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3,5-Disubstituted Isoxazolines as Potential Molecular Kits for Liquid-Crystalline Materials

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A collection of 3,5-disubstituted isoxazolines have been synthesized by 1,3-dipolar [3+2] cycloaddition reactions. Some isoxazolines were selected and transformed into liquid crystals. These new liquid crystals exhibit nematic and smectic C mesophases.

Introduction

The 1,3-dipolar [3+2] cycloaddition of nitrile oxides to olefins offers a convenient one-step route to the construction of a variety of five-membered heterocycles known as isoxazolines.[1] Pharmacologically, this class of heterocycle has been reported to possess interesting biological activities as well as analgesic, anti-inflammatory and hypoglycemic properties.[2–5] Isoxazolines are also synthetically versatile intermediates that readily undergo further transformations, such as alkylation,[6] dehydrogenation to isoxazoles[7] and reductive cleavage to expose functionalities such β-hydroxy ketones, α,β-unsaturated ketones,[8] β-amino acids or γ-amino alcohols.[9]

Nitrogen- and oxygen-containing heterocycles also play an important role in the synthesis of novel liquid-crystalline (LC) materials. One important heterocycle moiety used in LC materials is the isoxazole ring and its variants. Although the [3+2] cycloaddition approach has been used to synthesize isoxazole directly from activated alkynes and nitrile oxides, the literature reports only moderate yields and low regioselectivities.[10–12] To increase both the yield and regioselectivity of the cycloaddition step, we envisage that isoxazoline as an intermediate emerges as an excellent alternative to the preparation of the isoxazole ring in fair-to-good yields and high regioselectivity. The oxidation reaction of the corresponding 3,5-disubstituted isoxazoline[13b,13d] prepared by cycloaddition is an easy and efficient approach to the synthesis of the isoxazole ring. Moreover, by attaching suitable aryl groups at the C-3 and C-5 positions of the isoxazoline ring, interesting LC properties can emerge. In this sense, the isoxazoline moiety can be considered a useful molecular kit for the preparation of interesting organic materials.[13]

In this article we describe the 1,3-dipolar cycloaddition of nitrile oxides to dipolarophiles to produce 3,5-disubstituted isoxazoline rings which are potential candidates for liquid-crystalline materials. For this purpose we selected three 3,5-disubstituted isoxazoline compounds synthesized in this work to demonstrate that these heterocycles can serve as molecular kits in the synthesis of new compounds with mesogenic properties. Four LC compounds were prepared by a simple and easy modification of the original isoxazoline ring (Figure 1) by adding two "molecular wings" bearing one or more aromatic rings at the 3- and 5-positions of the isoxazoline system.

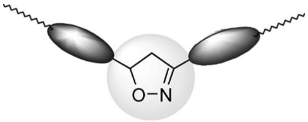

Figure 1. General structure of the isoxazoline liquid crystals.

Results and Discussion

Synthesis of the Isoxazolines 6–12

Two main methodologies were used to prepare the isoxazoline LC materials. First, to form the isoxazoline, a [3+2] cycloaddition reaction between a nitrile oxide (generated by in situ oxidation of the corresponding aldoxime) and an alkene was performed. The Sonogashira reaction was then used as the second methodology to install the triple bond into the molecular wings of the final compounds. The preparation of the aldoximes **3a**–**d** is outlined in Scheme 1. They were prepared from aldehyde **1** in two steps following classical procedures. In the first step, *p*-hydroxy-

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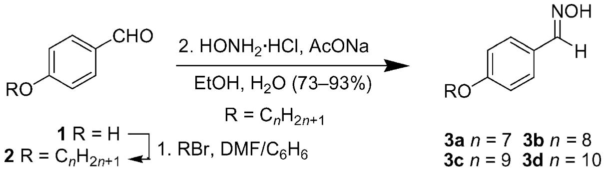
benzaldehyde (**1**) was alkylated by treatment with alkyl bromides to yield the corresponding *p*-alkoxybenzaldehydes **2a–d** in 70–90 % yields. In the second step the oximes were synthesized by the reaction of **2a–d** with a solution of hydroxylamine hydrochloride in good yields (73–93 %).

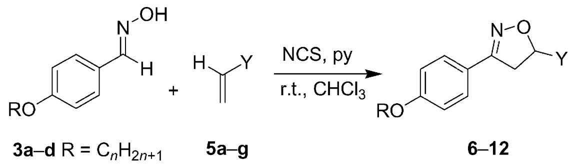


Scheme 1. Synthesis of aldoximes **3a–d**.

Oximes containing a polar group (X) at the *para* position of the aromatic ring **4e** (X = Br), **4f** (X = CN) and **4g** (X = NO_2) were also prepared in good yields by exposure of the corresponding 4-substituted benzaldehyde to a solution of hydroxylamine hydrochloride.

The oximes prepared in this work were obtained as a mixture of *E* and *Z* isomers. The structural assignments of these intermediates were made based on their ^{1}H and ^{13}C NMR chemical shifts. The signal of the iminyl hydrogen of the *Z* isomer always appears at a higher field than that of the *E* isomer, in accordance with the reported oxime analogues derived from anisaldehyde.[15a,15b] The ^{13}C NMR resonance line of the iminyl carbon atom follows the same tendency. For instance, the chemical shift of the iminyl carbon of the *E* isomer is always shifted downfield, whereas that of the *Z* isomer is shifted upfield. The chemical shift is an indication of the charge distribution on the iminyl carbon atom. In this situation, the charge distribution values observed for the *E* isomers were smaller than the those of the *Z* isomers.[14–19]

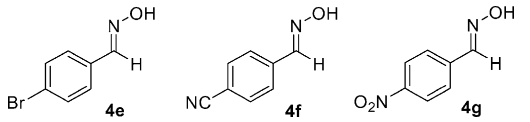
The 1,3-dipolar [3+2] cycloaddition reactions were carried out with seven different benzaldehyde oximes **3a–d** and **4e–g** and seven dipolarophiles **5a–g** (Scheme 2, Table 1). The yields of the isoxazolines **6–12** obtained are reported in Table 1. All the cycloadducts were characterized by ^{1}H and ^{13}C NMR spectroscopic techniques and melting points. The regiochemistries were established by ^{1}H and ^{13}C NMR spectroscopy. In all cases the reactions of the benzaldehyde oximes with **5a–g** (via the nitrile oxide intermediate) were completely regioselective giving only 3,5-disubstituted isoxazolines with no traces of the 3,4-regioisomers detected.[20]



Scheme 2. Preparation of isoxazolines **6–12**.

In nearly all cases, the yields were in the range of 40 to 90 %. Low yields were obtained with the allylic alcohol dipolarophile **5b**, which gave the 3,5-disubstituted isoxazolines **7a–d** and is known to be considerably less reactive than the other dipolarophiles used in this work. In the reactions of the cyano aldoxime **4f** with dipolarophile **5a** and **5d**, no cycloadducts were observed (entries 6 and 18).

Table 1. 1,3-Dipolar [3+2] cycloaddition of oximes **3a–d** and **4e–g** with dipolarophiles **5a–g**.[a]

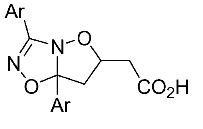


Entry	Aldoxime	Dipolarophile		Adduct	Yield [%][b]
1	**3a**	**5a**	Y = CO_2H	**6a**	80
2	**3b**			**6b**	66
3	**3c**			**6c**	83
4	**3d**			**6d**	89
5	**4e**			**6e**	47
6	**4f**			**6f**[c]	–
7	**4g**			**6g**	25
8	**3a**	**5b**	Y = CH_2OH	**7a**	36
9	**3b**			**7b**	36
10	**3c**			**7c**	38
11	**3d**			**7d**	41
12	**3a**	**5c**	Y = $CO_2{}^nBu$	**8a**	31
13	**3b**			**8b**	65
14	**3c**			**8c**	38
15	**3d**			**8d**	62
16	**3a**	**5d**	Y = $CONH_2$	**9a**	50
17	**3b**			**9b**	78
18	**4f**			**9f**[c]	–
19	**4g**			**9g**	45
20	**3c**	**5e**	Y = CN	**10c**	43
21	**3a**	**5f**	Y = CH_2CO_2H	**11a**[d]	30
22	**3b**	**5g**	Y = *p*-MeC_6H_4	**12b**	60

[a] Reaction conditions: dipolarophile (2.3 mmol), NCS (2.3 mmol), oxime (2 mmol), pyridine (3 mmol), solvent (8 mL). [b] Isolated yields. [c] No reaction. [d] 2:1 Cycloadduct, see discussion in the text.

The ^{13}C and ^{1}H NMR spectra of the isoxazolines exhibited well-defined resonance lines for the C-3 and C-5 carbon atoms and for the corresponding hydrogen atoms. The ^{1}H NMR spectrum of cycloadduct **7a**, for instance, showed four sets of doublet of doublets centred at δ = 3.24, 3.36, 3.68 and 3.86 ppm, which belong to ABX and AMX patterns arising from chemically and magnetically non-equivalent protons. The resonance lines of the selected carbon atoms of the isoxazoline ring confirm the correct regiochemistry of the [3+2] cycloaddition event. Thus, from the ^{13}C NMR spectrum of **7a** we can observe only two signals centred at δ = 36.5 and 80.9 ppm, which are consistent with the 3,5 regioisomer[20,21] (see the Supporting Information).

