Graphic Representation of Configuration in Two-Dimensional Space. Current Conventions, Clarifications, and Proposed Extensions[1,2]

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The chemical vocabulary can describe, in a single term, a racemate or a specific enantiomer or a compound that is enantiopure, but whose absolute configuration is unknown. Regardless of these differentiations, the corresponding conventional graphic representations display but one specific enantiomer. Because of this inflexibility, verbal annotations to stereostructures in chemical publications and databases are unavoidable. In the expanding era of chirotechnology, the limited descriptive power of stereostructures in two-dimensional space is of serious concern. To provide a solution to this problem, targeted redeployment of established stereobonds serve as stereodescriptors that differentiate between enantiopure and racemic compounds and those that are enantiopure but whose chirality sense is unknown. Graphic displays then share the explicitness and accuracy of the chemical vocabulary. Fischer projections, recently expanded to accommodate alkenes and axially stereogenic compounds, can display favorably comparative configurational aspects of molecules with a multiplicity of stereogenic units.

1. INTRODUCTION

Several types of molecular diagrams are in use to portray geometric and topographic information.[3] *Projections* are based on rigid conventions that readily allow the reconstruction of stereochemical information. *Perspective drawings*, by definition, provide the illusion of three-dimensional space so that the diagram itself elicits topographic perception.[4] Based on elementary laws of optics, a perspective drawing shows objects smaller and closer together as they recede in the distance. Consider a road leading toward the horizon, as illustrated in Figure 1. With increasing distance from the viewer's vantage point, the road seems to narrow and its shoulders appear to come closer and closer together, apparently meeting at the horizon. In a perspective drawing, the drawing surface is known as the picture plane, the horizon line is the horizontal eye-level line that divides the scene, and the vanishing point is the location on the horizon line where the "parallel" lines in the scene appear to converge. While we can readily identify the yz coordinates with the picture plane, it is the vanishing point, with the lines leading to it, that provides the latent *x* axis and hence the illusion of 3-D space. The number of a scene's potential vanishing points is not limited and depends only on the number of individual objects to be illustrated. The drawing of a single object, such as the ball-and-stick molecular model shown in Figure 1, is thus characterized by a single vanishing point.

Driven by the need for simple representations of stereocenters in structural diagrams, short-hand notations of stereounits have evolved. Central to the correct perception of a stereounit's topography is the stylized generation of a vanishing point, realized by the graphic stereodescriptor, or stereobond, commonly called a "wedge" as illustrated in Figure 1 as **1a** and **1b**. Three such *wedge* symbols as in **3**, **4**, and **6** are in use, each of them capable of portraying the ligand Z in **1** and **2** as being located in the front (**3** and **4**) or behind (**6**) the picture plane.

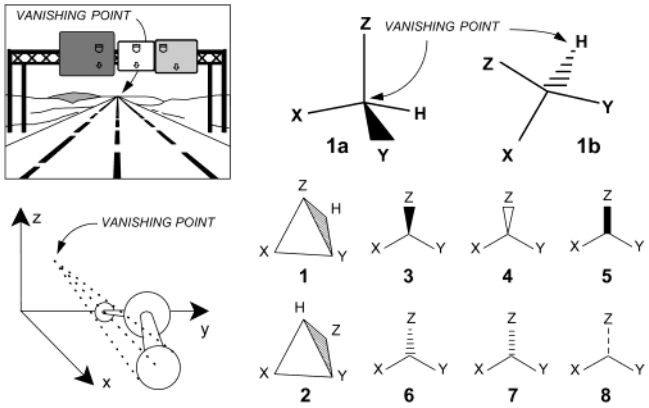

Figure 1. Perspective drawings of stereocenters with commonly used stereobonds.

In an apparent search for further simplification, *line* symbols **5**, **7**, and **8** were invented as wedge substitutes. Lacking differentiation of their termini, line-type symbols appear, a priori, to be inherently incapable of serving such a purpose; nevertheless, they provide a useful function in the context of a convention. Accordingly, the *stereogenic unit* to which the line-type bond symbol is attached is considered to lie in the picture plane so that the symbol printed in bold (**5**) reveals its ligand Z in front of that plane, whereas the hashed symbols (**7** and **8**) are intended to show that the ligand is behind it. In other words, symbol **5** portrays the stereocenter at the vanishing point and hence functions such as **3** and **4**. In symbols **7** and **8**, it is the ligand Z that is at the vanishing point, so that the stereocenter is perceived to be closer to the viewer than Z, as illustrated in **2**. Consequently, symbols **7** and **8** have been used interchangeably with **6**. To repeat, a stereobond without an apparent

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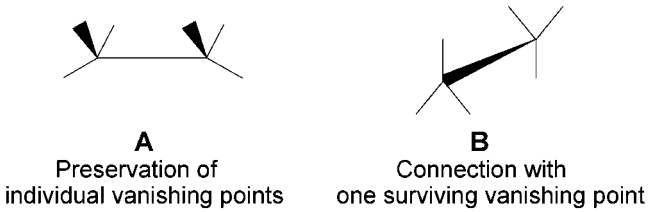


Figure 2. Connections of two stereocenters in 2-D space.

vanishing point (**5**, **7**, and **8**) places the *stereocenter* into the yz plane, while the chirotopic but nonstereogenic ligand Z assumes the relative position in front or behind the yz plane, irrespective of its CIP priority. Only with this convention can **5** unambiguously represent **1**, whereas **7** and **8** will be interpreted unmistakably as **2**.

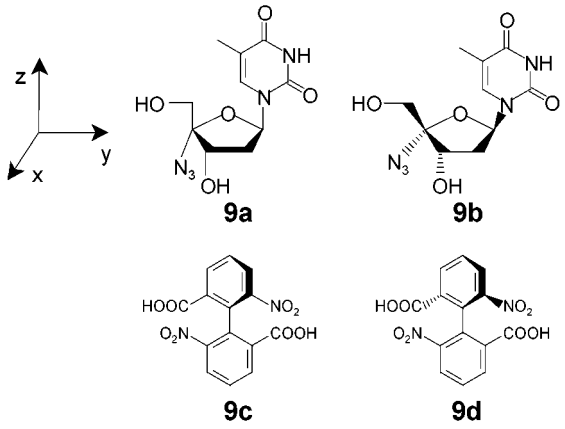
The simplest perspective rendition of a molecule with multiple stereounits is presented in 2-D space as a collection of individual stereogenic units, all linked together, each associated with its own vanishing point as in **A** (Figure 2). Alternatively, connecting two stereocenters by a stereodescriptor, as in **B**, relinquishes one of the two vanishing points. Whereas **A** requires at least two stereobonds, one for each stereocenter, only one defines the topography of **B**.

