans-form vitamin D structure as a replacement for the starting material of the Corrected Invention as of the filing date. Therefore, it is not recognized that a trans-form vitamin D structure was intentionally excluded from the scope of claims. Consequently, there is no reason for the appellants' allegation.

e. The appellants allege as follows: Although working examples using a starting material having a steroid ring structure are only stated in the Corrected Description, the invention is generalized and enlarged in the scope of claims to include the cases where a starting material has a cis-form vitamin D structure; if a third party sees such

description, he/she recognizes that structures that are not stated in the scope of claims were excluded. However, the statements in the scope of claims do not need to be identical with the scope of the invention stated in the working examples, although they need to be supported by the description. It is general practice that the invention whose content is more generalized than the content indicated in working examples is stated in the scope of claims. Such fact alone does not serve as a ground for objectively and externally recognizing that the applicant has recognized one other than the starting material stated in the scope of claims as a replacement for said starting material. Therefore, it cannot be said that there are special circumstances, such as the fact that the applicant intentionally limited the scope of claims. Consequently, there is no reason for the appellants' allegation.

f. The appellants allege that the applicant had no difficulty in including a trans-form vitamin D structure as Z of the starting material. However, even if the applicant can easily conceive of another structure that is outside the scope of claims as one that is substantially identical with the structure stated in the scope of claims as of the filing date, this fact alone cannot serve as a reason for saying that there are special circumstances, such as the fact that the applicant intentionally excluded said another structure, as mentioned in A.(A) above. Therefore, there is no reason for the appellants' allegation.

g. The appellants allege as follows: It is considered that the applicant limited the starting material to a cis form because it was highly likely to be unable to receive an examiner's decision to grant a patent based on the allegation of the effect of reducing the number of steps if it included a starting material having a trans-form vitamin D structure in the subject of the invention. However, as mentioned in (4)D. above, the function and effect of the Corrected Invention are not recognized as existing in the reduction of the number of steps, and rather, the essential part of the Corrected Invention is recognized as mentioned in (3)D. above. The use of a cis-form starting material is not at all related to the essential part. Taking this into account, it cannot be recognized that the appellee intentionally excluded trans-form starting materials from the starting material of the Corrected Invention in consideration of the function and effect alleged by the appellants. Therefore, there is no reason for the appellants' allegation.

h. According to the above, in this case, the applicant cannot be regarded as stating an invention using a starting material having a trans-form vitamin D structure in the Corrected Description, and it is not objectively and externally recognized that the applicant recognized a trans-form vitamin D structure as a replacement for the starting material of the Corrected Invention as of the filing date. Therefore, the applicant's

failure to state a structure wherein "Z" is a trans-form vitamin D structure in the scope of claims cannot be considered to fall under the "special circumstances" in the Fifth Requirement.

(C) The appellants allege that the statements in the document which the appellee sent prior to the commercialization of the Appellants' Products fall under an indication of intentional limitation of the scope of claims by the patentee.

However, in said document (written opinion prepared by the counsel attorney for the appellee), the appellee also made an allegation of infringement under the doctrine of equivalents to the effect that the Appellant's Process is equivalent to the Corrected Invention in the case of choosing a cis-form vitamin D structure as "Z" of the starting material and intermediate stated in the scope of claims. Therefore, even if the appellee also selectively made another allegation, it cannot be regarded as having intentionally limited the scope of claims by making said another allegation (incidentally, as mentioned above, in this lawsuit, the parties agree that the Appellant's Process does not constitute the literal infringement of the Invention prior to the Correction in the case of using a starting material having a CD ring structure). Therefore, there is no reason for the appellants' allegation.

(D) Even based on the other allegations of the appellants, it is not recognized that there are the special circumstances of the Fifth Requirement of the doctrine of equivalents.

Therefore, there are no special circumstances of the Fifth Requirement of the doctrine of equivalents in the Appellant's Process.

(8) Brief summary

On these bases, the Appellant's Process is equivalent to the Corrected Invention and is recognized as falling under the technical scope thereof.

2. Regarding the existence or absence of grounds for invalidation of the Corrected Invention

(1) Regarding the lack of an inventive step by citing Exhibit Otsu 14 Document as the primarily cited document (Ground for Invalidation A)

A. Content described in Exhibit Otsu 14 Document

Exhibit Otsu 14 Document is a paper written by Noboru Kubodera, who is one of the inventors of the Corrected Invention, which is titled "Active Vitamin D Analogs - Important and Various Roles by Medicinal Chemists during the Course of Development of Promising Candidates as Useful Medicines." The paper was published in "Journal of Synthetic Organic Chemistry, Japan, Vol. 54, No. 2" on February 1, 1996 prior to the Priority Date (September 3, 1996). There are the following statements in the paper.

(A) "1. Introduction

1α,25-dihydroxy-22-oxavitamin D_3 (2) (22-oxacalcitroiol; hereinafter abbreviated to "OCT" [note in this judgment: maxacalcitol]), which was produced for the purpose of separating various physiological activities of activated vitamin D, 1α,25-dihydroxyvitamin D_3 (1) (calcitriol; hereinafter abbreviated to "1,25$(OH)_2D_3$"), by means of structure modification has strong differentiation-inducing activity and growth-inhibiting activity on tumor cells, such as leukemia cells, while it is characterized by having weak blood calcium level increasing activity. It has been considered to be one of the derivatives which is most advanced in the separation of the activities of 1,25$(OH)_2D_3$ up to the present date. …

Incidentally, the work of researchers who are working in a synthesis laboratory of a pharmaceutical company tends to be focused on research to discover early active substances. However, in fact, their work not only includes such research but also various other roles, such as consideration of a manufacturing process for establishing a mass synthesis process and synthesis of isotope labeled substances, anticipated metabolites, and other related substances, which can be considered to be "thankless roles," during the course of producing medicines. … The authors would like to mention various roles which medicinal chemists play during the development of promising candidates as useful medicines, while focusing attention on some items in synthesis which they have engaged in for the last few years during the course of drug development, that is, the development research of OCT." (line 1 in the left column of page 139 to line 12 in the right column thereof)

(B) "3. Consideration of a mass synthesis process—problems in conventional processes and improvements thereto

Then, by the time when candidate specimens are narrowed down and the direction of development is decided, supply of a large number of specimens becomes necessary. …

The process whereby OCT was synthesized at first is indicated in Figure 5 [note in this judgment: same as the process described in the aforementioned Exhibit Ko 1 Publication]. The weak point of this process is that by-product (9) is produced in the alkylation of alcohol (8). 9 is separated as an unreacted substance in the next step, the Wacker oxidation, but it was a problematic loss. This production of by-product (9) arises from low reactivity caused by the steric hindrance of the hydroxyl group of 8. As a result of considering the alkylation reaction of 8 through dozens of series of reactions, it was revealed that the improved process that goes through the Michael Addition reaction-methylation reaction is efficient, as indicated in Figure 6. This process is adopted at present. However, even in this methylation reaction, $CeCl_3 \cdot 7H_2O$ is used by

subjecting it to dehydration and anhydration by an oven at 250°C. Therefore, the reaction is disadvantageous for mass synthesis though there is no problem at the laboratory level. Thus, further improvement is being considered." (fifth line from the bottom in the right column of page 140 to line 8 in the left column of page 142)

