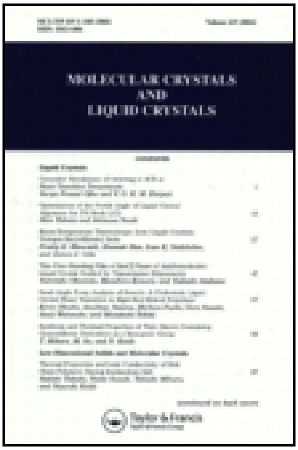

Molecular Crystals and Liquid Crystals

Liquid Crystals Containing the Isoxazole and Tetrazole Heterocycles

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Liquid Crystals Containing the Isoxazole and Tetrazole Heterocycles

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The influence of the bridging group between the mesogenic group and the terminal position on liquid-crystalline behavior was investigated. Two liquid-crystalline series containing pentagonal heterocycles were synthesized for this purpose. The liquid-crystal phase of mesogens with the isoxazole group was more stable than that of those with isoxazole and tetrazole groups in the same molecule. The mesogens with only the isoxazole group showed better thermal properties than those with isoxazoles and tetrazoles. Nematic and smectic phases were observed. The mesophase sequences of the materials were investigated by polarization microscopy and DSC (Differential Scanning Calorimetry).

Keywords: mesogens; phenylisoxazole; phenyltetrazole

INTRODUCTION

Our interest in heterocycle-based liquid crystals has been focused on developing novel types of polar liquid crystals [1]. Polar organizations are produced at the molecular level by electrostatic and molecular

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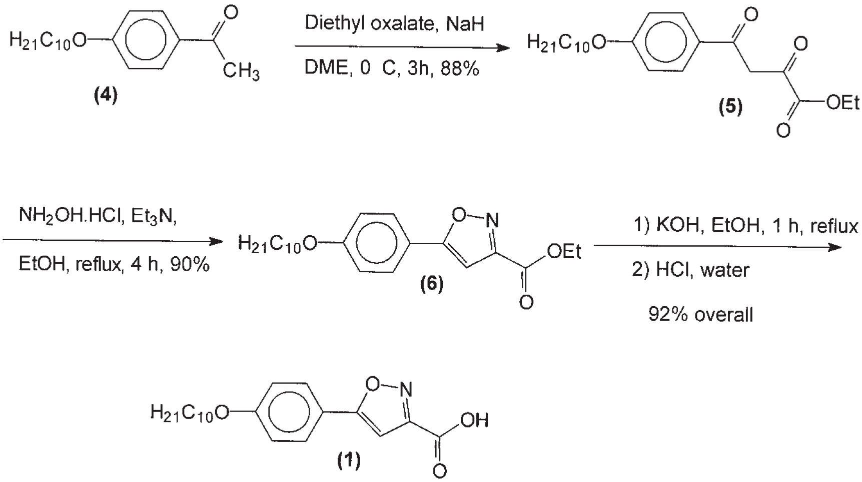
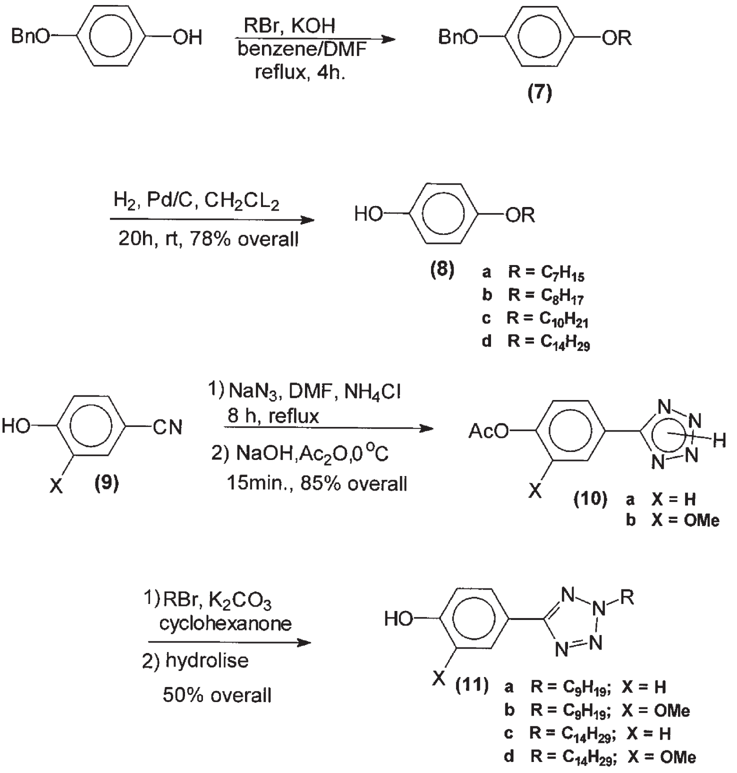
shape-dependent interactions between molecules (i.e., bowl-shaped liquid crystals) [2]. In this article, we describe the synthesis and properties of liquid crystals with very strong intermesogen interactions as a function of the presence of isoxazole and tetrazole heterocycles. The availability of liquid-crystal compounds with the pentagonal heterocycle is important for the study of the relation between structure and mesomorphic properties. The heterocyclic unit can be used to modify geometry and molecular polarizability. The isoxazole and tetrazole derivatives are ideal for these purposes because they are easily prepared and possess a sufficiently accented dipole moment [3]. They can be used to study the relationship between the structure and properties of liquid crystals. Also, azoles are a class of heterocyclic molecules that display a range of thermal and chemical stabilities that are exemplified by the parent members of the various families [4]. For example, 5-aminotetrazole monohydrate is a commercially available white crystalline solid (mp 203°C) that is frequently used as a building block for synthesis [5]. In this article, we describe the synthesis and mesomorphic properties of the 2,5-disubstituted tetrazole and 3,5-disubstituted isoxazole heterocycles.

