# Tetrahedron Letters 54 (2013) 3621-3623

Contents lists available at SciVerse ScienceDirect

**Tetrahedron Letters** 

journal homepage: www.elsevier.com/locate/tetlet



# The synthesis of chiral fluorinated 4-alkyl-4'-[(4-alkylphenyl)ethynyl]biphenyls

# Jakub Herman\*, Przemysław Kula

Institute of Chemistry, Department of Advanced Technologies and Chemistry, Military University of Technology, Kaliskiego 2, 00-908 Warsaw, Poland

#### ARTICLE INFO

Article history: Received 25 February 2013 Revised 18 April 2013 Accepted 26 April 2013 Available online 10 May 2013

Keywords: Coupling Alkylation Liquid crystal Biaryls Chirality

## ABSTRACT

We have designed, synthesized, and evaluated the physical properties of new fluorinated phenyltolane based chiral liquid crystal materials with 2-methylbutyl chains. This type of fluoro-substitution in chemical combination with a phenyltolane core brings a surprising improvement to the mesomorphic properties. The investigated compounds exhibit broad temperature ranges for the N<sup>\*</sup> phase and very low melting points. All homologues exhibited Blue Phase. We have applied a Cu-catalyzed cross-coupling reaction between aryl Grignard reagents and alkyl bromides for the synthesis of the products. © 2013 Elsevier Ltd. All rights reserved.

Significant attention has been focused on the search for new cholesteric liquid crystals having strong helical twisting power, wide mesogenic temperature ranges, and high chemical stability. These materials demonstrate a very broad number of unique applications.<sup>1</sup> In spite of their widespread specific applications they are utilized also as dopants in blue phase systems<sup>2</sup> and ferroelectric mixtures.<sup>3</sup> In this work we focused on the synthesis of a new class of liquid crystal materials with a 4-(phenylethynyl)biphenyl core, which imparts strong mesogenic stability and increased birefringence. Lateral fluoro-substitution, in particular a 2,6-difluorophenyl acetylene unit, brings unique and valuable nematic stability,<sup>4</sup> leading to a strong future application potential.

For the synthesis of the liquid crystal compounds described above we mainly utilized the Sonogashira–Hagihara cross-coupling reaction between 4-alkylaryl iodides and 4'-alkylbiphenyl acetylenes. The preparation of the substrates was achieved by introduction of an alkyl chain onto the aromatic system. The copper catalyzed cross-coupling reaction between aryl Grignard reagents and alkyl bromides was used to form an sp<sup>3</sup>–sp<sup>2</sup> C–C bond (Scheme 1). Transition metal catalyzed cross-coupling reactions have played an important role as carbon-carbon bond forming reactions in organic synthesis for many years.<sup>5</sup> Copper salts and complexes exhibit high catalytic activity for a wide range of substrates. Cu-catalyzed cross-coupling reactions between alkyl halides and Grignard reagents were first reported by Kochi and co-workers,<sup>6</sup> with many further reports on improved methods now available.<sup>7</sup>

Our approach is simply a modification of a known procedure,<sup>8</sup> which gives greater yields, and besides, non-branched alkyl chains can be easily used for chiral branched (2-methylbutyl)alkyl chain incorporation. The method presented here is mild, proceeds in one pot and requires cheap, easily accessible reagents. Furthermore it can be applied in large scale reactions. We used a tetrahydrofuran solution of Li<sub>2</sub>CuCl<sub>4</sub> complex as the catalyst system. Following this one-pot procedure, we obtained both alkyl fluorine substituted benzene 1-4 and 4-alkylbiphenyl derivatives 5-6 (Table 1), which were the main starting materials for mesogen synthesis, see Scheme 2. The alkyl fluorine substituted benzene derivatives 1-4 were then iodinated following ortho-directed lithiation. In parallel, 4-alkylbiphenyl derivatives 5-6 were iodinated in acetic acid. The formation of desired liquid crystals was subsequently accomplished by a copper catalyzed coupling of iodobiphenyl derivative 9 with 2-methyl-but-3-yn-2-ol followed by an alkaline cleavage of acetone and a second analogous coupling with compound **7** or **8**. The synthesis of (*S*)-4-(2-methyl-1-butyl) biphenyl 6 was also reported by Kaszynski and Jawdosiuk<sup>9</sup> He utilized Kumada cross-coupling,<sup>10</sup> using [1,3-bis(diphenylphosphino)propane]nickel(II) chloride as catalyst system. Although the Kumada



<sup>\*</sup> Corresponding author. Tel.: +48 (22) 683 98 73; fax: +48 (22) 683 95 82. *E-mail address*: jherman@wat.edu.pl (J. Herman).