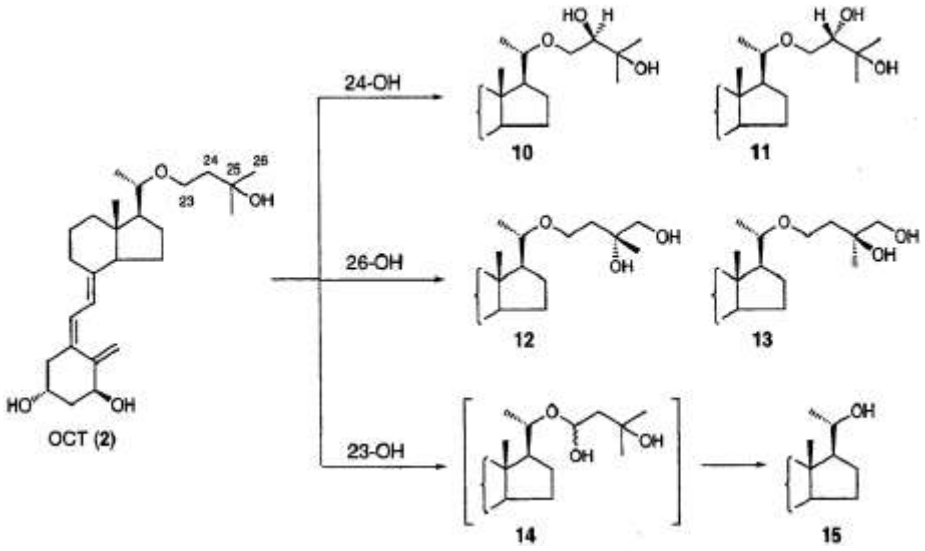
(C) "4. Synthesis of related compounds

4.1 Synthesis of anticipated metabolites

In deciding the structure of a metabolite, an important and also easier option is to directly compare those that were actually extracted and isolated from biological samples and those that were chemically synthesized. Assuming the part subjected to metabolism by looking at the structure of a medicine and synthesizing and providing an anticipated metabolite is of great help for researchers engaging in metabolic experiments.

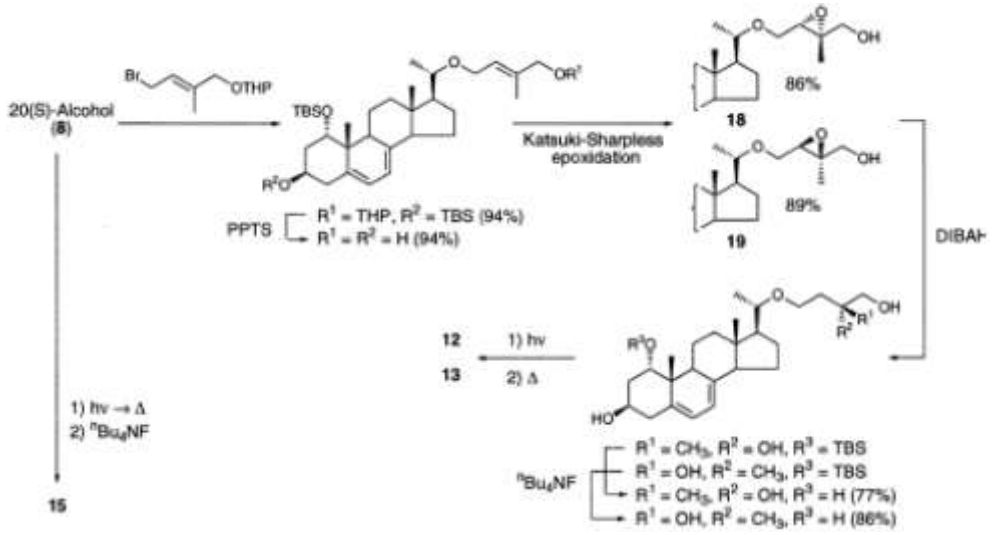
In the case of $1,25(OH)_2D_3$, it is well-known that the 23, 24, and 26-positions are hydroxylated and are finally metabolized to calcitroic acid. Then, in the case of OCT, the synthesis of 24-hydroxylated OCT (10) and (11), 26-hydroxylated OCT (12) and (13) [note in this judgment: a Maxacalcitol Side Chain of which the 26 position is hydroxylated], and pentanor OCT (15) deriving from hemiacetal (14), which is produced by the hydroxylation of the 23-position, was also considered as indicated in Figure 7." (line 17 in the left column of page 142 to line 12 of the right column thereof)

[Figure 7]



(D) "Furthermore, regarding 26-hydroxylated OCT (12) and (13), as indicated in Figure 9, epoxide (18) and (19) were obtained by using the Katsuki-Sharpless reaction in the key step, and each was led to 26-hydrozylated OCT of which the 25-position is R Coordination (12) and S Coordination (13), respectively. … (Figure 9)" (line 16 in the

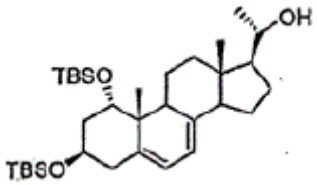
right column of page 142 to line 2 in the left column of page 143)
[Figure 9]



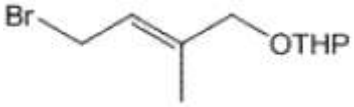
B. Content of Exhibit Otsu 14 Invention

According to A. above, Figure 9 of Exhibit Otsu 14 Document is recognized as disclosing the following process (Exhibit Otsu 14 Invention).

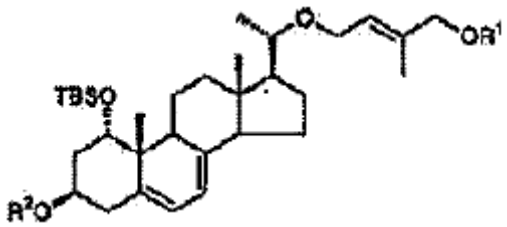
"A process for obtaining the anticipated metabolites of maxacalcitol indicated as (12) and (13) in Figure 9 (see Figure 7), which comprises the step of reacting the following 20(S)-alcohol (8):



(in the formula, TBS is t-butyldimethylsilyl that is a protective group)
with 4-bromo-2-methyl-tetrahydropyranyloxy-2-butene

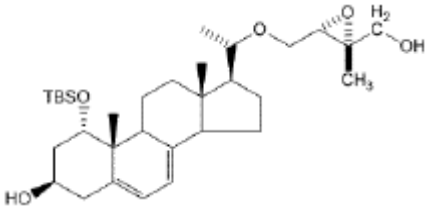


(in the formula, THP is tetrahydropyran)
to produce the following steroid compound [the same as the figure at the top center of Figure 9]:

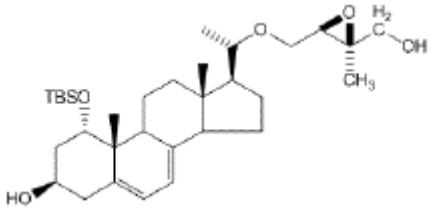


(in the formula, R^1=THP and R^2=H),

the step of subsequently producing the following epoxide compounds (18) and (19) by using the Katsuki-Sharpless reaction:



Compound 18



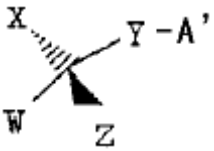
Compound 19

and the step of reducing these epoxide compounds with DIBAH (diisobutylaluminum hydride) and subsequently subjecting them to light illumination and thermal isomerization."

