ORIGINAL PAPER

Stereoisograms for three-membered heterocycles: III. *R/S*-stereodescriptors for characterizing the *RS*-stereogenic aspect of absolute configuration

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Abstract The stereoisogram approach presumes the presence of three pairs of attributes, i.e., chirality/achirality, *RS*-stereogenicity/*RS*-astereogenicity, and sclerality/asclerality, in contrast to the modern stereochemistry which presumes the presence of a single pair of chirality/achirality. From this viewpoint of the stereoisogram approach, the scope and limitations of *R/S*-stereodescriptors of the Cahn–Ingold–Prelog (CIP) system are discussed, where oxirane derivatives are used as probes. In particular, correlation diagrams of stereoisograms are used to comprehend the global and local symmetries of oxirane derivatives. Thereby, *R/S*-stereodescriptors of the CIP system are found to specify local symmetries at each positions of an oxirane derivative, so that the global symmetry of the oxirane derivative requires the other types of descriptors proposed in Part II of this series (R_a/S_a-descriptors and *Z/E*-descriptors). A correlation diagram of each position clarifies that *R/S*-stereodescriptors characterize the *RS*-stereogenic aspect of absolute configuration in the specification of local symmetries, but by no means the chiral aspect of absolute configuration. In other words, a pair of *R/S*-stereodescriptors is assigned to a pair of *RS*-diastereomers, not to a pair of enantiomers. This fact stems from the misleading foundation of the modern stereochemistry that it presumes a pair of chirality/achirality as a single pair of attributes. The pair of *R/S*-stereodescriptors originally assigned to a pair of *RS*-diastereomers should be interpreted subsidiarily to characterize the corresponding pair of enantiomers, where the concept of *chirality faithfulness* is necessary. Chirality-unfaithful cases are discussed by means of stereoisograms. Exceptional cases in the practices of the modern stereochemistry, e.g., pseudoasymmetry and 'geometric enantiomers', are discussed in a rational fashion according to the stereoisogram approach.

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1 Introduction

The global chirality or achirality of a given molecule is presumed to be characterized by a set of *R/S*-stereodescriptors due to the Cahn–Ingold–Prelog (CIP) system [1, 2]. For example, *meso*-tartaric acid is referred to by the name (*2R,3S*)-tartaric acid, where the set of *R/S*-stereodescriptors (*2R,3S*) is regarded as representing the global chirality or achirality. However, the set of *R/S*-stereodescriptors (*2R,3S*) does not directly characterize the global achirality of *meso*-tartaric acid, because each of the labels *2R* and *3S* is presumed to represent the local chirality of the carbon at 2- or 3-position. In fact, the achirality of *meso*-tartaric acid is indirectly represented by the compensation of the independent labels *2R* and *3S*.

The stereoisogram approach developed by the author [3,4] has demonstrated that there are three aspects of absolute configuration, i.e., the chiral aspect, the *RS*-stereogenic aspect, and the scleral aspect [5]. One of the important conclusions derived by the stereoisogram approach is that an *R/S*-stereodescriptor of the CIP system characterizes the *RS*-stereogenic aspect but not the chiral aspect of absolute configuration. This means that the state-of-the-art situations of the CIP system described in the preceding paragraph should be reexamined from the viewpoint of the stereoisogram approach, because only the chiral aspect of absolute configuration is presumed in the CIP system as well as in the theoretical foundations of organic stereochemistry.

In Part II of this series, the global symmetry of a promolecule derived from an oxirane skeleton has been discussed in term of the stereoisogram approach. As Part III of this series, the present paper deals with the local symmetries of oxirane derivatives. The assignment of *R/S*-stereodescriptors will be discussed in terms of the stereoisogram approach, where the global symmetry of an oxirane derivative and the local symmetries of its ring carbons are treated by means of correlation diagrams of stereoisograms, which have been developed to characterize binuclear and uninuclear promolecules [6–8].

2 Formulation of local symmetries by the stereoisogram approach

2.1 Global symmetry of oxirane derivatives

According to Part II of this series, the *RS*-stereogenic aspect of the global symmetry of a given oxirane derivative is characterized by the combination of an R_a/S_a-stereodescriptor and a *Z/E*-descriptor.

For example, *trans*-2,3-dimethyloxiranes (**1** and **$\overline{1}$**) shown in Fig. 1 (A = CH$_3$ and B = H) construct a stereoisogram of type I, which consists of a quadruplet of promolecules, i.e., **1** as a reference promolecule, **$\overline{1}$** as its enantiomer, **1$'$** (= **$\overline{1}$**) as its *RS*-diastereomer, and **$\overline{1}^{'}$** (= **1**) as its holantimer. The label 'R_a' is assigned to the reference promolecule **1**, while the counterpart label 'S_a' is assigned to its *RS*-diastereomer **1$'$** (=**$\overline{1}$**). Remember
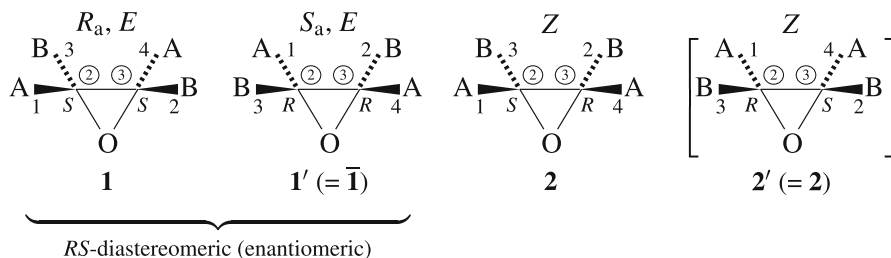
Fig. 1 Oxiranes with A^2B^2. The *RS*-stereogenic aspect of the global symmetry of each derivative is characterized by the combination of an R_a/S_a-stereodescriptor and a *Z/E*-descriptor. The *RS*-stereogenic aspect of the local symmetry of each ring carbon is characterized by an *R/S*-stereodescriptor

that a pair of stereodescriptors 'R_a/S_a' is assigned to a pair of *RS*-diastereomers, i.e., $\mathbf{1}/\mathbf{1'}$, but not to a pair of enantiomers, i.e., $\mathbf{1}/\overline{\mathbf{1}}$. Because this case is chirality-faithful, the label 'S_a' is interpreted to give to its enantiomer $\overline{\mathbf{1}}$ (= $\mathbf{1'}$). Thereby, the *RS*-stereogenic aspect of the global symmetry can be linked with the chiral aspect of the global symmetry.

On the other hand, *cis*-2,3-dimethyloxirane (**2**) shown in Fig. 1 (A = CH_3 and B = H) construct a stereoisogram of type IV, which consists of a quadruplet of pro-molecules i.e., **2** as a reference promolecule, $\overline{\mathbf{2}}$ (= **2**) as its enantiomer, $\mathbf{2'}$ (= **2**) as its *RS*-diastereomer, and $\overline{\mathbf{2}}'$ (= **2**) as its holantimer. Note that these four promolecules are identical with one another. Because of type IV, **2** is not labelled by R_a/S_a-stereodescriptors.

The *cis/trans*-isomerism of 2,3-dimethyloxiranes are determined by *Z/E*-descriptors according to Part II of this series. Note that the conversion of **1** into **2** (or into $\mathbf{2'}$) can be regarded as an epimerization at the 3-position (or the 2-position).

2.2 Local symmetries of oxirane derivatives

The *R/S*-stereodescriptors of the CIP system have been misleadingly regarded as specifying the local chirality of a molecule [1,2], although the CIP system gives precedence to stereogenicity over local chirality as stated by Helmchen [9]. This is because the stereogenicity connotes chirality in the CIP system, so that the 'stereogenic units' of the CIP system are subdivided into 'chirality units' (concerning enantiomers) and 'pseudoasymmetric units' (concerning diastereomers).

In contrast, the stereoisogram approach [3,4] recognizes that the *R/S*-stereodescriptors specify the *RS*-stereogenic aspect, not to specify the chiral aspect of the local symmetry of a promolecule [5]. As a result, a pair of *R/S*-stereodescriptors is assigned to a pair of *RS*-diastereomers, not to a pair of enantiomers.

For the purpose to obtain a priority sequence for the proligands at the 2-position of the *trans*-oxirane derivative (**1**), a hierarchical digraph is drawn as shown in Fig. 2, where each proligand is surrounded by an ellipse and labelled by p and q (chiral proligands) as well as A and B (achiral proligands, A = CH_3 and B = H). Thereby, the order of precedence of the proligands is established to be p > q > A > B. The assignment of an *R/S*-stereodescriptor '*S*' is confirmed by drawing the corresponding Fischer-type projection ($\mathbf{1}_{2f}$).
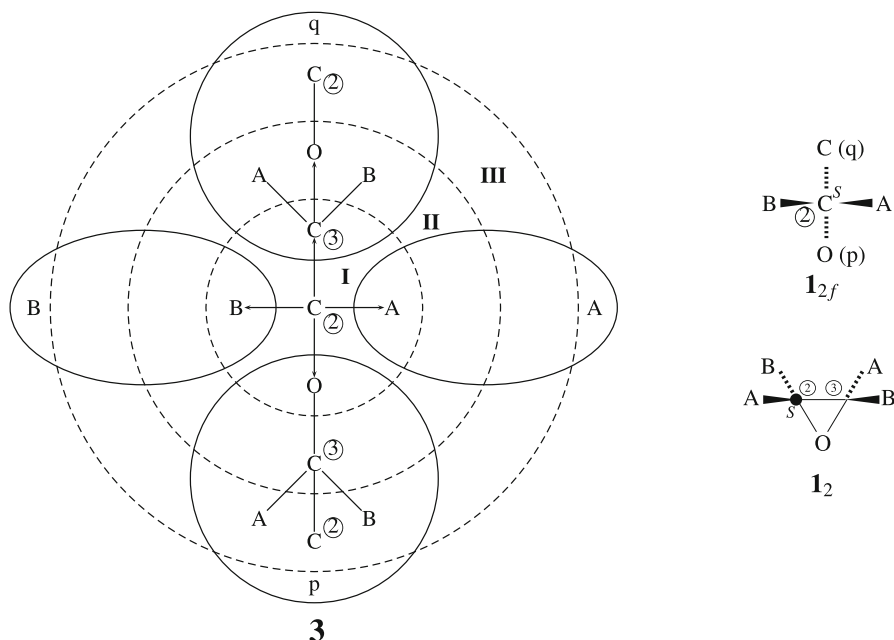
Fig. 2 Priority sequence for the proligands at the 2-position of an oxirane derivative (**1**) with A^2B^2, where a hierarchical digraph (**3**) is used to establish the order of precedence of the proligands (p > q > A > B) in the assignment of an *R/S*-stereodescriptor to the Fischer-type projection ($\mathbf{1}_{2f}$) or to the wedged projection ($\mathbf{1}_2$)

To compare the local symmetry with the global symmetry, the wedged projection ($\mathbf{1}_2$) is devised as an alternative expression, where a solid circle represents the 2-position to be examined.