RESULTS AND DISCUSSION

The synthetic routes used for the preparation of compounds **2** (**a**, **b**, **c**, and **d**) and **3** (**a**, **b**, **c**, and **d**) are shown in Scheme 1, Scheme 2, and



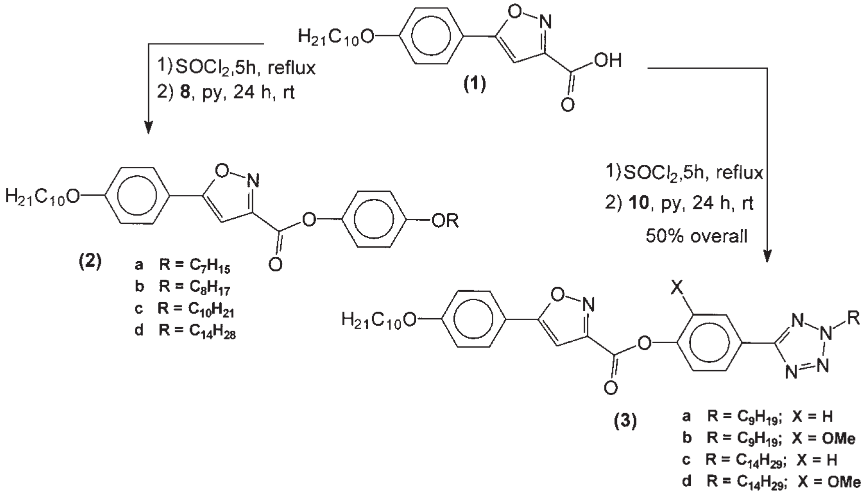
SCHEME 1



SCHEME 2

Scheme 3. All compounds were synthesized and fully characterized by elemental analysis, NMR, and IR spectroscopy. The mesophase sequences of the materials were investigated by polarization microscopy and differential scanning calorimetry (Perkin-Elmer DSC 781, heating and cooling rate 20 °C min^{-1}). The phase sequences are shown in Table I. All materials showed the smectic phase and four compounds (**2a**, **2b**, **2c**, and **3a**) additionally exhibited the nematic phase. It is important to note that the precursor **1** did not show mesomorphic behaviour, although it is a carboxylic acid. The formation of a symmetric dimeric structure that stabilizes the mesophase did not occur. This behavior might be directly due to the intramolecular hydrogen bond. The precursor **1**, when heated, passed from the crystalline state directly to the isotropic liquid (Cr–I).

The mesophase properties of compounds **2** (**a, b, c,** and **d**) are discussed first. When we compared the properties of these compounds with



SCHEME 3

the homologous structures without the ester linkage between the phenyl and isoxazole groups, we observed that their temperature range was greater (~20 °C) and their melting point was lower (~50 °C) [6]. This relationship is in agreement with data reported for liquid crystals [7]. It is well known from extensive research that the stability of the mesophase is mainly affected by the polarity of the mesogenic group and the aspect ration of the mesogenic molecules. The mesophase is stabilized through polar interaction between adjacent chains. The isoxazole group increases the polar interaction between adjacent chains, leading to the 3,5-biphenylisoxazole system, which has a higher melting point than the phenyl homologue. The polar molecules with dipole moments

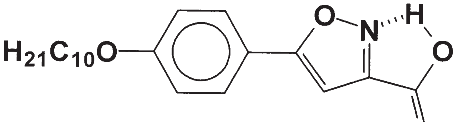
TABLE I Thermal Behaviors (°C) and Enthalpies [kJ · mol^{-1}] of the **1** intermediate and **2** (**a, b, c, d**) and **3** (**a, b, c, d**) Derivatives

Compound	R	X	Cr	Sc	N
1			>200		
2a	C_7H_{15}	H	82.0 [18.75]	145.6 [0.75]	153.3 [0.98]
2b	C_8H_{17}	H	80.2 [8.07]	146.6 [0.65]	151.2 [1.08]
2c	$C_{10}H_{21}$	H	87.8 [11.77]	148.9 [0.96]	151.5 [1.01]
2d	$C_{14}H_{28}$	H	85.7 [10.37]	148.1 [4.14]	
3a	C_9H_{19}	H	111.4 [12.73]	130.7 [1.05]	143.4 [0.91]
3b	C_9H_{19}	CH_3O	91.7 [51.97]	(64.3) [−1.56]	
3c	$C_{14}H_{29}$	H	104.9 [14.06]	123.12 [1.84]	
3d	$C_{14}H_{29}$	CH_3O	81.5 [33.11]	(66.3) [−2.96]	

perpendicular to the long molecular axis are associated in parallel orientations and this is favorable to the smectic phase. On the other hand, the electron-withdrawing ester linkage destabilizes the interaction between molecules, because it reduces the resonance interaction and modifies the dipole moment of the molecule. The ester group is bulkier than one bond and should reduce the anisotropy of the molecules, lowering the transition temperature of liquid crystals. This is easily understood by comparing the structures of compounds **2** and homologous structures without the ester linkage [6]. On comparing the structures of compounds **2** with the homologous biphenyl, we observed that their temperature ranges and melting points were the same, but the homologous biphenyl presented the formation of only the smectic A and nematic phases and not the smectic C mesophase, see Figure 1.

