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Prostaglandin Nomenclature

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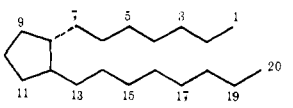
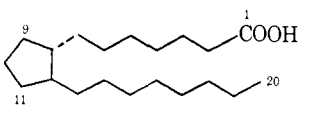
This prostaglandin nomenclature article emphasizes name derivations by semisystematic methods which are especially useful for rapid communication in the written and oral language. Currently used stem names are reviewed and special attention is given to problems of describing stereochemical configuration, homologs, nor compounds, and certain complex analogs.

Under ideal circumstances, a prostaglandin nomenclature system should permit names which (1) are communicable, (2) relate to prostaglandins, (3) allow convenient indexing and retrieval of information, (4) allow easy visualization of structures, and (5) allow scientists of different disciplines to arrive at unambiguous structure–biological activity relationships. In actual circumstances, it is quite difficult to achieve all these objectives for a compound using a single name. Names of compounds which are satisfactory and proper for indexing purposes may be unsatisfactory for rapid communication and quite possibly misleading to all but nomenclature experts when dealing with structure–biological activity studies. For reasons such as these, alternative systems of nomenclature usually emerge to fill the needs of a particular group.

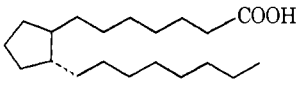
Current prostaglandin nomenclature used by *Chemical Abstracts* employs prostane (**1**)[1] and prostanoic acid (**2**)[2] (indirectly) as stereoparents or index heading parents. These names imply the absolute configuration and numbering system shown and prostaglandin-type compounds are then named as derivatives of prostane utilizing rules of terpene and steroid nomenclature[3] (for examples, see the last names listed for structures **12–19**). As to whether *ent*-prostanoic acid (**3**)[1] will be adopted as a stereoparent is not yet known.



1, prostane



2, prostanoic acid



3, *ent*-prostanoic acid

The *Chemical Abstracts* system for prostaglandin nomenclature is entirely satisfactory for indexing and information retrieval and is to be strongly recommended for most written work, especially of a chemical nature. Their system suffers a serious disadvantage in that the resulting names are often too cumbersome for oral communication. A need exists, therefore, for a semisystematic prostaglandin nomenclature, and such a system has emerged in recent years. It is not the purpose of this article to defend the semisystematic nomenclature, but rather to identify it and record some of its scope and limitations. What has occurred, basically, is that workers in the field have adopted a series of stereoparents or stem names, based on early developments in the field,[4] and have then applied general rules of nomenclature[5] (not always correctly) to arrive at names for prostaglandin analogs, derivatives, and metabolites. As with many semisystematic methods of nomenclature, the resulting names are not always perfect but serve the extremely important purpose of rapid communication.

This article will summarize the currently used stem names and how they can be modified to describe related compounds. Special attention will be given to problems of describing stereochemical configuration, homologs, nor compounds, and certain complex analogs. For organizational purposes, various aspects of prostaglandin nomenclature are itemized below. These items represent a tentative guide to prostaglandin nomenclature and should not be regarded as official rules of nomenclature.

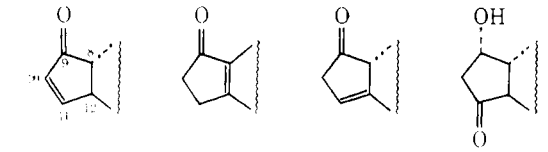
Items of Prostaglandin Nomenclature

1. Stem Names of Prostaglandins. Naturally occurring prostaglandins may be regarded as derivatives of prostanoic acid (**2**) in which the five-membered ring is substituted in a variety of ways; in which double bonds may occur in the cis-5, trans-13, or cis-17 arrangements; and in which an L-hydroxy group is attached to C-15 (except for PGG's). Prostaglandins have been divided into A,[4] B,[4] C,[6] D,[7] E,[4] F,[4] G,[8] H,[8] and R[9] families. These families differ from each other in the functionality of the five-membered ring as illustrated in partial structures **4–11**. Prostaglandins in the F family are subdivided (identified by the addition of the appropriate Greek letter subscript in the name) to distinguish configuration of the hydroxyl group at position 9. Prostaglandins of the G, H, and R families have the same substituted five-membered ring; PGH's (Karolinska Institute) and PGR's (Unilever Research Laboratories) are identical while PGG's differ from other

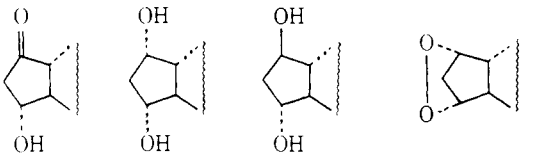
prostaglandins by the attachment of a 15L-hydroperoxy group instead of the usual 15L-hydroxy group.

The author and reviewers of this article recommend use of PGH in place of PGR for prostaglandins of partial structure **11** (the PGR abbreviation presumably arose from the mistaken belief that prostaglandin endoperoxides are rabbit aorta contracting substance). Prostaglandins of the PGG family may also be named as 15-deoxy-15-hydroperoxy-PGH's (see item 11).