2.3 Stereoisograms for characterizing local symmetries

The pairwise behavior of *R/S*-stereodescriptors is demonstrated by drawing the corresponding stereoisogram. For example, a stereoisogram of an oxirane with A^2B^2 at the 2-position is shown in Fig. 3a, where the Fischer-type projections are adopted. As found by Fig. 3a, a pair of *R/S*-stereodescriptors ('*S*' and '*R*') is assigned to a pair of *RS*-diastereomers $\mathbf{1}_{2f}$ and $\mathbf{2}'_{2f}$, where the 2-position of the *trans*-oxirane **1** is correlated to the 2-position of the *cis*-oxirane **2**. On the same line, a pair of *R/S*-stereodescriptors ('*R*' and '*S*') is assigned to a pair of *RS*-diastereomers $\overline{\mathbf{1}}_{2f}$ and $\overline{\mathbf{2}}'_{2f}$. It should be noted that, strictly speaking, the label '*S*' of the reference promolecule $\mathbf{1}_{2f}$ is not assigned to be paired with the label '*R*' of its enantiomeric promolecule $\overline{\mathbf{1}}_{2f}$. The pairing of the label '*S*' of $\mathbf{1}_{2f}$ and the label '*R*' of $\overline{\mathbf{1}}_{2f}$ stems from the chirality faithfulness of the stereoisogram of type I (Fig. 3a).

The correlation between the 2-position of the *trans*-oxirane **1** and the 2-position of the *cis*-oxirane **2** is more clearly demonstrated by drawing the corresponding stereoisogram of wedged projection (Fig. 3b), where the 2-position is labelled by a sold circle.
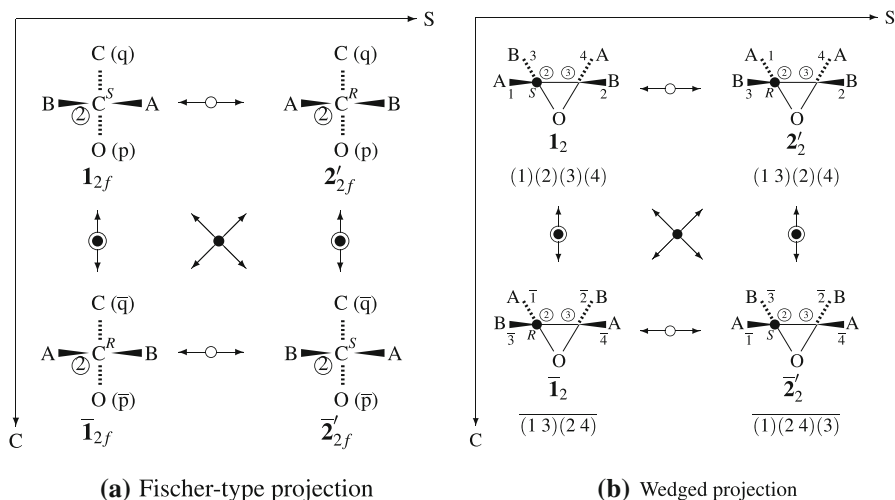
(a) Fischer-type projection   **(b)** Wedged projection

Fig. 3 Stereoisograms of an oxirane with A^2B^2 at the 2-position: **a** Fischer-type projection and **b** wedged projection. These two stereoisograms are equivalent to exhibit a type-III property

The epimerization at the 2-position of $\mathbf{1}_2$ generates its epimer $\mathbf{2}'_2$, where the epimerization process is controlled by the *RS*-permutation $(1\ 3)(2)(4)$. The relationship between $\mathbf{1}_2$ and $\mathbf{2}'_2$ is an *RS*-diastereomeric relationship. As a result, a pair of *R/S*-stereodescriptors ('*S*' and '*R*') is assigned to a pair of *RS*-diastereomers $\mathbf{1}_2$ and $\mathbf{2}'_2$. Note that the epimerization results in the *cis/trans*-isomerization of 2,3-dimethyloxiranes ($A = CH_3$ and $B = H$).

In contrast, the reflection at the 2-position of $\mathbf{1}_2$ results in the whole reflection, which generates its enantiomer $\overline{\mathbf{1}}_2$. The reflection is controlled by the reflection operation represented by $\overline{(1\ 3)(2\ 4)}$. Although an *R/S*-stereodescriptors ('*R*') is assigned to the 2-position of $\overline{\mathbf{1}}_2$, this assignment is independent of the assignment of $\mathbf{1}_2$, so that the direct pairing of the label '*R*' of $\overline{\mathbf{1}}_2$ and the label '*S*' of $\mathbf{1}_2$ is not permitted. In fact, a pair of *R/S*-stereodescriptors ('*R*' and '*S*') is assigned to a pair of *RS*-diastereomers $\overline{\mathbf{1}}_2$ and $\overline{\mathbf{2}}'_2$ by considering an epimerization at the 2-position. Because this case is chirality-faithful, the pairing of the label '*R*' of $\overline{\mathbf{1}}_2$ and the label '*S*' of $\mathbf{1}_2$ is interpreted to be be permitted subsidiarily.

It is worthwhile to examine the details of a ligand-reflection operation for the purpose of rationalizing the holantimeric relationship between $\mathbf{1}_2$ and $\overline{\mathbf{2}}'_2$. The ligand-reflection operation is represented by a product of cycles $\overline{(1)(2\ 4)(3)}$. The application of the 1-cycle $\overline{(1)}$ (or $\overline{(3)}$) to the proligand A (or B) generates $\overline{A}$ (or $\overline{B}$) which is identical with the original proligand A (or B). The application of the 2-cycle $\overline{(2\ 4)}$ to the remaining unit [C]–O–C(AB)–[C] (due to the ring cleavage of $\mathbf{1}_2$) generates another unit [C]–O–C(BA)–[C] (due to the ring cleavage of $\overline{\mathbf{2}}'_2$ with a reflected pair of A and B), where we use $\overline{A} = A$ and $\overline{B} = B$. As a result, the ligand-reflection operation converts the reference promolecule $\mathbf{1}_2$ into its holantimer $\overline{\mathbf{2}}'_2$.

When we place $I \sim (1)(2)(3)(4)$, $\sigma_{v(2)} \sim \overline{(1\ 3)(2\ 4)}$, $\widetilde{e}\widetilde{\sigma}_{v(2)} \sim (1\ 3)(2)(4)$, and $\widehat{eI} \sim \overline{(1)(2\ 4)(3)}$, we are able to construct a stereoisomeric group:

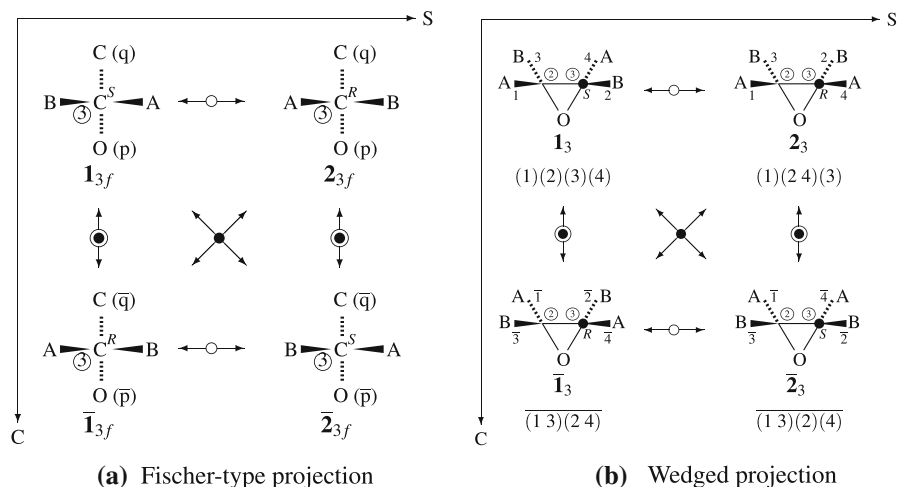**(a)** Fischer-type projection   **(b)** Wedged projection

Fig. 4 Stereoisograms of an oxirane with A^2B^2 at the 3-position: **a** Fischer-type projection and **b** wedged projection. These two stereoisograms are equivalent to exhibit a type-III property

$$\widetilde{\mathbf{C}}_{s\widetilde{e}\widehat{I}} = \left\{ I, \sigma_{v(2)}, \widetilde{e}\widetilde{\sigma}_{v(2)}, \widetilde{e}\widehat{I} \right\}, \tag{1}$$

which is a subgroup of the stereoisomeric group $\widetilde{\mathbf{C}}_{2v\widetilde{\sigma}\widehat{I}}$ (cf. Part II of this series). The type-III stereoisogram of Fig. 3 means that the reference promolecule $\mathbf{1}_2$ belongs to $\mathbf{C}_1$ ($= \{I\}$), which is a subgroup of $\widetilde{\mathbf{C}}_{s\widetilde{e}\widehat{I}}$, if we restrict our consideration to the stereoisomeric group $\widetilde{\mathbf{C}}_{s\widetilde{e}\widehat{I}}$.

The local symmetry at the 3-position is determined by examining the stereoisogram of Fischer-type projection (Fig. 4a) or of wedged projection (Fig. 4b). By means of Fig. 4a, a pair of R/S-stereodescriptors 'S' and 'R' (or 'R' and 'S') is assigned to a pair of RS-diastereomers $\mathbf{1}_{3f}$ and $\mathbf{2}_{3f}$ (or $\overline{\mathbf{1}}_{3f}$ and $\overline{\mathbf{2}}_{3f}$).

By means of Fig. 4b, on the same line, a pair of R/S-stereodescriptors 'S' and 'R' (or 'R' and 'S') is assigned to a pair of RS-diastereomers $\mathbf{1}_3$ and $\mathbf{2}_3$ (or $\overline{\mathbf{1}}_3$ and $\overline{\mathbf{2}}_3$). It should be noted that, strictly speaking, the label 'S' of the reference promolecule $\mathbf{1}_3$ is not assigned to be paired with the label 'R' of its enantiomeric promolecule $\overline{\mathbf{1}}_3$. The pairing of the label 'S' of $\mathbf{1}_3$ and the label 'R' of $\overline{\mathbf{1}}_3$ stems from the chirality faithfulness of the stereoisogram of type I (Fig. 4b).

