  Bull. Chem. Soc. Jpn., 60, 2067—2071 (1987)

Topological Ligand Design. III. Parent Ligand Graphs, Simple Cage Graphs, and Donor-Atomic Graphs for the Octahedral Coordination

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(Received December 23, 1986)

Various computer processes to determine all parent ligand graphs, simple cage graphs, and donor-atomic graphs for the octahedral coordination are described in order to design new sexidentate ligands. A complex ligand graph is represented by a numeral comprising of 12 figures, each of which indicates the code of a unit graph of six kinds placed on 12 edges of an octahedron. Then, 1055 parent ligand graphs, excluding chiral isomers, are selected from 6^{12} permutations of the complex ligand graphs. A simple cage graph is produced by fusing a pair of adjacent lines around every point of an octahedral graph; 102 kinds of simple cage graphs, excluding chiral isomers, have been obtained. Another more practical method for ligand design has been proposed by starting from 62 donor-atomic graphs.

Recently, the enumeration and classification of various complicated compounds have been enormously developed by the use of a graph theory and computer processing. However, such applications involving ligand design remain very few.

A ligand molecule can be considered to be a set of donor atoms joined by some carbon chains capable of forming a medium-sized chelate ring. A graph-theoretical path corresponding to such a carbon chain is called a "chelate path". One of the authors has already published a designing method for ligands using a simple ligand graph, which is defined as a set of m points and n lines representing m donor-atoms and n chelate-paths, respectively. Then, all the simple ligand graphs with $m \leqq 8$ were systematically derived and clearly documented by a numeral code of eight figures.[1]

However, a simple ligand graph cannot distinguish a ligand structure which has chelate paths branched at their carbon atoms. Thus, some modifications have been applied to the ligand graphs in order to represent all the structures of general chelating ligands.[2] Also, a complex ligand graph has been preferably adopted, which is a set of main points and sub-points connected by lines (where main points, sub-points, and lines correspond to donor atoms, carbon atoms forming chelate ring, and chemical bonds among these atoms, respectively). When a metal chelate ring is limited to five or six members, including a metal ion, each chelate path consists of two or three sub-points and three or four lines. Since no more than three chelate rings can branch at a donor atom or at a carbon atom, the maximum degree of a main point and a sub-point is three (the degree of a point is the number of lines incident on it).

Complex ligand graphs can faithfully express their original ligand structures, but they are so complicated that their systematic derivation and complete enumeration are quite difficult. In order to design all the chelate ligands for a given coordination structure, a "parent ligand graph" was defined.[2] This is a complex ligand graph to which no more sub-points nor lines can be added, i.e., highest density graphs in such coordination. Several kinds of parent ligand graphs may exist for a certain coordination structure. Then, all the other complex ligand graphs can be derived by neglecting some sub-points or by removing some lines from these parent ligand graphs.

Hence, finding all of the parent ligand graphs is a step in designing complex ligand graphs. Although the parent ligand graphs for the square planar and the tetrahedral coordinations have already been published,[2] it is difficult to obtain parent graphs for octahedral coordination by similar procedures, since four edges are incident on each vertex of an octahedron, whereas the degree of a main point cannot exceed three. Thus, the degree of each main point has to be reduced by a partial fusing of some adjacent graphs. Besides, an increasing number of donor atoms causes a much accelerated increase in the number of parent ligand graphs. But whatever difficulty may arise, designing sexidentate ligands should be achieved, since the octahedral coordination is one of the most popular and important structures in complex chemistry.

Methods

(1) Parent Ligand Graphs. Unit Graphs: In order to determine all of the parent ligand graphs for octahedral coordination, "unit graphs" of six kinds are defined. These unit graphs with direction and their own codes are shown in Fig. 1. Unconnected unit graph (0), and any unit graphs containing less than five-membered ring are omitted hereafter.

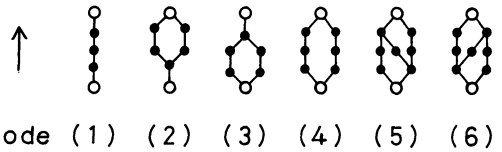

Fig. 1. Unit graphs for the parent ligand graph.

