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 separa-
tion 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-acylanthra-
cene was achieved efficiently by using this method (ref. 2). Enantioselec-
tive 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, $NaBH_4$ reduction of ketone,
phenol coupling with $FeCl_3$, and acetylene coupling with $CuCl_2$ 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 BH_3-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 $CDCl_3$
(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
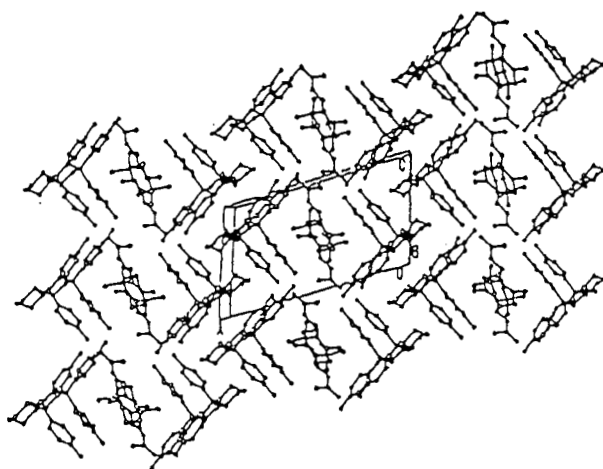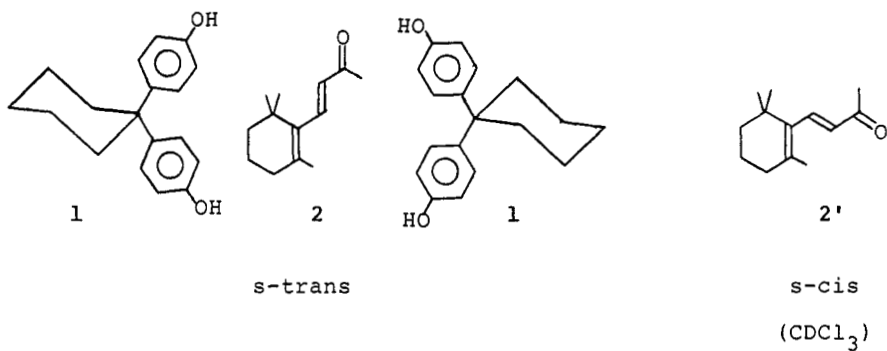by distillation because of almost the same boiling point, only the all

1

2

1

2'

s-trans

s-cis

(CDCl$_3$)

Fig. 1. Packing diagram in the crystal of
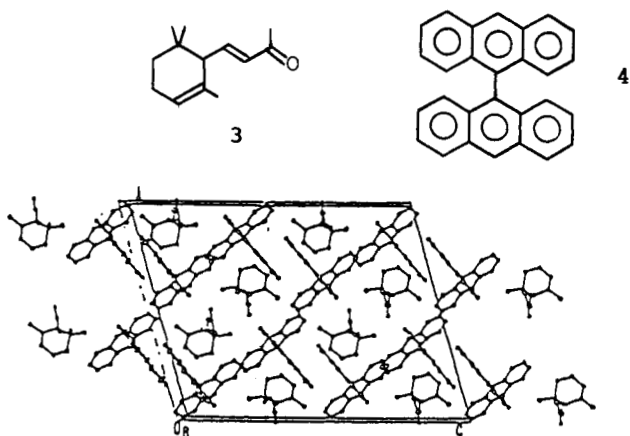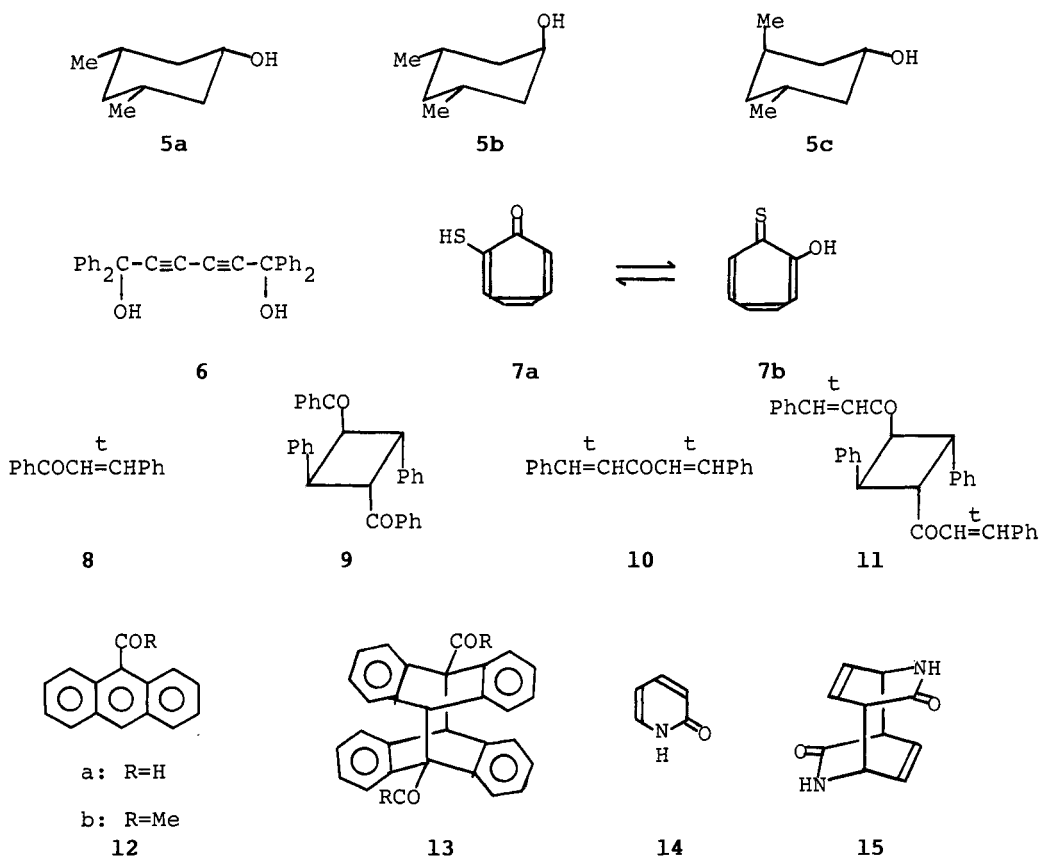2:1 inclusion compound of **1** and **2**.

