Synthesis and Enantioselective Coloration of Optically Active Azophenolic Acerands incorporating Two 1,1′-Binaphthyl Moieties as the Chiral Centre

Koji Yamamoto,*[a] Koichiro Isoue,[b] Yoshiteru Sakata[c] and Takahiro Kaneda*[c]

[a] *Department of Chemistry, Faculty of Integrated Arts and Sciences, University of Osaka Prefecture, Sakai, Osaka 593, Japan*

[b] *Department of Chemistry, Faculty of Engineering Science, Osaka University, Toyonaka, Osaka 560, Japan*

[c] *The Institute of Scientific and Industrial Research, Osaka University, Mihogaoka, Ibaraki, Osaka 567, Japan*

Two chiral azophenolic acerands **2** and **3** with two 1,1′-binaphthyl moieties as the chiral centre have been prepared, and their chiral recognition properties based on enantiomeric amine-selective coloration have been examined; the host **3** shows a higher enantioselective coloration than the host **2** with a variety of primary amines.

The recent discovery of the enantioselective coloration of the chiral azaphenolic acerand **1**[1] incorporating two hydrobenzoin units prompted us to investigate the design of another type of chiral azophenolic acerand having two axially dissymmetric moieties[2] as the chiral centre.

The attractive properties of the 1,1′-binaphthyl moiety, characterized by the presence of a powerful inherently chiral chromophore,[3] directed our continuing efforts to the synthesis of two types of novel optically active azophenolic acerand **2** and **3**,[4] which should display efficient enantioselective coloration with organic primary amines.

According to Cram's method,[5] except that the methoxymethyl protecting group was used, (+)-(*R*)-2,2′-dihydroxy-1,1′-binaphthyl **4** was converted into the (−)-(*R*,*R*)-diol **7** in a yield of 61% for the three steps. Condensation of (−)-(*R*,*R*)-**7** with 1,3-bis-(bromomethyl)-2,5-dimethoxybenzene **8**† [Cs_2CO_3, dimethylformamide (DMF)][6] afforded the crown ether (+)-(*R*,*R*)-**9**,‡ m.p. 236–237 °C, 42% yield, $[\alpha]_D^{24}$ + 125