All compounds **3** showed liquid-crystalline behavior. Only compound **3a** exhibited the smectic C and nematic phases. The other compounds **3** (**b, c,** and **d**) showed only smectic C. For the compounds **3c** and **3d**, the mesomorphic behavior was monotropic and was only observed when cooling the isotropic liquid. The mesophase was identified through the observation of focal conic fan regions and a schlieren optical texture when viewed through the polarizing microscope. When the smectic phase was formed during cooling of the isotropic liquid, the focal conic fans appeared more clearly. When the smectic phase was formed during cooling from the nematic phase with a schlieren texture, focal conic fans and a fine four-brush schlieren texture were observed. The mesomorphic behavior of compounds **3** can be explained as a function of the ring. The tetrazole ring reduces the stability of the mesophase, increasing the melting point of compounds and reducing the clearing point. With an increase in the alkyl chain, the temperature range of the mesophase stability, along with the mesomorphic stratification, is reduced.

Although in classic organic structures the basic question is, frequently, how to increase intermolecular contact to induce mesomorphism, in compounds **3** (**a, b, c,** and **d**) the problem was to avoid intermolecular contacts and strong dipolar interactions (associated with the high



(1)

FIGURE 1 Representative figure of the intramolecular hydrogen bond.

polarizability of the heterocycle) that would be sufficiently strong enough to cause a reduction in the stability of the mesophase. Based on these considerations, the reduction in the mesomorphic behaivor of compounds **3** can be interpreted as being due to the reduced anisometry of the molecule resulting from the deviation from linearity caused by the introduction of the tetrazole ring, which leads to a decrease in the intermolecular contact. On the other hand, the introduction of the lateral group makes the molecule become bulkier and should tend to reduce the anisotropy of the molecule, lowering the transition temperature. According to Gallardo, the mesomorphic behavior of the tetrazole derivative can be explained if it is assumed that the distortion of molecular shape is reduced to a certain degree because the tetrazole ring is shifted to the terminal position of the rigid aromatic core [9–11]. In this position, the flexible n-alkyl chain allows partial compensation of the molecular bending, and also the length-to-width ratio is increased.

EXPERIMENTAL

Materials and Methods

All reagents used in the synthesis were purchased from Aldrich Chemical Company (USA) and solvents were used as received from Merck. Elemental analyses were performed using a Perkin-Elmer model 2400. Infrared spectra were recorded on a Perkin-Elmer model 781 spectrometer in KBr disks or films. ^{1}H NMR and ^{13}C NMR spectra were recorded using a Bruker AC-200F spectrometer at 200 MHz and 50.4 MHz, respectively. Chemical shifts are reported relative to tetramethylsilane and in units of ppm. Textures and transition temperatures for compounds were observed by optical microscopy using a Leitz Ortholux polarizing microscope in conjunction with a Mettler FP 82 heating stage. Calorimetric measurements were performed to determine the transition temperatures and the transition enthalpies with a Perkin-Elmer DSC-2, using indium for the standard calibration.

Synthesis of the Materials

Synthesis of Ethyl-4-(4-Decyloxyphenyl)butanoate-2,4-dione, 5

4-Alkoxyacetophenone **4** was formed from the reaction of 4-hydroxyacetophenone with bromoalkane in the presence of potassium hydroxide [12]. 4-Decyloxyacetophenone (20.0 g, 72.0 mmol) and sodium hydride (2.0 g, 80.0 mmol) in DME (50 ml) were stirred at 0°C. Diethyloxalate was added dropwise to the solution. The reaction mixture was stirred for 2 h at room temperature and was then heated to 50–60°C for 1 h. After the reaction was completed, the mixture was poured into

200 ml of distilled water and neutralized with 1 M HCl. The yellow solid in solution was filtered off and washed three times with distilled water. Recrystallization from ethanol afforded 23.98 g as a yellow solid in 88% yield; mp. 77–78°C. IR (KBr, cm^{-1}) ν_{max}: 3452, 2926, 2858, 1736, 1602. ^1H NMR (200 MHz, $CDCl_3$) $\delta = 13.1$ (s, 1H), 7.90 (d, $J = 8.9$ Hz, 2H), 7.02 (s, 1H), 6.95 (d, $J = 8.9$ Hz, 2H), 4.39 (q, $J = 7.16$ Hz, 2H), 4.03 (t, $J = 6.5$ Hz, 2H), 1.81 (q, 2H), 1.60–1.10 (m, 17H), 0.87 (t, 3H). ^{13}C NMR (50.4 MHz, $CDCl_3$) $\delta = 190.34$, 167.98, 163.99, 162.50, 130.29, 127.40, 114.64, 97.71, 68.41, 62.46, 31.86, 29.51, 29.29, 29.03, 25.93, 22.65, 14.09. CHN: found 70.35% of C and 8.50% of H; required 70.21% of C and 8.51% of H.

