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PROVISIONAL

INTERNATIONAL UNION OF PURE AND APPLIED CHEMISTRY

and

INTERNATIONAL UNION OF BIOCHEMISTRY

JOINT COMMISSION ON BIOCHEMICAL NOMENCLATURE*

NOMENCLATURE OF VITAMIN D

Comments on these recommendations are welcome and should be sent within 8 months from August 1982 to the Secretary of the Commission

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Comments from the viewpoint of languages other than English are especially encouraged. These may have special significance regarding the publication in various countries of translations of the nomenclature eventually approved by IUPAC.

*Membership of the Commission for 1979-81 was as follows:

Chairman: P. KARLSON (FRG); *Secretary:* H. B. F. DIXON (UK); *Members:* B. L. HORECKER (USA); Y. JEANNIN (France); C. LIÉBECQ (Belgium — as Chairman of IUB Committee of Editors of Biochemical Journals); B. LINDBERG (Sweden); K. L. LOENING (USA); G. P. MOSS (UK); J. REEDIJK (Netherlands); S. F. VELICK (USA); J. F. G. VLIEGENTHART (Netherlands).

IUPAC-IUB Joint Commission on Biochemical Nomenclature (JCBN)

Nomenclature of Vitamin D

Recommendations 1981

CONTENTS

INTRODUCTION

In the 'IUPAC Definitive Rules for the Nomenclature of Vitamins', published in 1960 [1], and in the revised document of 1966 on Trivial Names of Miscellaneous Compounds of Importance in Biochemistry [2], the trivial names ergocalciferol for Vitamin D_2 and cholecalciferol for Vitamin D_3 were recommended. The recent revival of interest in vitamin D analogues and their chemistry as a result of the developments in vitamin D metabolism and function has rendered cumbersome some of the older systems for naming these compounds, resulting in the use of undesirable abbreviations like 1α,25-$(OH)_2D_3$ in the literature. Therefore, the Commission on Biochemical Nomenclature asked H. F. DeLuca to develop, in consultation with other experts, a simplified and extended system of trivial names for vitamin D metabolites. This proposal was submitted to the International Union of Nutritional Sciences and the IUB-IUPAC Joint Commission on Biochemical Nomenclature. The present recommendations are based on H. F. DeLuca's proposal after further consultation with other workers active in this field. They extend the scope of Section M-2 of the 1966 Rules [2] and recommend new, shorter trivial names. From the biochemical point of view, the most important ones are *calciol*, *calcidiol* and *calcitriol* for cholecalciferol, 25-hydroxycholecalciferol and 1α,25-dihydroxycholecalciferol, respectively. Calciol is not necessarily preferred to cholecalciferol for vitamin D_3 itself, but the new names are recommended for hydroxylated derivatives. A full list of recommended names is given in the appendix.

These recommendations are intended to give convenient short trivial names to the common, biologically important derivatives of vitamin D. Synthetic derivatives that have a more complicated structure may be named more conveniently according to the steroid rules [4], using 9,10-secocholestane and 9,10-secoergostane as parent compounds. Thus these recommendations do not supersede the steroid rules.

Document of the IUPAC-IUB Joint Commission on Biochemical Nomenclature (JCBN) whose members are: P. Karlson (chairman), H. B. F. Dixon, C. Liébecq (as chairman of the IUB Committee of Editors of Biochemical Journals), K. L. Loening, G. P. Moss, J. Reedijk, S. P. Velick, and J. F. G. Vliegenthart. JCBN thanks other members of the Nomenclature Committee of IUB (H. Bielka and N. Sharon) for consultation. Comments and suggestions for future revisions of these recommendations may be sent to its secretary: H. B. F. Dixon, University Department of Biochemistry, Tennis Court Road, Cambridge, England CB2 1QW, or to any member.

1. CLASS NAME

The term *vitamin D* should be used as a general term to describe all steroids that exhibit qualitatively the biological activity of calciol. This term should be used in derived terms such as vitamin D activity, vitamin D deficiency, vitamin D antagonist [5].

The term *vitamin* D_3 may be used as a synonym for calciol, but it should not be abbreviated to D_3 and then modified to forms like 1,25-$(OH)_2D_3$. This type of representation of vitamin D_3 metabolites is strongly discouraged.