Since these unit graphs are introduced for composing the parent ligand graphs, each chelate path in these unit graphs contains three sub-points. Unit graphs (2) and (3) have directions opposite to each other. Unit graphs (5) and (6) cause an antipode relation when placed on a solid surface. The order of the unit graphs in chelate-path density is (5), (6)>(4), (3), (2)>(1).

Then, a "composite graph" is assembled by placing one of above unit graphs on every line of a donor-atomic graph with common main point each other. (A donor-atomic graph is a set of main points and lines, each of which connects a pair of main points having at least one chelate path.[2]) Next a complex ligand graph is generated when these unit graphs in a composite graph are partially fused around every vertex. As a simplified example using a terdentate ligand, a derivation of these graphs is shown in Fig. 2.

When an octahedral graph is adopted as a starting donor-atomic graph, all the complex ligand graphs derived from it have a complete cage structure, where every pair of adjacent main points is connected; they must include all the parent ligand graphs of the octahedral coordination.

In this case the fusing manner of unit graphs is uniquely definable so that the ligand molecules may have its most strainless cage structure; hence, these complex ligand graphs have one-to-one correspondence with their composite graphs. Then, the design of the complex ligand graphs may be substituted for assembling of the composite graphs.

A parent ligand graph should have the highest density as to the chelate paths; that is, it should be assembled from unit graphs of higher order as possible. Although unit graphs (5) and (6) have the highest order as to the chelate paths (both of them are parent ligand graphs of the bidentate ligand), when four such unit graphs are incident on a vertex of an octahedron, the degree of the central main point exceeds three even if they are effectively fused. Therefore, some unit graphs of the lower order are still necessary as the constituents of the parent ligand graph.

Fusing Restrictions: There are some restrictions in partially fusing the unit graphs arround a main point, subjected to the limitation of the degree of main points and sub-points, and to the steric requirements which

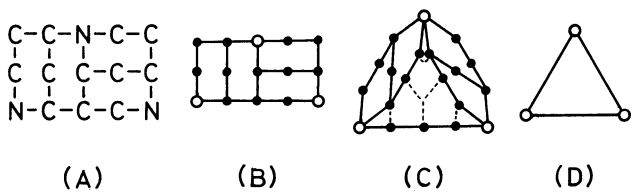

Fig. 2. Graph representations of a ligand. (A) Ligand, (B) complex ligand graph, (C) composite graph (Dotted lines indicate fusing sites.), (D) donor-atomic graph.

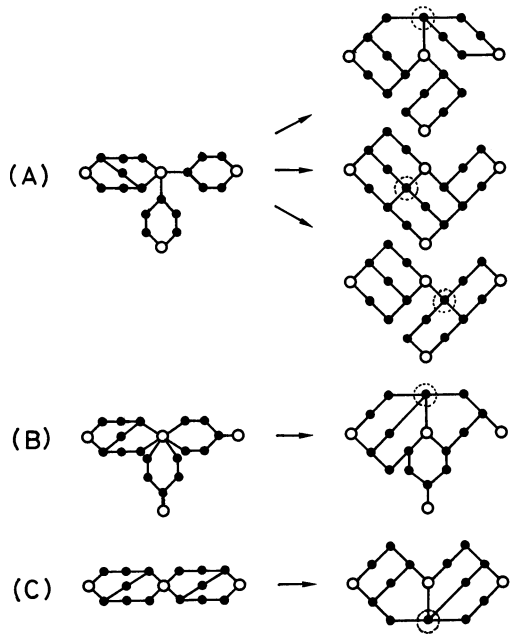

Fig. 3. Examples of impossible fusions. (A) (2)(2)(6), (B) (3)(3)(5), (C) trans (5)(5) (each dotted circle indicates over degree of a vertex.).

may be confirmed by use of molecular models.

The following fusions of unit graphs arround a main point (a vertex on an octahedron) are impossible, and some examples are shown in Fig. 3.

(i) Two unit graphs (5) and (5), or (6) and (6) in trans position.

(ii) Two unit graphs (5) and (6), or (6) and (5) in cis position.

(iii) Following arrangements of three unit graphs in clockwise order: (6)(6)(4), (6)(6)(3), (6)(4)(4), (6)(4)(3), (6)(3)(4), (6)(3)(3), (4)(5)(5), (3)(5)(5), (4)(4)(5), (4)(3)(5), (3)(4)(5), (3)(3)(5), (6)(4)(5), (6)(3)(5), (5)(2)(6), (2)(6)(6), (2)(6)(4), (2)(6)(3), (5)(5)(2), (4)(5)(2), and (3)(5)(2).

