COMMUNICATION

Design of new chiral tetraol host compounds, *trans*-1,4-bis[3-(*o*-chlorophenyl)-3-hydroxy-3-phenylprop-1-ynyl]-1,4-dihydroxycyclohexa-2,5-diene and its tetrahalogeno derivatives

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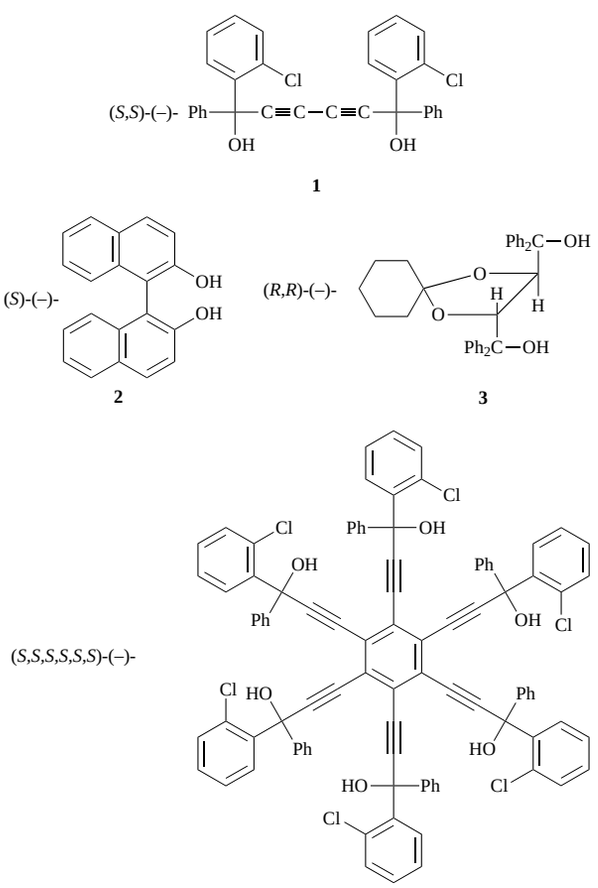
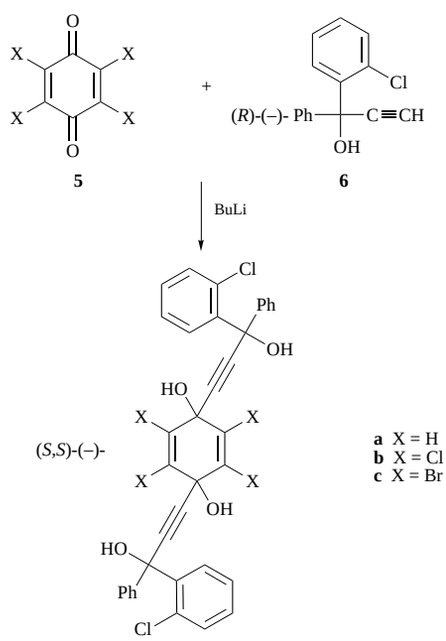
The title chiral tetraol host and its 2,3,5,6-tetrachloro and -tetrabromo derivatives have been prepared by the addition of the lithium acetylide derived from (*R*)-(−)-1-(*o*-chlorophenyl)-1-hydroxy-1-phenylprop-2-yne to benzoquinone, chloranil and bromanil, respectively and by complexation with these chiral host compounds, various kinds of *rac*-guest compounds have been resolved very efficiently.

In accordance with our simple principle for the design of host compounds, *i.e.* organic molecules which have a rigid structure and sterically hindered hydroxy groups are good host compounds, we have designed various achiral and chiral host compounds.[1] Of the chiral host compounds, (*S*,*S*)-(−)-1,6-bis(*o*-chlorophenyl)-1,6-diphenylhexa-2,4-diyne-1,6-diol **1**,[2] (*S*)-(−)-2,2′-dihydroxy-1,1′-binaphthyl **2**[3] and (*R*,*R*)-(−)-*trans*-2,3-bis(hydroxydiphenylmethyl)-1,4-dioxaspiro[4.5]decane **3**[4] were prepared as typical chiral diol hosts. These hosts were found to include various guest compounds and recognize their chirality precisely in the inclusion complex. By using the chiral discrimination ability of the host, optical resolution of *rac*-guests[1,5] and enantioselective reaction of prochiral guests in the inclusion complex have been accomplished.[6]