C. Common features and differences between the Corrected Invention and Exhibit Otsu 14 Invention

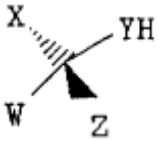
(A) The Corrected Invention and Exhibit Otsu 14 Invention are identical with each other in the following points.

"A process for preparing a compound having the following structure:



(in the formula, W is hydrogen, X is methyl; Y is O; and Z is a vitamin D structure) which comprises:

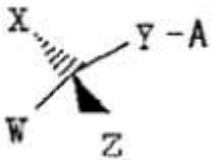
[a] the step of reacting a compound having the following structure:



(in the formula, W, X and Y are as defined above; Z is a steroid ring structure) with a reagent having the following structure:

E-B

(in the formula, E is an eliminating group)
to produce an epoxide compound having the following structure:

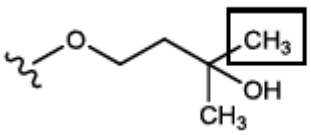


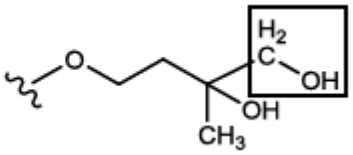
[b] the step of treating the epoxide compound with a reducing agent to produce the compound; and
[c] the step of recovering the compound so produced."

That is, the inventions are identical with each other in being a process for preparing a desired vitamin D compound by using the alcohol compound at the 20-position of a steroid ring structure as the starting material (Constituent Feature [B-1]), reacting said material with a reagent to produce an epoxide compound (part of Constituent Feature [B-3], excluding the side chain-related part), and treating the epoxide compound with a reducing agent (part of Constituent Feature [A-1], excluding the side chain-related part, and Constituent Features [A-2], [A-4] to [A-6], and [C] to [E]).

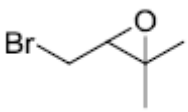
(B) The Corrected Invention and Exhibit Otsu 14 Invention differ in the following points.

(Difference 1) Regarding the objective substance "Y-A'," the side chain of the Corrected Invention is a Maxacalcitol Side Chain as indicated in the figure below on the left (the side chain-related part of Constituent Feature [A-1] and Constituent Feature [A-3]). On the other hand, the side chain of Exhibit Otsu 14 Invention is not a Maxacalcitol Side Chain as indicated in the figure below on the right.

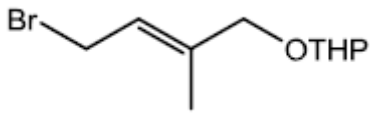




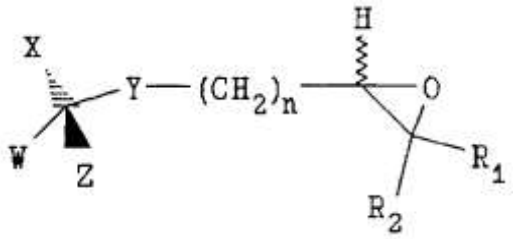
(Difference 2) In the Corrected Invention, Compound "E-B" (used as a reagent; E is Br, and B is a structure containing an epoxy group; the same applies hereinafter) is "4-bromo-2,3-epoxy-2-methylbutane" (the Reagent) having the following structure:



(the chemical formula part of Constituent Feature [B-2]). On the other hand, in Exhibit Otsu 14 Invention, Compound "E-B" is "4-bromo-2-methyl-tetrahydropyranyloxy-2-butene" having the following structure:

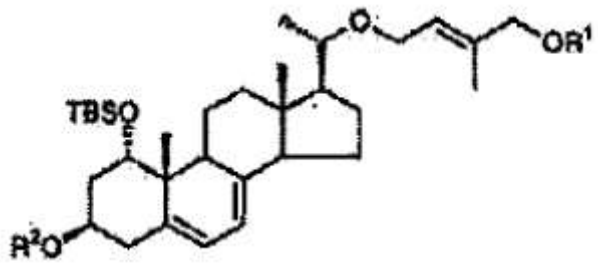


(Difference 3) In the Corrected Invention, the starting material and Compound "E-B" are reacted in the presence of a base to obtain an epoxide compound having the following structure:

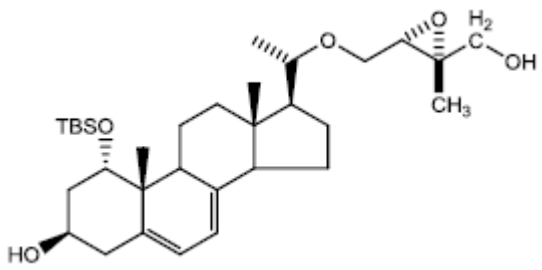


n=1, R_1 and R_2= methyl

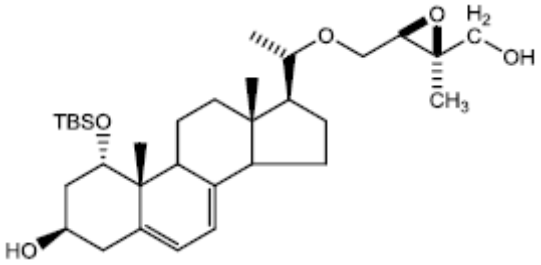
(part of Constituent Feature [B-2], excluding the chemical formula, and the side chain-related part of Constituent Feature [B-3]). On the other hand, in Exhibit Otsu 14 Invention, a compound having the following structure is produced through reaction of the starting material and Compound "E-B":



and then, epoxide compounds having the following structures are produced by using the Katsuki-Sharpless reaction:



Compound 18



Compound 19

D. Consideration concerning whether a person ordinarily skilled in the art can easily conceive of Differences 2 and 3

As mentioned in C. above, the Corrected Invention and Exhibit Otsu 14 Invention differ in the objective substance (Difference 1), the reagent reacted with the starting material (Difference 2), and the epoxide compound, which is the intermediate, and the step of producing said compound (Difference 3). The appellants allege that a person ordinarily skilled in the art can easily conceive of the structure pertaining to the Corrected Invention by combining the reagent described in Exhibit Otsu 9 Document (the Reagent) with Exhibit Otsu 14 Invention.