(iv) Four unit graphs (2).

(v) Four unit graphs other than (1) or (2).

We should thus determine all the composite graphs in which any arrangement of unit graphs does not offend against above fusing restrictions.

Canonical Name: If unit graphs of six kinds are simply placed on 12 edges of an octahedron, there exist 6^{12} (=2,176,782,848) permutations, including some duplications in each structure. Hence, it is necessary to define a "canonical name" which is the unique expression of a composite ligand graph (and also of a complex ligand graph) corresponding to a structure in one to one.

Labeling of Vertices and Edges of an Octahedron: Six vertices on an octahedron are labeled along one of the Hamiltonian paths, and twelve directed edges are labeled along one of Eulerian trails (like a picture drawn with a single stroke) in the graph theory as shown in Fig. 4. Hereafter, these labels of vertices and directed edges are represented by ①, ②, ③, ····, ⑥, and

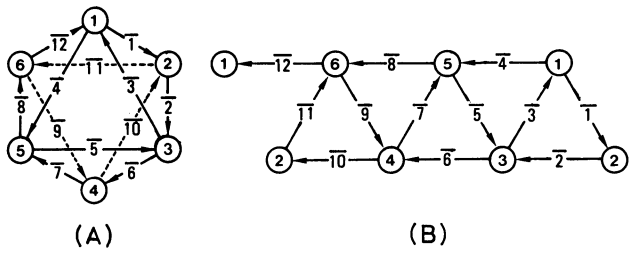

Fig. 4. Labeling of vertices and edges on an octahedron. (A) Perspective view, (B) developed diagram.

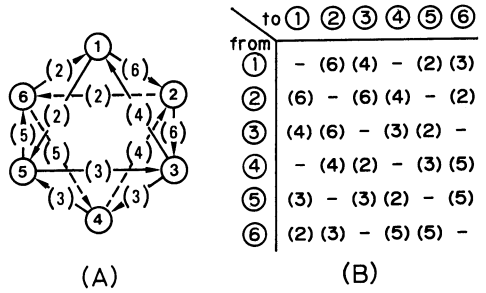

Fig. 5. An example of the composite graph. (A) Octahedral structure composing of 12 unit graphs, (B) its connection matrix.

$\overline{1}, \overline{2}, \overline{3}, \cdots, \overline{12}$ respectively, as well as (1), (2), (3), ····, (6) indicate codes of unit graphs.

Then a composite graph, as well as its complex ligand graph can be described by a numeral of 12 figures, each of which represents the code of a unit graph placed on every edge and lined up in the above-defined order. However, there exist 24 (=6×4) line-up ways of 12 edges in each octahedral structure, since such an Eulerian trail may start from any one of six vertices, and may take any one of four initial directions. The canonical name is defined as the maximum numerical in these 24 numerical names, thus the duplication of the same structure can be avoided.

For example, a composite graph for which the structure is shown in Fig. 5 can be expressed by 24 ways of numerical name given in Table 1. Then, their maximum numeral is 664 233 355 422, which becomes the canonical name of this graph.

The computer selects the possible arrangements of unit graphs from 6^{12} permutations under the above-mentioned fusing restrictions, and finds their canonical names.

Parent Ligand Graph: If a complex ligand graph becomes a parent ligand graph, it must contain neither a unit graph (2), (3), nor (4) on any edge which can be replaced with another unit graph of higher order (5) or (6) subjecting to the fusing restrictions; similarly, it must contain no unit graph (1) replaceable with (2), (3), (4), (5), or (6). The computer examines all such rearrangements of unit graphs in each structure, and if every replacement causes offense against the fusing restrictions, then the original structure can become a parent ligand graph. For example, in a structure named 664 214 553 222, if the unit graph (3) (the nineth figure) is replaced with (5), the resulting structure named 664 214 555 222 is allowed for the fusing around every vertex, then that the original structure is not a parent ligand graph. Also, the computer showed that no other unit graph in the latter structure can be replaced with any unit graph of higher order without breaking fusing restrictions; thus, the latter graph 664 214 555 222 is proved to be a parent ligand graph.