Each family is further subdivided and identified by a numeric subscript according to the number of specifically located double bonds in the side chains (see examples **12–19**). A PG_1 compound has a trans-13 double bond, a PG_2 compound has cis-5 and trans-13 double bonds, while a PG_3 compound has cis-5, trans-13, and cis-17 double bonds (this statement refers to parent prostaglandins before alterations in structure; a PG_2 compound must have a double bond at C-5 while a PG_3 compound must have a double bond at C-17 to be named as such). Currently used stem names and their abbreviations for the more common prostaglandins are given in Table I (however, see item 20F).



4. PGA 5. PGB 6. PGC 7. PGD

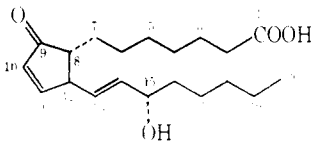


8. PGE 9. PGF_α 10. PGF_β 11. PGG or PGH or PGR (see text)

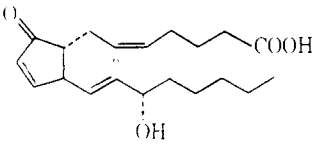
Structures and stem names for some representative prostaglandins are given in examples **12–19** along with their current *Chemical Abstracts* systematic names for comparison purposes. The structures, as written, correspond to the absolute configuration of prostaglandins from mammalian sources. The advantage of committing the stem names and corresponding structures of prostaglandins in this section to memory is that a wealth of structural and stereochemical detail is understood instantly. Structures of countless analogs, isomers, and derivatives can then be visualized quickly by use of names derived by existing methods of nomenclature.[5]

The lettered abbreviations for prostaglandins (*e.g.*, PGA_1, but see item 20F) are used almost exclusively in the spoken language, and often in written communications, after they have been defined as prostaglandins. The longer names (*e.g.*, prostaglandin A_1) are esthetically more pleasing and are less likely to be confused with other acronyms [for example, PGA is a common abbreviation for pteroylglutamic acid (folic acid) in the biochemical research literature].

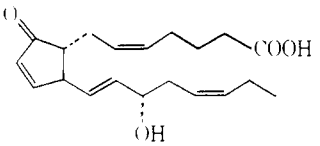
2. Structural Presentation of Prostaglandins. The structures of prostaglandins should be presented in a consistent format with the carboxy side chain extending to the upper right side and the terminal alkyl side chain extending to the lower right side of the five-membered ring as shown in examples **12–19**. The stereochemical configuration at a chiral (asymmetric) center, if known, should be indicated in one of the accepted ways such as a solid, heavy solid, or appropriate wedge-shaped line to indicate that a particular substituent is above the overall plane of the molecule or a dotted, broken, or appropriate wedge-shaped line for a substituent which is below the overall plane of the molecule. If the configuration of a substituent at a chiral center is unknown or is a mixture of two configurations, the situation can be indicated in the structure



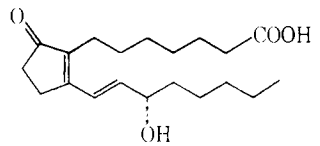
12. prostaglandin A_1 or PGA_1 or (13*E*,15*S*)-15-hydroxy-9-oxoprosta-10,13-dien-1-oic acid



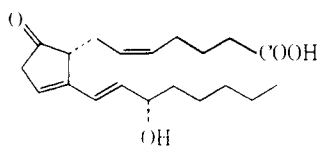
13. prostaglandin A_2 or PGA_2 or (5*Z*,13*E*,15*S*)-15-hydroxy-9-oxoprosta-5,10,13-trien-1-oic acid



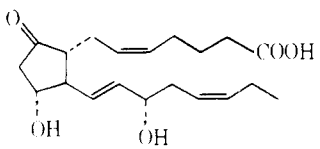
14. prostaglandin A_3 or PGA_3 or (5*Z*,13*E*,15*S*,17*Z*)-15-hydroxy-9-oxoprosta-5,10,13,17-tetraen-1-oic acid



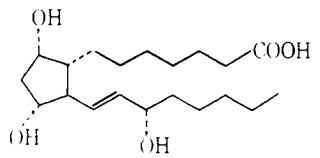
15. prostaglandin B_1 or PGB_1 or (13*E*,15*S*)-15-hydroxy-9-oxoprosta-8(12),13-dien-1-oic acid



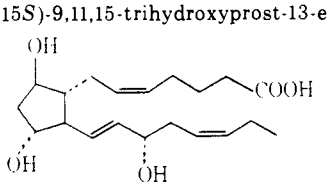
16. prostaglandin C_2 or PGC_2 or (5*Z*,13*E*,15*S*)-15-hydroxy-9-oxoprosta-5,11,13-trien-1-oic acid



17. prostaglandin E_3 or PGE_3 or (5*Z*,11α,13*E*,15*S*,17*Z*)-11,15-dihydroxy-9-oxoprosta-5,13,17-trien-1-oic acid



18. prostaglandin $F_{1\alpha}$ or $PGF_{1\alpha}$ or (9α,11α,13*E*,15*S*)-9,11,15-trihydroxyprost-13-en-1-oic acid