When we place $I \sim (1)(2)(3)(4)$, $\sigma_{v(2)} \sim \overline{(1\ 3)(2\ 4)}$, $\widetilde{e}I \sim (1)(2\ 4)(3)$, and $\widetilde{e}\sigma_{v(2)} \sim \overline{(1\ 3)(2)(4)}$, we are able to construct a stereoisomeric group:

$$\widetilde{\mathbf{C}}_{s\widetilde{e}} = \left\{ I, \sigma_{v(2)}, \widetilde{e}I, \widetilde{e}\sigma_{v(2)} \right\}, \tag{2}$$

which is a subgroup of the stereoisomeric group $\widetilde{\mathbf{C}}_{2v\widetilde{\sigma}\widehat{I}}$ (cf. Part II of this series). The type-III stereoisogram of Fig. 4 means that the reference promolecule $\mathbf{1}_3$ belongs to $\mathbf{C}_1$ ($= \{I\}$), which is a subgroup of $\widetilde{\mathbf{C}}_{s\widetilde{e}}$, if we restrict our consideration to the stereoisomeric group $\widetilde{\mathbf{C}}_{s\widetilde{e}}$.

2.4 Correlation diagrams of stereoisograms

Stereoisograms for characterizing the global symmetries of a set of stereoisomers are integrated to give a correlation diagram. Stereoisograms for characterizing the local symmetries of the set of stereoisomers at a common substitution position are integrated to give a correlation diagram. These correlation diagrams are gathered to show the total symmetrical features [6–8, 10].

Let us first construct a correlation diagram (Fig. 5a) for characterizing the global symmetries of a set of stereoisomers derived from **1**. The type-I stereoisogram labelled by #1 consists of the reference promolecule **1**, its enantiomer $\overline{\mathbf{1}}$, its *RS*-diastereomer **1**′, and its holantimer $\overline{\mathbf{1}}'$, where self-holantimeric relationships indicate $\mathbf{1} = \overline{\mathbf{1}}'$ and $\overline{\mathbf{1}} = \mathbf{1}'$. The type-IV stereoisogram labelled by #2 consists of the reference promolecule **2**, its enantiomer $\overline{\mathbf{2}}$, its *RS*-diastereomer **2**′, and its holantimer $\overline{\mathbf{2}}'$, all of which represent the same promolecule as indicated by equality symbols. The two stereoisograms #1 and #2 are arranged to give the correlation diagram for characterizing the global symmetries, as found in Fig. 5a.
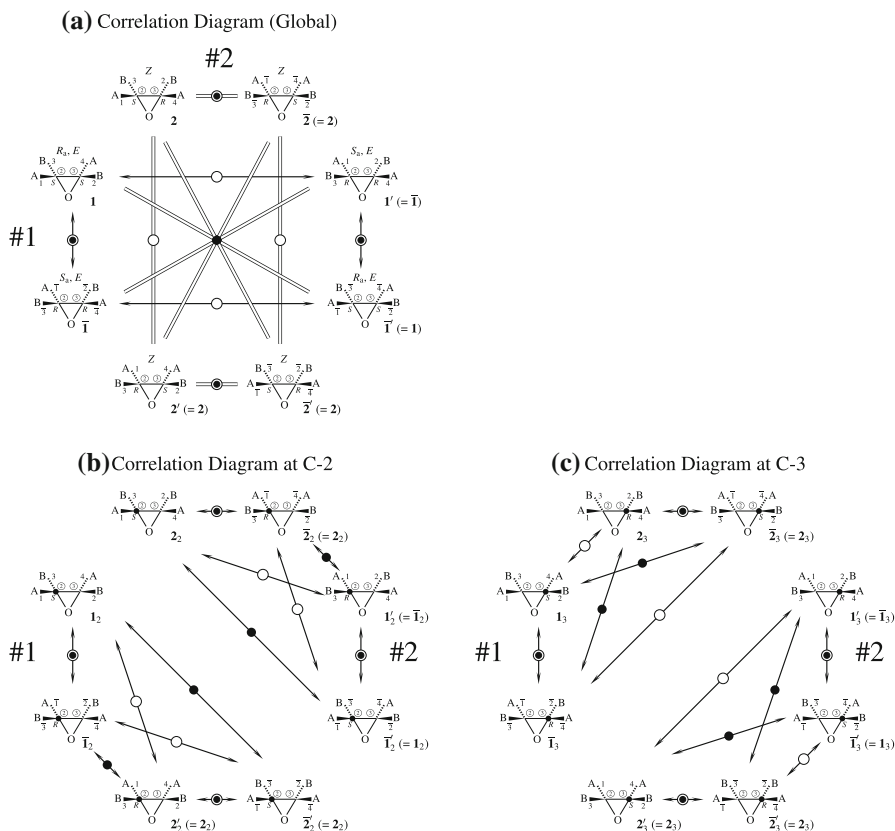

Fig. 5 Correlation diagrams of stereoisograms for oxiranes with A^2B^2. **a** For global symmetry (#1 of type I and #2 of type IV); **b** For 2-position (#1 of type III and #2 of type III); and **c** For 3-position (#1 of type III and #2 of type III)

Let us next construct a correlation diagram (Fig. 5b) for characterizing the local symmetries at the 2-positions. The type-III stereoisogram labelled by #1 consists of the reference promolecule $\mathbf{1}_2$, its enantiomer $\overline{\mathbf{1}}_2$, its *RS*-diastereomer $\mathbf{2}'_2$, and its holantimer $\overline{\mathbf{2}}'_2$. The stereoisogram #1 is identical with the stereoisogram shown in Fig. 3b. The other type-III stereoisogram labelled by #2 consists of the reference promolecule $\mathbf{1}'_2$, its enantiomer $\overline{\mathbf{1}}'_2$, its *RS*-diastereomer $\mathbf{2}_2$, and its holantimer $\overline{\mathbf{2}}_2$. The stereoisograms #1 and #2 in Fig. 5b coalesce with each other.

Let us finally construct a correlation diagram (Fig. 5c) for characterizing the local symmetries at the 3-positions. The type-III stereoisogram labelled by #1 consists of the reference promolecule $\mathbf{1}_3$, its enantiomer $\overline{\mathbf{1}}_3$, its *RS*-diastereomer $\mathbf{2}_3$, and its holantimer $\overline{\mathbf{2}}_3$. The stereoisogram #1 is identical with the stereoisogram shown in Fig. 4b. The other type-III stereoisogram labelled by #2 consists of the reference promolecule $\mathbf{1}'_3$, its enantiomer $\overline{\mathbf{1}}'_3$, its *RS*-diastereomer $\mathbf{2}'_3$, and its holantimer $\overline{\mathbf{2}}'_3$. The stereoisograms #1 and #2 in Fig. 5b coalesce with each other.

3 Examples of correlation diagrams

3.1 Oxiranes with ABXY

Among oxirane promolecules with ABXY, Fig. 6 lists a set of stereoisomers which have achiral proligands A and B at the 2-position and achiral proligands X and Y at the 3-position.

For the purpose of characterizing the global symmetries of the promolecules, let us construct correlation diagrams by starting from the set of stereoisomers. The promolecule $\mathbf{4}$ constructs a type-I stereoisogram (#1 of Fig. 7a), which contains $\mathbf{4}$ as a reference promolecule, $\overline{\mathbf{4}}$ as its enantiomer, $\mathbf{4}'$ ($= \overline{\mathbf{4}}$) as its *RS*-diastereomer, and $\overline{\mathbf{4}}'$ ($=\mathbf{4}$) as its holantimer. According to Part II of this series, a pair of R_a/S_a-descriptors is assigned to a pair of *RS*-diastereomers $\mathbf{4}$ ('R_a') and $\mathbf{4}'$ ('S_a') or another pair of *RS*-diastereomers $\overline{\mathbf{4}}$ ('S_a') and $\overline{\mathbf{4}}'$ ('R_a'). Because this case ($\mathbf{4}' = \overline{\mathbf{4}}$) is chirality-faithful, a pair of R_a/S_a-descriptors is interpreted to be assigned to a pair of enantiomers $\mathbf{4}$ ('R_a') and $\overline{\mathbf{4}}$ ('S_a'). Note that the priority sequence is presumed to be $(A > B) \gg (X > Y)$.
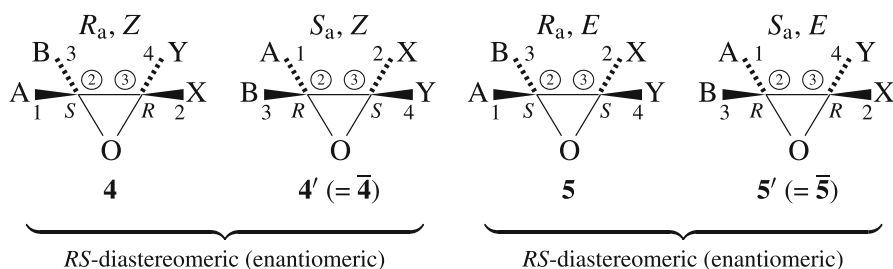

