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Spontaneous resolution of a chiral proton sponge

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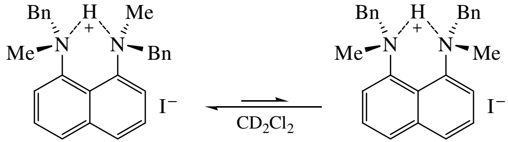
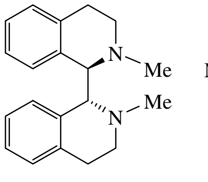
For the first time, the (+)- and (–)-enantiomers of chiral proton sponge (±)-3 have been obtained by spontaneous resolution.

The chemistry of superbasic proton sponges and their applications are known since 1968,[1,2] but chiral proton sponges are of considerable current interest. One of the first chiral proton sponges with non-symmetrically substituted nitrogen atoms (*d*,*l*-**1**) was prepared by Lloyd-Jones *et al.*[3]



d,*l*-**1** *meso*-**1**

However, it crystallises as a racemic compound (space group $P2_1/c$); therefore, its enantiomers cannot be obtained by spontaneous resolution. It is also impossible to resolve *d*,*l*-**1** *via* its diastereomeric salts with chiral acids due to fast enantiomerisation in solution through the intermediate *meso*-form ($\tau_{1/2} < 2$ min).[3(a)]



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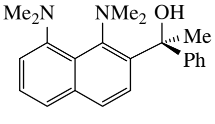

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Elliott *et al.*[4] reported highly basic sponge-like diamine **2** of C_2 symmetry. This compound also crystallises in achiral space group $P2_1/c$; hence, its spontaneous resolution is impossible. Nevertheless, it is basically feasible to carry out its optical resolution either by chiral chromatography or *via* diastereomeric salts with optically active acids.

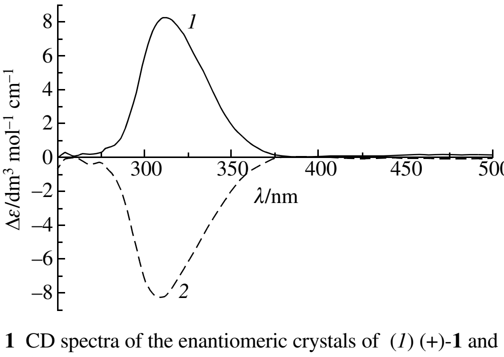

Figure 1 CD spectra of the enantiomeric crystals of (*1*) (+)-**1** and (*2*) (–)-**1** in methanol.

Chiral proton sponge **3** containing an asymmetric substituent at the 2-position has been synthesised, and this compound was found to crystallise in chiral space group $P2_12_12_1$ ($Z = 4$).[5] Thus, we could deal with a conglomerate and hope to effect its spontaneous resolution. Indeed, a number of conglomerates crystallising in the same space group are known to resolve easily;[6] however, not a few cases are found when the resolution was obstacled by recemic twinning.[6(a),(b)] It turned out that a racemic mixture of **3** is easily resolved by routine crystallisation from $CHCl_3$ or C_6H_6, and the single crystals (separated by triage) have a very high optical activity due to the presence of a naphthyl chromophore (Table 1).[†] For example, for a dibenzo analogue of the Tröger base containing two naphthyl fragments, $[\alpha]_{578}^{20} = +1166$ (c 0.4, $CHCl_3$).[6(c),(d)]

The two selected crystals with the opposite optical rotation signs were characterised by CD spectra (Figure 1):[†] $\Delta\varepsilon_{max} = +8.2$ and -8.2 dm³ mol⁻¹ cm⁻¹ ($\lambda = 310$ nm). An attempt to determine *ee* for the studied single crystals of **3** using NMR spectroscopy with the addition of chiral shift reagents such as Eu(tfc)$_3$ or (S)-1,1′-bi(2-naphthol) in $CDCl_3$ failed. However, it was performed using HPLC.[†] Analysis of the solutions presented in Table 1 shows *ee* = 100% for (–)-enantiomer and 99.5% for (+)-enantiomer. Upon crystallisation from benzene, (+)- and (–)-enantiomers were obtained with *ee* = 100%. Further studies