19. prostaglandin $F_{3\beta}$ or $PGF_{3\beta}$ or (5*Z*,9β,11α,13*E*,15*S*,17*Z*)-9,11,15-trihydroxyprosta-5,13,17-trien-1-oic acid

Table I. Stem Names and Abbreviations[a] of the More Common Prostaglandins

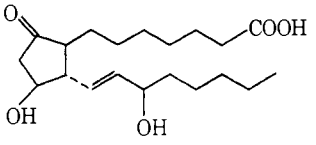
Prostaglandin A_1 or PGA_1	Prostaglandin D_1 or PGD_1
Prostaglandin A_2 or PGA_2	Prostaglandin D_2 or PGD_2
Prostaglandin A_3 or PGA_3	Prostaglandin D_3 or PGD_3
Prostaglandin B_1 or PGB_1	Prostaglandin E_1 or PGE_1
Prostaglandin B_2 or PGB_2	Prostaglandin E_2 or PGE_2
Prostaglandin B_3 or PGB_3	Prostaglandin E_3 or PGE_3
Prostaglandin C_1 or PGC_1	Prostaglandin $F_{1\alpha}$ or $PGF_{1\alpha}$
Prostaglandin C_2 or PGC_2	Prostaglandin $F_{2\alpha}$ or $PGF_{2\alpha}$
Prostaglandin C_3 or PGC_3	Prostaglandin $F_{3\alpha}$ or $PGF_{3\alpha}$
	Prostaglandin $F_{1\beta}$ or $PGF_{1\beta}$
	Prostaglandin $F_{2\beta}$ or $PGF_{2\beta}$
	Prostaglandin $F_{3\beta}$ or $PGF_{3\beta}$

[a]Currently used abbreviations, but see item 20F.

with a wavy line [further clarification as to whether the configuration is unknown or a mixture can be presented in the text of an article or in the assigned name of the substance (see items 20A and B below)].

If a substance is racemic, only one structure need be written; however, attention should be drawn to this fact near the structure, in the text, or in a footnote of the article as well as in the name of the substance. A racemic compound is usually referred to with a prefix of (±), *dl*, or *rac* in the name of the compound.

If all the chiral centers of a natural prostaglandin are reversed, the substance is an enantiomer, and this situation should be reflected in the name of the substance with the prefix *ent* or the appropriate sign of rotation in parentheses. The structure of the enantiomeric substance should be written following the format described at the beginning of item 2; see example **20**.[10] This structure should not be written with the side chains to the left or with the carboxy side chain to the lower right, because this can lead to confusion in assigning configuration to groups using the α,β system described in item 3.

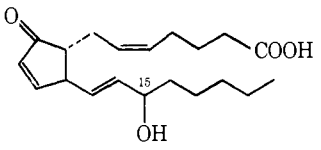


20, *ent*-prostaglandin E_1

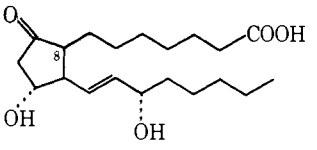
3. Denoting Stereochemical Configuration of Substituents. This section will describe four systems for expressing configuration in written or spoken language. The first three systems are used frequently for special situations while the fourth system is suggested for use in discussions of structure–biological activities.

A. Epi and Iso System. In compounds containing more than one chiral center, a numbered-*epi* prefix denotes an inversion of the normal configuration of a particular substituent (usually hydroxyl) at the numbered position; see example **21**.[10b,11] Similarly, a numbered-*iso* prefix denotes inversion of the normal chirality at the numbered center; in this instance, the substituent is usually one of the side chains; see example **22**.[12] The so-called *epi, iso* system for denoting configuration has been used widely and allows the visualization of new structures quickly. However, this system requires standard structures (*e.g.*, **12–19**) for comparison and is useless for denoting configuration at new chiral centers (*e.g.*, position 19 of structure **24**).

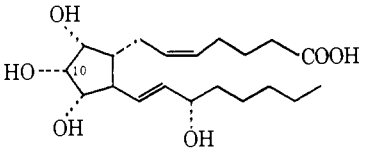
B. Alpha (α) and Beta (β) System. In describing a chiral center, the prefix α means that the substituent in question lies below the plane of the molecule *as drawn*, and the prefix β means that the substituent lies above the plane of the molecule; see example **23**.[13] For this system to be unambiguous, the structures of the parent prostaglandins must be drawn in a consistent format (see item 2). The chief disadvantage of the α,β system is that certain structural changes in flexible side chains (cis to trans isomerization or *vice versa*, saturation of double bonds, introduction of acetylenic or allenic groups or ring systems) can lead to confusion in how to draw the structures and, therefore, can result in ambiguity in assigning stereochemical configuration by this system. *It is suggested, therefore, that the α,β system be restricted to substituents attached to the five-membered ring.*



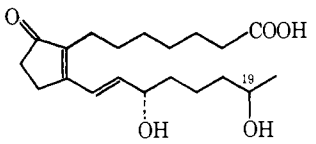
21, 15-*epi*-prostaglandin A_2 or (15*R*)-prostaglandin A_2



