

ENANTIOSELECTIVE SYNTHESIS OF 3-ARYL-3-HYDROXYPROPANOIC ESTERS AS SUBUNITS FOR CHIRAL LIQUID CRYSTALS

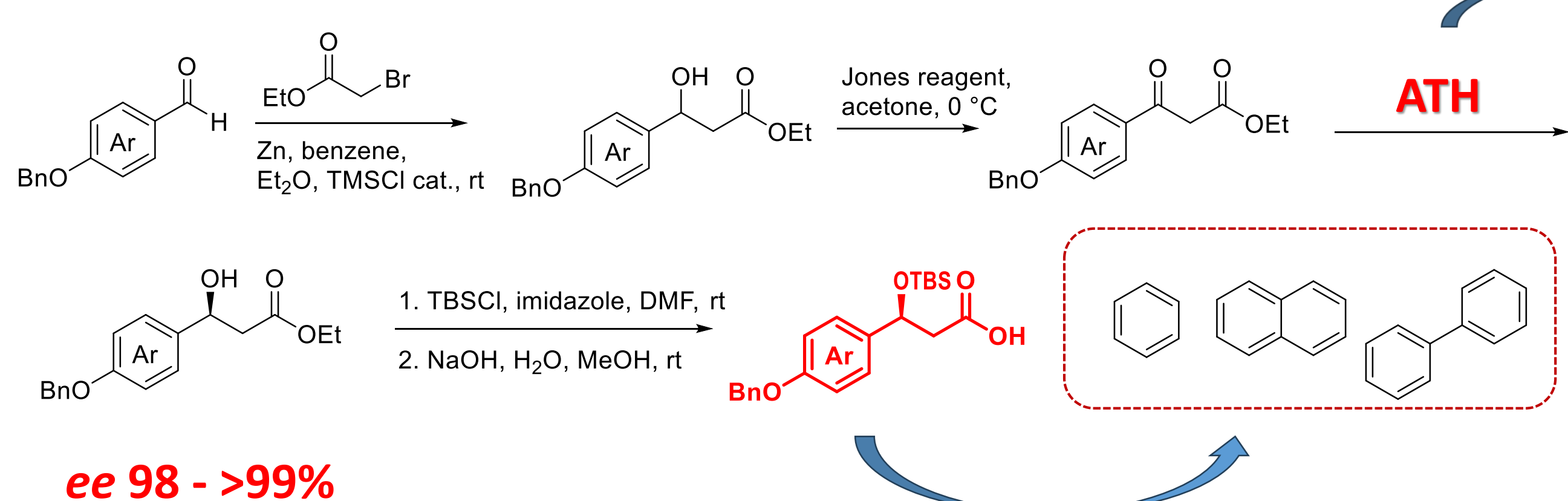
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INTRODUCTION

Liquid crystals (LCs) are dynamic functional soft materials that share the anisotropic properties of the crystalline state and the fluidity of a liquid. Chiral LCs with their unique optical and mechanical properties are perspective functional soft materials for fundamental science and advanced technological applications.^{1,2} The introduction of chirality into LCs results in various chiral liquid crystalline phases such as the cholesteric, chiral smectic, twist grain boundary (TGB), and blue phases (BP), each with unique properties.^{3,4} Our work aimed to develop a versatile chiral building block for liquid crystals that enables the preparation of molecules of various topologies and does not possess methyl branching. In addition, this building block needs to be available both in high enantiomeric purity and in racemic form. Herein, we introduce the chiral 3-aryl-3-hydroxypropanoic ester moiety as a building block that meets those requirements. We used asymmetric transfer hydrogenation (ATH) of β -ketoesters as a method to prepare chiral 3-hydroxypropanoic esters. Ever since the pioneering work of Noyori and Ikariya, catalytic ATH of ketones using Ru(II) complexes has become a widely used method for the synthesis of different chiral secondary alcohols, and many catalytic systems have been developed so far.⁵ Therefore, we believed that variations in both catalyst and ligand, could easily allow for a successful reaction optimization regarding enantioselectivity and scale-up.

