SYNTHESIS OF FLUORINATED LIQUID CRYSTALS

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List of Abbreviations

AcOH  acetic acid
AIBN  2,2’-azo-bisisotyronitrile
b      broad
b.p.   boiling point
BABH(n) 1,2-bis(4-n-alkoxybenzoyl) hydrazine where n = 9, 10 and 12
9-BBN  9-borabicyclo[3.3.1]nonane
BTMAC benzytrimethylammonium chloride
Bu₂SnO dibutyltin oxide
C₇H₁₅OH n-heptanol
CDCl₃ deuterated chloroform
(COCl)₂ oxalyl chloride
Cr     crystalline phase
Col₂hex hexagonal columnar phase
Cub phase cubic phase
d      doublet
dd     doublet of doublet
DCDHF dicyanomethylenedihydrofuran
DEAD  diethyl azodicarboxylate
DIAD  diisopropyl azodicarboxylate
<table>
<thead>
<tr>
<th>Acronym</th>
<th>Full Form</th>
</tr>
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<tbody>
<tr>
<td>DME</td>
<td>1,2-dimethoxyethane</td>
</tr>
<tr>
<td>DMF</td>
<td>dimethylformamide</td>
</tr>
<tr>
<td>DMSO</td>
<td>dimethyl sulfoxide</td>
</tr>
<tr>
<td>DMSO-\textit{d}_6</td>
<td>deuterated dimethyl sulfoxide</td>
</tr>
<tr>
<td>DSC</td>
<td>differential scanning calorimeter</td>
</tr>
<tr>
<td>E2</td>
<td>elimination reaction (type 2)</td>
</tr>
<tr>
<td>Et\textsubscript{3}N</td>
<td>triethylamine</td>
</tr>
<tr>
<td>FT-IR</td>
<td>Fourier Transform Infrared spectroscopy</td>
</tr>
<tr>
<td>H\textsubscript{2}O\textsubscript{2}</td>
<td>hydrogen peroxide</td>
</tr>
<tr>
<td>H\textsubscript{2}SO\textsubscript{4}</td>
<td>sulfuric acid</td>
</tr>
<tr>
<td>H</td>
<td>enthalpy or heat content</td>
</tr>
<tr>
<td>H\textsubscript{I}</td>
<td>normal hexagonal phase</td>
</tr>
<tr>
<td>H\textsubscript{II}</td>
<td>inverse hexagonal phase</td>
</tr>
<tr>
<td>HCl</td>
<td>hydrochloric acid</td>
</tr>
<tr>
<td>Hz</td>
<td>hertz</td>
</tr>
<tr>
<td>I</td>
<td>isotropic phase</td>
</tr>
<tr>
<td>i-Pr\textsubscript{2}NEt</td>
<td>Hunig’s base or \textit{N,N}-diisopropylethylamine</td>
</tr>
<tr>
<td>K\textsubscript{2}CO\textsubscript{3}</td>
<td>potassium carbonate</td>
</tr>
<tr>
<td>K-OtBu</td>
<td>potassium tert-butoxide</td>
</tr>
<tr>
<td>M</td>
<td>moles per liter</td>
</tr>
</tbody>
</table>
m multiplet
m.p. melting point
MHz hertz
mmol milli mole
mol mole
N nematic phase
N* chiral nematic phase or cholesteric phase
NaOH sodium hydroxide
$^1$H NMR proton nuclear magnetic resonance
$^{13}$C NMR carbon-13 nuclear magnetic resonance
$^{19}$F NMR fluorine-19 nuclear magnetic resonance
NaHCO$_3$ sodium bicarbonate
NH$_2$NH$_2$·H$_2$O hydrazine monohydrate
NMP $N$-methylpyrrolidone
Pd(PPh$_3$)$_4$ tetrakis(triphenylphosphine)palladium (0)
POCl$_3$ phosphorus oxychloride
POM polarized optical microscopy
ppm part per million
PPh$_3$ triphenylphosphine
rt room temperature
xxi
<table>
<thead>
<tr>
<th>Symbol</th>
<th>Definition</th>
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<tbody>
<tr>
<td>s</td>
<td>singlet</td>
</tr>
<tr>
<td>Sm</td>
<td>smectic</td>
</tr>
<tr>
<td>SmA</td>
<td>smectic A phase</td>
</tr>
<tr>
<td>SmC</td>
<td>smectic C phase, a tilted analog of SmA</td>
</tr>
<tr>
<td>SOCl₂</td>
<td>thionyl chloride</td>
</tr>
<tr>
<td>t</td>
<td>triplet</td>
</tr>
<tr>
<td>THF</td>
<td>tetrahydrofuran</td>
</tr>
<tr>
<td>TLC</td>
<td>thin layer chromatography</td>
</tr>
<tr>
<td>Δ</td>
<td>delta, the difference between two values or heating</td>
</tr>
<tr>
<td>δ</td>
<td>chemical shift</td>
</tr>
</tbody>
</table>
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Chapter 1

A general Introduction to Liquid Crystals
1.1 Introduction to Liquid Crystals

The study of liquid crystals began in 1888 when an Austrian botanist, Friedrich Reinitzer observed two distinct melting points in the compound cholesteryl benzoate. A German physicist, Otto Lehmann later confirmed this discovery and coined the name ‘liquid crystal’.\textsuperscript{1} Liquid crystals are known as the fourth state of matter and exhibit phases, which flow like a liquid but also have properties of crystalline solids. Most molecules with liquid crystalline properties are geometrically anisotropic with a rod or a disc-like shape. The molecules in crystals are ordered (positional and orientational) whereas in the liquid they are not.\textsuperscript{2} In crystals the molecules are held in fixed positions by intermolecular forces that need not be the same in all directions. On heating, the molecules vibrate and overcome the weaker organizing forces first but they remain bound by the stronger forces and lose some or all of their positional order, while maintaining the orientational order. The molecular axes of the individual molecules remain relatively aligned and parallel to each other leading to a preferred direction in space. In some cases the molecules tend to further associate in layers (a modulation in density in planes that intersect the molecular directors). Liquid crystals are usually anisotropic materials and the physical properties of the bulk system vary with the average alignment of the director in which large alignment tends towards anisotropic materials while small alignment tends towards isotropic materials.\textsuperscript{3} In the case of liquid crystals, the transition from the isotropic liquid phase to a crystal phase is not a single step but occurs by one or more intermediary steps. The shapes of the individual molecules and incompatibility of molecular segments are two key factors that drive organization in liquid crystal phases.
Research in this area was originally motivated by the desire to understand the behavior of this interesting state of matter. More recently research is motivated by applications of these materials which have led to significant invention and technological development. From the earliest days and even now over a century after their discovery, liquid crystals continue to provide surprises.

1.2 Types of liquid crystals

There are two very general types of liquid crystals, which can be distinguished by their composition and method of formation. Depending on their molecular ordering, each of these two types of liquid crystals may form a number of specific structures.4

1.2.1 Thermotropic liquid crystals

Thermotropic liquid crystals exhibit a variety of phases as the temperature is changed. At high temperature, the thermal motion destroys the ordering of the liquid crystal phase and transforms the material into a conventional isotropic liquid phase. At low temperature, most liquid crystal materials form a conventional crystal. A liquid crystal phase may be formed either by cooling an isotropic liquid below the clearing point or by heating a solid crystal above the melting point. There are two types of thermotropic liquid crystals which are called enantiotropic where the liquid crystal phase can be achieved either by heating or cooling (reversible cycles) and monotropic which is an irreversible process where the liquid crystal phase can only be reached from one direction.
(upon cooling) in the thermal cycle. Of course, a liquid crystal phase may also be obtained by heating or cooling from a different adjacent liquid crystal phase.

Thermotropic calamitic liquid crystals usually consist of rigid units (usually one or more rings) which comprise the molecular long axis to which is attached some flexible alkyl chains. These molecules are able to orient themselves so their long axes (along the director, $\mathbf{n}$) are on average parallel to each other. The simplest thermotropic bulk liquid crystal order is the nematic (N) where the molecules have no positional order but possess a spontaneous long range orientational order. As the chains are elongated, further segregation of the rigid units and the alkyl chains may occur. In such a case, the calamitic molecules tend to also become arranged in layers to form smectic phases.

On the other hand, discotic molecules form the discotic nematic phase or columns to exhibit either the columnar nematic (N$_C$) or other columnar phases (Col$_h$, Col$_r$). The discotic nematic phase is composed of flat-shaped disc molecules without long-range order. The discotic nematic molecules do not form specific columnar assemblies but are organized with their short axes parallel to the director. The columnar nematic (N$_C$) has no long-range order and are less organized than other columnar liquid crystals which have long-range order with two-dimensional lattices, such as the hexagonal (Col$_h$), rectangular (Col$_r$), oblique, plastic and helical. Our discussion will only focus on the columnar hexagonal phase. Relatively few thermotropic compounds with cubic phases are known. The mesophase morphologies for thermotropic LCs are summarized, as shown in Figure 1.1.
1.2.2 Lyotropic liquid crystals

Lyotropic liquid crystals were discovered well before their thermotropic counterparts were known. In 1850, their texture was noticed in a mixture of the phospholipid myelin and water.¹⁴ For both the thermotropic and lyotropic liquid crystals, temperature is an important condition for the appearance of liquid crystal phases. Because lyotropics are comprised of at least two chemical constituents, concentration is a much more important parameter compared to temperature.¹⁵ Lyotropic liquid crystal transitions occur with the primary influence of solvents, not by a change in temperature. Different phases can be observed as the concentrations of the solutions change.¹⁶ In these phases, solvent molecules fill the space around (and/or in) the structures to provide fluidity to the system. The mesophase morphologies for lyotropic LCs are summarized, as shown in Figure 1.2.
Figure 1.2: Mesophase morphologies for lyotropic mesogens.

- Mean interfacial curvature

Type 1

Type 2

- Lamellar
- Cubic (I1, Cm3m)
- Hexagonal (H1, P63m)
- Lamellar
- Cubic (I1, Cm3m)
- Hexagonal (H1, P63m)
- Bicontinuous cubic
- Cubic (V1, Pm3m)
- Bicontinuous cubic
- Cubic (V1, Pm3m)

Type 1

Type 2

- Inverse micellar solution
- Microemulsion solution
At very low concentrations, the molecules are distributed randomly without order throughout the water but as the concentration increases, the molecules agglomerate as amphiphiles called *micelles*, with the hydrophobic tail inside the micelle core, exposing a hydrophilic head to the aqueous component. These micelles separate into two shapes that are either spherical or rod-like. These shapes are influenced by the relative volume of the alkyl chains and the headgroups. As the concentration increases, the micelles increase in size and eventually coalesce to separate the newly formed liquid crystalline state from the solvent. Since lyotropic liquid crystals rely on a subtle balance of intermolecular interactions amongst more diverse components, it is sometimes more difficult to analyze their structures and properties than those of thermotropic liquid crystals.

When the concentration is increased, cubic phases are formed where spherical molecules form the I-type cubic phases and the rod-like molecules form the V-type cubic phases. Further increase in the concentration forms the hexagonal phase. At even higher concentration, a lamellar phase may be formed where the polar head is now at the outer layer and the non-polar tails are sandwiched in the middle. The normal phase (type 1) is common where the hydrophobic tails are located inside the aggregates surrounded by the polar head groups. For some systems, inverse phase (type 2) liquid crystals can also be observed at high concentration where the polar head groups are inside the core.

The driving forces for the formation of liquid crystalline phases of these amphiphilic molecules are the micro-segregation of hydrophilic and hydrophobic molecular parts into different regions (interface curvature), as well as the strong attractive forces between the hydrophilic headgroups, such as intermolecular hydrogen bonding.
The interface curvature between hydrophilic and hydrophobic regions is directed away from the water with stronger cohesive interaction (hydrogen bonding). The normal phase (type 1) shows positive interface curvature where the interface is curved away from the water while on the other hand, the inverse phases (type 2) show negative interface curvature in which the interface is curved towards the water with stronger cohesive interaction. At zero interface curvature, the lamellar (Smectic A) phase occurs. The interface curvature (ratio between the hydrophilic and hydrophobic regions) determines the structure, its mesophase and also whether it is the normal (type 1) or inverse (type 2) phases.

1.2.3 Amphotropic or Amphitropic Liquid Crystals

Another type of liquid crystal which has received special attention is termed amphotropic or amphitropic. These materials can form liquid crystalline phases not only in the lyotropic systems but also as pure compounds in the thermotropic systems. However, the mesophases observed in these two regimes are often quite different owing to the temperature, shapes and chemical structures. Examples of such amphotropic molecules are amphiphilic polyhydroxy compounds and carbohydrate derivatives.

1.3 Structural Classification of Thermotropic Liquid Crystals

There are different types of liquid crystal phases which can be distinguished based on their distinct optical texture and the amount of order in the material, depending on the
These liquid crystalline phases are characterized by molecular orientational order when cooling from the isotropic phase to the crystalline phase. The observation of the optical textures of these phases by polarized optical microscopy is one of the most important methods for the identification and classification of different liquid crystalline phases.

### 1.3.1 Nematic phase

The nematic (N) phase is the most common liquid crystal phase. The molecules have long-range orientational order but no positional order. As such, it is the least ordered thermotropic phase and thus the closest to the isotropic liquid. They have the ease of fluidity in which molecules slide past one another while retaining their average parallel positions (Figure 1.3).

Figure 1.3: Schematic representation of molecular order in the crystalline, nematic and isotropic phases.
A nematic phase may be comprised of individual molecules with substantially anisotropic electrical and optical properties. In such a case, and because of their tendency to organize themselves in a parallel fashion, they may also demonstrate corresponding interesting and useful bulk electrical and optical properties. The nematic to isotropic liquid transition phase is a first order transition with relatively small transition energy. In general, the transition energies increase with increasing molecular length within a homologous series.

Viewed by POM (polarizing optical microscope), on cooling from the isotropic liquid, nematic layers between glass plates show the defect regions linking these domains as a threaded schlieren texture which appears between crossed polarizers in POM (Figure 1.4). The simple nematic with a single axis (uniaxial) perpendicular to the director (actually the two minor axes are identical in the case of the simple nematic) is different from the biaxial nematic which is a spatially homogeneous liquid crystal with three distinct optical axes. Some nematic liquid crystals are biaxial, meaning that in addition to orienting along their long axis, they also can orient preferentially along one of the pair of secondary orthogonal axes. For example, a biaxial nematic with a boomerang-shaped oxadiazole bent-core mesogen was first reported in 2004.
Figure 1.4: (a) POM photographs of the schlieren texture of nematic phase
(magnification: 10 × 10); (b) schlieren texture showing four brushes disclination
(magnification: 50 × 10).

1.3.2 Smectic phases

There are a number of different categories of smectic phases amongst which the
best known are the smectic A (SmA) and smectic C (SmC) phases.

1.3.2.1 Smectic A phase

The smectic phases are found at temperatures below the nematic and they have at
least one more increased degree of order, which means that the smectic state is more
‘solid-like’ than the nematic. They maintain the general orientational order of nematics
but also show a degree of translational order not present in the nematic. As such, they
form well-defined layers that can slide by one another. Molecules in SmA possess the
least order amongst all smectic phases and they align with their directors on the average
perpendicular to the layer planes. These molecules are able to rotate freely about their
long axes and the individual molecules are able to move from one layer to another but spend most of their time associated with a layer. Most mesogens that exhibit the SmA phase have molecular structures that consist of a rigid core and one or two alkyl chain(s). The molecular order of the SmA phase is as illustrated in Figure 1.5.