Table 1. 24 Expressions of a Composite Graph in Fig. 5

Start	Name	Start	Name
①→②	664 233 355 422	④→⑤	333 464 622 255
①→③	423 352 534 266	④→③	264 536 353 422
①→⑤	252 625 463 334	④→②	425 352 234 663
①→⑥	336 464 222 553	④→⑥	552 223 466 334
②→③	646 222 553 334	⑤→⑥	522 346 634 253
②→①	633 455 222 346	⑤→①	342 226 453 635
②→⑥	254 633 342 526	⑤→③	333 554 226 642
②→④	425 642 335 253	⑤→④	255 333 646 422
③→④	333 425 262 546	⑥→①	225 533 346 462
③→⑤	234 663 345 522	⑥→⑤	525 342 664 233
③→①	466 342 535 223	⑥→④	542 266 423 335
③→②	642 225 533 364	⑥→②	363 534 222 645

Chiral Isomers: In oreder to search the chiral-isomer couples in the parent ligand graphs, the mirror-image graphs of a given graph should be generated. Since an octahedron is reflected by a mirror (as shown in Fig. 6(A)), the correspondences of each vertex and edge between original and mirror-image graphs would be obvious.

Vertices ①, ②, ③, ④, ⑤, and ⑥, are converted into ①, ⑥, ⑤, ④, ③, and ②, respectively; also edges $\overline{1}$, $\overline{2}$, $\overline{3}$, $\overline{4}$, $\overline{5}$, $\overline{6}$, $\overline{7}$, $\overline{8}$, $\overline{9}$, $\overline{10}$, $\overline{11}$, and $\overline{12}$ are converted into $\overline{12}$, $\overline{8}$, $\overline{4}$ $\overline{3}$, $\overline{5}$, $\overline{7}$, $\overline{6}$, $\overline{2}$, $\overline{10}$, $\overline{9}$, $\overline{11}$, and $\overline{1}$, respectively, by a mirror-image transformation. As this transformation inverts also the chirality and direction of the unit graph, the unit graphs (5) and (6), as well as (2) and (3) should be converted each other.

For example, in Fig. 6(B), the graph 664 233 355 422 is transformed into its mirror-image graph 363 422 254 635; however, this representation is not its canonical name. Then the computer produces 24 kinds of numeral espressions for this structure, and finds the maximum numeral in them. Thus, 663 334 545 222 is obtained as the canonical name of the chiral isomer for the original graph.

If the canonical name of the mirror image is identical with that of the original graph, e.g. the graph named 643 541 624 522, it has no chiral isomer; in other words, its structure is achiral.

(2) Simple Cage Graph. A simple cage graph is a

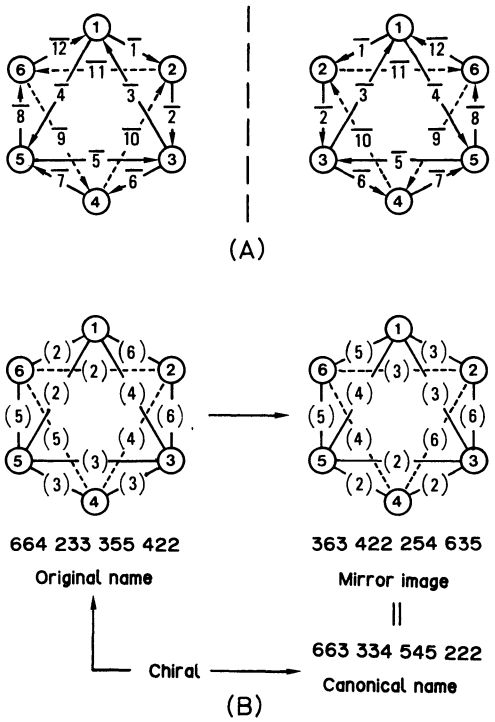

Fig. 6. An example of chiral couples. (A) Mirror reflection, (B) mirror-image transformation.

