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Highly efficient and practical resolution of 1,1′-spirobiindane-7,7′-diol by inclusion crystallization with *N*-benzylcinchonidinium chloride

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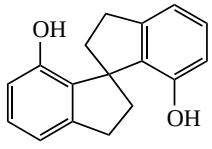
Abstract—The chiral spirobiindane ligand, 1,1′-spirobiindane-7,7′-diol has been resolved efficiently by inclusion complexation with commercially available *N*-benzylcinchonidinium chloride. The resolved complex was studied by X-ray crystallography in order to characterize the intermolecular interactions and recognition nature. © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

C_2-Symmetric biaryl compounds, especially 1,1′-binaphthalene derivatives,[1,2] are widely used in asymmetric synthesis.[3] In contrast, spiranes, another class of molecules with axial chirality, have received limited attention in asymmetric synthesis. For example, chiral spiro compounds that have been employed in asymmetric synthesis include spirobisphosphinite and spirobis(isoxazoline).[4] Recently, a novel chiral spirobiindane derivative, 1,1′-spirobiindane-7,7′-diol (tentatively named SPINOL) **1**, was successfully prepared by Birman and co-workers.[5] The structure of **1** offers a promising combination of chemical robustness and conformational rigidity, and the two OH groups at positions 7 and 7′ will be available for chelating. It was expected that the spiro diol **1** would be an excellent framework for chiral ligands, and this was indeed the case. Compound **1** has been utilized in the synthesis of a monodentate chiral phosphorus ligand that provided extremely high enantioselectivities in the rhodium-catalyzed asymmetric hydrogenation of dehydroamino acids and itaconic acid derivatives.[6]



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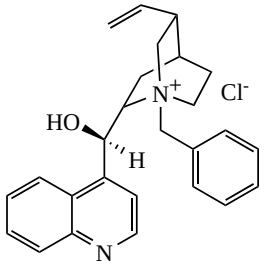

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In order to obtain chiral compound **1**, resolution is considered to be the most convenient method. However, the reported resolution method was a troublesome task.[5] Herein, we describe a more practical approach, commonly used for BINOL and its derivatives,[7] employing co-crystallization of the inclusion complex with *N*-benzylcinchonidinium chloride **2**. A comprehensive evaluation of the structure of the resolved complex and of the intermolecular interaction mode within this crystal is also presented below.

2. Results and discussion

To a suspension of **2** in solvent was added the racemic **1**, and the resulting mixture was stirred for 1 h under

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reflux. The precipitated crystals were collected by filtration and characterized as a 1:1 molecular crystal of **1** and **2** by ^{1}H NMR and elemental analysis.[8] The predominant (*S*)-(−)-form of **1** was obtained by decomposition of the solid diastereomeric complex. Several solvents were examined for improving the efficiency of the resolution, and toluene was found to be the most effective (Table 1). In this case, both enantiomers of **1** were obtained in good enantioselectivity and yield (entry 1, 93% e.e., 86% yield and 92% e.e., 80% yield from the inclusion complex and mother liquor, respectively). When hexane was used as the solvent, a racemic mixture was obtained.

Following these results, the resolution of racemic **1** was performed in toluene, varying the ratio of **2** and **1**, which affected the efficiency of the resolution (Table 2). Satisfactory results were obtained with ratios between 0.5:1 and 0.6:1 (entries 1–3). The best molar ratio of **2** and **1** is 0.55:1, which gave 96% e.e. with 93% yield from the inclusion complex and 90% e.e. with 88% yield from the mother liquor, respectively (entry 2). After the two complexes decomposed, recrystallization from ethyl acetate–hexane gave enantiomerically pure (*S*)-(−)-**1** (>99% e.e.) and (*R*)-(+)-**1** (>99% e.e.) with 82 and 75% overall yields, respectively. Thus, an efficient and practical method for the resolution of **1** has been successfully achieved.