SYNTHESIS OF CHIRAL BUILDING BLOCKS USING ATH REACTION

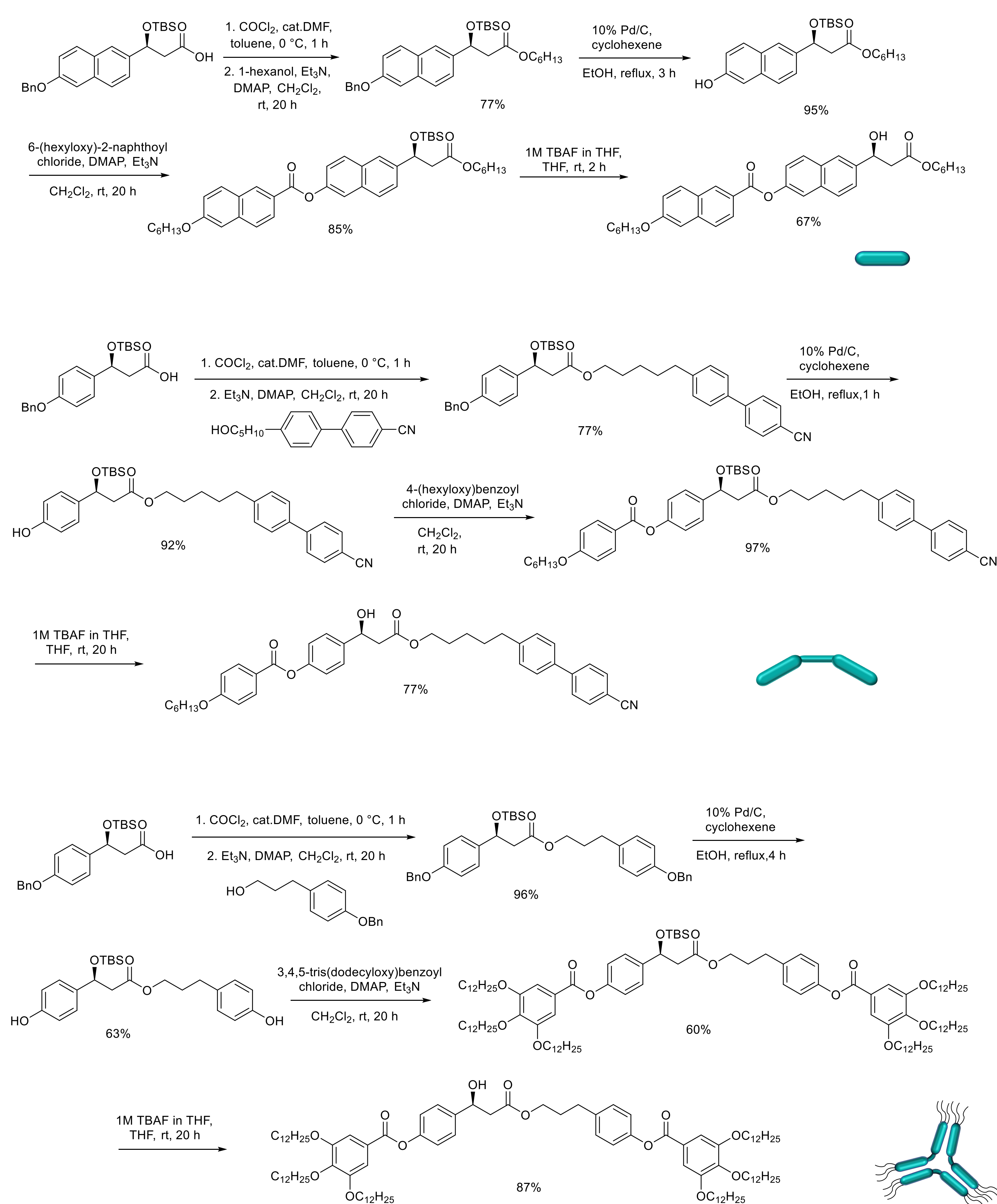


OPTIMIZATION OF ASYMMETRIC HYDROGEN TRANSFER (ATH) REACTION

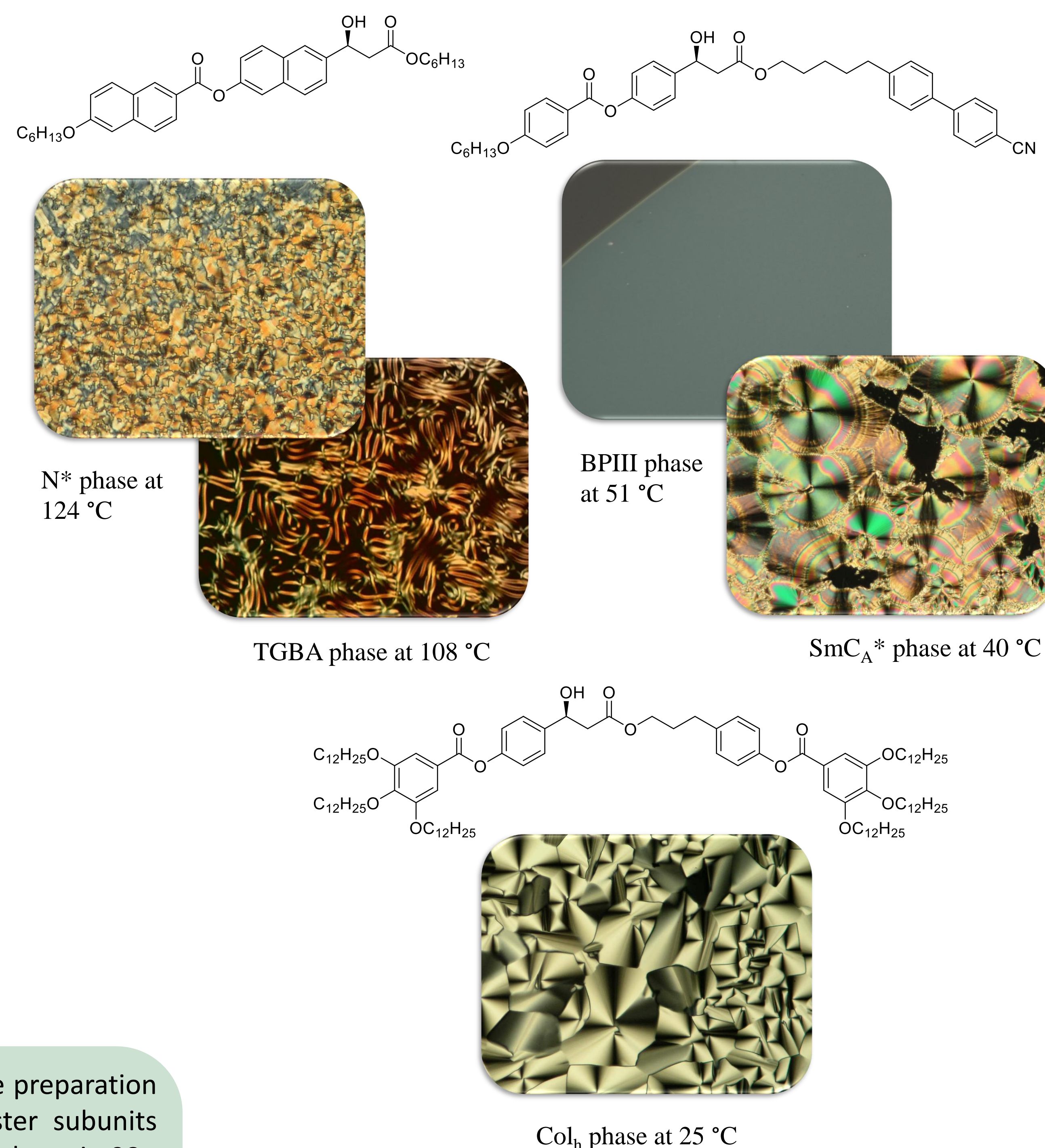
Product	[RuCl ₂ (η ⁶ -arene)] ₂ (mol%)	Ligand	Time (h)	Conversion (%) ^a	Yield (%)	ee (%) ^b	
BnO-CH ₂ -CH(OH)-CH ₂ -CO-OEt	<i>p</i> -cymene (10 mol%), 40 °C	L1	48	70	31	38	
	mesitylene (10 mol%), 40 °C	L1	24	95	81	90	
	benzene (10 mol%), 40 °C	L1	24	100	92	92	
	<i>p</i> -cymene (10 mol%), 40 °C	L2	48	90	70	82	
	mesitylene (10 mol%), 40 °C	L2	3	100	97	97	
	benzene (10 mol%), 40 °C	L2	24	95	73	93	
BnO-CH ₂ -CH(OH)-CH ₂ -CO-OEt	mesitylene (5 mol%), 40 °C	L2	24	100	88	98	
	mesitylene (2 mol%), 40 °C	L2	24	100	82	>99	
	mesitylene (2 mol%), rt	L2	48	95	69	98	
	mesitylene (2 mol%), rt	L2	48	93	78	99	
	BnO-CH ₂ -CH(OH)-CH ₂ -CO-OEt	<i>p</i> -cymene (10 mol%), 40 °C	L1	24	100	87	90