22, 8-*iso*-prostaglandin E_1



23, 10α-hydroxyprostaglandin $F_{2\alpha}$

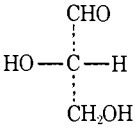


24, (19*R*)-19-hydroxyprostaglandin B_1

C. *R* and *S* System. Perhaps the most used and least ambiguous system of denoting the absolute configuration of a chiral center involves use of the sequence rules of the Cahn–Ingold–Prelog system.[5b,14] This system is normally employed to describe chiral centers on the side chains of prostaglandins, especially for indexing purposes; see example **24**.[15]

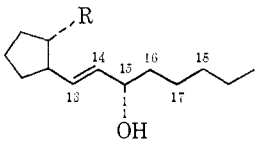
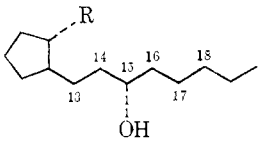
Unfortunately, this highly refined system of denoting configuration has certain disadvantages. Remembering the sequence rules and applying them quickly for the visualization of structures from names require frequent practice and mental agility. Therefore, this system is somewhat weak, especially for the spoken language. A more serious criticism of the system is the fact that minor structural changes adjacent to, or even remote to, a chiral center may result in reversal (because of the arbitrary definitions of the sequence rules) of the *R* and *S* configuration of the center (see examples in Table II). This can lead to great confusion in interpreting changes in biological activity with assigned changes in configuration at a chiral center. Therefore, *in describing structure–activity data*, it is suggested that chiral centers be referred to by some system (see items 3A and 3D) other than *R* or *S*.

D. D and L System. Asymmetric or chiral centers in prostaglandins can be assigned absolute configuration by relating them to D- or L-glyceraldehyde using the standard Fischer convention.[4c] Thus, all of the compounds represented in Table II have the L configuration. Since this sys-



L-glyceraldehyde

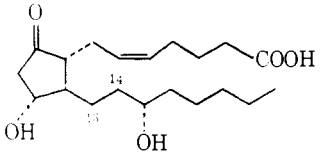
Table II. Effect of Structural Changes on Configurational Assignments at C-15 of Prostaglandins

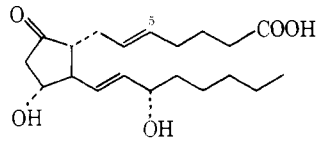
C-15 configuration	Structural change	C-15 configuration
15*S*	None	15*S*
15*S*	15-Methyl	15*S*
15*S*	16-Methyl	15*R*
15*R*	16,16-Dimethyl	15*R*
15*S*	17,17-Dimethyl	15*R*
15*R*	16-Fluoro	15*R*
15*S*	17,18-Didehydro (PG_3)	15*R*
15*S*	16-Deuterio	15*R*
15*R*	17-Oxa	15*R*
15*S*	17-Phenyl-18,19,20-trinor	15*R*

tem is insensitive to nearby structural changes and also to how a structural formula is presented, the system may have considerable merit especially in communicating structure–biological activity work.

4. Saturation of Carbon–Carbon Double Bonds. To denote reduced carbon–carbon double bonds, a numbered prefix (*e.g.*, 13,14-dihydro) may be used; see example **25.**[16] Products corresponding to reduction of the 10,11 double bond of prostaglandin A compounds are normally referred to as 11-deoxyprostaglandin E's (see item 10).



25. 13,14-dihydroprostaglandin E_2

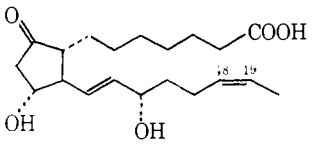


26. *trans*-5-prostaglandin E_2

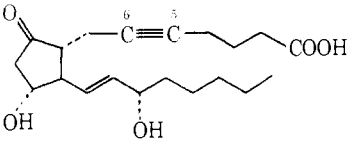
5. Denoting Unsaturation. A. To denote a change in cis–trans isomerism in a parent, a prefix followed by its locant (*e.g.*, *trans*-5, *cis*-13, or *trans*-17) may be used; see example **26.**[17] The more refined system of using the letters *Z* (for cis) and *E* (for trans) may also be used.[18]

B. For new unsaturation, a numbered prefix giving its location and configuration, if pertinent (*e.g.*, 18,19-*cis*-didehydro, 5,6-didehydro, *trans,trans*-$\Delta^{2,4}$, etc.), may be used; see examples **27**[19] and **28.**[20] Compound **28** might also be called (±)-5,5,6,6-tetradehydroprostaglandin E_1; however, this name requires a greater number of changes than the name based on prostaglandin E_2 and, therefore, is less preferable. Note use of the prefix didehydro rather than dehydro or bisdehydro. The prefix dehydro finds use in describing the conversion of an alcohol to an oxo group (see item 6). The prefix bisdehydro represents incorrect use of "bis" and is ambiguous in that with different people it may mean the introduction of one or two double bonds.

6. Introduction of Carbonyl Groups. A. To denote replacement of a methylene group with a carbonyl group, the appropriate numbered-oxo prefix (*e.g.*, 18-oxo) may be used; see example **29.**[21] Many scientists prefer the prefix



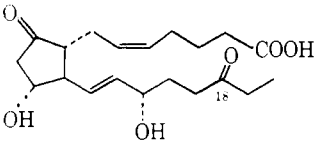
27. 18,19-*cis*-didehydroprostaglandin E_1



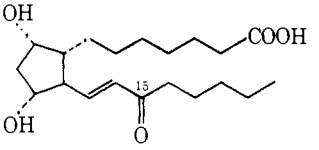
28. (±)-5,6-didehydroprostaglandin E_2

keto instead of oxo; however, the latter prefix is recommended in *IUPAC* and *Chemical Abstracts* nomenclature.