All six stereobonds described in Figure 1 are in use and are available in most software packages for chemists. Their crucial function in the graphics of molecules is obvious; yet there are no written rules to guide their usage. We attempt, therefore, to consolidate and unify current conventions, as poorly defined as they are, and to forward proposals aimed at maximizing the stereochemical information implied in drawings of chemical structures.

2. FUNCTIONS AND USES OF STEREODESCRIPTORS

2.1. Number of Stereodescriptors per Stereocenter. Correct topographic perception of a molecular assembly must allow the identification, in a *3-D* environment, of the position of an atom, or groups thereof, with respect to the vicinal partners. In a perspective drawing, the location of ligands surrounding a stereocenter is provided by the position in a 3-*D* Cartesian coordinate system, where the yz plane furnishes two axes, but the x coordinate, simulated by the stereobond, determines the atoms' relative positions in the third dimension. Since three corners of a tetrahedron can be placed into a plane, only one stereobond is required to define the position of its fourth corner, either in front or behind that plane. Thus, for simplicity's sake, it is usually appropriate to employ only one stereobond per stereocenter. This practice is particularly fitting if one of the ligands on a stereocenter is hydrogen. The deletion of this ligand from the display usually furnishes a less encumbered diagram with uncompromised clarity. The latent position of the hydrogen substituent is usually presumed opposite to the stereobond's ligand with respect to the yz plane. The renditions of **1** and **2** as **3**−**5** and **6**−**8**, respectively, serve as examples (Figure 1). Notwithstanding, line symbols **5**, **7**, and **8** may occasionally require a second descriptor on a stereogenic unit to clarify the vanishing point, i.e., when Z itself is stereogenic.

In view of these premises simple lines represent bonds intended to show connectivities between atoms that lie in the picture plane or in any plane parallel to it. They show that a particular substituent is on the right or left or up or down. It is the prerogative of the stereobonds to depict what is to be perceived to be in front or behind the picture plane. To illustrate this point, we inspect molecule **9a**, where the stereobonds are part of a ring drawn as a "Haworth projection". Because of the firmly established ring topography, ring ligands appear either above or below with respect to the xy-plane in accordance with the z coordinate. Simple lines as in **9a** can therefore show the corresponding bonds; in contrast, **9b**, an example taken from a recent publication,[5a] illustrates the awkward appearance of a diagram where stereobond usage defy the rules spelled out so far. Equally inappropriate is the representation of (*S*)-2,2′-dinitro-6,6′-diphenic acid (**9c**) as **9d**, where three sets of stereobonds, portraying three vanishing points, are used to illustrate a single stereogenic axis.[5b]



2.2. Use of the Hashed-Wedge Stereodescriptor 6. Stereobond **3**, contained in the five-point figure **10a** shown in Figure 3, describes the chirality sense of **10**. Similarly, symbol **6** in **10b** portrays the same object. These stereobonds define the vanishing points: in **10a** we recognize ligand A in the foreground and the stereocenter at the vanishing point; in **10b** ligand D is at the vanishing point. Reversing the direction of a stereobond, as exemplified by the conversions **10a** → **11a** and **10b** → **11b**, places the vanishing point to the opposite terminus of the stereobond. Vanishing point reversal is equivalent to the reversal of the sign of the x coordinate, which defines the three-dimensional space, and hence changes the chirality sense of the stereocenter. As a result, **11a** and **11b** are valid representations of **11**, which is the enantiomer of **10**.

If two stereodescriptors on the same stereocenter are to be used, two vanishing points are implied to suggest

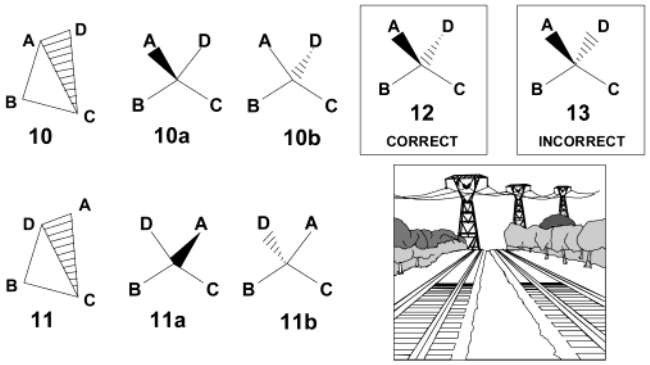


Figure 3. Directional change of a stereodescriptor reverses the vanishing point and the chirality sense of the object.

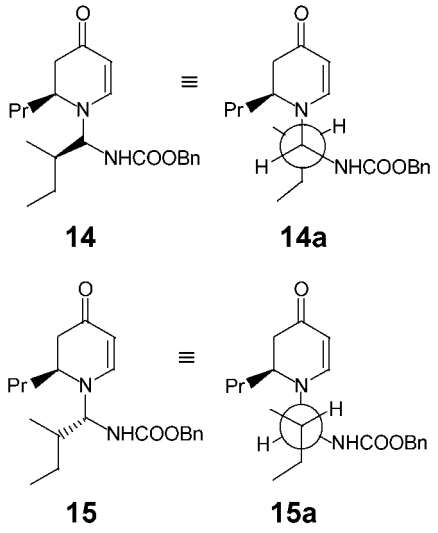


Figure 4. Interpretations of carbamic acid benzyl ester **14** and **15**.