Gratifyingly, we were able to obtain a single crystal of the inclusion complex of *S*-(−)-**1** and **2** suitable for X-ray crystallography.[9] The ORTEP view of the crystal structure is shown in Fig. 1A, which indicates that the molecular complex consists of one molecule of (−)-**1** and one molecule of **2**. In contrast to the structure of the molecular crystals of BINOL and its derivatives with *N*-benzylcinchonidinium halides,[7a,7c] a perspective view (Fig. 1B) showed that a remarkable feature of the crystal is the stacking of a nanotube.[10] However, it is filled with the benzyl group of **2**, rather than being hollow. Fig. 2C shows a unit of hollow nanotube, resembling a rectangle of approximate dimensions 12×5 Å. The side view down the *a* axis of the assembly (Fig. 2D) displays a right-handed helical strand[11] with a pitch of 9.083 Å, which involves two types of hydrogen bonds. The chloride anion links the two hydroxyl groups of *S*-(−)-**1** and **2** by bridging hydrogen bonds between O(1) and O(3) with distances of 3.020(2) and 3.047(2) Å, respectively. The second intermolecular hydrogen bond forms between N(2) of **2** and O(2) of (−)-**1** with a distance of 2.865(3) Å. Such hydrogen bonds thus serve as a driving force for

Table 1. Resolution of (±)-**1** with **2** in different solvents[a]

Entry	Solvent (v/v)	Inclusion complex		Mother liquor	
		E.e.(%)[b]	Yield (%)[c,d]	E.e.(%)[b]	Yield (%)[c,e]
1	Toluene	93	86	92	80
2	Toluene/hexane (3:1)	61	116	92	40
3	Acetone	95	72	69	72
4	Acetone/hexane (1:1)	88	85	79	60
5	Butanone	89	82	70	72
6	Butanone/hexane (1:1)	90	88	91	48
7[f]	Ethanol/hexane (1:6)	84	87	89	76
8	Ether	37	98	83	72

[a] The mol ratio of host **2** and guest **1** is 0.6:1, and resolved by suspension method.
[b] Enantiomeric excess of **1** was determined by chiral HPLC analysis (Chiralcel AD).
[c] Yield based on half of the starting (±)-**1**.
[d] Yield based on 1:1 inclusion complex of **1** and **2**.
[e] Yield of **1** enriched (*R*)-(+)-form, after **2** was separated.
[f] Resolved by crystallization method.

Table 2. Results of resolution in different ratio of **2** and (±)-**1**[a]

Entry	Ratio (**2**:**1**)	Inclusion complex		Mother liquor	
		E.e.(%)[b]	Yield (%)[c]	E.e.(%)[b]	Yield (%)[c,d]
1	0.5:1	98	92	81	107
2	0.55:1	96	93	90	88
3	0.6:1	93	86	92	80
4	0.8:1	58	134	87	56
5	1:1	56	164 (136)[e]	91	44

[a] Resolved in toluene by suspension method.
[b] Enantiomeric excess of **1** was determined by a chiral HPLC analysis (Chiralcel AD).
[c] Yield based on half of the starting (±)-**1**.
[d] Yield of **1** enriched (*R*)-(+)-form, after **2** was separated.
[e] The complex was verified to contain the insoluble **2** by ^{1}H NMR analysis, and yield in parentheses based on 1:1 inclusion complex of **1** and **2**.