However, no chiral tetraol host which has two different types of hydroxy groups has ever been prepared, although a hexaol host, a kind of dendrimer host which has one type of hydroxy group, (*S*,*S*,*S*,*S*,*S*,*S*)-(−)-hexakis[3-(*o*-chlorophenyl)-3-hydroxy-3-phenylprop-1-ynyl]benzene **4** has been reported.[7] Nevertheless, **4** did not show any chiral discrimination ability with a *rac*-guest. We report here the preparation of the title new chiral tetraol host **7a**, and its 2,3,5,6-tetrachloro (**7b**) and -tetrabromo (**7c**) derivatives by addition of the lithium acetylide



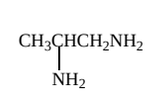


derived from (*R*)-(−)-3-(*o*-chlorophenyl)-3-hydroxy-3-phenylprop-1-yne **6**[8] and BuLi to benzoquinone **5a**, chloranil **5b** and bromanil **5c**, respectively.[9] Very efficient optical resolutions of various guest compounds by complexation with these hosts were also reported.

For example, to a solution cooled by a dry ice-bath of BuLi (5.27 g, 82.4 mmol) in dry THF (5 ml)–hexane (50 ml), a solution of **6** (10 g, 41.2 mmol) in dry THF (20 ml) was added under N_2 over 30 min. To this cooled mixture, a solution of **5a** (1.78 g, 16.5 mmol) in dry THF (50 ml) was added over 1 h and the mixture was stirred for a further 3 h while cooling was continued. The reaction mixture was kept at room temperature overnight and then dil. HCl was added and the mixture

Table 1 Host:guest ratios in the inclusion complexes of **7a–c** with typical guest compounds

Guest compound	Host compound		
	7a	**7b**	**7c**
MeOH	—	1:2	1:2
EtOH	—	1:2	1:2
THF	—	1:4	—
Dioxane	1:2	1:2	1:4
DMSO	1:2	1:2	1:4
DMF	1:2	1:2	1:4
Acetone	1:1	1:2	1:2
Cyclopentanone	1:2	1:2	1:4



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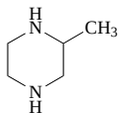

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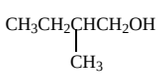

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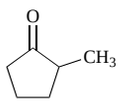

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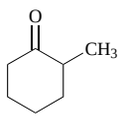

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extracted with toluene. From the toluene solution, **7a** was obtained, after recrystallization from toluene, as colourless prisms (6.26 g, 64%), mp 193–195 °C, $[\alpha]_D$ −90.2† (*c* 0.51, MeOH); ν_{max}(Nujol)/cm^{-1} 3370 (OH) (Calc. for $C_{36}H_{26}O_4Cl_2$: C, 72.85; H, 4.42. Found: C, 73.11; H, 4.28%). By the same method, **7b** and **7c** were prepared from **5b** and **5c**, respectively. **7b** was obtained as colourless prisms (52%), mp 189–191 °C, $[\alpha]_D$ −51.9 (*c* 1.1, MeOH); ν_{max}(Nujol)/cm^{-1} 3545, 3330 and 3275 (OH) (Calc. for $C_{36}H_{22}O_4Cl_6$: C, 59.13; H, 3.03. Found: C, 59.21; H, 3.15%). **7c** was obtained as colourless prisms (42%), mp 185–187 °C, $[\alpha]_D$ −48.1 (*c* 0.51, MeOH); ν_{max}(Nujol)/cm^{-1} 3505 and 3420 (OH) (Calc. for $C_{36}H_{22}O_4Br_4Cl_2$: C, 47.56; H, 2.44. Found: C, 47.66; H, 2.48%). In all the reactions, only a single product was obtained. **7a–c** should all have the sterically less hindered *trans* structure, since addition of phenylmagnesium bromide to 9.10-anthraquinone gave only the *trans*-9,10-dihydroxy-9,10-diphenyl-9,10-dihydroanthracene.[1]

The inclusion tendency of the hosts **7a–c** for some typical guest compounds was studied, and **7b** and **7c** were found to show relatively good inclusion ability compared with **7a** (Table 1). In particular **7c** usually includes four guest molecules to form a 1:4 host–guest inclusion complex. This suggests that **7c**, which has more bulky Br atoms, constructs a crystalline lattice with a relatively large space in the inclusion complex compared with **7a** and **7b** and accommodates four guest molecules. DSC measurement of a 1:4 complex of **7c** with dioxane showed that two dioxane molecules are released at about 60 °C and then the other two molecules are released at about 130 °C. This result shows that two of the dioxane molecules are bound more strongly to the OH groups of **7c** than the other two. Unfortunately, however, the crystal structure was not clarified directly by X-ray analysis because a suitable crystal for the analysis was not available.