Fig. 6 Oxiranes with ABXY. The *RS*-stereogenic aspect of the global symmetry of each derivative is characterized by the combination of an R_a/S_a-stereodescriptor and a *Z/E*-descriptor. The *RS*-stereogenic aspect of the local symmetry of each ring carbon is characterized by an *R/S*-stereodescriptor. The priority sequence is presumed to be $(A > B) \gg (X > Y)$
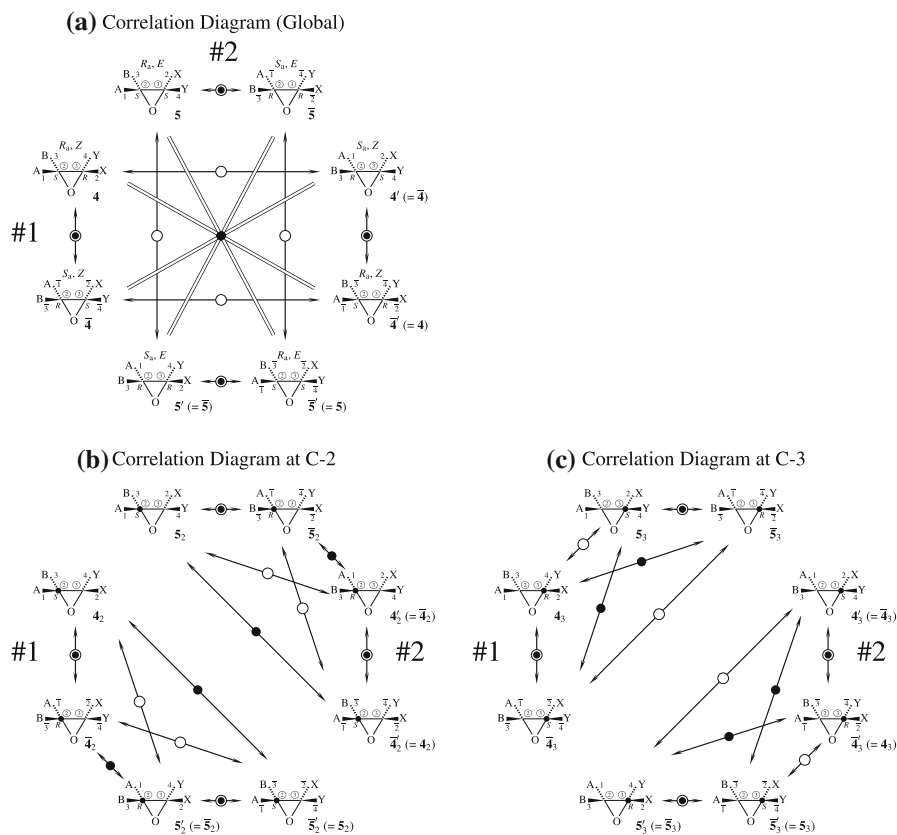
Fig. 7 Correlation diagrams of stereoisograms for oxiranes with ABXY. **a** For global symmetry (#1 of type I and #2 of type I); **b** For 2-position (#1 of type III and #2 of type III); and **c** For 3-position (#1 of type III and #2 of type III)

On the other hand, the promolecule **5** constructs another type-I stereoisogram (#2 of Fig. 7a), which contains **5** as a reference promolecule, $\overline{\mathbf{5}}$ as its enantiomer, $\mathbf{5}'$ ($= \overline{\mathbf{5}}$) as its *RS*-diastereomer, and $\overline{\mathbf{5}}'$ ($= \mathbf{5}$) as its holantimer. A pair of R_a/S_a-descriptors is assigned to a pair of *RS*-diastereomers **5** ('R_a') and $\mathbf{5}'$ ('S_a') or another pair of *RS*-diastereomers $\overline{\mathbf{5}}$ ('S_a') and $\overline{\mathbf{5}}'$ ('R_a'). Because this case ($\mathbf{5}' = \overline{\mathbf{5}}$) is chirality-faithful, a pair of R_a/S_a-descriptors is interpreted to be assigned to a pair of enantiomers **5** ('R_a') and $\overline{\mathbf{5}}$ ('S_a').

As for *Z/E*-descriptors, a pair of *Z/E*-descriptors is assigned to a pair of *cis/trans*-isomers **4** ('*Z*') and **5** ('*E*'). These labels for oxirane derivatives are assigned in a similar way to the *Z/E*-descriptors of ethylene derivatives according to Part II of this series. Note that the priority sequence is presumed to be $(A > B) \gg (X > Y)$.

The local symmetries at the 2-positions are examined by means of a correlation diagram shown in Fig. 7b. The type-III stereoisogram labelled by #1 consists of the reference promolecule $\mathbf{4}_2$, its enantiomer $\overline{\mathbf{4}}_2$, its *RS*-diastereomer $\mathbf{5}'_2$, and its holantimer $\overline{\mathbf{5}}'_2$. The other type-III stereoisogram labelled by #2 consists of the reference

promolecule $\mathbf{4}'_2$, its enantiomer $\overline{\mathbf{4}}'_2$, its *RS*-diastereomer $\mathbf{5}_2$, and its holantimer $\overline{\mathbf{5}}_2$. The stereoisograms #1 and #2 in Fig. 7b coalesce with each other.

The *RS*-stereogenic aspect of the local symmetries at the 2-positions of the respective promolecules appearing in the stereoisogram #1 of Fig. 7b relates to the assignment of *R/S*-stereodescriptors at the 2-positions. The 2-position attached by A and B in **4** is determined to have the label '*S*' by examining the reference promolecule $\mathbf{4}_2$, while the 2-position in $\mathbf{5}'$ is determined to have label '*R*' by examining the corresponding *RS*-diastereomer $\mathbf{5}'_2$. Thus, a pair of *R/S*-stereodescriptors is assigned to a pair of *RS*-diastereomers $\mathbf{4}_2$ ('*S*') and $\mathbf{5}'_2$ ('*R*'). Note that the priority sequence is presumed to be ring O > ring C > A > B. In a similar way, a pair of *R/S*-stereodescriptors is assigned to a pair of *RS*-diastereomers $\overline{\mathbf{4}}_2$ ('*R*') and $\overline{\mathbf{5}}'_2$ ('*S*'). Because the type-III stereoisogram #1 of Fig. 7b exhibits chirality faithfulness, the pair of *R/S*-stereodescriptors, which is originally assigned to a pair of *RS*-diastereomers $\mathbf{4}_2$ ('*S*') and $\mathbf{5}'_2$ ('*R*'), is interpreted to characterize a pair of enantiomers $\mathbf{4}_2$ ('*S*') and $\overline{\mathbf{4}}_2$ ('*R*').

The local symmetries at the 3-positions are characterized by drawing a correlation diagram shown in Fig. 7c. The type-III stereoisogram labelled by #1 consists of the reference promolecule $\mathbf{4}_3$, its enantiomer $\overline{\mathbf{4}}_3$, its *RS*-diastereomer $\mathbf{5}_3$, and its holantimer $\overline{\mathbf{5}}_3$. The other type-III stereoisogram labelled by #2 consists of the reference promolecule $\mathbf{4}'_3$, its enantiomer $\overline{\mathbf{4}}'_3$, its *RS*-diastereomer $\mathbf{5}'_3$, and its holantimer $\overline{\mathbf{5}}'_3$. The stereoisograms #1 and #2 in Fig. 7b coalesce with each other.

In a similar way to the 2-positions, the assignment of *R/S*-stereodescriptors at the 3-positions depends upon the *RS*-stereogenic aspect of the local symmetries at the 3-positions of the respective promolecules appearing in the stereoisogram #1 of Fig. 7c. The 3-position attached by X and Y in **4** is determined to have the label '*R*' by examining the reference promolecule $\mathbf{4}_3$, while the 3-position in **5** is determined to have label '*S*' by examining the corresponding *RS*-diastereomer $\mathbf{5}_3$. Note that the priority sequence is presumed to be ring O > ring C > X > Y. Thus, a pair of *R/S*-stereodescriptors is assigned to a pair of *RS*-diastereomers $\mathbf{4}_3$ ('*R*') and $\mathbf{5}_3$ ('*S*'). In a similar way, a pair of *R/S*-stereodescriptors is assigned to a pair of *RS*-diastereomers $\overline{\mathbf{4}}_3$ ('*S*') and $\overline{\mathbf{5}}_3$ ('*R*'). Because the type-III stereoisogram #1 of Fig. 7c exhibits chirality faithfulness, the pair of *R/S*-stereodescriptors, which is originally assigned to a pair of *RS*-diastereomers $\mathbf{4}_3$ ('*R*') and $\mathbf{5}_3$ ('*S*'), is interpreted to characterize a pair of enantiomers $\mathbf{4}_3$ ('*R*') and $\overline{\mathbf{4}}_3$ ('*S*').

3.2 Oxiranes with ABXp or ABX$\overline{\text{p}}$

Stereoisomers which have achiral proligands A and B at the 2-position as well as an achiral proligand X and a chiral proligand p (or $\overline{\text{p}}$) at the 3-position are categorized into *Z*- and *E*-isomers according to Part II of this series. A quadruplet of *Z*-isomers constructs a type-III stereoisogram (Fig. 8a), which contains the reference promolecule **6**, its enantiomer $\overline{\mathbf{6}}$, its *RS*-diastereomer $\mathbf{6}'$, and its holantimer $\overline{\mathbf{6}}'$. A quadruplet of *E*-isomers constructs a type-III stereoisogram (Fig. 8b), which contains the reference promolecule **7**, its enantiomer $\overline{\mathbf{7}}$, its *RS*-diastereomer $\mathbf{7}'$, and its holantimer $\overline{\mathbf{7}}'$.

After the priority sequence is presumed to be (A > B) $\gg$ (X > p) or (A > B) $\gg$ (X > $\overline{\text{p}}$), a pair of R_a/S_a-descriptors is assigned to each pair of *RS*-diastereomers

(a) *Z*-oxiranes   **(b)** *E*-oxiranes
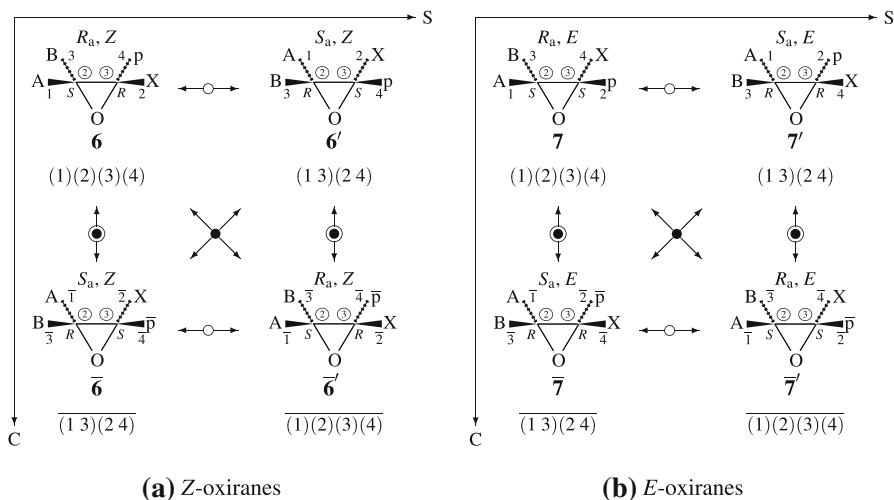
Fig. 8 Stereoisograms for representing the global symmetries of oxiranes, which have achiral proligands A and B at the 2-position as well as an achiral proligand X and a chiral proligand p (or $\bar{\text{p}}$) at the 3-position. **a** *Z*-oxiranes and **b** *E*-oxiranes. These two stereoisograms exhibit type-III properties. The priority sequence is presumed to be $(A > B) \gg (X > p)$

according to Part II: $\mathbf{6}/\mathbf{6'}$ ('R_a'/'S_a') and $\overline{\mathbf{6}}/\overline{\mathbf{6}}'$ ('S_a'/'R_a') for the *Z*-series; as well as $\mathbf{7}/\mathbf{7'}$ ('R_a'/'S_a') and $\overline{\mathbf{7}}/\overline{\mathbf{7}}'$ ('S_a'/'R_a') for the *E*-series.

