Azophenolic Acerands Having Chiral 1-Phenyl-*cis*-1,2-cyclohexanediol Units: A Correlation between Enantiorecognitive Coloration and Host–Guest Complementarity

Koichiro Naemura,*,† Koji Ueno,† Sachiko Takeuchi,† Yoshito Tobe,† Takahiro Kaneda,*,‡ and Yoshiteru Sakata‡

Department of Chemistry, Faculty of Engineering Science Osaka University, Toyonaka, Osaka 560, Japan
The Institute of Scientific and Industrial Research Osaka University, Mihogaoka, Ibaraki, Osaka 567, Japan

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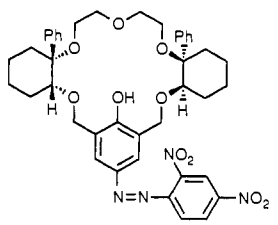
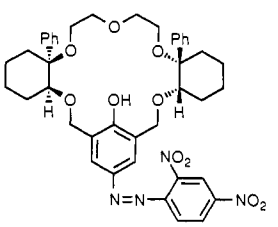
Studies of host–guest color complexation,[1] defined as complexation causing synchronous coloration, provide basic information for the development of color indicators or sensors for special guests. For such studies, an azophenolic acerand[2] is a suitable system because of its chromogenic and binding abilities in the same molecule. In previous reports on the enantiorecognitive coloration of chiral indicators containing hydrobenzoin[3a] and 1,1′-binaphthyl[4] units, the observed blue shift, the difference in transition energy between the two diastereomeric saltexes,[2] could be correlated with the better host–guest complementarity, although the complementarity was examined using only the CPK molecular model. We describe here a correlation between the enantiorecognitive coloration of indicator **1** and the complementarity judged by the association constants in addition to the CPK modeling.



(R,R,R,R)-1



(S,S,S,S)-1

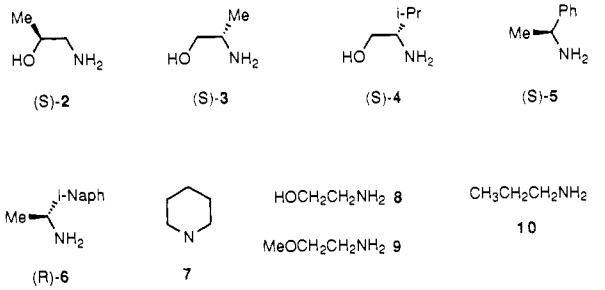
An enantiomeric pair of chiral acerands (**1**) was synthesized via six steps involving quinone hydrazone–azophenol tautomerization from optically pure 1-phenyl-*cis*-1,2-cyclohexanediol[5] with a known absolute configuration,[6] protection of the diol with $CH_2(OCH_3)_2$, etherification with diethylene glycol ditosylate/NaH, deprotection, cyclization with 1,4-dimethoxy-2,6-bis(bromomethyl)benzene,[7] oxidation with ceric ammonium nitrate, and 2,4-dinitrophenylhydrazonation.[8]

Enantiorecognitive color saltexation of **1** with five chiral amines **2**–**6** was examined in ethanol by the same procedure as previously reported[3] except for the guest/host molar ratio of $1–3 \times 10^3$, and the association constants for the saltexation were determined by the Benesi–Hildebrand method[9] with the aid of the self-color indicating properties of **1**. Between the diastereomeric set of the **1**-(S)-valinol (**4**) salts, the ratio of K_a values is close to 1.00, and no differences in the λ_{max} values were observed in either solvent (Table I). However, *when the guests were (S)-1-amino-2-propanol (**2**), (S)-α-phenethylamine (**5**), and (S)-1-(1-naphthyl)ethylamine*[10] *(antipode of (R)-**6**), indicator (SSSS)-**1** caused blue shifts (up to 10 nm in ethanol) of the absorption bands compared with the enantiomer (RRRR)-**1**.* The table also demonstrates that *the combination exhibiting the blue shift shows a higher value of K_a*, in other words, a better host–guest complementarity (a more stable saltex) than the other diastereomeric counterparts, although there have been no parallel relationships between the observed blue shift and the complementarity in the general sense.[1]

Table I. Association Constants and Absorption Maxima of Acerand **1**–Amine Systems[a]

amine[b]	acerand **1**	K_a/M^{-1}	relative ratio of K_a	λ_{max}/nm in $CHCl_3$	λ_{max}/nm in EtOH
(*S*)-**2**	(*RRRR*)	197 ± 1	1	583	570
(*S*)-**2**	(*SSSS*)	270 ± 2	1.37	577	565
(*S*)-**3**	(*RRRR*)	78.4 ± 2.3	1	577	575
(*S*)-**3**	(*SSSS*)	88.3 ± 0.6	1.13	578	573
(*S*)-**4**	(*RRRR*)	18.6 ± 0.3	1	574	575
(*S*)-**4**	(*SSSS*)	19.3 ± 0.2	1.04	574	575
(*S*)-**5**	(*RRRR*)	5.3 ± 0.3	1	588	571
(*S*)-**5**	(*SSSS*)	11.1 ± 0.4	2.01	585	564
(*R*)-**6**	(*RRRR*)	8.3 ± 0.3	1.95	584	561
(*R*)-**6**	(*SSSS*)	4.3 ± 0.2	1	586	571
7	(*RRRR*)	13.1 ± 0.2		592	
8	(*RRRR*)	413 ± 3		579	
9	(*RRRR*)	59.4 ± 0.7		600	
10	(*RRRR*)	256 ± 9		598	

