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Synthesis and Thermal Behavior of New *N*-Heterotolan Liquid Crystals

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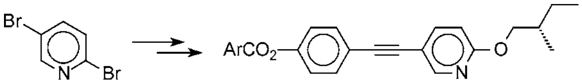
ABSTRACT



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9 a = *n*-heptyl, **b** = *n*-octyl
c = *n*-nonyl, **d** = *n*-decyl
Ar = *p*-$C_nH_{2n+1}OC_6H_4$

The synthesis of liquid crystal series 9a–d was achieved using the Buchwald protocol and Sonogashira reaction.

Liquid crystals are the fascinating condensed state of soft matter with unique electrical, optical, and mechanical properties. The anisotropic properties of liquid crystals make them very attractive materials, which can be found in many practical technological applications such as displays. The self-ordering of the LC may be also extended to living processes such as the cell membrane, which has a bilayer structure self-organized in water. The biological function of the cell membrane is related to cyclic or linear topological shape and is also dependent on the physiological temperature, thus showing fascinating properties.[1]

Among many types of liquid-crystalline architecture, the tolan (diphenylacetylene) and its N-hetero version (pyridylphenylacetylene) play a prominent role in the field of liquid crystals science. The main outstanding features of tolans and related systems are high polarizability, stability, linearity, and phase behavior such as nematic and smectic phases,[2] twist grain boundary phases[3] (TGB), an antiferroelectric smectic phase,[4] and NLO properties.[5]

Liquid crystals containing nitrogen heterocycles present great possibilities in the variations of their permanent dipole moment (value and direction), as well as in their dielectric anisotropy.[6] *N*-Heterocycle mesogens are less symmetric and have lower melting points than analogue phenyl mesogens. However, they present high birefringence and other properties.[7] *N*-Heterotolans may be considered as potential candidates for application to liquid crystal displays, and many synthetic efforts should be put into making them in an acceptable yield.

To observe the relationship between structure and mesomorphic properties, we have introduced a pyridine moiety to produce *N*-heterotolans using the Buchwald protocol[8] and Sonogashira reaction.[9]

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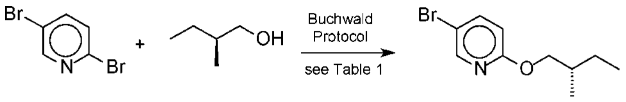
The first is a copper-catalyzed cross-coupling reaction developed by the Buchwald group, and the second is a well-established Sonogashira reaction to introduce an acetylene unit into the final compounds **9a**−**d**.

The Ullmann synthesis is a classical methodology for the construction of aromatic ethers and amines. High temperatures and extended reaction times are needed to ensure reasonable yields. In addition, a high quantity of copper catalyst is often needed. As opposed to the traditional copper-mediated Ullmann ether synthesis, the Buchwald protocol is an efficient and mild method for N-arylation and O-arylation coupling of aryl halides with amines and alcohols, respectively. This prompted us to disclose our preliminary results in the arylation reaction of **1** and the synthesis of chiral liquid crystals by double Sonogashira reaction. In our approach, we were guided by the possibility of constructing chiral ether **3**. The preparation of that key compound provided us the entry to a new class of precursors to high-performance liquid crystal materials.

Synthesis of the Chiral Intermediate 3 by Buchwald Protocol. Our synthetic strategy is outlined in the scheme below. The key intermediate **3** was obtained using the Buchwald protocol.[8] This protocol was particularly suitable for the conversion of **1** into the chiral precursor **3** in acceptable yields, according to Scheme 1.

Scheme 1



1 **2** **3**

We have repeated this protocol several times with different molar quantities of **1**, looking at the yields and regiochemistry of the reaction. We found that the conversion of **1** into **3** can be made even on the scale of 20 mmol of compound **1** (MM 237 g mol^{-1}) and that the O-arylation reaction of **1** occurs regiospecifically at position 2.[10]

Arylation reaction using 2,5-dibromopyridine (**1**) with (*S*)-(−)-2-methyl-1-butanol (**2**) in the presence of cesium carbonate as a mild base, as well as 1,10-phenanthroline as a bidentate nitrogenous ligand and a catalytic amount of copper iodide, provided the chiral intermediate **3** in the yield range of 60−70% (entry 4 in Table 1, Scheme 1).

Under aromatic nucleophilic substitution (S_NAr), arylation reaction of the chiral alcohol **2** using potassium carbonate[10a] or sodium hydride, a more powerful base, provided the desired product, though in a yield of <50% (entries 1 and 2, Table 1).

Table 1. Arylation Reaction under S_NAr and Copper-Catalyzed Coupling

entry	reaction conditions	yield
1	DMSO, K_2CO_3	<50%
2	NaH, DMSO	<50%
3[a]	NaH, DMF	70%
4[b]	CuI, Cs_2CO_3, phenanthroline, toluene	60−70%

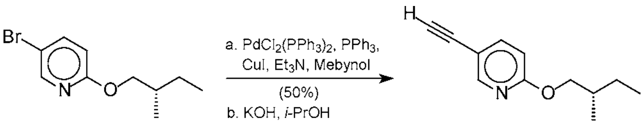
[a] Experimental conditions had not been reproduced on the scale of 10 mmol of reagent **1**. [b] Experimental conditions had been reproduced on the scale of 20 mmol of reagent **1**.

