A modern aspect of classical aromatic compounds

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Abstract - Host compounds which have classical aromatic rings were found to include a wide variety of guest compounds by surrounding these with the aromatic rings in crystal. Since the inclusion occurs selectively, it can be used for separation of isomers and optical resolution of racemic compounds. Reaction of guest in its inclusion compound with an appropriate host proceeds selectively. By utilizing this method, some regio-, stereo-, and enantioselective syntheses were achieved efficiently.

INTRODUCTION
Classical aromatic compound contains rigid and planar ring such as benzene, naphthalene, or anthracene. These rings work as curtain, wall, and/or spacer in crystal of molecular assembly, and classical aromatic compounds can be good hosts and form host-guest inclusion compounds by surrounding guests with their aromatic rings in crystal lattice. By this idea, we designed many new host compounds (ref. 1). Some of them are chiral hosts. Since these hosts include guests selectively, the inclusion phenomena can be used for separation and purification of isomers. Some such examples are described.

Since guest molecules are arranged regularly at close positions to each other in the crystal of host-guest compound, reaction of the guest compound in the crystal would occur efficiently and selectively. Regio- and stereoselective photodimerization of chalcone, dibenzalacetone, pyridone, and 9-acylanthracene was achieved efficiently by using this method (ref. 2). Enantioselective photoreaction of nitrone, tropolone alkylether, oxoamide, pyridone, cycloocta-2,4,6-trien-1-one, and cycloocta-2,4-dien-1-one was also achieved (ref. 2).

We also found that some usual organic reactions such as pinacol rearrangement, Baeyer-Villiger oxidation, Grignard reaction, NaBH₄ reduction of ketone, phenol coupling with FeCl₃, and acetylene coupling with CuCl₂ proceed in the solid state and that some reactions proceed much faster than in solution. We further succeeded to carry out the solid state reaction stereoselectively. For example, when a mixture of BH₃-ethylenediamine complex and an inclusion compound of ketone with optically active host is kept at room temperature, optically active alcohol was obtained (ref. 3).

ROLE OF AROMATIC RINGS AS CURTAIN, WALL, AND/OR SPACER IN CRYSTAL OF INCLUSION COMPOUND AND SEPARATION OF ISOMERS BY THE INCLUSION COMPOUND FORMATION

1,1-Di(p-hydroxyphenyl)cyclohexane (1) includes β-ionone (2) but not α-ionone (3). X-Ray crystal structural study of the 2:1 inclusion compound of 1 and 2 shows that 2 is surrounded by four p-hydroxyphenyl rings of two moles of 1 in crystal lattice (Fig. 1). Although 2 exists in the s-cis form (2') in CDCl₃ (ref. 4), it does in the s-trans form in the inclusion compound (Fig. 1). The space which is constructed by surrounding with four p-hydroxyphenyl walls would fit to accommodate the s-trans isomer. Non-planar molecule of 3 is more bulky and is not accommodated in the space. However, 9,9'-bianthryl (4) includes 3 selectively. Large anthryl rings construct much larger space which accommodates the bulky 3 (Fig. 2).

Of three isomeric 3,5-dimethylcyclohexan-1-ol (5a-c) which are not isolable by distillation because of almost the same boiling point, only the all...
Fig. 1. Packing diagram in the crystal of 2:1 inclusion compound of 1 and 2.

Fig. 2. Packing diagram in the crystal of 1:1 inclusion compound of 3 and 4.
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equatorial isomer (5a) formed a 1:1 inclusion compound with 1,1,6,6-tetraphenylhexa-2,4-diyne-1,6-diol (6). The phenyl rings of 6 probably can form the space which includes the least bulky 5a (ref. 5). Since thiotropolone exists as an equilibrium mixture of 2-mercaptopropone (7a) and 2-hydroxytropolone (7b) in solution, structural study of each in pure state has not been done. However, 6 includes 7a selectively to form a 1:1 inclusion compound, and its X-ray crystal structural study disclosed that 7a has a π-electron delocalized structure in the inclusion compound (ref. 6).