The two stereoisograms of type III (Fig. 8a, b) are combined to give a correlation diagram for characterizing the global symmetries, as shown in Fig. 9a. The stereoisogram labelled by #1 is identical with Fig. 8a, while the other stereoisogram labelled by #2 is identical with Fig. 8b.

By drawing a correlation diagram shown in Fig. 9b, we are able to discuss the local symmetries at the 2-positions. The type-III stereoisogram labelled by #1 consists of a quadruplet of promolecules, i.e., the reference promolecule $\mathbf{6}_2$, its enantiomer $\overline{\mathbf{6}}_2$, its *RS*-diastereomer $\mathbf{7}'_2$, and its holantimer $\overline{\mathbf{7}}'_2$. The other type-III stereoisogram labelled by #2 consists of a quadruplet of promolecules, i.e., the reference promolecule $\mathbf{6}'_2$, its enantiomer $\overline{\mathbf{6}}'_2$, its *RS*-diastereomer $\mathbf{7}_2$, and its holantimer $\overline{\mathbf{7}}_2$.

The assignment of *R/S*-stereodescriptors at the 2-positions is accomplished by examining the *RS*-stereogenic aspect of the local symmetries at the 2-positions of the respective promolecules appearing in the stereoisogram #1 of Fig. 9b. The 2-position attached by A and B in $\mathbf{6}$ is determined to have the label '*S*' by examining the reference promolecule $\mathbf{6}_2$, while the 2-position in $\mathbf{7'}$ is determined to have label '*R*' by examining the corresponding *RS*-diastereomer $\mathbf{7}'_2$. Note that the priority sequence is presumed to be ring O > ring C > A > B. Thus, a pair of *R/S*-stereodescriptors is assigned to a pair of *RS*-diastereomers $\mathbf{6}_2$ ('*S*') and $\mathbf{7}'_2$ ('*R*'). In a similar way, a pair of *R/S*-stereodescriptors is assigned to a pair of *RS*-diastereomers $\overline{\mathbf{6}}_2$ ('*R*') and $\overline{\mathbf{7}}'_2$ ('*S*'). Because the type-III stereoisogram #1 of Fig. 9b exhibits chirality faithfulness, the pair of *R/S*-stereodescriptors, which is originally assigned to a pair of *RS*-diastereomers $\mathbf{6}_2$ ('*S*') and $\mathbf{7}'_2$ ('*R*'), is interpreted to characterize a pair of enantiomers $\mathbf{6}_2$ ('*S*') and $\overline{\mathbf{6}}_2$ ('*R*').

(a) Correlation Diagram (Global)

(b) Correlation Diagram at C-2   **(c)** Correlation Diagram at C-3

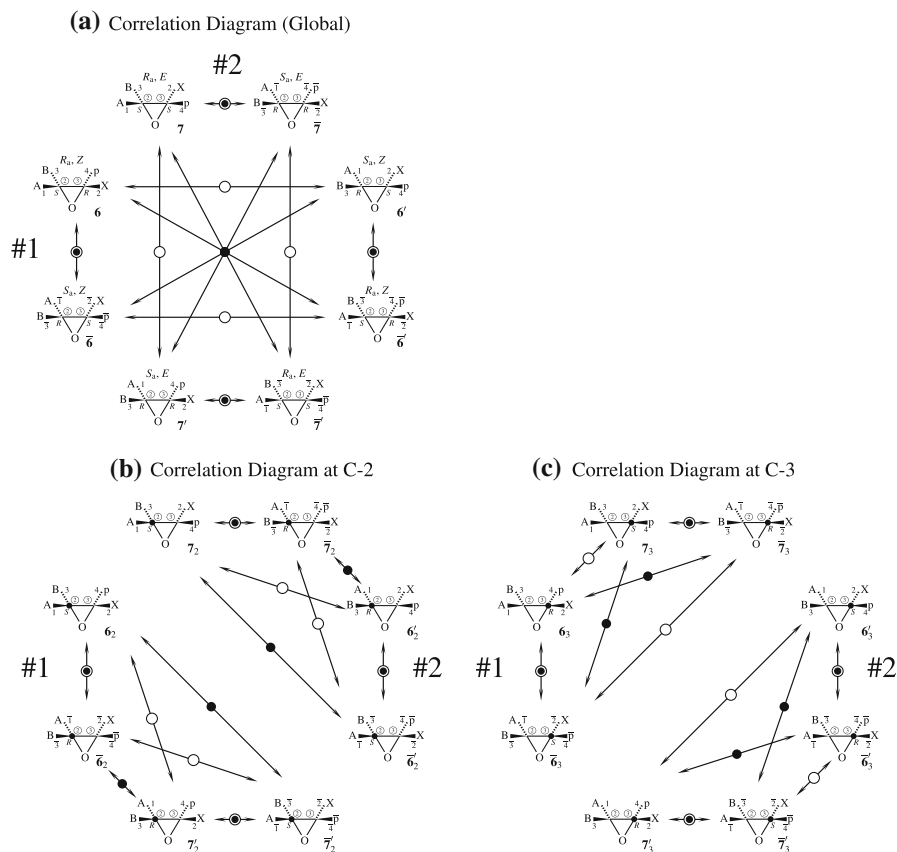**Fig. 9** Correlation diagrams of stereoisograms for oxiranes with ABXp or ABXp̄. **a** For global symmetry (#1 of type III and #2 of type III); **b** For 2-position (#1 of type III and #2 of type III); and **c** For 3-position (#1 of type III and #2 of type III)

As for the stereoisogram #2 of Fig. 9b, a pair of *R/S*-stereodescriptors is assigned to each pair of *RS*-diastereomers. The result is interpreted to be given to a pair of enantiomers because of chirality faithfulness.

The local symmetries at the 3-positions are characterized by drawing a correlation diagram shown in Fig. 9c. The type-III stereoisogram labelled by #1 consists of the reference promolecule $\mathbf{6}_3$, its enantiomer $\overline{\mathbf{6}}_3$, its *RS*-diastereomer $\mathbf{7}_3$, and its holantimer $\overline{\mathbf{7}}_3$. The other type-III stereoisogram labelled by #2 consists of the reference promolecule $\mathbf{6}'_3$, its enantiomer $\overline{\mathbf{6}}'_3$, its *RS*-diastereomer $\mathbf{7}'_3$, and its holantimer $\overline{\mathbf{7}}'_3$.

The assignment of *R/S*-descriptors at the 3-positions depends upon the *RS*-stereogenic aspect of the local symmetries at the 3-positions of the respective promolecules appearing in the stereoisogram #1 of Fig. 9c. Note that the priority sequence is presumed to be ring O > ring C > X > p (or p̄). Thus, a pair of *R/S*-stereodescriptors is assigned to a pair of *RS*-diastereomers $\mathbf{6}_3$ ('*R*') and $\mathbf{7}_3$ ('*S*'). In a similar way, a pair of *R/S*-stereodescriptors is assigned to a pair of *RS*-diastereomers $\overline{\mathbf{6}}_3$ ('*S*') and $\overline{\mathbf{7}}_3$ ('*R*'). Because the type-III stereoisogram #1 of Fig. 9c exhibits chirality faithfulness, the pair

of *R/S*-stereodescriptors, which is originally assigned to a pair of *RS*-diastereomers **6**$_3$ ('*R*') and **7**$_3$ ('*S*'), is interpreted to characterize a pair of enantiomers **6**$_3$ ('*R*') and $\overline{\textbf{6}}_3$ ('*S*').

As for the stereoisogram #2 of Fig. 9c, a pair of *R/S*-stereodescriptors is assigned to each pair of *RS*-diastereomers. The result is interpreted to be given to a pair of enantiomers because of chirality faithfulness.

3.3 Oxiranes with ABp$\overline{p}$

Among oxirane promolecules with ABp$\overline{p}$, Fig. 10 shows a type-III stereoisogram in which each promolecule has achiral proligands A and B at the 2-position and an enantiomeric pair of chiral proligands p and $\overline{p}$ at the 3-position.

This case exhibits alternation of chirality faithfulness, as discussed in Part II of this series. If we adopts the priority sequence (A > B) $\gg$ (p > $\overline{p}$), the assignment of R_a/S_a-descriptors exhibits chirality faithfulness. Thereby, a pair of R_a/S_a-descriptors, which is originally assigned to a pair of *RS*-diastereomers **8** ('R_a') and **8**′ ('S_a'), is interpreted to be given to a pair of enantiomers **8** ('R_a') and $\overline{\textbf{8}}$ ('S_a'). On the other hand, if we adopts the priority sequence (p > $\overline{p}$) $\gg$ (A > B), the assignment of R_a/S_a-descriptors exhibits chirality unfaithfulness. Thereby, a pair of R_a/S_a-descriptors, which is originally assigned to a pair of *RS*-diastereomers **8** ('S_a') and **8**′ ('r_a'), cannot be interpreted to be given to a pair of enantiomers **8** ('S_a') and $\overline{\textbf{8}}$ ('S_a'). Because of chirality unfaithfulness, the lowercase labels 'r_a/s_a' are used to specify global symmetries.
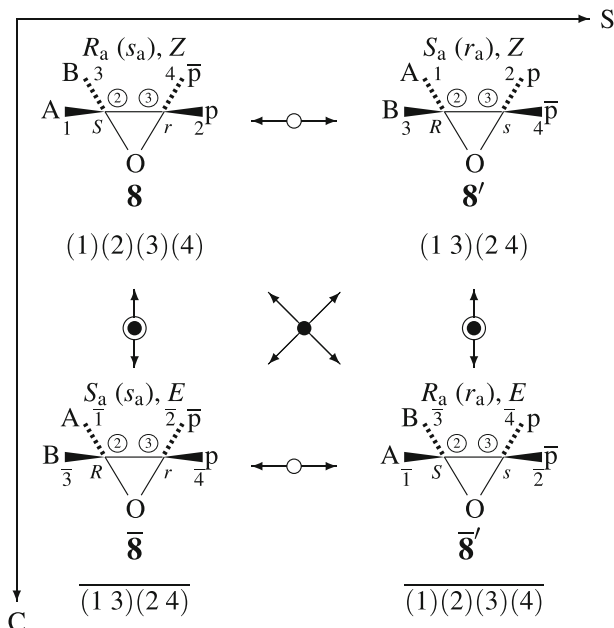