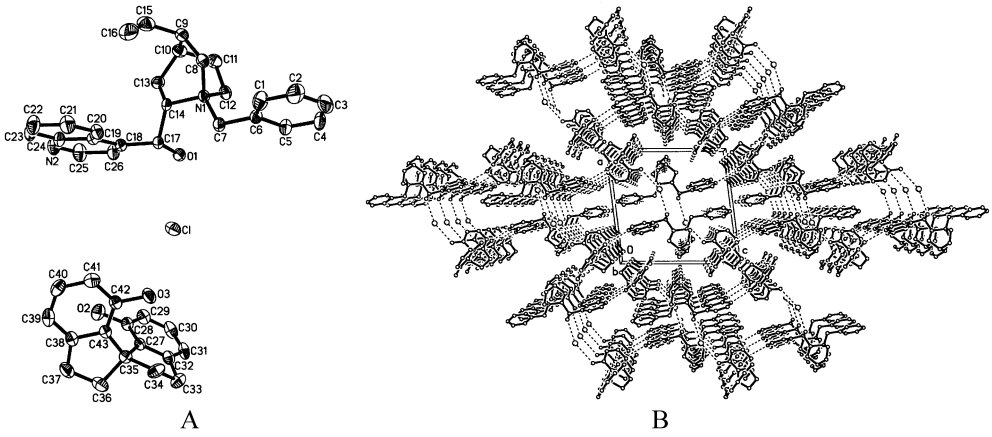

Figure 1. (A) ORTEP drawing of crystal with atom numbering scheme. (B) A perspective view of crystal packing (top view down the *b* axis).

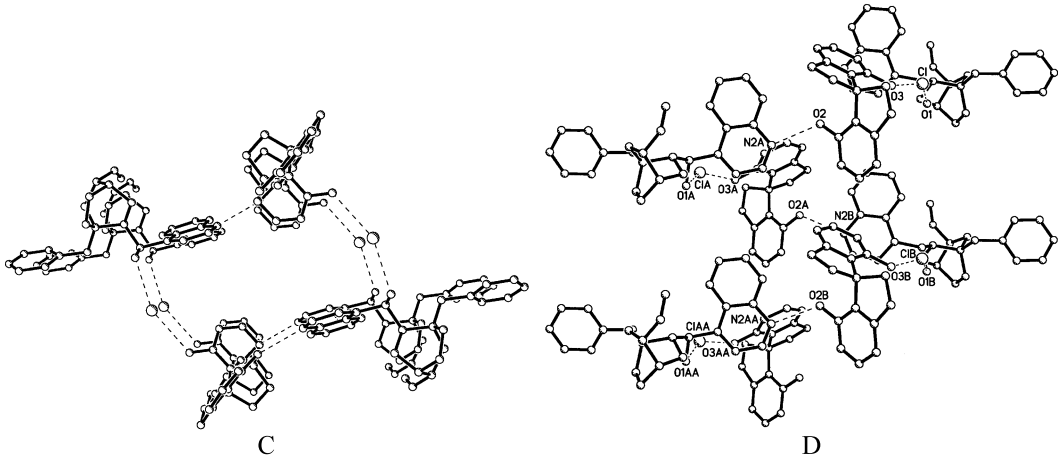

Figure 2. (C) Tubular structure of (−)-**1**·**2** (top view down the *b* axis). (D) Right-handed helical motif (side view down the *a* axis).

the formation of the stable supramolecular nanotube structure.

3. Conclusion

A highly efficient and practical resolution of racemic 1,1′-spirobiindane-7,7′-diol (±)-**1** has been achieved, with the (*S*)-(−)- and (*R*)-(+)-forms of **1** obtained with >99% e.e. in 82% yield from the inclusion complex and 75% yield from the mother liquor, respectively. In the less soluble inclusion complex, (*S*)-(−)-**1** and **2** self-assemble into a supramolecular nanotube with a right-handed helical structure in a 1:1 molar ratio, by a chloride anion bridging hydrogen bond and another common hydrogen bond between (*S*)-(−)-**1** and **2**.

4. Experimental

4.1. Materials and methods

^{1}H NMR were measured on a Bruker 300 (300 MHz) spectrometer. Infrared spectra were measured on a Nicolet 200SXV FT-IR spectrometer. Melting points were determined on a digital melting point apparatus and uncorrected. Optical rotations were measured on a Perkin–Elmer 341 polarimeter. Liquid chromatographic analyses were conducted on a Beckman 110 instrument equipped with a model 168 detector (ultra violet light, 254 nm).