The SmA phase can be obtained by cooling either a nematic or the isotropic phase. Two important microscopic textures of SmA are the homeotropic texture and the focal-conic fan texture. Observation using POM shows a black area of homeotropic texture except the area around air bubbles. The common texture for SmA is the focal-conic fan, which is formed upon cooling the isotropic phase. The phase separates out initially in the form of bâtonnets which then coalesce to form the focal-conic fan texture (Figure 1.6).
1.3.2.2 Smectic C phase

Closely related to the SmA phase is the smectic C (SmC) phase. Here the molecules are not on average orthogonal to the layer plane, and hence the molecular directors, lie at an average angle, $\theta$ to the layer plane (Figure 1.7).
This angle is temperature dependent and the SmC phase is the tilted analogue of a SmA phase. The tilt is caused by dipole-induced intermolecular interactions. The formation of SmC is influenced by the molecular structure; particularly symmetrical molecules with two terminal alkyl or alkoxy chains. In some cases, branching in the terminal chain can increase the chances for a material to exhibit the SmC phase. The zig-zag molecular shapes produce the necessary tilting within the layers to form the SmC phase. The usual microscopic textures exhibited by the SmC phase are the *schlieren* and the broken focal-conic fan textures. The SmC can be obtained either by cooling the isotropic, the nematic or the SmA phases. Cooling the focal-conic fan texture of SmA shows the broken focal-conic fan texture of the SmC phase (Figure 1.8).

![POM photographs](image)

Figure 1.8: POM photographs of (a) broken focal-conic fan texture of SmC (magnification: 10 × 10); (b) *schlieren* texture of SmC (magnification: 10 × 10).
1.3.3 Cholesteric phase

Intrinsically chiral molecules can also form a special nematic phase called the chiral nematic but usually called the cholesteric phase \( (N^*) \) because it was first observed for cholesterol derivatives.\(^{38}\) The cholesteric phase can also be produced by mixing a nematic material with a chiral dopant. These molecules often have a chiral center and the molecular order remains the same as the nematic except the director makes a twist about a single axis with a constant angle in the preferred direction throughout the sample. The twist produces the molecules perpendicular to the director with the molecular axis parallel to the director and this creates the intermolecular forces between alignments of the molecules at a slight angle to one another.\(^{39}\) This can be visualized as a stack of very thin 2-D nematic-like layers with the director in each layer twisted with respect to those above and below,\(^{16}\) as illustrated in Figure 1.9. The distance over which the director rotates by 360 degrees is called the chiral pitch, \( p \). When the temperature is altered (and/or the amount of chiral dopant is altered), the pitch often changes and can be tuned accordingly.\(^{38}\) The structure of the cholesteric phase repeats itself every half-pitch, since in this phase directors at 0 degrees and +/-180 degrees are equivalent. In this structure, the directors actually form a continuous helical pattern about the layer normal.\(^{40}\)
1.3.4 Blue phase

Blue phases are among the most interesting self-organized structure in the field of liquid crystals. This topic will be further discussed in Chapter 6.

1.3.5 Cubic phase

Thermotropic cubic phases show a variety of morphologies as the temperature is changed. This topic will be further discussed in Chapter 4.

1.3.6 Columnar phase

Columnar liquid crystals are different from the previous types because the molecules that form them are usually shaped like disks instead of long rods. The discotic molecules tend to arrange themselves and become the discotic nematic, the nematic columnar and other more stable columnar phases with two dimensional lattices. The
discotic nematics are composed of flat-shaped discotic molecules stacked in one
dimension.\textsuperscript{8} The nematic columnar phase do not form two-dimensional lattice but display
a positional short-range order and an orientational long-range order.\textsuperscript{41} They are less
organized than other columnar liquid crystals which have long-range order with two-
dimensional lattices\textsuperscript{8} (Figure 1.10).

\begin{center}
\includegraphics[width=0.2\textwidth]{figure1_10.png}
\end{center}

Figure 1.10: Schematic representation of the nematic columnar phase.\textsuperscript{42}

These latter phases consist of five types of columnar arrangements based on the
gometry of molecular stacking (Figure 1.11).\textsuperscript{43}

\begin{center}
\includegraphics[width=0.8\textwidth]{figure1_11.png}
\end{center}

Figure 1.11: Schematic representation of columnar: (a) hexagonal (Col\textsubscript{h}) (b) rectangular
\textsuperscript{(Col\textsubscript{r}) (c) oblique (d) plastic (Col\textsubscript{p}) (e) H phase helical columns which interdigitate
in groups of three columnar stacks.\textsuperscript{43}
The typical columnar liquid-crystalline molecules have a \( \pi \)-electron-rich aromatic core surrounded by multiple flexible alkyl chains. The \( \pi-\pi \) interaction is a noncovalent interaction caused by intermolecular overlapping of p-orbitals in \( \pi \)-conjugated systems. As flexible long aliphatic chains surround the core, the intercolumnar distance is usually 20–40 Å, depending on the lateral chain length. Therefore, the interactions between neighbor molecules stacked in the same column are stronger than the interactions between molecules in the neighboring columns.\(^{43}\)

1.4 Structural Classification of Lyotropic Liquid Crystals

There are different types of lyotropic liquid crystal phases which can be distinguished by their bulk organization depending on the temperature and concentration.\(^{14}\) At certain conditions of concentration and temperature, the amphiphilic molecules form aggregates with different shapes. Ordering of the structural units forms specific structures such as cubic, hexagonal and lamellar.\(^{15}\)

1.4.1 Cubic phase

Cubic phases in the lyotropic system are more commonly observed than in thermotropic systems.\(^{44}\) By changing the concentration of the solvent, several different cubic phases may be observed in lyotropic systems.\(^{45}\) Just as the cubic phases in the thermotropic system, this topic will also be further discussed in Chapter 4.
1.4.2 Hexagonal phase

If the solvent concentration in the cubic phase is increased, the hexagonal phase may occur and depending on the solvent polarity, the normal (H₁) or inverse structures (H₁I) will be formed. Micelles aggregate themselves and become cylindrical shaped micelles of indefinite length, forming hexagonal arrays with six rods grouped around a central one where the micelle surface is composed of hydrophilic heads while the hydrophobic tails are isolated inside the micelle. This phase has long-range orientational order.46 In the normal hexagonal phases (type 1), hydrocarbon chains are contained within the cylindrical aggregates and shows positive mean curvature for polar-apolar interface (H₁). The inverse hexagonal phases (H₁I) have water within the cylindrical aggregates and the hydrocarbon chains fill the voids between the hexagonally packed cylinders.46 Both normal and inverse phases are highly viscous and show textures as smoke-like, fan-like or mosaic (Figure 1.12).

![Hexagonal Phase](image)

Figure 1.12: Schematic representation of hexagonal phase of (a) rod micelle close up (b) normal and (b) inverse types⁴⁶.
1.4.1 Lamellar phase

At even higher concentrations (Figure 2) the molecules move into another liquid crystalline phase – the lamellar phase. This structure has a double layer of molecules with one dimensional stacking and zero interfacial curvature. This lamellar structure is formed with the polar heads on the outer layer and the nonpolar tails sandwiched in the middle. This pattern is similar to that of smectic liquid crystals in the thermotropic category, which form a focal conic texture. This lamellar phase is less viscous than the hexagonal phase because the sheet-like layers can slide easily past each other despite its lower water content. If the molecules are placed on the surface of water without actually being dissolved in it, they can form a monolayer in which the polar heads are in contact with the water and the hydrophobic tails point into the air. These monolayers are often referred to as Langmuir films (Figure 1.13).

![Figure 1.13: Schematic representation of lamellar structure (a) bilayer (b) monolayer](image)

A precursor to the bilayer is the ribbon phase which involves finite bilayers that end in cylindrical half-micelles. These ribbons will fuse together to form the bilayers. If the
amphiphile concentration is lower, the mixture reverts to a hexagonal phase or a solution of micelles.  

1.5 Scope of this dissertation

This dissertation describes most of the research work I have completed in Dr Twieg’s lab. The overall goal of my work is to synthesize and characterize different series of liquid crystals, often focusing on semifluorinated and perfluorinated liquid crystal materials. Information on the structure-property relationships and the behavior of the liquid crystal textures (Chapter 1) helps to further confirm the structure identification for these studies.

The research work described in Chapter 2 involves fluorination at the tail positions of \( N,N'\)-bis(4-alkoxybenzoyl) hydrazines and examines on how this fluorination influences the mesophase behavior. These liquid crystal properties are compared with their perhydrogenated analogs. Our interest in the relationships between molecular structure and mesomorphic behavior has led us to further the work in Chapter 3. Notably, the precursors for these heterocycles are the same bis(alkoxybenzoyl) hydrazines examined in Chapter 2. Here we examine the influence of the fluorinated block in the tail of a new series of 2,5-diaryl-1,3,4-oxadiazoles and 2,5-diaryl-1,3,4-thiadiazoles with semifluorinated alkoxy chains and their properties are compared with their perhydrogenated analogs.

The research work in Chapter 4 involves some thermotropic cubic phase liquid crystals which have attracted considerable attention due to their three-dimensional
structures and their appearance in different self-organizing systems. Cubic phases have been found intermittently in many types of liquid crystals, for example the bisbenzoyl hydrazines,\textsuperscript{47-62} as discussed in Chapter 2. Here, we are interested to further understand the thermotropic cubic phases in amphiphilic polyhydroxybenzamide materials. Earlier work by several groups investigated how slight variations of the lipophilic and polar regions in amphiphilic compounds can influence the appearance of different cubic mesophases. We intend to better understand the influence of the different components of the amphiphilic polyhydroxy molecules on their mesophase behavior. A number of new hydroxylated amides derived from 3,4,5-tris(\textit{n}-nonyloxy)benzoic acid have been synthesized and characterized. Different mesophases have been determined depending on the size of the hydrophilic units. We are also taking a brief look at some ester versions of these molecules (as opposed to the known amide mesogens). Eventually the related semifluorinated molecules in this series will be made but these were not prepared during the course of this study.

The research work in Chapter 5 focused less on liquid crystals but generally more on other applications of the oxadiazole substructure already found in other studies in this thesis. The focus here is on three different types of intermediates, namely ethyl 5-(4-fluorophenyl)-1,3,4-oxadiazole-2-carboxylate as intermediate 1; 2-(4-fluorobenzoyl)-5-(chloromethyl)-1,3,4-oxadiazole as intermediate 2 and 5-(4-fluorophenyl)-1,3,4-oxadiazole-2-carbonitrile as intermediate 3. Intermediates 1 and 3 are used in separate synthetic studies which involves reactions of these intermediates with different functional groups on the benzene-oxadiazole systems. As novel fluorophores DCDHF dyes have
been intensively prepared in Dr Twieg’s group, intermediate 2 is used in a synthesis of new type of DCDHF chromophore. Detailed synthetic discussion will be elaborated in Chapter 5.

The research work in Chapter 6 initiates an examination of a particular class of bimesogens with potential flexoelectric and blue phase properties. Blue phases which occur in chiral liquid crystals are very interesting three dimensional self-organized structures with unusual cubic symmetry.\textsuperscript{63,64} It was reported by Coles that certain blue phases possess enhanced thermal stability from the typical 1\degree C range to up to a 30\degree C range and the flexoelectricity effects observed in them are more profound.\textsuperscript{65} We are interested to learn how the flexoelectricity may be related to the stability of these wide temperature range blue phase liquid crystals. A further component of this investigation is to investigate whether the quadrupolar electrostatic interactions involving arene-perfluoroarene systems may further enhance this blue phase stability and flexoelectric behavior. Our initial part of the work focused on the preparation of different dimers with single heptyloxy tail shared between the two conjugated end sections.

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Chapter 2

Liquid Crystals Derived from Semifluorinated Alkoxybenzoyl Hydrazines

The content of this chapter has been recently submitted to

*Mol Cryst Liq Cryst* for consideration for publication

Khairuddean, M.; Twieg, R. J., *2008*
2.1 Introduction

2.1.1 Fluorinated liquid crystals

For a long time, fluorination has been a productive strategy in liquid crystal science owing to the considerable influence of fluorine on mesomorphic behavior and on related physical properties. Prior to discussing any specific fluorinated liquid crystal molecules it is useful to look at mesogenic behavior as part of a more overall picture. Molecules with a liquid crystalline mesophase have a degree of intermolecular association intermediate between that of a three dimensional crystal and an isotropic liquid. To modify these intermolecular associations, a perturbing substituent or group can be included in the molecular structure which changes the separation of the molecules and modifies the strength of the intermolecular forces. The fluorine atom is often used in the design of liquid crystal molecules to obtain many interesting effects such as a stronger dipole moment, a lower viscosity and a higher chemical stability. The introduction of a fluorine atom generally leads to a subtle modification of properties and sometimes imparts advantageous properties due to its small size (1.47 Å) comparable to the size of hydrogen (1.20 Å). Because of this, the fluorine atom is a suitable hydrogen mimic due to its insignificant steric impact while it can simultaneously introduce substantial electronic and polarity influences.

2.1.2 Where to introduce fluorine in the molecules

There are numerous ways to introduce a fluorine atom into liquid crystal molecules. It may be introduced at different locations or combination of locations, within the core,
the terminal chains or the linking groups which produce materials with different physical properties\textsuperscript{5-7} (Figure 2.1).

![Figure 2.1: A typical structural template for a calamitic liquid crystal\textsuperscript{8}. A and B are core ring units; R and R’ are terminal tail units; X, Y and Z are linking groups amongst the rings and tails; M and N are lateral core substituents.]

2.1.2.1 Fluoro substitution at lateral position

Fluorine substitution at a lateral position within the core exerts a small steric effect because, relative to a hydrogen atom, the fluorine atom that protrudes from the side of the molecules will sterically force the molecules apart and disrupt the smectic molecular packing.\textsuperscript{9,10} In most cases the melting temperature will be reduced and so sometimes the liquid crystalline phase stability as well. Therefore, a lateral fluoro substituent tends to increase the lateral dipole within a molecule and this may promote tilted smectic phases, such as the SmC phase,\textsuperscript{11,12} and hence shows promise in the formulation of ferroelectric compounds. By combining the steric and polarity effects of fluorine, some significant changes in the physical properties can result without too much disruption of the molecular packing.
2.1.2.2 Fluoro substitution at the terminal position as a single unit

Fluoro substitution at the terminal position of a liquid crystal was reported to be poor at generating mesophases\(^4\) due to its small size. However, this type of fluoro substituent has reasonable polarity to provide positive dielectric anisotropy which can be used advantageously in nematic mixtures for active matrix displays.