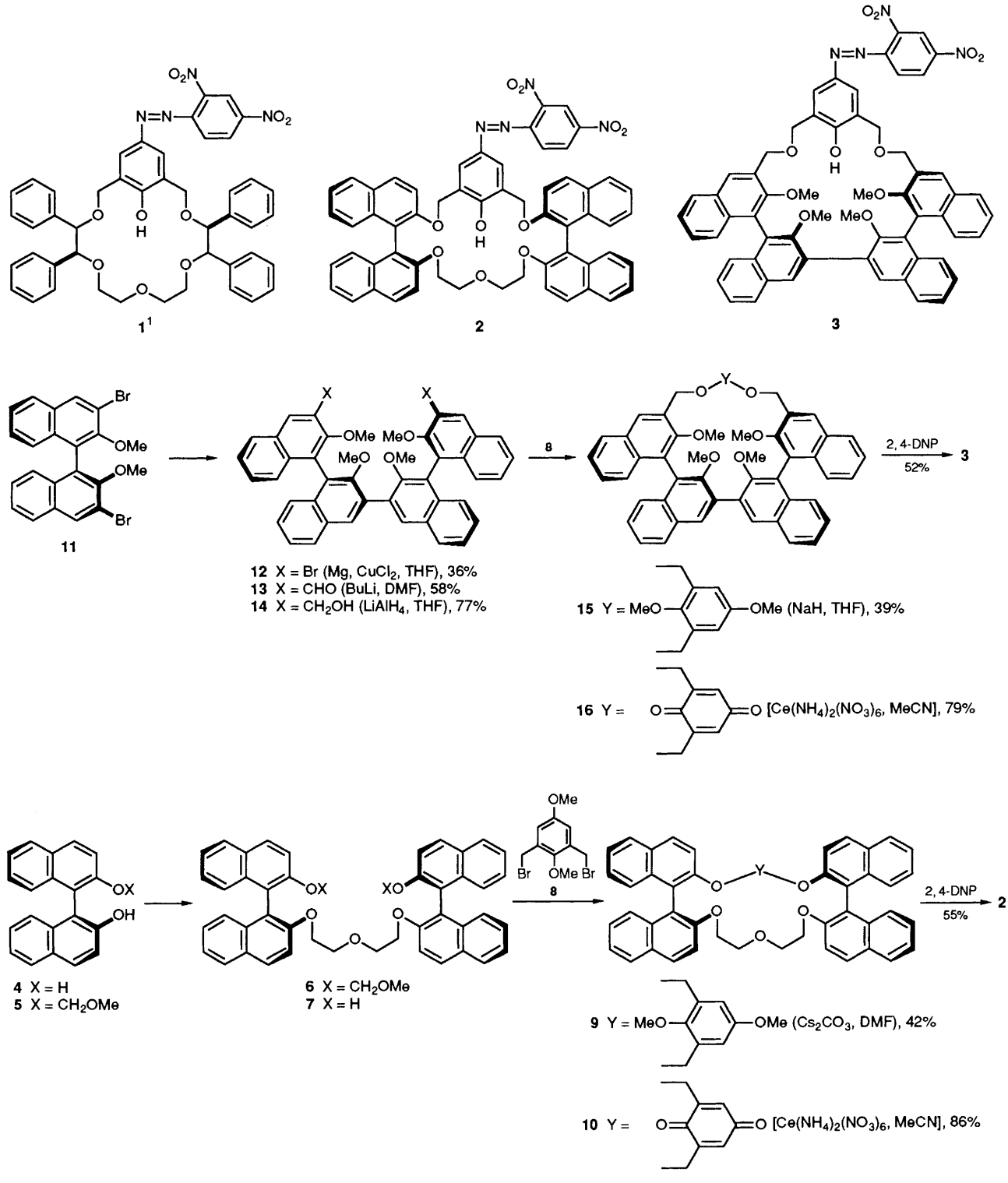
† Compound **8** was prepared by the bromination (PBr_3) of 1,3-bis(hydroxymethyl)-2,5-dimethoxybenzene which was derived by the hydroxymethylation (37% formalin, NaOH) of *p*-methoxyphenol followed by methylation with dimethyl sulfate.

‡ Satisfactory analytical and spectroscopic data have been obtained for all new compounds.

Table 1 Absorption maxima of the coloured salts of acerands **2** and **3** with chiral amines in chloroform[a]

Guest[b]	Host[c]	Temp/°C	λ_{max}/nm (ε)	$\Delta\lambda_{max}$
A	(*S*,*S*)-**2**	0	564 (36 500)	3
	(*R*,*R*)-**2**	0	561 (36 100)	
	(*S*,*S*)-**3**	0	574 (23 700)	5
	(*R*,*R*)-**3**	0	579 (24 500)	
B	(*S*,*S*)-**2**	25	571 (41 300)	4
	(*R*,*R*)-**2**	25	576 (42 100)	
	(*S*,*S*)-**2**	0	570 (41 300)	5
	(*R*,*R*)-**2**	0	575 (42 100)	
	(*S*,*S*)-**3**	25	582 (29 100)	4
	(*R*,*R*)-**3**	25	586 (29 600)	
	(*S*,*S*)-**3**	0	579 (30 100)	8
	(*R*,*R*)-**3**	0	587 (31 300)	
C	(*S*,*S*)-**2**	0	575 (40 500)	3
	(*R*,*R*)-**2**	0	578 (40 900)	
	(*S*,*S*)-**3**	0	582 (29 100)	5
	(*R*,*R*)-**3**	0	587 (29 700)	

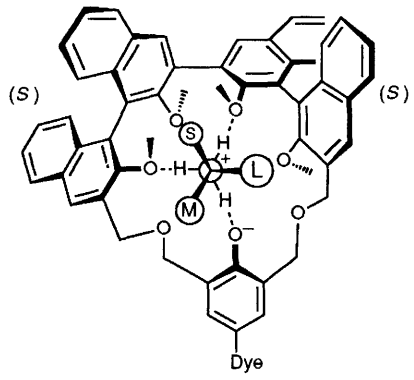
[a] An acerand to amine molar ratio of 1 : 10^3 was employed in all cases. [b] Commercially available chiral amines were used without further purification after checking their rotation: **A** = (*S*)-2-aminopropan-1-ol; **B** = (*S*)-1-(1-naphthyl)ethylamine; **C** = (*S*)-1-phenylethylamine. [c] Chloroform solutions of an enantiomeric pair of acerands were adjusted to *ca.* 10^{-5} mol dm^{-3} concentration.