4.2. General procedure for the resolution

N-Benzylcinchonidinium chloride **2** (0.92 g, 2.18 mmol) was added to a solution of racemic **1** (1.00 g, 3.97 mmol) in toluene (30 mL). The mixture was heated under reflux for 1 h and then allowed to cool to room temperature. The resulting white crystalline solid was collected by filtration and washed with toluene to afford (−)-**1**·**2** (1.24 g, 96% e.e., 93% yield). The solid was characterized as a two-component molecular crystal of (*S*)-(−)-**1** and **2** in a 1:1 molar ratio.[8] To a suspension of crystals in ethyl acetate (20 mL) was added 10% HCl (to pH 3) and the mixture was stirred for a few minutes until the white solid was dissolved. The organic layer was separated, washed with brine (2×20 mL) and then dried over Na_2SO_4. After concentration under reduced pressure, recrystallization from ethyl acetate–hexane (1:10 v/v) gave enantiomerically

pure (*S*)-(−)-**1** (>99% e.e.) in 82% overall yield (determined by HPLC on a Chiralcel AD column with 20:80 isopropanol–hexane as eluent, 1.0 mL/min, $t_R = 5.9$ min, $t_S = 7.8$ min). Mp: 156–158°C; $[\alpha]_D^{20} = -38.8$ (*c* 0.6, $CHCl_3$); ^1H NMR ($CDCl_3$): 2.15–2.37 (m, 4H), 2.98–3.14 (m, 4H), 6.70 (d, $J = 8.1$ Hz, 2H), 6.91(d, $J = 7.5$ Hz, 2H), 7.19 (t, $J = 7.5$, 8.1 Hz, 2H); IR (KBr, cm^{-1}): 776, 1298, 1467, 1588, 1614, 3484 (O–H). Anal. calcd for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39. Found: C, 80.88; H, 6.40%. The mother liquor was concentrated to dryness and (*R*)-(+)-**1** was obtained with 90% e.e. by following the procedure for the decomposition of (*S*)-(−)-**1**. Further recrystallization from ethyl acetate–hexane (1:30 v/v) gave enantiomerically pure (*R*)-(+)-**1** (>99% e.e.) with 75% overall yield. Mp: 156–158°C; $[\alpha]_D^{20} = +39.3$ (*c* 0.6, $CHCl_3$); ^1H NMR ($CDCl_3$): 2.19–2.36 (m, 4H), 3.03–3.09 (m, 4H), 4.64 (s, 2H, -OH), 6.70 (d, $J = 8.1$ Hz, 2H), 6.91(d, $J = 7.5$ Hz, 2H), 7.19 (t, $J = 7.8$ Hz, 2H); IR (KBr, cm^{-1}): 776, 1298, 1467, 1588, 1614, 3484 (O–H). Anal. calcd for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39. Found: C, 80.89; H, 6.42%.

4.3. X-Ray investigation and crystal data

Colorless crystals of (*S*)-(−)-**1**·**2** were grown from acetonitrile at room temperature. The X-ray diffraction data were collected on a Siemens P4 automatic four-circle diffractometer using graphite monochromated Mo Kα radiation ($\lambda = 0.71073$ Å) at room temperature. The structure was solved by direct methods using SHELXS-97[12] and refined by full-matrix least-square calculation on F^2 with SHELXL-97.[13] Crystal data for (*S*)-(−)-**1**·**2** ($C_{43}H_{45}ClN_2O_3$): $M_w = 673.26$, crystal size 0.58×0.42×0.22 mm, monoclinic, space group $P2(1)$, $a = 13.944(2)$, $b = 9.083(2)$, $c = 14.316(3)$ Å, $\alpha = 90$, $\beta = 97.03(2)$, $\gamma = 90°$, $V = 1799.5(6)$ Å^3, $Z = 2$, $D_{calcd} = 1.243$ Mg m^{-3}, $F(000) = 716$, $T = 288$ K. All non-hydrogen atoms were refined anisotropically, whereas the hydrogen atoms were generated geometrically. Final R indices [$I > 2\sigma(I)$]: $R_1 = 0.0428$, $wR_2 = 0.0853$. Calculations were performed on a PII-350 computer using the Siemens SHELXTL program package.[14] Further data have been deposited with the Cambridge Crystallographic Data Centre.[9]