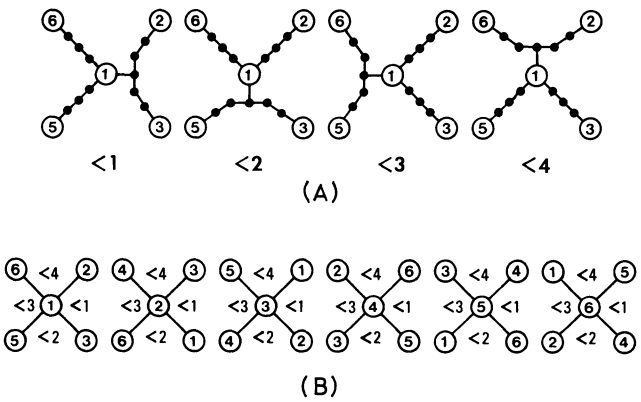

Fig. 7. Labeling of the fusing sites in the simple cage graph. (A) Four sites of fusing around the vertex 1, (B) fusing sites around each vertex.

complex ligand graph where every pair of adjacent main points is joined by only one chelate path. Accordingly, both its donor-atomic graph and its composite graph are an octahedron. Since the degree of every vertex on an octahedron is four, one adjacent pair of unit graphs (1) around every vertex must be partially fused so that the degree of each main point may become three. As there are four adjacent pairs of four edges at each of six vertices, the permutations of fusing ways come to 4^6=4096 kinds including symmetrical duplications.

Labeling of the sites, where each adjacent pair of unit graphs (1) is partially fused around every vertex, are defined as Fig. 7.

Then, a simple cage graph is expressed by a numeral consisting of six figures, each of which represents the label of fusing site around each of six vertices which are lined up in the previous order. Also, in this case 24 expressions are possible in a given structure; thus, a canonical name may be defined as the minimum numeral in these expressions. An example is shown in Fig. 8. The chiral isomers are found by the same method in the parent ligand graphs.

(3) Direct Designing of Complex Ligand Graphs. Simpler complex ligand graphs may be produced directly from some donor-atomic graphs not having complete-cage structure through neither the parent ligand graph nor the simple cage graph. When unit graphs in Fig. 9 are placed on every line of a certain donor-atomic graph in Fig. 10, a composite graph is directly generated.

Directed or chiral isomers of unit graphs are neglected in Fig. 9 for symplifying. Geometrical (or configurational) isomers of donor-atomic graphs are also omitted in Fig. 10. Then several complex ligand graphs are designed by proper fusing around main points under similar restrictions. In this case fusing is not alwalys necessary unless the degree of a main point exceeds three; thus, one-to-one correspondence is lost between a composite graph and its complex ligand graph.

These donor-atomic graphs in Fig. 10 are partial graphs of an octahedral graph, and can be systematically derived from it by removing some lines. Then each of them consists of six points and n lines ($5 \leqq n < 12$), and maximum degree of its points is four. Naturally, a pair of points in trans position of an octahedron is never connected.

The above calcurations are performed by use of a HP9831A Desktop Computer (Hewlett & Packard Co.) and a PC9801F2 Personal Computer (Nippon Electric Co.).

Results and Discussion

It was already discussed[2] that the complex ligand

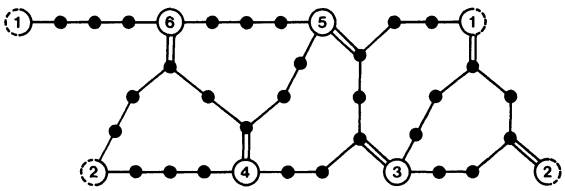

Fig. 8. An example of the simple cage graph.

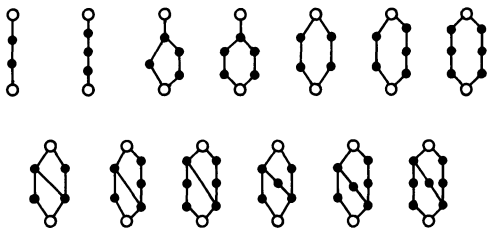

Fig. 9. General unit graphs.