(A) However, as the reagent of Exhibit Otsu 14 Invention differs from the reagent of the Corrected Invention, a person ordinarily skilled in the art needs to be motivated to use the reagent of the Corrected Invention in place of the reagent of Exhibit Otsu 14 Invention in order to conceive of the Corrected Invention from Exhibit Otsu 14 Invention. In this regard, although the structure of the Reagent itself was publicly known (Exhibit Otsu 9), according to what is described in A. above, the process described in Figure 9 of Exhibit Otsu 14 Document (Exhibit Otsu 14 Invention) is a manufacturing process for selectively synthesizing anticipated metabolites of maxacalcitol (12) and (13) which have a side chain end structure including two kinds of steric configurations, unlike maxacalcitol. Then, in Exhibit Otsu 14 Invention, the Katsuki-Sharpless reaction (by using said reaction, a side chain including a double bond is subjected to asymmetric epoxidation, and thereby, two kinds of compounds that differ in the steric configuration can be synthesized) is used for the purpose of selectively producing two kinds of epoxide compounds (18) and (19) (these compounds are isomers that differ in the steric configuration of the end of the side chain [R-stereoisomer and S-stereoisomer]) to synthesize the aforementioned two kinds of anticipated metabolites of maxacalcitol. A specific reagent having a double bond at its side chain (4-bromo-2-methyl-tetrahydropyranyloxy-2-butene) is selected as a reagent

used for introducing a double bond that is necessary for the Katsuki-Sharpless reaction into the side chain of the starting material. Using the Reagent in place of said reagent is neither described nor suggested in Exhibit Otsu 14 Document and Exhibit Otsu 9 Document.

In that case, a person ordinarily skilled in the art cannot be considered to be motivated to combine the Reagent with Exhibit Otsu 14 Invention. Therefore, the structure of the Corrected Invention pertaining to Difference 2 (difference in the reagent) cannot be considered to be one which a person ordinarily skilled in the art could have easily conceived of.

(B) In addition, neither Exhibit Otsu 14 Document nor other publicly known documents submitted in this lawsuit describe or suggest any motivation of a person ordinarily skilled in the art to intend to obtain an epoxide compound, which is the intermediate of the Corrected invention, in place of the epoxide compound of Exhibit Otsu 14 Invention.

Therefore, the structure of the Corrected Invention pertaining to Difference 3 (difference in the epoxide compounds) cannot also be considered to be one which a person ordinarily skilled in the art could have easily conceived of.

E. Regarding the appellants' allegations

In response to the above, the appellants allege as follows: It is easy to change the objective substance of Exhibit Otsu 14 Invention from the anticipated metabolites of maxacalcitol to maxacalcitol whose structure of the side chain is very similar to those of the anticipated metabolites of maxacalcitol (Difference 1); in that case, [i] when seeing Figure 9 of Exhibit Otsu 14 Document, a person ordinarily skilled in the art, who considers an efficient process for preparing maxacalcitol, can conceive of using and is motivated to use compounds in which the hydromethyl group of epoxide compounds (18) and (19) is replaced with a methyl group as the precursors of maxacalcitol for the purpose of synthesizing maxacalcitol, focusing attention on the fact that the structures of the side chains of the anticipated metabolites of maxacalcitol indicated in said figure and the structure of a Maxacalcitol Side Chain are very similar to each other (hereinafter referred to as "Allegation [i]"); [ii] by applying retrosynthesis and common general technical knowledge to such replaced epoxide compounds, a person ordinarily skilled in the art conceives of first cutting between the oxygen atom of the ether bond and the carbon atom on its right side and then reacting the Reagent obtained by the cutting and the starting material of Exhibit Otsu 14 Invention, and also considers that the reaction between said materials proceeds well; therefore, it is easy for a person ordinarily skilled in the art to conceive of both of the structures of the Corrected Invention pertaining to

Differences 2 and 3 (hereinafter referred to as "Allegation [ii]"). The appellants' allegations are considered below.

(A) As mentioned in Allegation [i], the appellants allege that a person ordinarily skilled in the art, who considers an efficient process for preparing maxacalcitol, can conceive of using and is motivated to use compounds in which the hydromethyl group of epoxide compounds (18) and (19) is replaced with a methyl group as the precursors of maxacalcitol based on Figure 9 of Exhibit Otsu 14 Document.

However, as mentioned in D.(A) above, the process described in Figure 9 of Exhibit Otsu 14 Document is a manufacturing process for selectively synthesizing two different kinds of anticipated metabolites of maxacalcitol (12) and (13), which differ in that the steric configuration at the 25-position is R-stereoisomer or S-stereoisomer. The process comprises a series of steps: specifically, the step of first carrying out the two-step reaction of introducing a side chain having a double bond by applying a reagent to the starting material and using the Katsuki-Sharpless reaction to selectively synthesize two kinds of epoxide compounds (18) and (19), which are intermediates in which the double bond is converted into an epoxy group; the step of then opening the ring of the epoxy group of each epoxide compound to produce two kinds of steroid compounds as graphically illustrated in the lower right of Figure 9; and the final step of subjecting each of the steroid compounds to light illumination and thermal isomerization to produce the aforementioned anticipated metabolites (12) and (13), which are the final objective substances, from each of these steroid compounds. In the aforementioned Allegation [i] of the appellants, they only extract the point that the process goes through a step involving epoxide compounds as the intermediates (precursors) in the final phase of the series of steps, and allege that the steps before obtaining said epoxide compounds are changed to those that completely differ from those of Exhibit Otsu 14 Invention. Therefore, it requires a technical idea of focusing attention especially on the point that the process goes through a step involving epoxide compounds out of the series of steps of Exhibit Otsu 14 Invention (given that one intends to apply this Exhibit Otsu 14 Invention to the synthesis of maxacalcitol, it is natural for him/her to conceive of a manufacturing process using 4-bromo-2-methyl-2-butene (prenyl bromide) indicated in the following figure, which does not have a tetrahydropyranyloxy group (OTHP group) that is excess for a Maxacalcitol Side Chain, in place of 4-bromo-2-methyl-tetrahydropyranyloxy-2-butene, as the reagent of Exhibit Otsu 14 Invention, and other than this, going through a series of steps, specifically, the step of introducing a side chain, the epoxidation step, and the step of opening the ring of the epoxy group, which are the same as those of Exhibit Otsu 14 Invention).

Reagent described in Exhibit Otsu 14 Document　　4-bromo-2-methyl-2-butene

In this regard, in Exhibit Otsu 14 Document, there is no statement suggesting that the series of steps indicated in Figure 9 is focused on the point that the process goes through a step involving epoxide compounds. Rather, it is considered that the epoxide compounds were produced during the steps just as a result of adopting the Katsuki-Sharpless reaction for the purpose of selectively synthesizing two kinds of anticipated metabolites of maxacalcitol (12) and (13), which differ in the steric configuration of the end of the side chain of which the 26-position is hydroxylated. In addition, Exhibit Otsu 14 Document only describes that anticipated metabolites of maxacalcitol were obtained in a good yield by the synthesis process indicated in Figure 9. There is neither statement describing problems nor statement suggesting the points which are not required to be changed and which should be improved when improving (changing) the series of steps of Exhibit Otsu 14 Invention (even if the issue of the number of steps is taken up as a point to be improved, there is no suggestion about which step should be cut down, the step of introducing a side chain, the epoxidation step, or the step of opening the ring of the epoxy group, and it is also possible to assume an option of direct hydroxylation from a double bond without going through epoxidation).