The chiral discrimination ability of the hosts **7a–c** towards some chiral compounds was studied, and their extremely high chiral recognition ability was observed. Finally, a new optical resolution method of *rac*-guest compounds by complexation with **7a–c** was established. For example, when a solution of **7a** (0.58 g, 0.98 mmol) and *rac*-1,2-diaminopropane **8** (0.29 g, 3.92 mmol) in toluene (3 ml) was kept at room temperature for 12 h, a 1:2 complex of **7a** and (+)-**8** was obtained as colourless prisms (0.59 g, 81%, mp 115–117 °C). Heating of the complex at 200 °C/15 mmHg gave (+)-**8** of 100% ee {0.1 g, 69% yield, $[\alpha]_D$ +32.2 (*c* 0.31, benzene)}. By complexation with **7a**, *rac*-2-methylpiperazine **9** was also resolved efficiently and gave (+)-**9** of 90% ee in 65% yield. The optical purities of **8** and **9** were determined by measurement of their ^{1}H NMR spectra using **2** and **1**, respectively, as a chiral shift reagent.[10] By using **7b** and **7c** instead of **7a**, resolutions of **8** and **9** were accomplished more efficiently (Table 2).

Table 2 Optical resolution of **8** and **9** by complexation with **7a–c**[a]

Host	Guest	Product	Yield (%)[b]	Optical purity (% ee)[c]
7a	**8**	(+)-**8**	69	100
7b	**8**	(+)-**8**	71	100
7c	**8**	(+)-**8**	73	100
7a	**9**	(+)-**9**	65	90
7b	**9**	(+)-**9**	75	100
7c	**9**	(+)-**9**	74	100

[a] In all complexes, host:guest ratio was 1:2. [b] Yields were calculated on the basis of the theoretical amount of the optical isomer contained in the initial *rac*-compound. [c] Optical purities of **8** and **9** were determined by the measurement of ^{1}H NMR spectra using **2** and **1**, respectively, as a chiral shift reagent.[10]

Table 3 Optical resolution of **10–13** by complexation with **7b** and **7c**

Host	Guest	Host:Guest	Product	Yield (%)[a]	Optical purity (% ee)
7b	**10**	1:2	(−)-**10**	48	95[b]
7c	**10**	1:2	(−)-**10**	39	90[b]
7b	**11**	1:2	(−)-**11**	42	32[c]
7b	**12**	1:1	(−)-**12**	60	83[c]
7b	**13**	1:1	(−)-**13**	53	67[c]

[a] Yields were calculated on the basis of the theoretical amount of the optical isomer contained in the initial *rac*-compound. [b] Optical purity was determined by HPLC on the chiral stationary phase, Chiralcel OB using hexane–Pr^{i}OH (9:1) as an eluent. [c] Optical purities of **11**,[12] **12**[13] and **13**[14] were determined by comparison of their $[\alpha]_D$ values with those of the corresponding authentic sample.

1-Phenylethanol **10**, 2-methylbutanol **11**, 2-methylcyclopentanone **12** and 2-methylcyclohexanone **13** were also resolved by complexation with **7b** and **7c**, although **7a** was not effective for these resolutions (Table 3). The resolution of **10–13** by one complexation with a host compound is very efficient but not complete. When the complexation is repeated again, the resolution becomes complete and an optically pure sample is obtained. For example, complexation with **7b** of (−)-**12** of 83% ee and (−)-**13** of 67% ee obtained by the first resolution experiment (Table 3) followed by distillation *in vacuo* gave (−)-**12** of 100% ee {58%, $[\alpha]_D$ −110.5 (*c* 0.52, MeOH)} and (−)-**13** of 99% ee {57%, $[\alpha]_D$ −13.9 (*c* 0.65, MeOH)}, respectively. The optical purity of **10** was determined by HPLC on the chiral stationary phase, Chiralcel OB.[11] The optical purities of **11–13** were determined by comparison of their $[\alpha]_D$ values with those of a corresponding authentic sample of **11**,[12] **12**[13] and **13**.[14]

Of these results, the success in resolving **12** and **13** is extremely valuable, since no method for their direct resolution has been reported so far. Although the resolution of 3-methylcyclopentanone and 3-methylcyclohexanone can be accomplished by complexation with **1**, the method is not applicable to the resolution of **12** and **13**.[2] Optically active **12** of about 95% ee has been prepared from 5-methylcyclopentadiene *via* several reaction steps including an enantioselective hydroboration process.[13] Optically active **13** of 82% ee has also been prepared *via* several reaction steps including an enenatioselective methylation process.[14] In comparison with the synthetic method, the resolution method by complexation with **7b** is rather simple and can give an optically pure sample easily. Furthermore, the reso-

† $[\alpha]_D$ Values are given in units of 10^{-1} deg cm^2 g^{-1}.

lution method is more economical since the host compound can be recovered and used repeatedly.

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