The cycloaddition reaction between the oxime **3a** and the dipolarophile **5f** reported in Table 1 gave the product **11a** (Figure 2) exclusively in 30 % yield and not the expected 3,5-disubstituted isoxazoline. The structure of the new condensed product **11a**, which was characterized as the 2:1 cycloadduct, was confirmed by NMR, mass spectrometry, elemental analysis and thermal analysis. These results can be rationalized by the low dipolarophilic reactivity of the vinylacetic acid (**5f**) in comparison with the 3,5-disubstituted isoxazoline formed in situ. Once the 3,5-disubstituted isoxazoline has formed by the reaction of the aryl nitrile oxide and **5f**, polarization of the C=N bond by the oxygen atom enhances the dipolarophilic character of the C=N bond and drives the addition of a second equivalent of aryl nitrile oxide to the initially formed isoxazoline.[22]



Ar = $p\text{-}C_nH_{2n+1}OC_6H_4$

11a *n* = 7

Figure 2. The 2:1 cycloadduct **11a**.

Synthesis of Selected Liquid-Crystalline Materials

Having accomplished the preparation of 3,5-disubstituted isoxazolines (Table 1) we could then explore the potential of this heterocycle as a molecular kit for obtaining a new class of calamitic liquid crystals. In this way, potential LC materials can be obtained from these key intermediates by an elongating molecular strategy. The elongation builds on the rigid isoxazoline core to form a more polarizable and mesogenic one. Our idea was to explore the synthetic potential of this class of compounds bearing a functional group by attaching a suitable aromatic moiety. The isoxazolines **6a** and **7a** were chosen because they possess carboxy and hydroxy functional groups, which could be used to obtain the desired LC materials. In addition, simple oxidation of the isoxazoline ring, such as **12b**, affords the liquid crystal compound in a straightforward fashion.

By a Sonogashira reaction an arylacetylenic group was installed on one side of the isoxazoline ring. Figure 3 shows the two acetylene derivatives used to elongate the isoxazolines **6a** and **7a**. Compounds **15** and **16** were synthesized in three steps following a methodology described previously.[23] Thus, the alkylation of 6-bromo-2-naphthol (**13**) or *p*-bromophenol (**14**) with *n*-alkyl bromide gave the corresponding alkyl aryl ethers in 85–95% yields. Installation of the acetylene unit was accomplished by Sonogashira alkynylation[24] of the alkyl aryl ethers derived from **13** or **14** with 2-methyl-3-butyn-2-ol (mebynol). The terminal acetylenes **15** and **16** were smoothly obtained by the release of acetone using KOH and 2-propanol.[25]

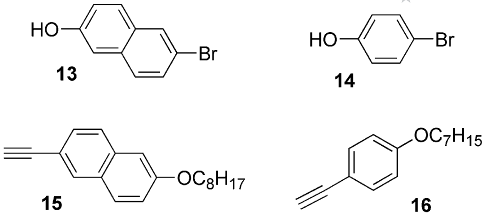
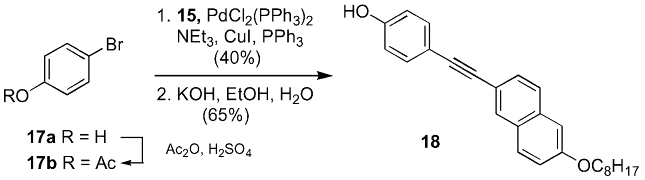


Figure 3. Terminal acetylenes **15** and **16**.

The second Sonogashira reaction allowed further elongation of the acetylene derivatives **15** and **16** by connection of another aromatic ring. Thus, the reaction of the protected bromophenol[26] **17b** and **15** under palladium/copper cross-coupling conditions[24,27] gave the desired phenol **18** after hydrolysis of the acetyl group in good yields (Scheme 3).



Scheme 3. Synthesis of **18**.

The chemical linkage between **18** and **6a** to obtain the final liquid crystal compound **19** was mediated by the DCC/DMAP protocol[28] in 70% of yield (Figure 4). Thermal analysis (DSC) and polarized optical microscopy studies (POM) showed that **19** is a thermotropic liquid crystal. When compound **19** was cooled from the isotropic phase, it clearly presented typical schlieren textures with singularity points and two- and four-brush defects characteristic of the nematic phase. The optical, thermal and thermodynamic data for the liquid crystals prepared in this work are summarized in Table 2.

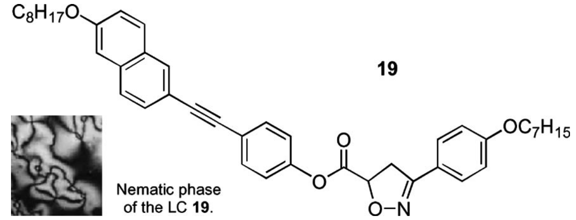


Figure 4. Chemical structure of **19**.

Table 2. Transition temperatures and enthalpies (Δ*H*) for compounds **19**, **21**, **23** and **24**.[a]

Entry	Phase transition temperature [°C]		Δ*H* [kcal mol⁻¹]	
	Heating	Cooling	Melt[d]	Iso phase K[e]
19	K 144.5[b] N 148.0 I	I 144.9 N 136.9 K	6.74	I 0.015 N 6.59 K
21	K 138.4 I	I 134.3[c] N 120.2 K	13.91	I 0.67 N 13.53 K
23	K 102.5 I	I 75.7[c] SmC[f] 71.2 K	13.40	I 2.81 SmC 11.79 K
24	K 105.9 N 132.2 I	I 131.1 N 82.2 K	5.82	I 0.076 N 5.87 K

[a] Scan rate: 10 °C min⁻¹ for all samples. K denotes crystal phase, SmC = smectic C phase and N = nematic phase. [b] Data obtained from POM study. [c] Monotropic behaviour. [d] Enthalpies (second heating/cooling stage) were determined from the crystal phase to the LC phase. [e] Cooling. [f] On slow cooling the samples crystallized. On fast cooling the sample displayed an unstable mesophase SmC during the crystallization process.

The DSC traces (Figure 5) for **19** exhibit I → N → K on cooling. However, this compound showed enantiotropic behaviour when analyzed by POM. On slow heating the sample **19** enters into the nematic phase at 144.5 °C and melts to an isotropic liquid at 148.0 °C. The temperature range for the mesophase is small for **19** (ΔT = 3.5 °C). The transition enthalpy for the isotropic-to-nematic transition of **19** is rather low (0.015 kcal mol^{-1}). This value is consistent with a less-ordered nematic mesophase.

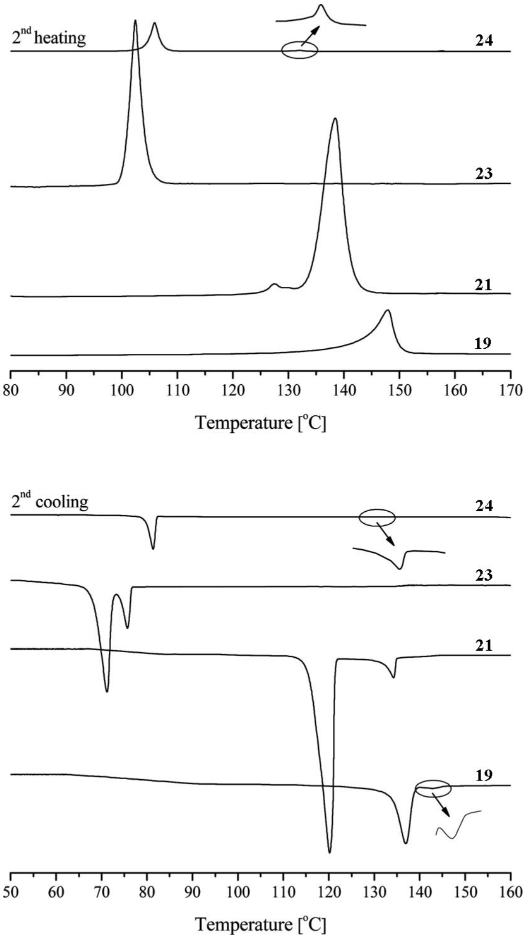


Figure 5. DSC curves for the LC compounds **19**, **21**, **23** and **24** on second heating and cooling.

