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Novel synthesis of liquid crystalline compounds of 5-substituted 2-(4-alkylphenyl)pyridines

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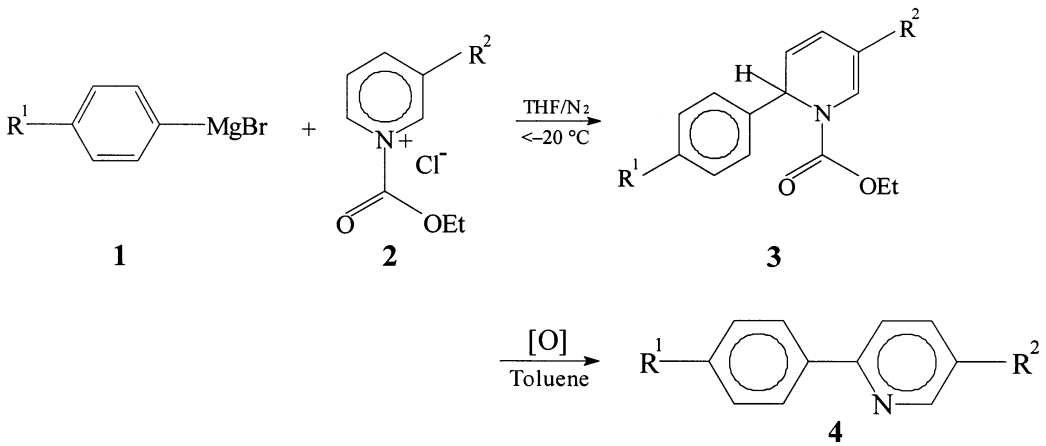
Abstract—This study describes a novel and efficient synthesis of pyridine-containing liquid crystalline 5-substituted 2-(4-alkylphenyl)pyridines. 4-Alkylphenylmagnesium bromide was reacted with 3-substituted *N*-ethoxycarbonylpyridinium chloride to give regioselective 1,2-dihydropyridine intermediates, which were subsequently oxidized by *o*-chloranil. Good yields and high α-regioselectivity on the pyridine ring were observed in all cases.

1. Introduction

Regioselective addition of organometallic reagents to 1-acylpyridinium salts has been found to be increasingly important in the preparation of 2- and 4-substituted pyridines.[1] It has been suggested that the regioselectivity of nucleophilic attack on the pyridinium cation can be explained by the hard and soft acids and bases (HSAB) principle.[2] For example, it has been demonstrated that relatively hard nucleophiles show a preference for addition at the 2-position of the pyridine ring and relatively soft nucleophiles at the 4-position. Previously, we have prepared various 2- or 4-substituted pyridines and alkaloids by the above-mentioned methodology.[3]

Recently, we have focused our interests on the synthesis of new liquid crystalline materials. For such device chemicals, it is necessary to achieve a delicate balance of the nematogenic character, viscous and elastic properties as well as electro-optical anisotropy. It is the optimum combination of these parameters that makes a particular liquid crystal useful for display applications.[4] Although some pyridine-containing liquid crystalline compounds have been synthesized before,[5–8] there is a high demand for new liquid crystalline materials for



1 2 3 4

Scheme 1.

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Table 1. Synthesis of 5-substituted 2-(4-alkylphenyl)-pyridines **4a**–**4g**

Entry	R^1	R^2	Bp/mp (°C)	Yield[a] (%)
4a	Bu	H	225 (2 torr)	71
4b	Bu	Me	230 (2 torr)	58
4c	Bu	Et	250 (2 torr)	55
4d	Bu	Bu	247 (0.2 torr)	71
4e	Bu	Ph	113.8[b]	75
4f	Pentyl[c]	H	225 (2 torr)	88
4g	Pentyl[c]	Ph	111.7[b]	73

[a] Isolated yield by column chromatography (methylene chloride/hexane) on silica gel.
[b] Recrystallized from hexane and according to the second heating cycle.
[c] *p*-Bromopentylbenzene was synthesized according to a known procedure.[11]

more advanced displays. Herein, we wish to report a novel and efficient synthetic method (Scheme 1) to prepare liquid crystalline 5-substituted 2-(4-alkylphenyl)pyridines **4**.

2. Results and discussion

2.1. Synthesis of 5-substituted 2-(4-alkylphenyl)-pyridines

Previously, syntheses of pyridine-containing liquid crystalline compounds were usually carried out by condensation reactions.[5–7] The variety of these pyridine derivatives that could be prepared was limited and yields of these compounds were low. On the contrary, in this work synthesis of various 5-substituted 2-(4-alkylphenyl)pyridines was completed in an efficient way by allowing 4-alkylphenylmagnesium bromide **1** to react with 3-substituted *N*-ethoxycarbonylpyridinium chloride **2** followed by oxidation by *o*-chloranil[9] (Scheme 1). There are various 3-substituted pyridines readily available commercially that could be used in this regioselective addition reaction. A portion of these results, mainly involving electron-donating 3-substituents on the pyridine, is presented in this paper (Table 1). These 5-substituted 2-(4-alkylphenyl)-pyridines[10] were obtained in good yields (55–88%). α-Regioselectivity on the pyridine rings was found to be completely dominant in the products isolated from all these reactions.