(CHCl$_3$). Oxidation of (+)-(*R*,*R*)-**9** with cerium(IV) ammonium nitrate (CAN)[1] gave the quinone (+)-(*R*,*R*)-**10** (86% yield) whose condensation with 2,4-dinitrophenylhydrazine (2,4-DNP) gave the azophenolic acerand (+)-(*R*,*R*)-**2** as orange needles, m.p. 163–164 °C, 55% yield, $[\alpha]_D^{24}$ + 119 (CHCl$_3$).§ By the parallel sequence of reactions with the (*S*)-enantiomer, (−)-(*S*)-**4** was converted into (−)-(*S*,*S*)-**2**, m.p. 164–165 °C, $[\alpha]_D^{24}$ −121 (CHCl$_3$).

The optically active hemispherands[7] (−)-(*R*,*R*)-**15**: m.p. 178–180 °C, $[\alpha]_D^{24}$ −245 (CHCl$_3$); and (+)-(*S*,*S*)-**15**: m.p. 179–181 °C, $[\alpha]_D^{24}$ +241 (CHCl$_3$), were prepared *via* a sequence of conversions involving Grignard coupling of 3,3′-dibromo-2,2′-dimethoxy-1,1′-binaphthyl **11**[8] [Mg, $CuCl_2$, tetrahydrofuran (THF)] (34–36% yield), formylation of **12** (BuLi, DMF; 55–58% yield), reduction of **13** ($LiAlH_4$, THF; 78–80%), and coupling of **14** with **8** (Cs_2CO_3, DMF; 37–40%). Oxidation of the hemispherands (+)-(*S*,*S*)-**15** and (−)-(*R*,*R*)-**15** with CAN followed by condensation with 2,4-dinitrophenylhydrazine gave the other type of acerand as

§ Selected spectroscopic data for (+)-(*R*,*R*)-(**2**): ^{1}H NMR (270 MHz, CDCl$_3$) δ 2.91–3.07 (m, CH$_2$, 4H), 3.66–3.75 (m, CH$_2$, 4H), 5.12 (d, *J* 12.5 Hz, CH$_2$, 2H), 5.23 (d, *J* 12.5 Hz, CH$_2$, 2H), 7.16–8.04 (m, ArH, 25H), 8.56 (dd, *J* 2.2, 8.5 Hz, ArH, 1H), 8.79 (d, *J* 2.2 Hz, ArH, 1H) and 8.90 (s, ArH, 1H); UV(CHCl$_3$) λ_{max} (ε) 270 (5.47 × 10^4), 291 (4.47 × 10^4), 335 (3.29 × 10^4) and 401 nm (3.67 × 10^4).



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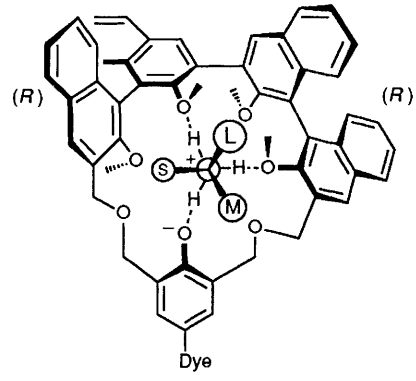

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L (large) = naphthyl
M (medium) = Me
S (small) = H

orange needles, (+)-(*S*,*S*)-**3**, m.p. 246–248 °C, $[\alpha]_D^{24}$ +228 ($CHCl_3$), 45% yield; and (−)-(*R*,*R*)-**3**, (m.p. 245–247 °C, $[\alpha]_D^{24}$ −224 ($CHCl_3$), 43% yield,¶ respectively.