The isoxazoline **7a** was selected to prepare the liquid-crystalline compounds **21** and **23**. Figure 6 shows the chemical structures of the final liquid crystals as well as the optical texture micrographs of their mesophases. For these purposes, the ester linkage was introduced by esterification of the bromo acid **20** with **7a** by the DCC/DMAP protocol. Application of the same cross-coupling reaction conditions to the alkyne **16** and the ester derivative from acid **20** afforded the liquid-crystalline compound **21** in 40% yield (two steps). The data collected in Table 2 for this compound show that the mesophase appears only during the cooling cycle. No mesophase was observed on heating when the sample was analysed by POM. Compound **21** displayed a planar thread-like texture, which is characteristic of a liquid-crystalline nematic phase. Note that the enthalpy for the nematic↔isotropic transition of **21** is larger than conventional nematic↔isotropic transition enthalpies (<0.50 kcal mol^{-1}) of calamitic liquid crystals. This may indicate that relatively strong intermolecular interactions exist in the nematic phase and could be attributed to an inversion of the carboxylate group in **21** compared with in **19**.

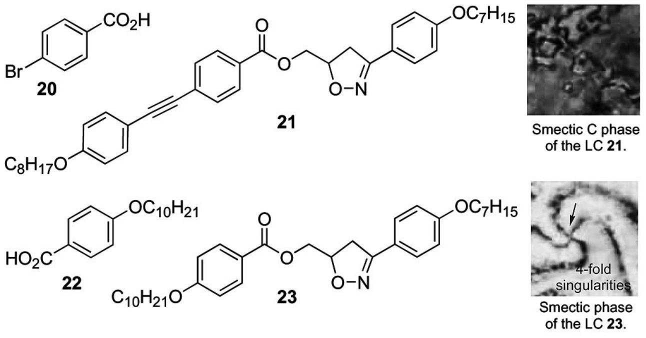
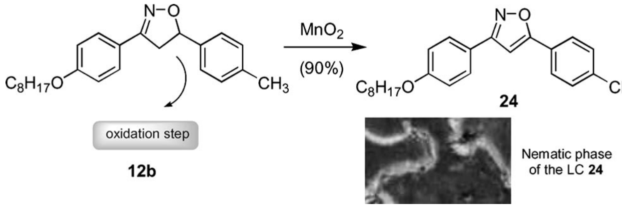


Figure 6. Chemical intermediates **20** and **22** and final liquid crystal isoxazolines **21** and **23**.

Liquid crystal **23** was prepared from **7a** by a short and fast method. The esterification reaction (DCC/DMAP) between **7a** and the popular acid **22** widely used in LC synthesis[29] gave the LC product. The phase behaviour of compound **23** is similar to that of compound **21**. On heating the sample **23** melts to the isotropic state at 102.5 °C. However, on cooling, the sample enters into the smectic C phase at 75.7 °C and finally crystallizes at 71.2 °C (Table 2, Figure 5). The schlieren texture observed for this sample shows a disclination point at which four black brushes (disclination lines) meet and this was assigned as the smectic C phase. In the smectic C phase, only four-fold singularities were observed; nematics may in addition show singularities with two brushes, as shown by compound **19**. For comparison, the mesophase range of LC **21** is larger than that of LC **23** due to the phenylacetylene substructure present in **21**. The transition enthalpy for the isotropic-to-smectic transition of **23** is higher than that for **21**. The enthalpy value suggests a more ordered phase on going from the isotropic to the smectic phase compared with compound **21**.

The final demonstration of the potential of isoxazolines in LC materials is outlined in Scheme 4. Isoxazoline **12b** was oxidized to the isoxazole **24** by exposure to manganese(IV) dioxide.[30] Compound **24** was easily purified by simple filtration to remove the inorganic materials and recrystallized from ethanol. The optical, thermal and thermodynamic data (Table 2) and the DSC traces (Figure 5) for compound **24** clearly reveal that it exhibits a large enantiotropic nematic mesophase. When the sample is cooled from its isotropic phase, the nematic phase appears exhibiting planar thread-like texture, which is characteristic of a liquid-crystalline nematic phase.[31] On heating, sample **24** enters into the nematic phase at 105.9 °C and finally melts to an isotropic liquid at 132.2 °C. The temperature range for the mesophase is 26.3 °C. The two peaks observed at 105.9 and 132.2 °C were associated with K→N and

N → I transitions, respectively. As expected for isotropic ↔ nematic transition enthalpies, the value of 0.076 kcal mol^{-1} is in accordance with a less-ordered nematic mesophase.



Scheme 4. Preparation of isoxazole LC **24**.

Conclusions

We have synthesized and characterized a number of isoxazolines with aryl and polar groups at the 3- and 5-positions by 1,3-dipolar [3+2] cycloaddition reactions of nitrile oxides and alkenes. The straightforward access to 2-isoxazolines is excellent for obtaining molecular kits for the preparation of versatile intermediates that can be transformed into LC materials. In this work, isoxazolines **6a** and **7a** were chosen and chemically modified by linkage of an arylacetylenic moiety at the polar group. Also we selected isoxazoline **12b** and performed the oxazoline → oxazole transformation by an oxidation reaction. In this way four new LC materials **19**, **21**, **23** and **24** were synthesized. In all the chemical operations, the compounds exhibited mesomorphic behaviour; the nematic phase was observed for compounds **19**, **21** and **24** and the smectic C phase was detected for compound **23**. With the less reactive dipolarophile vinylacetic acid (**5f**), the 2:1 cycloadduct was obtained exclusively and not the expected 1:1 cycloadduct. The synthesis of new liquid crystals derived from the isoxazolines listed in Table 1 is in progress and will be reported in due course.

Experimental Section

Instruments and Techniques: 4-Hydroxybenzaldehyde, 1-bromoalkanes, hydroxylamine hydrochloride, acrylic acid, *N*-chlorosuccinimide (NCS), KOH, sodium acetate, ethanol, chloroform, butyl acrylate, acrylonitrile, 4-bromobenzaldehyde, acetonitrile and toluene were from Aldrich and used without further purification. Pyridine and allylic alcohol were distilled under reduced pressure. All other commercial solvents and reagents were used without further purification. The melting points and mesophase transition temperatures and textures of the samples were measured with a Mettler Toledo FP82HT Hot Stage FP90 Central Processor and DSC 2910 TA Instruments. NMR spectra were obtained with a Varian 300 MHz instrument. Chemical shifts are given in parts per million (δ) and are referenced to tetramethylsilane (TMS). Infrared spectra were recorded with a Perkin–Elmer Spectrum One FTIR spectrometer using NaCl plates in the case of solids and as thin films supported between NaCl plates in the case of liquids and are reported in wavenumbers (cm^{-1}). Low-resolution mass spectra were obtained with a Shimadzu GC-MS-QP5050 mass spectrometer interfaced with a Shimadzu GC-17A gas chromatograph equipped with a DB-17 MS capillary column. ESI-MS data were collected with a Waters® Micromass® Q-Tof micro™ mass spectrometer with a Z-spray electrospray source. Samples were infused from a 100 µL gastight syringe at 5 µL min^{-1} through a syringe pump. Instrument settings were unexceptional: capillary voltage 4500 V, cone voltage 50 V, source temperature 100 °C, desolvation gas temperature 100 °C. Nitrogen was used as the desolvation gas. CHN analyses were performed with a Perkin–Elmer 2400 CHN Elemental Analyzer. All reactions involving the Sonogashira coupling were performed in a one-neck round-bottomed flask equipped with septum stoppers and charged with triethylamine (Et_3N), aromatic iodide and alkyne under argon for 30 min. Copper(I) iodide (CuI), triphenylphosphane (PPh_3) and bis(triphenylphosphane)palladium(II) chloride [$PdCl_2(PPh_3)_2$] were then added.

Alkylation Reactions: The 4-(*n*-alkyloxy)benzaldehydes **2a–d** were prepared from benzaldehyde (**1**) following previously reported procedures.[23b,32]

Synthesis of Aldoximes: The 4-(*n*-alkyloxy)benzaldehyde oximes **3a–d** and **4e–g** were synthesized from the corresponding 4-substituted benzaldehydes according literature procedures.[13a,33–36] See the Supporting Information for experimental procedure and spectral characterization.

Cycloaddition Reactions: A solution of the corresponding oxime (2 mmol) in $CHCl_3$ (2 mL) was added dropwise to an ice-cooled solution of $CHCl_3$ (8 mL), dipolarophile (2.3 mmol), pyridine (3 mmol) and *N*-chlorosuccinimide (NCS) (2.3 mmol) under argon for 40 min. The reaction was then stirred at room temperature for 4 h. The solution was washed with water and dried with Na_2SO_4. The filtrate was evaporated under a reduced pressure and the residue purified by recrystallization from toluene.