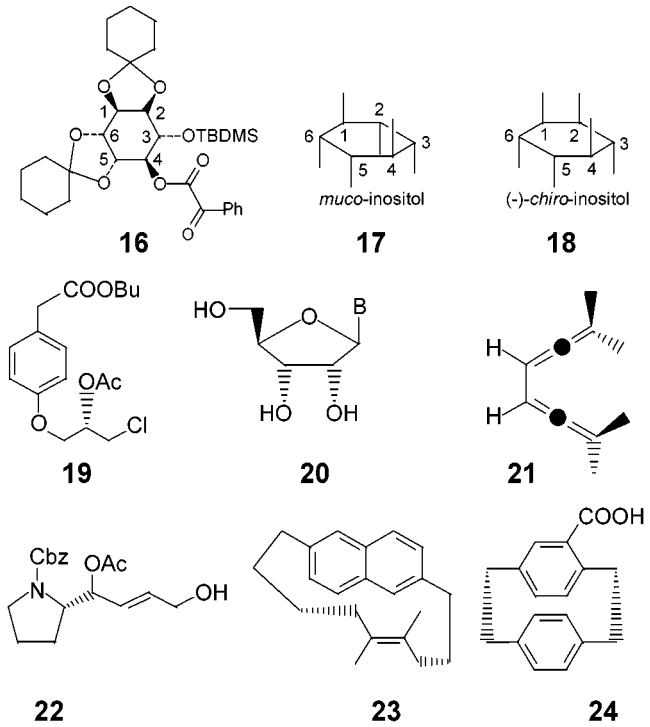
progressively increasing distance from the viewer. As illustrated in Figure 3, railroad tracks originating at the foreground recede into the distance to the first vanishing point; a second one is created to display high-tension wires, mounted on masts of apparently decreasing size to provide the illusion of further recedence into the distance. Diagram **12** reflects the same drawing technique and suggests the stereocenter to be located in the yz plane, while ligands A and D are situated in front of, or behind that plane, respectively. In a curious bow to Bohemianism, some of us insist to use descriptor **6** inversely, as in **13**, with the intent to portray **10b**. This misuse of **6** is caused by the erroneous application of the convention, specifically intended and reserved for the *line-type symbols*, to symbols that are wedges. Of necessity, line symbols **5**, **7**, and **8** must be employed in conjunction with a *convention that defines the vanishing point*, as explained in the Introduction. Wedge symbols, on the other hand, are *inherently vanishing-point defined* and, for this very reason, are self-explanatory, as seen in examples **1a** and **1b** (Figure 1). In other words, *wedge symbols are not, and may not be, subject to the same convention that defines the vanishing point of a line-type descriptor*. With this statement in force, the erroneous interpretation of **11b** as **10** is no longer possible.

To override the obvious ambiguity generated by the inconsistent usage of **6**, it is common practice to add, to the same stereocenter, an additional descriptor such as a solid wedge, whose meaning is usually uncontested. The resulting symbol **13** may then perhaps be interpreted as **10**, although correct perception places the stereocenter in the yz plane where *both* stereobonds share one vanishing point so that the ligands A and D are situated in front of the yz plane, while B and C reside in the yz plane. Symbol **12**, by contrast, shows the atom sequence A-stereocenter-D to extend from A in the foreground to the first vanishing point, which is coincidental with the position of the stereocenter, and then further into the distance toward D, leading to an unambiguous representation of **10**.

The incorrect use of the hashed wedge symbol **6** can cause serious problems when employed to connect two stereogenic units. To portray the two stereocenters in **14** (Figure 4), for example, a single stereobond on each stereocenter as shown should suffice for complete topographic description. As a tribute to the lucidity of the solid wedge symbol, compound **14** will be perceived as **14a**. The reader is now invited to view **15**, shown exactly as it appeared in a recent publication.[6a] Because of the incoherent use of **6**, it is impossible to decide which of the two diastereomers (**14a** or **15a**) it is supposed to represent: interpretation in the sense of **12** leads to **15a**, but a vista in the sense of **13** establishes **15** as **14a**.[6b]

Even solid wedges are occasionally used thoughtlessly. The stereocenters 1 and 2 in **16** shown as it appeared in print will certainly be interpreted as trans by most of us and hence as a derivative of *muco*-inositol **17**, yet the *chiro*-inositol **18** is actually implied![7]

At this time, the usage of the hashed stereobond **6** is totally inconsistent. One may find it applied in the sense of **13** in one paper (e.g., **19**)[8] and as **12** in another (e.g., **20**),[9] both in the same issue of a journal; on occasion it is even employed in the sense of **12** and **13** within the same molecular display as exemplified by **21**.[10] As a result, the seemingly lucid configurational display of **22**, also taken from a recent



publication,[11] can no longer be deciphered when taken out of context: Interpretation according to **12** leads to the enantiomer of the compound implied by the authors.

As we reach the stage where the absolute configuration in ostensibly obvious displays such as **22**−**24** is no longer obvious, an agreement is required that should be easy to implement: discontinue the use of the hashed-wedge symbol in the sense **13** and unanimously adopt **12** in its place.

3. EQUIVALENCE OF CHEMICAL VOCABULARY AND GRAPHIC DISPLAY

Concomitant with the evolution of stereochemistry, a vocabulary has developed that addresses the needs of the practicing chemist as well as those concerned exclusively with documentation and computational databases. A single term will completely describe a racemate or a substance deemed to be enantiopure but of unknown chirality sense,

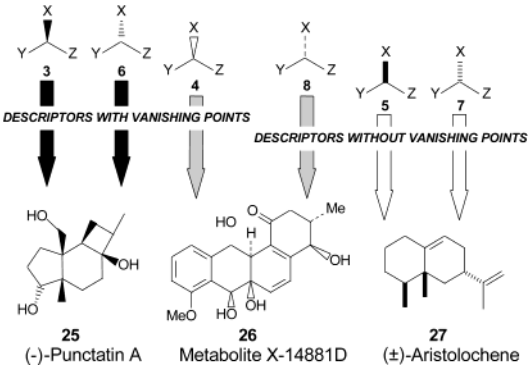


Figure 5. Allocation of stereobonds.

although two enantiomers are the subject of consideration. Enantiomerically or diasteomerically enriched materials are also named by single terms, the measure of the enantiomeric or diastereomeric excess, respectively, is appropriately added to the name of the predominating species. But our needs to specify stereochemical information go further, occasionally requiring the description of incomplete stereochemical features, all of which can be achieved verbally.

