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Buchwald protocol applied to the synthesis of *N*-heterotolan liquid crystals

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Abstract

A homologous series of the new *N*-heterotolans **8a–d** were synthesized using two cross-coupling reactions mediated by copper and palladium/copper. The final compounds present the phenyl-pyridyl framework connected by the acetylene group. The evaluation of thermal properties for this series is described. All compounds exhibit the smectic A and X mesophase. For comparison were also synthesized compounds **10**, **12**, and **14**. Their LC properties are reported.

Keywords: Liquid crystal; *N*-Heterotolan; Phenylpyridyl framework; Buchwald protocol; Sonogashira coupling

1. Introduction

Liquid crystal displays (LCDs) have become essential as information displays in our technological society. Since highly birefringent liquid crystal materials are required,[1,2] many display parameters such as response time, contrast ratio, brightness, and viewing angle are important parameters to be considered.[1b] High birefringence liquid crystals are useful materials for application in reflective-type LCDs, spatial light modulators, compensation film reflectors, and polarizers.

A number of calamitic nematic liquid crystals showing high birefringence of relevance to LCDs such as cyanobiphenyls,[3] phenylpyrimidines,[4] phenylcyclohexanes,[5] and cyanopyridines[6] have been synthesized.

Tolan (diphenylacetylene) and its *N*-hetero version (pyridylphenylacetylene) play a prominent role in the field of liquid crystals science. From academic and technological research point of view, the planning and construction of new molecular materials containing such connectivity mentioned above have recently received much effort since they exhibit interesting electrical and optical properties.[7]

N-Heterotolan represents an interesting class of materials considering that the nitrogen atom in pyridine alters the optical, electrical, and thermal properties. Pyridine derivatives are aimed to provide a satisfactory selection of the best components of liquid crystals materials for TN and STN applications.[8] They also can be used as a template for high performance LC materials when substituted adequately by polar groups or alkyl/alkoxy tails.

Aromatic nucleophilic substitution using π-electron deficient systems such as halopyridines is sometimes used for the synthesis of pyridine derivatives. The major limitations of this methodology are related to the substrate availability and reactivity.[9]

The copper-mediated Ullmann-type condition[10] is an alternative method to synthesize aromatic and heteroaromatic derivatives. The nucleophilic aromatic substitution mediated by copper between nucleophiles (e.g., substituted phenoxides and amines) with aryl or heteroaryl halides allows the synthesis of the corresponding aryl/heteroaryl ethers and amines. However, the harsh reaction (125–220 °C in neat phenol or solvents such as pyridine, collidine, or DMF), which requires

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stoichiometric (or greater) quantities of the copper complex, and the fact that inactivated aryl halides usually react in low yields have limited the utility of this reaction. These drawbacks commonly result in low functional group tolerance and low and/or irreproducible yields.

Buchwald[11] and Hartwig[12] were pioneers in developing interesting and practical protocols to construct aryl carbon and aryl–heteroatom bond mediated by metals, affording many compounds that have important biological, pharmaceutical, and materials properties.

For the synthesis of diaryl ethers, Buchwald et al. established a general procedure using aryl bromides and iodides with a variety of phenols catalyzed by copper complex, cesium carbonate as a base, and 1,10-phenanthroline as a bidentate nitrogenous ligand. The reaction conditions were compatible with a wide range of functionalized substrates.[13] Starting from their initial reports concerning on the Ullmann diaryl ether synthesis and the observation that the yields of N-arylation of imidazoles could be better when carried out in nonpolar solvents,[14] Buchwald's group were able to demonstrated in 2002 that the copper-based protocols could be used to synthesize alkyl aryl ethers by Ullmann type reaction.[15a]

The authors reported a mild, practical, and efficient Cu-catalyzed arylation of aryl halides with alcohols. The method exhibit large substrate and reagent scope and it is extremely selective. Both primary and secondary alcohols can be used, which clearly distinguish this method from Pd-catalyzed reaction, in which secondary alcohols give side products due to ready PdH elimination.[15b] Allylic alcohols give the ethers without allylic rearrangement, even for alcohols with a terminal double bond, which are extremely liable to rearrangements. For chiral alcohols, full retention of configuration is observed.

