



Preparation and Absolute Configuration of Hexahydroxyter- and Octahydroxyquaternaphthalene Derivatives

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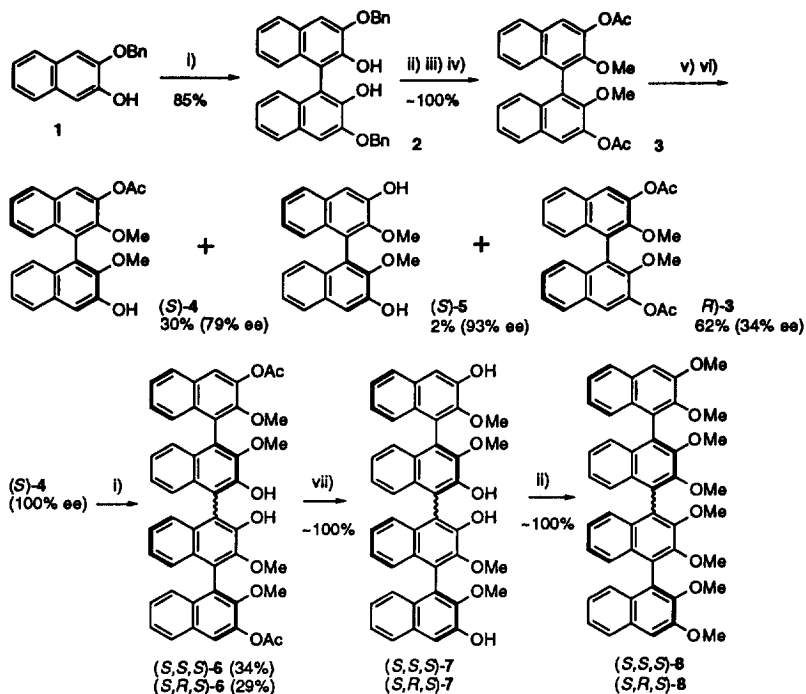
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Abstract: Oxidative coupling reactions of the stereochemically defined *S*-tetrahydroxybinaphthalene derivative gave a separable mixture of two diastereomers of the quaternaphthalenes of *S, S, S* and *S, R, S* configurations, whose stereostructures were confirmed by an alternative chemical transformation through the ternaphthalenes as well as the X-ray structure analysis. The CD spectra of the corresponding diastereomers were indicative of the stereochemistry across the axis. Copyright © 1996 Elsevier Science Ltd

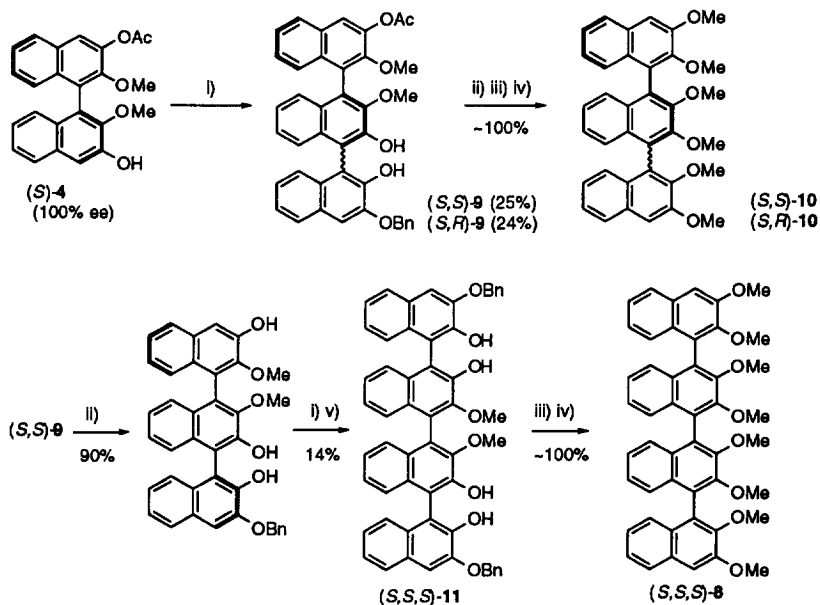
Polyaryls linking at the 1,4-positions (*para*-polyaryls) are attractive molecules possessing a rigid, long and rod-like structures, from which unusual physical properties¹ might be expected, besides their usage as spacer units.² More interesting is that a high rotational barrier along the main axis causes the occurrence of dissymmetry of the molecules, hence the stereochemically controlled construction of polyaryls, such as polynaphthyls, permits a unique molecular architecture of special functions including helicity. Although some preparation methods of polyaryls are available,³ there has been a relatively small number of reports describing optically active and ordered *para*-polyaryls.⁴ In this context, the preparation and characterization of conformationally and/or configurationally defined ter- and quaternaphthyl derivatives are of great value for the construction of the higher oligomers. We report here the preparation and absolute stereochemistry of the titled derivatives using a dimer unit of definite configuration.