3-[4-(Heptyloxy)phenyl]-4,5-dihydroisoxazole-5-carboxylic Acid (6a): Yield 240 mg, 80%; white solid; m.p. 149 °C. ^1H NMR ($CDCl_3$): δ = 0.89 (m, 3 H, CH_3), 1.38 [m, 8 H, $(CH_2)_4$], 1.79 (m, 2 H, CH_2CH_2O), 3.62 (d, J = 9.0 Hz, 2 H, CH_2CH), 3.98 (t, J = 6.6 Hz, 2 H, CH_2O), 5.12 (t, J = 9.0 Hz, 1 H, CH_2CH), 6.90 (d, J = 8.7 Hz, 2 H, Ar), 7.60 (d, J = 8.7 Hz, 2 H, Ar), 8.10 (br., 1 H, OH) ppm. ^{13}C NMR ($CDCl_3$/[D$_6$]DMSO): δ = 13.7, 22.2, 25.5, 28.6, 28.7, 31.3, 38.8, 67.7, 77.4, 114.3, 120.5, 128.0, 155.3, 160.5, 172.0 ppm. IR: $\tilde{\nu}$ = 3182, 2925, 2854, 1720, 1610, 1517, 1461, 1377, 1252, 1183, 1043, 1010, 897, 829, 721, 666 cm^{-1}. $C_{17}H_{23}NO_4$ (305.37): calcd. C 66.86, H 7.59, N 4.59; found C 66.96, H 7.62, N 4.71.

3-[4-(Octyloxy)phenyl]-4,5-dihydroisoxazole-5-carboxylic Acid (6b): Yield 105 mg, 66%; white solid; m.p. 143 °C. ^1H NMR ($CDCl_3$): δ = 0.89 (m, 3 H, CH_3), 1.39 [m, 10 H, $(CH_2)_5$], 1.79 (m, 2 H, CH_2CH_2O), 3.63 (d, J = 9.0 Hz, 2 H, CH_2CH), 3.98 (t, J = 6.6 Hz, 2 H, CH_2O), 5.13 (t, J = 9.0 Hz, 1 H, CH_2CH), 5.80 (br., 1 H, OH), 6.90 (d, J = 8.7 Hz, 2 H, Ar), 7.60 (d, J = 8.7 Hz, 2 H, Ar) ppm. ^{13}C NMR ($CDCl_3$/[D$_6$]DMSO): δ = 13.7, 22.2, 25.6, 28.7, 28.8, 29.0, 31.4, 38.9, 67.7, 77.4, 114.3, 120.5, 128.1, 155.3, 160.5, 172.1 ppm. IR: $\tilde{\nu}$ = 3184, 2925, 2854, 1720, 1610, 1519, 1461, 1377, 1253, 1183, 1045, 1010, 895, 828, 721, 665 cm^{-1}. $C_{18}H_{25}NO_4$ (319.40): calcd. C 67.69, H 7.89, N 4.39; found C 67.58, H 7.92, N 4.51.

3-[4-(Nonyloxy)phenyl]-4,5-dihydroisoxazole-5-carboxylic Acid (6c): Yield 138 mg, 83%; white solid; m.p. 141 °C. ^1H NMR ($CDCl_3$): δ = 0.88 (m, 3 H, CH_3), 1.38 [m, 12 H, $(CH_2)_6$], 1.78 (m, 2 H, CH_2CH_2O), 3.62 (d, J = 9.0 Hz, 2 H, CH_2CH), 3.98 (t, J = 6.6 Hz, 2 H, CH_2O), 5.11 (t, J = 9.0 Hz, 1 H, CH_2CH), 6.70 (br., 1 H, OH), 6.90 (d, J = 8.7 Hz, 2 H, Ar), 7.59 (d, J = 8.7 Hz, 2 H, Ar) ppm. ^{13}C NMR (CDCl$_3$/[D$_6$]DMSO): δ = 13.8, 22.3, 25.6, 28.8, 28.9, 29.0, 29.1, 31.5, 38.9, 67.8, 77.4, 114.3, 120.6, 128.1, 155.3, 160.5, 172.2 ppm. IR: $\tilde{\nu}$ = 3183, 2925, 2854, 1721, 1608, 1518, 1461, 1377, 1253, 1182, 1045, 1010, 898, 828, 721, 667 cm^{-1}. $C_{19}H_{27}NO_4$ (333.43): calcd. C 68.44, H 8.16, N 4.20; found C 68.32, H 8.09, N 4.32.

3-[4-(Decyloxy)phenyl]-4,5-dihydroisoxazole-5-carboxylic Acid (6d): Yield 309 mg, 89%; white solid; m.p. 138 °C. ^{1}H NMR (CDCl$_3$): δ = 0.88 (m, 3 H, CH$_3$), 1.38 [m, 14 H, (CH$_2$)$_7$], 1.79 (m, 2 H, C*H*$_2$CH$_2$O), 3.62 (d, *J* = 9.0 Hz, 2 H, C*H*$_2$CH), 3.98 (t, *J* = 6.6 Hz, 2 H, CH$_2$O), 5.12 (t, *J* = 9.0 Hz, 1 H, CH$_2$C*H*), 6.90 (d, *J* = 8.7 Hz, 2 H, Ar), 7.59 (d, *J* = 8.7 Hz, 2 H, Ar) ppm. ^{13}C NMR (CDCl$_3$/[D$_6$]DMSO): δ = 13.8, 22.3, 25.6, 28.8, 28.9, 29.0, 29.2, 30.6, 31.5, 38.9, 67.7, 77.4, 114.3, 120.5, 128.1, 155.3, 160.5, 172.1 ppm. IR: $\tilde{\nu}$ = 3183, 2925, 2854, 1720, 1610, 1517, 1461, 1377, 1251, 1183, 1042, 1010, 898, 830, 721, 665 cm^{-1}. $C_{20}H_{29}NO_4$ (347.45): calcd. C 69.14, H 8.41, N 4.03; found C 69.23, H 8.33, N 4.12.

3-(4-Bromophenyl)-4,5-dihydroisoxazole-5-carboxylic Acid (6e): Yield 127 mg, 47%; brown solid; m.p. 173–175 °C. ^{1}H NMR (CDCl$_3$): δ = 3.62 (d, *J* = 9.3 Hz, 2 H, C*H*$_2$CH), 5.16 (t, *J* = 9.3 Hz, 1 H, CH$_2$C*H*), 7.55 (s, 4 H, Ar) ppm. ^{13}C NMR (CDCl$_3$/[D$_6$]-DMSO): δ = 38.5, 77.8, 124.4, 127.4, 128.1, 131.7, 155.0, 171.8 ppm. IR: $\tilde{\nu}$ = 3200–3100, 2924, 2854, 1726, 1592, 1462, 1377, 1225, 899, 824 cm^{-1}. $C_{10}H_8BrNO_3$ (270.08): calcd. C 44.47, H 2.29, N 5.19; found C 44.56, H 2.41, N 5.25.

3-(4-Nitrophenyl)-4,5-dihydroisoxazole-5-carboxylic Acid (6g): Yield 118 mg, 25%; white solid; m.p. 130 °C. ^{1}H NMR (CDCl$_3$/[D$_6$]-DMSO): δ = 3.69 (d, *J* = 9.3 Hz, 2 H, C*H*$_2$CH), 5.25 (m, 1 H, CH$_2$C*H*), 7.45 (br., 1 H, OH), 7.87 (d, *J* = 8.4 Hz, 2 H, Ar), 8.27 (d, *J* = 8.4 Hz, 2 H, Ar) ppm. $C_{10}H_8N_2O_5$ (236.18): calcd. C 50.85, H 3.41, N 11.86; found C 50.78, H 3.49, N 12.01.

{3-[4-(Heptyloxy)phenyl]-4,5-dihydroisoxazol-5-yl}methanol (7a): Yield 419 mg, 36%; white solid; m.p. 96 °C. ^{1}H NMR (CDCl$_3$): δ = 0.89 (m, 3 H, CH$_3$), 1.41 [m, 8 H, (CH$_2$)$_4$], 1.79 (m, 2 H, C*H*$_2$CH$_2$O), 2.10 (br., 1 H, OH), 3.24 (dd, *J* = 16.5, 7.8 Hz, 1 H, N=CC*H*HCH), 3.36 (dd, *J* = 16.5, 10.5 Hz, 1 H, N=CCH*H*CH), 3.67 (dd, *J* = 12.0, 4.8 Hz, 1 H, CHC*H*HOH), 3.85 (dd, *J* = 12.0, 3.3 Hz, 1 H, CHCH*H*OH), 3.97 (t, *J* = 6.6 Hz, 2 H, CH$_2$O), 4.83 (m, 1 H), 6.89 (d, *J* = 9.0 Hz, 2 H, Ar), 7.58 (d, *J* = 8.7 Hz, 2 H, Ar) ppm. ^{13}C NMR (CDCl$_3$): δ = 13.9, 22.5, 25.8, 28.9, 29.0, 31.6, 36.5, 63.4, 68.0, 80.9, 114.5, 121.5, 128.1, 156.5, 160.5 ppm. IR: $\tilde{\nu}$ = 3294, 3187, 2923, 2854, 1610, 1517, 1463, 1377, 1253, 1181, 1049, 875, 820, 721, 665 cm^{-1}. $C_{17}H_{25}NO_3$ (291.39): calcd. C 70.07, H 8.65, N 4.81; found C 70.12, H 8.71, N 4.89.