B. To denote a carbonyl group derived from oxidation of an alcohol function, a numbered-dehydro prefix (*e.g.*, 15-dehydro) may be used; see example **30.**[22]

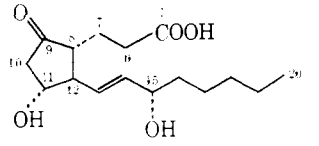


29. 18-oxoprostaglandin E_2

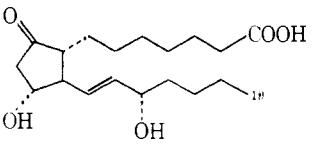


30. 15-dehydroprostaglandin $F_{1\alpha}$

7. Shortening the Side Chains. A methylene group or groups missing from a parent prostaglandin can be identified by a locant or locants and the appropriate prefix nor, dinor, trinor, tetranor, etc. (*e.g.*, 2-nor, 2,3,20-trinor); see examples **31**[23] and **32.**[24] An advantage of this method is that the parent numbering system of the prostaglandin is retained, which simplifies communication especially in structure–biological activity reports. As a limitation to this system, it is suggested that if more than six methylene groups are missing, the substance be named by systematic methods.

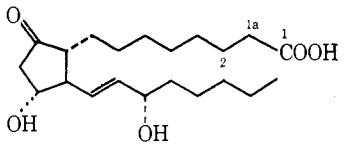


31. 2,3,4,5-tetranorprostaglandin E_1

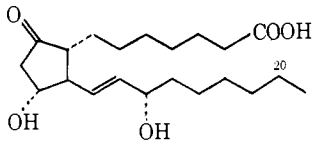


32. 20-norprostaglandin E_1

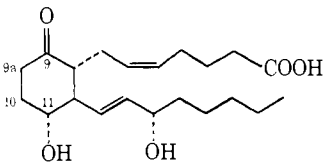
8. Lengthening the Side Chains. A methylene group or groups added to a parent prostaglandin in the carboxy side chain should be identified by a locant or locants and the appropriate prefix homo, dihomo, trihomo, tetrahomo, etc. It is tentatively suggested that new methylene groups be listed as 1a-homo, 1a,1b-dihomo, 1a,1b,1c-trihomo, 1a,1b,1c,1d-tetrahomo, etc., so as to avoid altering the parent numbering system of prostaglandins. Lengthening



33, 1a-homoprostaglandin E_1



34, 20-methylprostaglandin E_1

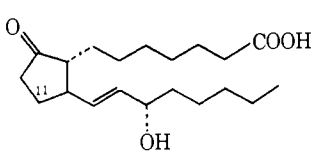


35, 9a-homoprostaglandin E_2

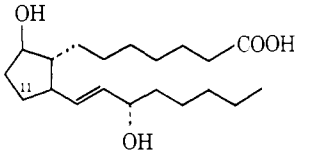
the alkyl side chain is handled most easily by indicating the group added to C-20. Examples **33**[25] and **34**[24] illustrate the methods.

9. Changing the Size of the Ring. A decrease in the size of the five-membered ring may be indicated with a numbered-nor prefix while an increase in the size of the ring may be indicated with a numbered-homo prefix (*e.g.*, 9a-homo); see example **35**.[26] The numbers preceding the prefixes nor and homo should be chosen so as to avoid assigning new numbers to the functionalized 9 and 11 positions of PGE and PGF compounds.

10. Deoxygenated Prostaglandins. Replacement of a hydroxyl group with hydrogen may be designated with a numbered-deoxy (not desoxy) prefix; see examples **36**[27] and **37**.[28]

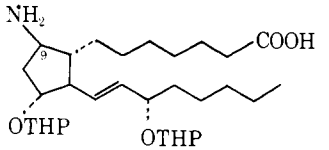


36, 11-deoxyprostaglandin E_1

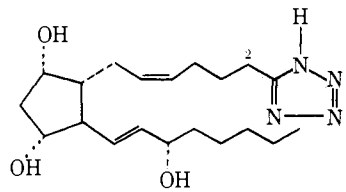


37, 11-deoxyprostaglandin $F_{1\beta}$

If compound **36** had been prepared by selective hydrogenation of PGA_1 (**12**), a logical and easily understood name for the product would be 10,11-dihydroprostaglandin A_1. However, we are suggesting that such compounds be named 11-deoxyprostaglandins, since this system of nomenclature can be extended to 11-deoxy-PGF compounds as well as other prostaglandins where a hydroxyl group is replaced by hydrogen.



