distilled at 98° (14 mm.), n_D^{20} 1.5563–1.5576, reported b.p. 104° (17 mm.).[9] *p-Chlorobenzyl chloride* was redistilled Eastman practical grade, b.p. 100.5–101° (15 mm.), reported b.p. 94–96° (14 mm.).[10]

p-Bromobenzoyl chloride, obtained in 82% yield from *p*-bromobenzoic acid and phosphorus pentachloride, distilled at 220–225°. *p-Chlorobenzoyl chloride*, obtained by treating the acid with thionyl chloride, distilled at 107–108° (17 mm.).

The *chloro-* and *bromo-2,4-dihydroxydiphenylmethanes* were all obtained by the same general procedure. Typically, *4'-bromo-2,4-dihydroxydiphenylmethane* was prepared from 70 g. (0.636 mole) resorcinol, 64.7 g. (0.31 mole) *p*-bromobenzyl chloride and 50 g. (0.378 mole) anhydrous aluminum chloride in nitrobenzene solvent (400 g.) by the procedure of Klarmann and von Wowern.[4] Distillation of the resulting heavy red oil from an Allihn flask, the column of which was wrapped with asbestos tape and heated by a nichrome wire winding, gave 33.7 g. (38.4%) of a light colored viscous oil distilling at 200–219° (2 mm.). After standing several days or after repeated stirring the crude product solidified. Recrystallization from 1:1 ligroin-xylene gave colored needles of m.p. 90–92°. A product of slight gray color, m.p. 92.5–93.5°, was obtained after treatment with charcoal and repeated recrystallization from ligroin-xylene.

Derivatives. The *dibenzoates* and the *di-p-bromobenzoates* were made in the customary manner[11] by heating the dihydroxy compound and the appropriate acid chloride in pyridine. Attempts to prepare the *di-p-chlorobenzoates* of the 2'-chloro and 3'-chloro isomers in a similar fashion yielded small amounts of the impure derivative plus large quantities of a difficulty soluble crystalline material, m.p. 194–197°, which was identified as *p*-chlorobenzoic acid anhydride. The desired derivatives could be purified only with considerable

difficulty because of their like solubility with the acid anhydride. Larger quantities of an initially purer di-*p*-chlorobenzoate could be made more conveniently by heating the dihydroxy compound with about 2.5 times its weight of *p*-chlorobenzoyl chloride at temperatures approximating 130° for about 4 hr.[12] The solid which resulted on cooling was broken up and dissolved in ether and the acidic materials were extracted with sodium bicarbonate solution. After evaporation of the ether, the residual solid or oil was dissolved in ethanol and permitted to crystallize. Recrystallization was from ethanol.

The *aryloxydiacetic acid* of the 3'-bromo isomer resulted in minute amounts when the 3'-bromo isomer was heated for one hour with chloroacetic acid in the presence of base.[13] The resulting solid, after crystallization from aqueous acetic acid melted at 172.5–174°. This derivative was not further investigated.

The attempted *purification* of the *3'-bromo isomer* consisted of: converting a sample, consisting of flat plates of m.p. 59–66°, into the dibenzoate, which melted at 95.5–96° after recrystallization from ethanol and which possessed the analysis shown in Table I; hydrolysis of 3 g. of the dibenzoate by refluxing it for one hour with 5 g. of potassium hydroxide in 25 ml. of diethylene glycol and 8 ml. of water; and isolating the liberated dihydroxy compound. The latter was accomplished by cooling and acidifying the alkaline diethylene glycol solution. The solid was separated and dissolved in ether and the acidic materials removed by extraction into sodium bicarbonate solution. Evaporation of the ether left a red oil which, after solution in toluene, yielded crystals of the 3'-bromo isomer of m.p. 59–66°, even after repeated recrystallization.

Bromine determination was carried out by the method of Lemp and Broderson.[14]

EAST LANSING, MICH.

(9) G. M. Bennet and B. Jones, *J. Chem. Soc.*, 1818 (1935).

(10) E. H. Huntress, *Organic Chlorine Compounds*, John Wiley and Sons, Inc., New York, 1948, p. 44.

(11) R. L. Shriner, R. C. Fuson and D. Y. Curtin, *Systematic Identification of Organic Compounds*, 4th Ed., John Wiley and Sons, Inc., New York, 1956, p. 212.

(12) R. C. Huston and K. R. Robinson, *J. Am. Chem. Soc.*, **73**, 2483 (1951).

(13) C. F. Koelsch, *J. Am. Chem. Soc.*, **53**, 304 (1931).