2. SEMISYSTEMATIC NAMES

Although all compounds with vitamin D activity may be described using a semisystematic steroid name [4], the names tend to be cumbersome for general use. A new and shorter name for (5*R*,10*R*)-9,10-secocholestane was considered as a parent molecule, but it was decided that the shortening achieved was not worth the disruption involved in the change. The main confusion in the application of Steroid Rule 2S-8.1 [4] to vitamin D derivatives is that the descriptors 'α' and 'β' only apply when ring A is orientated as in the parent steroid, although the vitamin is often represented in its alternative conformation [compare (1) with (2), (3) with (4), or (8) with (9)]. We recommend that these descriptors should never be applied to ring A or to C-6 or C-7 of vitamin D compounds; chiral centres should be designated *R* or *S*, and double bonds *E* or *Z* [6]. Examples are given in Table 1.

Because of the nature of the sequence rules it is not possible to transfer *R* or *S* from one compound to its derivatives. Examples of the effects of this are shown in Fig. 1.

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Table 1. *Nomenclature for vitamin D compounds*

Current trivial name	Recommended trivial name	Systematic steroid name[a]
Cholecalciferol	calciol or cholecalciferol	(5*Z*,7*E*)-(3*S*)-9,10-seco-5,7,10(19)-cholestatrien-3-ol
25-Hydroxycholecalciferol	calcidiol	(5*Z*,7*E*)-(3*S*)-9,10-seco-5,7,10(19)-cholestatriene-3,25-diol
1α,25-Dihydroxycholecalciferol	calcitriol	(5*Z*,7*E*)-(1*S*,3*R*)-9,10-seco-5,7,10(19)-cholestatriene-1,3,25-triol
Ergocalciferol	ercalciol or ergocalciferol	(5*Z*,7*E*,22*E*)-(3*S*)-9,10-seco-5,7,10(19),22-ergostatetraen-3-ol[b]
1α,25-Dihydroxyergocalciferol	ercalcitriol	(5*Z*,7*E*,22*E*)-(1*S*,3*R*)-9,10-seco-5,7,10(19),22-ergostatetraen-1,3,25-triol[c]
22,23-Dihydroergocalciferol	(24*S*)-methylcalciol or 22,23-dihydroercalciol	(5*Z*,7*E*)-(3*S*)-9,10-seco-5,7,10(19)-ergostatrien-3-ol[c]
1α,24*R*,25-Trihydroxycholecalciferol	calcitetrol	(5*Z*,7*E*)-(1*S*,3*R*,24*R*)-9,10-seco-5,7,10(19)-cholestatriene-1,3,24,25-tetrol
Previtamin D_3	(6*Z*)-tacalciol	(6*Z*)-(3*S*)-9,10-seco-5(10),6,8-cholestatrien-3-ol
$Tachysterol_3$	tacalciol	(6*E*)-(3*S*)-9,10-seco-5(10),6,8-cholestatrien-3-ol
Isovitamin D_3	(5*E*)-isocalciol	(5*E*,7*E*)-(3*S*)-9,10-seco-1(10),5,7-cholestatrien-3-ol
$Dihydrotachysterol_3$	dihydroercalciol	(5*E*,7*E*)-(3*S*,10*S*)-9,10-seco-5,7-cholestadien-3-ol

[a] To conform with the convention used in the Steroid Rules (Rule 2S-4.1.1 [4]) and IUPAC Nomenclature of Organic Chemistry [7] double bond locants are cited before the stem name.
[b] 24*R*-configuration.
[c] 24*S*-configuration.

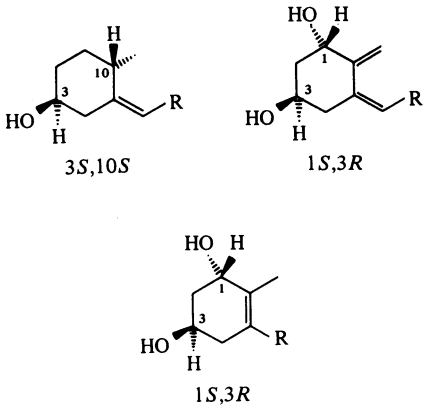
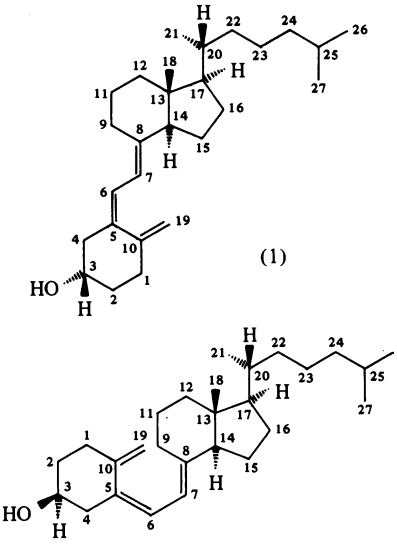


Fig. 1. *Examples of stereochemistry in ring A.* Note that the hydroxyl group in formulae (1) to (6) is 3*S*



(1)

(2)
Calciol

These recommendations do not apply to compounds in which ring B is unbroken. Thus lumisterol remains (22*E*)-9β,10α-ergosta-5,7,22-trien-3β-ol (Steroid Rule 2S-5.2 in [4]).