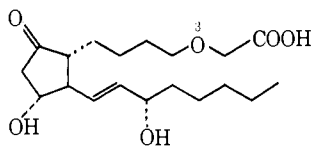
38, 9β-amino-9-deoxyprostaglandin F_1 bis(tetrahydropyran-2-yl ether)



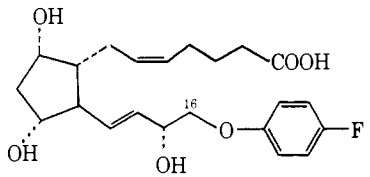
39, 2-decarboxy-2-(1*H*-tetrazol-5-yl)prostaglandin $F_{2\alpha}$

11. Replacement of Functional Groups with Other Functional Groups. When a functional group such as a hydroxyl or carboxyl group is replaced by a new functional group, the new substance may be named by substracting the removed group and adding the new group with appropriate numbers and prefixes; see examples **38**[29] and **39**.[30]

12. Hetero Prostaglandins. Replacement of a methylene group with a hetero radical or group may be designated with a numbered prefix (oxa for replacement with -O-, thia for replacement with -S-, aza for replacement with -NH-); see example **40**.[31]



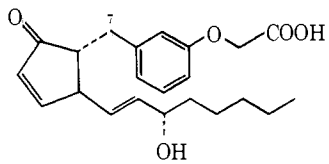
40, (±)-3-oxaprostaglandin E_1



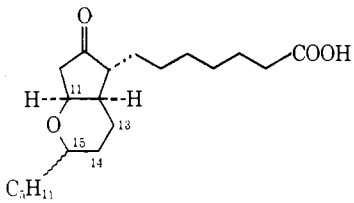
41, 16-(4-fluorophenoxy)-17,18,19,20-tetranorprostaglaglandin $F_{2\alpha}$

13. Modifications of the Alkyl Side Chain. Most modifications in the alkyl side chain can be described by standard substitutive nomenclature. Example **41**[32] is given to illustrate the additional need to report missing methylene groups.

14. Introduction of Complex Radicals into the Carboxy Side Chain. The naming of analogs which have a complex radical inserted into the carboxy side chain may result in rather complex names when using existing rules. We suggest the following method for naming such analogs. Any methylene groups missing from or added to the carboxy side chain are indicated with a numbered prefix (see items 7 and 8). The atoms to which the inserted radical are attached are numbered and are followed by an expression describing the inserted radical (*inter*-name of radical); see example **42**.†



42, (±)-4,5,6-trinor-3,7-*inter*-*m*-phenylene-3-oxaprostaglandin A_1



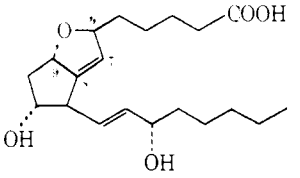
43, 11,15-anhydro-13,14-dihydro-11-*epi*-15ζ-prostaglandin E_1

15. Intramolecular Oxygen-Bridged Prostaglandins. A. Anhydro nomenclature may be applied to cyclic ethers derived from the corresponding dihydroxy compounds; see example **43**.[33]

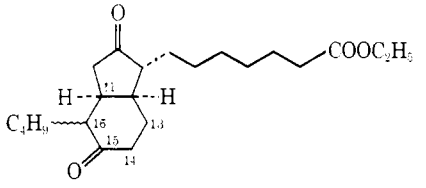
† N. A. Nelson, unpublished results.

B. Epoxy nomenclature may be applied to situations where two carbon atoms are bridged with oxygen to form a cyclic ether. When one of the carbon atoms is substituted with a hydroxyl which becomes involved in the cyclic ether formation, subtractive-additive nomenclature is necessary to define the product; see example **44.**[34]

16. Carbon-Bridged Prostaglandins. Prostaglandin analogs in which carbon atoms are connected to form a new ring system may be named by a numbered-cyclo prefix where the numbers correspond to the carbon atoms being connected; see example **45.**[35]

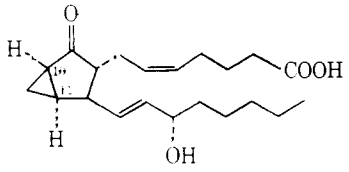


44. 7,8-didehydro-9-deoxy-6,9α-epoxyprostaglandin $F_{1\alpha}$

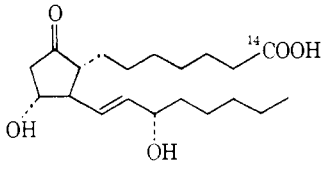


45. 11-deoxy-13,14-dihydro-15-dehydro-11β,16ζ-cycloprostaglandin E_1 ethyl ester

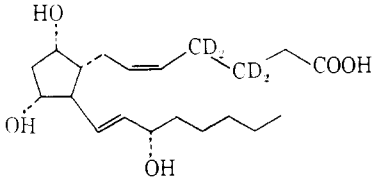
17. Prostaglandins with Fused Ring Systems. In cases where the new group attached can be easily identified (*e.g.*, methylene, ethylene), a simplified nomenclature may be used as illustrated in the first name of example **46.**[36] For more complex ring systems, it may be necessary to employ the systematic nomenclature for fused ring steroid names[5c] as illustrated in the second name of example **46.**



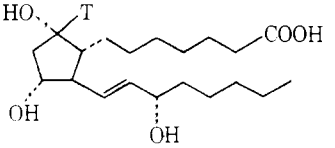
46. 11-deoxy-10β,11β-methyleneprostaglandin E_2 or 10α,11α-dihydro-2'*H*-cyclopropa[10,11]prostaglandin A_2



