Tetrahedron 71 (2015) 5296–5307

Contents lists available at ScienceDirect

Tetrahedron

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

Mesogenic bis-heterocycles incorporating both pyrazole and isoxazole

Yu-Lun Li [a], Gene-Hsiang Lee [a,b], Chung K. Lai [a,*]

[a] Department of Chemistry, National Central University, Chung-Li, Taiwan, ROC
[b] Instrumentation Center, National Taiwan University, Taipei 10660, Taiwan, ROC

ARTICLE INFO

Article history:
Received 3 May 2015
Received in revised form 1 June 2015
Accepted 3 June 2015
Available online 10 June 2015

Keywords:
Heterocycles
Mesogens
Pyrazoles
Isoxazoles
Smectic

ABSTRACT

Two new series of mesogenic bis-heterocyclic derivatives containing pyrazoles and isoxazoles **1a**–**b** were reported. One single crystallographic structure of mesogenic **2a** (n=8) was determined by X-ray analysis, and it crystallizes in a triclinic space group P-1, with a=7.0511(2), b=7.6303(2) and c=21.2143(5) Å, and Z=2. The crystal was considered as slightly bent-shaped molecule with a molecular length of ca. ~24.9 Å. A dimeric correlated structure induced by H-bonds was observed in the crystal lattice, which was favorable to the formation of mesophases. All compounds **1**–**2** exhibited N, SmA, N/SmC or SmA/SmC phases, as expected for linear-shaped molecules. All compounds **1** have higher clearing temperatures and wider ranges of mesophases than those of their precursors **2**, which might be attributed to have higher dipoles polarized by two heterocyclic rings in **2**.

1. Introduction

Heterocyclic structures as core moiety have been used to generate novel mesogenic materials in the past decades. Most of heterocyclic compounds are considered as electron-deficient or electron acceptors and these structures were constituted with heteroatoms, such as oxygen, nitrogen, sulfur and others. Heterocycles often have chemical or/and physical properties different from other all carbon rings. An enhanced dipole of donor-to-acceptor interaction was easily induced within molecules or between molecules, which were required to generate potential materials with preferred molecular orientation in a particular state. A larger size or heavier atom with many electrons lone-pair electrons often executes a higher polarizability than other smaller atoms, thus the importance of London dispersion forces greatly increases as atomic size increases. Polarization abilities inherent from heterocyclic atoms; N, S or O atoms might electronically impart the overall structural flexibility and its resulting physical behavior. This is particularly important on the formation or induction of mesogenic structures.

Among them, pyrazoles and isoxazoles, considered as two of the most important five-membered rings are excellent candidates. Higher dipole moment inherent from their heterocyclic core could significantly contribute to the molecular dipoles. Both heterocycles were easy to prepare and also chemically and thermally stable. The first mesogens derived from 1,3-diphenylpyrazoles and 1,3-diphenylisoxazole derivatives exhibited smectic mesomorphism. More and more pyrazoles[1–4] and isoxazoles[5–10] were prepared and their mesomorphic properties investigated. The effect of non-linear shapes, caused by a larger exocyclic angle[11] ($\varepsilon \sim 157°$ for pyrazoles, $\varepsilon \sim 159°$ for isoxazoles) played an important key factor in forming mesophases. In general, the more linear geometry favored the appearance of mesophases. A few other similar mesogenic structures derived from pyrazoles[12] **Ia**–**d** and isoxazoles[13] **IIa**–**c** were also previously reported by this group (see Fig. 1).

In this work, two new series of rod-like unsymmetric compounds **1a**–**b** incorporating both pyrazole and isoxazole were reported. Two heterocycles incorporated might be particularly interesting not only in overall molecular structures, but also in their potential formation of novel mesomorphism. A higher unsaturation or/and greater polarization induced might facilitate the formation of mesophases. All compounds **2** exhibited N, N/SmA or N/SmA/SmC phases. These are the fewer examples of bis-heterocyclic[14] and tris-heterocyclic[15] derivatives known to exhibit mesomorphic behavior. All compounds **1a**–**b** exhibited enantiotropic mesophases, giving N, SmA, N/SmA or SmA/SmC phases. An improvement in observed mesomorphism over derivatives with mono-heterocycles was attributed to the larger dipole results from both heterocycles incorporated.

* Corresponding author. Tel.: +886 03 4259207; fax: +886 03 4277972; e-mail address: cklai@cc.ncu.edu.tw (C.K. Lai).

http://dx.doi.org/10.1016/j.tet.2015.06.021
0040-4020/

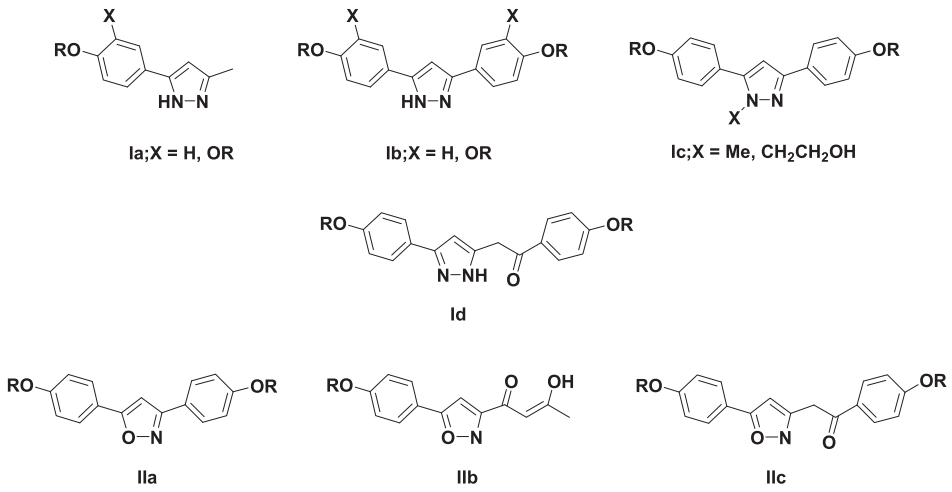


Fig. 1. The molecular structures of known mesogens derived from pyrazoles and isoxazoles.