2.1.2.3 Fluoro substitution in terminal chains

The mesomorphic properties of liquid crystals depend strongly on the nature of the terminal chain(s) that are present. Fluorination of a block of carbons in the terminal chain(s) causes stiffening which generates a lamellar packing and thus contributes to smectic phase stability.\(^6\) The research work in this chapter involves liquid crystal molecules with such semifluorinated chains. Semifluorinated alkanes self-assemble in smectic phases, as an incompatibility exists between the fluorinated and the alkylated parts which are tied together by a covalent bond. Both hydrocarbon and fluorocarbon segments are incompatible with water and other such highly polar substances.\(^1,6,7\) Likewise, but to a lesser extent, the hydrocarbon and the perfluorocarbon segments are also incompatible. The fluorinated segment also has reduced conformational freedom producing a net helical conformation. This fluorinated segment is more rigid than the hydrogenated part owing to the steric hindrance between fluorine atoms since the van der Waals radius of fluorine is larger (1.35 Å) than that of hydrogen (1.10 Å).\(^14\) The hydrogen bearing segment is more flexible and this in turn leads to a structure as illustrated in Figure 2.2, with the lowest energy of planar zig-zag conformation.
The combination of a suitable length and ratio of the perfluorinated alkyl segment within the same molecule produces a microsegregation which plays an important role in the manifestation of mesomorphic properties. Another bulk property resulting from the fluorinated chain involves low intermolecular interactions leading to a low surface tension.\(^\text{15}\)

A major challenge is to rationalize fluorine substitution effects on mesogenic behavior because there is no unique site to consider for introduction of a substituent. However, structure-property relationships can be used to quantify the effect of the substitution on phase transition temperatures. For example, liquid crystals incorporating heavily fluorinated alkyl chains (especially semifluorinated blocks) are known to display smectic properties relative to their perhydrogenated counterparts. Likewise, earlier work on liquid crystals containing one or more perfluoroalkyl or perfluoroalkyloxy tails indicated that smectic phases are enhanced\(^\text{16-18,14}\). Even simple \(n\)-alkanes which contain a hydrocarbon and a fluorocarbon block (and no ring-containing core section) form smectic phases.\(^\text{19-24}\) Some molecules with only a single aromatic ring and fluorinated tail segments show smectic phases, while their hydrocarbon tail counterparts are non-
mesomorphic.\textsuperscript{25,26} Just as the attachment of fluorinated alkyl chains often leads to stabilization or induction of smectic phases in rod-like molecules\textsuperscript{27,14,28} these same fluorinated chains are also known to influence the columnar phases in disc-shaped\textsuperscript{29,30} and taper-shaped molecules.\textsuperscript{31,32}

2.1.3 Hydrogen bonding in 1,2-bis-alkoxybenzoyl hydrazine molecules

Hydrogen bonding plays a crucial role in some examples of mesophase formation and stabilization.\textsuperscript{33-35} The 1,2-bis-alkoxybenzoyl hydrazine, denoted BABH\(_n\) where \(n\) indicates the number of carbon atoms in the alkoxy chain, are one of the simplest chemical structures possessing a thermotropic cubic phase. Early studies by Schubert \textit{et al.}\textsuperscript{36} and Demus \textit{et al.}\textsuperscript{37} on these types of molecules provided detailed reports on their mesophase behavior. The hydrazide derivatives have an ability to form hydrogen bonds between CO and NH groups. These intermolecular hydrogen bonds were recognized to play an important role in the formation of the cubic phase.\textsuperscript{37} Compared to compounds containing a \(-\text{CO}–\text{NH}–\text{NH}–\text{CO}–\) structure, it was reported that compounds containing a \(-\text{CH}=\text{N}–\text{N}=\text{CH}–\) structure cannot form either hydrogen bonds or the cubic phase.\textsuperscript{38} The amide hydrogen bridge is close to linear although the \(-\text{N}–\text{H}⋯\text{O}\) angle at the central position is about 140 to 180\(^{\circ}\). Most amides prefer to form hydrogen bonded centrosymmetric rings (Figure 2.3).\textsuperscript{39} The \(\text{N}–\text{H}⋯\text{O}\) hydrogen bond is very strong as the bonding energy of a single amide H-bond is around 7-12 kJ/mol.\textsuperscript{33}
2.2 Research Proposal

We have been interested in the influence of fluorination in liquid crystals for some time. In particular, we have studied the semifluorinated hydrocarbons\textsuperscript{19-23} and the role of semifluorinated alkoxy chains in ferroelectric materials\textsuperscript{40-43} wherein the introduction of semifluorinated chains tends to suppress the nematic phase and enhance the breadth of the smectic phases.\textsuperscript{44-46} The combination of suitable lengths and length ratios of these fluorinated and hydrogenated segments within the same molecule influences the microsegregation between these incompatible moieties which acts as a driving force for the mesogenic properties of these compounds.\textsuperscript{26} The properties of the fluorinated chains are somewhat larger and stiffer than the perhydrogenated chains and thus can be employed to modify liquid crystal behavior.

Only a few 1,2-bis(4-\textit{n}-alkoxybenzoyl) hydrazine derivatives with liquid crystal properties have been reported.\textsuperscript{36,47-56} The BABH(\textit{n}) reported thus far possess only perhydrogenated alkoxy chains. The BABH(\textit{n}) where \textit{n} = 9, 10 and 12 are of special
significance as they exhibit a Cub phase and, thus, here we are particularly interested in
the influence of fluorination on this Cub phase. Our ultimate goal is to understand the
behavior of the Cub phases in these different series of molecules for optical application.

This chapter describes the influence of semifluorination in some simple 4-
alkoxybenzoic acids, 1a-h as well as their hydrazine derivatives, namely, the
corresponding 4-alkoxybenzoyl hydrazine, 2a-h and the asymmetric and symmetrical
N,N’-bis(4-alkoxybenzoyl)hydrazine derivatives, 3a-m. The new compounds that have
been synthesized are shown in Figure 4. The N,N’-bis(4-alkoxybenzoyl)hydrazine
compounds 3a-m are also precursors for the synthesis of 1,3,4-oxadiazoles and 1,3,4-
thiadiazoles derivatives which will be discussed in Chapter 3.
Figure 2.4: The structures of the perhydrogenated (a-c), mono semifluorinated (d-h) and doubly semifluorinated (i-m) series studied here (here, and elsewhere, when $n = 0$ the terminal carbon on the tail bears three hydrogens).

2.3 Synthesis

The perhydrogenated, 1a-c and semifluorinated, 1d-h 4-alkoxybenzoic acids can be synthesized according to a standard method. A systematic approach to synthesize some five semifluorinated 4-alkoxybenzoic acid derivatives, 1d-h was investigated in earlier work but was not documented. The synthesis route is shown in Scheme 2.1, involving the semifluorinated iodoalkane intermediates with a variable ratio $(m/n)$ of their perhydrogenated $[(\text{CH}_2)_m]$ to perfluorinated $[\text{F(CF}_2)_n]$ segments. The overall chain length $(m + n)$ is controllable as well. Reaction of an alkyl 4-hydroxybenzoate and a commercially available $\alpha$-alken-$\omega$-ol in a Mitsunobu reaction, followed by AIBN (2,2'-...
azo-bisisobutyronitrile) catalyzed radical addition of perfluoroalkyl iodide produces semifluorinated alkyl iodides of variable chain lengths. The removal of the iodo group with zinc, followed by saponification afforded the semifluorinated 4-alkoxybenzoic acid derivatives, 1d-h.

Scheme 2.1: The general synthesis route for compounds 1d-h. In the final product(s) 1d-h, the number of perhydrogenated carbons is \( m \) and the number of perfluorinated carbons is \( n \) and the total number of carbons in the tail is \( m+n \).

The synthesis route for the asymmetric and symmetrical \( N,N' \)-bis(4-alkoxybenzoyl) hydrazine compounds is as shown in Scheme 2.2. The 4-alkoxybenzoic acids were converted to their acid chloride derivatives using oxalyl chloride. Semifluorinated 4-alkoxybenzoyl hydrazines, 2d-h were prepared by a two-step reaction involving esterification of the semifluorinated 4-alkoxybenzoic acid in methanol with acid catalysis, followed by addition of excess hydrazine hydrate.\(^{32} \) The semifluorinated \( N,N' \)-bis(4-alkoxybenzoyl) hydrazine derivatives 3a-m were prepared by reaction of the
appropriate 4-alkoxybenzoyl chloride with the companion 4-alkoxybenzoyl hydrazine.

This latter method also permitted the preparation of unsymmetrical N,N'-bis(4-
alkoxybenzoyl) hydrazines with non-identical alkoxy groups. The n-nonyloxy chain was
chosen for compounds with perhydrogenated chains, 3a-c and one semifluorinated chain,
3d-h for comparison with the perhydrogenated compounds. Most of the reported studies
on bis(alkoxybenzoyl) hydrazine compounds involve chains with nine carbons.

\[
\begin{align*}
\text{F(F}_2\text{C)}_n\text{(H}_2\text{C)}_m\text{O} & \quad \text{O} \\
\text{1a-h} & \quad \text{OH} \\
\text{F(F}_2\text{C)}_n\text{(H}_2\text{C)}_m\text{O} & \quad \text{O} \\
\text{2a-h} & \quad \text{Cl} \\
\text{F(F}_2\text{C)}_n\text{(H}_2\text{C)}_m\text{O} & \quad \text{O} \\
\text{NH-NH}_2 & \quad \text{NH-NH}_2
\end{align*}
\]

\[
\begin{align*}
\text{1a-h} & \quad \text{(COCl)}_2, \text{CH}_2\text{Cl}_2 \\
45 ^\circ \text{C}, 8 \text{ h} & \quad \text{F(F}_2\text{C)}_n\text{(H}_2\text{C)}_m\text{O} \\
\text{Cl} & \quad \text{2a-h} \\
\text{1a-h} & \quad \text{CH}_3\text{OH/H}_2\text{SO}_4 \\
\text{reflux} & \quad \text{2a-h} \\
\text{NH}_2\text{NH}_2, \text{H}_2\text{O,} & \quad \text{F(F}_2\text{C)}_n\text{(H}_2\text{C)}_m\text{O} \\
\text{reflux} & \quad \text{2a-h} \\
\text{3a-h} & \quad \text{CH}_2\text{Cl}_2, \text{Et}_3\text{N} \\
\text{room temperature} & \quad \text{8 h} \\
\text{3a-h} & \quad \text{3i-m}
\end{align*}
\]

<table>
<thead>
<tr>
<th>Compound</th>
<th>a</th>
<th>b</th>
<th>c</th>
<th>d</th>
<th>e</th>
<th>f</th>
<th>g</th>
<th>h</th>
<th>i</th>
<th>j</th>
<th>k</th>
<th>l</th>
<th>m</th>
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<td>0</td>
<td>0</td>
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</tr>
</tbody>
</table>

Scheme 2.2: The preparative routes for the semifluorinated members (d-h) of series 1,2
and the semifluorinated members (d-m) of series 3 studied here.
The synthesis of some additional compounds 8 and 9 with lateral core fluorine substitution involved the reaction of the appropriate 4-dodecyloxybenzoyl chloride or its fluorinated analog with the companion of 4-dodecyloxybenzoyl hydrazine or its fluorinated analog, as illustrated in Scheme 2.3. Benzoic acid derivative 5 was converted to its acid chloride using oxalyl chloride. Precursor 5 itself was prepared by a two-step reaction, wherein the dodecyloxy chain is first introduced, followed by hydrolysis of the benzonitrile to the benzoic acid. Compound 6, 2-fluoro-4-dodecyloxybenzoyl hydrazine was prepared by a two-step reaction involving esterification of 2-fluoro-4-dodecyloxybenzoic acid, followed by addition of excess hydrazine hydrate.

Scheme 2.3: The synthesis routes for compounds 8 or 9 studied here with lateral core fluorine substitution.
2.4 Results and Discussion

The thermal properties for all the compounds were investigated using differential scanning calorimetry (DSC) and polarized optical microscopy (POM). The literature data for mesomorphic behavior of some nonfluorinated and semifluorinated 4-alkoxybenzoic acids is summarized in Table 2.1. Related data for the 4-alkoxybenzoic acids from our experiments is provided in Table 2.2.

Table 2.1: Transition temperatures (°C) for some perhydrogenated and semifluorinated 4-alkoxybenzoic acids (literature data is compiled here for comparative purposes).

<table>
<thead>
<tr>
<th>R</th>
<th>Cr</th>
<th>Sm</th>
<th>SmC</th>
<th>SmA</th>
<th>N</th>
<th>I</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>C₉H₁₉</td>
<td>92</td>
<td>−</td>
<td>−</td>
<td>118</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>1b</td>
<td>C₁₀H₂₁</td>
<td>97</td>
<td>−</td>
<td>−</td>
<td>122</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>1c</td>
<td>C₁₂H₂₅</td>
<td>95</td>
<td>−</td>
<td>−</td>
<td>129</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>1g</td>
<td>F(CF₂)₆(CH₂)₆</td>
<td>156*</td>
<td>−</td>
<td>−</td>
<td>177</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>1h</td>
<td>F(CF₂)₄(CH₂)₄</td>
<td>165*</td>
<td>178</td>
<td>190</td>
<td>193</td>
<td>−</td>
<td>−</td>
</tr>
</tbody>
</table>

*a This compound exhibits several crystalline phases; *b This is an undetermined high-order smectic mesophase (e.g. SmB, SmE, SmH, SmK); *c the transition here was reported as Cr₁-Cr₂ phase transition. (Literature data in Table 2.1 were obtained from heating)
Table 2.2: Transition temperatures and enthalpies ($\Delta H$, kJ mol$^{-1}$) for perhydrogenated and semifluorinated 4-alkoxybenzoic acids, 1a-h (experimental data).

![Chemical Structure]

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<th></th>
<th>R</th>
<th>Cr$_1$</th>
<th>Cr$_2$</th>
<th>SmC</th>
<th>N</th>
<th>I</th>
</tr>
</thead>
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<td>91.1</td>
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<td>97.0</td>
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<tr>
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<td>–</td>
<td>186.2</td>
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<td>–</td>
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<td></td>
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<tr>
<td>1e</td>
<td>F(CF$_2$)$_4$(CH$_2$)$_6$</td>
<td>125.8</td>
<td>147.0</td>
<td>167.5</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
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<td>7.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1f</td>
<td>F(CF$_2$)$_7$(CH$_2$)$_3$</td>
<td>181.6</td>
<td>–</td>
<td>191.5</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>m=3, n=7</td>
<td>23.4</td>
<td></td>
<td>12.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1g$^a$</td>
<td>F(CF$_2$)$_6$(CH$_2$)$_6$</td>
<td>140.9</td>
<td>158.2</td>
<td>178.8</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>m=6, n=6</td>
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<td>9.4</td>
<td>6.2</td>
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<td>F(CF$_2$)$_8$(CH$_2$)$_4$</td>
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<td>180.2</td>
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<td>17.5</td>
<td>12.4</td>
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</table>

$^a$ This compound exhibits two crystalline phases in the first DSC run but only one crystalline phase can be observed in the second run for the same sample. Data in Table 2.2 were obtained on heating.

Compounds containing a single benzene ring might be expected to have small molecular shape anisotropy and therefore would not be mesomorphic. However, 4-
alkoxybenzoic acids, 1a-c (Table 2.2) show both SmC and nematic mesophases involving the formation of an H-bonded dimer with a larger aspect ratio.\(^6^6\) In a simple benzoic acid derivative such as 4-methoxybenzoic acid all the atoms in the two benzene rings and the two carboxylic acid groups are close to co-planar.\(^6^7\) Each of the two hydrogen atoms involved in hydrogen bonding is located between a doubly bonded oxygen of one acid group (1.654 Å) and a single bonded oxygen of the other acid group (1.009 Å). There are a number of other close intermolecular contact sites amongst atoms of the \(p\)-anisic acid molecules in the crystal but none are as influential in dictating the bulk structure as the co-planar set of two carbons, four oxygen and two hydrogen atoms comprising the hydrogen bonded pair of carboxylic acids (Figure 2.5).

![Figure 2.5: Schematic representation of hydrogen bonding forming a centrosymmetric ring in 4-alkoxybenzoic acids.](image)

Modifications of the tails influence the phase behavior of these 4-alkoxybenzoic acid derivatives. A simple increase in the chain lengths lowers the clearing temperature. However, introduction of a terminal semifluorinated segment in the 4-alkoxybenzoic acid system leads to the suppression of the nematic phase and generally increased transition temperatures. Only enantiotropic SmC phases were observed for all the semifluorinated 4-alkoxybenzoic acids, 1d-h used in this study. The perfluoroalkyl block tends to
enhance the thermal stability of these phases due to its increased rigidity. In a layered morphology, the fluorinated chains lie adjacent to each other, leading to an enhanced crystallization tendency.\textsuperscript{68} From Table 2.2 it can be seen that the semifluorinated compounds, 1d-h show higher melting points and clearing temperatures compared to their hydrogenated homologs. For compounds of $n + m = 10$ and 12 where $n$ is larger than $m$, the melting points and clearing temperatures are higher than compounds having $n$ smaller than $m$. For example, compound 1e ($n + m = 10$) with a shorter fluorinated segment and longer alkyl segment shows a lower melting point (147.0°C) and a lower clearing temperature (167.5°C) with a broad mesophase range of 20.5°C. On the other hand, compound 1f with a longer fluorinated segment and shorter alkyl segment shows a higher melting point (181.6°C) and a higher clearing temperature (191.5°C) with a net smaller mesophase range of 9.9°C.