[a] Determined by the Benesi–Hildebrand method at 25 °C in $CHCl_3$. [b] The structures are presented below.



The prediction of which indicator can form a more stable saltex was made by examining of the CPK molecular models using the assumption, as accepted from a previous work,[3] that the phenolate oxygen atom necessarily participates in binding the guest. The following prediction has been drawn as mentioned below: *the indicator (SSSS)-**1** should show better complementarity than the (RRRR)-isomer to the amine (S)-**2**, (S)-**5**, and (S)-**6**.*[10] *These combinations are compatible with the combinations exhibiting the previously described blue shift.*

The more favorable combination (*SSSS*)-**1**:(*S*)-**5** leads to the most stable geometry, **11**, where the smallest hydrogen atom of the guest occupies the most hindered area near the bulky phenyl group and the largest phenyl group of the guest is allowed to occupy the least hindered area, and here the two-point binding model rather than Cram's three-point binding model[11] is accepted by the following steric requirement. One of the axial hydrogens of the cyclohexane moiety of the chiral unit covers one of the

† Department of Chemistry, Faculty of Engineering Science.
‡ The Institute of Scientific and Industrial Research.

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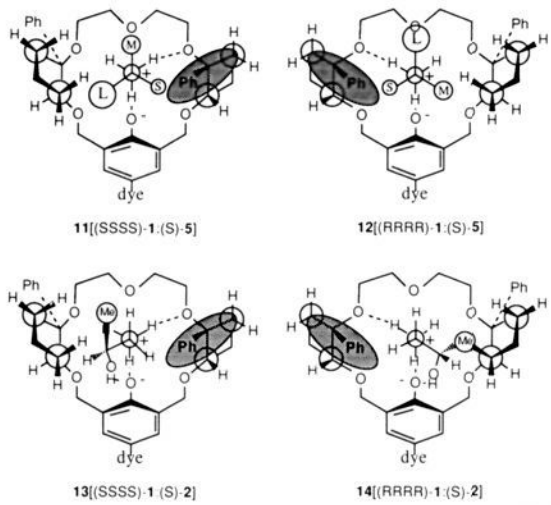

Figure 1. Predicted structures of the saltexes consisting of (*SSSS*)-**1**:(*S*)-**2** and (*SSSS*)-**1**:(*S*)-**5** combinations, where "dye" = 2,4-dinitrophenylazo group. The Ph group above the plane of the cyclic polyether ring is shown as an ellipse.

donor oxygen atoms of the polyether ring to prevent the third hydrogen-bonding formation. This may be one reason for the relative weakness in the binding ability of the present acerand, even toward unbranched primary amines **8**–**10** in Table I. The two-point model[12] seems to be quite reasonable for this system when one compares the K_a value for (*S*)-**5** with that for piperidine (**7**), to which the three-point model is inapplicable. A similar argument can be applied to the case of (*R*)-**6**.

The unfavorable combination (*RRRR*)-**1**:(*S*)-**5** leads to the predicted structure **12**, where the largest phenyl group of the guest occupies the diethylene glycol group area in the host. The steric repulsion between these groups must destabilize this saltex (see Figure 1).

The ethanolamine derivative (*S*)-**2** was predicted to form the most stable saltex, having geometry **13**, where the hydroxyl group of the guest is bound to the phenolate oxygen by the additional hydrogen bonding to make the saltex more stable. A similar $O^-\cdots H—O$-type hydrogen bonding must be responsible for the highest stability constant for ethanolamine (**8**) among the three amines **8**–**10** and the blue shift (20 nm in Table I) of the absorption band compared with the other two amines. In the less stable saltex with geometry **14** from the unfavorable combination, however, such hydrogen bonding may be prevented by steric repulsion between the methyl group of the guest and the cyclohexane barrier in the host.

We have demonstrated that, at least in the present system, the combinations exhibiting the blue shift are compatible with the combinations leading to better host–guest complementarity, as judged by both approaches, the association constant determined in $CHCl_3$, and examination of the CPK molecular models. The observed coloration-complementarity correlation allows us to make efforts to create "absolute configuration indicators".

(12) This type of two-point binding was observed in the crystal structure of a piperidine saltex.[13]

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