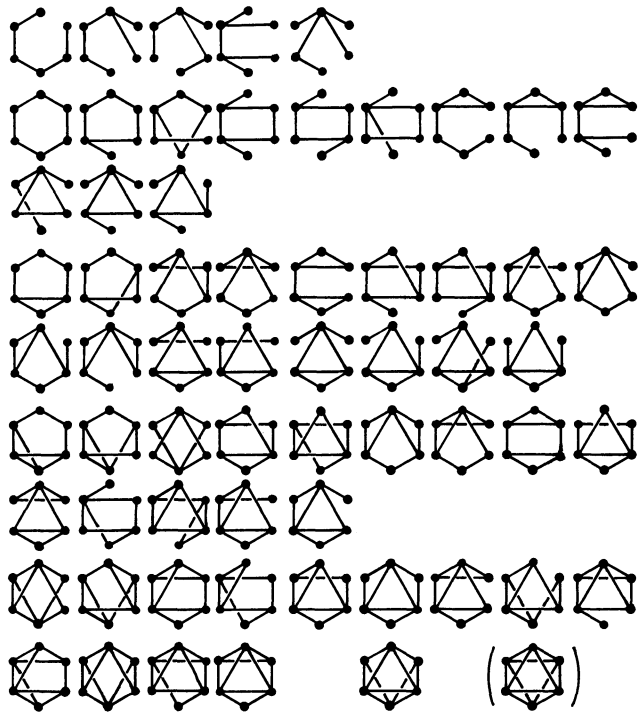

Fig. 10. Donor-atomic graphs for the octahedral coordination.

graph is the best mean for the expression of a ligand structure. The complex graph which has main points and sub-points would be very useful especially in designing of hetero-atomic compounds. The complex ligand graph can be "uniquely" decomposed into several unit graphs, and reversely assembled from them. These procedures may be also available in complicated chemical designs. In this case "uniquely" is important, because any complicated graph should have definable components as if a chemical compound consists of definite atoms. The concept of "fusing" is extensively applicable not only to the graph but also to other geometrical figures in various designings, e.g. a naphthalene frame is formed by fusing of two benzene rings.

Simple numerical expressions of molecular structures are necessary for computer processing. Since an arrangement of six kinds of unit graphs can fully express intricate ligand structures, including optical isomers, the above procedures can be extended to determine the parent ligand graphs for any other coordinations.

Computer calculations show that as many as 1055 kinds of parent ligand graphs for the octahedral coordination may exist even if chiral isomers are excluded, whereas the number of parent ligand graphs for the tetrahedral structure is only nine. They would be too many and too complicate for the application to ligand design. Although more severe restriction to the local fusing of unit graphs around a main point would be difficult, some sifting out may be possible with the totally steric hindrance as to the whole structure of a graph. Neverthless, a drastic reduction of their number would be hopeless, even upon applying such modifications. Moreover, the ligands which will be synthesized in near future will not have such complicated networks as the parent ligand graphs.

The simple cage graphs are the least complete cage-graph, where every pair of adjacent main points is connected, and they are much simpler and much fewer than the parent ligand graphs for the octahedral coordination. Computer calculations have proved that 90 chiral couples and 12 achiral graphs exist in these simple cage graphs. Therefore, they may be preferably adopted as the new starting points of the ligand design instead of parent ligand graphs, and many complex ligand graphs can be introduced by adding or omitting some sub-points and/or lines on them. Especially, this method would be well suited for designing ligands with cage or nearly cage structures.

Method (3) is most useful and most hopeful for the practical designing of ligands. When one or more donor-atomic graphs are selected from Fig. 10 for a certain purpose, some series of related structures can be systematically derived by diverse combinations of unit graphs. Since almost known ligands have topologically simple structure, various new ligands of quite different from old ones would be easily created. As the geometrical structure of a ligand largely effects on the properties and the reactions of the metal chelates, such design would extensively contribute to the development of the coordination chemistry. The applications of these ligand graphs to the designing of new ligands have already been discussed in previous papers.[1-3]

The donor-atomic graph is regarded as a back-bone of a ligand, then all ligands can be classified by their donor-atomic graphs. As this graph is one of the most simplified expression of a ligand, it is available for an easy determination of several geometrical (or configurational) isomers of a metal chelate with a complicated ligand. The donor-atomic graph resembles the simple ligand graph[1] in the graph shape. The only difference is that the degree of each point in the simple ligand graph cannot exceed three. Therefore, the donor-atomic graphs completely include the simple ligand graphs. Although the configurational isomers of donor-atomic graphs are omitted here, most of them were shown as those of the simple ligand graphs in a previous paper.[1]

References

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