(*S*)-2,2',3,3'-Tetrahydroxy-1,1'-binaphthalene derivative **4**, a useful candidate for the construction of conformationally locked polynaphthalenes, was prepared by the oxidative coupling⁵ of the monobenzyl ether of 2,3-dihydroxynaphthalene **1** followed by transformations with the aid of the enzyme Lipase P⁶ as shown in Scheme 1.⁷ Purification by repeated recrystallization led to an enantiomerically pure sample⁸ of (*S*)-**4** whose stereostructure was deduced from a comparison of CD spectra of related compounds (Figure 1), and determined chemically by the transformation to the known (*S*)-2,2'-dimethoxy-1,1'-binaphthalene.⁹

Oxidative coupling⁵ of (*S*)-**4** in the presence of the racemic phenylethylamine and copper chloride gave the *S,S,S*-isomer and the *S,R,S*-isomer of quaternaphthyl derivatives **6** in 34 and 29% yield, respectively, after chromatographic separation. These compounds were independently converted to the corresponding octamethoxyquaternaphthalenes **8** (Scheme 1).



Scheme 1. i) phenylethylamine / CuCl_2 / CH_2Cl_2 / MeOH, r. t. 18 h ii) MeI / K_2CO_3 / acetone, reflux iii) 10% Pd/C- H_2 iv) Ac_2O / pyr. v) Lipase P / MeOH / *i*-Pr₂O, 37° C, 26 h vi) SiO_2 column chromatography vii) K_2CO_3 / MeOH



Scheme 2. i) 1 / phenylethylamine / CuCl_2 / CH_2Cl_2 / MeOH, r. t. 18 h ii) K_2CO_3 / MeOH iii) 10% Pd/C- H_2 iv) MeI / K_2CO_3 / acetone v) SiO_2 column chromatography

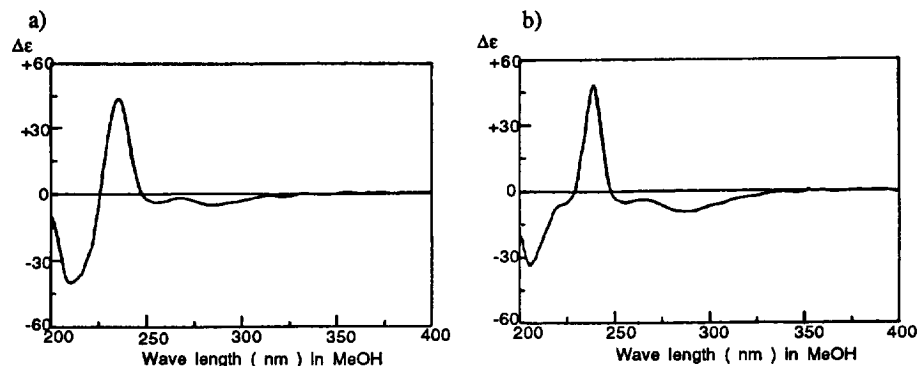


Figure 1. CD spectra of (*S*)-4 (a) and (*S,S*)-10 (b).