2.2. Thermotropic behavior of 5-substituted 2-(4-alkylphenyl)pyridines

Thermotropic behavior of 5-substituted 2-(4-alkylphenyl)pyridines can be clearly observed by differential scanning calorimetry (dsc). Only two of these 5-substituted 2-(4-alkylphenyl)pyridines were found to be liquid crystals, they were 2-(4-*n*-butylphenyl)-5-phenylpyridine (**4e**) and 2-(4-*n*-pentylphenyl)-5-phenylpyridine (**4g**).

Both **4e** and **4g** were found to be enantiotropic and their mesomorphic ranges were identified to be between 80.44 and 113.37°C and between 66.57 and 111.84°C, respectively, when a second heating cycle was conducted. The magnitudes of the enthalpy changes between crystal-to-mesophase are found to be about only one-third of those between mesophase-to-isotropic phase for both **4e** and **4g**, which indicates that highly ordered mesophases occur in these liquid-crystal-forming compounds.[12] A parallel thermo-optical study of

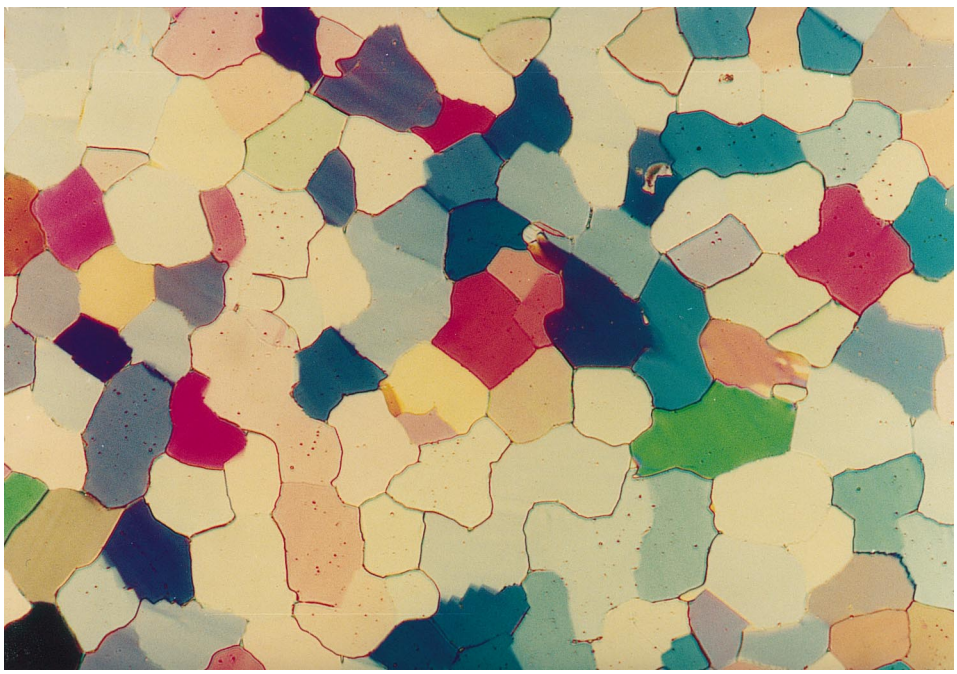

Figure 1. Mosaic texture of the mesophase of 2-(4-*n*-pentylphenyl)-5-phenylpyridine (**4g**) arises from crystalline phase on heating to 75°C. Polarized optical micrographs with magnification of ×200.

2-(4-*n*-butylphenyl)-5-phenylpyridine (**4e**) and 2-(4-*n*-pentylphenyl)-5-phenylpyridine (**4g**) was done by using a polarized optical microscope, which further confirmed the phase transitions of these two compounds. Both **4e** and **4g** in the mesophases showed mosaic textures during their second heating cycles, which complimented the results found by dsc that highly ordered mesophases (presumably smectic) occur in these mesophases. The immobility of those colorful domains in mosaic textures (Fig. 1) provides additional evidence of the presence of highly crystalline mesophases. However, the exact identification of the mesophases of these two compounds needs to be further characterized by X-ray diffraction methods.