3

4

Fig. 2. Packing diagram in the crystal of
1:1 inclusion compound of **3** and **4**.

equatorial isomer (5a) formed a 1:1 inclusion compound with 1,1,6,6-tetra-
phenylhexa-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-mercaptotropone (7a) and 2-hydroxy-
tropothione (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 com-
pound, 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 dibenzal-
acetone (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).

Me⟋⟍OH   MeOH   Me⟋OH

5a   5b   5c

Ph₂C-C≡C-C≡C-CPh₂   HS⟍O ⇌ S⟍OH
   | |
   OH   OH

6   7a   7b

PhCOCH=CHPh   PhCO⟋Ph COPh   PhCH=CHCOCH=CHPh   PhCH=CHCO⟋Ph COCH=CHPh

8   9   10   11

COR   COR   N-O(H)   NH ... HN
a: R=H   O

b: R=Me
12   13   14   15

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).

16
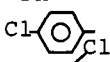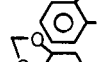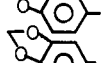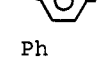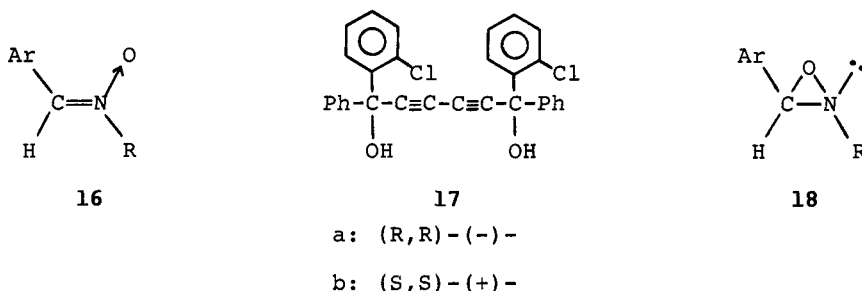
17

a: (R,R)-(-)-

b: (S,S)-(+)-

18

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

16		Irradiation time (h)	18		
Ar	R		Yield (%)	$[\alpha]_D$ (°) (c, $CHCl_3$)	ee (%)
Ph	iPr	24	56	+40.7 (0.31)	---
Ph	tBu	36	41	+8.2 (0.55)	9.5
Cl〇Cl	tBu	32	74	+16.0 (0.61)	30
〇	tBu	12	51	-4.3 (0.83)	100
〇	iPr	16	63	+20.0 (0.21)	28
〇	tBu	21	52	+78.5 (0.38)	94
Ph	iPrMeCH	24	40	+53.9 (0.50)	100

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).
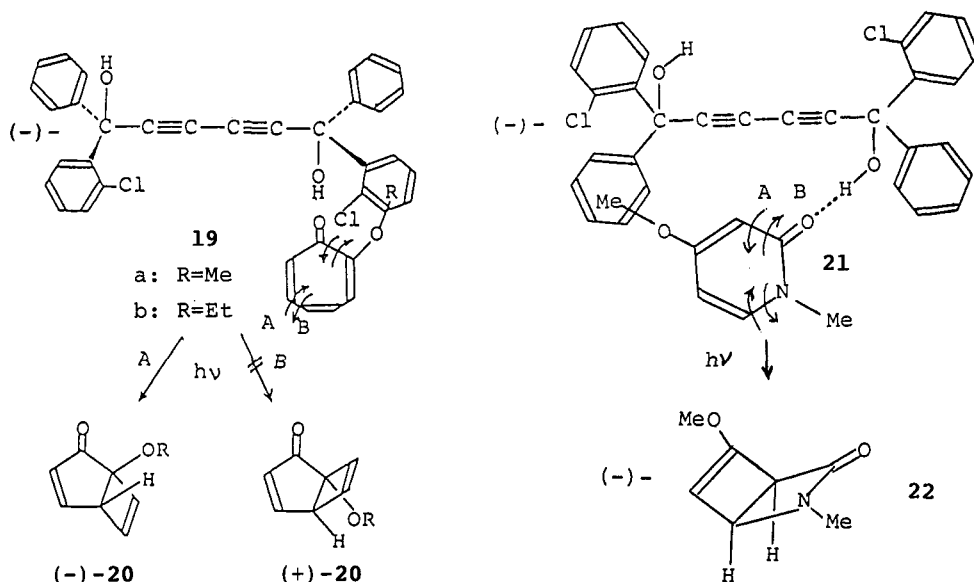