(14) J. F. Lemp and H. J. Broderson, *J. Am. Chem. Soc.*, **39**, 2069 (1917).

Stereo Numbers: A Short Designation for Stereoisomers[1]

ALFRED FELDMAN

A new method of designation for stereoisomers is proposed. Its advantage is conciseness.

The practice of designating a stereoisomer by individual reference to its asymmetric centers, as in, *e.g.*, *trans-anti-trans*-perhydrophenanthrene,[2] leads to cumbersome names for compounds containing several asymmetric centers. As a consequence, methods of nomenclature have been elaborated which achieve shorter names. These shorter names, however, were attained at the expense of uniformity in nomenclature, by taking advantage of peculiarities inherent in each particular field of stereochemistry. This fragmentation was aided by the requirement of correlating compounds to a steric prototype (which has become unnecessary since the advent of methods for determining absolute configurations).

Thus, carbohydrate chemists have developed a system of prefixes,[3] each one of which denotes the configuration at several asymmetric carbon atoms (Table I).

Carbohydrates containing more than 4 asymmetric centers can be named by combining the

(1) Paper presented before the 135th ACS meeting, Boston, Mass., April 1959.

(2) R. P. Linstead, *Chem. & Ind. (London)*, **15**, 510 (1937).

(3) Rules of Carbohydrate Nomenclature, *Chem. and Eng. News*, **31**, 1776 (1953).

TABLE I

PREFIXES FOR CARBOHYDRATE STEREOISOMERS[3]

No. of Asymmetric Carbons	Prefixes
2	D- or L-erythro-, threo-
3	D- or L-arabino-, lyxo-, ribo-, xylo-
4	D- or L-allo-, altro-, galacto-, gluco-, gulo-, ido-, manno-, talo-

prefixes of Table I as, e.g., methyl L-erythro-β-D-galacto octopyranoside (Fig. 1) which expresses the configuration at seven carbon atoms.

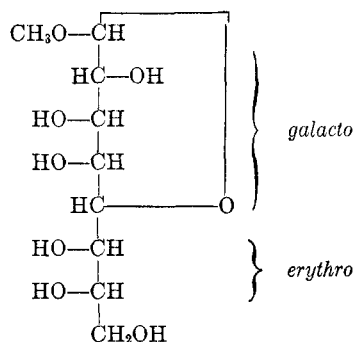Fig. 1. Methyl L-erythro-β-D-galacto-octopyranoside

In other methods for carbohydrate nomenclature, the asymmetric positions are designated only by their number. A comma (,)[4] or a fraction bar (/)[5] separates those having a substituent above a plane from those having one below (Fig. 2).
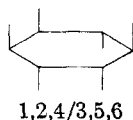

1,2,4/3,5,6

Fig. 2. Maquenne's[5] notation for dextro-inositol

Steroid chemists take advantage of the fortuitous circumstance that natural steroids are amazingly similar in their configuration. They implicitly assume this "natural" configuration, designating only those positions that are at variance with it.[6] Thus, in 5β-pregnane, the positions 8β,9α,10β,13β, 14α, and 17β are implied. If the compound differs much from the natural configuration, the system fails to provide short names. Thus, the compound commonly known as lumistane[7] should properly be called 5α,8α,13α,14β,17α,20α,24α-ergostane.

To avoid this, it has been proposed to distinguish between a lumi- and an ergo-sterol series.[8] Similarly,

(4) M. R. Lespiau, Bull. soc. chim. France [3], 13, 105 (1895).

(5) L. Maquenne, Les Sucres et leurs Principaux Dérivés, Gauthier-Villars, Paris, 1900, p. 15 ff.

(6) International Union of Pure and Applied Chemistry, Nomenclature of Organic Chemistry 1957, Butterworths, London, 1958, pp. 73–82.

(7) J. Castells, E. R. H. Jones, G. D. Meakins, and R. W. J. Williams, J. Chem. Soc. 1159 (1959).

butyrospermol, the structure of which has recently been elucidated, was described as 9α-eupha-7,24-dien-3β-ol,[9] from the parent name "euphol," a compound with the lanostane skeleton but related to lumistane in its configuration. Such instances of alternative nomenclatures are quite common.