Acknowledgements

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9. Representative experimental procedure for **3a**: To a (Grignard) solution of 1-bromo-4-butylbenzene (10 mmol) in 20 ml THF was added freshly dried magnesium granules (11 mmol) under an inert atmosphere. The Grignard solution **1** was then slowly added by syringe into a preformed solution of pyridinium chloride **2** (10 mmol ethyl chloroformate, 10 mmol pyridine, 20 ml dry THF at −20°C, 0.5 h) at −20°C. The resulting solution was warmed slowly to room temperature and stirred for another 8 h. After evaporating the THF, the residue was extracted with ether. The organic layer was further washed twice with 10% HCl solution and brine and dried with magnesium sulfate. Yields of the intermediates were found to be 70–90%. For **4a**: To a solution of 20 ml dry toluene and crude **3a** was added about 1.5 equiv. *o*-chloranil. The reaction mixture was heated to reflux for a number of hours under inert atmosphere and then quenched by adding 25 ml 1N NaOH solution and 25 ml ethyl ether and filtered through Celite. Normal aqueous work up and isolation with column chromatography affords the products **4a** (71%). These crude products were further purified by either recrystallization from hexane or by vacuum distillation.
10. ^{1}H NMR (400 MHz, $CDCl_3$). **4a**: 8.66 (d, 1H, $J=4.7$ Hz), 7.89 (d, 2H, $J=8.3$ Hz), 7.72–7.67 (m, 2H), 7.27 (d, 2H, $J=8.3$ Hz), 7.19–7.15 (m, 1H), 2.65 (t, 2H, $J=7.6$ Hz), 1.66–1.59 (m, 2H), 1.41–1.33 (m, 2H), 0.92 (t, 3H, $J=7.3$ Hz); **4b**: 8.52 (dd, 1H, $J_1=1.4$ Hz, $J_2=0.6$ Hz), 7.89 (d, 2H, $J=8.3$ Hz), 7.6 (d, 1H, $J=8.1$ Hz), 7.53 (dd, 1H, $J_1=8.0$ Hz, $J_2=0.5$ Hz), 7.28 (d, 2H, $J=8.3$ Hz), 2.67 (t, 2H, $J=7.6$ Hz), 2.35 (s, 3H), 1.68–1.61 (m, 2H), 1.44–1.34 (m, 2H), 0.95 (t, 3H, $J=7.3$ Hz); **4c**: 8.55 (d, 1H, $J=1.6$ Hz), 7.9 (d, 2H, $J=8.2$ Hz), 7.67 (d, 1H, $J=8.1$ Hz), 7.63 (d, 1H, $J=8.2$ Hz), 7.29 (d, 2H, $J=8.2$ Hz), 2.73–2.65 (m, 4H), 1.68–1.60 (m, 2H), 1.43–1.34 (m, 2H), 1.29 (t, 3H, $J=7.6$ Hz), 0.948 (t, 3H, $J=7.3$ Hz); **4d**: 8.51 (d, 1H, $J=1.9$ Hz), 7.89 (d, 2H, $J=8.3$ Hz), 7.63 (d, 1H, $J=8.1$ Hz), 7.55 (dd, 1H, $J_1=8.1$ Hz, $J_2=2.3$ Hz), 7.28 (d, 2H, $J=8.3$ Hz), 2.68–2.63 (m, 4H), 1.68–1.60 (m, 4H), 1.42–1.35 (m, 4H), 0.97–0.93 (m, 6H); **4e**: 8.91 (dd, 1H, $J_1=2.4$ Hz, $J_2=0.7$ Hz), 7.95 (d, 2H, $J=8.3$ Hz), 7.92 (dd, 1H, $J_1=8.2$ Hz, $J_2=2.4$ Hz), 7.77 (dd, 1H, $J_1=8.2$ Hz, $J_2=0.8$ Hz), 7.63 (dt, 2H, $J_1=6.8$ Hz, $J_2=1.4$ Hz), 7.48 (td, 2H, $J_1=7.0$ Hz, $J_2=1.5$ Hz), 7.4 (t, 1H, $J=5.31$ Hz), 7.30 (d, 2H, $J=8.4$ Hz), 2.67 (t, 2H, $J=7.6$ Hz), 1.7–1.61 (m, 2H), 1.41–1.36 (m, 2H), 0.94 (t, 3H, $J=7.3$ Hz); **4f**: 8.69 (d, 1H, $J=4.9$ Hz), 7.93 (d, 2H, $J=8.1$ Hz), 7.71 (d, 2H, $J=3.5$ Hz), 7.31 (d, 2H, $J=8.1$ Hz), 7.19 (dd, 1H, $J_1=8.4$ Hz, $J_2=4.7$ Hz), 2.67 (t, 2H, $J=7.6$ Hz), 1.71–1.64 (m, 2H), 1.4–1.33 (m, 4H), 0.92 (t, 3H, $J=6.9$ Hz); **4g**: 8.91 (dd, 1H, $J_1=2.4$ Hz, $J_2=0.7$ Hz), 7.95 (d, 2H, $J=8.3$ Hz), 7.90 (dd, 1H, $J_1=8.3$ Hz, $J_2=2.4$ Hz), 7.76 (dd, 1H, $J_1=10.9$ Hz, $J_2=0.8$ Hz), 7.61 (dt, 2H, $J_1=8.3$ Hz, $J_2=1.4$ Hz), 7.47 (td, 2H, $J_1=7.0$ Hz, $J_2=1.4$ Hz), 7.38 (t, 1H, $J=7.4$ Hz), 7.29 (d, 2H, $J=8.3$ Hz), 2.69 (t, 2H, $J=7.9$ Hz), 1.73–1.65 (m, 2H), 1.41–1.34 (m, 4H), 0.93 (t, 3H, $J=6.9$ Hz). All compounds gave satisfactory data by ^{13}C NMR (75 MHz, $CDCl_3$) and IR spectrum.
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