Ethyl 5-(4-Decyloxyphenyl)-3-isoxazolylcarboxylate, 6

A solution of ethyl 4-(4-decyloxyphenyl)butanoate-2,4-dione **5** (10 g, 26.59 mmol), hydroxylamine hydrochloride (1.85 g, 26.62 mmol), triethylamine (99%) (4 ml, 28.75 mmol), and ethanol (50 ml) was refluxed for 4 h. The mixture was poured into iced water, the precipitate was filtered off, dried in air, and then recrystallized three times from ethanol. Yield 7.8 g (90%); mp. 74.0–75.0°C. IR (KBr, cm^{-1}) ν_{max}: 2948, 2856, 1724, 1614, 1592, and 1260. ^1H NMR (200 MHz, $CDCl_3$) $\delta = 7.71$ (d, $J = 8.7$ Hz, 2H, $-C_6H_4-$), 6.96 (d, $J = 8.7$ Hz, 2H, $-C_6H_4-$), 6.78 (s, 1H, isoxazole), 4.46 (q, $J = 7.14$, 2H), 3.99 (t, $J = 6.46$ Hz, 2H), 1.8 (q, 2H, $-CH_2-$), 1.6–1.2 (m, 11H), 0.89 (t, 3H, $-CH_3$).^{13}C NMR (50.4 MHz, $CDCl_3$) $\delta = 171.73$, 161.11, 160.11, 156.81, 127.47, 119.09, 114.94, 98.35, 68.17, 62.05, 31.69, 29.06, 28.96, 25.88, 22.53, 14.09, 14.00. CHN: found 69.02% of C and 7.44% of H; required 68.88% of C and 7.55% of H.

5-(4-Decyloxyphenyl)-3-isoxazolylcarboxylic Acid, 1

Ethyl 5-(4-decyloxyphenyl)-3-isoxazolylcarboxylate **6** (5 g, 12.0 mmol) was dissolved in 50 ml of ethanol. An equimolar amount of potassium hydroxide dissolved in 10 ml of water was then added to the ethanol solution. The mixture was refluxed for 1 h and cooled slowly to room temperature. The resulting mixture was neutralized with 1 M HCl. The white solid was filtered off and purified by recrystallization three times from ethanol. Yield 4.3 g (92%); mp.> 200°C (dec.). IR (KBr, cm^{-1}) ν_{max}: 3440, 2956, 2850, 1734, 1614. ^1H NMR (200 MHz, $CDCl_3$) $\delta = 7.75$ (d, $J = 8.7$ Hz, 2H, $-C_6H_4-$), 6.96 (d, $J = 8.7$ Hz, 2H, $-C_6H_4-$), 6.84 (s, 1H, isoxazole), 4.02 (t, $J = 6.50$ Hz, 2H), 1.8 (q, 2H, $-CH_2-$), 1.6–1.2 (m, 11H), 0.89 (t, 3H, $-CH_3$). ^{13}C NMR (50.4 MHz, $CDCl_3$) $\delta = 172.03$, 161.41, 160.01, 156.89, 125.87, 118.69, 112.84, 98.55, 67.97, 31.44, 29.26, 27.96, 26.58, 22.53, 14.19, 14.10. CHN: found 69.42% of C and 7.54% of H; required 69.56% of C and 7.83% of H.

5-(4-Decyloxyphenyl)-3-isoxazolylcarboxyl Chlorides

The 5-(4-decyloxyphenyl)-3-isoxazolylcarboxylic acid **1** (0.626 g, 5.08 mmol) was refluxed with thionyl chloride (20 ml) for 5 h. The unreacted thionyl chloride was then removed under vacuum, and the crude product thus obtained was used for the next step without further purification.

General Procedure for Conversion of Benzyloxyphenol to its Corresponding 4-alcoxyphenol, 8

A solution of 4-benzyloxyphenol (5 g, 25 mmol), hepthyl bromide (4.5 g, 25 mmol) KOH (25 mmol), and benzene/dimethylformamide (DMF) (100 mL, 1:1) was refluxed for 6 h, and the solid formed was filtered off. The solvent was concentrated in a rotary evaporator and the crude product was chromatographed to furnish 7 ($R = C_7H_{15}$).

The benzyl ether **7** ($R = C_7H_{15}$) (6.0 g, 20 mmol) was hydrogenated with 20% Pd/C (Pearlman catalyst) (50 mg) in dichloromethane at 55 psi pressure in a Parr apparatus for 6 h. The catalyst was then filtered off and washed thoroughly with dichloromethane. After evaporation of the solvent, the crude product was recrystallized from EtOH to give 3.3 g (78%) of the phenol **8a** ($R = C_7H_{15}$): mp. 62–63°C; IR (KBr, cm^{-1}) ν_{max}: 3450, 3020, 2950, 2850, 1600, 1500, 1450, 1380, 1280, 1230, 1100, 1020, 910, 820, 730, 690. (Table II)

General Procedure for Conversion of 4-Acetylbenzonitrile to its Corresponding Tetrazole

5-(4-Hydroxyaryl)tetrazole, **9**: A suspension of 0.15 mol of 4-hydroxyarylnitrile, 37.5 g (0.60 mol) of sodium azide, and 30.9 g (0.60 mol) of ammonium chloride in 100 ml of dimethylformamide was stirred overnight at 160°C. After cooling, the solvent was concentrated in a rotary evaporator, and the reaction mixture was poured into 250 ml of iced water and acidified with hydrochloric acid. The white precipitate was isolated by filtration, washed with iced water, and recrystallized.

TABLE II Data for 4-Alkoxyphenols

Compound	R	Purified % yield	Mp (°C)	Mp (°C) [14]
8a	C_7H_{15}	78	62–63	60–61
8b	C_8H_{17}	70	60–62	63–64
8c	$C_{10}H_{21}$	89	70–72	70–73
8d	$C_{12}H_{25}$	85	76–78	80–82

5-(4-Hydroxyphenyl)tetrazole, **9a**: Recrystallization from water gave a white solid; yield 80.0% (19.4 g), mp 241.8°C.

5-(4-Hydroxy-2-metoxyphenyl)tetrazole, **9b**: Recrystallization from water gave a white solid; yield 61.0% (5.5 g), mp 215.6–217.1°C.