3. STEREOPARENT COMPOUNDS

Many investigators have used modifications of purely trivial names to show relationships between compounds. This aim can be combined with considerable shortening of names based on cholecalciferol and ergocalciferol if the name calciol is used for cholecalciferol [(1) which is the same as (2)]; cholecalciferol may still be used as an alternative trivial name for calciol but should not be used for naming metabolites. Although calciol is the parent name for the vitamin D_3 series and is capable of further modification (see below), no new parent hydrocarbon is named. Hence the name should only be used for compounds containing a 3-hydroxyl group and a system of (or derived from) three conjugated double bonds. Unless otherwise specified the configuration of the 3-hydroxyl group remains unchanged from that of the 3β-hydroxyl of the parent tetracyclic steroid, i.e. in the absence of 2- and 4-substitution it is 3*S* if position 1 is unsubstituted and 3*R* if position 1 also carries a hydroxyl. The triene system is 5,7,10(19) with 5*Z*,7*E* stereochemistry unless otherwise specified.

4. NUMBERING

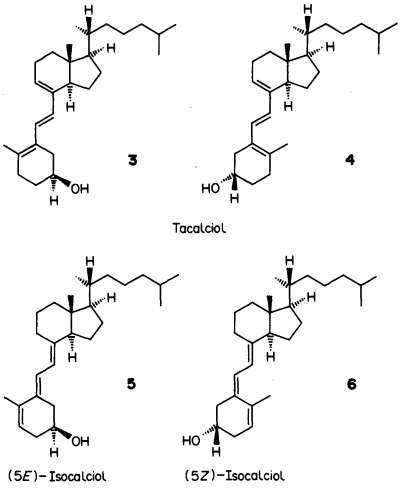
The numbering of the parent steroid is maintained as shown in formulae (1) and (2).

5. MODIFICATION OF THE TRIENE SYSTEM

As mentioned in rule 3 the stem calci- includes the 5,7,10(19)-triene system with 5*Z*,7*E* stereochemistry unless otherwise specified. The prefix 'ta' is applied to calciol (Table 2) to change the location of the triene to 5(10),6,8 with 6*E* configuration implied, e.g. *tacalciol* [(3) which is the same as (4)]. The prefix 'iso' is applied to calciol (Table 2) to change the location of the triene to 1(10),5,7 with 7*E* configuration implied; this prefix requires designation of the stereochemistry at position 5, e.g. *(5E)-isocalciol* (5).

6. SIDE CHAIN MODIFICATION

The prefix 'er' is used (Table 2) to indicate the side chain (7) for the vitamin D_2 series, e.g. *ercalciol.* This prefix implies



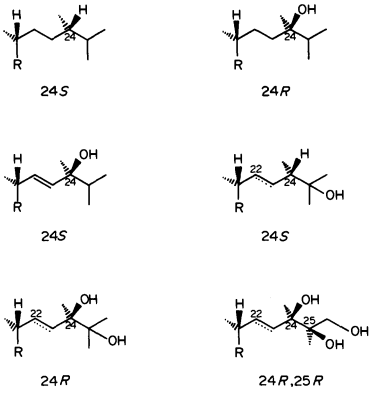
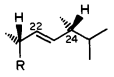


Fig. 2. *Examples of stereochemistry at position 24 (and 25) in the vitamin D_2 series.* Note that the presence or absence of a 22(23) double bond in the bottom three examples does not change in this series the designation at position 24 (or 25)

Table 2. *Modification of trivial names*

Stem or prefix	Origin	Effect
calci	calciferol	indicates 9,10-seco-5,7,10(19)-cholestatriene with 5*Z*,7*E*-configuration
ta	tachysterol	changes the triene of calciol to 5(10),6,8 with 6*E*-configuration
iso	isovitamin D_3	changes the triene of calciol to 1(10),5,7 with 7*E*-configuration
er	ergosterol	introduces 22(23) double bond with 22*E*-configuration and 24-methyl group in the configuration that is 24*R* if no other changes are made

the 22*E*,24*R* configuration shown in (7) unless otherwise specified. Ergocalciferol may still be used as an alternative trivial name for ercalciol but should not be used for naming metabolites.