The temperature and enthalpy phase transition data for the perhydrogenated 2a-c and 2d-h semifluorinated 4-alkoxybenzoyl hydrazines is summarized in Table 2.3.

Table 2.3: Transition temperatures and enthalpies ($\Delta H$, kJ mol\textsuperscript{-1}) for perhydrogenated 2a-c and semifluorinated 4-alkoxybenzoyl hydrazines, 2d-h.

<table>
<thead>
<tr>
<th>Compounds</th>
<th>R</th>
<th>Cr\textsubscript{1}</th>
<th>Cr\textsubscript{2}</th>
<th>SmA</th>
<th>I</th>
</tr>
</thead>
<tbody>
<tr>
<td>2a</td>
<td>C\textsubscript{9}H\textsubscript{19}</td>
<td>*</td>
<td>99.6</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>
The perhydrogenated 4-alkoxybenzoyl hydrazines 2a-c (C9, C10 and C12), possess similar melting points and none of them are mesogenic (Table 2.3) and we do not find any literature reports that such compounds are mesogenic. Remarkably, introduction of a terminal semifluorinated segment into these 4-alkoxybenzoyl hydrazine systems, 2d-h induces mesomorphic properties and these semifluorinated compounds now exhibit enantiotropic SmA mesophases. From Table 2.3, compounds 2d-h show only a SmA phase. Compound 2d \((n + m = 9)\) with a long fluorinated segment shows the SmA phase at 147.6°C with a clearing temperature of 171.3°C. Its fully hydrogenated homolog, 2a did not show any liquid crystalline properties and exhibits a low melting point of 99.6°C.
Compounds \((n + m = 10 \text{ and } 12)\) with a longer fluorinated segment, \(2f\) and \(2h\), exhibit a higher clearing temperature than the compounds with shorter fluorinated segments, \(2e\) and the compound with the same fluorinated and hydrogenated length, \(2g\).

The crystal structures of a variety of benzoyl hydrazine derivatives are known. Just as in the case of the 4-alkoxybenzoic acids, the 4-alkoxybenzoyl hydrazine molecules tend to arrange as dimers. However, due to the extra hydrogen bonding sites in the hydrazide functional group, the hydrogen bonding network becomes three dimensional (3-D), as three different hydrogen atoms (based on location and orientation) are available on the two nitrogens in the hydrazide vs. the single hydrogen atom available in the carboxylic acid. In the carboxylic acid dimer all the atoms involved in the hydrogen bonds are highly co-planar and also co-planar with the aromatic rings. In contrast, the carbonyl groups in the benzoyl hydrazine aggregates are twisted \((30^\circ\) in the case of anisic hydrazide) out of the plane of the benzene ring. The term *aggregates* is applied here as the hydrazide carbonyl groups participate in a more 3-D hydrogen bonding network than in the case of carboxylic acid *dimers*.\(^{69}\) The hydrogen bonding pattern of anisic hydrazide has a primary interaction (a pair of H-bonds, C=O \(\cdots\) H\(_a\)H\(_b\)N\(-\)NH\(-\), each with length of 2.086 Å) that resembles the one found in the carboxylic acid dimers but with additional short contacts between the hydrazide carbonyl and the other amine hydrogen of the other adjacent molecules (these short contacts, C=O \(\cdots\) H\(_a\)H\(_b\)N\(-\)NH\(-\) are just slightly longer at 2.121 Å). No doubt, this 3-D hydrogen bonding network plays an important role in the formation of the mesophases found in some of these hydrazide materials (Figure 2.6).
The importance of H-bonds in formation of the novel Cub phases found in some of the bis(4-alkoxybenzoyl) hydrazines has been discussed in detail.\textsuperscript{36}

![Diagram of 3-D hydrogen bonding network in some 4-alkoxybenzoyl hydrazines.](image)

Figure 2.6: Schematic representation of the 3-D hydrogen bonding network in some 4-alkoxybenzoyl hydrazines.
Table 2.4: Transition temperatures and enthalpies ($\Delta H$, kJ mol$^{-1}$) for some perhydrogenated $N,N'$-bis(4-alkoxybenzoyl) hydrazines (literature data is compiled here for comparative purposes).

\[
\begin{array}{cccccccc}
\text{Ref} & \text{R}_1 & \text{R}_2 & \text{Cr}_1 & \text{Cr}_2 & \text{Cr}_3 & \text{Cub} & \text{SmC} & \text{I} \\
35 & \text{C}_9\text{H}_{19} & \text{C}_9\text{H}_{19} & \bullet & 124.0 & - & - & \bullet & 143.5 & \bullet & 158.0 & \bullet & 167.0 & \bullet \\
36 & & & & 124.0 & - & - & \bullet & 143.0 & \bullet & 157.0 & \bullet & 165.0 & \bullet \\
 & & & & 44.5 & 21.3 & 1.1 & 9.0 & & & & & & \\
37 & \text{C}_{10}\text{H}_{21} & \text{C}_{10}\text{H}_{21} & \bullet & 122.0 & - & - & \bullet & 129.0 & \bullet & 152.0 & \bullet & 166.0 & \bullet \\
38 & & & & 122.0 & 127.1 & 141.2 & \bullet & 153.0 & \bullet & 163.9 & \bullet \\
 & & & & 24.3 & 4.9 & 23.1 & 0.4 & 7.2 & & & & & \\
53 & \text{C}_{12}\text{H}_{25} & \text{C}_{12}\text{H}_{25} & \bullet & 124.0 & 128.0 & 143.0 & \bullet & 152.0 & \bullet & 165.0 & \bullet \\
 & & & & 26.5 & 5.8 & 23.3 & 0.6 & 7.6 & & & & & \\
36,37 & \text{C}_{12}\text{H}_{25} & \text{C}_{12}\text{H}_{25} & \bullet & 100.0 & 128.1 & 134.6 & \bullet & 161.2 & - & - & - \\
 & & & & - & 33.9 & 24.8 & 7.1 & & & & & \\
\end{array}
\]

Data in Table 2.4 were obtained upon heating.
Table 2.5: Transition temperatures and enthalpies ($\Delta H$, kJ mol$^{-1}$) for perhydrogenated and semifluorinated $N,N'$-bis(4-alkoxybenzoyl) hydrazines, 3a-m.

<table>
<thead>
<tr>
<th>R$_1$</th>
<th>R$_2$</th>
<th>Cr$_1$</th>
<th>Cr$_2$</th>
<th>Cub</th>
<th>Sm</th>
<th>Sm</th>
<th>I</th>
</tr>
</thead>
<tbody>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C$<em>9$H$</em>{19}$</td>
<td>C$<em>9$H$</em>{19}$</td>
<td>125.9</td>
<td>142.4</td>
<td>159.3</td>
<td>165.9</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td></td>
<td>34.6</td>
<td>15.4</td>
<td>0.4</td>
<td>4.4</td>
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</tr>
<tr>
<td>C$<em>9$H$</em>{21}$</td>
<td>C$<em>{10}$H$</em>{31}$</td>
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<td>134.5</td>
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<td>–</td>
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<td>–</td>
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<tr>
<td></td>
<td></td>
<td>112.0</td>
<td>5.1</td>
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<td></td>
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</tr>
<tr>
<td>C$<em>9$H$</em>{19}$</td>
<td>C$<em>{12}$H$</em>{25}$</td>
<td>111.6</td>
<td>132.8</td>
<td>162.6</td>
<td>–</td>
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<td>–</td>
</tr>
<tr>
<td></td>
<td></td>
<td>9.7</td>
<td>6.9</td>
<td>2.4</td>
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</tr>
<tr>
<td>C$<em>9$H$</em>{19}$</td>
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<td>124.3</td>
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<td>–</td>
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<td>233.2</td>
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<td>118.8</td>
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<tr>
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<td>172.9</td>
<td>183.2</td>
<td>228.2</td>
<td>232.1</td>
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<td>–</td>
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<tr>
<td>F(CF$_2$)$_m$(CH$_2$)$_n$</td>
<td>F(CF$_2$)$_m$(CH$_2$)$_n$</td>
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<td>–</td>
<td>187.1</td>
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<td>13.7</td>
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<tr>
<td>F(CF$_2$)$_m$(CH$_2$)$_n$</td>
<td>F(CF$_2$)$_m$(CH$_2$)$_n$</td>
<td>118.5</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>165.6</td>
<td>•</td>
</tr>
<tr>
<td>m=6, n=6</td>
<td>m=6, n=6</td>
<td>56.7</td>
<td>0.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F(CF$_2$)$_m$(CH$_2$)$_n$</td>
<td>F(CF$_2$)$_m$(CH$_2$)$_n$</td>
<td>90.1</td>
<td>125.7</td>
<td>–</td>
<td>–</td>
<td>194.4</td>
<td>•</td>
</tr>
<tr>
<td>m=4, n=8</td>
<td>m=4, n=8</td>
<td>0.4</td>
<td>48.3</td>
<td>1.4</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* This compound exhibits several crystalline phases. Data in Table 2.5 were obtained on heating.

The temperature and enthalpy phase transition data for mesomorphic behavior of the $N,N'$-bis(4-alkoxybenzoyl) hydrazines is summarized in Table 2.5. Lengthening of
the alkoxy chain destabilizes the SmC phase and favors the formation of only the Cub phase of the \(N,N'\)-bis(4-alkoxybenzoyl) hydrazines with fully hydrogenated chains. Compound 3a (symmetrical, C9) shows the Cub phase at 142.4 °C. Further heating gives a SmC phase at 159.3°C and a clearing temperature at 165.9°C. These values are quite similar with those reported in the literature.\(^{36}\) Upon cooling from the isotropic phase, compound 3a exhibits a SmC phase at 162.8°C, in which a schlieren texture having point singularity with four brushes was also observed. Further cooling of 3a converts the SmC into a featureless black area of the Cub phase at 152.4°C, followed by the appearance of a colorful crystalline phase at 101.3°C. At the SmC-Cub phase transition, a complete black area in the SmC texture is first developed and grows until the entire field of view is black and this Cub phase is confirmed to appear reversibly by the DSC and POM observations. The Cub phase has also been referred to as a SmD\(^{70}\) phase which is optically isotropic and has no texture in the real sense. It presents an optically black area and its transformation from the isotropic liquid or a homeotropic smectic phase is hard to observe (black to black area). The Cub phase could be mistaken for an isotropic liquid, except that this Cub phase is highly viscous and its phase detection can be facilitated by observing the effects of stress on any air bubbles in the thin film.\(^{71}\) The confirmation for this Cub phase can also be supported by a DSC peak in the heating and cycles and enthalpy changes on the DSC thermogram.

\(N,N'\)-bis(4-alkoxybenzoyl) hydrazine compounds with asymmetrical hydrocarbon chains, 3b (C9, C10) and 3c (C9, C12) possess only the Cub phase between the crystalline solid and the isotropic liquid at 134.5 and 132.8°C, respectively. From Table
5, \textit{N,N’}-bis(4-alkoxybenzoyl) hydrazine compounds 3d-h, with only one semifluorinated chain, show a lower melting temperature but also a higher clearing temperature than their perhydrogenated homologs. All the mesomorphic compounds in this series display SmA and SmC phases. These phases have classical optical textures with focal-conic fan texture for SmA and broken focal-conic fan texture for SmC. The single semifluorinated tail in these compounds suppresses the Cub phase and induces a SmA phase. As usual, this semifluorinated chain tends to enhance the thermal stability of smectic mesophase due to its rigidity and the fluorophobic effect.\textsuperscript{72-74} For each series of \( n + m = 10 \) and 12, compounds with the longer fluorinated segment show higher clearing temperatures compared to those with the shorter fluorinated segment. Compounds with two semifluorinated chains, 3i-m show higher melting and clearing temperatures compared to their perhydrogenated analogs.

Compound 3a (C9) with symmetrical two perhydrogenated chains displays the Cr-Cub-SmC-I transition sequence. Introduction of a single semifluorinated chain in the asymmetric compound 3d (\( n=6, m=3 \)) interestingly suppresses the Cub phase, retains the SmC and induces a SmA phase. Compound 3i which has two semifluorinated chains is again symmetrical and exhibits the Cub, SmC and SmA phases. All the mesophases for these compounds were observed and identified by POM upon cooling from the isotropic phase. Figures 2.7, 2.8 and 2.9 show the representative textures of compounds \textit{N,N’}-bis(4-alkoxybenzoyl) hydrazines (C9): 3a (two perhydrogenated chains), 3d (one perhydrogenated and one semifluorinated chain) and 3i (two semifluorinated chains), respectively.
Figure 2.7: POM photographs of 3a on cooling (I-SmC-Cub-Cr): (a) SmC at 164.5°C (magnification: 10 × 10); (b) Cub phase (dark area) at 162.85°C (magnification: 10 × 10).

Figure 2.8: POM photographs of 3d on cooling (I-SmA-SmC-Cr): (a) SmA (batonnet texture) at 223.1°C (magnification: 10 × 10); (b) SmA (focal-conic fan texture) at 217.0°C (magnification: 20 × 10); (c) SmC (broken focal-conic fan texture) at 175.9°C (magnification: 10 × 10).
A further investigation involves some binary mixtures. An individual liquid crystal material has its own specific structure which confers a certain phase morphology and phase transition temperatures. The combination of different structural moieties determines new mesogenic and physical properties. In binary mixtures of liquid crystalline substances, different mechanisms operate for the stabilization or the induction of certain phases which includes electron donor-acceptor interactions\textsuperscript{75-81} or steric factors.\textsuperscript{82} Binary solutions with limited solubility between two isotropic liquid phases are usually the result of the mixing of two molecules with different polarity, chemical nature or size.\textsuperscript{83,4,84} Here, the mesophase behavior of several binary mixtures of the $N,N'$-bis(4-alkoxybenzoyl) hydrazine compounds just discussed with one semifluorinated compound have been investigated. Transition temperatures as measured by DSC and the mesophase identification by POM for these mixtures are summarized in Table 2.6.
Table 2.6: Transition temperatures and enthalpies ($\Delta H$, J/g) for selected binary mixtures.