19

a: R=Me

b: R=Et

(-)-20

(+)-20

Fig. 3. Photoreaction of a 1:1 inclusion compound of **17a** and **19**.

21

22

Fig. 4. Photoreaction of a 1:1 inclusion compound of **17a** and **21**.

Cyclooca-2,4,6-trien-1-ol (23) exists as an equilibrium mixture of two flip-
ping 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 cyclooca-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
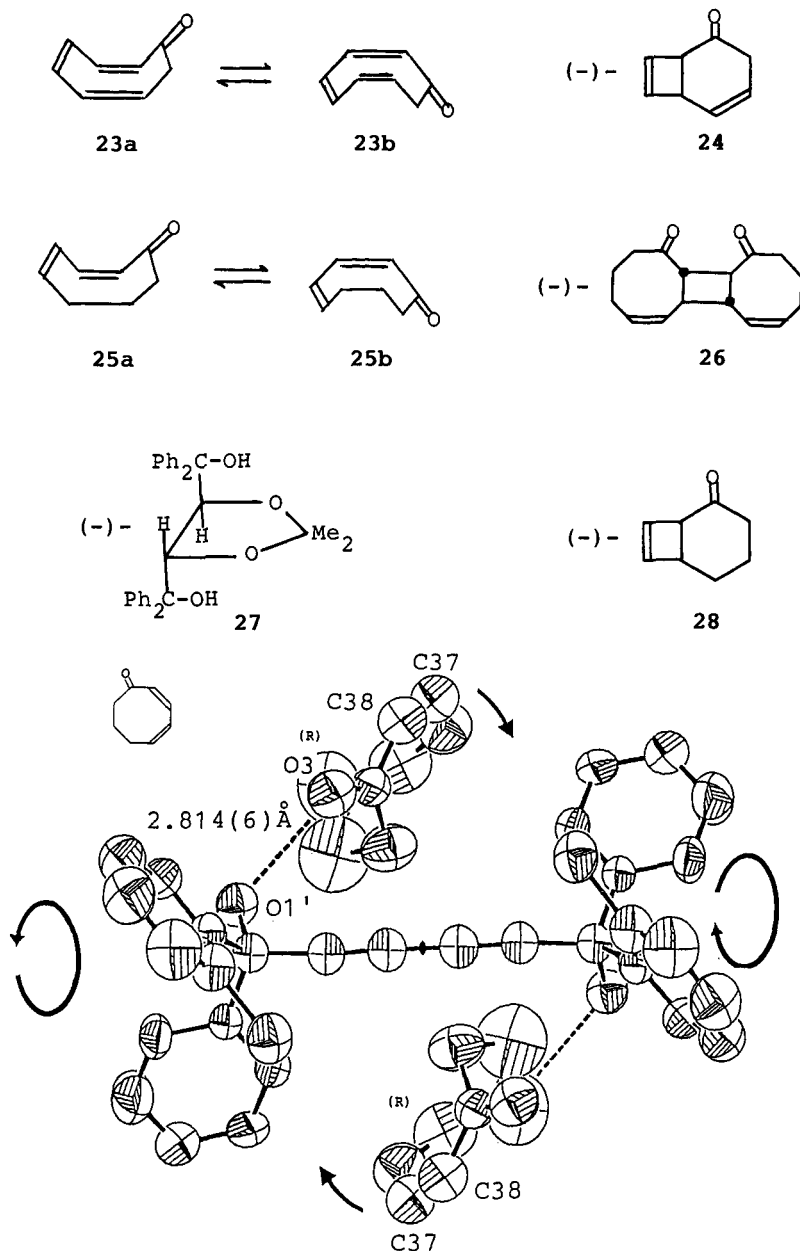is the first example which is not fit to the Schmidt rule.

23a   23b   (-)- 24

25a   25b   (-)- 26

27   (-)- 28

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.

$$BH_3 \cdot H_2NCH_2CH_2NH_2 \cdot BH_3$$
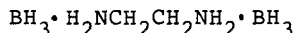
30

TABLE 2. Enantioselective reduction of ketone (29) with **30** in inclusion compound with **17a**.[a]

ArCOR (29)		ArCH(OH)R (31)	
Ar	R	Yield (%)	Optical purity (% ee)
Ph	Me	96	44
Ph	·Et	20	38
4-Me-C6H4 (Me)	Et	64	42
α-naphthyl	Me	29	22

[a] Reaction was carried out at room temperature for one day by occasionally griding with pestle and mortar.

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