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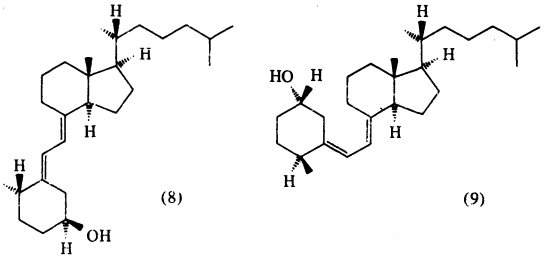
Note. Because of the nature of the sequence rules it is not possible to transfer *R* or *S* from one compound to its derivatives. Examples of the effect of this are shown in Fig. 2.

7. DIHYDRO DERIVATIVES

Dihydrotachysterol is an important member of the vitamin D family. It should be called dihydrocalciol, although a more systematic name would be (5*E*)-(10*S*)-10,19-dihydrocalciol [(8) which is the same as (9)].



(5*E*)-(10*S*)-10,19-Dihydrocalciol

Note 1. Although this compound is derived from calciol by hydrogenation of the 10(19) double bond it may also be considered as a derivative of tacalciol formed by 1,6-addition of hydrogen to the 5(10),6,8-triene system, i.e. positions 9 and 10.

Note 2. A new chiral centre is present at position 10. If a synthetic sample contains a mixture of both isomers, not necessarily in equimolar proportions, the affix *ambo* may be used [8] to indicate the presence of such a mixture, e.g. (5*E*)-10-*ambo*-10,19-dihydrocalciol. If only one isomer is present, but with unknown stereochemistry, then this may be indicated by the use of *xi*, e.g. (5*E*)-(10ξ)-10,19-dihydrocalciol. When the absolute stereochemistry at C-10 is known this is shown in the normal way, e.g. (5*E*)-(10*S*)-10,19-dihydrocalciol.

8. OTHER MODIFICATIONS

Other modifications of the parent compound may be named by the appropriate prefix as outlined in the IUPAC Nomenclature of Organic Chemistry, Section F [9]. Table 3 indicates possible modifications.

If there is a change of configuration from that implied by the stem and its suffix (see sections 3 and 10a), and by any of the prefixes listed in Table 2, then this is stated by means of the appropriate locant and affix (*R* or *S* at positions 1, 3, 20

Table 3. *Prefixes for modifying a parent compound*
Further details for the application of these prefixes may be found in the appropriate section of the F-rules [9] as indicated in column 3

Prefix	Effect	Rule
cyclo	an additional ring	F-4.1
didehydro	an additional double bond	F-3.3
homo	an additional methylene group	F-4.5
dihydro	reduction of a double bond	F-3.1, see section 7 above
nor	loss of a methylene group	F-4.2, F-4.4
aza	replacement of carbon by nitrogen	F-4.11
oxa	replacement of carbon by oxygen	F-4.11

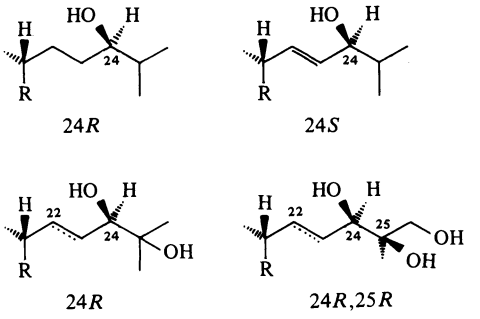


Fig. 3. *Examples of stereochemistry at position 24 (and 25) in the vitamin D_3 series.* Note that the presence or absence of a 22(23) double bond in the last two examples does not change the designation at position 24 (or 25)

or 24; *E* or *Z* at positions 5, 6, 7 or 22; and α or β at 13, 14 or 17). Further details of these modifications are given in Rule F-6.3 [9] and Steroid Rules 2S-5.2 and 2S-5.4 [4]; the use of the prefixes '*ent*-' and '*rac*-' is also given in these references (F-6.4, F-6.5, F-6.6; 2S-5.1, 2S-5.3 and 2S-5.4). Examples: *D*-homocalciol, 24-azaercalciol, (3*R*)-calciol, and (22*Z*)-ercalciol.

9. COMBINATION OF PREFIXES

Modifying prefixes may be combined and are cited in the order (a) stereochemistry of double bonds requiring *E* or *Z*, (b) stereochemistry at chiral centres requiring *R* or *S*, (c) detachable prefixes (see sections 10a and 11b below), (d) modifying prefixes in the order given in Table 3, (e) changes in configuration at positions 13, 14 or 17, and (f) modifying prefixes given in Table 2 in alphabetical order.