{3-[4-(Octyloxy)phenyl]-4,5-dihydroisoxazol-5-yl}methanol (7b): Yield 219 mg, 36%; white solid; m.p. 94 °C. ^{1}H NMR (CDCl$_3$): δ = 0.89 (m, 3 H, CH$_3$), 1.41 [m, 10 H, (CH$_2$)$_5$], 1.78 (m, 2 H, C*H*$_2$CH$_2$O), 2.99 (br., 1 H, OH), 3.24 (dd, *J* = 16.8, 8.1 Hz, 1 H, N=CC*H*HCH), 3.34 (dd, *J* = 16.8, 10.5 Hz, 1 H, N=CCH*H*CH), 3.67 (dd, *J* = 12.0, 4.8 Hz, 1 H, CHC*H*HOH), 3.83 (dd, *J* = 12.0, 3.3 Hz, 1 H, CHCH*H*OH), 3.96 (t, *J* = 6.6 Hz, 2 H, CH$_2$O), 4.81 (m, 1 H), 6.87 (d, *J* = 9.0 Hz, 2 H, Ar), 7.56 (d, *J* = 8.7 Hz, 2 H, Ar) ppm. ^{13}C NMR (CDCl$_3$): δ = 13.9, 22.5, 25.8, 29.0, 29.1, 29.2, 31.7, 36.5, 63.4, 68.0, 80.9, 114.5, 121.4, 128.1, 156.5, 160.5 ppm. IR: $\tilde{\nu}$ = 3294, 3189, 2923, 2854, 1608, 1517, 1463, 1377, 1254, 1181, 1049, 876, 820, 721, 668 cm^{-1}. $C_{18}H_{27}NO_3$ (305.42): calcd. C 70.79, H 8.91, N 4.59; found C 70.65, H 8.86, N 4.80.

{3-[4-(Nonyloxy)phenyl]-4,5-dihydroisoxazol-5-yl}methanol (7c): Yield 122 mg, 38%; white solid; m.p. 98 °C. ^{1}H NMR (CDCl$_3$): δ = 0.89 (m, 3 H, CH$_3$), 1.43 [m, 12 H, (CH$_2$)$_6$], 1.79 (m, 2 H, C*H*$_2$CH$_2$O), 2.10 (br., 1 H, OH), 3.24 (dd, *J* = 16.8, 8.1 Hz, 1 H, N=CC*H*HCH), 3.36 (dd, *J* = 16.8, 10.5 Hz, 1 H, N=CCH*H*CH), 3.67 (dd, *J* = 12.0, 4.8 Hz, 1 H, CHC*H*HOH), 3.86 (dd, *J* = 12.0, 3.3 Hz, 1 H, CHCH*H*OH), 3.97 (t, *J* = 6.6 Hz, 2 H, CH$_2$O), 4.84 (m, 1 H), 6.89 (d, *J* = 9.0 Hz, 2 H, Ar), 7.58 (d, *J* = 8.7 Hz 2 H, Ar) ppm. ^{13}C NMR (CDCl$_3$): δ = 13.9, 22.5, 25.8, 29.0, 29.1, 29.2, 29.3, 31.7, 36.5, 63.3, 68.0, 80.9, 114.4, 121.5, 128.0, 156.4, 160.5 ppm. IR: $\tilde{\nu}$ = 3294, 3189, 2923, 2854, 1611, 1515, 1463, 1377, 1254, 1182, 1048, 876, 820, 721, 666 cm^{-1}. $C_{19}H_{29}NO_3$ (319.44): calcd. C 71.44, H 9.15, N 4.38; found C 71.65, H 9.25, N 4.50.

{3-[4-(Decyloxy)phenyl]-4,5-dihydroisoxazol-5-yl}methanol (7d): Yield 273 mg, 41%; white solid; m.p. 95 °C. ^{1}H NMR (CDCl$_3$): δ = 0.89 (m, 3 H, CH$_3$), 1.43 [m, 14 H, (CH$_2$)$_7$], 1.79 (m, 2 H, C*H*$_2$CH$_2$O), 2.05 (br., 1 H, OH), 3.24 (dd, *J* = 16.5, 7.8 Hz, 1 H, N=CC*H*HCH), 3.37 (dd, *J* = 16.5, 10.5 Hz, 1 H, N=CCH*H*CH), 3.67 (dd, *J* = 12.0, 4.8 Hz, 1 H, CHC*H*HOH), 3.86 (dd, *J* = 12.0, 3.3 Hz, 1 H, CHCH*H*OH), 3.98 (t, *J* = 6.6 Hz, 2 H, CH$_2$O), 4.84 (m, 1 H), 6.90 (d, *J* = 9.0 Hz, 2 H, Ar), 7.58 (d, *J* = 8.7 Hz, 2 H, Ar) ppm. ^{13}C NMR (CDCl$_3$): δ = 14.0, 22.6, 25.9, 29.1, 29.2, 29.3, 29.4, 29.5, 31.8, 36.5, 63.5, 68.0, 80.9, 114.5, 121.5, 128.1, 156.6, 160.6 ppm. IR: $\tilde{\nu}$ = 3294, 3187, 2923, 2854, 1610, 1515, 1463, 1377, 1256, 1182, 1047, 877, 820, 721, 667 cm^{-1}. $C_{20}H_{31}NO_3$ (333.47): calcd. C 72.04, H 9.37, N 4.20; found C 71.98, H 9.24, N 4.45.

Butyl 3-[4-(Heptyloxy)phenyl]-4,5-dihydroisoxazole-5-carboxylate (8a): Yield 112 mg, 31%; yellow solid; m.p. 34 °C. ^{1}H NMR (CDCl$_3$): δ = 0.91 [m, 6 H, (CH$_3$)$_2$], 1.38 [m, 10 H, (CH$_2$)$_5$], 1.67 (m, 2 H, C*H*$_2$CH$_2$OCO), 1.79 (m, 2 H, C*H*$_2$CH$_2$O), 3.60 (d, *J* = 10.2 Hz, 1 H, C*H*HCH), 3.61 (d, *J* = 8.4 Hz, 1 H, CH*H*CH), 3.98 (t, *J* = 6.6 Hz, 2 H, CH$_2$O), 4.20 (t, *J* = 6.6 Hz, 2 H, CH$_2$OCO), 5.13 (dd, *J* = 8.4, 10.2 Hz, 1 H, CHHC*H*), 6.90 (d, *J* = 9.0 Hz, 2 H, Ar), 7.60 (d, *J* = 9.0 Hz, 2 H, Ar) ppm. ^{13}C NMR (CDCl$_3$): δ = 13.5, 13.9, 18.9, 22.4, 25.8, 28.9, 29.0, 30.3, 31.6, 39.0, 65.6, 68.0, 77.7, 114.5, 120.7, 128.3, 155.5, 160.8, 170.3 ppm. IR: $\tilde{\nu}$ = 2923, 2854, 1737, 1610, 1519, 1456, 1377, 1264, 1210, 1017, 879, 828, 722, 664 cm^{-1}. $C_{21}H_{31}NO_4$ (361.48): calcd. C 69.78, H 8.64, N 3.87; found C 69.58, H 8.59, N 3.98.

Butyl 3-[4-(Octyloxy)phenyl]-4,5-dihydroisoxazole-5-carboxylate (8b): Yield 244 mg, 65%; yellow solid; m.p. 35 °C. ^{1}H NMR (CDCl$_3$): δ = 0.91 [m, 6 H, (CH$_3$)$_2$], 1.38 [m, 12 H, (CH$_2$)$_6$], 1.67 (m, 2 H, C*H*$_2$CH$_2$OCO), 1.79 (m, 2 H, C*H*$_2$CH$_2$O), 3.60 (d, *J* = 9.9 Hz, 1 H, C*H*HCH), 3.61 (d, *J* = 8.1 Hz, 1 H, CH*H*CH), 3.98 (t, *J* = 6.6 Hz, 2 H, CH$_2$O), 4.20 (t, *J* = 6.6 Hz, 2 H, CH$_2$OCO), 5.13 (dd, *J* = 8.1, 9.9 Hz, 1 H, CHHC*H*), 6.90 (d, *J* = 9.0 Hz, 2 H, Ar), 7.60 (d, *J* = 9.0 Hz, 2 H, Ar) ppm. ^{13}C NMR (CDCl$_3$): δ = 13.5, 14.0, 18.9, 22.5, 25.9, 29.0, 29.1, 29.2, 30.3, 31.7, 39.0, 65.6, 68.0, 77.7, 114.5, 120.6, 128.3, 155.5, 160.8, 170.4 ppm. IR: $\tilde{\nu}$ = 2923, 2854, 1738, 1612, 1519, 1458, 1377, 1264, 1210, 1019, 881, 827, 722, 666 cm^{-1}. $C_{22}H_{33}NO_4$ (375.51): calcd. C 70.37, H 8.86, N 3.73; found C 70.18, H 8.69, N 3.90.