The regioselective copper-catalyzed O-arylation of **1** obtained in this work is in accordance with the results achieved in a previous work reported for the synthesis of 2-alkyl-5-bromopyridine[11] and carboalkoxylation[12] of 2,5-dibromopyridine (**1**). We believe that this method should provide expedient access to a variety of 2,5-disubstituted pyridine liquid crystals.

Entry 2 (Table 1) failed to reproduce the desired product in an acceptable yield. When the solvent was changed to DMF, the product was obtained in 70% yield (entry 3). However, it was possible to reproduce this result only in small quantities, i.e., on the 1 mmol scale. The low yield (entries 1 and 2) and nonreproducibility (entry 3) may be associated with harsh reaction conditions involving high temperature and a strongly basic medium.

Ethynylation Reaction of 3 by Sonogashira Coupling. After accomplishing the synthesis of **3**, we started to build the next key intermediate **4** through a copper−palladium-catalyzed cross-coupling alkynylation reaction,[9] according to Scheme 2.

Scheme 2



3 **4**

Sonogashira alkynylation with 2-methyl-3-butyn-2-ol (Mebynol) followed by deprotection with KOH and 2-propanol[10b] provided (*S*)-5-ethynyl-2-(2-methylbutoxy) pyridine (**4**) in 90% yield, $[\alpha]_D = +13$ (c 1, CH_2Cl_2).

The classical deprotection method[10c] that uses potassium hydroxide in toluene under heating failed. Under those conditions, we observed some decomposition and a degree of polymerization of the starting material.

Convergent Synthesis of the Chiral Heterotolan Liquid Crystal 9a−d. As the synthesis of compound **4** was

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(9) (a) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, *16*, 4467−4470. (b) Sonogashira, K.; Yatake, T.; Tohda, Y.; Takahashi, S.; Hagihara, N. *J. Chem. Soc., Chem. Commun.* **1977**, 291−292. (c) Takahashi, K.; Kuroyama, Y.; Sonogashira, K.; Hagihara, N. *Synthesis* **1980**, 627−630. (d) General review, see: Sonogashira, K. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weiheim, 1998; Chapter 5. (e) Negishi, E.-I.; Anastasia, L. *Chem. Rev.* **2003**, *103*, 1979−2017. Verkade, J. G.; Urgaonkar, S. *J. Org. Chem.* **2004**, *69*, 5752−5755.

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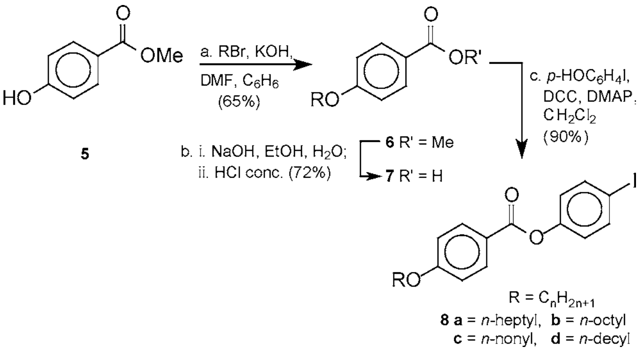
(12) Chambers, R. J.; Marfat, A. *Synth. Commun.* **1997**, *27*, 515−520.

achieved, we started to synthesize other chemical structures, **8a**−**d** (Scheme 3). Alkylation reaction of methyl *p*-hydroxybenzoate (**5**) with alkyl bromides resulted in product **6** in the yield range of 65−80%. Saponification reaction of the ester **6** provided the *p*-*n*-alkoxybenzoic acid (**7**) in 70−80% yield.

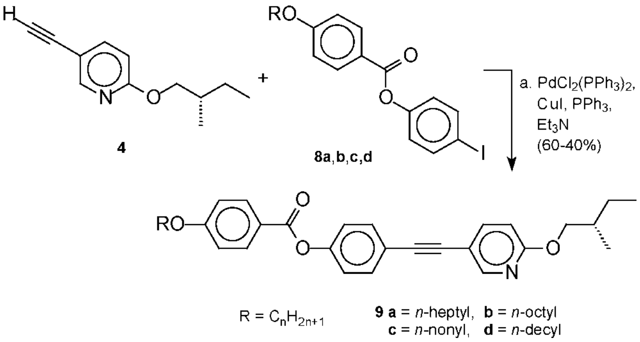
Scheme 3



Esterification reaction[13] using dicyclohexylcarbodiimide as a dehydrating agent, 4-(*N*,*N*-dimethylamino)pyridine (DMAP) as a catalyst, and *p*-iodophenol yielded the target molecules **8a**−**d** in 70−95% yield.

The last step was a second Sonogashira coupling between **4** and **8**. The homologous series was obtained in 40−60% yield as a pale yellow solid after purification through column chromatography. The cross-coupling product **9a**−**d** is outlined in Scheme 4.