Chemical communication, either in conversation or documentation, relies not only on the *chemical names* but especially on *structural diagrams*. The advent of the era of chirotechnology,[12a,b] which infests our vocabulary with terms such as "chiral drugs", "chiral pools", and "racemic switches" should arouse our longing to extend the exactness of the science to the tools that portray her products. Foremost, we should strive to parallel the verbal description of a chiral molecule, whatever the nuances of available chemical information may be, with an equally descriptive, graphic representation.[13] To achieve this goal, we redeploy the available stereobonds **3**−**8** and provide them with certain privileges that reach beyond the rudimentary concepts discussed before.

3.1. Diagrams of Enantiopure/Enantioenriched Compounds. As a first step, we group the available descriptors into two categories, those with vanishing points and those without, as illustrated in Figure 5. Stereobonds **3**, **6**, and **4** lend themselves ideally for the portrayal of enantiopure and enantioenriched compounds, as they elicit three-dimensional impressions with uncompromised chirality sense of the object. More specifically, the wedges **3** and **6** are now designated to represent enantiopure/enantioenriched compounds of known chirality sense as depicted in **25**. Just as the verbal description of such a compound is often incomplete without a statement revealing the degree of enantio- or diastereopurity, a similar supplement as a numerical signature to the graphic display would maintain the equivalence of verbal and graphic information.

In an analogy to the physical appearance of the graphic stereodescriptor and the enantiostatus it should serve to display, the *open* wedge **4**, and the stereobond in **8**, the *simplest* of the available line symbols, imply *less than complete* stereochemical information and are proposed to depict enantiopure/enatioenriched compounds but whose absolute configurations are unknown, as illustrated in **26**, Figure 5.

3.2. Diagrams of Racemates. The descriptors **5** and **7** do not inherently reveal their vanishing points and are employed, appropriately, to represent racemates. Compound **27** in Figure 5 should serve as example.

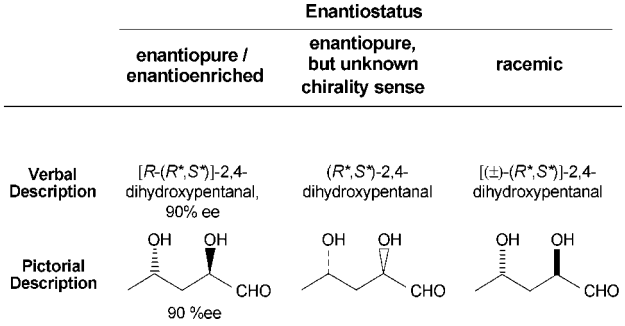
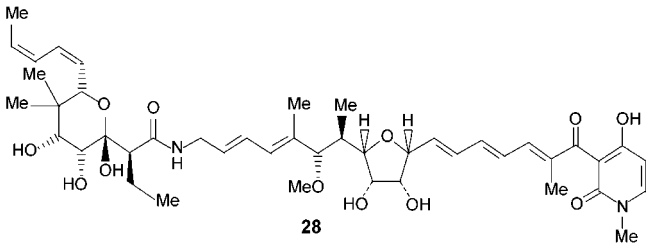


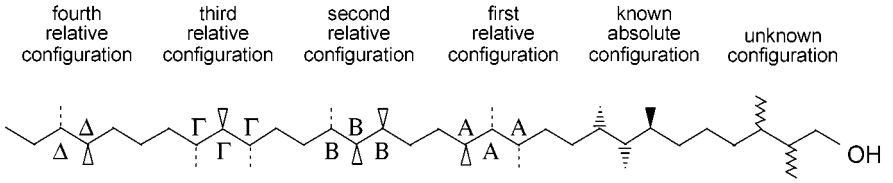
Figure 6. Equivalence of verbal and pictorial description.

To use the words of Tavernier,[14] we have now a *graphic representation of the three levels of information*, (*R*,*R*), (*R**,*R**), *and* (*RR*,*SS*). Figure 6 summarizes these tools that generate verbal and graphic equivalence. It is reassuring to see that this simple convention is gaining increasing recognition, including authoritative textbooks.[15]

3.3. Diagrams of Molecules with Incomplete Stereochemical Information. For a drawing to reveal partial stereochemical details, we use the symbol pair **4**/**8** assigned to the exposition of enantiopure compounds with known relative, but unknown absolute, configurations. The illustration of a mixture of stereounits with known and unknown absolute configurations is then easily accomplished using both pairs **3**/**6** and **4**/**8**, as shown in **28**. The diagram describes complete topographic details with the exception of the central tetrahydrofuran ring, which is perceived as a relative configuration and reflects accurately the stereochemical information available at a certain point in time during the structure elucidation.[16]



Whereas the descriptor pair **4**/**8** symbolizes relative configuration adequately, it is occasionally necessary to describe multistereocentered molecules where certain *sets* of stereocenters are of known relative configuration but the stereochemical connectivities between those sets are unknown. This is easily described verbally by providing appropriate sets of stereocenter with the corresponding stereochemical jargon. The equivalent graphic description now designates stereocenters comprising a certain relative configuration by a certain Greek capital letter; the same letter is assigned to each stereocenter that is part of a coherent group.[13,17] To illustrate this feature, we inspect the hypothetical molecule **29** in Figure 7, assumed to contain, as viewed from right to left, two stereocenters of unknown configuration, three contiguous centers with known topography, and four independently established sets of relative configurations. Whereas 65 536 stereoisomeric possibilities exist for the configurationally undefined **29**, the cited information reduces the isomeric possibilities to 64. Revealing these details, **29** now