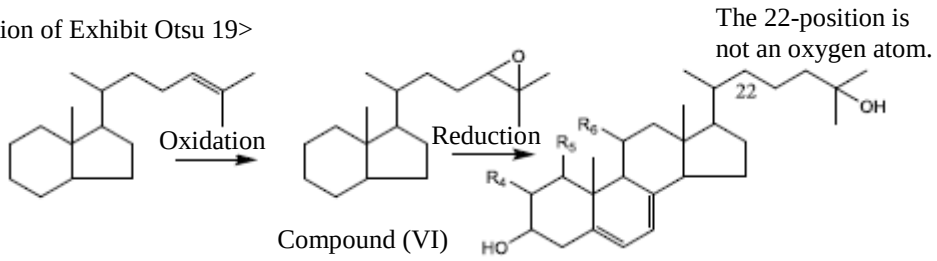
In that case, even if a person ordinarily skilled in the art could have conceived of applying Exhibit Otsu 14 Invention to the synthesis of maxacalcitol based on similarity between the side chains of the anticipated metabolites of maxacalcitol that are the final objective substances of Exhibit Otsu 14 Invention (or the steroid compounds that are the precursors thereof) and a Maxacalcitol Side Chain, he/she is not recognized as having been able to easily conceive of changing the step of introducing a side chain and the epoxidation step, which are steps before the step of opening the ring of the epoxy group of the epoxide compounds that is the final step, without changing said step of opening the ring of the epoxy group of the epoxide compounds, focusing special attention on the point that the process goes through a step involving epoxide compounds out of the series of steps.

(B) In this regard, the appellants allege as follows as a ground for Allegation [i]: Exhibit Otsu 19 Document (International Publication No. 1993/21204) describes that an epoxide compound is used when forming the same side chain as that of calcitriol, and the inventors of the Corrected Invention themselves also conceived of maxacalcitol by

replacing the carbon atom at the 22-position of the side chain of calcitriol with an oxygen atom; therefore, a person ordinarily skilled in the art, who has the technical knowledge of Exhibit Otsu 19 Document, has no difficulty in conceiving of the idea of synthesizing the precursors of maxacalcitol (epoxide compounds) from the epoxide compounds of Exhibit Otsu 14 Invention.

However, as indicated in the figure below, Exhibit Otsu 19 Document describes a process for the synthesis of calcitriol wherein the 22-position of the side chain is bonded not by an oxygen atom but by a carbon atom (it is not bonded by an ether bond unlike a Maxacalcitol Side Chain) (Exhibit Otsu 19 and the entire import of argument). The Williamson reaction between the alcohol compound at the 20-position and the reaction reagent is not carried out, and the objective substance is not maxacalcitol.

<Reaction of Exhibit Otsu 19>



In addition, as mentioned above, the manufacturing process described in Exhibit Otsu 19 Document comprises a series of steps, specifically, the step of oxidizing the double bond of the side chain of the starting material to introduce an epoxy group into the side chain and the step of opening the ring of the epoxy group of the epoxide compound with a reducing agent to produce the side chain of the objective substance. It is not recognized that there is a statement suggesting that attention is focused only on the point that the process goes through a step involving the epoxide compound as the intermediate out of said steps.

In that case, even a person ordinarily skilled in the art, who has the technical knowledge of Exhibit Otsu 19 Document, cannot be considered to have been able to easily conceive of the idea of changing the step of introducing a side chain and the epoxidation step, which are steps before the final step of the synthesis of the objective substance, focusing attention only on the point that epoxide compounds are used as the precursors in said final step, based on the series of steps of Exhibit Otsu 14 Invention.

Incidentally, the appellants also point out that the inventors of the Corrected Invention themselves said that they considered the synthesis of a substance by replacing the carbon atom at the 22-position of calcitriol with an oxygen atom and thereby invented maxacalcitol (Exhibit Otsu 14). However, even if the inventors considered as

such, this fact does not serve as a ground for proving that it is easy for a person ordinarily skilled in the art to conceive of a process for preparing maxacalcitol by changing the step of introducing a side chain and the epoxidation step, which are steps before the final step in the aforementioned process for preparing calcitriol, focusing attention only on the point that epoxide compounds are used as the precursors in said final step.

(C) The appellants also allege as follows: [a] A person ordinarily skilled in the art, who sees Figure 9 of Exhibit Otsu 14 Document, can understand that the Katsuki-Sharpless reaction is used due to existence of two different kinds of steric configurations and that such issue of steric configuration does not arise in relation to maxacalcitol; therefore, existence of two kinds of isomers in Figure 9 does not reduce the easiness of conceiving of the idea alleged by the appellants; [b] A person ordinarily skilled in the art would not bother to adopt a roundabout synthesis process which comprises a larger number of steps; therefore, he/she never adopts a process wherein the reagent is replaced with prenyl bromide when applying Exhibit Otsu 14 Invention to the synthesis of maxacalcitol.

However, regarding the allegation of [a] above, it is not recognized that similarity in the structures of the side chains and Exhibit Otsu 19 Document, which are originally alleged by the appellants as the grounds for the easiness of conceiving of the idea, are sufficient to have a person ordinarily skilled in the art conceive of extracting only the point that the process goes through a step involving epoxide compounds as the intermediates (precursors) out of the series of steps described in Figure 9 of Exhibit Otsu 14 Document and changing the steps before obtaining said epoxide compounds to those that are completely different from those of Exhibit Otsu 14 Invention, as indicated in the holdings in (A) and (B) above. Even if a person ordinarily skilled in the art, who sees the steps of Figure 9 of Exhibit Otsu 14 Document, can have an understanding as alleged above by the appellants, this fact cannot be considered to suggest that a person ordinarily skilled in the art focuses attention on the point that the process goes through the step involving epoxide compounds as the intermediates out of the series of steps, and it thus does not affect the content of said holdings.

In addition, regarding the allegation of [b] above, as indicated in the holding in (A) above, even if it can be said that a person ordinarily skilled in the art, who intends to apply Exhibit Otsu 14 Invention to the synthesis of maxacalcitol, naturally conceives of changing the structure of the side chain of the reagent within the limits of difference in the structures of the side chains of the final objective substances due to said difference, he/she is not recognized as being motivated to maintain only the step involving epoxide

compounds out of the series of steps and change the synthesis steps before said step to completely different ones for the purpose of further reducing the number of steps. Therefore, said allegation of the appellants also does not affect the content of said holding.

(D) On these bases, regarding the appellants' allegations, Allegation [i] is originally unacceptable. Therefore, it is not recognized that a person ordinarily skilled in the art could have easily conceived of the structures of the Corrected Invention pertaining to Differences 2 and 3 based on Exhibit Otsu 14 Invention, without the need of considering another Allegation [ii].