47. prostaglandin E_1-*1-*^{14}*C*



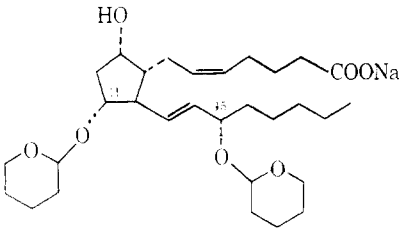
48. prostaglandin $F_{2\alpha}$-*3,3,4,4-*d_4



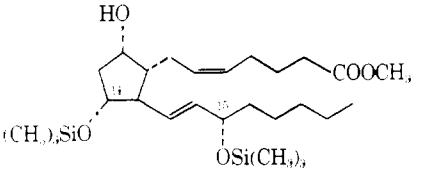
49. prostaglandin $F_{1\alpha}$-*9-t*

18. Isotopically Labeled Prostaglandins. The nomenclature for isotopically labeled prostaglandins is illustrated with examples **47,**[37] **48,**[38] and **49.**[39] The names given are based on current practices of *Chemical Abstracts.*[3] Editorial policy of some journals may favor the following equally satisfactory names: [1-^{14}C]prostaglandin E_1 [3,3,4,4-$^2H_4$]prostaglandin $F_{2\alpha}$, and [9β-^{3}H]prostaglandin $F_{1\alpha}$ for **47, 48,** and **49,** respectively.

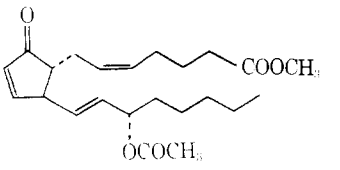
19. Prostaglandin Derivatives. Simple derivatives of prostaglandins, in some cases, have included combinations, such as (a) salts, esters, and amines, (b) derivatives of hydroxyl groups such as esters and ethers, (c) derivatives of oxo groups such as oximes, methoximes, semicarbazones, and substituted hydrazones, and (d) derivatives of double bonds such as oxides. Such derivatives should be listed alphabetically after the prostaglandin name proper, using numbers, if necessary, to avoid confusion as to the exact location of the derivative(s). It should be recalled that the prefixes di, tri, and tetra are used to denote two, three, or four (respectively) simple, but identical groups; these prefixes do not take alphabetical precedence over the groups they modify. The prefixes bis, tris, and tetrakis are used to denote two, three, or four (respectively) complex, but identical groups; again, these prefixes do not take alphabetical procedence over the groups they modify. Examples of prostaglandin derivatives are **50,**[40] **51,**[41] **52,**[42] and **53.**[43]



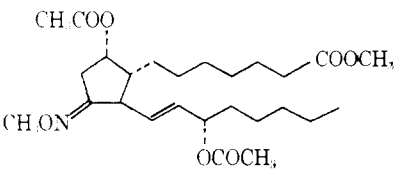
50. prostaglandin $F_{2\alpha}$ 11,15-bis(tetrahydropyran-2-yl ether) sodium salt



51. prostaglandin $F_{2\alpha}$ methyl ester 11,15-bis(trimethylsilyl ether)



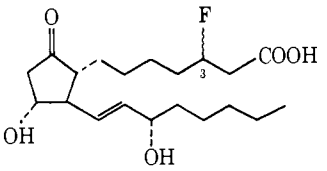
52. prostaglandin A_2 acetate methyl ester



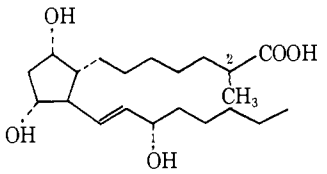
53. prostaglandin D_1 diacetate methoxime methyl ester

20. Other Nomenclature Considerations. A. Substituents of Unknown Configuration. If the configuration at a chiral center in an epimerically pure substance is unknown, an appropriate prefix in the name should indicate this; see example **54.**[44]

B. Epimeric Mixtures. If the configuration at a chiral



54, (3*R* or *S*)-3-fluoroprostaglandin E_1 or 3ζ-fluoroprostaglandin E_1

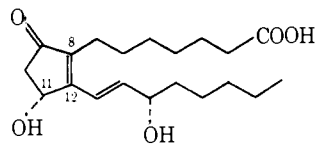


55, (2*RS*)-2-methylprostaglandin $F_{1\alpha}$

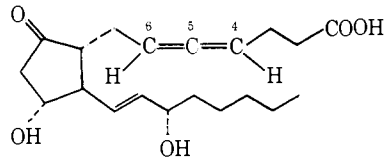
center represents two epimers, an appropriate prefix in the name should indicate this; see example **55**.[45]

C. Multiple Inversions of Chiral Centers. Compounds in which all chiral centers of a parent prostaglandin are inverted are referred to as *ent*-prostaglandins; see example **20**. Some workers in the field refer to *ent*-prostaglandins as those prostaglandins in which both side chains are inverted from the normal configuration (any other noninverted chiral centers are then identified in some appropriate way). As long as prostaglandin structures are pictured in the format outlined in item 2, no ambiguities should result.