Fig. 10 Stereoisogram for representing the global symmetry of an oxirane of ABp$\overline{p}$, which has achiral proligands A and B at the 2-position as well as a pair of chiral proligands p and $\overline{p}$ at the 3-position. This stereoisogram exhibits a type-III property

(a) Correlation Diagram (Global)

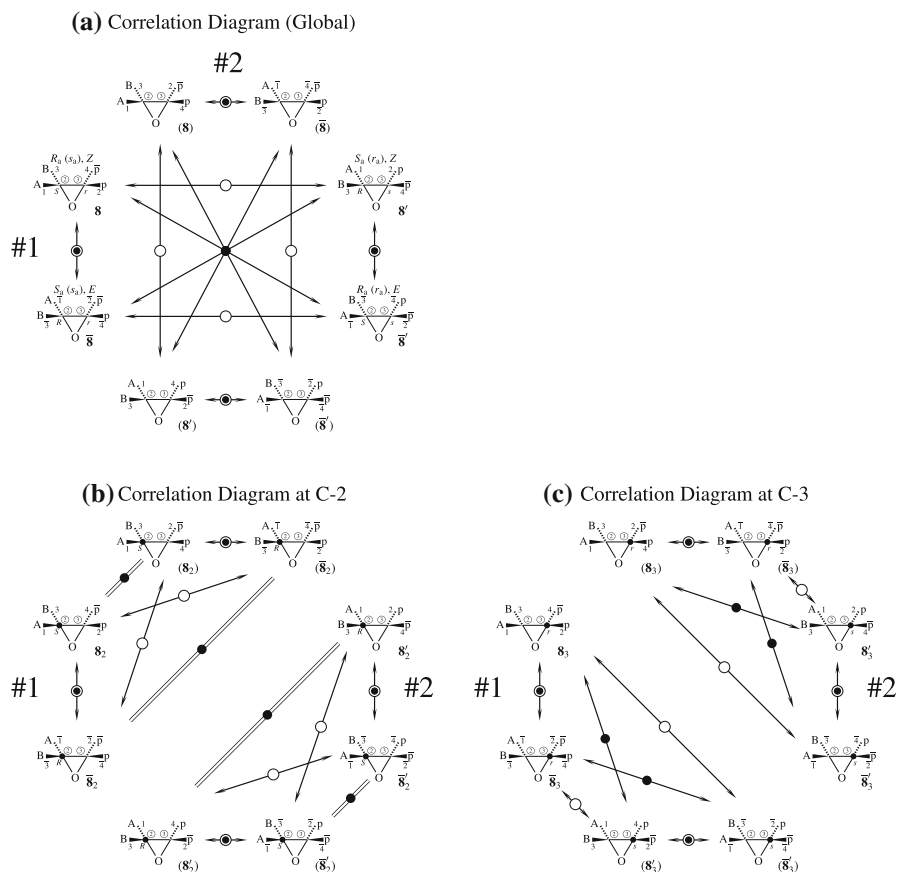**(b)** Correlation Diagram at C-2   **(c)** Correlation Diagram at C-3

Fig. 11 Correlation diagrams of stereoisograms for oxiranes with ABpp̄. **a** For global symmetry (#1 of type III and #2 of type III); **b** For 2-position (#1 of type III and #2 of type III); and **c** For 3-position (#1 of type III and #2 of type III)

The stereoisogram of Fig. 10 exhibits another specific feature, as discussed in Part II of this series, Thus, **8** ('*Z*') and **8̄** ('*E*') is enantiomeric and at the same time *Z/E*-isomeric (diastereomeric, conventionally speaking). This point will be discussed later.

The type-III stereoisogram (Fig. 10) is duplicated to give a correlation diagram for characterizing the global symmetries, as shown in Fig. 11a. Both the stereoisograms labelled by #1 and #2 are based on the stereoisogram shown in Fig. 10.

The local symmetries at the 2-positions are discussed by drawing a correlation diagram shown in Fig. 11b, which consist of two type-I stereoisograms. The type-I stereoisogram labelled by #1 consists of a quadruplet of promolecules, i.e., the reference promolecule $\mathbf{8}_2$, its enantiomer $\overline{\mathbf{8}}_2$, its *RS*-diastereomer '$(\overline{\mathbf{8}}_2)$', and its holantimer '$(\mathbf{8}_2)$'. The other type-I stereoisogram labelled by #2 consists of a quadruplet of promolecules, i.e., the reference promolecule $\mathbf{8}_2'$, its enantiomer $\overline{\mathbf{8}}_2'$, its *RS*-diastereomer '$(\overline{\mathbf{8}}_2')$', and its holantimer '$(\mathbf{8}_2')$'.

The stereoisogram #1 of Fig. 11b indicates that a pair of *R/S*-stereodescriptors is assigned to a pair of *RS*-diastereomers $\mathbf{8}_2$ ('*S*') and '$(\overline{\mathbf{8}}_2)$' ('*R*'), where the

RS-diastereomer '($\overline{\bf 8}_2$)' is identical with the enantiomer $\overline{\bf 8}_2$. This means that this case is chirality-faithful. Note that the priority sequence is presumed to be ring O > ring C > A > B. In a similar way, the stereoisogram #2 of Fig. 11b indicates that a pair of *R/S*-stereodescriptors is assigned to a pair of *RS*-diastereomers ${\bf 8}_2'$ ('*R*') and '($\overline{\bf 8}_2'$)' ('*S*'), where the *RS*-diastereomer '($\overline{\bf 8}_2'$)' is identical with the enantiomer $\overline{\bf 8}_2'$. The result is interpreted to be given to a pair of enantiomers because of chirality faithfulness.

The local symmetries at the 3-positions are characterized by drawing a correlation diagram shown in Fig. 11c. By examining the type-III stereoisogram labelled by #1, a pair of *R/S*-stereodescriptors is assigned to a pair of *RS*-diastereomers ${\bf 8}_3$ ('*r*') and '($\overline{\bf 8}_3'$)' ('*s*'). Note that the priority sequence is presumed to be ring O > ring C > p > $\overline{\rm p}$. In a similar way, a pair of *R/S*-stereodescriptors is assigned to a pair of *RS*-diastereomers $\overline{\bf 8}_3$ ('*r*') and '($\overline{\bf 8}_3'$)' ('*s*'). The type-III stereoisogram #1 of Fig. 11c exhibits chirality unfaithfulness, so that the lowercase labels are used.

By examining the type-III stereoisogram labelled by #2 in Fig. 11c, a pair of *R/S*-stereodescriptors is assigned to a pair of *RS*-diastereomers ${\bf 8}_3'$ ('*s*') and '($\overline{\bf 8}_3$)' ('*r*'). In a similar way, a pair of *R/S*-stereodescriptors is assigned to a pair of *RS*-diastereomers $\overline{\bf 8}_3'$ ('*s*') and '(${\bf 8}_3$)' ('*r*'). The type-III stereoisogram #2 of Fig. 11c exhibits chirality unfaithfulness, so that the lowercase labels are used.

3.4 Oxiranes with $A^2 p\overline{p}$

Among oxirane promolecules with $A^2 p\overline{p}$, Fig. 12 lists a set of stereoisomers which have a pair of an achiral proligand A and a chiral proligand p at the 2-position as well as a pair of an achiral proligand A and a chiral proligand $\overline{\rm p}$ at the 3-position.

The promolecules of *E*-isomers (**9** and **9**' ($= \overline{\bf 9}$)) and those of *Z*-isomers (**10** and **10**') listed in Fig. 12 are characterized by a correlation diagram shown in Fig. 13a, which demonstrates global symmetries.

First, a quadruplet of *E*-isomers constructs a type-I stereoisogram (#1 of Fig. 13a), which contains the reference promolecule **9**, its enantiomer $\overline{\bf 9}$, its *RS*-diastereomer **9**' ($= \overline{\bf 9}$), and its holantimer $\overline{\bf 9}'$ ($= {\bf 9}$). After the priority sequence is presumed to be (A > p) $\gg$ (A > $\overline{\rm p}$), a pair of R_a/S_a-descriptors is assigned to each pair of *RS*-diastereomers
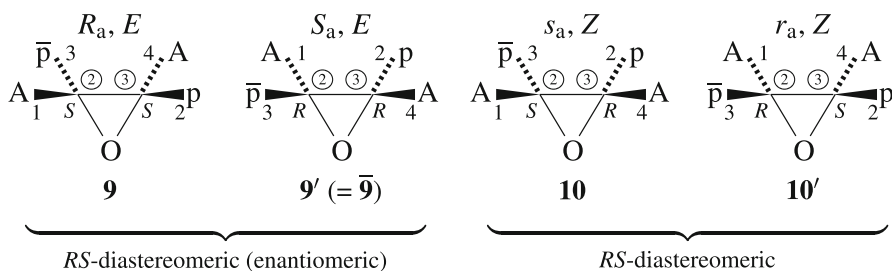

Fig. 12 Oxiranes with $A^2 p\overline{p}$. The *RS*-stereogenic aspect of the global symmetry of each derivative is characterized by the combination of an R_a/S_a-stereodescriptor and a *Z/E*-descriptor. The *RS*-stereogenic aspect of the local symmetry of each ring carbon is characterized by an *R/S*-stereodescriptor

(a) Correlation Diagram (Global)