5-(4-Acetoxyaryl)tetrazole, **10**: To a suspension of 5-(4-hydroxyaryl) tetrazole **9** (50 mmol) in 30 ml of water, a solution of 3 M of sodium hydroxide in suspension was added until the solid was completely dissolved. Ice and acetic anhydride (53 mmol) were then added and the mixture was vigorously stirred for 10 to 15 min. The reaction mixture was acidified with hydrochloric acid. The acetate was isolated by filtration, washed with cool water, and recrystallized.

5-(4-Acetoxyphenyl)tetrazole, **10a**: Recrystallization from ethanol/water gave a white solid, yield 98.0% (10 g), mp 182°C. IR (KBr, cm^{-1}) ν_{max}: 2716–2620 (broad), 1754, 1614, 1502, 1212, 912. ^1H NMR (200 MHz, DMSO$-d_6$) $\delta = 8.18$ (d, $J = 8.7$ Hz, 2H, $-C_6H_4-$), 7.49 (d, $J = 8.7$ Hz, 2H, $-C_6H_4-$), 6.21 (br s, 1H, $-CN_4H-$), 2.39 (s, 3H, CH_3CO_2-). CHN: found 54.82% of C, 5.10% of H, and 25.59% of N; required 54.79% of C, 5.06% of H, and 25.46% of N.

5-(4-Acetoxy-2-metoxyphenyl)tetrazole, **10b**: Recrystallization from ethanol/water gave a white solid; yield 94.0% (6.3 g), mp 202.8–203.8°C. IR (KBr, cm^{-1}) ν_{max}: 2980–2652 (br), 1754, 1508, 1270, 1212, 1020, 866. ^1H NMR (200 MHz, DMSO$-d_6$) $\delta = 7.85$ (d, $J = 1.7$ Hz, 1H, $-C_6H_3-$), 7.74 (dd, $J = 8.2$ Hz, $J = 1.7$ Hz, 1H, $-C_6H_3-$), 7.43 (d, $J = 8.2$ Hz, 1H, $-C_6H_3-$), 3.98 (s, 3H, $-OCH_3$), 3.61 (br s, 1H, $-CN_4H$), 2.39 (s, 3H, $-CH_3CO_2-$). CHN: found 53.02% of C, 5.29% of H, and 22.51% of N; required 53.11% of C, 5.26% of H, and 22.48% of N.

5-(4-Hydroxyaryl)-2-alkyltetrazole, **11**: A solution of 5-(4-acetoxyaryl)tetrazole **10** (8.0 mmol), appropriate alkylbromide (8.0 mmol), potassium carbonate (8.0 mmol), and cyclohexanone (100 ml) was refluxed for 56 h, cooled to room temperature, and the solid formed was filtered off. The solvent was concentrated in a rotary evaporator and the residue was recrystallized with ethanol/water to give the pure 5-(4-acetoxyaryl)-2-alkyltetrazole.

A solution of 5-(4-acetoxyaryl)-2-alkyltetrazole (8.0 mmol) in 50 ml of ethanol and a solution of potassium hydroxide (8.0 mmol of KOH in 10 ml of water) was refluxed for 4 h. After cooling to room temperature, the reaction mixture was poured into 100 g of ice and acidified with hydrochloric acid. The aqueous mixture was shaken three times with ether. The ether extracts were washed with water and then dried over sodium sulphate, and the solvent evaporated. The crude product was recrystallized.

5-(4-Hydroxyphenyl)-2-nonyltetrazole, **11a**: Recrystallization from ethanol gave a white solid; yield 100.0% (2.8 g), mp 72.0°C. IR (KBr, cm^{-1}) ν_{max}: 3144, 2924, 2852, 1614, 1460, 842. ^1H NMR (200 MHz, $CDCl_3$) $\delta = 8.00$ (d, $J = 8.7$ Hz, 2H, $-C_6H_4-$), 6.97 (d, $J = 8.7$ Hz, 2H, $-C_6H_4-$), 4.62 (t, $J = 7.2$ Hz, 2H, $-NC\underline{H}_2CH_2-$), 2.05 (quint., 2H, $-NC\underline{H}_2CH_2-$ 1.30 (m, 12H, $-CH_2-$), 0.87 (t, $J = 6.3$ Hz, 3H, $-CH_3$). ^{13}C NMR (50.4, $CDCl_3$) $\delta = 164.9$ $-(CN_4-)$, 158.2, 128.6, 119.4, 116.0, 53.3 ($-NCH_2-$), 31.9, 29.6, 29.3, 28.9, 26.3, 22.7 (7C, $-CH_2-$, nonyl chain), 14.1 (1C, $-CH_3$). CHN: found 66.68% of C, 8.41% of H, and 19.45% of N; required 66.54% of C, 8.33% of H, and 19.31% of N.

5-(4-Hydroxy-3-metoxyphenyl)-2-nonyltetrazole, **11b**: Recrystallizaion from hexane gave a white solid; yield 78.0% (1.98 g) mp 50°C. IR (KBr, cm^{-1}) ν_{max}: 3200, 2928, 2840, 1612, 1480, 1252, 888, 796, 765. ^1H NMR (200 MHz, $CDCl_3$) $\delta = 7.62$ (m, 2H, $-C_6H_3-$), 6.72 (d, $J = 7.9$ Hz, 1H, $-C_6H_3-$), 4.78 (t, $J = 7.2$ Hz, 2H, $-NC\underline{H}_2CH_2-$), 3.90 (s, 3H, $-OCH_3$), 2.0 (m, 2H, $-NC\underline{H}_2CH_2-$), 1.25 (m, 12H, $-CH_2-$), 0.87 (t, $J = 6.6$ Hz, 3H, $-CH_3$). ^{13}C NMR (50.4 MHz, $CDCl_3$) $\delta = 165.0$, 162.0, 164.9 ($-CN_4-$), 120.8, 120.2, 115.0, 110.3, 56.9 ($-OCH_3$), 53.5 ($-NCH_2-$), 32.8, 30.9, 30.2, 30.0, 29.8, 27.0, 26.6, 23.3, (12C, $-CH_2-$, nonyl chain), 14.8 (1C, $-CH_3$). CHN: found 64.05% of C, 8.19% of H, and 17.56% of N; required 64.15% of C, 8.17% of H, and 17.61% of N.