Scheme 4



Mesomorphic Behavior. Thermal behavior of all *N*-heterotolans was characterized by a combination of differential scanning calorimetry (DSC) and thermal optical polarized microscopic techniques and is compiled in Table 2. The DSC thermograms of **9a**−**d** showed that all samples are thermally stable and present an enantiotropic behavior. Phase transition temperatures and enthalpy values were collected from second heating scans.

Table 2. Transition Temperatures (°C) of the Series of Heterotolans **9a**−**d** and Enthalpy Values (Δ*H*, kcal mol^{-1})

entry	R	K	*T* [Δ*H*]	Sa	*T* [Δ*H*]	N*	*T* [Δ*H*]	I
9a	C_7H_{15}	•	101.4 [4.4]	•	132.8 [0.20]	•	151.6 [0.15]	•
9b	C_8H_{17}	•	111.9 [6.2]	•	137.4 [0.35]	•	148.6 [0.18]	•
9c	C_9H_{19}	•	106.7 [6.4]	•	143.0 [0.52]	•	149.1 [0.25]	•
9d	$C_{10}H_{21}$	•	85.6 [2.8]	•	144.0 [0.12]	•	144.7[a]	•

[a] Enthalpy value was not determined, and the N* phase was observed only through microscopic analysis.

Mesophase textures[14] were identified by microscopy observations. When the sample was cooled, the isotropic liquid of heterotolans provided a chiral nematic phase, which showed typical cholesteric texture, as well as a smectic phase showing both homeotropic (black) and focal-conic texture for smectic A phase, respectively.

All heterotolan derivatives display a broad, stable smectic A phase range, and the temperature range of the smectic A increases as the alkyl tail changes from **9a** to **9d**. However, this homologue series has no smectic C phase.

The opposite behavior was found in the nematic phase. It was observed that there is a wide nematic range for the first member of the series. As *n* increases, the nematic range is reduced. It was also dependent on the size of the alkyl chain. The thermal stability of the nematic phase decreased with an increased alkyl chain length. For example, $\Delta T_{\mathrm{Sa-N}}$ is 18.8 °C for **9a**, $\Delta T_{\mathrm{Sa-N}}$ is 11.2 °C for **9b**, $\Delta T_{\mathrm{Sa-N}} = 6.1$ °C for **9c**, and $\Delta T_{\mathrm{Sa-N}} = 0.7$ °C for **9d**. A narrow enantiotropic nematic phase was observed in **9d** with an increase in the length of the alkyl chain attached to the benzene moiety.

In contrast, the thermal stability of the smectic A phase increases as the alkyl tail increases. As pointed out by Gray and Winsor,[15] this behavior has been attributed to the fact that lateral attractions grow stronger as the alkoxy group is lengthened, while the terminal attractions grow relatively weaker; thus, the net result will be an increase in the van der Waals attraction responsible for the parallel alignment in the smectic phase. Gray[16] discusses the effects of molecular structure changes on the nematic phase and smectic polymorphism.

The clearing point (cp N*/isotropic or Sa/isotropic) of heterotolans **9a**−**d** follows the same tendency. These observations are a general behavior in the liquid crystal field. This means that the nematic phase is shifted to the more ordered smectic phase when the alkyl chain becomes longer, as it can be seen from enthalpy values compiled in Table 2.

The mesomorphic behavior observed in this liquid-crystalline series can be compared with the tolan homologue series reported in our previous paper.[2b]

For the comparison between the transition temperatures, we notice that the compounds belonging to the heterotolans

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[13] Neises, B.; Steglich, W. *Angew. Chem., Int. Ed. Engl*. **1978**, *17*, 522−524.

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[15] Gray, G. W.; Winsor, P. A. *Liquid Crystals and Plastic Crystals*; Ellis Horwood: Chichester, 1974, Vol. 1.

[16] Gray, G. W. *Molecular Structure and the Properties of Liquid Crystals*; Academic Press: New York, 1962.

9a−d have lower melting and clearing points than the equivalent homologue diphenylacetylene with the same terminal alkyl chain. Furthermore, the nature and range of the mesophase is changed when the aromatic ring has a nitrogen atom. The mesomorphic phase in **9a−d** is less stable than those in the corresponding diphenylacetylene. This corroborates the statement about the influence of the nitrogen atom and its lone pair of electrons on liquid crystal properties. The loss of symmetry by the pyridyl ring weakens the interactions between liquid crystal molecules.

In conclusion, we have synthesized new *N*-heterotolan liquid crystals using two powerful methodologies. Using the Buchwald protocol, we prepared a chiral intermediate **3** as a promising candidate for a variety of 2,5-disubstituted pyridine liquid crystals. And, through a double Sonogashira reaction on **3**, we have prepared a final series **9a−d** containing a nitrogen atom at position 2 on the aromatic ring. The final compounds show an enantiotropic nematic phase, as well as a smectic A phase.

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Supporting Information Available: Experimental details of representative reactions, as well as spectral and analytical data on isolated products, including ^{1}H and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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