<table>
<thead>
<tr>
<th></th>
<th>Cr$_1$</th>
<th>Cr$_2$</th>
<th>Cr$_3$</th>
<th>Cub</th>
<th>SmC</th>
<th>SmA</th>
<th>I</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>125.9</td>
<td>142.4</td>
<td>–</td>
<td>–</td>
<td>159.3</td>
<td>165.9</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>34.6</td>
<td>15.4</td>
<td>0.4</td>
<td>4.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3b$^a$</td>
<td>89.6</td>
<td>112.4</td>
<td>134.5</td>
<td>158.7</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>1.8</td>
<td>20.0</td>
<td>11.0</td>
<td>5.1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3c</td>
<td>111.6</td>
<td>132.8</td>
<td>–</td>
<td>–</td>
<td>162.6</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>9.7</td>
<td>6.9</td>
<td>2.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3d</td>
<td>77.6</td>
<td>128.3</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>186.8</td>
<td>225.6</td>
</tr>
<tr>
<td></td>
<td>14.3</td>
<td>8.2</td>
<td>0.5</td>
<td>1.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3a + 3b$^b$</td>
<td>72.7</td>
<td>90.5</td>
<td>113.1</td>
<td>126.3</td>
<td>126.3</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>(1:1)</td>
<td>8.8</td>
<td>15.7</td>
<td>27.0</td>
<td>5.0</td>
<td>5.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3a + 3c$^c$</td>
<td>89.8</td>
<td>100.4</td>
<td>–</td>
<td>100.4</td>
<td>110.6</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>(1:1)</td>
<td>26.2</td>
<td>5.5</td>
<td>5.5</td>
<td>0.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3a + 3d$^d$</td>
<td>86.6</td>
<td>–</td>
<td>–</td>
<td>124.6</td>
<td>124.6</td>
<td>158.9</td>
<td></td>
</tr>
<tr>
<td>(1:1)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$^a$ This compound exhibits three crystalline phases in the first DSC run but only two crystalline phases can be observed in the second run for the same sample.; $^b$ At 126.3°C, the Cub phase becomes SmC and an isotropic, almost simultaneously. $^c$ At 100.4°C, the crystalline phase becomes Cub and SmC, almost simultaneously. $^d$ At 86.6°C, the crystalline phase becomes Cub and SmC phase, almost simultaneously. Mesophase values for this mixture observed using POM. Data in Table 2.6 were obtained on heating.
In Table 2.6, pure 3a exhibits the phase sequences of Cr-Cr$_2$-Cub-SmC-I, pure 3b shows Cr$_1$-Cr$_2$-Cr$_3$-Cub-I, pure 3c shows Cr$_1$-Cr$_2$-Cub-I and pure 3d shows Cr$_1$-Cr$_2$-SmC-SmA-I. Compound 3a was separately mixed with 3b, 3c and 3d in a 1:1 ratio. The mixture of 3a + 3b displays the phase sequence of Cr$_1$-Cr$_2$-Cr$_3$-Cub-SmC-I. Heating under POM shows the dark area of Cub phase at 113.1°C, followed by the formation of the broken focal conic fan texture of SmC and the isotropic phase almost at the same time (126.3°C). The mixture of 3a + 3c shows the phase sequence of Cr$_1$-Cr$_2$-Cub-SmC-I, with the melting temperature at 89.8°C, followed by the formation of Cub and SmC phase at 100.4°C, almost at the same time. The clearing temperature for this mixture is observed at 110.6°C. Mixture of 3a + 3d exhibits the phase sequence of Cr-Cub-SmC-SmA-I. Heating under POM at 86.6°C shows the transformation of crystalline to Cub and SmC phase, almost at the same time, followed by the formation of SmA phase at 124.6°C and then the isotropic liquid at 158.9°C. Pure 3a exhibits only Cub and SmC phases while pure 3d shows only SmC and SmA phases. The mixture of 3a + 3d shows a combination of Cub, SmC and SmA phases. All these mixed systems are homogeneous and their melting and clearing temperatures are lower compared to the pure components.

Another fluorination position that we are interested in involves lateral fluorine substitution on the core, as is often used to alter the mesomorphic behavior of liquid crystalline compounds. Lateral core substitution with fluorine is used due to its relatively small size and high electronegativity. This study involved the examination of mesophase behavior of some selected $N,N'$-bis(4-dodecyloxybenzoyl) hydrazine compounds and
their precursors. Transition temperatures measured by DSC and mesophase identification by POM for these mixtures are summarized in Tables 2.7 and 2.8.

Table 2.7: Transition temperatures and enthalpies ($\Delta H$, kJ mol$^{-1}$) for precursors 4, 4-(dodecyloxy)-2-fluorobenzoyl nitrile; 5, 4-(dodecyloxy)-2-fluorobenzoic acid and 6, 4-(dodecyloxy)-2-fluorobenzoyl hydrazine.

<table>
<thead>
<tr>
<th></th>
<th>Cr$_1$</th>
<th>Cr$_2$</th>
<th>SmC</th>
<th>N</th>
<th>I</th>
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<tr>
<td>1c</td>
<td>94.1</td>
<td>–</td>
<td>–</td>
<td>132.2</td>
<td>138.4</td>
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<tr>
<td></td>
<td>46.0</td>
<td>–</td>
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<tr>
<td>4</td>
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<td>–</td>
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<td>30.7</td>
<td>–</td>
<td>–</td>
<td>14.4</td>
<td></td>
</tr>
<tr>
<td>6$^a$</td>
<td>127.9</td>
<td>147.2</td>
<td>–</td>
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<td>–</td>
</tr>
<tr>
<td></td>
<td>3.5</td>
<td>0.1</td>
<td>–</td>
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</tbody>
</table>

$^a$ Compound exhibits several crystalline phases. Data in Table 2.7 were obtained on heating

The intermediates methyl 4-dodecyloxybenzoate, 4-dodecyloxybenzoyl hydrazine, 2c, 4-(dodecyloxy)-2-fluorobenzonitrile, 4 and 4-(dodecyloxy)-2-fluorobenzoyl hydrazine, 6 did not show any liquid crystalline properties. The 4-dodecyloxybenzoic acid, 1c exhibits SmC and nematic mesophases with a melting point at 94.1°C and clearing temperature of 138.4°C. Fluorination at the lateral core position of compound 1c
gives compound 5, which suppresses the SmC phase but retains the nematic phase. This compound shows a lower melting point of 86.7°C and lower clearing temperature of 94.5°C compared to its counterpart with no fluorine.

Table 2.8: Transition temperatures and enthalpies ($\Delta H$, kJ mol$^{-1}$) for $N,N'$-bis(4-dodecyloxy)benzoyl hydrazine, 7; 4-(dodecyloxy)-$N'$-(4-(dodecyloxybenzoyl)-2-fluorobenzoyl hydrazine, 8 and $N,N'$-bis(4-(dodecyloxy)-2-fluorobenzoyl) hydrazine, 9.

<table>
<thead>
<tr>
<th></th>
<th>Cr$_1$</th>
<th>Cr$_2$</th>
<th>Cub</th>
<th>SmC</th>
<th>N</th>
<th>I</th>
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</thead>
<tbody>
<tr>
<td>7$^a$</td>
<td>•</td>
<td>129.0</td>
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<td>160.5</td>
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<td>•</td>
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<td></td>
<td>32.0</td>
<td>25.0</td>
<td>7.2</td>
<td>5.7</td>
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<tr>
<td>8</td>
<td>•</td>
<td>100.0</td>
<td>•</td>
<td>115.0</td>
<td>•</td>
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<td></td>
<td>3.9</td>
<td>55.2</td>
<td>12.6</td>
<td>12.6</td>
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<tr>
<td>9</td>
<td>•</td>
<td>127.8</td>
<td>•</td>
<td>157.0</td>
<td>•</td>
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<td></td>
<td>47.1</td>
<td>•</td>
<td>5.6</td>
<td>5.6</td>
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</tr>
</tbody>
</table>

$^a$ This compound exhibits several crystalline phases. Data in Table 2.8 were obtained on heating.

In Table 2.8, compound 7 exhibits Cub phase while 8 and 9 possess SmC and nematic phases, respectively. Compound 7 without lateral core fluorination has a clearing temperature of 160.5°C. Addition of a single fluorine atom in only one of the rings as in
compound 8 lowers the clearing temperature to 157.0°C. Addition of a single fluorine atom in both of the rings as in compound 9 lowers the clearing temperature still more to 142.9°C. Remarkably, the presence of a single fluorine on two rings (symmetric 9) or even just one ring (asymmetric 8) completely suppresses the Cub phase in both cases and instead induces a nematic phase or a SmC phase, respectively.

2.5 Conclusion

The replacement of hydrogen by fluorine atoms in the alkoxy chain modifies the molecular interactions and this causes changes in the mesomorphic properties. Semifluorinated 4-alkoxybenzoic acids (1a-e) have suppressed nematic phases while the perhydrogenated 4-alkoxybenzoic acids often have a nematic phase. Semifluorinated 4-alkoxybenzoyl hydrazines (2a-e) exhibit mesogenic behavior while none is found in their perhydrogenated counterparts. Perhydrogenated N,N'-dialkoxybenzoylhydrazines derivatives (3a-c) display Cub and SmC phases. Compounds 3d-h with one semifluorinated chain suppress the Cub phase but induce a SmA phase, with lower melting but higher clearing temperatures compared to compounds with two semifluorinated chains, 3i-m. All bis-semifluorinated compounds show higher melting and clearing temperatures compared to their hydrocarbon counterparts. The few selected binary mixtures (3a+3b, 3a+3b, 3a+3c, 3a+3d) show mesogenic texture combination of both of the pure compounds. For all these mixed systems, the melting and clearing temperatures are lower compared to their pure components. In the selected lateral fluoro substituted N,N'-dialkoxybenzoylhydrazines, compounds with a single fluorine on the
ring, either asymmetric, 8 or symmetric, 9 suppresses the Cub phase (compound 7) but induces a SmC or a nematic phase.

2.6 References


Chapter 3

Synthesis and Characterization of 2,5-diphenyl-1,3,4-oxadiazole and 2,5-diphenyl-1,3,4-thiadiazole Liquid Crystals with Semifluorinated Alkoxy Tails.

The content of this chapter has been recently submitted to Mol Cryst Liq Cryst for consideration for publication

Khairuddean, M.; Twieg, R. J.
3.1 **Introduction to liquid crystals with heterocyclic rings**

In the course of structure-property studies of liquid crystals, much attention has been paid to compounds containing heterocyclic ring units. During the last decade, a large number of liquid crystalline materials containing heterocyclic rings have been synthesized. Many heterocyclic mesogens investigated contain 1,4-disubstituted (*para* disubstituted) six-membered heteroaromatic rings that provide a high linearity in structure as is preferred for the calamitic systems. Compounds with five-membered heterocyclic rings have also been examined but were deemed less suitable for the formation of mesogenic materials due to their deviation from linearity. Nevertheless, many series of mesomorphic compounds containing such heterocyclic units have been synthesized due to their potential applications, for example, in electro-optical devices.\(^1\-^8\)

Interest in such structures has attracted much attention and work in this area continues as the introduction of such heterocyclic units produces considerable changes in polarity, polarizability and geometry of the molecules.\(^9\-^11\) These can, in turn, influence the types of mesophase and their phase transition temperatures.\(^12\,^13\) In addition, the presence of lone-pair electrons on heteroatoms with differing electronegativities may introduce a transverse dipole moment, resulting in a change of dielectric anisotropy.\(^14\)

Most recently, a study of the molecular biaxiality structure-property relationships in some heterocyclic liquid crystals has been inspired by Cai and Samulski\(^11\) who explored the non-linear molecular shape effects of oxadiazole and related heterocyclic compounds.
3.1.1 The 1,3,4-oxadiazole system

The parent oxadiazole unit is an aromatic heterocyclic molecule with carbon, hydrogen, nitrogen and oxygen atoms. As illustrated in Figure 1, there are a few possibilities for the arrangement of atoms in these molecules (Figure 3.1). Substitution at the two open positions in the 1,3,4-oxadiazole in some cases enables the formation of certain bend-shape molecules with liquid crystal behavior.15

![Four types of oxadiazoles.](image)

The first 1,3,4-oxadiazole derivatives reported by Dimitrowa et al.12 were non-mesogenic. Later, a variety of other mesogenic 1,3,4-oxadiazole compounds were eventually reported.16-27 The suppression of mesomorphic behavior observed for many 1,3,4-oxadiazole derivatives is at least in part due to the bend (~134°) associated with the exocyclic bonds in the 2- and 5-positions of the oxadiazole ring (Figure 3.2). This bend is often too severe to sustain the required ordered packing in calamitic mesophases.20 The tendency for compounds to exhibit liquid crystalline properties if they contain any of the set of heterocyclic compounds seen in Figure 3.2 roughly decreases in the order depicted.28,29 However, compounds still might be able to exhibit the liquid crystalline mesophase (in general) if this severe bend in the mesogenic core can restrict the free rotation of the mesogenic units around them.30
Due to the bent-shaped structure, these 1,3,4-oxadiazole compounds produce a spontaneous break in symmetry and are prone to form the banana-shaped molecules which were reported to show the ferroelectric behavior.\textsuperscript{31} These rigid bent-shaped compounds with a large angle were also reported to be suitable for the formation of the biaxial nematic phase.\textsuperscript{32}

Another interesting area involves the discovery of electroluminescence (EL)\textsuperscript{33,34} in low molecular weight organic molecules\textsuperscript{35} and in conjugated polymers.\textsuperscript{36} This discovery led to the synthesis of new materials incorporated into the organic light emitting diodes (OLEDs).\textsuperscript{37-41} Such compounds have received a great deal of attention due to their potential application in display technologies. Most EL materials are hole-transporting wherein most cases the holes are injected and transported instead of electrons due to their weak electronic affinity and consequently the device will exhibit low efficiency.\textsuperscript{34,33} In order to enhance the device efficiency, a material with electron-transporting characteristics which usually contains a π-electron deficient heterocyclic moiety is
needed to provide balance between the number of positive and negative carriers. Thus, the 1,3,4-oxadiazole units have attracted considerable interest because they have strong electron affinity and often possess electron transporting character. Among the heterocyclic compounds, they have been quite widely used for OLEDs.\textsuperscript{42-45}

### 3.1.2 The 1,3,4-Thiadiazole system

Thiadiazole is an aromatic heterocyclic molecule with carbon, hydrogen, nitrogen and sulfur atoms and it is the sulfur analogue of oxadiazole. The two most common thiadiazole molecules are illustrated in Figure 3.3.

![1,3,4-Thiadiazole 1,2,4-Thiadiazole](image)

**Figure 3.3:** Common thiadiazoles.

Along with 1,3,4-oxadiazole compounds, many analogous 1,3,4-thiadiazole derivatives have also been reported.\textsuperscript{46-49} For example, numerous mesogenic compounds with 1,3,4-thiadiazole unit are known in chiral Schiff’s bases.\textsuperscript{50-53} Compounds with 1,3,4-thiadiazole ring are also known to possess useful biological\textsuperscript{54,55} and electro-optical\textsuperscript{56,57} properties. Compared to a 1,3,4-oxadiazole ring, a 1,3,4-thiadiazole ring deviates less from the co-linear 180-degree configuration due to the larger sulfur atom and longer C-S bonds and provides a more linear overall bond arrangement (Figure 2). It was reported that compounds with a 1,3,4-thiadiazole ring can be used in the nonlinear optical (NLO) applications\textsuperscript{58} and the presence of this ring has the ability to promote SmC phases\textsuperscript{59-61}
with broad temperature ranges.\textsuperscript{53,16} 1,3,4-Thiadiazole compounds with properties of photoluminescent (PL) and electroluminescent (EL) properties behave as electron-
transporting and light-emitting materials which exhibit smectic and/or nematic phases.\textsuperscript{62} These types of compounds have also initiated a significant interest in ferroelectric liquid crystals due to their potential application in fast switching devices.\textsuperscript{61,49,47}

3.2 Research Proposal

Our current interest has focused on the preparation of new types of liquid crystalline 1,3,4-oxadiazole and 1,3,4-thiadiazole compounds with semifluorinated tails. The semifluorinated tails are known to have a profound impact on the mesomorphic behavior of both calamitic\textsuperscript{63-74} and discotic systems\textsuperscript{75-86} and the semifluorination of tails is already discussed in Chapter 2. Here we examine their influence on the properties of diaryl 1,3,4-oxadiazoles and diaryl 1,3,4-thiadiazoles. The fluorinated block in the tail, due to its restricted conformational freedom, is very different from the perhydrogenated block in the tail. The fluorinated section is a relatively stiff helical chain in contrast to the more flexible hydrocarbon chain with a planar zig-zag alignment of the backbone carbon atoms.\textsuperscript{67} Our interest in the relationships between molecular structure and mesomorphic behavior has led us to synthesize a series of symmetric and asymmetric compounds of diphenyl 1,3,4-oxadiazole, 1 and diphenyl 1,3,4-thiadiazole, 2 units with semifluorinated alkoxy tails (Figure 4).
3.3 Synthesis

The \(N,N'\)-bis(4-alkoxybenzoyl) hydrazines are common precursors for the synthesis of both 2,5-bis(4-alkoxyphenyl)-1,3,4-oxadiazole and 2,5-bis(4-alkoxyphenyl)-1,3,4-thiadiazole-based derivatives. In our initial work,\(^87\) we reported the preparation of these \(N,N'\)-bis(4-alkoxybenzoyl) hydrazine compounds and their own interesting mesophase behavior. The \(N,N'\)-bis(4-alkoxybenzoyl) hydrazine compounds were prepared by standard methods, usually by reaction between a 4-alkoxybenzoyl hydrazine and the acid chloride of a companion 4-alkoxybenzoic acid. The routes adopted for the synthesis of the new 1,3,4-oxadiazole (1a-m) and 1,3,4-thiadiazole (2a-m) compounds are outlined in Figure 3.4: The 1,3,4-oxadiazole and 1,3,4-thiadiazole compounds (without core fluorination) examined in this paper. In all cases when \(n=0\) the terminal methyl group on the chain has three hydrogens.
Scheme 3.1. The 1,3,4-oxadiazole derivatives were synthesized by cyclodehydration of $N,N'$-bis(4-alkoxybenzoyl) hydrazine with phosphorus oxychloride\textsuperscript{88} while reaction of $N,N'$-bis(4-alkoxybenzoyl) hydrazine with Lawesson’s reagent\textsuperscript{89} produced the 1,3,4-thiadiazole derivatives. The alkoxy tails in these systems differ in overall length ($m + n$ carbons) and in the ratio of fluorinated ($n$ carbons) to hydrocarbon ($m$ carbons) block size.
Scheme 3.1: Synthesis method and structures of the 1,3,4-oxadiazole and 1,3,4-
thiadiazole compounds (without core fluorination) examined in this paper.