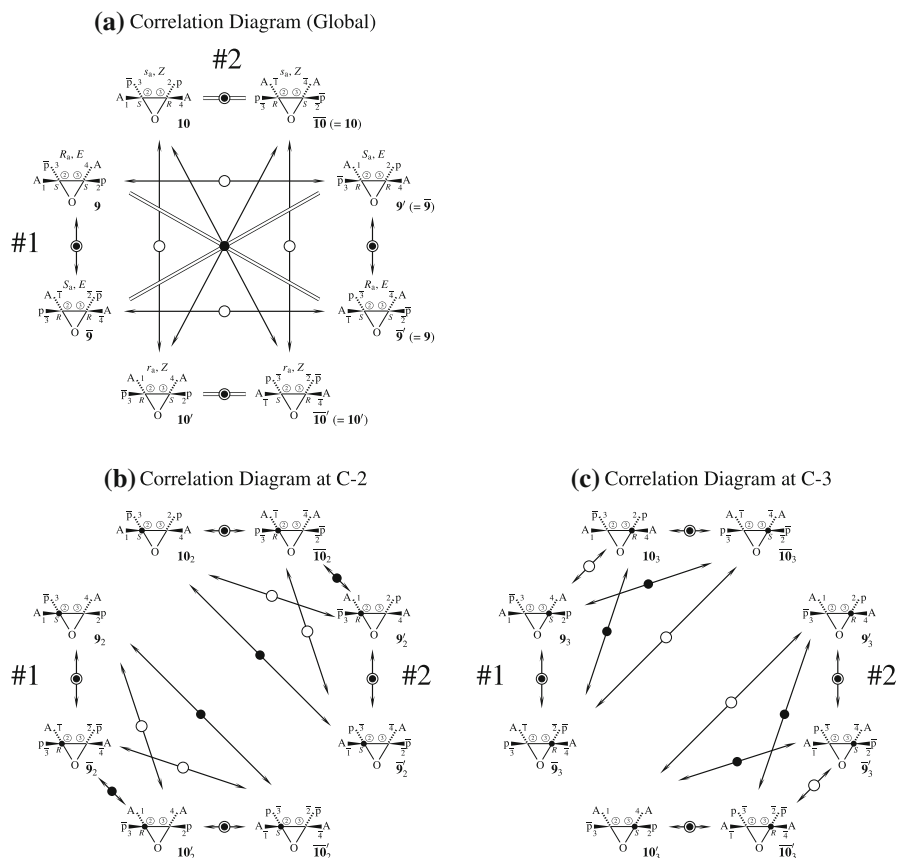**(b)** Correlation Diagram at C-2   **(c)** Correlation Diagram at C-3

Fig. 13 Correlation diagrams of stereoisograms for oxiranes with $A^2p\bar{p}$. **a** For global symmetry (#1 of type I and #2 of type V); **b** For 2-position (#1 of type III and #2 of type III); and **c** For 3-position (#1 of type III and #2 of type III)

according to Part II. By examining the stereoisogram #1 of Fig. 13a, the following assignments are obtained: **9**/**9**′ ('R_a'/'S_a') and $\overline{\mathbf{9}}$/$\overline{\mathbf{9}}'$ ('S_a'/'R_a') for the E-isomers. The assignments exhibit chirality faithfulness.

Second, a quadruplet of Z-isomers constructs a type-V stereoisogram (#2 of Fig. 13a), which contains the reference promolecule **10**, its enantiomer $\overline{\mathbf{10}}$ (= **10**), its RS-diastereomer **10**′, and its holantimer $\overline{\mathbf{10}}'$ (=**10**′). By examining the stereoisogram #2 of Fig. 13a, the following assignments are obtained: **10**/**10**′ ('s_a'/'r_a') for the Z-isomers. Because of chirality unfaithfulness, the lowercase labels are used. Note that **10** and **10**′ are achiral. They exhibit an extended pseudoasymmetric feature, although an oxirane skeleton is considered in place of a carbon center of a usual pseudoasymmetric case.

By drawing a correlation diagram shown in Fig. 13b, we are able to discuss the local symmetries at the 2-positions. The type-III stereoisogram labelled by #1 consists of a quadruplet of promolecules, i.e., the reference promolecule $\mathbf{9}_2$, its enantiomer $\overline{\mathbf{9}}_2$, its RS-diastereomer $\mathbf{10}'_2$, and its holantimer $\overline{\mathbf{10}}'_2$. The other type-III stereoisogram labelled

by #2 consists of a quadruplet of promolecules, i.e., the reference promolecule $\mathbf{9}'_2$, its enantiomer $\overline{\mathbf{9}}'_2$, its RS-diastereomer $\mathbf{10}_2$, and its holantimer $\overline{\mathbf{10}}_2$.

The 2-position attached by A and $\overline{\mathrm{p}}$ in $\mathbf{9}$ is determined to have the label 'S' by examining the reference promolecule $\mathbf{9}_2$ of the stereoisogram #1 of Fig. 13b, while the 2-position in $\mathbf{10}'$ is determined to have label 'R' by examining the corresponding RS-diastereomer $\mathbf{10}'_2$. Note that the priority sequence is presumed to be ring O > ring C > A > $\overline{\mathrm{p}}$. Thus, a pair of R/S-stereodescriptors is assigned to a pair of RS-diastereomers $\mathbf{9}_2$ ('S') and $\mathbf{10}'_2$ ('R'). In a similar way, a pair of R/S-stereodescriptors is assigned to a pair of RS-diastereomers $\overline{\mathbf{9}}_2$ ('R') and $\overline{\mathbf{10}}'_2$ ('S'). Note that the priority sequence is presumed to be ring O > ring C > A > p. Because the type-III stereoisogram #1 of Fig. 9b exhibits chirality faithfulness, the pair of R/S-stereodescriptors, which is originally assigned to a pair of RS-diastereomers $\mathbf{9}_2$ ('S') and $\mathbf{10}'_2$ ('R'), is interpreted to characterize a pair of enantiomers $\mathbf{9}_2$ ('S') and $\overline{\mathbf{9}}_2$ ('R').

As for the stereoisogram #2 of Fig. 13b, a pair of R/S-stereodescriptors is assigned to each pair of RS-diastereomers in a similar way to the stereoisogram #1 of Fig. 13b. The result is interpreted to be given to a pair of enantiomers because of chirality faithfulness.

The local symmetries at the 3-positions are characterized by drawing a correlation diagram shown in Fig. 13c. The type-III stereoisogram labelled by #1 consists of the reference promolecule $\mathbf{9}_3$, its enantiomer $\overline{\mathbf{9}}_3$, its RS-diastereomer $\mathbf{10}_3$, and its holantimer $\overline{\mathbf{10}}_3$. The other type-III stereoisogram labelled by #2 consists of the reference promolecule $\mathbf{9}'_3$, its enantiomer $\overline{\mathbf{9}}'_3$, its RS-diastereomer $\mathbf{10}'_3$, and its holantimer $\overline{\mathbf{10}}'_3$.

The assignment of R/S-stereodescriptors at the 3-positions is based on the RS-stereogenic aspect of the local symmetries at the 3-positions of the respective promolecules appearing in the stereoisogram #1 of Fig. 13c. Note that the priority sequence is presumed to be ring O > ring C > A > p. Thus, a pair of R/S-stereodescriptors is assigned to a pair of RS-diastereomers $\mathbf{9}_3$ ('S') and $\mathbf{10}_3$ ('R'). In a similar way, a pair of R/S-stereodescriptors is assigned to a pair of RS-diastereomers $\overline{\mathbf{9}}_3$ ('R') and $\overline{\mathbf{10}}_3$ ('S'). Note that the priority sequence is presumed to be ring O > ring C > A > $\overline{\mathrm{p}}$. Because the type-III stereoisogram #1 of Fig. 13c exhibits chirality faithfulness, the pair of R/S-stereodescriptors, which is originally assigned to a pair of RS-diastereomers $\mathbf{9}_3$ ('S') and $\mathbf{10}_3$ ('R'), is interpreted to characterize a pair of enantiomers $\mathbf{9}_3$ ('S') and $\overline{\mathbf{9}}_3$ ('R').

As for the stereoisogram #2 of Fig. 13c, a pair of R/S-stereodescriptors is assigned to each pair of RS-diastereomers in a similar way to the stereoisogram labelled by #1. The result is interpreted to be given to a pair of enantiomers because of chirality faithfulness.

3.5 Oxiranes with A^2p^2 or $A^2\overline{p}^2$

Among oxirane promolecules with A^2p^2 or $A^2\overline{p}^2$, let us examine a set of stereoisomers which have a pair of an achiral proligand A and a chiral proligand p (or $\overline{\mathrm{p}}$) at the 2-position as well as another pair of A and p (or A and $\overline{\mathrm{p}}$) at the 3-position.

The correlation diagram for characterizing global symmetries is shown in Fig. 14a. A quadruplet of E-isomers constructs a type-III stereoisogram (#1 of Fig. 14a), which
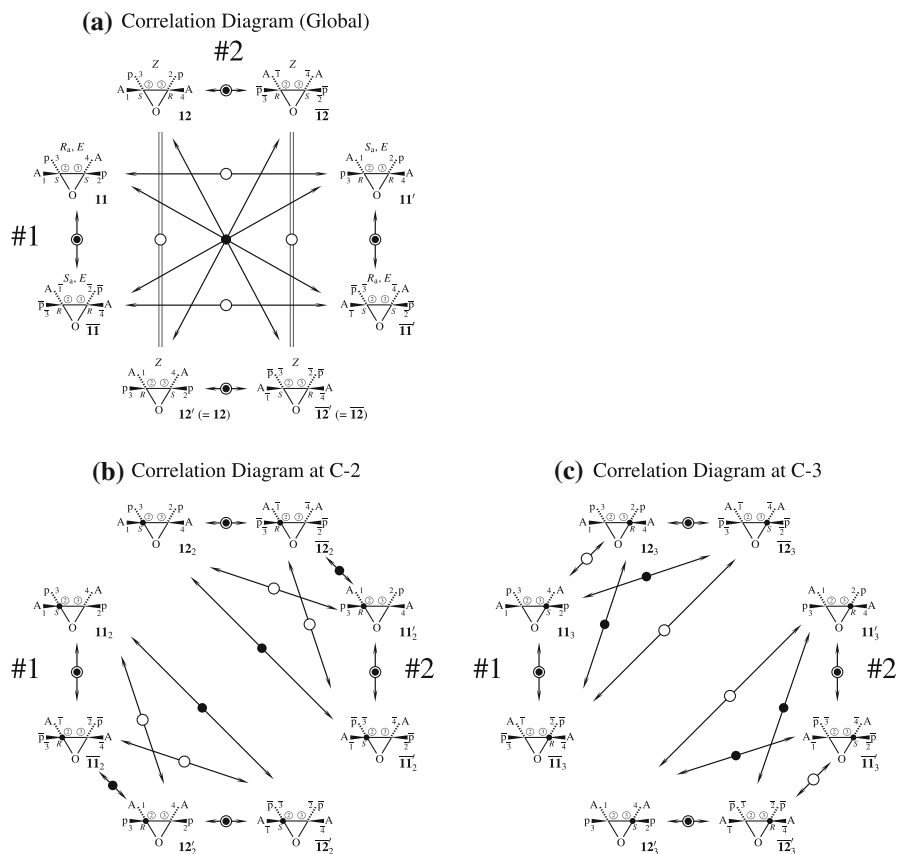
(a) Correlation Diagram (Global)

(b) Correlation Diagram at C-2   **(c)** Correlation Diagram at C-3

Fig. 14 Correlation diagrams of stereoisograms for oxiranes with A^2p^2 or $A^2\bar{p}^2$. **a** For global symmetry (#1 of type III and #2 of type II); **b** For 2-position (#1 of type III and #2 of type III); and **c** For 3-position (#1 of type III and #2 of type III)

contains the reference promolecule **11**, its enantiomer $\overline{\bf 11}$, its *RS*-diastereomer **11**′, and its holantimer $\overline{\bf 11}'$. After the priority sequence is presumed to be $(A > p) \gg (A > p)$, a pair of R_a/S_a-descriptors is assigned to each pair of *RS*-diastereomers according to Part II. The assigned labels are attached at the tops of the respective promolecules.