The more the field of stereoisomer nomenclature is subdivided, the more tenaciously trivial prefixes from early times survive, and the more the need arises for a system of general applicability. Several such systems have been proposed recently.[10-12] However, because of their scope, they no longer can take advantage of some inherent peculiarity of a class of compounds in order to obtain short names. Instead, each asymmetric center is mentioned separately.[13] Thus, α-iso-sparteine (Fig. 3) is designated by the method of Cahn, Ingold, and Prelog[11] as $(1R:6R:7S:9S:11R:16R)$-sparteine. No wonder then, that these authors feel compelled to state that a universal system "need not be allowed to disturb any local system in an area in which the latter is preserving good order. But a general system could provide for the unregulated areas; and it could be used to circumvent ambiguities caused by the overlapping of local systems."
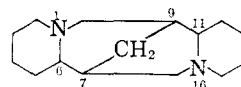
$(1R:6R:7S:9S:11R:16R)$-Sparteine

Fig. 3. α-iso-Sparteine, and its name by the universal system of Cahn, Ingold, and Prelog[11]

(8) A. Butenandt and L. Poschmann, Ber., 73B, 893 (1940).

(9) W. Lawrie, W. Hamilton, F. S. Spring, H. S. Watson, J. Org. Chem. 21, 491 (1956).

(10) G. E. McCasland, A New General System for the Naming of Stereoisomers, available from Chemical Abstracts, Columbus (Ohio), 1953.

(11) R. S. Cahn, C. K. Ingold, V. Prelog, Experientia, 12, 81 (1956).

(12) A. P. Terentiev and V. M. Potapov, Tetrahedron, 1, 119 (1957).

(13) This author is aware of one other attempt to provide a more general system with short prefixes. In a personal communication, Dr. Charles D. Hurd, of Northwestern University, suggested that carbohydrate configurational prefixes could be adapted readily to designate the steric arrangement of the sequences of asymmetric carbons in steroids. He would adopt the convention that in


$(CH_3 or)H$
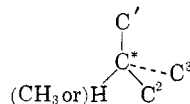
H to C^2 to C^3 is clockwise (or $+$) if viewed from underneath, that the terminal atom of the asymmetric sequence (C^*) is held by C' which is of lower number than C^2 or C^3, and that for the next asymmetric carbon of the sequence C' becomes C^*, and the atom C^2 is attached to the prior ring and C^3 to the succeeding ring. With this convention, pregnane (and related 5β compounds) would have the sequence 5β, 10β, 9α, 8β, 14α, 13β, 17β or D-arabino-L-talo-;

    $+$ $+$ $+$ $-$ $+$ $+$

the 5α isomer of pregnane, as found in androstane or cholestane, would be $- + + - - + +$ or D-arabino-L-galacto-.

To overcome the above difficulties, this writer wishes to propose a system by which explicit designations for stereoisomers can be drastically reduced in length, without causing loss of information. This method is not a new nomenclature system, but rather a technique that can be applied to any system of nomenclature, universal or specialized. But in the case of the above-mentioned general designations, the availability of prefixes of trivial proportions may well prove to be the simplification needed to carry one of these designations over into general acceptance.
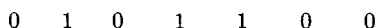
The system is based on the fact that no more than two symbols are necessary to describe an asymmetric position in a compound. Thus, in the steroids, the Greek letters α and β suffice; in the sugars, the asymmetry can be denoted by drawing substituents to the left or the right of a Fischer projection; etc. Conceivably, stereoisomeric positions could be differentiated by using the symbols 0 and 1.

The advantage of using the latter symbols instead of α and β, D and L, etc., is that the 0's and 1's can be assembled (in the same order in which they occur along a compound's skeleton) to constitute a *binary* (or *dyadic*) number.[14] This can be converted, by table or by routine methods (shown in parts A and B of appendix) into a short *decimal number*.[15] It is proposed to call this number, to be used as a prefix, the "stereo number" of the compound concerned.

For instance, the full configuration of 17-*iso-allo*-pregnane is:

$$5\alpha, \quad 8\beta, \quad 9\alpha, \quad 10\beta, \quad 13\beta, \quad 14\alpha, \quad 17\alpha$$
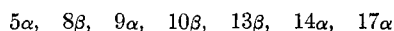
In binary notation this is:

$$0 \quad 1 \quad 0 \quad 1 \quad 1 \quad 0 \quad 0$$

In decimal notation this is:

$$44$$

(*The procedure for this conversion is given in the appendix.*)

Forty-four is thus the stereo number of 17-*iso-allo*-pregnane, which can be written as follows: /44/-pregnane. It is a complete and unequivocal yet utterly concise description of this stereoisomer.

Similarly, the sugar methyl L-*erythro-β-D-galacto*-octopyranoside (Fig. 1) can be named, as shown in the appendix C, as methyl /36/-octopyranoside. The compound α-*iso*-sparteine could be named (using the R and S of Cahn *et al.*, and setting $R = 0$ and $S = 1$) /12/-Sparteine (see appendix D).