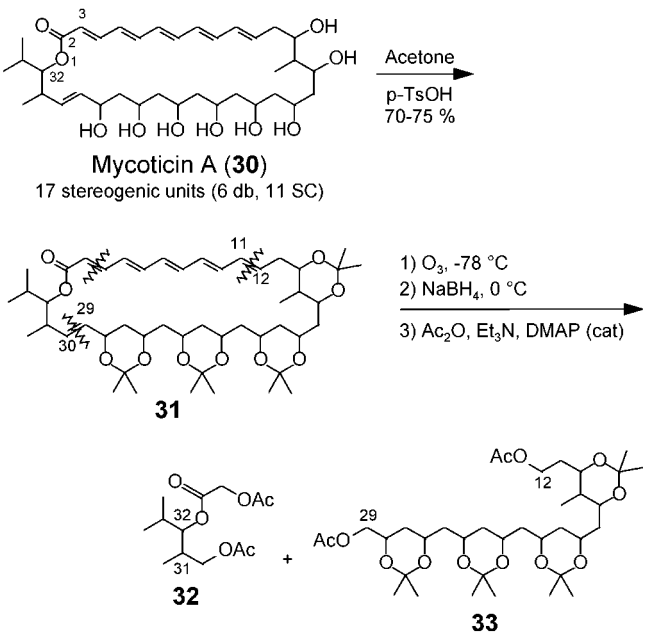


29

Total number of possible diastereomers = $2^{n-k-r+g} = 2^{16-3-11+4} = 64$

n = total number of stereogenic centers (16)
k = total number of stereogenic centers with known topography (3)
r = total number of stereogenic centers associated with greek letters (11)
g = total number of different greek letters used (4)

Figure 7. Illustration of incomplete stereochemical information.

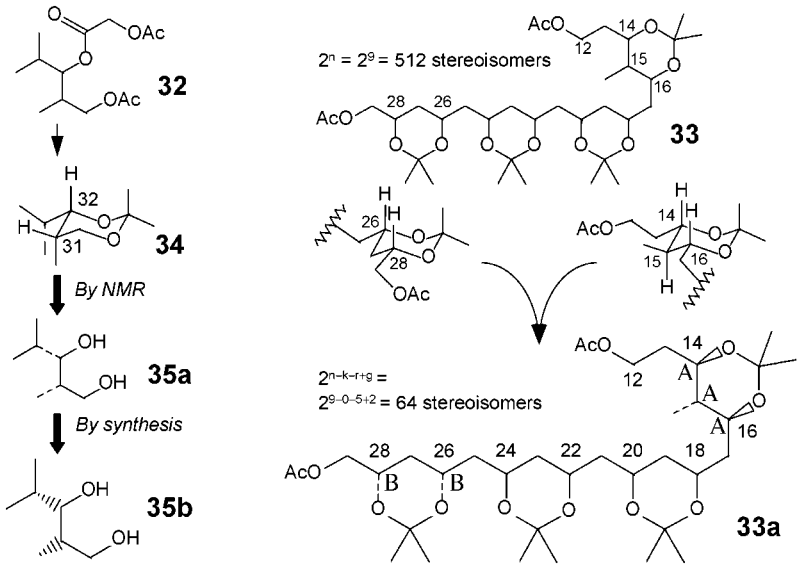


reflects the entire stereochemical information in complete equivalence with the corresponding name: [(7S-(7R*,8S*, 9R*))-(2ξ,3ξ,12,13-syn,13,14-anti,17,18-syn,18,19-anti,22, 23-anti,23,24-anti,28,29-anti)]-2,3,7,8,9,12,13,14,17,18,19, 22,23,24,28,29-hexadecamethylhentriacontan-1-ol.

The determination of mycoticin's stereochemistry[18−20] demonstrates the practical utility of this concept: that it is now possible to illustrate, unambiguously, fragmentary stereochemical results as they become available in the course of time. Of the 17 stereogenic units in **30**, six are substituted double bonds whose *E*-configurations were established at the outset. The remaining 11 left 2048 possible stereoisomers for consideration. Ozonolysis of the tetra-O-isopropylidene derivative **31**, followed by reductive workup and acetylation, furnished fragments **32** and **33**, which contained all of the 11 stereogenic centers.

Fragment **32** was converted to **34**, whose synclinal coupling constant $J_{31,32}$ established the *erythro* configuration, so that the parent diol can now be represented as **35a**. A comparison with a synthetic specimen established the (*S*,*S*) configuration, **35b**.

Of the residual nine stereocenters, two sets, 14−15−16 and 26−28, containing three and two stereocenters, respectively, were then established as relative configurations by the analysis of **33**. The results are reflected in diagram **33a**, where the independence of the two established relative configurations is emphasized by the association of descriptor type **4**/**8** with the two different Greek letters A and B.



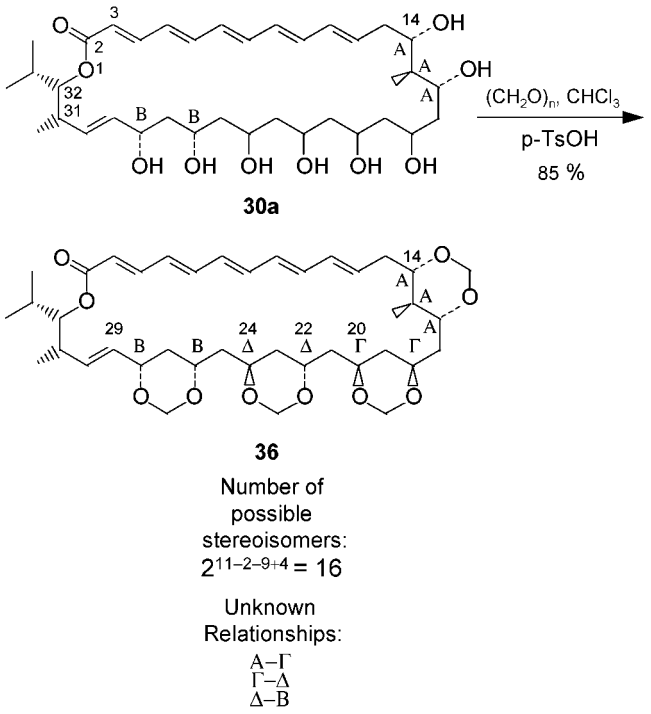


Diagram **33a** summarizes the available stereochemical results. Incorporating these findings into a mycoticin-A structure leads to **30a**. This single diagram is equivalent to a single term: [*S*-(14,15-*l*,15-16-*u*,18ξ,20ξ,22ξ,24ξ,26,28-*l*,31*R**,32*R**)-(*all-E*)]-14,16,18,20,22,24,26,28-octahydroxy-15,31-dimethyl-32-(1-methylethyl)oxacyclodotriacontan-2-one, encompassing 64 diastereomeric possibilities.