Acknowledgements

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References

1. Rosini, C.; Franzini, L.; Raffaelli, A.; Salvadori, P. *Synthesis* **1992**, 503.
2. (a) BINAP: Miyashita, A.; Takaya, H.; Souchi, T.; Noyori, R. *Tetrahedron* **1984**, *40*, 1245; (b) BINAPO: Grubbs, R. H.; Devries, R. A. *Tetrahedron Lett*. **1977**, *17*, 1879.
3. Whitesell, J. K. *Chem. Rev*. **1989**, *89*, 1581.
4. (a) Chan, A. S. C.; Hu, W.; Pai, C.-C.; Lau, C.-P.; Jiang, Y.; Mi, A.; Yan, M.; Sun, J.; Lou, R.; Deng, J. *J. Am. Chem. Soc*. **1997**, *119*, 9570; (b) Srivastava, N.; Mital, A.; Kumar, A. *J. Chem. Soc., Chem. Commun*. **1992**, 493; (c) Arai, M. A.; Kuraishi, M.; Arai, T.; Sasai, H. *J. Am. Chem. Soc*. **2001**, *123*, 2907.
5. Birman, V. B.; Rheingold, A. L.; Lam, K.-C. *Tetrahedron: Asymmetry* **1999**, *10*, 125.
6. Fu, Y.; Xie, J.-H.; Hu, A.-G.; Zhou, H.; Wang, L.-X.; Zhou, Q.-L. *Chem. Commun*. **2002**, 480.
7. (a) Ding, K.; Wang, Y.; Yun, H.; Liu, J.; Wu, Y.; Terada, M.; Okubo, Y.; Mikami, K. *Chem. Eur. J*. **1999**, *5*, 1734; (b) Tanaka, K.; Okada, T.; Toda, F. *Angew. Chem., Int. Ed. Engl*. **1993**, *32*, 1147; (c) Toda, F; Tanaka, K.; Stein, Z.; Goldberg, I. *J. Org. Chem*. **1994**, *59*, 5748; (d) Toda, F.; Tanaka, K. *Chem. Commun*. **1997**, 1087; (e) Cai, D.; Hughes, D. L.; Verhoeven, T. R.; Reider, P. J. *Tetrahedron Lett*. **1995**, *36*, 7991; (f) Hu, Q.-S.; Vitharana, D.; Pu, L. *Tetrahedron: Asymmetry* **1995**, *6*, 2123.
8. Mp 201–203°C (decomp.). Anal. calcd for $C_{43}H_{45}ClN_2O_3$: C, 76.71; H, 6.74; Cl, 5.27; N, 4.16. Found: C, 76.70; H, 6.75; Cl, 5.28; N, 4.19%.
9. Crystallographic data has been deposited with the Cambridge Crystallographic Data Center supplementary publication no. CCDC-180391. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44(0)-1223-336033; e-mail: deposit@ccdc.cam.ac.uk).
10. For review of organic nanotubes, see: Bong, D. T.; Clark, T. D.; Granja, J. R.; Ghadiri, M. R. *Angew. Chem., Int. Ed*. **2001**, *40*, 988.
11. (a) Rowan, A. E.; Nolte, R. J. M. *Angew. Chem., Int. Ed*. **1998**, *47*, 63; (b) Piguet, C.; Bernardinelli, G.; Hopfgartner, G. *Chem. Rev*. **1997**, *97*, 2005; (c) Dapporto, P.; Paoli, P.; Roelens, S. *J. Org. Chem*. **2001**, *66*, 4930.
12. Sheldrick, G. M. SHELXS-97: Program for Crystal Structure Determination, University of Göttingen, 1997.
13. Sheldrick, G. M. SHELXL-97: Program for Crystal Structure Refinement, University of Göttingen, 1997.
14. (a) XSCANS, Version 2.1, Siemens Analytical X-ray Instruments, Madison, WI, 1994; (b) SHELEXTL, Version 5.1, Siemens Industrial Automation, Analytical Instruments, Madison, WI, 1995.