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Exploration of Chiral Aminophenols and Aminonaphthols with C_2-Symmetry

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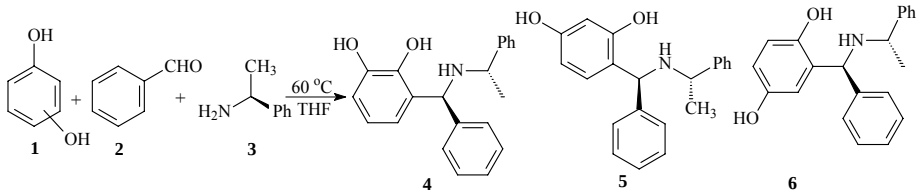
Abstract: The exploration of C_2-symmetric chiral aminophenols and aminonaphthols is described. Seven new ligands have been successfully synthesized using Mannich reaction as a key step. Four of them have C_2-symmetry and their structure has been fully characterized by means of NMR and X-ray crystallography.

Keywords: Aminophenol, aminonaphthol, C_2-symmetry, chiral ligand.

Optically active chiral aminophenols and aminonaphthols have attracted considerable attention as they show excellent enantioselectivities in a wide range of asymmetric reactions, such as asymmetric additions of Et_2Zn to aldehydes[1-3], asymmetric Michael addition[4], asymmetric cyclopropanation[5], asymmetric aldol reactions[6] and *etc*. A variety of aminophenols and aminonaphthols have been reported recently[7, 8]. It is also found that ligands with C_2-symmetry always exhibit high catalytic efficiency, for example the Salen catalyst[9], Corey catalyst[10], Narasaka catalyst[11] and so on. However the studies on aminophenols and aminonaphthols with C_2-symmetry are still rare. In this report we describe the synthesis of C_2-symmetric chiral aminophenols and aminonaphthols. Three new aminophenols **4**-**6** and four new aminonaphthols **9**, **11**, **12**, **13** were obtained. Among them, the aminonaphthols are C_2-symmetric.

Scheme 1 Synthesis of ligands **4**-**6**



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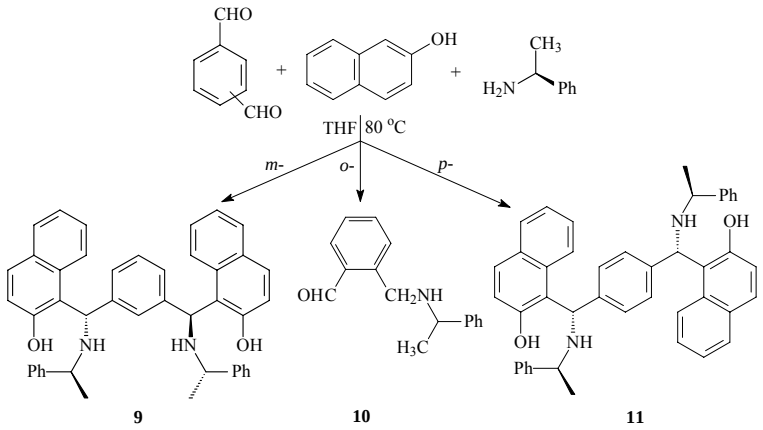
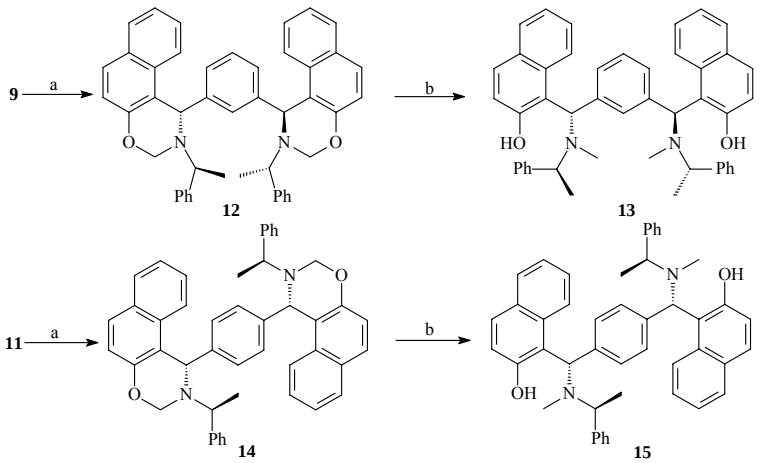
Scheme 2 Synthesis of ligands **9**, **11**