We have also synthesized a few new compounds to examine the influence of lateral
core substitution with a single fluorine atom. The 2,5-bis(2-fluoro-4-alkoxyphenyl)-
1,3,4-oxadiazole compounds 4 and 5 and the respective 1,3,4- thiadiazole derivatives 7
and 8 were prepared from their lateral core fluorinated $N,N'$-bis(2-fluoro-4-$n$-alkoxybenzoyl) hydrazine derivatives according to the synthesis route mentioned earlier.

### 3.4 Results and Discussion

Transition temperatures and phase behavior were determined by optical texture observations using a hot stage polarizing microscope (POM) and differential scanning calorimetry (DSC). The optical, thermal and thermodynamic phase transition data for perhydrogenated and semifluorinated 2,5-(4-alkoxyphenyl)-1,3,4-oxadiazoles, 1a-m are summarized in Table 3.1.
Table 3.1: Transition temperatures and enthalpies data from DSC for perhydrogenated and semifluorinated 2,5-(4-alkoxyphenyl)-1,3,4-oxadiazoles, 1a-m.

![Chemical structure](image)

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<th>R&lt;sub&gt;2&lt;/sub&gt;</th>
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<td>(●) 136.9</td>
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<td>• 164.7</td>
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<td>–</td>
<td>• 153.9</td>
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<td>• 170.4</td>
<td>(●) 170.4</td>
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<td>• 142.5</td>
<td>• 174.6</td>
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<td>m=4, n=8</td>
<td>m=4, n=8</td>
<td>18.0</td>
<td>33.6</td>
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a At 136.9°C, the crystalline becomes SmA phase, almost at the same time. b At 164.7°C and 170.4°C, respectively, a transient SmA phase was observed. Data in Table 3.1 were obtained on heating. The enthalpy (ΔH) is reported in units of kJ mol⁻¹.

In Table 3.1, the first series for the diaryl 1,3,4-oxadiazole compounds involves compounds with only perhydrogenated alkoxy chains, 1a-c which are not mesogenic. As the chain length increases, the melting temperature decreases (Table 3.1). These compounds containing the 1,3,4-oxadiazole bend (134°) and simple alkoxy chains did not achieve the required ordered mesophase packing and simply increasing the chain length (in the modest range examined) did not induce liquid crystalline properties. Nevertheless, such compounds might still be able to exhibit liquid crystal mesophases if this severe bend in the mesogenic core can restrict the free rotation of the units around them. When either one or two semifluorinated chains are introduced (in lieu of the simple alkoxy tails) into these diaryloxadiazoles, SmC or/and SmA liquid crystalline mesophases appear.

The second series consists of compounds with one semifluorinated chain (1d-h) which exhibit SmC and SmA phases if the fluorinated segment in the single semifluorinated tail is longer than the hydrogenated part, as in the case of compounds 1d,f and h. Compounds show only a SmA phase if the fluorinated segment is shorter, as in 1e or has the same length as the hydrogenated part, as in 1g. From Table 1, heating 1e under POM shows the crystalline phase is transformed to a SmA phase at 136.9°C and becomes isotropic almost at the same time. For compounds 1f and 1h with a longer fluorinated segment, at 164.7 and 170.4°C respectively, the SmC becomes a SmA phase.
and isotropic almost simultaneously. In this series, compounds $n + m = 10$ and $12$ shows that a longer fluorinated segment in the chain for compounds $1f$ and $1h$ produces higher melting and clearing temperatures.

The third series involves symmetrical compounds with two semifluorinated chains ($1i-m$). For compounds $n + m = 10$ and $12$, compounds with a longer fluorinated segment, $1k$ and $1m$ show only SmC phases but compounds with shorter fluorinated segment, $1j$ or have the same fluorinated and hydrogenated segment, $1l$ show only SmA phases. It is also true for this series ($n + m = 10$ and $12$) that longer fluorinated segments in the chain exhibit higher melting and clearing temperatures.

The mesophase transitions apparent in the DSC curves are accompanied by the typical changes in the textures observed with hot stage POM. Figure 3.5 illustrates the representative textures observed during cooling from the isotropic melt. In Figure 3.5, compound $1e$ with one semifluorinated chain shows (a) batonnet formation and (b) further cooling shows the typical focal-conic fan texture of SmA phase.
Figure 3.5: POM photographs of 1e on cooling (I-SmA-Cr): (a) batonnets at 135.9°C (magnification: 10 × 10); (b) SmA at 130.9°C (magnification: 10 × 10).

The transition temperatures and phase behavior for the analogous set of perhydrogenated and semifluorinated 2,5-(4-alkoxyphenyl)-1,3,4-thiadiazole compounds, 2a-m were determined by optical texture observations using POM and DSC. The optical, thermal and thermodynamic phase transition data for these compounds are summarized in Table 3.2.
Table 3.2: Transition temperatures and enthalpies data from DSC for perhydrogenated and semifluorinated 2,5-(4-alkoxyphenyl)-1,3,4-thiadiazoles, \(2\text{a-m}\).

\[
\begin{align*}
2\text{a}: \quad & \text{C}_9\text{H}_{19} \quad \text{C}_9\text{H}_{19} \quad \bullet \quad 93.7 \quad - \quad - \quad \bullet \quad 184.0 \quad - \quad - \\
2\text{b}: \quad & \text{C}_9\text{H}_{19} \quad \text{C}_{10}\text{H}_{21} \quad \bullet \quad 89.2 \quad - \quad - \quad \bullet \quad 164.0 \quad - \quad - \\
2\text{c}: \quad & \text{C}_9\text{H}_{19} \quad \text{C}_{12}\text{H}_{25} \quad \bullet \quad 84.6 \quad - \quad - \quad \bullet \quad 170.8 \quad - \quad - \\
2\text{d}: \quad & \text{C}_9\text{H}_{19} \quad \text{F(CF}_2)_m(\text{CH}_2)_n \quad \bullet \quad 89.4 \quad - \quad - \quad \bullet \quad 217.9 \quad - \quad - \\
2\text{e}: \quad & \text{C}_9\text{H}_{19} \quad \text{F(CF}_2)_m(\text{CH}_2)_n \quad \bullet \quad 94.0 \quad - \quad - \quad \bullet \quad 212.2 \quad - \quad - \\
2\text{f}: \quad & \text{C}_9\text{H}_{19} \quad \text{F(CF}_2)_m(\text{CH}_2)_n \quad \bullet \quad 96.9 \quad - \quad - \quad \bullet \quad 211.0 \quad - \quad - \\
2\text{g}: \quad & \text{C}_9\text{H}_{19} \quad \text{F(CF}_2)_m(\text{CH}_2)_n \quad \bullet \quad 106.0 \quad - \quad - \quad \bullet \quad 126.3 \quad - \quad - \\
2\text{h}: \quad & \text{C}_9\text{H}_{19} \quad \text{F(CF}_2)_m(\text{CH}_2)_n \quad \bullet \quad 126.5 \quad - \quad - \quad \bullet \quad 204.2 \quad - \quad - \\
2\text{i}: \quad & \text{F(CF}_2)_m(\text{CH}_2)_n \quad \text{F(CF}_2)_m(\text{CH}_2)_n \quad \bullet \quad 119.5 \quad - \quad - \quad \bullet \quad 164.4 \quad - \quad - \\
2\text{j}: \quad & \text{F(CF}_2)_m(\text{CH}_2)_n \quad \text{F(CF}_2)_m(\text{CH}_2)_n \quad \bullet \quad 103.5 \quad - \quad - \quad \bullet \quad 161.0 \quad - \quad - \\
2\text{k}: \quad & \text{F(CF}_2)_m(\text{CH}_2)_n \quad \text{F(CF}_2)_m(\text{CH}_2)_n \quad \bullet \quad 133.2 \quad - \quad - \quad \bullet \quad 185.7 \quad - \quad - \\
2\text{l}: \quad & \text{F(CF}_2)_m(\text{CH}_2)_n \quad \text{F(CF}_2)_m(\text{CH}_2)_n \quad \bullet \quad 153.4 \quad - \quad - \quad \bullet \quad 169.8 \quad - \quad -
\end{align*}
\]
This compound exhibits two crystalline phases in the first DSC run but only one crystalline phase in the second run for the same sample. Data in Table 3.2 were obtained on heating. The enthalpy ($\Delta H$) is reported in units of kJ mol$^{-1}$.

In Table 3.2, the first series of diaryl 1,3,4-thiadiazole compounds involves compounds with only perhydrogenated alkoxy chains, $2a$-$c$ which exhibit only SmC phases. Compound $2a$ with symmetrical nonyloxy chains shows a SmC phase at 93.7°C with clearing temperature at 184.0°C. This experimental data is within the range of the reported literature values$^{90-93,12}$ with a phase sequence of Cr-SmC-I. Elongating one of the alkoxy chains by replacement with a decyloxy, $2b$ or dodecyloxy chain, $2c$ did not change the phase behavior (Table 3.2).

The second series consists of compounds with just one semifluorinated chain ($2d$-$h$) which exhibit SmC and SmA phases. For compounds $n + m = 10$ and 12, chains with the fluorinated segment longer than the hydrogenated part (as in $2f$ and $2h$) show higher clearing temperatures compared to those with a shorter fluorinated segment, as in $2e$ or have the same fluorinated and hydrogenated length, as in $2g$. The third series involves symmetrical compounds with two semifluorinated chains ($2i$-$m$) which show SmA and SmC phases. For compounds $n + m = 10$ and 12, chains with longer fluorinated segment, $2k$ and $2m$ show lower clearing temperatures compared to compounds with shorter fluorinated segment, $2j$ or have the same fluorinated and hydrogenated segment, $2l$. When cooling under POM, a SmA phase can be observed from the formation of
batonnets and becomes the focal-conic fan texture. Further cooling of the SmA phase leads to broken focal-conic fan texture of the SmC phase.

The mesophase transitions apparent in the DSC curves are accompanied by typical changes in the textures observed by POM. Figure 3.6 illustrates representative textures observed during cooling from the isotropic melt. In Figure 3.6, these textures were observed during cooling from the isotropic melt of compound 2f which has only one semifluorinated chain.

![Figure 3.6: POM photographs of 2f on cooling (I-SmA-SmC-Cr): (a) SmA with focal-conic fan texture at 225.2°C; (magnification: 20 × 10); (b) further cooling shows SmC with broken focal-conic fan texture at 188.0°C (magnification: 10 × 10).](image)

A further brief investigation involved the examination of lateral core substitution of the compounds with perhydrogenated tails, which can be used to alter the mesomorphic behavior of these liquid crystalline compounds. Lateral core fluorine substitution is used in this case due to its relatively small size and high electronegativity. Some selected
compounds of 2,5-bis(dodecyloxyphenyl)-1,3,4-oxadizole, 3-5 and 2,5-
bis(dodecyloxyphenyl)-1,3,4-thiadiazole, 6-8 were chosen. Transition temperatures, as measured by DSC and mesophase identification by POM, for these mixtures are summarized in Table 3.3 and Table 3.4.

Table 3.3: Transition temperatures and enthalpies of compounds 3, 4 and 5.

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<th>Compound</th>
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<td>92.0</td>
<td>125.4</td>
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<td>0.5</td>
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³ Compound shows several crystalline phases. Data in Table 3.3 were obtained on heating. The enthalpy (ΔH) is reported in units of kJ mol⁻¹.
Table 3.4: Transition temperatures and enthalpies of compounds 6, 7 and 8.

<table>
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<td></td>
<td>16.9</td>
<td>33.3</td>
<td>6.8</td>
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</tr>
<tr>
<td>7</td>
<td>• 99.4</td>
<td>–</td>
<td>• 162.0</td>
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<td></td>
<td>28.1</td>
<td>–</td>
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<td>10.4</td>
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Data in Table 3.4 were obtained on heating. The enthalpy (ΔH) is reported in units of kJ mol⁻¹.

Compound 3, 2,5-(4-dodecyloxyphenyl)-1,3,4-oxadiazole with symmetric perhydrogenated chains did not show any liquid crystalline properties (Table 3.3). Lateral core fluorine substitution in either one or both aromatic rings, 4 or 5 respectively, did not induce any liquid crystalline mesophase. On the other hand, compound 6, 2,5-Bis(4-dodecyloxyphenyl)-1,3,4-thiadiazole with symmetric perhydrogenated chains exhibits a SmC phase. Compounds with lateral core fluorine substitution in one (7) and two aromatic rings (8) still exhibit a SmC phase. For both 1,3,4-oxadiazole and 1,3,4-thiadiazole systems, core fluorination produces lower melting and clearing temperatures, for example compound 5 compared to 4 and compound 8 compared to 7.
3.5 Conclusion

A group of mesomorphic semifluorinated heterocyclic molecules based on 2,5-diphenyl-1,3,4-oxadiazole and 2,5-diphenyl-1,3,4-thiadiazole core groups has been prepared. The critical difference between these two series, 2a-m and 3a-m, is their central heterocyclic core. Diphenyl 1,3,4-thiadiazole compounds with perhydrogenated alkoxy chains show a SmC phase but when the sulfur atom is replaced by oxygen in the oxadiazoles, all mesogenic behavior disappears. All compounds with either one or two semifluorinated chains attached to the 1,3,4-thiadiazole unit show higher clearing temperatures than their corresponding 1,3,4-oxadiazole derivatives. For 1,3,4-oxadiazole compounds, semifluorination in the terminal chain induces a liquid crystalline mesophase but fluorination at the lateral positions did not enhance any liquid crystalline properties. For the 1,3,4-thiadiazole compounds, fluorination at both the core and the tail still provides mesogenic activity. We see here in the case of the diphenyl oxadiazoles another system where the introduction of fluorinated blocks in the tails of these molecules can induce liquid crystal behavior where none is otherwise found in the perhydrogenated analogs.