Example: (24*S*)-24-hydroxy-22,23-didehydrotacalciol (cf. second example in Fig. 3).

10. ADDITIONAL HYDROXYL GROUPS

a) *Designated by a Suffix*

The name calcidiol is reserved for the 3,25-diol, calcitriol for the 1,3,25-triol, and calcitetrol for the 1,3,24,25-tetrol. The configuration of the hydroxyl group(s) corresponds to the 3β-hydroxy or 1α,3β-dihydroxy tetracyclic steroid (see Fig. 1) or 24*R*-hydroxy group.

b) *Designated by a Prefix*

Any hydroxyl groups not included in the suffixes (see rules 3 and 10a) shall be designated by the prefix hydroxy, dihydroxy etc. together with the appropriate locant and where necessary indicating the stereochemistry of this substituent. Examples: (1*S*)-1-hydroxycalciol, 16β-hydroxycalciol, and 26-hydroxycalciol [or if the full stereochemistry is known, (25*R*)-26- or (25*S*)-26-hydroxycalciol].

Note. Because of the nature of the sequence rules it is not possible to transfer *R* or *S* from one compound to its derivatives. Examples of the effects of this are shown in Fig. 2 and Fig. 3.

11. OTHER SUBSTITUENTS

a) *Modification of the Suffix*

Esters of the hydroxyl groups cited by a suffix (rules 3 and 10a) are given by the acyloxy group(s) in its anionic form, with locants when necessary (see Steroid rule 2S-4.1 [4]).

The ketone corresponding to calciol may be called *calcione*, but this name is restricted to the 3-ketone. Oxidation of calcidiol will give a hydroxy ketone, which should be named 25-hydroxycalcione. Examples: calciol acetate, and calcitriol 1-acetate 3-formate.

Note. If a methyl group of a vitamin D compound is oxidized to a carboxyl group (or derivative), the compound needs to be named using the appropriate suffix. The name calciol is not suitable for this, because its suffix indicates the oxygen function at C-3; we therefore recommend that carboxylic acids should be named as 9,10-secocholestane or 9,10-secoergostane derivatives. Example: (5*Z*,7*E*)-(3*S*,23*R*,-25*S*)-3β,25-dihydroxy-9,10-seco-5,7,10(19)-cholestatrieno-26,23-lactone.

b) *Designated by a Prefix*

Substituents not cited by the parent compound and suffixes (sections 3, 10a and 11a) should be designated by a prefix together with the appropriate locant, indicating, where necessary, the stereochemistry with an affix. Vitamin D analogues where the hydroxyl group at C-3 is absent or is replaced by an amino group are named by the use of the prefix 3-deoxy (see Carbohydrate Rule 14 [10]). Examples: 25-fluorocalciol, (3*S*)-3-amino-3-deoxycalciol, and 11α-acetoxycalciol.

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Appendix. *Trivial names of vitamin D compounds*

Recommended name	Current trivial name	Other names
Calciol or cholecalciferol	cholecalciferol	vitamin D_3, colecalciferol[a]
Ercalciol or ergocalciferol	ergocalciferol[a]	vitamin D_2, calciferol
Calcidiol	25-hydroxycholecalciferol	calcifediol[a]
(1*S*)-Hydroxycalciol	1α-hydroxycholecalciferol	alfacalcidol[a]
(24*R*)-Hydroxycalcidiol	24(*R*),25-dihydroxycholecalciferol	
Calcitriol[a]	1,25-dihydroxycholecalciferol	
Calcitetrol	1,24(*R*),25-trihydroxycholecalciferol	
25-Fluorocalciol	25-fluorocholecalciferol	
Ercalcidiol	25-hydroxyergocalciferol	
Ercalcitriol	1,25-dihydroxyergocalciferol	
Ertacalciol	tachysterol$_2$	
Tacalciol	tachysterol$_3$	
(5*E*)-Isocalciol	isovitamin D_3	
22,23-Dihydroercalciol or (24*S*)-methylcalciol	vitamin D_4	
(5*E*)-(10*S*)-10,19-Dihydroercalciol	dihydrotachysterol$_2$	hytakerol, dihydrotachysterol[a]
(6*Z*)-Tacalciol	precalciferol	previtamin D
(24*S*)-Ethylcalciol	vitamin D_5	
(22*E*)-(24*R*)-Ethyl-22,23-didehydrocalciol	vitamin D_6	

[a] WHO-approved nonproprietary name.