Three colourless chiral amines, (*S*)-2-aminopropan-1-ol, (*S*)-1-(1-naphthyl)ethylamine, and (*S*)-1-phenylethylamine, were treated in chloroform with two enantiomeric pairs of yellow azophenolic acerands **2** and **3** to give six diastereoisomeric sets of purple ammonium phenolates, whose visible spectra were determined. The absorption maxima for the phenolates appeared in the long wavelength region and varied from 561 to 587 nm for the same type of electronic transition as shown in Table 1. From these results, it can be seen that the rigid host **3** with a tetranaphthyl sequence has a higher enantiomer selective coloration than the less rigid host **2** with two separated binaphthyl sequences and exhibits a significant difference (up to 8 nm) in λ_{max} values between diastereoisomeric sets of the salts towards a sterically bulky amine such as (*S*)-1-(1-naphthyl)ethylamine at 0 °C.

This observation is compatible with the host (*S*,*S*)-**3** showing better complementarity on steric grounds than the (*R*,*R*)-isomer for (*S*)-1-(1-naphthyl)ethylamine, as shown by the three-point binding models **17** and **18**.[9] Hence, hydrogen bonding between the phenolate oxygen of the host and an HN^+ hydrogen of the guest in **17** stabilizes the energy of the polar ground state leading to a blue-shift.

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References

1 T. Kaneda, Y. Ishizaki and S. Misumi, *J. Am. Chem. Soc.*, 1988, **110**, 2970; T. Kaneda, S. Umeda, Y. Ishizaki, H.-S. Kuo and S. Misumi, *J. Am. Chem. Soc.*, 1989, **111**, 1881; T. Kaneda, H. Hirose and S. Misumi, *J. Am. Chem. Soc.*, 1989, **111**, 742.
2 K. Yamamoto, H. Fukushima, Y. Okamoto, K. Hatada and M. Nakazaki, *J. Chem. Soc., Chem. Commun.*, 1984, 1111; K. Yamamoto, K. Noda, and Y. Okamoto, *J. Chem. Soc., Chem. Commun.*, 1985, 1065; K. Yamamoto, T. Ikeda, T. Kitsuki, Y. Okamoto and M. Nakazaki, *J. Chem. Soc., Perkin Trans. 1*, 1990, 271.
3 D. J. Cram and J. M. Cram, *Acc. Chem. Res.*, 1978, **11**, 8; J. M. Timko, R. C. Helgeson and D. J. Cram, *J. Am. Chem. Soc.*, 1978, **100**, 2828; S. C. Peacock, L. A. Domeier, F. C. A. Gaeta, R. C. Helgeson, D. M. Walba, F. C. A. Gaeta, R. C. Helgeson and D. J. Cram, *J. Am. Chem. Soc.*, 1980, **102**, 2043.
4 Presented in part at the 61st Annual Meeting of the Chemical Society of Japan, 29th March, 1991, Abstracts II, p. 1135.
5 E. P. Kyba, G. W. Gokel, F. de Jong, K. Koga, L. R. Sousa, M. G. Siegel, L. Kaplan, G. D. Sogah and D. J. Cram, *J. Org. Chem.*, 1977, **42**, 4173.
6 J. Buter and R. M. Kellog, *J. Chem. Soc., Chem. Commun.*, 1980, 466.
7 D. J. Cram, *Angew. Chem., Int. Ed. Engl.*, 1986, **25**, 1039.
8 D. S. Lingenfelter, R. C. Helgeson and D. J. Cram, *J. Org. Chem.*, 1981, **46**, 393.
9 J. van Gent, E. J. R. Sudholter, P. V. Lambeck, T. J. A. Popma, G. J. Gerritsma and D. N. Reinhoudt, *J. Chem. Soc., Chem. Commun.*, 1988, 893.

¶ Selected spectroscopic data for (+)-(*S*,*S*)-**3**: ^1H NMR (270 MHz, $CHCl_3$) δ 3.03 (s, OCH_3, 6H), 3.35 (s, OCH_3, 6H), 4.62 (d, *J* 12.9 Hz, CH_2, 2H), 4.66 (d, *J* 8.6 Hz, CH_2, 2H), 4.68 (d, *J* 12.9 Hz, CH_2, 2H), 5.13 (d, *J* 8.6 Hz, CH_2, 2H), 7.17–7.58 (m, ArH, 10H), 7.80–8.43 (m, ArH, 13H), 8.58 (s, ArH, 1H), 8.77 (s, ArH, 1H) and 9.82 (s, OH, 1H); UV($CHCl_3$) λ_{max} (ε) 327 (1.54×10^4) and 405 nm (2.14×10^4).

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