In view of the ability of stereo numbers to fit many nomenclature systems, it might be advisable to prefix them by a symbol denoting the nomenclature used. For instance, in /s44/-pregnane, the "s" might signify that the steroid numbering has been used; in /c12/-sparteine, the "c" will indicate the numbering according to Cahn *et al.* Obviously, some convention must be adopted in this matter before stereo numbers are to be used by authors.

It is worthwhile noting some interesting properties of stereo numbers. Depending upon whether the first asymmetric carbon in a steroid is α or β, its stereo number will be within the lower or upper half of the possible number of stereoisomers.[16] In steroids, as it happens, C-5 is a special case, warranting separate designation. Since this carbon atom is frequently the first asymmetric center, its configuration can be deduced from the stereo number at a glance. (Thus, /44/-pregnane must be an allo (5α) compound because $44 < \frac{128}{2}$.) Again, depending upon whether the last asymmetric carbon is α or β, the stereo number will be even or odd. As it happens in steroids, the positions next to C-5 most likely to vary are C-17 and C-14, both frequent candidates for the asymmetric center with the highest number. (Thus, /44/-pregnane must be a 17-*iso* compound because 44 is an even number.)

Similarly, in sugars, the position that is specifically designated by α or β is frequently the lowest, while the highest position determines whether the compound is D or L. Here too, then, a glance at the stereo number will tell the configuration at these positions.(Thus, methyl /36/-octopyranoside is a L sugar because 36 is even; and it is β because $36 < \frac{128}{2}$.) Octal numbers may prove even more advantageous in this respect.

Finally, it might be pointed out that the stereo numbers of a pair of enantiomorphs will add to $2^n - 1$, where n is the number of asymmetric carbons in the molecule. This particularity may solve the problem of designating steroid enantiomorphs.[17] (Thus, the enantiomorph of /44/-pregnane is necessarily /83/-pregnane, since $44 + 83 = 127 = 2^7 - 1$.)

All such mathematical niceties notwithstanding, it remains a fact that stereo numbers do not indicate at first glance *all* the steric relations shown by the "extended" prefixes. This could be construed as

---

(14) A binary notation uses only the digits 0 and 1. Values greater than 1 are expressed by the position of the digits, as in our common (decimal) system. Thus, the binary 10, 100, 1000, 10,000 equal, respectively, 2, 4, 8, 16. This notation was proposed by Leibnitz. It also has been found in actual use among primitive Australian and South American tribes. Because of their use by digital computers, binary numbers have ceased to be a mathematical curiosity.

(15) H. Friedman, of our research department, suggests that the binary numbers be expressed as the corresponding octal numbers. Although somewhat longer than the equivalent decimal numbers, they are even easier to convert, as shown in the appendix E.

(16) The number "s" of possible sterioisomers of a compound containing n asymmetric carbon atoms is given by the equation: $s = 2^n$.

(17) A. Horeau, J. Jacques, J. P. Mathieu, A. Petit, *Bull. soc. chim. France* [5], **22**, 1304 (1955); T. Reichste in *Helv. Chim. Acta*, **40**, 677 (1957).

a serious shortcoming, but it is not. The chemist specifically interested in these relations can revert at will to the extended prefixes. Any annoyance in this respect is more than compensated for, whenever names have merely to be "handled." Stereo numbers combine the convenience of trivial names with the accuracy of the systematic names. Anyone who has been aware of the amount of information lost in the literature because authors assumed too much stereoisomerism known, will appreciate this advantage.
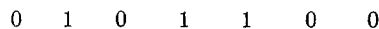
APPENDIX

Stereo numbers can be obtained by using a conversion table.[18] The actual calculations, however, are shown here:

A. To obtain the stereo number corresponding to 17-*iso-allo*-Pregnane ($5\alpha,17\alpha$-Pregnane):

The full configuration of the compound is:

$$5\alpha, \quad 8\beta, \quad 9\alpha, \quad 10\beta, \quad 13\beta, \quad 14\alpha, \quad 17\alpha$$
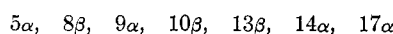
Step 1. Assign arbitrarily the digits of the binary numbers: $\alpha = 0$ and $\beta = 1$:

$$0 \quad 1 \quad 0 \quad 1 \quad 1 \quad 0 \quad 0$$

Step 2. Make a table of the powers of the number two, as shown below (column 1).

Step 3. Write the digits of the binary number so that the lowest (rightmost) binary digit matches the lowest number (which is 1) in the table of powers of 2 (column 2).

Step 4. Multiply each number in column 1 by the corresponding number in column 2, and enter result in column 3.