5-(4-Hydroxyphenyl)-2-tetradecyltetrazole, **11c**: Recrystallization from ethanol gave a white solid; yield 100.0% (3.4 g), mp 81.5°C. IR (KBr, cm^{-1}) ν_{max} : 3151, 2922, 2850, 1614, 1464, 910, 840. ^1H NMR (200 MHz, $CDCl_3$) $\delta = 8.01$ (d, $J = 8.7$ Hz, 2H, $-C_6H_4-$), 6.97 (d, $J = 8.7$ Hz, 2H, $-C_6H_4-$), 4.62 (t, $J = 7.2$ Hz, 2H, $-NC\underline{H}_2CH_2-$), 2.05 (quint., 2H, $-NC\underline{H}_2CH_2-$), 1.25 (m, 22H, $-CH_2-$), 0.87 (t, $J = 6.3$ Hz, 3H, $-CH_3$). ^{13}C NMR (50.4 MHz, $CDCl_3$) $\delta = 164.9$ ($-CN_4-$), 158.2, 128.6, 119.4, 116.0, 53.3 ($-NCH_2-$), 31.9, 29.6, 29.3, 28.9, 26.3, 22.7 (12C, $-CH_2-$, tetradecyl chain), 14.1 (1C, $-CH_3$). CHN: found 70.39% of C, 9.59% of H, and 15.67% of N; required 69.98% of C, 9.46% of H, and 15.43% of N.

5-(4-Hydroxy-3-metoxyphenyl)-2-tetradecyltetrazole, **11d**: Recrystallization from hexane gave a white solid; yield 60.0% (2.17 g), mp 53.5°C. IR (KBr, cm^{-1}) ν_{max}: 3244, 2922, 2848, 1602, 1488, 1282, 880, 794, 760. ^1H NMR (200 MHz, $CDCl_3$) $\delta = 7.66$ (m, 2H, $-C_6H_3-$), 6.99 (d, $J = 7.9$ Hz, 1H, $-C_6H_3-$), 4.61 (t, $J = 7.2$ Hz, 2H, $-NC\underline{H}_2CH_2-$), 3.98 (s, 3H, $-OCH_3$), 2.05 (m, 2H, $-NCH_2C\underline{H}_2-$), 1.25 (m, 22H, $-CH_2-$), 0.87 (t, $J = 6.6$ Hz, 3H, $-CH_3$). ^{13}C NMR (50.4 MHz, $CDCl_3$) $\delta = 165.7$, 165.0, 164.9 ($-CN_4-$), 121.2, 120.1, 115.5, 109.9, 56.8 ($-OCH_3$), 53.3 ($-NCH_2-$), 32.6, 30.3, 30.2, 30.0, 29.6, 27.0, 26.6, 23.3 (12C, $-CH_2-$, tetradecyl chain), 14.8 (1C, $-CH_3$). CHN: found 68.05% of C, 9.39% of H, and 14.46% of N; required 68.11% of C, 9.34% of H, and 14.42% of N.

Acylation of Phenol Intermediate

The 5-(4-decyloxyphenyl)-3-isoxazolylcarboxyl chloride (0.64 g, 1.77 mmol) was dissolved in anhydrous pyridine (30 ml) and cooled at 0°C. To the solution, the phenol compound (1.77 mmol) obtained through the method previously described (General Procedure for Conversion of Benzyloxyphenol to its Corresponding 4-alcoxyphenol, 8), and anyhydrous pyridine (30 ml) was added. The suspension was shaken at room temperature for 24 h. The reaction mixture was then poured into 100 g of iced water and acidified with hydrochloric acid. The product was isolated by filtration and washed with water, then dried and recrystallized from ethanol.

For derivative with $R = C_7H_{15}$, **2a**: Yield = 0.613 g, 70.4%, mp 88.5–90.0°C. IR (KBr, cm^{-1}) ν_{max}: 2940, 2850, 1748, 1748, 1614, 1510, 1256. ^1H NMR (200 MHz, $CDCl_3$) $\delta = 7.75$ (d, $J = 8.7$ Hz, 2H, $-C_6H_4-$), 7.43 (d, $J = 8.9$ Hz, 2H, $-C_6H_4-$), 6.95 (m, 4H, $-C_6H_4-$), 6.90 (s, 1H, isoxazole), 3.95 (m, 4H, 2-$OC\underline{H}_2CH_2-$), 1.81 (m, 4H, 2-$OCH_2C\underline{H}_2-$), 1.28 (m, 22H, $-CH_2-$), 0.88 (m, 6H, 2-CH_3). ^{13}C NMR (50.4 MHz, $CDCl_3$) $\delta = 172.8$, 161.9, 159.7, 157.9, 157.1, 144.1, 128.3, 122.8, 119.7, 115.8, 115.7, 99.4, 69.1, 68.9, 32.5, 32.4, 30.2, 30.1, 30.0, 29.9, 29.8, 29.7, 26.7, 23.3, 14.7. CHN: found 73.02% of C, 8.47% of H, and 2.84% of N; required 73.30% of C, 8.67% of H, and 2.70% of N.