F. Therefore, there is no reason for the appellants' allegation of Ground for Invalidation A.

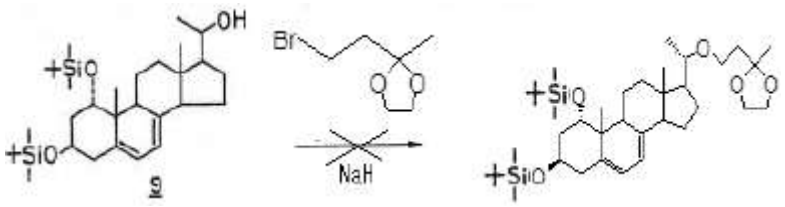
(2) Regarding lack of an inventive step by citing Exhibit Ko 12 Document as the primarily cited document (Ground for Invalidation B)

A. Content described in Exhibit Ko 12 Document

Exhibit Ko 12 Document (the translation thereof is Exhibit Otsu 43) is a paper titled "Synthetic studies of vitamin D_3 analogues VIII," which was written by five researchers of the new medicine research laboratory of the appellee, including Noboru Kubodera, who is one of the inventors of the Corrected Invention. The paper was published in "Chem. Pharm. Bull." which was distributed in 1986 prior to the Priority Date (September 3, 1996). There are following statements in the paper.

(A) "In contrast to the formation of [compound] 10, attempted alkylation of 9 with 1-bromo-3,3-ethylenedioxybutane … failed. [note in this judgment: see Reaction Formula A] (note 10)" (fifth line from the bottom of page 2 to the third line from the bottom thereof)

[Reaction Formula A]



9

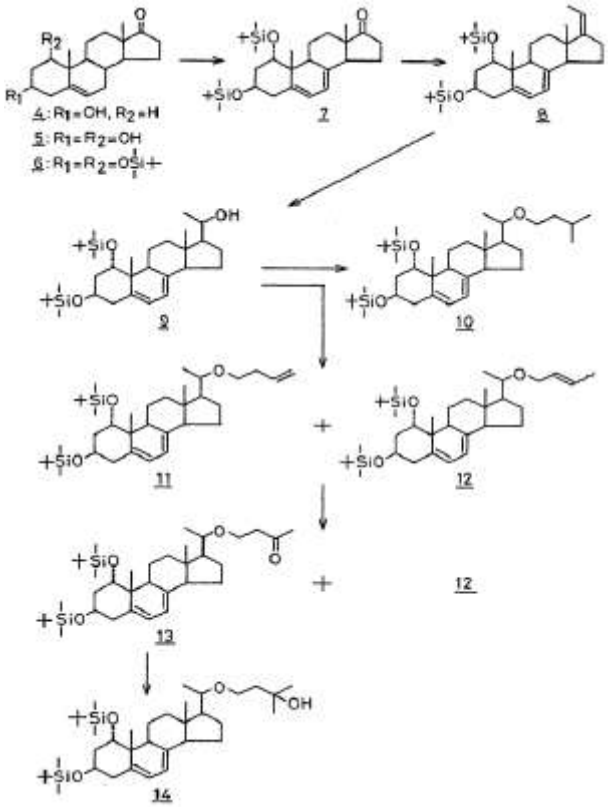
The alkylation failed.

(B) "However, the desired 25-keto derivative (13) was obtained by the following two-step procedure; the alcohol 9 was treated with 4-bromo-1-butene and a large excess of NaH in refluxing xylene for 18 h, then the resulting 1:1 mixture of the double bond isomers (11 and 12) was oxidized by the Wacker process (catalytic amounts of $PdCl_2$

and excess CuCl in DMF-H_2O, O_2 atmosphere, room temperature, 19 h) to give the ketone (13) in 44% yield based on the consumed [compound] 9, together with the unchanged isomer 12. The reaction of [compound] 13 with MeMgBr in THF at 0°C for 1 h gave the pro-D_3 derivative (14) in 79% yield.

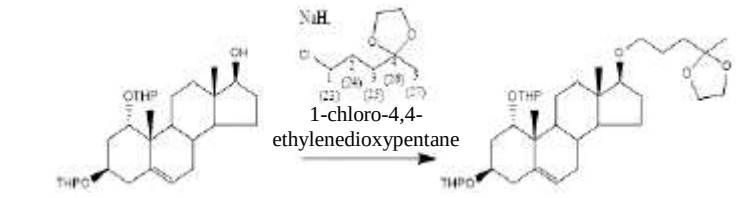
[Compound] 14 was successively subjected to the irradiation, thermal isomerization and deprotection in the same manner as mentioned above to give 1α,25-$(OH)_2$-22-oxa-D_3 3b in 9% yield [note in this judgment: see Reaction Formula C]." (third line from the bottom of page 2 to line 10 of page 3)

[Reaction Formula C]



(C) (Note 10) "The alkylation of 1α,3β-bis(tetrahydropyranyloxy)-5-androsten-17β-ol with 1-chloro-4,4-ethylenedioxypentane in the presence of NaH in boiling xylene gave the desired ether in good yield [note in this judgment: see Reaction Formula B]. The failure in this work might be due to the bulkiness of 1-halo-3,3-ethylenedioxybutane compared with the former one." (seventh line from the bottom of page 5 to the third line from the bottom thereof)

[Reaction Formula B]



1α,3β-bis(tetrahydropyranyloxy)-
5-androsten-17β-ol

B. Content of Exhibit Ko 12 Invention

According to A.(A) above, Exhibit Ko 12 Document is recognized as disclosing the following process (Exhibit Ko 12 Invention).

"A manufacturing process for the synthesis of a steroid compound having a Maxacalcitol Side Chain wherein Compound 9 (alcohol compound at the 20-position of a steroid ring structure) of Reaction Formula A was reacted with 1-bromo-3,3-ethylenedioxybutane (Exhibit Ko 12 Reagent 1) but the reaction failed and the desired compound could not be obtained"

C. Common features and differences between the Corrected Invention and Exhibit Ko 12 Invention

(A) The Corrected Invention and Exhibit Ko 12 Invention are identical with each other in the following point.

"A process for preparing a steroid compound having a Maxacalcitol Side Chain by using the alcohol compound at the 20-position of a steroid ring structure (Constituent Feature [B-1]) as the starting material and reacting said material with a reagent (Constituent Features [A] and [E])"

(B) The Corrected Invention and Exhibit Ko 12 Invention differ in the following points.

(Difference 1) In the Corrected Invention, the compound used as the reagent (in the case of a structure containing an epoxy group wherein the eliminating group is Br) is 1-bromo-3-methyl-2,3-epoxybutane (the Reagent) (the chemical formula part of Constituent Feature [B-2]). On the other hand, in Exhibit Ko 12 Invention, the compound used as the reagent is 1-bromo-3,3-ethylenedioxybutane (Exhibit Ko 12 Reagent 1).

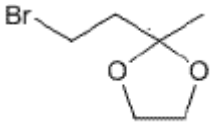
(Difference 2) The Corrected Invention is a process for obtaining the objective substance which comprises the step of reacting the starting material and the reagent in the presence of a base to obtain an epoxide compound and the step of subsequently treating the epoxide compound with a reducing agent to open the ring of the epoxy group (part of Constituent Feature [B-2], excluding the chemical formula part, and Constituent Features [B-3] [C], and [D]). On the other hand, in Exhibit Ko 12 Invention,

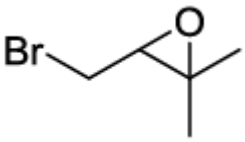
the starting material and the reagent were reacted, but the reaction failed and the objective substance could not be obtained.