D. Priority Considerations. Application of semisystematic nomenclature often results in two or more names for a substance; see items 4b and 10 and examples **56**[46] and **57**.[47] In the absence of priority recommendations from nomenclature committees, the use of multiple names is, perhaps, permissible for the spoken and written language, as long as the names fulfill most of the requirements of good nomenclature described at the outset of this article.



56, 11α-hydroxyprostaglandin B_1 or 8,12-didehydroprostaglandin E_1



57, 4,5-didehydroprostaglandin E_2 or 4,5,5,6-tetradehydroprostaglandin E_1

E. Structure-Modifying Prefixes. If there is more than one structure-modifying prefix needed (*e.g.*, aza, homo, nor, oxa, thia), it is suggested that the prefixes be listed alphabetically directly in front of prostaglandin (or PG) in the name of the compound. Ordinary substituents (*e.g.*, dihydro, hydroxy, fluoro, methyl, oxo) should be listed alphabetically before the structure-modifying prefixes.

F. Future Considerations. It has come to the attention of the author that the currently used abbreviations for prostaglandins do not conform to proper practices of biochemical nomenclature.‡ A proper chemical abbreviation should begin with a capital letter and continue with lower case letters. The choice of letters would, hopefully, evoke the name of the material. Thus, prostaglandin might be abbreviated Prs rather than PG, and abbreviations such as PGA_1 would become $PrsA_1$ [another abbreviation for prostaglandin might be Pgn; however, Prs (pronounced pros, as in prostaglandin) is easier to handle in oral communications and would apply to the term prostanoid,[48] should this term come into wide use].

The word prostaglandin was conceived at a time when it was believed that the material was unique to prostate glands. With the development of sensitive analytical techniques and additional research, the truly ubiquitous occurrence of prostaglandins has been revealed.[4a] The recent suggestion[48] to employ the term prostanoids (*cf.* steroids) to designate compounds within the prostaglandin family has already received some acceptance.[49]

Finally, it is the opinion of this author that the semisystematic method for prostaglandin nomenclature may become unwieldy if the proliferation of stem names (item 1) continues. Even now, some of the existing stem names could be consolidated; however, such action is best left to the anonymity of committee action.

Acknowledgments. The author is indebted to Robert C. Anderson, John C. Babcock, and Earl C. Spaeth for helpful advice, to Laura VanVlack and A. Vern McIntosh who supplied a number of references, and to the many scientists and nomenclature experts who responded to an earlier unpublished draft of this article.

‡ W. E. Cohn, Secretary, IUPAC-IUB Commission on Biochemical Nomenclature, private communication.

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Chemoimmunotherapy of Cancer. 1†

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The use of a multiple-component system for the selective destruction of neoplastic cells is considered with emphasis on chemoimmunotherapy. The synthesis of potential tumor-tagging compounds is described against which antibodies can be prepared. The rationale is presented for the design and preparation of such compounds and the chemical features that are necessary.

The rationale for using a multiple-component system for the selective destruction of cancer cells is founded on the premise that each agent of this system must be relatively innocuous but their interaction at the tumor cell level produces a cytotoxic reaction. This approach is the basis for the attempts to destroy neoplasms by neutron capture irradiation using ^{10}B and other neutron absorbers.[2-4] This same rationale is the foundation for the use of certain dyes, oxygen, and visible light in the photoradiation of malignancies.[5] Similarly related is the use of masked alkylating agents which are enzymatically activated within the tumor[6] and the use of radiation sensitizers.[7]

Chemoimmunotherapy is yet another possible multicomponent system for cancer therapy. The basic concept involves the preparation of tagging haptens which may be infused to label neoplastic cells. This is the first component of a two-component system. The second is a cytotoxic antibody which may be generated against these haptens. Alternative to such a soluble system is the stimulation of a cell-mediated response to these attached haptens. In either case, the combination of the antibody or sensitized lymphocyte with the antigen at the level of the tumor cell membrane may produce a cytotoxic reaction. This approach offers several advantages *vis-à-vis* conventional cancer chemotherapy. In the latter case, these drugs inhibit mitosis by modifying intracellular metabolism. The need for high intracellular concentrations has prevented the regression of certain solid tumors. Cellular destruction at the membrane level may obviate such restrictions. The background for this approach was that antimelphalan antibodies, when used with this mustard, produced cytotoxic effects in a murine ependymoblastoma. The combination was more effective than either agent alone.[8] Two distinct steps occurred: (1) the mustard became attached to the tumor by alkylation and (2) these labeled cells were destroyed by antihapten antibodies. This same approach has been used against Walker 256 carcinosarcoma.[9]

In order to refine this chemoimmunotherapeutic approach, the synthesis and evaluation of better haptens was undertaken. Ideally, one would want a tumor specific agent. Though we do not have such compounds yet, we can design haptens with several key attributes. In the first place, the compound must readily bind to tumor cells under *in vivo* conditions. For this purpose monofunctional alkylators were prepared since polyfunctional alkylating agents could crosslink proteins and produce mixtures of antigens and these compounds are frequently cytotoxic *per se*. This fact could becloud the question of whether

†Preliminary presentation of this work was made; see ref 1.