Analysis of the remaining four stereocenters, 18, 20, 22, and 24, was possible spectroscopically after conversion of mycoticin A (**30a**) to the tetramethylidene derivative **36**. An NMR study revealed two additional sets of relative configurations comprising centers 18−20 and 22−24. Four sets of relative configurations, namely 14−15−16, 18−20, 22−24, and 26−28, were now established as (*l*, *u*), *l*, *l*, and *l*, respectively. The use of four different Greek letters reflects the number of the known, independent relative configurations.

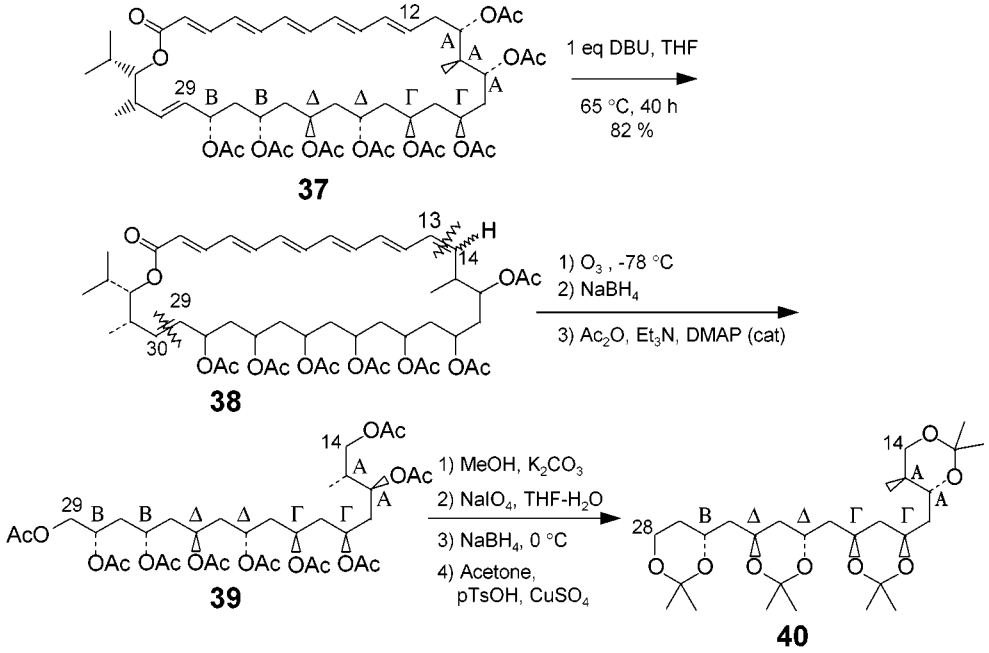
Still unknown at this stage were the three geometric relationships linking the four sets of stereocenters designated by the four Greek capital letters and the absolute configuration of the entire system, leaving only 16 stereoisomers as final candidates. All stereochemical findings available at that point in time are reflected in diagrams **36** and **37**, the octa-O-acetyl derivative of mycoticin A. Precisely the same information is offered by a single chemical name, although 16 stereoisomeric possibilities persist: [*S*-(14,15-*l*,15-16-*u*,18,20-*l*,22,24-*l*,26,28-*l*,31*R**,32*R**)-(*all-E*)]-14,16,18,20,22,24,26,28-octaacetoxy-15,31-dimethyl-32-(1-methylethyl)-oxacyclodotriacontan-2-one (**37**).

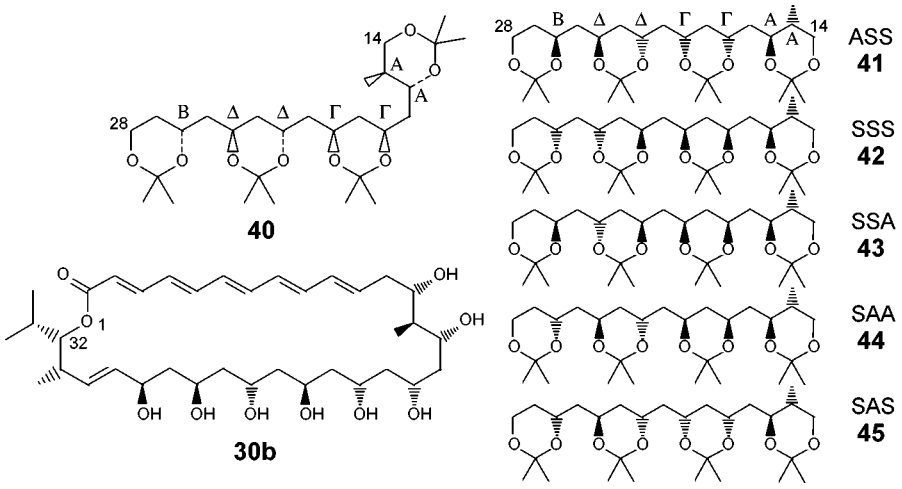
To solve the stereochemical connectivities among the four individual relative configurations in **37** required selecting one out of eight possible arrangements, each containing the established relative configurations but joined by different connectivities between A−Γ, Γ−Δ, and Δ−B (*ASS*, *ASA*, *AAA*, *AAS*, *SAS*, *SAA*, *SSA*, *SSS*; *A* = *anti*, *S* = *syn*). After the appropriate selection from the pool of these eight candidates, the correct absolute configuration would have to be determined. To enable this choice, the general structure of the minimal synthetic target, **40**, was made accessible by a degradative sequence via **38** and **39**.

Five of the eight diastereomeric variants of **40**, namely **41**−**45** had to be synthesized until a mach was found; **44** was identical with **40** by spectroscopic criteria. Based on its chiroptical properties, however, the synthetic target was antipodal to the isolated molecular fragment **40**, so that the absolute configuration of mycoticin was established by default, as shown in **30b**.