D. Consideration concerning whether a person ordinarily skilled in the art can easily conceive of Difference 1

As mentioned in C. above, the Corrected Invention and Exhibit Ko 12 Invention differ in the reagent reacted with the starting material (Difference 1) and the point of whether the starting material and the reagent react and thereby lead to the synthesis of an epoxide compound, which is the intermediate, and the objective substance (Difference 2). The appellants allege that a person ordinarily skilled in the art can easily conceive of the structures of the Corrected Invention pertaining to the differences by combining the Reagent of Exhibit Otsu 9 Document with Exhibit Ko 12 Invention.

However, as the reagent of Exhibit Ko 12 Invention differs from the reagent of the Corrected Invention, a person ordinarily skilled in the art is required to have a motivation to use the reagent of the Corrected Invention in place of the reagent of Exhibit Ko 12 Invention in order to conceive of the Corrected Invention based on Exhibit Ko 12 Invention. In this regard, although the structure of the Reagent itself was publicly known (Exhibit Otsu 9), Exhibit Ko 12 Reagent 1 (left figure below) completely differs from the Reagent (right figure below) in the specific cyclic structure. In addition, neither Exhibit Ko 12 Document nor Exhibit Otsu 9 Document describes or suggests that the Reagent is used in place of Exhibit Ko 12 Reagent 1 with which the reaction failed.





In that case, it cannot be said that a person ordinarily skilled in the art has a motivation to combine the Reagent with Exhibit Ko 12 Invention. Therefore, it cannot be said that a person ordinarily skilled in the art could have easily conceived of the structure of the Corrected Invention pertaining to Difference 1 (difference in the reagent).

E. Regarding the appellants' allegations

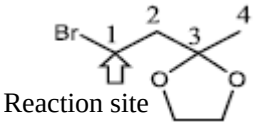
In response to the above, the appellants allege as follows: [i] As of the Priority Date, a person ordinarily skilled in the art only had to find an alkylation reagent which can alkylate the hydroxyl group of the Steroid Starting Material in a good yield; [ii] If a person ordinarily skilled in the art, who saw Exhibit Ko 12 Invention, sees the statement in note 10 of Exhibit Ko 12 Document, he/she can conceive of using the Reagent, which is a compound that has a cyclic structure while maintaining a four carbon straight alkyl

structure and whose number of elements that constitute the cyclic part is reduced, as the alkylation reagent in place of Exhibit Ko 12 Reagent 1 with which alkylation reaction failed; [iii] Then, seeing Exhibit Otsu 9 Document that describes the Reagent, a person ordinarily skilled in the art considers that the reaction between the Reagent and the Steroid Starting Material proceeds well; therefore, a person ordinarily skilled in the art can easily conceive of the structures of the Corrected Invention pertaining to Differences 1 and 2.

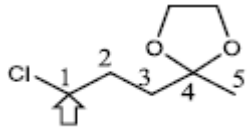
(C) However, regarding the aforementioned allegation [i] of the appellants, it is not recognized that a person ordinarily skilled in the art was naturally motivated to change the alkylation reagent of Exhibit Ko 12 Invention to another alkylation reagent and was also motivated to seek an alkylation reagent that replaces Exhibit Ko 12 Reagent 1 based on the step that failed to introduce a Maxacalcitol Side Chain, by daringly focusing attention on said step out of the processes described in Exhibit Ko 12 Document, if taking into account that Exhibit Ko 12 Document describes as follows: The reaction of Exhibit Ko 12 Invention failed; therefore, 4-bromo-1-butene (Exhibit Ko 12 Reagent 2) was applied to Compound 9 as a process for preparing maxacalcitol in place of said reaction; in that case, alkylation reaction proceeded, and steroid compound (14) having a Maxacalcitol Side Chain could be synthesized by going through 25-keto derivative (13) (Reaction Formula C in A.(B) above).

(B) In addition, considering the aforementioned allegation [ii] of the appellants, it is stated in parallel in note 10 of Exhibit Ko 12 Document that Reaction Formula B achieved a good yield but that Reaction Formula A failed. It is specifically stated that "The failure in this work might be due to the bulkiness of 1-halo-3,3-ethylenedioxybutane compared with the former one." The "former one" mentioned here is recognized as meaning "1-chloro-4,4-ethylenedioxypentane" (Exhibit Ko 12 Reagent 3) of Reaction Formula B.

Comparing the reagents used in the aforementioned two reactions, the number of carbons of the main chain of Exhibit Ko 12 Reagent 1 (left figure below) with which alkylation failed is one fewer than that of Exhibit Ko 12 Reagent 3 (right figure below) with which alkylation succeeded, and the position at which a five-membered ring is bonded is closer to bromide, which is an eliminating group. Therefore, it is reasonable to understand that "bulkiness" includes the perspective of distance between the eliminating group and the cyclic structure and does not merely mean the size of the cyclic structure.



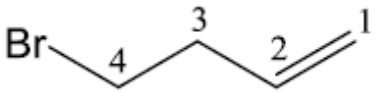
1-bromo-3,3-ethylenedioxybutane



1-chloro-4,4-ethylenedioxypentane

Moreover, the statement in note 10 of Exhibit Ko 12 Document is nothing more than analyzing that the failure "might be due to the bulkiness." In addition, Reaction Formula B originally differs from Reaction Formula A not only in the reagent but also in the structure of the starting material. Therefore, the statement cannot be understood as suggesting that the reaction of Reaction Formula A naturally proceeds in the same manner as that of Reaction Formula B and the reagent of Reaction Formula A reacts with Compound 9 if the reagent of Reaction Formula A is changed to a reagent obtained by reducing the "bulkiness" of Exhibit Ko 12 Reagent 1.

Even based on the understanding that the "bulkiness" of Exhibit Ko 12 Reagent 1 is the "size of the cyclic structure" and that it inhibits the reaction, there is no statement suggesting that the reagent should maintain the cyclic structure in Exhibit Ko 12 Document. Rather, as mentioned above, 4-bromo-1-butene (Exhibit Ko 12 Reagent 2; see the following figure), which is used in the working example in which the reaction succeeded in Exhibit Ko 12 Document, does not have a cyclic structure. Therefore, it cannot be said that a person ordinarily skilled in the art conceives of a reagent maintaining a cyclic structure as a reagent with reduced "bulkiness."



Therefore, there is no reason for the appellants' allegation that note 10 in Exhibit Ko 12 Document suggests that alkylation reaction can be expected to proceed in relation to Compound 9 if the five-membered ring cyclic ether of Exhibit Ko 12 Reagent 1 is less bulky, that is, a compound whose number of elements that constitute the cyclic part is reduced. Consequently, the aforementioned allegation [ii] of the appellants on this premise is unacceptable.

(C) On these bases, it cannot be said that a person ordinarily skilled in the art had a motivation to consider the use of the Reagent whose cyclic structure is reduced in size in place of Exhibit Ko 12 Reagent 1 based only on the suggestion that the failure "might be due to the bulkiness," by daringly focusing attention on Exhibit Ko 12 Invention using Exhibit Ko 12 Reagent 1 with which reaction failed as a process for preparing maxacalcitol. It is thus not recognized that a person ordinarily skilled in the art could

have easily conceived of the structures of the Corrected Invention pertaining to Differences 1 and 2 based on Exhibit Ko 12 Invention, without the need of considering other points.