Butyl 3-[4-(Nonyloxy)phenyl]-4,5-dihydroisoxazole-5-carboxylate (8c): Yield 151 mg, 38%; yellow solid; m.p. 40 °C. ^{1}H NMR (CDCl$_3$): δ = 0.91 [m, 6 H, (CH$_3$)$_2$], 1.38 [m, 14 H, (CH$_2$)$_7$], 1.67 (m, 2 H, C*H*$_2$CH$_2$OCO), 1.79 (m, 2 H, C*H*$_2$CH$_2$O), 3.60 (d, *J* = 9.9 Hz, 1 H, C*H*HCH), 3.61 (d, *J* = 8.4 Hz, 1 H, CH*H*CH), 3.98 (t, *J* = 6.6 Hz, 2 H, CH$_2$O), 4.20 (t, *J* = 6.6 Hz, 2 H, CH$_2$OCO), 5.13 (dd, *J* = 8.4, 9.9 Hz, 1 H, CHHC*H*), 6.91 (d, *J* = 9.0 Hz, 2 H, Ar), 7.60 (d, *J* = 9.0 Hz, 2 H, Ar) ppm. ^{13}C NMR (CDCl$_3$): δ = 13.5, 14.0, 18.9, 22.5, 25.8, 29.0, 29.1, 29.2, 29.4, 30.3, 31.7, 39.0, 65.6, 68.0, 77.7, 114.5, 120.7, 128.3, 155.5, 160.8, 170.4 ppm. IR: $\tilde{\nu}$ = 2923, 2854, 1737, 1610, 1517, 1456, 1377, 1264, 1210, 1017, 880, 828, 722, 667 cm^{-1}. $C_{23}H_{35}NO_4$ (389.54): calcd. C 70.92, H 9.06, N 3.60; found C 70.98, H 9.12, N 3.69.

Butyl 3-[4-(Decyloxy)phenyl]-4,5-dihydroisoxazole-5-carboxylate (8d): Yield 250 mg, 62%; yellow solid; m.p. 44 °C. ^{1}H NMR (CDCl$_3$): δ = 0.91 [m, 6 H, (CH$_3$)$_2$], 1.38 [m, 16 H, (CH$_2$)$_8$], 1.67 (m, 2 H, C*H*$_2$CH$_2$OCO), 1.79 (m, 2 H, C*H*$_2$CH$_2$O), 3.60 (d, *J* = 10.2 Hz, 1 H, C*H*HCH), 3.61 (d, *J* = 8.4 Hz, 1 H, CH*H*CH), 3.98 (t, *J* = 6.6 Hz, 2 H, CH$_2$O), 4.20 (t, *J* = 6.6 Hz, 2 H, CH$_2$OCO), 5.13 (dd, *J* = 8.4, 10.2 Hz, 1 H, CHHC*H*), 6.90 (d, *J* = 9.0 Hz, 2 H, Ar), 7.60 (d, *J* = 9.0 Hz, 2 H, Ar) ppm. ^{13}C NMR (CDCl$_3$): δ = 13.5, 14.0, 18.9, 22.5, 25.9, 29.0, 29.1, 29.2, 29.4, 29.5, 30.3, 31.7, 39.0, 65.6, 68.0, 77.7, 114.5, 120.7, 128.3, 155.5, 160.8, 170.3 ppm. IR: $\tilde{\nu}$ = 2923, 2854, 1737, 1611, 1519, 1457, 1377, 1264, 1210, 1018, 879, 829, 722, 667 cm^{-1}. C$_{24}$H$_{37}$NO$_4$ (403.56): calcd. C 71.43, H 9.24, N 3.47; found C 71.52, H 9.34, N 3.59.

3-[4-(Heptyloxy)phenyl]-4,5-dihydroisoxazole-5-carboxamide (9a): Yield 152 mg, 50%; white solid; m.p. 185 °C. ^{1}H NMR (CDCl$_3$/[D$_6$]DMSO): δ = 0.88 (m, 3 H, CH$_3$), 1.39 [m, 8 H, (CH$_2$)$_4$], 1.79 (m, 2 H, C*H*$_2$CH$_2$O), 3.68 (m, 2 H, C*H*$_2$CH), 3.99 (t, *J* = 6.6 Hz, 2 H, CH$_2$O), 5.11 (dd, *J* = 6.6, 9.9 Hz, 1 H, CH$_2$C*H*), 5.57 (s, 1 H, N*H*H), 6.79 (s, 1 H, NH*H*), 6.92 (d, *J* = 9.0 Hz, 2 H, Ar), 7.59 (d, *J* = 9.0 Hz, 2 H, Ar) ppm. ^{13}C NMR (CDCl$_3$/[D$_6$]DMSO): δ = 12.2, 20.4, 23.8, 26.8, 26.9, 29.6, 65.9, 76.7, 112.8, 119.1, 126.5, 153.9, 158.6, 170.7 ppm. IR: $\tilde{\nu}$ = 3394, 3186, 2925, 2854, 1655, 1610, 1460, 1377, 1255, 1114, 1048, 906, 875, 822, 722, 667 cm^{-1}. C$_{17}$H$_{24}$N$_2$O$_3$ (304.39): calcd. C 67.08, H 7.95, N 9.20; found C 67.06, H 7.89, N 9.30.

3-[4-(Octyloxy)phenyl]-4,5-dihydroisoxazole-5-carboxamide (9b): Yield 496 mg, 78%; white solid; m.p. 185 °C. ^{1}H NMR (CDCl$_3$/[D$_6$]DMSO): δ = 0.88 (m, 3 H, CH$_3$), 1.37 [m, 10 H, (CH$_2$)$_5$], 1.80 (m, 2 H, C*H*$_2$CH$_2$O), 3.64 (m, 2 H, C*H*$_2$CH), 3.99 (t, *J* = 6.6 Hz, 2 H, CH$_2$O), 5.11 (dd, *J* = 6.6, 10.5 Hz, 1 H, CH$_2$C*H*), 5.58 (s, 1 H, N*H*H), 6.79 (s, 1 H, NH*H*), 6.92 (d, *J* = 8.1 Hz, 2 H, Ar), 7.59 (d, *J* = 8.1 Hz, 2 H, Ar) ppm. ^{13}C NMR (CDCl$_3$/[D$_6$]DMSO): δ = 12.1, 20.3, 23.7, 26.8, 26.9, 27.0, 29.5, 65.8, 76.7, 112.7, 119.0, 126.4, 153.4, 158.5, 170.5 ppm. IR: $\tilde{\nu}$ = 3394, 3187, 2924, 2854, 1655, 1610, 1460, 1377, 1256, 1114, 1049, 906, 875, 823, 722, 667 cm^{-1}. C$_{18}$H$_{26}$N$_2$O$_3$ (318.42): calcd. C 67.90, H 8.23, N 8.80; found C 67.92, H 8.16, N 8.85.

3-[4-(Nitrophenyl)]-4,5-dihydroisoxazole-5-carboxamide (9g): Yield 106 mg, 45%; white solid; m.p. 220 °C (thermal degradation above the isotropic temperature). ^{1}H NMR (CDCl$_3$/[D$_6$]DMSO): δ = 3.67 (m, 2 H, C*H*$_2$CH), 5.15 (dd, *J* = 11.4, 6.6 Hz, 1 H, CH$_2$C*H*), 6.41 (s, 1 H, N*H*H), 6.84 (s, 1 H, NH*H*), 7.78 (d, *J* = 9.0 Hz, 2 H, Ar), 8.21 (d, *J* = 9.0 Hz, 2 H, Ar) ppm. ^{13}C NMR (CDCl$_3$/[D$_6$]DMSO): δ = 36.9, 78.4, 122.4, 126.4, 133.5, 146.9, 153.8, 170.7 ppm. IR: $\tilde{\nu}$ = 3310, 3192, 1670, 1578, 1346, 875, 851, 752, 722 cm^{-1}. C$_{10}$H$_9$N$_3$O$_4$ (235.20): calcd. C 51.07, H 3.86, N 17.87; found C 51.12, H 3.89, N 17.94.

3-[4-(Nonyloxy)phenyl]-4,5-dihydroisoxazole-5-carbonitrile (10c): Yield 136 mg, 43%; white solid; m.p. 65 °C. ^{1}H NMR (CDCl$_3$): δ = 0.92 (m, 3 H, CH$_3$), 1.35 [m, 12 H, (CH$_2$)$_6$], 1.80 (m, 2 H, C*H*$_2$CH$_2$O), 3.68 (dd, *J* = 16.5, 6.6 Hz, 1 H, C*H*HCH), 3.75 (dd, *J* = 16.5, 10.2 Hz, 1 H, CH*H*CH), 3.99 (t, *J* = 6.6 Hz, 2 H, CH$_2$O), 5.34 (dd, *J* = 6.6, 10.2 Hz, 1 H, CHHC*H*), 6.93 (d, *J* = 8.7 Hz, 2 H, Ar), 7.59 (d, *J* = 8.7 Hz, 2 H, Ar) ppm. ^{13}C NMR (CDCl$_3$): δ = 14.0, 22.5, 25.8, 29.0, 29.1, 29.2, 29.4, 31.7, 41.3, 66.2, 68.1, 114.8, 117.2, 119.4, 128.6, 155.8, 161.4 ppm. IR: $\tilde{\nu}$ = 2924, 2853, 1607, 1516, 1461, 1377, 1362, 1257, 1175, 1014, 935, 876, 860, 839, 812, 723, 666 cm^{-1}. C$_{19}$H$_{26}$N$_2$O$_2$ (314.43): calcd. C 72.58, H 8.33, N 8.91; found C 72.51, H 8.58, N 8.94.