**Scheme 1.** Copper-catalyzed cross-coupling of aryl Grignard reagents with alkyl bromides.

<sup>0040-4039/\$ -</sup> see front matter @ 2013 Elsevier Ltd. All rights reserved. http://dx.doi.org/10.1016/j.tetlet.2013.04.118

#### Table 1

Results of the Li\_2CuCl\_4-catalyzed cross-coupling of aryl Grignard reagents with alkyl bromides  $^{\rm a}$ 



 $^a$  Reaction conditions: 1. aryl bromide (1.5 mol), Mg (1.5 mol), 2. alkyl bromide (1.57 mol), Li\_2CuCl\_4 (45 mmol), 70 °C, N\_2 atmosphere, 72 h.

<sup>b</sup> Isolated yields



# Table 2

Phase transition temperatures (°C) and enthalpies (J/mol) of the investigated liquid crystals

Product	Temperature (°C) and enthalpy [J/mol]of the phase transitions
<b>11</b> <sup>a</sup>	Cr 103.2 (18,330) N* 124.8 (13) BP* (366) 126.6 Iso
12 <sup>a</sup>	Cr 56.5 (17,990) N* 105.1 (10) BP* 106.5 (330) Iso
13 <sup>0</sup>	$Cr_1 68.7 (5525) Cr_2 89.2 (12,608) N^* 158.0 BP^* 158.2 Iso$
14 <sup>-</sup> 15 <sup>b</sup>	Cr 30.9 (18,715) N° 140.0 BP 140.2 ISO Cr 55.6 (5100) Cr 75.2 (11,400) N* 152.8 PD* 152.0 Ico
15 16 <sup>b</sup>	$(r_1 33.6 (3100) Cr_2 73.2 (11,400) (133.8 Br 133.8 IS)$

The melting temperatures are determined from heating, while N\*-BP and clearing temperatures are derived from cooling.

<sup>a</sup> Obtained from differential scanning calorimetry DSC.

<sup>b</sup> Obtained from polarizing thermomicroscope.

protocol can bring higher yields in small to medium scale reactions, it is our belief that the combination of a one-pot procedure with an easily accessible and cheap catalyst like Li<sub>2</sub>CuCl<sub>4</sub>, brings noticeable benefits for large scale procedures<sup>11</sup>. The characterized liquid crystal compounds possess (S)-2-methylbutyl chain as a source of chirality either at one or both terminals of the molecule. In the case where only one branched chiral chain is present, the other side of the molecule is terminated with an *n*-pentyl alkyl chain. The temperatures and enthalpies of the phase transitions of the products are listed in Table 2.

In summary we have designed and synthesized a new family of cholesteric liquid crystals<sup>12</sup>. We show that the products are interesting materials for applicable mixture formulation. They are characterized by a broad range of chiral nematic phases. Liquid crystals incorporating 2,6-difluorophenyl acetylene unit 12, 14, and 16 proved to be valuable components exhibiting a broad nematic phase with very low melting temperatures, still maintaining high clearing temperatures. In addition, they can also play the role of blue phase sources, as all of homologues exhibit a narrow range blue phase. The high stability of the chiral nematic mesophase originates mainly from the rigid core which consists of previously mentioned 2,6-difluorophenyl acetylene structural substructure. It was proven that such a sequence of structural units was built into the liquid crystal molecule which brings unusual properties with very stable mesophases.<sup>4</sup> In order to obtain the intended mesogens we have modified and improved a copper-catalyzed coupling method between alkyl bromides and aryl Grignards.

## Acknowledgment

This work was supported by the Military University of Technology Grant 08-714.

# Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2013.04. 118.

#### **References and notes**

- (a) Lu, M. H. J. Appl. Phys. **1997**, 81, 1063; (b) Kim, K. H.; Song, D. H.; Shen, Z. G.; Park, B. W.; Park, K. H.; Lee, J. H.; Yoon, T. H. Opt. Expr. **2011**, 19, 10174; (c) Manabe, T.; Sonoyama, K.; Takanishi, Y.; Ishikawa, K.; Takezoe, H. J. Mater. Chem. **2008**, 18, 3040.
- 2. Chojnowska, O.; Dabrowski, R. Phot. Lett. Poland 2012, 4, 81.
- 3. Hird, M. Liq. Cryst. 2011, 38, 1467.
- (a) Kula, P.; Aptacy, A.; Herman, J.; Wójciak, W.; Urban, S. *Liq. Cryst.* 2013, 40, 482; (b) Buchecker, R.; Marck, G.; Schadt, M. *Mol. Cryst. Liq. Cryst.* 1995, 260, 93; (c) Seils, F.; Schadt, M. *Mol. Cryst. Liq. Cryst.* 1995, 260, 127.
- (a) Ulmann, F.; Bielecki, J. Ber. Dtsch. Chem. Ges. 1901, 34, 2174; (b) Ulmann, F. Justus Liebigs An. Chem. 1904, 332, 38.
- 6. Tamura, M.; Kochi, J. K. J. Organomet. Chem. 1972, 42, 205.