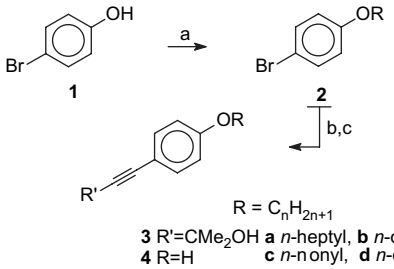
As part of our ongoing studies dealing with the synthesis of pyridine liquid crystals, we had previously reported that 2,5-disubstituted pyridine could easily be prepared[16] using the powerful protocol developed by Buchwald followed by Sonogashira reaction. We now wish to present an extension of application of this protocol to the other *N*-heterotolan compounds.

2. Results and discussion

2.1. Synthesis

The synthesis of the title compounds was carried out according to the synthetic methods outlined in Schemes 1–3. In order to establish the relationship between molecular structure and mesomorphic properties, we have introduced a pyridine moiety to produce *N*-heterotolans using Buchwald protocol[15] and the alkynylation coupling through Sonogashira reaction.[17]

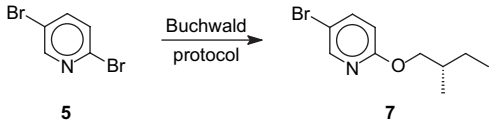
The first step was the synthesis of the intermediates **4a–d** according to Scheme 1. The alkylation of *p*-bromophenol with *n*-alkylbromide gave the products **2a–d** in 65–75% yields. Installation of the acetylene unit was accomplished by Sonogashira alkynylation of **2a–d** with 2-methyl-3-butyn-2-ol



Scheme 1. Alkynylation reaction by Sonogashira coupling. Conditions: (a) RBr, KOH, DMF/C_6H_6 (65–75%); (b) mebynol, PPh_3, $PdCl_2(PPh_3)_2$, CuI, Et_3N (75–90%); (c) KOH, isopropanol (85–90%).

(mebynol) followed by de-protection with KOH and isopropanol.[18] The final compounds **4a–d** were obtained in 70–80% yield from **2**.

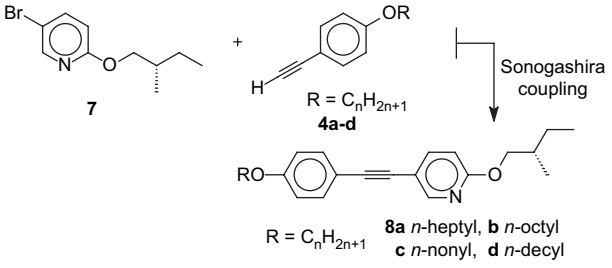
With compounds **4a–d** in hands, the synthesis of chiral key intermediate **7**[16a] was achieved by using the Buchwald protocol. This method was particularly suitable for the conversion of **5** to the chiral precursor **7** in acceptable yields according to Scheme 2.



Scheme 2. Arylation reaction under copper-mediated Buchwald protocol. Buchwald conditions: $CsCO_3$, CuI, 1,10-phenanthroline, toluene, (*S*)-**6**.

Thus, the arylation reaction using 2,5-dibromopyridine (**5**) with (*S*)-(−)-2-methyl-1-butanol (**6**) in the presence of cesium carbonate as a mild base, as well as 1,10-phenanthroline as a bidentate nitrogenous ligand and catalytic amount of copper iodide furnished the chiral intermediate **7** in 60% yield.

The synthesis of the *N*-heterotolan homologues **8a–d** was achieved using a second Sonogashira coupling between **7** and **4a–d**, according to Scheme 3 (45–60%).



Scheme 3. Synthesis of **8a–d** using Sonogashira coupling. Sonogashira conditions: $PdCl_2(PPh_3)_2$, CuI, PPh_3, Et_3N (45–60%).

Attempting to compare the influence on liquid-crystalline behavior of the carboxylate group and the relative position of the nitrogen atom on the pyridine ring, we also synthesized compounds **10** and **12**. The liquid crystals properties were compared with the series **8a–d**.

The synthesis of compound **10** was accomplished by alkynylation reaction between the chiral ester **9** and the selected