The most interesting application of host-guest inclusion is for control of reaction. Since guest molecules are arranged regularly at close positions in the inclusion compound, reaction of guests in the solid state is expected to proceed efficiently and selectively. Although photodimerization of chalcone (8) can not be achieved neither in solution nor in the solid state, irradiation of a 1:2 inclusion compound of 6 and 8 in the solid state for 6 h gave syn-head-to-tail dimer (9) selectively in 90% yield (ref. 7). X-Ray crystal structural study of the inclusion compound showed that chalcone molecules are arranged at close positions (distance between reaction centers of 8 is 3.86 Å) (ref. 8). This tight packing is due to a surrounding of 7 with phenyl groups of 6. By the same method, photodimerization of dibenzalacetone (10) to its syn-head-to-tail dimer (11), 9-acylanthracene (12) to its anti-dimer (13), and pyridone (14) to its anti-dimer (15) has been achieved easily (ref. 9). All of these efficient photodimerization reactions have been studied by X-ray crystal structural analysis (ref. 8, 10).

When optically active host is used at the reaction of guest in host-guest inclusion compound, enantioselective reaction of the guest is expected. Irradiation of a 1:1 inclusion compound of nitrone (16) and (R,R)-(+)-1,6-di(o-chlorophenyl)-1,6-diphenylhexa-2,4-diyne-1,6-diol (17a) in the solid state gave optically active oxaziridine (18) of the optically purity shown in Table 1 (ref. 11). Mechanism of the enantioselective photocyclization of 16 has been studied by X-ray crystal structural analysis (ref. 12).
Irradiation of a 1:1 inclusion compound of 17a and tropolone alkylether (19) in the solid state gave the photocyclization product (20) of 100% ee (ref. 13). X-Ray crystal structural study of the inclusion compound showed that 19 is surrounded with phenyl rings of 17a and disrotatory ring closure of 19 is allowed only to the A direction by a steric factor of phenyl ring to afford finally (-)-20 (Fig. 3) (ref. 14). Similar irradiation of a 1:1 inclusion compound of 17a and pyridone (21) gave (-)-22 of 100% ee (ref. 15). The enantio-control is also due to a steric factor of phenyl ring (Fig. 4) (ref. 16).

![Chemical structures](image)

**TABLE 1.** Irradiation time to the 1:1 inclusion compound of 16 and 17a, and yield, [α]D value, and optical purity of 18

<table>
<thead>
<tr>
<th>Ar</th>
<th>R</th>
<th>Irradiation time (h)</th>
<th>Yield (%)</th>
<th>[α]D(°) (c, CHCl₃)</th>
<th>ee (%)</th>
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<tbody>
<tr>
<td>Ph</td>
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<tr>
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<tr>
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<td>+53.9 (0.50)</td>
<td>100</td>
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Fig. 3. Photoreaction of a 1:1 inclusion compound of 17a and 19. Fig. 4. Photoreaction of a 1:1 inclusion compound of 17a and 21.
Cycloocta-2,4,6-trien-1-ol (23) exists as an equilibrium mixture of two flipping enantiomers (23a and 23b) in solution. 17a includes one enantiomer (23a or 23b) selectively and irradiation of the inclusion compound gives optically active photocyclization product (24). Of the two flipping enantiomers (25a and 25b) of cycloocta-2,4-dien-1-ol (25), one (25a or 25b) is included with 17a, and irradiation of the inclusion compound gives (-)-dimer of 78% ee (ref. 17). X-Ray crystal structural study of the inclusion compound of 17a and 25 showed that the distance between the reaction centers of two 25 is about 10 Å. Schmidt rule for photodimerization of olefin in the solid state says that distance between the reaction centers should not be longer than 4.2 Å (ref. 18). Therefore, in order to dimerize, two molecules of 25 should move to a close position in crystal. One possible movement is by a rotation around the triple bond of 17a in the inclusion compound (Fig. 5). In any way, this is the first example which is not fit to the Schmidt rule.

![Chemical structures](image)

**Fig. 5.** X-Ray crystal structure of the inclusion compound of 17a and 25a (or 25b).
ENANTIOSELECTIVE SOLID–SOLID REACTION

When a mixture of the inclusion compound of ketone (29) with 17a and BH$_3$-ethylenediamine complex (30) is kept at room temperature for one day, optically active alcohol (31) was obtained in the yield shown in TABLE 2.

\[
\text{BH}_3\cdot \text{H}_2\text{NCH}_2\text{CH}_2\text{NH}_2\cdot \text{BH}_3
\]

<table>
<thead>
<tr>
<th>ArCOR (29)</th>
<th>ArCH(OH)R (31)</th>
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<td>Ar</td>
<td>R</td>
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<td>Ph</td>
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<tr>
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<td>Et</td>
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<tr>
<td>α-naphthyl</td>
<td>Me</td>
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*Reaction was carried out at room temperature for one day by occasionally grinding with pestle and mortar.*

REFERENCES