F. Therefore, there is no reason for the appellants' allegation of Ground for Invalidation B.

(3) Regarding the lack of an inventive step by citing Exhibit Otsu 4 Document as the primarily cited document (Ground for Invalidation C)

The Corrected Invention is not recognized as one which a person ordinarily skilled in the art could have easily conceived of based on the invention described in Exhibit Otsu 4 Document. The reason therefor is as held in No. 4, 7. in "Facts and reasons" in the judgment in prior instance. Therefore, the relevant part is cited.

3. Summary

On these bases, the Appellant's Process is recognized as falling under the technical scope of the Corrected Invention as an equivalent to the Corrected Invention. In addition, there is no reason for all of the grounds for invalidation alleged by the appellants in relation to the Corrected Invention. Therefore, the Patent Pertaining to the Corrected Invention is not recognized as one that should be invalidated by a trial for patent invalidation.

According to the aforementioned facts on which the decision is premised, all of the Appellants' Products were prepared by the Appellant's Process. Consequently, both the act of importing or assigning Appellant's Product 1 and the act of assigning or offering for assignment Appellants' Products 2 constitute infringement of the Patent Right. Therefore, there is a reason for all of the appellee's claims for an injunction against the import or assignment of Appellant's Product 1 and disposal thereof in relation to Appellant DKSH and claims for an injunction against the assignment or offer for assignment of Appellants' Products 2(1) to (3) and disposal thereof in relation to Appellant Iwaki Seiyaku, Appellant Takata Pharmaceutical, and Appellant Pola Pharma, respectively, for the period up to September 3, 2017, which is the last day of the duration of the Patent Right before the registration of extension of the duration of the Patent Right.

No. 5 Conclusion

On these bases, the judgment in prior instance that upheld all of the appellee's claims is reasonable, and there is no reason for all of the appeals in question filed by the appellants.

Therefore, the judgment shall be rendered in the form of the main text.

Intellectual Property High Court, Special Division

Presiding judge: SHITARA Ryuichi
Judge: SHIMIZU Misao
Judge: TAKABE Makiko
Judge: OTAKA Ichiro
Judge: OHYORI Asayo

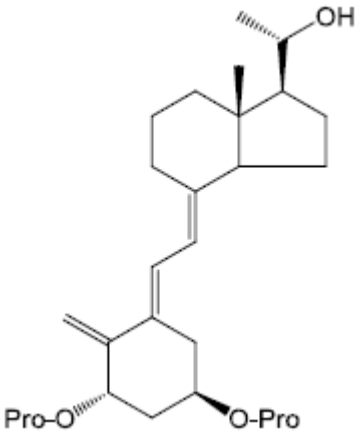
(Attachment)

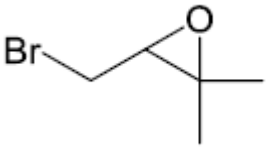
Process List

A process for preparing maxacalcitol comprising the following steps:

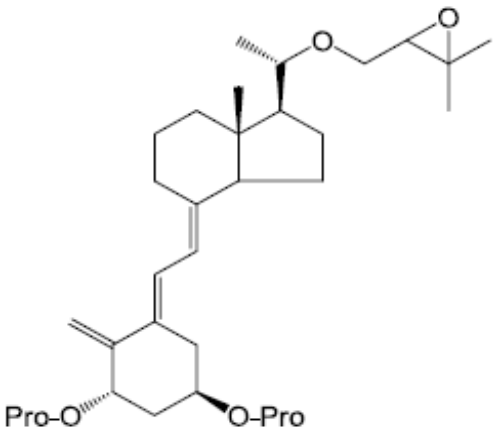
1. (Step I) The step of reacting the following Starting Material A with the following Reagent B in the presence of a base to synthesize the following Intermediate C of an epoxide compound

Starting Material A + Reagent B



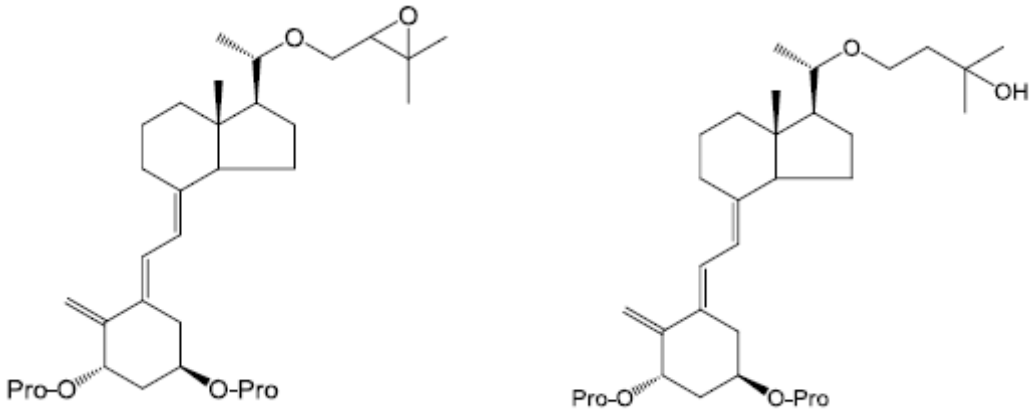


→ Intermediate C



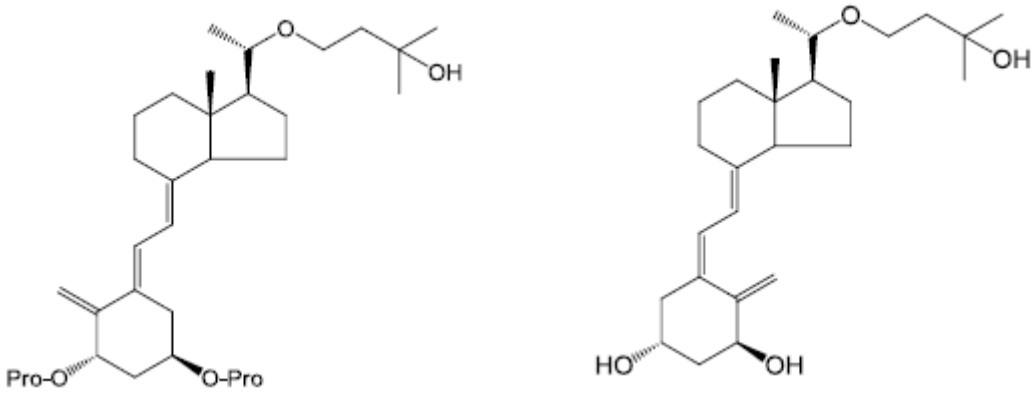
2. (Step II) The step of opening the epoxide ring (epoxy group) by treating the following Intermediate C with a reducing agent to obtain the following Substance D

Intermediate C → Substance D



3. (Step III) The step of converting the following trans-form Substance D to a cis form and removing protective groups to obtain maxacalcitol

Substance D → Maxacalcitol



4. (Step IV) The step of recovering the obtained maxacalcitol

(Note: In each of the aforementioned structural formulas, Pro means a "protective group.")