2. Results and discussions

2.1. Synthesis and characterization

The synthetic routes used to prepare final bis-heterocyclic compounds **1** are listed in Scheme 1. The procedures to prepare ethyl 4-(4-alkoxyphenyl)-2,4-dioxobutanoates and ethyl 5-(4-alkoxyphenyl)isoxazole-3-carboxylates were followed by our previous routes. A characteristic peak occurred at δ 15.46–15.47 and δ 6.72–6.77 assigned for diketonate–O*H* and isoxaloze–C=C*H* confirmed the formation of both compounds. Compounds **2a**–**b** were obtained by reactions of 1-(2-hydroxyphenyl)ethanones or 1-(2-hydroxy-4-alkoxy phenyl)ethanones and ethyl 5-(4-(dodecyloxy)phenyl)isoxazole-3-carboxylates and NaH were gently refluxed in THF for 6 h. Both compounds isolated as yellow solids were obtained after recrystallization from THF/methanol. On the ^{1}H NMR spectra, two characteristic peaks assigned for diketonate–OH and phenolic–OH occurred at δ 14.88–14.92 and δ 11.90–11.93 for compounds **2a** and at δ 14.77–14.84 and δ 12.30–12.42 for compounds **2b** were observed. On the other hand, the characteristic peak for isoxazole–C=CH also moved from δ 6.72–6.77 to δ 7.10–7.17 (for **2a**) and δ 6.95–7.00 (for 2b). The final compounds **1**; 2-(3-(5-(4-alkoxyphenyl)isoxazol-3-yl)-1H-pyrazol-5-yl) phenols were prepared by reactions of compounds **2**, excess hydrazine solution and few drops of acetic acid in refluxing ethanol/THF for 10 h. The products isolated as white solids were obtained after recrystallization from THF/methanol. The formation of final pyrazoles was confirmed by a characteristic peak appeared at δ 10.37–10.42 and 10.23–10.30 ppm assigned to the pyrazole–*H*(–NH=C), for compounds **1a** and **1b**, respectively. All these compounds were characterized by ^{1}H NMR and ^{13}C NMR spectroscopy, mass spectroscopy and elemental analysis. The ^{1}H NMR spectra of all compounds **1**–**2** showed a few characteristic signals due to their features of keto-enol forms in d-chloroform solution, listed in Table 1. However, the ^{13}C NMR spectroscopic data for compounds 1b are not available due to their poor solubilities in d-solvents, for example, d-chloroform and d-DMSO. The elemental analyses of all compounds **1a**–**b** were also performed to confirm their purities.

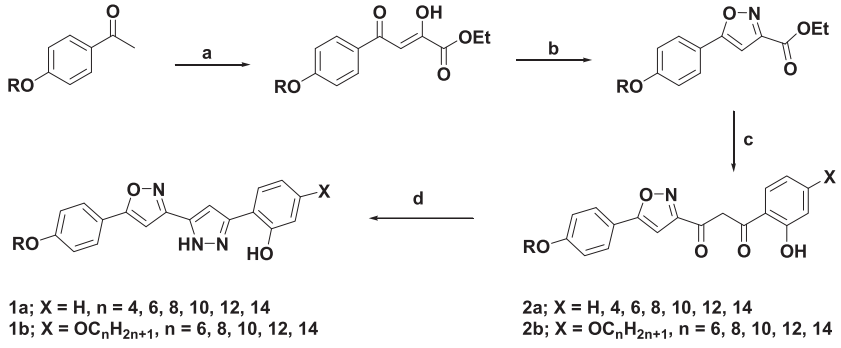
Table 1
The characteristic chemical peaks[a] on ^{1}H NMR spectroscopes for compounds **1**–**2**

Compds	1a	1b	2a	2b
–C=C***H*** (diketonate)	—	—	6.77–6.86	6.77–6.82
–C=C***H*** (isoxazole)	7.19–7.21	7.06–7.08	7.10–7.17	6.95–7.00
–C=C***H*** (pyrazole)	7.24	7.18–7.21	—	—
–N***H***	10.37–10.42	10.23–10.30	—	—
–O***H*** (phenolic)	13.30–13.34	13.06–13.13	11.90–11.93	12.30–12.42
–O***H*** (diketonate)	—	—	14.88–14.92	14.77–14.84

[a] **1a**–**b** measured in dimethyl sulfoxide-d_6 and **2a**–**b** measured in $CDCl_3$, unit (δ) in ppm.

2.2. Single crystal and molecular structures of (*Z*)-3-hydroxy-3-(2-hydroxyphenyl)-1-(5-(4-(octyloxy)phenyl)isoxazol-3-yl) prop-2-en-1-one 2a (n=8)

In order to understand the correlation between the molecular structure and mesomorphic behavior, a single crystal of the mesogenic compound **2a** (n=8) suitable for crystallographic



Scheme 1. Reagents and conditions: (a) diethyl oxalate (1.1 equiv), NaOEt (3.0 equiv), stirred in THF at 0 °C, 3 h, 81–85%; (b) NH_2OH (1.5 equiv), AcOH (drops), refluxed in THF/EtOH, 3 h, 70–72%; (c) NaH (3.0 equiv), refluxed in THF, 3 h, 42–46%; (d) N_2H_4 (1.5 equiv), AcOH (drops), refluxed in THF/EtOH, 3 h, 72–75%.