

An Investigation of the Inherent Chiral Induction Ability of Axially Chiral 1,1'-Binaphthalene Framework in the Prelog's Atrolactic Acid Synthesis

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In the Prelog's atrolactic acid synthesis using 2'-substituted 1,1'-binaphthalen-2-ols as the chiral auxiliaries, the sense of the diastereoselection could not solely be determined by the helicity of the 1,1'-binaphthalene framework. A revised steric model is proposed to explain the selectivity.

Recently axially chiral 1,1'-binaphthalene derivatives have attracted much attention as highly efficient chiral inducers for a wide range of asymmetric reaction. In the course of our study on the remote asymmetric induction using 2'-substituted 1,1'-binaphthalen-2-ols (**1**) as the chiral auxiliary,¹⁾ we recently reported that the Prelog's atrolactic acid synthesis²⁾ using 1,1'-binaphthalen-2-ol (**1a**) as the chiral alcohol resulted in a poor diastereoselectivity [$<20\%$ diastereoisomeric excess (d.e.)],³⁾ in contrast to the high value (85% d.e.) reported previously.⁴⁾ Furthermore, it has been shown that the proposed steric model could not explain the observed sense of diastereoselection.^{3,5)} These discrepancies prompted us to investigate the inherent chiral induction ability of the axially chiral 1,1'-binaphthalene framework. In this letter, we wish to report the Prelog's atrolactic acid synthesis by use of **1** and a steric model to explain the effect of the 2'-substituent.

Homochiral 2'-substituted 1,1'-binaphthalen-2-yl benzoylformates (**2a-2f**), having respectively the same helicity as depicted below, were synthesized in 80 - 90% yields by treatment of the corresponding hydroxyl compounds **1a-1f**^{3,6)} with benzoylformyl chloride. The nucleophilic addition of MeMgI (1.0 mol dm⁻³ in ether) to **2a-2f** in ether at -78 °C afforded the corresponding atrolactic acid esters **3a-3f** and **4a-4f** in high yields with moderate diastereoselectivity (Table 1). The ratio between **3** and **4** was determined by 250 MHz ¹H NMR analysis. The absolute configuration of the newly formed chiral center was determined from the specific rotation of the corresponding atrolactic acid after the complete hydrolysis of the diastereomer mixture.

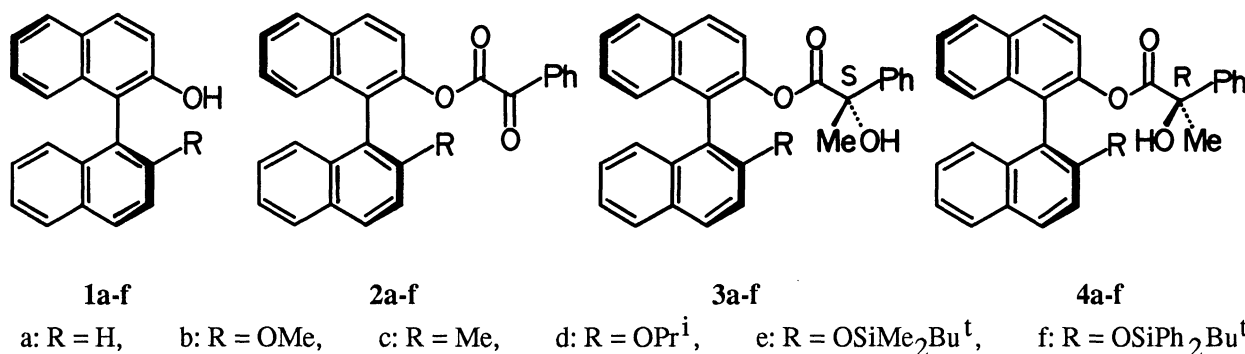


Table 1. Addition of MeMgI to 2a-2f

Ester	R	Yield ^{a)} /%	Ratio (3 : 4) ^{b)}
2a	H	95	52 : 48
2b	OMe	76	53 : 47
2c	Me	74	42 : 58
2d	OPr ⁱ	91	37 : 63
2e	OSiMe ₂ Bu ^t	98	25 : 75
2f	OSiPh ₂ Bu ^t	98	24 : 76

a) Isolated yields were based on the consumed 2.

b) Ratios were determined by 250 MHz ¹H NMR.

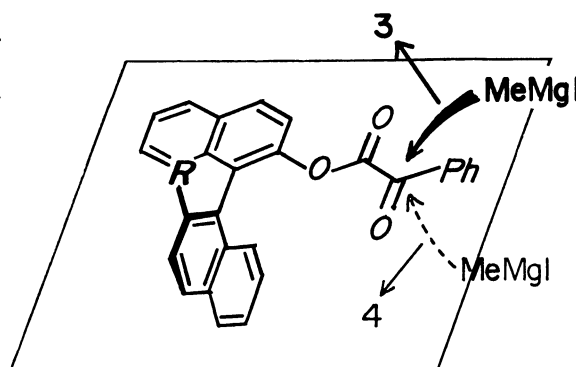


Fig. 1. A revised steric model.

The reaction of 2a and 2b preferentially induced (*S*)-centro-chirality on the atrolactic acid residue, while (*R*)-centro-chirality was preferred in the reaction of 2c-2f. Moreover, the content of 4 increased with increasing the bulkiness of the 2'-substituent. Since the dihedral angle of the two naphthalene plains seems to be around 90°, ⁷⁾ and the α -keto ester moiety of 2a-2f should exist as *s*-trans conformer due to the dipole-dipole repulsion of the two carbonyl groups in the transition state, a steric model depicted in Fig. 1 may explain the diastereoselectivity. Thus, the steric hindrance imposed by C2'-R is smaller than that of the C5'-C8' moiety when the 2'-substituent is H or OMe; MeMgI attacks the keto carbonyl group preferentially from the less hindered upper side to give the diastereomer 3. On the other hand, less hindered site is reversed when 2'-substituent is Me or a bulkier group to give 4 preferentially.

In conclusion, in the Prelog's atrolactic acid synthesis using 2'-substituted 1,1'-binaphthalene-2-ols, the sense of the diastereoselection could not solely be determined by the helicity of the 1,1'-binaphthalene skeleton. It should be noted that the low selectivity observed in the reaction of 2a suggests that the difference of the actual bulkiness between the C2'-R and C5'-C8' moieties of the 1,1'-binaphthalene skeleton is rather smaller than might be expected.

References

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- 6) Compound 1b was prepared from 2'-methoxy-1,1'-binaphthalene-2-carboxylic acid by the following reactions. i, LiAlH₄/THF; ii, HBr/AcOH; iii, LiAlH₄/ether; iv, BBr₃/CH₂Cl₂. Synthesis of 1c and 1d, see: W. H. Pirkle and J. L. Schreiner, *J. Org. Chem.*, **46**, 4988 (1981). Synthesis of 1e and 1f, see: A. Aigner, F. Vögtle, S. Franken, and H. Puff, *Chem. Ber.*, **118**, 3643 (1985).
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