3,7a-Bis[4-(heptyloxy)phenyl]-7,7a-dihydro-6*H*-isoxazolo[2,3-*d*]-[1,2,4]oxadiazol-6-ylacetic Acid (11a): Yield 83 mg, 30%; white solid; m.p. 110–113 °C. ^{1}H NMR (CDCl$_3$): δ = 0.89 [m, 6 H, (CH$_3$)$_2$], 1.38 [m, 16 H, (CH$_2$)$_8$], 1.79 [m, 4 H, (C*H*$_2$CH$_2$O)$_2$], 2.87 (dd, *J* = 15.6, 7.5 Hz, 1 H, NCC*H*HCH), 3.05 (dd, *J* = 15.6, 6.0 Hz, 1 H, NCCH*H*CH), 3.28 (dd, *J* = 16.8, 6.9 Hz, 1 H, CHC*H*HCO$_2$H), 3.59 (dd, *J* = 16.8, 10.5 Hz, 1 H, CHCH*H*CO$_2$H), 3.98 [m, 4 H, (CH$_2$O)$_2$], 5.17 (m, 1 H), 6.89 (d, *J* = 8.4 Hz, 2 H, Ar), 6.93 (d, *J* = 8.4 Hz, 2 H, Ar), 7.60 (d, *J* = 8.7 Hz, 2 H, Ar), 7.85 (d, *J* = 8.7 Hz, 2 H, Ar) ppm. ^{13}C NMR (CDCl$_3$/[D$_6$]DMSO): δ = 14.0, 22.5, 25.8, 25.9, 28.9, 29.0, 29.1, 31.7, 37.5, 40.4, 68.1, 68.2, 76.3, 114.4, 114.6, 121.3, 122.4, 128.3, 129.5, 156.4, 160.8, 162.7, 166.3, 168.8 ppm. IR: $\tilde{\nu}$ = 3228, 2924, 2854, 1787, 1684, 1608, 1517, 1464, 1377, 1254, 1176, 1098, 1015, 876, 834, 812, 722, 666 cm^{-1}. HRMS (ESI): calcd. for [M]$^+$ 552.3199; found [M + 1]$^+$ 553.3298; calcd. for [M + Na]$^+$ 575.3097; found 575.3068. EIMS: *m*/*z* (%) = 233, 135 (100), 134, 107, 106, 90, 78. C$_{32}$H$_{44}$N$_2$O$_6$ (552.71): calcd. C 69.54, H 8.02, N 5.07; found C 68.93, H 8.03, N 4.79.

5-(4-Methylphenyl)-3-[4-(octyloxy)phenyl]-4,5-dihydroisoxazole (12b): Yield 220 mg, 60%; white solid; m.p. 110–113 °C. ^{1}H NMR (CDCl$_3$): δ = 0.89 (m, 3 H, CH$_3$), 1.38 [m, 10 H, (CH$_2$)$_5$], 1.80 (m, 2 H, C*H*$_2$CH$_2$O), 2.31 (s, 3 H, CH$_3$), 3.30 (dd, *J* = 16.6, 7.8 Hz, 1 H, C*H*HCH), 3.71 (dd, *J* = 16.4, 10.7 Hz, 1 H, CH*H*CH), 4.0 (t, *J* = 6.4 Hz, 2 H, CH$_2$O), 5.60 (dd, *J* = 10.8, 8.0 Hz, 1 H, CHHC*H*), 6.93 (d, *J* = 8.8 Hz, 2 H, Ar), 7.28 (d, *J* = 8.4 Hz, 2 H, Ar), 7.32 (d, *J* = 8.6 Hz, 2 H, Ar), 7.68 (d, *J* = 8.8 Hz, 2 H, Ar) ppm. ^{13}C NMR (CDCl$_3$): δ = 14.1, 21.1, 22.6, 25.9, 29.1, 29.2, 29.3, 31.8, 43.3, 68.0, 82.2, 114.5, 121.6, 125.8, 128.1, 129.3, 137.8, 137.9, 155.7, 160.6 ppm. IR: $\tilde{\nu}$ = 2922, 2853, 1904, 1701, 1605, 1515, 1460, 1376, 1255, 1174, 1112, 1044, 1021, 904, 837, 812, 714, 657 cm^{-1}. C$_{24}$H$_{31}$NO$_2$ (365.52): calcd. C 78.87, H 8.55, N 3.83; found C 78.89, H 8.53, N 3.79.

2-Ethynyl-6-(octyloxy)naphthalene (15): Compound **15** was synthesized according to previously reported procedures.[23–25] Yield 1.55 g, 69%; white solid; m.p. 36 °C. ^{1}H NMR (CDCl$_3$): δ = 0.89 (m, 3 H, CH$_3$), 1.40 [m, 10 H, (CH$_2$)$_5$], 1.83 (m, 2 H, C*H*$_2$CH$_2$O), 3.10 (s, 1 H, HCC), 4.04 (t, *J* = 6.6 Hz, 2 H, CH$_2$O), 7.07 (d, *J* = 2.4 Hz, 1 H, Ar), 7.15 (dd, *J* = 9.0, 2.4 Hz, 1 H, Ar), 7.47 (dd, *J* = 8.4, 1.5 Hz, 1 H, Ar), 7.65 (m, 2 H, Ar), 7.93 (s, 1 H, Ar) ppm. ^{13}C NMR (CDCl$_3$): δ = 14.1, 22.6, 26.1, 29.1, 29.2, 29.3, 31.8, 68.1, 76.6, 84.2, 106.4, 116.7, 119.7, 126.7, 128.1, 129.0, 129.2, 132.1, 134.4, 157.9 ppm. IR: $\tilde{\nu}$ = 3314, 2904, 2109, 1630, 1602, 1500, 1466, 1377, 1266, 1225, 1173, 1030, 891, 849, 812, 722, 646 cm^{-1}.

1-Ethynyl-4-(octyloxy)benzene (16):[23–25] Compound **16** was synthesized according to previously reported procedures.[23–25] Yield 1.10 g, 60%; colourless liquid. ^{1}H NMR (CDCl$_3$): δ = 0.90 (m, 3 H, CH$_3$), 1.38 [m, 10 H, (CH$_2$)$_5$], 1.77 (m, 2 H, C*H*$_2$CH$_2$O), 2.99 (s, 1 H, HCC), 3.94 (t, *J* = 6.6 Hz, 2 H, CH$_2$O), 6.82 (d, *J* = 8.4 Hz, 2 H, Ar), 7.41 (d, *J* = 8.4 Hz, 2 H, Ar) ppm. ^{13}C NMR (CDCl$_3$): δ = 14.1, 22.6, 26.0, 29.1, 29.2, 29.3, 31.8, 68.1, 75.6, 83.7, 113.9, 114.4, 133.5, 159.5 ppm. IR: $\tilde{\nu}$ = 3318, 2927, 2856, 2108, 1607, 1507, 1469, 1289, 1248, 1170, 1026, 832, 724, 641 cm^{-1}.

4-Bromophenyl Acetate (17b): This compound was prepared according to a previous report.[26] Yield 3.78 g, 88%; pale-yellow liquid. ^{1}H NMR (CDCl$_3$): δ = 2.29 (s, 3 H, CH$_3$), 6.98 (d, *J* = 8.7 Hz, 2 H, Ar), 7.48 (d, *J* = 8.7 Hz, 2 H, Ar) ppm. ^{13}C NMR (CDCl$_3$): δ = 20.9, 118.7, 123.3, 132.3, 149.6, 168.9 ppm. IR: $\tilde{\nu}$ = 1761, 1485, 1369, 1197, 1068, 1013, 908, 843, 794, 710, 674 cm^{-1}.

4-[(6-Octyloxy-2-naphthyl)ethynyl]phenol (18): This compound was prepared according to a literature procedure.[27] Yield 204 mg, 65%; brown solid; m.p. 126–128 °C. ^{1}H NMR (CDCl$_3$/[D$_6$]DMSO): δ = 0.89 (m, 3 H, CH$_3$), 1.38 [m, 10 H, (CH$_2$)$_5$], 1.82 (m, 2 H, C*H*$_2$CH$_2$O), 4.06 (t, *J* = 6.3 Hz, 2 H, CH$_2$O), 6.84 (d, *J* = 8.1 Hz, 2 H, Ar), 7.12 (m, 2 H, Ar), 7.40 (d, *J* = 8.1 Hz, 2 H, Ar), 7.50 (d, *J* = 8.4 Hz, 1 H, Ar), 7.64 (d, *J* = 8.4 Hz, 1 H, Ar), 7.68 (d, *J* = 9.0 Hz, 1 H, Ar), 7.91 (s, 1 H, Ar) ppm. ^{13}C NMR (CDCl$_3$/[D$_6$]DMSO): δ = 13.9, 22.5, 25.9, 29.0, 29.1, 29.2, 31.6, 67.9, 87.9, 89.3, 106.4, 113.9, 115.6, 118.3, 119.4, 126.5, 128.2, 128.7, 128.9, 130.5, 132.9, 133.7, 157.3, 157.5 ppm. IR: $\tilde{\nu}$ = 2925, 2855, 1727, 1466, 1377, 1251, 1182, 898, 876, 829, 721, 666 cm^{-1}.