For the purpose of determination of the stereostructure of the products **6-8**, an alternative synthesis of quaternaphthalene derivatives was carried out through prior construction of ternaphthalene derivatives (Scheme 2).⁷ The dimer possessing a stereochemically defined structure, (*S*)-4, again served as a building unit for the establishment of the configuration of quaternaphthalene derivatives. Thus, the coupling of (*S*)-4 with **1** afforded a easily separable mixture of nearly equal amounts of two ternaphthalenes **9** in 49% combined yield, together with bi- and quat-naphthalenes. The CD spectra of the derived hexamethoxy compounds **10** indicated that one of the isomers possesses an *S,S*-configuration, whereas that of the other isomer lacks a clear Cotton effect due to the *meso* structural element of an *S,R*-configuration (Figure 1). The following transformation proved that CD data were consistent with the proposed structure. Further coupling reaction of the compound derived from (*S,S*)-9 with **1** resulted in formation of a mixture of two diastereomers of quaternaphthalenes **11**. The mixture was separated and then one of the diastereomers was transformed into the octamethoxyquaternaphthalene **8**, which was completely identical with the sample prepared previously in Scheme 1 in terms of the retention time in HPLC analysis on the chiral stationary phase,⁸ and CD, ¹H- and ¹³C-NMR, IR spectra. These experiments unambiguously established the absolute configuration of each of the two quaternaphthalene derivatives **8** obtained by the coupling of (*S*)-4 as *S,S,S* and *S,R,S*.

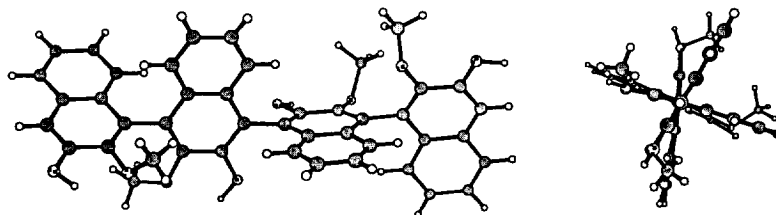


Figure 2. Crystal structure of (*S,S,S*)-7; side view (left) and top view (right).

A single X-ray crystallographic analysis¹⁰ was carried out with the (*S,S,S*)-compound **7**, and it was found that **7** cocrystallized with a molecule of EtOAc and each dihedral angle between naphthalene π -systems is 74.7°, 79.7° and 113.0° in solid state (Figure 2). It is interesting that the repeat of the same configuration around the axis of the polyhydroxypolynaphthalene enforces the molecule helical like (*S,S,S*)-**8**; on the other hand, alternate *R* and *S* configuration might result in formation of a unique

molecule, where the hydrophilic moiety locates in one site and the hydrophobic in the other site. In this study, configurationally unequivocal (*S,S*)- and (*S,R*)-2,2',2'',3,3',3'''-tetrahydroxy-1,1':4',1''-ternaphthalene, and (*S,S,S*)- and (*S,R,S*)-2,2',2'',2''',3,3',3'''-octahydroxy-1,1':4',1''':4'',1''''-quaternaphthalene derivatives were first synthesized and characterized. Further investigation of the preparation of higher oligomers of controlled length and configurations as well as their specific functions is in progress.