For derivative with $R = C_8H_{17}$, **2b**: Yield = 0.613 g, 70.4%, mp 80.0–81.2°C. IR (KBr, cm^{-1}) ν_{max}: 2928, 2847, 1747, 1746, 1614, 1509, 1254. ^1H NMR (200 MHz, $CDCl_3$) $\delta = 7.72$ (d, $J = 8.7$ Hz, 2H, $-C_6H_4-$), 7.22 (d, $J = 8.8$ Hz, 2H, $-C_6H_4-$), 6.95 (m, 4H, $-C_6H_4-$), 6.90 (s, 1H, isoxazole), 3.96 (m, 4H, 2 $-OC\underline{H}_2CH_2-$), 1.82 (m, 4H, 2-$OCH_2C\underline{H}_2-$), 1.27 (m, 24H, $-CH_2-$), 0.88 (m, 6H, 2-CH_3). ^{13}C NMR (50.4 MHz, $CDCl_3$) $\delta = 172.8$, 162.0, 159.7, 157.9, 157.1, 144.2, 128.3, 122.8, 119.7, 115.8, 115.7, 99.4, 69.1, 68.9, 32.0, 29.8, 29.5, 26.1, 23.0, 14.3. CHN: found 73.28% of C, 8.50% of H, and 2.56% of N; required 74.32% of C, 8.56% of H, and 2.55% of N.

For derivative with $R = C_{10}H_{21}$, **2c**: Yield = 0.613 g, 70.4%, mp 86.0–87.3°C. IR (KBr, cm^{-1}) ν_{max}: 2920, 2850, 1748, 1747, 1614, 1510, 1450, 1256, 1228, 808. ^1H NMR (200 MHz, $CDCl_3$) $\delta = 7.78$ (d, $J = 8.7$ Hz, 2H, $-C_6H_4-$), 7.16 (d, $J = 8.9$ Hz, 2H, $-C_6H_4-$), 6.96 (m, 4H, $-C_6H_4-$), 6.90 (s, 1H, isoxazole), 3.99 (m, 4H, 2-$OC\underline{H}_2CH_2-$), 1.79 (m, 4H, 2-$OCH_2C\underline{H}_2-$), 1.28 (m, 28H, $-CH_2-$), 0.89 (m, 6H, 2-CH_3). ^{13}C NMR (50.4 MHz, $CDCl_3$) $\delta = 172.2$, 161.3, 159.0, 157.3, 156.5, 143.4, 127.6, 122.1, 119.0, 115.1, 98.7, 68.4, 68.3, 31.9, 29.5, 29.3, 26.0, 22.7, 14.1. CHN: found 74.22% of C, 8.70% of H, and 2.35% of N; required 74.87% of C, 8.84% of H, and 2.43% of N.

For derivative with $R = C_{14}H_{29}$, **2d**: Yield = 0.613 g, 70.4%, mp 79.0–79.5°C. IR (KBr, cm^{-1}) ν_{max}: 2920, 2853, 1748, 1745, 1614, 1510, 1450, 1256, 1228, 808. ^1H NMR (200 MHz, $CDCl_3$) $\delta = 7.78$ (d, $J = 8.7$ Hz, 2H, $-C_6H_4-$), 7.16 (d, $J = 8.9$ Hz, 2H, $-C_6H_4-$), 6.95 (m, 4H, $-C_6H_4-$), 6.90 (s, 1H, isoxazole), 3.98 (m, 4H, 2-$OC\underline{H}_2CH_2-$), 1.80 (m, 4H, 2-OCH_2CH_2-), 1.26 (m, 36H, $-CH_2-$), 0.87 (m, 6H, 2-CH_3). ^{13}C NMR (50.4 MHz, $CDCl_3$) $\delta = 172.2$, 161.3, 159.0, 157.3, 156.5, 143.4, 127.6, 122.1, 119.0, 115.1, 98.7, 68.4, 68.3, 31.9, 29.5, 29.3, 26.0, 22.7, 14.1. CHN: found 75.62% of C, 9.27% of H, and 2.20% of N; required 75.83% of C, 9.32% of H, and 2.21% of N.

For derivative with $R = C_9H_{19}$, **3a**: Yield = 0.613 g, 70.4%, mp 104.0–105.6°C. IR (KBr, cm^{-1}) ν_{max}: 2918, 2850, 1752, 1614, 1508, 1448, 1258, 1226, 834. ^1H NMR (200 MHz, $CDCl_3$) $\delta = 8.23$ (d, $J = 8.7$ Hz, 2H, $-C_6H_4-$), 7.77 (d, $J = 8.7$ Hz, 2H, $-C_6H_4-$), 7.41 (d, $J = 8.7$ Hz, 2H, $-C_6H_4-$), 7.00 (d, $J = 8.7$ Hz, 2H, $-C_6H_4-$), 6.93 (s, 1H, isoxazole), 4.65 (t, 2H, $-NC\underline{H}_2CH_2-$), 4.02 (t, 2H, $-OC\underline{H}_2CH_2-$), 2.09 (m, 2H, $-NCH_2C\underline{H}_2-$), 1.81 (m, 2H, $-OCH_2C\underline{H}_2-$), 1.27 (m, 26H, $-CH_2-$), 0.87 (m, 6H, 2-CH_3). ^{13}C NMR (50.4 MHz, $CDCl_3$) $\delta = 172.5$, 164.3, 161.4, 158.4, 156.3, 151.6, 128.3, 127.7, 126.0, 122.1, 119.0, 115.2, 98.8, 68.4, 53.3, 31.94, 29.6, 29.4, 29.2, 28.9, 26.4, 22.7, 14.1. CHN: found 70.26% of C, 7.90% of H, and 11.31% of N; required 70.24% of C, 7.97% of H, and 11.38% of N.