		mesitylene (10 mol%), 40 °C	L1	3	100	92	95
benzene (10 mol%), 40 °C		L1	3	100	94	89	
mesitylene (10 mol%), 40 °C		L2	2	100	81	97	
benzene (10 mol%), 40 °C		L2	3	100	82	91	
mesitylene (5 mol%), 40 °C		L2	3	100	90	98	
BnO-CH ₂ -CH(OH)-CH ₂ -CO-OEt	mesitylene (5 mol%), rt	L2	24	100	73	98	
	mesitylene (2 mol%), 40 °C	L2	24	100	80	98	
	mesitylene (2 mol%), rt	L2	24	100	89	98	
	mesitylene (2 mol%), rt	L2 ^c	24	100	86	>98 ^d	
	BnO-CH ₂ -CH(OH)-CH ₂ -CO-OEt	<i>p</i> -cymene (10 mol%), 40 °C	L1	24	100	91	88
		mesitylene (10 mol%), 40 °C	L1	3	100	82	97
benzene (10 mol%), 40 °C		L1	3	100	89	93	
mesitylene (10 mol%), 40 °C		L2	2	100	81	98	
benzene (10 mol%), 40 °C		L2	3	100	82	94	
mesitylene (5 mol%), 40 °C		L2	24	100	92	98	
BnO-CH ₂ -CH(OH)-CH ₂ -CO-OEt	mesitylene (5 mol%), rt	L2	24	100	83	98	
	mesitylene (2 mol%), 40 °C	L2	24	100	74	98	
	mesitylene (2 mol%), rt	L2	24	100	80	99	