References and Notes

- 1) a) Müller, U.; Adam, M.; Müllen, K. *Chem. Ber.* **1994**, *127*, 437-444. b) Scherf, U.; Müllen, K. *Synthesis* **1992**, 23-38. c) Müller, U.; Baumgarten, M. *J. Am. Chem. Soc.* **1995**, *117*, 5840-5850. d) Kreyenschmidt, M.; Baumgarten, M.; Tyutyulkov, N.; Müllen, K. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1957-1959. e) Tour, J. M.; Sthephens, E. B.; *J. Am. Chem. Soc.* **1991**, *113*, 2309-2311. f) Pelter, A.; Maud, J. M.; Jenkins, I.; Sadecka, C.; Coles, G. *Tetrahedron Lett.* **1989**, *30*, 3461-3464.
- 2) Cristofaro, M. F.; Chamberlin, A. R. *J. Am. Chem. Soc.* **1994**, *116*, 5089-5098.
- 3) a) Unrau, C. M.; Campbell, M. G.; Snieckus, V. *Tetrahedron Lett.* **1992**, *33*, 2773-2776. b) Martin, G. H.; Horak, V. *J. Org. Chem.* **1994**, *59*, 4267-4271. c) Belohradsky, M.; Budesínský, M.; Günterová, J.; Hodacová, J.; Holy, P.; Závada, J.; Čísarová, I.; Podlaha, J. *J. Org. Chem.* **1996**, *61*, 1205-1210. d) Hiyama, T.; Sato, K.-i. *Synlett* **1990**, 53-54. e) Unroe, M. R.; Reinhardt, B. A. *Synthesis* **1987**, 981-986. f) Harada, K.; Hart, H.; Du, C.-J. *J. Org. Chem.* **1985**, *50*, 5524-5528.
- 4) a) Hayashi, T.; Hayashizaki, K.; Ito, Y. *Tetrahedron Lett.* **1989**, *30*, 215-218. b) Yamamoto, K.; Yumioka, H.; Okamoto, Y.; Chikamatsu, H. *J. Chem. Soc., Chem. Commun.* **1987**, 168-169. c) Harada, N.; Hiyoshi, N. *Abstracts of Papers II*, p854, The 69th Annual Meeting of Chemical Society of Japan, Kyoto, March 1995.
- 5) a) Brussee, J.; Groenendijk, J. L. G.; te Koppele, J. M.; Jansen, A. C. A. *Tetrahedron* **1985**, *41*, 3313-3319. b) Hovorka, M.; Scigel, R.; Gunterová, J.; Tichý, M.; Závada, J. *Tetrahedron* **1992**, *48*, 9503-9516. c) Smrcina, M.; Poláková, J.; Vyskocil, S.; Kocovsky, P. *J. Org. Chem.* **1993**, *58*, 4534-4538. d) Noji, M.; Nakajima, M.; Koga, K. *Tetrahedron Lett.* **1994**, *35*, 7983-7984.
- 6) a) Santaniello, E.; Ferraboschi, P.; Grisenti, P.; Manzocchi, A. *Chem. Rev.* **1992**, *92*, 1071-1140. b) Otera, J. *ibid.* **1993**, *93*, 1449-1470.
- 7) All new compounds in this paper provided satisfactory spectroscopic and analytical data.
- 8) HPLC analysis was performed with CHIRALPAK AS or AD (Daicel Chemical Ind., LTD.) column with a solvent system of hexane / 2-PrOH = 9~19 / 1 as eluent.
- 9) (*S*)-**4** was converted straightforward to the known compound, (*S*)-2,2'-dimethoxy-1,1'-binaphthalene, by the following successive procedures in good overall yield; i) K₂CO₃ / MeOH, ii) Tf₂O / pyr / DMAP, iii) 10% Pd-C / H₂.
- 10) Crystal data for (*S,S,S*)-**7**: C₄₄H₃₄O₈·C₄H₈O₂, *M* = 778.85, monoclinic, space group *P*2₁, *a* = 9.469 (4) Å, *b* = 22.477 (3) Å, *c* = 9.590 (3) Å, β = 105.33 (3)°, *V* = 1969 (2) Å³, *Z* = 2, *D*_c = 1.314 gcm⁻³, *R* = 0.0622, reflections used = 4824.