3.6 References


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89. Sybo, B.; Bradley, P.; Grubb, A.; Miller, S.; Proctor, K. J. W.; Clowes, L.;
Chapter 4

Synthesis and Characterization of Some Amphiphilic Polyhydroxy Benzamide

Liquid Crystalline Materials

This Chapter is in progress to be submitted to

*Mol Cryst Liq Cryst* for consideration for publication

Khairuddean, M.; Twieg, R. J.
4.1 Introduction

4.1.1 Amphiphilic molecules

An amphiphile is a compound that consists of both hydrophilic (polar groups) and hydrophobic (non-polar or hydrocarbon) components. These molecules are called *amphiphilic* and they behave as amphotropic\(^1\) or amphitropic\(^2-4\) molecules where they can form liquid crystalline phases not only in the lyotropic systems but also as pure compounds in the thermotropic systems.\(^5-7\) The amphiphilic polyhydroxy compounds\(^8-11\) and carbohydrate derivatives\(^12-16\) are examples of the amphotropic materials. The hydrogen bonding networks amongst the hydroxy groups is very important in the self-organization system as is the microsegregation of the hydrophilic and hydrophobic parts of the molecules.\(^17\) It was reported that amphiphiles with double chains often form columnar mesophases (Col\(_{h2}\)) or bicontinuous cubic mesophases (Cub\(_{v}\)).\(^9\) Amphiphiles with three long aliphatic chains can organize to form micellar cubic mesophases built up from spherical closed micelles (Cub\(_l\)). The strong hydrogen bonding which is located inside the aggregates surrounded by the flexible alkyl chains makes this cubic phase similar to the inverse cubic phase in the lyotropic system.\(^7\)

4.1.2 Lyotropic cubic mesophase

Cubic phases are more commonly observed in the lyotropic systems.\(^18\) The individual micelles arrange themselves and form the cubic phase, which may exist in
three different packing arrangements including the cubic, cubic face-centered and cubic body-centered lattices. By changing the concentration of the solvent, several different cubic phases may be observed in lyotropic systems.\textsuperscript{19} Micellar aggregates separate into two distinct shapes; the spherical shape which forms the I-phase (discontinuous cubic phase) while the other shape is rod-like which is interconnected in three dimensional patterns to form the V-phase (bicontinuous cubic phase).\textsuperscript{20} In a lyotropic system, there are four different cubic structures of the I- and V-phases in the normal and inverted types (Figure 4.1).

![Diagram of cubic phases](image)

**Figure 4.1:** Schematic representation of cubic phases from spherical molecules, I-phase (top) and from rod-like molecules, V-phase (below), in the lyotropic system.\textsuperscript{20}

The microphase separation between hydrophilic and hydrophobic parts of the aggregates formed by the amphiphilic molecules is known as interfacial curvature.\textsuperscript{21} This is an important factor that determines the structure and the phase sequence of the
molecules based on the concentration of the solvent. If both regions are equal with respect to the required space, a lamellar structure ($L_\alpha$) with a zero curvature is observed. Smaller deviations show the bicontinuous cubic phase ($V$-phase) while greater deviations show the micellar structure ($I$-phase). Detailed information from the crystallographic point of view helps to distinguish different types of cubic lattices. In the $I$-phase, the spherical the normal structure of the primitive ($Pm3n$), cubic face centered ($Fm3m$) and cubic body centered ($lm3m$). This $I$-phase also shows one inverse structure ($Fd3m$). In the $V$-phase, the rod-like shows three different structures of 3-D interwoven networks consist of short rod-like micelles with the face curvature facing water ($V_1$) or nonpolar solvent ($V_2$). These arrangements organize into different bicontinuous cubic lattices of $Pn3m$, $lm3m$ and $la3d^6$ (Figure 4.1).

These cubic phases ($I$- and $V$-phases) can be differentiated from one another by their position in sequence between other phases. In the increasing surfactant concentration, the $I$-phase is located in between the isotropic micellar and the hexagonal phase while the $V$-phase is between the hexagonal and the lamellar phase.

### 4.1.3 Thermotropic cubic mesophase

Thermotropic cubic mesophases have received considerable attention due to their complex three dimensional (3-D) structures in different self-organizing systems. Their molecules are often highly anisotropic, and the bulk phase is optically isotropic and highly viscous in their cubic phase even when it appears between adjacent SmA and SmC
phases. Examples of molecular structures producing these thermotropic Cub phases include the bisbenzoyl hydrazines, disk-shaped molecules, block copolymers, polyhydroxy amphiphiles and carbohydrates. They have been widely used as a building block of supramolecular materials and have a wide variety of different mesophases driven by the intermolecular hydrogen bonding between the hydroxy groups in the molecules and the segregation of the non-polar hydrophobic chains. Therefore, the number, length, location and composition of the alkyl chains attached to the rigid moiety and the number and type of hydrogen bonding sites determines the identity of the resulting mesophase(s).

These types of cubic phases show a variety of morphologies. The most common is the bicontinuous la3d, followed by the space group lm3m and the Pm3n. In order to determine the exact symmetry of these cubic phases, X-ray diffraction studies are required. The Bragg peaks in the X-ray detects the cubic polar and apolar interfaces due to the electron density contrast but it is not sensitive to the position of the alkyl chain regions with respect to the polar/apolar interfaces thus is not sufficient to identify whether it is a normal or inverted type. Examples of the cubic phases (I- and V-phases) structures in thermotropic mesogens include the bicontinuous structures with a body centered lattice (la3d, lm3m) and the primitive cubic lattice (Pm3n), as shown in Figure 4.2.
Cubic phases are characterized by a long range positional order but without orientational order. The cubic phase was initially called the SmD phase. Under POM, the cubic phases do not show any texture in both lyotropic and thermotropic systems. They look isotropic but have a highly viscous character. In the lyotropic system, the cubic phases were often called a ringing phase. Earlier work on the refractive index and X-ray diffraction of this phase showed no layered structure in the molecules. Instead, the structure was discovered to have positional order similar to that of the isotropic liquid but it coexists with a crystalline cubic lattice. Etherington et al argued that SmD phase should not be called a smectic phase, but simply the D phase since it is clearly established to have three dimensional order and is definitely cubic. Later, it was known as D phase and now is known as the cubic phase. It presents an optically black area and its transformation from the isotropic liquid or from a homeotropic smectic phase is hard to observe (black to black area) and it could be mistaken for an isotropic liquid.
4.2 Research Proposal

We are interested in synthesizing a new series of amphiphilic polyhydroxybenzamide compounds with semifluorinated chains. However, prior to that investigation, we decided first to investigate the phase transformations of some non-fluorinated amphiphilic polyhydroxy molecules. The present investigation expands the variety of hydrophilic polar end groups and a subsequent investigation will expand the composition (by fluorination) of the hydrophobic tails. Our intention is to better understand the influence of the different components of the amphiphilic polyhydroxy molecules on the mesophase behavior; in particular the thermotropic cubic phases in amphiphilic polyhydroxybenzamide materials. Our ultimate goal is to further understand the behavior of the Cub phases in these different series of molecules for optical applications.

As a starting point, a series of new hydroxylated amides derived from 3,4,5-tris(n-nonyloxy)benzoic acid have been synthesized and characterized (Figure 4.3). Different mesophases have been determined depending on the size of the hydrophilic units.
Figure 4.3: Compounds of 3,4,5-trialkoxybenzamides, 3a, 3b and 4-10 with different hydrophilic groups.

4.3 Synthesis

The homologous polyhydroxybenzamide derivatives were synthesized according to Scheme 1 where a derivative of 1-amino-2,3-propanediol is exemplary.
Scheme 4.1: The synthesis route for polyhydroxybenzamide 3a and 3b is representative of the method employed for a variety of aminoalcohols.

Alkylation of methyl gallate with an excess of the appropriate alkyl bromide and potassium carbonate followed by saponification gave the 3,4,5-trialkoxybenzoic acid. The resulting benzoic acid was transformed into the corresponding benzoyl chloride by treatment with thionyl chloride. The crude acid chloride was converted to a series of amides by reaction with amino alcohols in the presence of dimethylformamide (DMF). The final products were purified by crystallization. Details of the syntheses are reported in the experimental section.

4.4 Results and Discussion

The thermal properties for all the compounds were investigated using differential scanning calorimetry (DSC) and polarized optical microscopy (POM). The literature data of the melting temperatures of some intermediates is summarized in Table 1. None of the intermediates, the methyl 3,4,5-trialkoxybenzoates 1a-b and 3,4,5-trialkoxybenzoic acids 2a-b, showed any liquid crystalline properties.
Table 4.1: Melting temperatures of the intermediates, methyl 3,4,5-trialkoxybenzoates, 1a-b and 3,4,5-trialkoxybenzoic acids, 2a-b.

<table>
<thead>
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<th>Structures</th>
<th>α</th>
<th>β</th>
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</thead>
<tbody>
<tr>
<td><img src="image" alt="Methyl 3,4,5-trialkoxybenzoate" /></td>
<td>α52.7-53.8</td>
<td>α49.3-50.5</td>
</tr>
<tr>
<td><img src="image" alt="3,4,5-trialkoxybenzoic acid" /></td>
<td>α57.9-58.2</td>
<td>α46.8-47.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Structures</th>
<th>T/°C</th>
<th>ΔH, kJ mol⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>αMicroscope values (°C). βLiterature values (°C).</td>
<td></td>
<td></td>
</tr>
<tr>
<td><img src="image" alt="Methyl 3,4,5-trialkoxybenzoate" /></td>
<td>Cr1 45.6 Cr2 52.3 Cub 121.4</td>
<td>38.5 40.3 1.1</td>
</tr>
<tr>
<td><img src="image" alt="3,4,5-trialkoxybenzoic acid" /></td>
<td>Cr1 46.2 Cr2 59.9 Cub 102.0</td>
<td>23.2 15.6 0.4</td>
</tr>
</tbody>
</table>

The temperature and enthalpy phase transition data for some amphiphilic polyhydroxybenzamides is summarized in Table 4.2.

Table 4.2: Transition temperatures and enthalpies (ΔH, kJ mol⁻¹) of 3,4,5-trialkoxybenzamides, 3a-b and 4-10 with different hydrophilic groups (All the reported values correspond to the heating cycles).

<table>
<thead>
<tr>
<th>Structures</th>
<th>T/°C</th>
<th>ΔH, kJ mol⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="3,4,5-trialkoxybenzamide" /></td>
<td>Cr 48.9 Colh2 104.1 Cub 148.8</td>
<td>57.1 0.1 0.3</td>
</tr>
<tr>
<td>5</td>
<td><img src="" alt="Chemical Structure" /></td>
<td>( \text{Cr}_1 \ 40.1 \ \text{Cr}_2 \ 53.0 \ \text{Cub} \ 61.9 \ \text{Iso} \ 29.4 \ 14.3 \ 0.9 )</td>
</tr>
<tr>
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<td>---</td>
</tr>
<tr>
<td>6</td>
<td><img src="" alt="Chemical Structure" /></td>
<td>( \text{Cr} \ (&lt;25.0) \ \text{Col}_{h2} \ 74.6 \ \text{Iso} \ 86.2 )</td>
</tr>
<tr>
<td>7</td>
<td><img src="" alt="Chemical Structure" /></td>
<td>( \text{Cr} \ 43.0 \ \text{Cub} \ 51.0 \ \text{Iso} \ 18.8 \ 0.31 )</td>
</tr>
<tr>
<td>8</td>
<td><img src="" alt="Chemical Structure" /></td>
<td>( \text{Cr} \ 100.1 \ \text{Col}_{h2} \ 110.6 \ \text{Iso} \ 25.8 \ 46.7 )</td>
</tr>
<tr>
<td>9</td>
<td><img src="" alt="Chemical Structure" /></td>
<td>( \text{Cr} \ 47.6 \ \text{Cub} \ 54.5 \ \text{Iso} \ 19.4 \ 18.0 )</td>
</tr>
<tr>
<td>10</td>
<td><img src="" alt="Chemical Structure" /></td>
<td>( \text{Cr} \ 93.0 \ \text{Cub} \ 103.6 \ \text{Iso} \ 78.4 \ 1.0 )</td>
</tr>
</tbody>
</table>

\( ^a \) These are known compounds. \( ^b \) Columnar to crystalline or vice-versa could not be observed under DSC because the texture transformation might be very small and insignificant.

Temperatures below 25°C are not easily observed by POM with our hardware.

All the compounds examined here have the same hydrophobic 3,4,5-tris(\( n \)-nonyloxy)benzoic acid segment but differ in the number of hydroxy groups and their relative positions in the hydrophilic amide segment. It was reported that the nonyloxy and decyloxy derivatives of triple chain amphiphilic polyhydroxy molecules display a columnar-cubic dimorphism. \( ^7 \) The triple chain polyhydroxybenzamide shows the Cub
phase as high temperature mesophases above the hexagonal columnar (Colh₂) phase. The hexagonal columnar (Colh₂) phases of these compounds consist of extended aggregates of the hydrogen bonding networks (polar region) which are surrounded effectively by the triple alkoxy chains. This forms a circular shape of the Colh₂ phase. For cubic phase compounds, the triple tails form strongly curved aggregates due to the increased bulk of the lipophilic moiety which are not directly attached to the polyhydroxy unit, but are connected via an aromatic linking unit. All the compounds that exhibit Cub phases could be distinguished from cooling the isotropic liquid using POM only by the movement of air bubbles, which suddenly stopped at the phase transition. On heating, these compounds show Cub phases with higher transition temperatures above the hexagonal columnar (Colh₂) phases.

In Table 4.2, some known compounds 3a, 3b and 4 which were reported by Borisch et al have also been synthesized and characterized here again for comparison. Compounds 3a and 3b are racemic mixtures with similar structures but differ in their alkyl chain lengths (C₁₂ and C₉) which are attached to the rigid moiety. These homologues were reported to have exclusively Cub phases and according to the diffraction pattern of the Cub phase, compound 3a exhibits the inverted micellar structure of the primitive cubic lattice. It was also discussed that on cooling, the transition from isotropic to Cub phase is often supercooled and on heating it can be overheated. Based on the heating and cooling rate, the values could be different. On heating under POM, the transition from Cub to isotropic liquid can be detected by the increase of fluidity which shows some liquid movement.
Compounds 3b and 4 are structurally related to each other; wherein compound 4 is chiral, made from a pure carbohydrate and it has five hydroxy groups while compound 3b has only two. Due to the increased number of hydrogen bonds in compound 4, the phase transition temperatures are shifted to higher values. By using POM, compound 4 can be observed as circular shape of a hexagonal columnar phase where three nonyloxy chains are able to surround the five hydrogen bondings in the polar region. On heating compound 4, a transition from columnar to Cub phase is observed at 104.1°C before it becomes the isotropic phase at 148.8°C. On cooling compound 4 from the isotropic a Cub phase appears and further cooling shows the formation of columnar phase being supercooled at 84.0°C with very low melting enthalpy of 0.07 kJ/mol.

In Table 4.2, compound 5 is achiral and has only one hydroxy group. On heating, it exhibits Cub phase at 53.0°C and this dark area becomes isotropic at 61.9°C. On cooling compound 5 using POM, the isotropic becomes more viscous and a slow movement of some air bubbles can be observed. However, temperatures below 25.0°C are not accessible by POM with our hardware. In the DSC for compound 5, the cooling cycle shows a small curve at 25.0°C with low enthalpy value of 0.96 kJ/mol. This might refer to the isotropic-Cub phase transition. The second cooling curve is at 21.3°C (enthalpy value of 27.9 kJ/mol), which might refer to the Cub-crystalline phase transition.

Compound 6 is a racemic mixture with one chiral center, one hydroxy group and one branched methyl chain in the amide segment. On heating compound 6, its clearing temperature of columnar to isotropic phase occurs at 74.6°C. On cooling, the isotropic to hexagonal columnar phase occurs at 53.5°C. No crystalline phase reappeared even after
the temperature dropped to 25.0°C. In the DSC spectra, only one peak is observed at 53.4°C in the cooling cycle, which involves the isotropic-hexagonal columnar phase. No other peak is observed between 53.4 to 0°C. A phase transition from columnar to crystalline or vice-versa could not be observed under DSC because the texture transformation might be very small and insignificant. Temperatures below 25°C are not easily observed by POM with our hardware.