^a Determined by HPLC on InfinityLab Poroshell 120 EC-C18 column in MeOH/H₂O gradient; ^b Determined by HPLC on Chiralcel OD-3 and Chiralpak IA; ^c (1*R*,2*R*)-(-)-*N*-Ts-1,2-DPEN was used instead of (1*S*,2*S*); ^d opposite (*R*) enantiomer obtained

SYNTHESIS OF COMPOUNDS WITH DIFFERENT TOPOLOGIES USING CHIRAL 3-ARYL 3-HYDROXYPROPANOIC ACIDS



MESOMORPHIC PROPERTIES – different for molecules of diverse topologies



CONCLUSION

The chiral 3-aryl-3-hydroxypropanoic ester has demonstrated its versatility as a building block for the preparation of chiral LC compounds with a variety of topologies. Three chiral 3-aryl-3-hydroxypropanoic ester subunits differing in aromatic part were obtained through asymmetric transfer hydrogenation using Ru(II) complexes in 98 - >99% ee.⁶ These subunits were further used for preparation of chiral LC compounds of diverse topologies (rod-like, bent-shaped, and hexacatenar bent-shaped) without deterioration of the ee during the synthesis. Mesomorphic behavior of final LCs was investigated - chiral nematic and smectic phases were identified, as well as rarely observed twist grain boundary A and blue phases.

The utilization of synthetic chiral building blocks offers the possibility of fine-tuning the intermolecular interactions by subtle changes in the molecular structure, as well as the preparation of corresponding racemic forms. This paves the way for the study of self-organization and the structure-property relationship in chiral soft materials.

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REFERENCES

- [1] Wang, L.; Urbas, A. M.; Li, Q. *Advanced Materials* **2020**, *32* (41), 1801335.
- [2] Ariga, K.; Mori, T.; Kitao, T.; Uemura, T. *Advanced Materials* **2020**, *32* (41), 1905657.
- [3] Tschierske, C.; Ungar, G. *ChemPhysChem* **2016**, *17* (1), 9–26.
- [4] Goodby, J. W. *Proc. R. Soc. A* **2012**, *468* (2142), 1521–1542.
- [5] Hashiguchi, S.; Fujii, A.; Takehara, J.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1995**, *117* (28), 7562–7563
- [6] Dokli, I.; Ožegović, A.; Šimanović, A.; Hromin, M.; Knežević, A.; Višnjevac, A.; Lesac, A. *J. Org. Chem.* **2022**, *87* (21), 14045–14057.