For derivative with $R = C_{14}H_{29}$, **3c**: Yield = 0.613 g, 70.4%, mp 101.9–103.0°C. IR (KBr, cm^{-1}) ν_{max}: 2919, 2850, 1751, 1614, 1500, 1450, 1258, 1230, 835. ^1H NMR (200 MHz, $CDCl_3$) $\delta = 8.22$ (d, $J = 8.7$ Hz, 2H, $-C_6H_4-$), 7.76 (d, $J = 8.7$ Hz, 2H, $-C_6H_4-$), 7.41 (d, $J = 8.7$ Hz, 2H, $-C_6H_4-$), 6.98 (d, $J = 8.7$ Hz, 2H, $-C_6H_4-$), 6.93 (s, 1H, isoxazole), 4.65 (t, 2H, $-NC\underline{H}_2CH_2-$), 4.02 (t, 2H, $-OC\underline{H}_2CH_2-$), 2.09 (m, 2H, $-NCH_2C\underline{H}_2-$), 1.81 (m, 2H, $-OCH_2C\underline{H}_2-$), 1.27 (m, 26H, $-CH_2-$), 0.87 (m, 6H, $2-CH_3$). ^{13}C NMR (50.4 MHz, $CDCl_3$) $\delta = 172.5$, 164.3, 161.4, 158.4, 156.3, 151.6, 128.3, 127.7, 126.0, 122.1, 119.0, 115.2, 98.8, 68.4, 53.3, 31.94, 30.1, 29.8, 29.5, 29.2, 28.9, 26.4, 26.0, 22.7, 14.1. CHN: found 71.65% of C, 8.58% of H, and 10.20% of N; required 71.82% of C, 8.61% of H, and 10.22% of N.

For derivative with $R = C_9H_{19}$, **3b**: Yield = 0.613 g, 70.4%, mp 89.0–90.0°C. IR (KBr, cm^{-1}) ν_{max}: 2922, 2852, 1746, 1612, 1446, 1258, 1224, 1174, 1126, 868. ^1H NMR (200 MHz, $CDCl_3$) $\delta = 7.77$ (m, 2H, $-C_6H_4-$, 2H, $-C_6H_3-$), 7.31 (d, $J = 8.0$ Hz, 1H, $-C_6H_3-$), 6.98 (d, $J = 8.7$ Hz, 2H, $-C_6H_4-$), 6.93 (s, 1H, isoxazole), 4.64 (t, 2H, $-NC\underline{H}_2CH_2-$), 4.01 (t, 2H, $-OC\underline{H}_2CH_2-$), 3.93 (s, 3H, CH_3), 2.00

(m, 2H, $-NCH_2C\underline{H}_2-$), 1.80 (m, 2H, $-OCH_2C\underline{H}_2-$), 1.27 (m, 26H, $-CH_2-$), 0.87 (m, 6H, $2-CH_3$). ^{13}C NMR (50.4 MHz, $CDCl_3$) $\delta = 172.2$, 164.3, 161.2, 157.7, 156.0, 151.3, 140.5, 127.6, 126.9, 123.1, 119.4, 119.0, 115.0, 110.9, 98.8, 68.2, 56.2, 53.2, 31.82, 31.7, 29.5, 29.3, 29.1, 28.9, 26.3, 25.9, 22.6, 14.0. CHN: found 68.74% of C, 7.88% of H, and 10.81% of N; required 68.84% of C, 7.91% of H, and 10.85% of N.

For derivative with $R = C_{14}H_{29}$, **3d**: Yield = 0.613 g, 70.4%, mp 81.5–92.6°C. IR (KBr, cm^{-1}) ν_{max}: 2922, 2852, 1746, 1612, 1446, 1258, 1224, 1174, 1126, 868. ^{1}H NMR (200 MHz, $CDCl_3$) $\delta = 7.77$ (m, 2H, $-C_6H_4-$, 2H, $-C_6H_3-$), 7.31 (d, $J = 8.0$ Hz, 1H, $-C_6H_3-$), 6.98 (d, $J = 8.7$ Hz, 2H, $-C_6H_4-$), 6.93 (s, 1H, isoxazole), 4.64 (t, 2H, $-NC\underline{H}_2CH_2-$), 4.01 (t, 2H, $-OC\underline{H}_2CH_2-$), 3.93 (s, 3H, CH_3), 2.00 (m, 2H, $-NCH_2C\underline{H}_2-$), 1.80 (m, 2H, $-OCH_2C\underline{H}_2-$), 1.27 (m, 36H, $-CH_2-$), 0.87 (m, 6H, 2-CH_3). ^{13}C NMR (50.4 MHz, $CDCl_3$) $\delta = 172.2$, 164.3, 161.2, 157.7, 156.0, 151.3, 140.5, 127.6, 126.9, 123.1, 119.4, 119.0, 115.0, 110.9, 98.8, 68.2, 56.2, 53.2, 31.82, 31.7, 29.5, 29.3, 29.1, 28.9, 26.3, 25.9, 22.6, 14.0. CHN: found 70.45% of C, 8.52% of H, and 9.71% of N; required 70.49% of C, 8.53% of H, and 9.79% of N.

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