Table 1 Optical rotation of the enantiomers of **3**.[†]

λ/nm	$[\alpha]_\lambda^{20}$	
	(+)-**3** (c 0.068, $CHCl_3$)	(–)-**3** (c 0.047, $CHCl_3$)
578	+434.8	–438.6
546	+497.0	–514.3
436	+1367.0	–1379.0
406	+2274.0	–2314.0

[†] *1,8-Bis(dimethylamino)-2-(α-hydroxy-α-phenylethyl)naphthalene* **3** was obtained by the earlier described method[5] and identified by ¹H NMR using a Bruker WM-400 spectrometer. For a single crystal of 0.25 mg with $[\alpha]_{406}^{20} = +2087$ (c 0.006, $CHCl_3$), mp 218.5–219 °C, whereas for the ground racemic mixture mp 187–189 °C (lit.,[5] mp 191–193 °C). The optical rotation angles (Table 1) were measured using Polamat A (cell lengths 5 and 10 cm). CD spectra for the crystals with $[\alpha]_{546}^{20} = +240$ and –225 were measured in methanol using a CDS dichrometer (2 mm cell). HPLC: column, chiralcel OD (25 cm length × 4.6 mm diameter); UV detector, 254 nm; mobile phase, propan-2-ol in hexane 5%; flow rate, 1 ml min⁻¹; temperature, 18 °C. The retention times for (+)-enantiomer $t_1 = 5.0 \pm 0.2$ min, for (–)-enantiomer $t_2 = 6.4 \pm 0.2$ min.

on determination of the absolute configuration of **3** [by XRD of the salt of (+)-**3** with (*S*)-(+)-mandelic acid], as well as developing a more efficient method for the synthesis of **3**, are in progress.

Thus, for the first time, superbasic chiral proton sponge **3** was obtained in both enantiomerically pure forms. This gives a new outlook for the use of chiral proton sponges in enantioselective processes.

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References

1 R. W. Alder, P. S. Bowman, W. R. S. Steele and D. R. Winterman, *J. Chem. Soc., Chem. Commun.*, 1968, 723.

2 A. F. Pozharskii and V. A. Ozeryanskii, in *The Chemistry of Anilines*, ed. Z. Rappoport, J. Wiley & Sons, Chichester, 2007, ch. 17, pp. 931–1026.

3 (*a*) J. P. H. Charmant, G. C. Lloyd-Jones, T. M. Peakman and R. L. Woodward, *Tetrahedron Lett.*, 1998, **39**, 4733; (*b*) J. P. H. Charmant, G. C. Lloyd-Jones, T. M. Peakman and R. L. Woodward, *Eur. J. Org. Chem.*, 1999, **5**, 2501; (*c*) P. Hodgson, G. C. Lloyd-Jones, M. Murray, T. M. Peakman and R. L. Woodward, *Chem. Eur. J.*, 2000, **6**, 4451.

4 M. C. Elliott, E. Williams and S. T. Howard, *J. Chem. Soc., Perkin Trans. 2*, 2002, 201.

5 A. F. Pozharskii, A. V. Degtyarev, O. V. Ryabtsova, V. A. Ozeryanskii, M. E. Kletskii, Z. A. Starikova, L. Sobczyk and A. Filarowski, *J. Org. Chem.*, 2007, **72**, 3006.

6 (*a*) P. A. Levkin, V. Yu. Torbeev, D. A. Lenev and R. G. Kostyanovsky, in *Topics in Stereochemistry*, eds. S. E. Denmark and J. S. Siegel, Wiley-Interscience, New York, 2006, ch. 4, pp. 81–134; (*b*) V. Yu. Torbeev, K. A. Lyssenko, O. N. Kharybin, M. Yu. Antipin and R. G. Kostyanovsky, *J. Phys. Chem., B*, 2003, **107**, 13523; (*c*) R. G. Kostyanovsky, V. R. Kostyanovsky, G. K. Kadorkina and K. A. Lyssenko, *Mendeleev Commun.*, 2003, 111; (*d*) R. G. Kostyanovsky, V. R. Kostyanovsky, G. K. Kadorkina and K. A. Lyssenko, *Mendeleev Commun.*, 2001, 1.

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