Scheme 2. General synthetic path to the investigated compounds.

15 for F,H 16 for F.F

- (a) Hamze, A.; Brion, J. D.; Alami, M. Org. Lett. 2012, 14, 2782; (b) Cahiez, G.; Gager, O.; Buendia, J. Angew. Chem., Int. Ed. 2010, 49, 1278; (c) Cahiez, G.; Gager, O.; Buendia, J. Synlett 2010, 299; (d) Erdik, E.; Eroglu, F. Synth. React. Inorg. Met. 2000, 30, 955.
- 8. Cahiez, G.; Chaboche, C.; Jezequel, M. Tetrahedron 2000, 56, 2733.
- 9. Kaszynski, P.; Jawdosiuk, M. Mol. Cryst. Liq. Cryst. 1989, 174, 21.
- 10. Kiso, Y.; Yamamoto, K.; Tamao, K.; Kumada, M. J. Am. Chem. Soc. 1972, 94, 4374.
- 11. Representative procedure for the one pot coupling of alkyl bromides with aryl Grignards: (S)-1-Fluoro-3-(2-methyl-1-butyl)benzene **3**: A solution of (262.5 g, 1.5 mol) 1-bromo-3-fluorobenzene in anhydrous THF (1 L) was added dropwise to Mg chips (36.5 g, 1.5 mol) with vigorous stirring under N<sub>2</sub> atmosphere. The mixture was refluxed for 1 h, then a 1 mol/dm<sup>3</sup> solution of catalyst Li<sub>2</sub>CuCl<sub>4</sub> in anhydrous THF (45 mL, 3 mol %) was added. Next, (S)-1-bromo-2-methylbutane (214.2 g, 1.58 mol) was added dropwise to the mixture which was stirred under reflux for 2 days. When the reaction was completed the mixture was poured into 1500 mL of H<sub>2</sub>O and 100 mL of 10% HCl. The crude product was extracted with pentane. The organic layer was washed with H<sub>2</sub>O (2 × 300 mL), separated, dried over MgSO<sub>4</sub>, and the solvent evaporated. The

product was distilled under reduced pressure: bp 98–100 °C (28 mmHg), yield 205 g (83%),  $[\alpha]_D^{25}9.5$  (*c*, 5.1; CHCl<sub>3</sub>). MS(EI) *m/z*: 166 (M<sup>+</sup>), 133, 110, 96. <sup>1</sup>H NMR (CDCl<sub>3</sub>),  $\delta$  7.65–7.60 (m, 1H), 7.53 (t, *J* = 2.2, 3.1 Hz, 1H), 6.82–6.75 (m, 2H), 2.50 (d, *J* = 8.8 Hz, 2H), 1.60–1.58 (m, 1H), 1.35–1.25 (m, 2H), 0.93 (t, *J* = 12.2 Hz, 3H), 0.86 (t, *J* = 11.4 Hz, 3H). <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  11.65, 19.0, 29.4, 36.6, 42.3, 109.0, 115.5, 121.7, 124.9, 126.4, 128.9, 145.0, 161.4.

12. 4S,4'S-[2-Fluoro-4-(2-methyl-1-butyl)phenyl]ethynyl-4'-(2-methyl-1-butyl)biphenyl (11): Compounds 11–16 were obtained via Sonogashira reactions. The products were purified using silica gel and hexane as eluent, and then recrystallized from EtOH. Mp.103.2 °C, MS(EI): 412 (M\*); 299. <sup>1</sup>H NMR (CDCl<sub>3</sub>),  $\delta$  7.62–7.58 (m, 4H), 7.55 (d, J = 7.9 Hz, 2H), 7.44–7.40 (m, 1H), 7.25–7.22 (d, J = 7.3 Hz, 2H), 6.95–6.9 (m, 2H), 2.65–2.60 (m, 2H), 2.45–2.40 (m, 2H), 1.65–1.60 (m, 2H), 1.45–1.40 (m, 2H), 1.25–1.20 (m, 4H), 0.95–0.90 (m, 6H). <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  11.65, 19.0, 27.8, 29.4, 33.9, 36.6, 42.3, 83.3, 93.8, 109.0, 115.5, 121.7, 124.9, 126.4, 128.9, 132.2, 133.2, 137.7, 142.8, 145.0, 161.4, 163.5. Anal. Calcd for C<sub>30</sub>H<sub>33</sub>F: C, 87.33; H, 8.06; F, 4.61. Found: C, 87.87; H 8.15; F, 4.56.