4. GRAPHIC DISPLAY OF STEREOCHEMICAL SIMILARITIES

The comparison of stereochemical features of related molecules is greatly facilitated by identical arrangements of





the molecular skeletons. Certain multicyclic systems, such as steroids, are typically shown in standardized fashions; in contrast, graphic representations of most chiral molecules are not governed by any rules. It appears on occasion that the variety of structural diagrams of a given molecule symbolizes the idiosyncrasies of scientists. The Fischer projection, however, is a tool par excellence for comparative purposes as it furnishes the same diagram of a molecule, regardless of the individual who drew it. While stereocenters have been portrayed for more than a century, it was only recently that rules for the Fischer projection of stereogenic axes and planes have been proposed.[17,21]

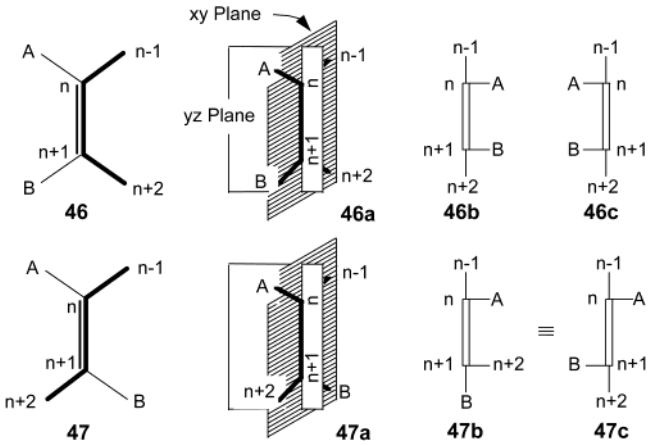
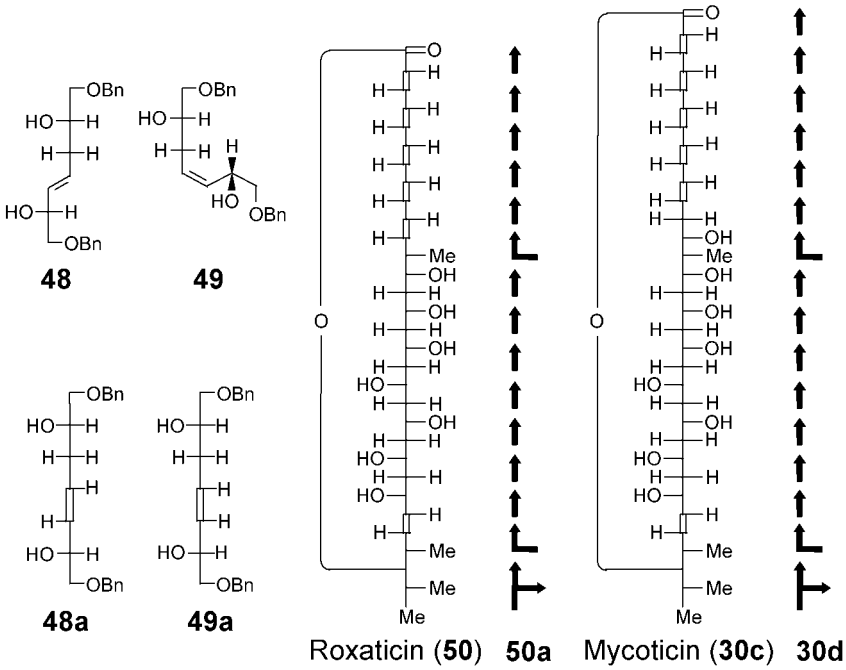


Figure 8. Fischer projection of alkenes.

To project an alkene such as **46** (Figure 8), the double bond is placed into the intersection of two planes, perpendicular to each other, and in such a fashion that the substituents lie in one of the two planes as shown in **46a**. In this display the letters A and B denote the substituents, and the sequence n−1 → n → n+1 → n+2 stands for the molecular skeleton. As customary for Fischer projections, the chain members preceding the first stereogenic unit to be projected is positioned below the projection plane (the yz plane). A slight rotation of the xy plane that bisects the molecular diagram around the axis of intersection generates a lateral bias of the substituents relative to the yz plane. The



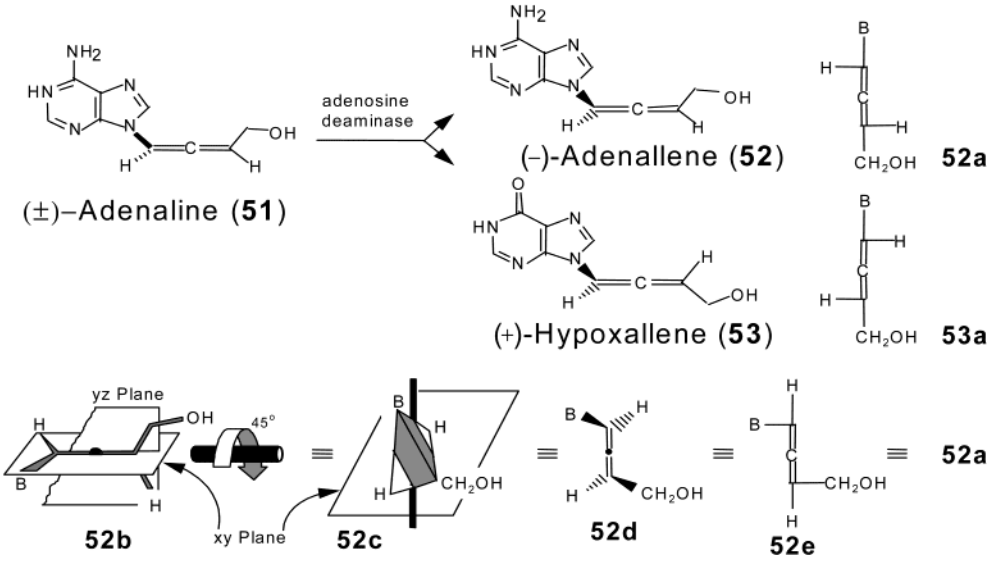
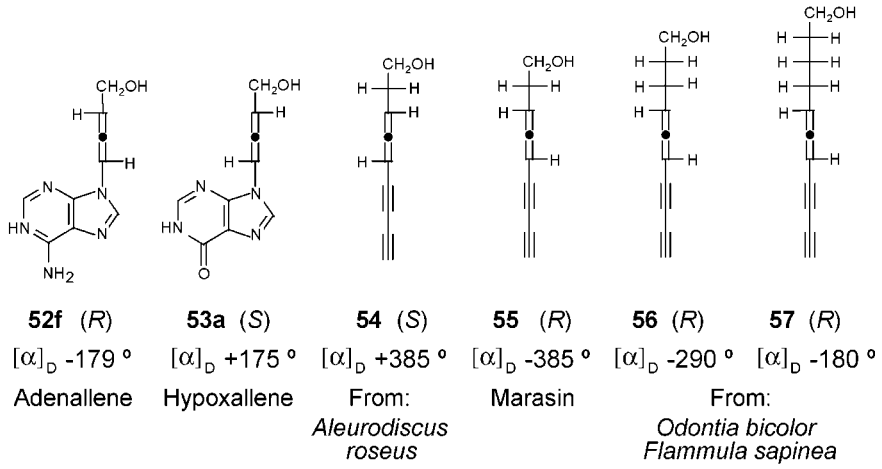