Scheme 3 Synthesis of ligands **13**, **15**

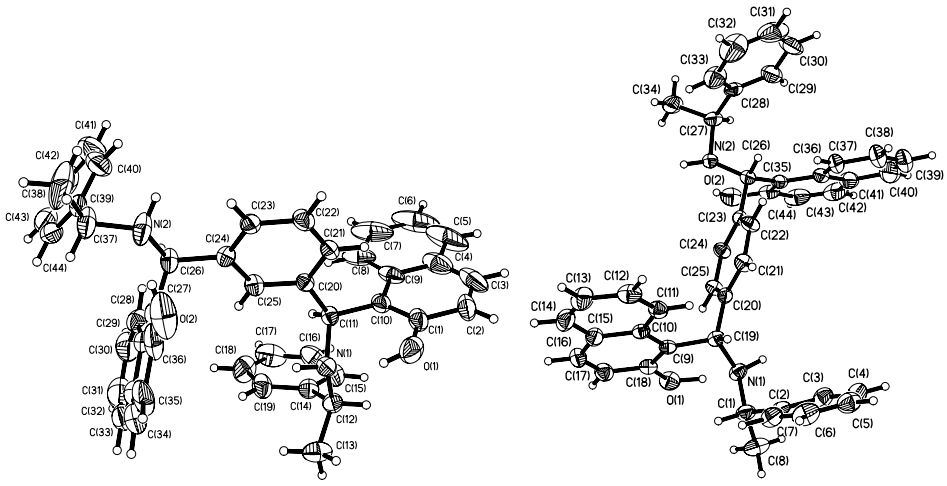


(a) CH_2O, TFA, THF, rt, 4 h; (b)$LiAlH_4$, THF, 80°C,5h.

Table 1 Physical data and elemental analysis of new ligands

Compd.	Yield (isolated %)	m. p. (°C)	$[\alpha]_D^{20}$ (c, THF)	Elemental analysis (Calcd.) C	H	N
4	58	152-154	+216.4 (1.04)	79.07 (78.97)	6.77 (6.63)	4.35 (4.39)
5	26	99-100	+105.6 (0.77)	79.23 (78.97)	6.28 (6.63)	4.21 (4.39)
6	43	141-142	+81.1 (1.03)	78.68 (78.97)	6.48 (6.63)	4.51 (4.39)
9	32	192-194	+306.7 (0.60)	83.95 (84.04)	6.04 (6.41)	4.30 (4.46)
11	45	173-175	+223.5 (0.51)	83.93 (84.04)	6.55 (6.41)	4.72 (4.46)
13	60	145-147	+174.5 (0.47)	83.74 (84.11)	6.51 (6.75)	4.27 (4.26)
15	69	168-170	+164.0 (0.50)	84.07 (84.11)	6.81 (6.75)	4.16 (4.26)

Figure 1 Ortep views of compounds **9** and **11**



The synthetic routes and the products are outlined in **Scheme 1** to **Scheme 3**. Compounds **4**-**6**, **9**, **11** are synthesized through Mannich reaction. The *o*, *m*, *p*-benzenediols **1** and *o*, *m*, *p*-benzenedialdehydes **7** are used as the starting material. And the (*S*)-α-methylbenzyl amine **3** is the resource of the chirality. Condensation of **9** and **11** with formaldehyde afforded **12** and **14**. Reduction of the resulting products with $LiAlH_4$ gave *tert*-aminonaphthols **13** and **15**. The structure of the new compounds has been determined by IR, ^{1}H NMR, ^{13}C NMR, EA, and MS. Selected physical character and elemental analysis of the new ligands are listed in **Table 1**. The absolute configurations of compounds **9** and **11** are established by X-ray crystallography (**Figure 1**).

Although we failed to gain the desired C_2-symmetric products when using benzenediols as the starting material, we obtained three new chiral aminophenols which have three chelating atoms. This may cause different chelation manner of these ligands with metal compared with traditional aminophenols. The catalytic efficiency and mechanism are still worth of studying. Compounds **9**, **11**, **13** and **15** have C_2-symmetry.

In summary, seven new chiral catalysts **4**-**6**, **9**, **11**, **13**, **15** were synthesized, four of which are C_2-symmetric. The synthetic details will be published elsewhere. And the detailed studies of their applications concerning enantio- and diastereoselectivity in some catalytic reactions are under active progressing.

Acknowledgment

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