On the other hand, a quadruplet of *Z*-isomers constructs a type-II stereoisogram (#2 of Fig. 14a), which contains the reference promolecule **12**, its enantiomer $\overline{\bf 12}$, its *RS*-diastereomer **12**′ (= **12**), and its holantimer $\overline{\bf 12}'$ (= $\overline{\bf 12}$). Because of type II, R_a/S_a-descriptors are not assigned to the *Z*-isomers. Note that **12** and $\overline{\bf 12}$ can be identified by specifying the label 'Z'.

By drawing a correlation diagram shown in Fig. 14b, we are able to discuss the local symmetries at the 2-positions. The type-III stereoisogram labelled by #1 consists of a quadruplet of promolecules, i.e., the reference promolecule $\mathbf{11}_2$, its enantiomer $\overline{\bf 11}_2$, its *RS*-diastereomer $\mathbf{12}'_2$, and its holantimer $\overline{\bf 12}'_2$. A pair of *R/S*-stereodescriptors is assigned to a pair of *RS*-diastereomers $\mathbf{11}_2$ ('*S*') and $\mathbf{12}'_2$ ('*R*'), because the priority sequence is presumed to be ring O > ring C > A > p. In a similar way, a pair of

R/S-stereodescriptors is assigned to a pair of RS-diastereomers $\overline{\mathbf{11}}_2$ ('R') and $\overline{\mathbf{12}}'_2$ ('S'), where the priority sequence is presumed to be ring O > ring C > A > $\bar{\mathrm{p}}$. Because the type-III stereoisogram #1 of Fig. 14b exhibits chirality faithfulness, the pair of R/S-stereodescriptors, which is originally assigned to a pair of RS-diastereomers $\mathbf{11}_2$ ('S') and $\mathbf{12}'_2$ ('R'), is interpreted to characterize a pair of enantiomers $\mathbf{11}_2$ ('S') and $\overline{\mathbf{11}}_2$ ('R').

The other type-III stereoisogram labelled by #2 in Fig. 14b consists of a quadruplet of promolecules, i.e., the reference promolecule $\mathbf{11}'_2$, its enantiomer $\overline{\mathbf{11}}'_2$, its RS-diastereomer $\mathbf{12}_2$, and its holantimer $\overline{\mathbf{12}}_2$. A pair of R/S-stereodescriptors is assigned to each pair of RS-diastereomers in a similar way to the stereoisogram #1 of Fig. 13b. The result is interpreted to be given to a pair of enantiomers because of chirality faithfulness.

The local symmetries at the 3-positions are characterized by drawing a correlation diagram shown in Fig. 14c. Because $\mathbf{11}_3$ is superimposable onto $\mathbf{11}_2$ by a two-fold vertical rotation (C_2), the assignment of R/S-stereodescriptors to the 3-positions can be conducted in a similar way to the above-mentioned practices for the 2-positions.

4 Discussions

4.1 *cis/trans*-isomerism

When we obey the CIP system, *trans*-2,3-dimethyloxiranes ($\mathbf{1}$ and $\overline{\mathbf{1}}$) shown in Fig. 1 (A = CH_3 and B = H) are respectively referred to by using the labels '($2S,3S$)' and '($2R,3R$)', while *cis*-2,3-dimethyloxirane ($\mathbf{2}$) shown in Fig. 1 (A = CH_3 and B = H) is referred to by using the label '($2R,3S$)'. Thus, the *trans*-configurations of $\mathbf{1}$ and $\overline{\mathbf{1}}$ as well as the *cis*-configuration of $\mathbf{2}$ are not directly but subsidiarily specified by the CIP system.

On the other hand, the *Z/E*-descriptors proposed in Part II of this series directly specify the *cis/trans*-isomerism. As shown in Fig. 5a, the label E is assigned to *trans*-2,3-dimethyloxiranes ($\mathbf{1}$ and $\overline{\mathbf{1}}$); and the label Z is assigned to *cis*-2,3-dimethyloxirane ($\mathbf{2}$).

4.2 Lowercase labels 'r' and 's'

Prelog and Helmchen [11] has originally stated that "because enantiotopic spaces can exist only in achiral stereomodels and molecules, there cannot be any pseudoasymmetry in chiral stereomodels and molecules". However, the revision of the CIP system [2,9] has finally recognized that pseudoasymmetric atoms can exist in chiral as well as achiral molecules after the introduction of 'reflection-invariant descriptors r/s'.

The stereoisogram approach succeeds the original definition of pseudoasymmetry after the formulation of type-V stereoisograms. The final definition permitting the presence of pseudoasymmetry in chiral molecules should be abandoned on the basis of the type-III stereoisograms, where lowercases labels 'r' and 's', however, are maintained under the concept of *chirality unfaithfulness* in place of the term 'reflection-invariance' [5].

Let us examine the 3-position of **8** shown in Fig. 10, where the 3-position accommodates a pair of chiral proligands p and p̄. By examining the type-III stereoisogram labelled by #1 in Fig. 11c, the pair of *R/S*-stereodescriptors assigned to the *RS*-diastereomers **8**$_3$ ('*r*') and '(**8̄**$_3'$)' ('*s*') is the same as the pair of *R/S*-stereodescriptors assigned to the pair of *RS*-diastereomers **8̄**$_3$ ('*r*') and '(**8**$_3'$)' ('*s*'). Because the holantimers **8**$_3$ ('*r*') and '(**8**$_3'$)' ('*s*') have opposite labels, the type-III stereoisogram #1 of Fig. 11c exhibits chirality unfaithfulness [5]. This means that the reference promolecule **8**$_3$ ('*r*') and its enantiomeric promolecule **8̄**$_3$ ('*r*') has the same label, so that the lowercase labels are used. Although the labels of **8**$_3$ ('*r*') and enantiomeric promolecule **8̄**$_3$ ('*r*') exhibit 'reflection invariance', this invariance is only concerned with the labels. The 3-position of **8**$_3$ is enantiotopic (in an extended fashion) to the 3-position of **8̄**$_3$ in parallel ways to the behaviors of the other type-III stereoisograms (e.g., #1 of Fig. 7c), although the latter require no lowercase labels. The term *chirality-unfaithful* demonstrates what happens, more essentially than the term 'reflection invariance' does. Remember again that a pair of *R/S*-stereodescriptors is originally assigned to a pair of *RS*-diastereomers, not to a pair of enantiomers.

4.3 Extended pseudoasymmetry

The type-V stereoisogram labelled #2 in Fig. 12a exhibits pseudoasymmetry in an extended fashion. From the viewpoint of the global symmetries, the promolecules **10** and **10'** are *RS*-diastereomeric to each other, where the oxirane units can be regarded as locally achiral skeletons in a similar way to the locally achiral central atoms of pseudoasymmetric 2,3,4-trihydroxyglutaric acids. Because of exhibiting pseudoasymmetry in an extended fashion, they are respectively labelled as S_a and r_a according to the proposal described in Part II of this series. Note that the lowercase letters are used to emphasize chirality unfaithfulness.

In contrast, such extended pseudoasymmetry as describe in the preceding paragraph cannot be detected by the CIP system. By the examination of Fig. 13b, c, a set of labels '(*S*, *R*)' is assigned to **10**; and another set of labels '(*R*, *S*)' is assigned to **10'**. The *meso*-feature can be detected by examining each sets of labels, where the intramolecular compensation is implied by the label '(*S*, *R*)' or '(*R*, *S*)' in a parallel way to the case of *meso*-tartaric acid. In contrast, the extended pseudoasymmetric feature is not deduced by comparing the set of labels '(*S*, *R*)' of **10** with the other set of labels '(*R*, *S*)' of **10'**, because **10** and **10'** are 'diastereomeric' under the conventional terminology of the modern stereochemistry. It should be noted that the label '(2*S*, 3*R*)' for **10** and the label '(2*R*, 3*S*)' for **10̄** (=**10**) coalesce each other.

4.4 Coalescence of enantiomerism and *cis/trans*-isomerism

The term 'geometric enantiomers' is used to refer to olefines which exhibit the coalescence of enantiomerism with *cis/trans*-isomerism [12,13]. This case has been discussed in terms of the stereoisogram approach [14].

A similar phenomenon appears in **8** shown in Fig. 10. The relationship between **8** and **8̄** is determined to be enantiomeric because they are interchangeable by a reflection

operation. They are characterized by a pair of R_a/S_a-descriptors (chirality-faithful) or a pair of r_a/s_a-descriptors (chirality-unfaithful). At the same time, the relationship between **8** and $\overline{\textbf{8}}$ is determined to be *cis/trans*-isomeric as indicated by a pair of *Z/E*-descriptors. Because the *cis/trans*-isomeric relationship is a kind of diastereomeric relationship according to the modern stereochemistry, this case exhibits coalescence of enantiomerism and diastereomerism. It follows that this case is a counter-example against the conventional dichotomy between enantiomers and diastereomers.

5 Conclusion

The scope and limitations of *R/S*-stereodescriptors of the Cahn–Ingold–Prelog (CIP) system are discussed in terms of the stereoisogram approach, where correlation diagrams of stereoisograms are used to comprehend the global and local symmetries by selecting oxirane derivatives as examples. Such *R/S*-stereodescriptors specify local symmetries at each positions of an oxirane derivative, so that the global symmetry of the oxirane derivative requires the other types of descriptors proposed in Part II of this series. In the specification of local symmetries, a correlation diagram of each position clarifies that a pair of *R/S*-stereodescriptors is assigned to a pair of *RS*-diastereomers, not to a pair of enantiomers. The concept of *chirality faithfulness* is necessary in order that the pair of *R/S*-stereodescriptors originally assigned to a pair of *RS*-diastereomers is translated to be applied to a pair of enantiomers. Chirality-unfaithful cases are discussed by means of stereoisograms. Exceptional cases in the conventional stereochemistry, e.g., pseudoasymmetry and 'geometric enantiomers', are discussed in a rational fashion according to the stereoisogram approach.

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