Figure 9. Fischer projection of allenes.



direction of rotation is chosen to conform to a Fischer projection in the yz plane in which the first substituent (A) at the double bond is positioned on the right when viewing the sequence n−1→ n+2 from top to bottom.

The resulting Fischer projection reflects this lateral disposition in the form of **46b** and **46c**, depending on the direction of rotation used to disturb the bond coplanarity with the xy plane shown in **46a**. To attain consistency of display, the convention demands that the laterally displayed ligands be located on the right side in the Fischer projection, as in **46b**.

The same rule applies, of course, to the projection of *E*-alkenes. The ligand n−1 that precedes the double bond in **47** is positioned below the plane and ligands A and n+2 appear above the plane, as seen in **47a**. The resulting projection **47b** is readily changed to **47c** by effecting *two* substitutional changes: interchange of n+2 with B and directional change of B from right to left. In summary, *Z*-alkenes will exhibit their ligands always on the right side, whereas *E*-alkenes will be recognized by their ligand positions on the right and left, as shown in **48a**. Exotic diagrams such as **48** and **49**, encountered in the literature,[21] now assume the uncomplicated forms **48a** and **49a**.

In view of different ring sizes, a configurational comparison of roxaticin and mycoticin, for example, is most readily accomplished by Fischer projections as seen in **50** and **30c**. Further, Fischer projections allow rapid biosynthetic pattern recognition. In roxaticin (**50a**), for example, we immediately discern the valine-derived C_4 starter unit (bottom), followed by propionate, seven acetates, propionate, and five additional acetate units. Mycoticin's biogenesis is very similar (**30d**).

Axially stereogenic molecules, such as allenes, are Fischer-projected similarly as illustrated in Figure 9. As example, we consider racemic adenallene (**51**), which was recently resolved enzymically to (−)-adenallene (**52**) and (+)-hypoxallene (**53**).[23] A Fischer projection of **52** as **52a** is obtained by placing the stereogenic axis into the projection plane (xy plane) as illustrated in **52b**. A small rotational increment around the allenic axis in either direction will disturb the alignment of the ligand bonds with the xy and yz planes.

More specifically, the allene in diagram **52b** is rotated to the extent of 45° as shown. As a consequence of this rotation, both hydrogen ligands are now positioned below the projection plane (here the xy plane), while the remaining ligands B and CH_2OH are located above that plane and are biased laterally with respect to the yz plane as seen in **52c** and **52d**.

As customary, the ligands below the xy plane become Fischer-chain members and are denoted vertically, while the lateral bias of the supraplanar ligands is reflected in the Fischer projection as illustrated in **52e**. The option to change the Fischer chain members can always be realized by *two* substitutions at the orthogonal axis. Such a change converts **52e** to **52a**. The enforced uniformity greatly facilitates comparisons of similar structures as illustrated by allenols **52f**−**57**.

5. EPILOG

To scientists, proficient graphic communication should be a paramount priority because it supports an overarching ambition: to delineate information that precisely and unambiguously reflects reality, to present molecular architecture as uncomplicated as possible, and to facilitate pattern recognition and pattern memory. Rudy Baum[24] may very well be correct when he says that "Chemistry is the most rigorous science, making it a priori difficult to communicate." This communication problem may have a special reason. Precise graphic formulation of reality, the lifeblood of information management in chemistry, is intimately associated with a predicament clearly spelled out by the mathematician Kline:[25] "That one can draw pictures to represent what one is thinking about in geometry has its drawbacks. One is prone to confuse the abstract concept with the picture and to accept unconsciously properties of the picture." The tools summarized here are expressly designed to allow accurate graphic communication by avoiding the danger Kline is alluding to. The object of a conventional picture is locked in Euclidean space. By the stroke of a pen we can now lift this restriction in a chemical diagram and implicitly reveal only geometric relationships for the entirety or any part of the object. Alternatively, we can enforce the topographic realm, inherently present in a picture, not only for the entire object but also selectively for any of its components. To aid us in the acceptance of this paradigm shift we should perhaps turn for support to the American painter Jasper Johns, who said: "Draw an object. Do something to it. Do something else to it."

REFERENCES AND NOTES

(1) This paper is dedicated to the memory of Professor George Buechi whose life and work has touched many of us and who ardently supported of the concepts described herein.

(2) The thoughts presented here have been discussed with numerous colleagues whose encouragement and constructive comments are gratefully acknowledged.

(3) The understanding of the terms *geometry* and *topography* is of importance and has been emphasized repeatedly. The *chirality* (orientability in Euclidean space) of a figure is a *geometric* property, whereas the *chirality sense* (orientation of that figure and its algebraic sign, i.e., absolute configuration) is a *topographical* one, see: Prelog, V.; Helmchen, G. Basic Principles of the CIP−System and Proposals for a Revision. *Angew. Chem., Int. Ed. Engl*. **1982**, *21*, 567−583.

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