Step 5. Add column 3; the total is the sought decimal, or *stereo number*.

Column 1		Column 2		Column 3
64	×	0	=	0
32	×	1	=	32
16	×	0	=	0
8	×	1	=	8
4	×	1	=	4
2	×	0	=	0
1	×	0	=	0
				44
				(stereo number)

Thus, /44/-pregnane = 17-*iso-allo*-pregnane.

B. To obtain the configuration of /93/-Cortisol: The above procedure could be reversed, but a simpler method will be illustrated in this example:

Step 1. Draw a horizontal line and write the stereo number above and on the extreme right of the line.

(18) Available, *e.g.*, in *Reference Manual, 704 Data Processing System* (appendix C), by International Business Machines Corp.
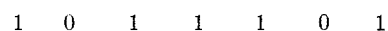
Step 2. Divide this number by two. Write the remainder (0 or 1) below the stereo number, and the result to the left of the stereo number (on the line). Repeat this operation on the result, and continue till numbers are exhausted. The number below the line will be the sought binary number.

$$\frac{1 \quad 2 \quad 5 \quad 11 \quad 23 \quad 46 \quad 93}{1 \quad 0 \quad 1 \quad 1 \quad 1 \quad 0 \quad 1}$$

We know that the asymmetric centers in cortisol are located at the positions:

$$8, \quad 9, \quad 10, \quad 11, \quad 13, \quad 14, \quad 17$$
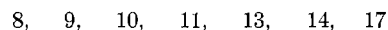
Step 3. Align these with the corresponding digits of the binary number:

$$1 \quad 0 \quad 1 \quad 1 \quad 1 \quad 0 \quad 1$$

Step 4. Set $0 = \alpha$ and $1 = \beta$:

$$8\beta, \quad 9\alpha, \quad 10\beta, \quad 11\beta, \quad 13\beta, \quad 14\alpha \quad 17\beta$$
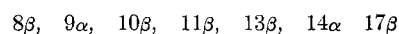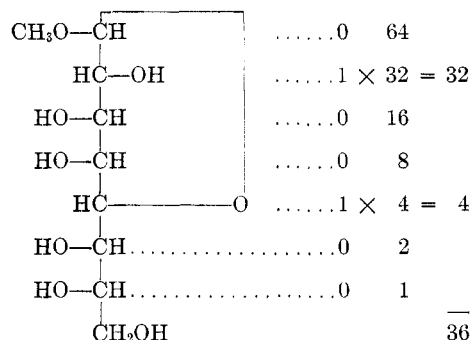
which is the configuration sought.

C. To obtain the stereo number for methyl L-*erythro*-β-D-*galacto*-octopyranoside. The convention adopted here is to assign 0 to all substituents to the left of the Fischer projection, and 1 to those on its right:

$$
\begin{array}{llll}
\text{CH}_3\text{O---CH} & & \dots\dots 0 & 64 \\
\text{HC---OH} & & \dots\dots 1 \times 32 = & 32 \\
\text{HO---CH} & & \dots\dots 0 & 16 \\
\text{HO---CH} & & \dots\dots 0 & 8 \\
\text{HC-----O} & & \dots\dots 1 \times 4 = & 4 \\
\text{HO---CH} & & \dots\dots 0 & 2 \\
\text{HO---CH} & & \dots\dots 0 & 1 \\
\text{CH}_2\text{OH} & & & \overline{36}
\end{array}
$$

D. The compound α-*iso*-Sparteine can be named (using the R and S of Cahn *et al.*, and setting $R=0$ and $S=1$) as /12/-Sparteine:

$$
\begin{array}{cccccc}
1R: & 6R: & 7S: & 9S: & 11R: & 16R \\
0 & 0 & 1 & 1 & 0 & 0 \\
& & & 12
\end{array}
$$
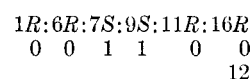
E. Octal numbers: Another method of expressing binary numbers in a shorter form is the use of the equivalent octal number. In the octal system numbers run from 0 through 7.

Binary No.	Octal No.	Binary No.	Octal No.
000	0	100	4
001	1	101	5
010	2	110	6
011	3	111	7

In the first example, 17-*iso-allo*-Pregnane, the binary number is given as 0 1 0 1 1 0 0. To obtain the equivalent octal number the binary number is broken into groups of three:

0 101 100

and the equivalent octal number is expressed:

0 5 4

Thus, in an octal system the compound becomes [54]-Pregnane.

Translation of an octal number back into its binary equivalent is also very simple. In the second example, the octal number would have been [135]-Cortisol. The binary equivalent is easily written down: 1 3 5
001 011 101

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