4-[(6-Octyloxy-2-naphthyl)ethynyl]phenyl 3-(4-Heptyloxyphenyl)-4,5-dihydroisoxazole-5-carboxylate (19): Compound **19** was prepared according to the DCC/DMAP/DCM reaction protocol following a previously described experimental procedure.[28] Yield 115 mg, 70%; white solid; m.p. 144.5 °C. ^{1}H NMR (CDCl$_3$): δ = 0.88 [m, 6 H, (CH$_3$)$_2$], 1.38 [m, 18 H, (CH$_2$)$_9$], 1.82 [m, 4 H, (C*H*$_2$CH$_2$O)$_2$], 3.75 (m, 2 H, C*H*$_2$CH), 3.98 (t, *J* = 6.6 Hz, 2 H, CH$_2$O), 4.07 (t, *J* = 6.6 Hz, 2 H, CH$_2$O), 5.37 (dd, *J* = 7.2, 11.1 Hz, 1 H, CH$_2$C*H*), 6.92 (d, *J* = 8.7 Hz, 2 H, Ar), 7.14 (m, 4 H, Ar), 7.50–7.72 (m, 7 H, Ar), 7.96 (s, 1 H, Ar) ppm. ^{13}C NMR (CDCl$_3$): δ = 14.0, 14.1, 22.5, 22.6, 25.9, 26.1, 28.9, 29.0, 29.1, 29.2, 29.3, 31.7, 31.8, 39.2, 68.0, 68.1, 77.7, 87.9, 90.4, 106.5, 114.7, 117.6, 119.7, 120.5, 121.3, 121.6, 126.8, 128.3, 128.5, 128.8, 129.2, 131.3, 132.7, 134.2, 149.9, 155.6, 157.9, 161.0, 168.5 ppm. IR: $\tilde{\nu}$ = 2924, 2854, 1763, 1596, 1464, 1378, 1224, 1045, 897, 859, 818, 722, 666 cm^{-1}. C$_{43}$H$_{49}$NO$_5$ (659.85): calcd. C 78.27, H 7.48, N 2.12; found C 78.48, H 7.58, N 2.07.

[3-(4-Heptyloxyphenyl)-4,5-dihydroisoxazol-5-yl]methyl 4-[(Octyloxyphenyl)ethynyl]benzoate (21): Compound **21** was prepared according to the DCC/DMAP/DCM reaction protocol following a previously described experimental procedure.[28] Yield 63.0 mg, 40%; orange solid; m.p. 138.4 °C. ^{1}H NMR (CDCl$_3$): δ = 0.89 [m, 6 H, (CH$_3$)$_2$], 1.38 [m, 18 H, (CH$_2$)$_9$], 1.79 [m, 4 H, (C*H*$_2$CH$_2$O)$_2$], 3.24 (dd, *J* = 16.5, 6.6 Hz, 1 H, N=CC*H*HCH), 3.52 (dd, *J* = 16.5, 10.5 Hz, 1 H, N=CCH*H*CH), 3.98 [m, 4 H, (CH$_2$O)$_2$], 4.43 (dd, *J* = 12.0, 5.4 Hz, 1 H, CHC*H*HOCO), 4.50 (dd, *J* = 12.0, 4.2 Hz, 1 H, CHCH*H*OCO), 5.08 (m, 1 H), 6.87 (d, *J* = 9.0 Hz, 2 H, Ar), 6.92 (d, *J* = 8.7 Hz, 2 H, Ar), 7.45 (d, *J* = 9.0 Hz, 2 H, Ar), 7.51 (d, *J* = 8.4 Hz, 2 H, Ar), 7.62 (d, *J* = 9.0 Hz, 2 H, Ar), 7.97 (d, *J* = 8.4 Hz, 2 H, Ar) ppm. ^{13}C NMR (CDCl$_3$): δ = 14.0, 22.5, 22.6, 25.8, 25.9, 28.9, 29.0, 29.1, 29.3, 31.6, 31.7, 37.5, 65.7, 68.0, 77.8, 87.3, 92.9, 114.3, 114.5, 114.6, 121.3, 128.1, 128.3, 128.6, 129.6, 131.2, 133.1, 155.8, 159.6, 160.7, 165.7 ppm. IR: $\tilde{\nu}$ = 2924, 2855, 1723, 1600, 1517, 1465, 1377, 1286, 1251, 1177, 1108, 1045, 890, 834, 765, 721, 695, 666 cm^{-1}. C$_{40}$H$_{49}$NO$_5$ (623.82): calcd. C 77.01, H 7.92, N 2.25; found C 76.96, H 8.07, N 2.14.

[3-(4-Heptyloxyphenyl)-4,5-dihydroisoxazol-5-yl]methyl 4-Decyloxybenzoate (23): Compound **23** was prepared according to the DCC/DMAP/DCM reaction protocol following a previously described experimental procedure.[28] Yield 83.0 mg, 60%; white solid; m.p. 102.5 °C. ^{1}H NMR (CDCl$_3$): δ = 0.89 [m, 6 H, (CH$_3$)$_2$], 1.38 [m, 22 H, (CH$_2$)$_{11}$], 1.79 [m, 4 H, (C*H*$_2$CH$_2$O)$_2$], 3.22 (dd, *J* = 16.5, 6.9 Hz, 1 H, N=CC*H*HCH), 3.49 (dd, *J* = 16.5, 10.8 Hz, 1 H, N=CCH*H*CH), 3.98 [t, *J* = 6.6 Hz, 4 H, (CH$_2$O)$_2$], 4.44 (m, 2 H, CHC*H*$_2$OCO), 5.06 (m, 1 H), 6.85 (d, *J* = 8.7 Hz, 2 H, Ar), 6.91 (d, *J* = 8.4 Hz, 2 H, Ar), 7.61 (d, *J* = 8.7 Hz, 2 H, Ar), 7.95 (d, *J* = 9.0 Hz, 2 H, Ar) ppm. ^{13}C NMR (CDCl$_3$): δ = 14.0, 14.1, 22.5, 22.6, 25.9, 28.9, 29.0, 29.1, 29.2, 29.3, 29.5, 31.7, 31.8, 37.6, 65.2, 68.0, 68.1, 78.0, 114.0, 114.6, 121.5, 121.6, 128.2, 131.7, 155.8, 160.7, 163.1, 166.0 ppm. IR: $\tilde{\nu}$ = 2924, 2854, 1715, 1606, 1510, 1466, 1377, 1249, 1169, 1127, 1014, 882, 834, 768, 722, 699, 666, 649 cm^{-1}. C$_{34}$H$_{49}$NO$_5$ (551.76): calcd. C 74.01, H 8.95, N 2.54; found C 74.15, H 9.13, N 2.54.

3-(4-Octyloxyphenyl)-5-(4-methylphenyl)isoxazole (24): This compound was prepared according to a previous report.[30] Yield 131 mg, 90%; white solid; m.p. 105.9 °C. ^{1}H NMR (CDCl$_3$): δ = 0.89 (m, 3 H, CH$_3$), 1.38 [m, 10 H, (CH$_2$)$_5$], 1.80 (m, 2 H, C*H*$_2$CH$_2$O), 2.41 (s, 3 H, CH$_3$), 4.00 (t, *J* = 6.6 Hz, 2 H, CH$_2$O), 6.72 (s, 1 H), 6.97 (d, *J* = 8.7 Hz, 2 H, Ar), 7.28 (d, *J* = 8.1 Hz, 2 H, Ar), 7.72 (d, *J* = 8.1 Hz, 2 H, Ar), 7.78 (d, *J* = 8.7 Hz, 2 H, Ar) ppm. ^{13}C NMR (CDCl$_3$): δ = 14.1, 21.5, 22.6, 26.0, 29.1, 29.2, 29.3, 31.8, 68.1, 96.7, 114.8, 121.5, 124.9, 125.7, 128.1, 129.6, 140.4, 160.6, 162.6, 170.3 ppm. IR: $\tilde{\nu}$ = 2924, 2854, 1618, 1464, 1377, 1270, 1180, 951, 875, 837, 807, 722, 666 cm^{-1}. C$_{24}$H$_{29}$NO$_2$ (363.50): calcd. C 79.30, H 8.04, N 3.85; found C 79.24, H 8.09, N 3.80.

Supporting Information (see also the footnote on the first page of this article): Spectral and analytical data for the isolated products, including ^{1}H and ^{13}C NMR, IR, DSC and polarizing optical micrographs of the texture of the LCs, are supplied.

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