![Figure 4.4: POM photographs of the hexagonal columnar phase observed for compound 6 on cooling at 51.3°C (magnification: 50 × 10).](image)

Compound 7 is achiral and has an additional methyl group in the amide segment compared to compound 6. On heating under POM, compound 7 shows two phase transitions of crystal to Cub and Cub to isotropic at 44.2 and 52.8°C, respectively. On cooling, there is a slow movement of the isotropic liquid and it becomes Cub phase at 40°C when the small air bubble in the thin film stop moving. In DSC spectra, no cooling event in this temperature range can be observed which might be due to a supercooling
effect. In the subsequent cooling cycle, the Cub phase remains as oily streaks without any clear crystalline phase. After prolonged storage, only very little crystallization takes place. The DSC spectra shows a heating cycle of crystal to Cub phase transition at 43.0°C with an enthalpy value of 18.8 kJ/mol and a Cub to isotropic phase transition at 51.0°C with an enthalpy value of 0.31 kJ/mol. Having the same number of attractive hydrogen bonds in compound 6 and 7, more branching in the amide segment lowers the phase transition values.

Compound 8 is a chiral non-racemic compound with one chiral center, one hydroxy group and one phenyl ring in the amide segment. On heating compound 8, the crystalline to hexagonal columnar phase occurs at 100.1°C and further heating converts columnar to isotropic phase at 110.6°C. On cooling from the isotropic, a columnar phase was observed at 88.6°C and it becomes a crystalline phase at a low temperature of 14.6°C, which could be observed in the DSC spectra as a small peak in the cooling cycle.

Figure 4.5: POM photographs of the hexagonal columnar phase observed for compound 8 on cooling at 80.5°C (magnification: 10 × 10).
Both compounds 9 and 10 are also chiral non-racemic compounds with two hydroxy groups and one benzene ring branching in the chain of the amide segment. In compound 10, there is also a nitro group attached to the benzene ring at the para position. On heating compounds 9 and 10, the crystalline to Cub phases occur at 47.6 and 93.0°C, respectively. Further heating of these compounds transforms the Cub to isotropic phases at 54.5 and 103.6°C, respectively. On cooling, the isotropic phases become highly viscous domain and remain as oily streaks without any clear crystalline phases. This indicates that the crystalline phase is strongly supercooled. Even after prolonged storage, only very little crystallization takes place. In the second DSC run using the same sample, these phases are supercooled and no peaks can be observed either in the DSC heating or cooling cycles.

It was reported that increasing the number of hydroxy groups destabilizes the cubic phase and prefers the formation of a columnar phase along with a shift of the phase transition temperature to a higher temperature. Compounds 8 and 9 have very similar molecular structures but there is only one hydroxy group in compound 8 and two hydroxy groups in compound 9. Despite the fact that there are more hydroxy groups, compound 9 shows a Cub phase with lower clearing temperature value compared to compound 8 which exhibits a hexagonal columnar phase at a higher clearing temperature value. This result contradicts the earlier report. Both compounds 8 and 9 have one phenyl ring attached at the amide segment and probably this group contributes to the stabilizing effect which might be the reason for the reverse factor.
Compounds 9 and 10 have the same molecular structure, with two hydroxy groups and one phenyl ring attached at the amide segment. Both compounds exhibit Cub phases at different temperatures. In these compounds, the hydroxyl groups are positioned close to the hydrophilic-lipophilic interface curvature which gives rise to the curved aggregate of the Cub phase. Compound 10 has an additional nitro group at the para position of the phenyl ring and shows higher melting and clearing temperatures, compared to compound 9. The electron withdrawing nitro group is at least partially responsible for the higher phase transition values.

4.5 Conclusion

A study on a series of trialkoxy benzamides derived from different amino alcohols with a range of hydroxy groups has been undertaken seeking substances with Cub mesophases. Compounds 3a and 3b with two hydroxy groups show Cub phases while compound 4 with five hydroxy groups exhibits both columnar and Cub phases. Compounds 5-8 with only one hydroxy group show different mesophases depending on the group attached to the amide segment. Compound 5 has straight alkyl chain at the amide segment and shows a Cub phase. Compound 7 with more branching at the amide segment prone to exhibit Cub phase which is due to the formation of curved aggregate, compared to compound 6.

Compounds 9 and 10 with two hydroxy groups and one phenyl ring on the amide segment. The hydroxy groups are positioned in the close hydrophilic-lipophilic interface curvature which gives rise to the curved aggregate of the Cub phase. Compound 8 has
only one hydroxy group which is positioned in an extended aggregate to exhibit columnar phase. We have identified some additional Cub phase materials in this study and the next step, remaining to be done, will be to synthesize a comparable series of semifluorinated materials.

4.6 References


Chapter 5

Studies of some selected 2,5-disubstituted-1,3,4-oxadiazole compounds

- Synthesis, characterization and potential applications
5.1 Introduction

In recent years, compounds with a 1,3,4-oxadiazole ring system have received much attention due to their unique properties. Heterocyclic compounds of 2,5-disubstituted 1,3,4-oxadiazoles have attracted significant interest because of their potential use in the areas of medicine, agricultural, polymer, liquid crystals and materials science. Some of these compounds are known for their high thermal and hydrolytic stability. It was also reported that compounds with the oxadiazole ring are often chemically stable and the electron-accepting property of the oxadiazole ring enables substances incorporating it to be use as electron transport layers in applications of organic light-emitting devices (OLEDs). Some liquid crystalline compounds with a 1,3,4-oxadiazole ring have been discussed earlier in Chapter 3. Another interesting liquid crystal category, which has been extensively developed, involves fluorine-containing compounds.

5.2 Research Proposal

We are interested to merge these two categories, fluorine-containing compounds and 1,3,4-oxadiazoles, to form new types of improved 2,5-functionalized-1,3,4-oxadiazole compounds which are able to show an increase in their functionality through modification at the substituent positions. There are three types of main intermediates of 1,2 and 3, which were synthesized and used separately for different synthesis studies (Figure 5.1). Studies of substitution at different positions in the molecules were also
initiated to understand how the 1,3,4-oxadiazole unit influences the reactions and whether such transformations may help to induce liquid crystalline properties.

![Figure 5.1: Some of the intermediates used in the synthesis studies here include ethyl 5-(4-fluorophenyl)-1,3,4-oxadiazole-2-carboxylate, 1; 2-(chloromethyl)-5-(4-fluorophenyl)-1,3,4-oxadiazole, 2 and 5-(4-fluorophenyl)-1,3,4-oxadiazole-2-carbonitrile, 3.](image)

### 5.3 Synthesis, Results and Discussion

Functionalized 1,3,4-oxadiazole derivatives can be synthesized by several general preparative methods. Ester substituted intermediate 1 can be readily synthesized according to the synthesis route shown in Scheme 1 which first involves the transformation of 4-fluorobenzonitrile to 5-(4-fluorophenyl)-1H-tetrazole, 19 4.  

![Scheme 5.1: The preparative routes for the intermediate 1 via tetrazole intermediate, 4.](image)
The tetrazole moiety is a nitrogen-rich ring system. The most direct method to form tetrazoles is the reaction between an azide and a nitrile. In this case, the reaction involves the activation of the nitrile by protonation which proceeds through a 4-fluorobenzimidoyl azide intermediate. The proposed mechanism for the transformation of 4-fluorobenzonitrile to the tetrazole intermediate 4 is illustrated in Figure 5.2. Heating the reaction mixture of 4-fluorobenzonitrile, sodium azide and glacial acetic acid in n-butanol provides compound 4 in excellent yield, 85%. Intermediate 1 did not show any liquid crystalline behavior. Under polarized optical microscopy (POM) the melting temperature for compound 1 is 212.0°C.

![Diagram of proposed mechanism](image)

Figure 5.2: Proposed mechanism for the transformation of a nitrile to a tetrazole.

The free N-H bond of the tetrazole makes the molecule acidic and interestingly, the pKa values of tetrazoles correspond approximately to those of carboxylic acids. This substituted tetrazole was further transformed into substituted 1,3,4-oxadiazoles by reaction with a variety of acid chlorides. Intermediate 4 can exist in two tautomeric forms, 4 and 5, as illustrated in Figure 3. However, compound 5 preferentially reacts with ethyl oxalyl chloride to form the acylated derivative 6, followed by loss of nitrogen and ring opening to give intermediate 7, which then finally closes to give oxadiazole.
intermediate 1. This compound is not a liquid crystal and has a melting temperature of 104.1°C. The proposed mechanism for the transformation of tetrazole 4-5 to oxadiazole intermediate 1 is illustrated in Figure 5.3.

Figure 5.3: Scheme for the transformation of a substituted tetrazole to a 2,5-disubstituted-1,3,4-oxadiazole.22

Several synthetic studies to exploit the reactivity of intermediate 1 have been undertaken here. A series of different reactions using intermediate 1 is illustrated in Scheme 2. Transesterification is one of the most important organic reactions and a convenient method for ester preparation.23 From a dibutyltin oxide-catalyzed transesterification24 of intermediate 1 and n-heptanol shown in Scheme 5.2, the formation of compound 8, heptyl 5-(4-fluorophenyl)-1,3,4-oxadiazole-2-carboxylate was accomplished but in low yield. The reaction mixture was refluxed in a vacuum distillation setup and the toluene was continuously removed from the system to drive the reaction to completion.24
Scheme 5.2: Synthesis routes for different target compounds using intermediate 1

A few transesterification attempts were made and most of the reactions did not give a high yield and the best yield was only 20%. Compound 8 was identified based on the \(^1\)H NMR spectrum. The aromatic protons show a multiplet at 8.16-8.20 ppm and a triplet at 7.24 ppm while a quartet at 4.52-4.58 ppm and a triplet at 1.48 ppm confirm the ester protons. Compound 8 is not a liquid crystal and has a low melting point of 42.5°C.

Hydrolysis is one of the common reactions to make an acid from an ester. This nucleophilic acyl substitution type reaction, which is also known as saponification, is one of the most studied reactions. Hydrolysis\(^{25}\) of intermediate 1 provided only the
decarboxylated product compound 10 and none of compound 9 (Scheme 5.2).

Saponification of intermediate 1 with potassium hydroxide (10 N) in ethanol and THF at 0°C to room temperature yielded the decarboxylated compound 10. Compound 10 was identified based on the 1H NMR spectrum where the aromatic protons show a multiplet at 8.08-8.12 ppm, a triplet at 7.22 ppm a singlet at 8.46 ppm for one proton. Another reaction26 adopts the same method but instead of THF, diethyl ether was used to mix with intermediate 1, and potassium hydroxide in ethanol was added dropwise into the reaction mixture. Compound 10 was formed where characterization using 1H NMR shows a singlet at 8.46 ppm for one proton in compound 10. No other peaks for an ethyl ester are observed.

In general, the nature of the leaving group influences the rate and the course of nucleophilic substitution reaction. The reaction usually benefits from polar aprotic solvents such as dimethyl formamide, DMF or dimethyl sulfoxide, DMSO and is performed at temperatures between 0 – 100 °C and in the case of less reactive precursors or less reactive nucleophiles still higher boiling solvents such as N-methylpyrrolidone, NMP may be used. The aromatic precursor in intermediate 1 bears a strong electron-withdrawing group, the ester substituted 1,3,4-oxadiazole heterocycle ring in the para position. The electron deficient oxadiazole ring activates the benzene ring towards nucleophilic attack during which the fluorine is displaced by the nucleophile. In this particular compound, the reactive site for possible nucleophilic substitution reaction is not only at the fluorine position but also at the ester position as the oxadiazole also activates the carbonyl of the ester towards nucleophilic acyl attack. In our experiments, as
illustrated in Scheme 5.2, we tested the addition of piperidine (nucleophile) to intermediate 1 in DMSO under different reaction conditions.

Several different products were observed. Reaction of intermediate 1 under vigorous conditions, in the presence of potassium tert-butoxide, K-OtBu as base, produced compound 11, 2-(4-(piperidin-1-yl)phenyl)-1,3,4-oxadiazole with low yield (24%). In the $^1$HNMR spectrum, two doublets at 6.95 and 7.92 ppm refer to the aromatic protons and a singlet at 8.36 ppm refers to a proton attached directly to the 1,3,4-oxadiazole ring. Two multiplets at 3.32-3.35 ppm and 1.62-1.74 ppm refer to the four and six protons in the piperidine ring which displaced the fluorine atom. No carbonyl (C=O) band was observed in the IR spectrum, which indicates that compound 11 has undergone decarboxylation. Compound 11 is not a liquid crystal and has a melting point of 162.8°C.

The postulated mechanism of reaction of intermediate 1 with piperidine might proceed via zwitterionic intermediates, as illustrated in Figure 5.4. At high temperature and in the presence of base, it can be postulated that an E2 type reaction may occur where ethylene and CO$_2$ are released to yield compound 12.

Figure 5.4: Postulated mechanism of intermediate 1 to compound 11.
Using the same reaction conditions but with an excess piperidine without any base, the two products 11 (18%) and 12 (38%) were obtained. Compound 11 was formed after decarboxylation where the second piperidine acts as a base and undergoes the E2 type reaction, as postulated in pathway 3 (Figure 5). Compound 12 piperidin-1-yl(5-(4-(piperidin-1-yl)phenyl)-1,3,4-oxadiazol-2-yl)methanone shows that nucleophilic substitution can occur at both fluorine and ester positions, as postulated in pathway 1 (Figure 5.5). The $^1$H NMR spectrum for compound 12 shows two doublets at 6.94 and 7.97 ppm. There are two triplets at 4.06 and 3.76 ppm, each integrates two protons for the piperidine ring, which displaced the fluorine atom. One multiplet at 3.34-3.37 ppm integrates four piperidine protons at the amide position and a multiplet at 1.65-1.72 ppm integrates twelve protons for both piperidine rings. Compound 12 is not a liquid crystal and has a melting point of 131.5 °C.

![Figure 5.5: Postulated mechanism of intermediate 1.](image)
In Figure 5.5, there are three possible pathways for these reactions to occur. In the tetrahedral intermediate, kicking out the ethoxide group gives compound 12 or kicking out the piperidine gives ethyl 5-(4-(piperidin-1-yl)phenyl)-1,3,4-oxadiazole-2-carboxylate. The third pathway gives the decarboxylated product, 11.

The same reaction run at room temperature, either with or without base, provides two possible products of compounds 12, and 13, (5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl)(piperidin-1-yl)methanone. Reaction without base at room temperature produces compounds 12 (30%) and 13 (35%) while reaction with Hunig’s base at room temperature also produces compounds 12 (8%) and 13 (58%). Compound 13 is not a liquid crystal and has a melting point of 106.1°C.

Further investigation of the nucleophilic substitution of intermediate 1 with alkoxide was done by reaction with n-heptanol and sodium hydride in N-methylpyrrolidone, NMP as shown in Scheme 5.3.28 A mixture of sodium heptyloxide in NMP was first prepared before the addition of intermediate 1. The product of nucleophilic aromatic substitution of heptyloxide at the fluorine position was not detected but instead, decarboxylation occurs to give compound 10. The 1HNMR spectrum shows a singlet at 8.46 ppm, which is due to the proton at 5-position in the 1,3,4-oxadiazole ring.
Our next attempt was to produce compound 15 using a more conventional synthetic route\textsuperscript{29,30} (Scheme 5.3). Here, the \(n\)-nonyloxy chain (the alkoxy group) was attached to the benzene ring from the beginning. The reaction with hydrazine hydrate formed the hydrazide compound, which then was further reacted with ethyl oxalyl chloride to produce compound 14 in good yield. Cyclization of compound 14 with phosphorus oxychloride, POCl\(_3\) yielded compound 15 also in a good yield.

Compound 14, ethyl 2-(2-(4-(nonyloxy)benzoyl)hydrazinyl)-2-oxoacetate shows two bishydrazone protons at 9.91 and 9.07 ppm. Two doublets at 6.92 and 7.70 ppm refer to the aromatic protons. A quartet at 4.38-4.43 ppm and a triplet at 1.40 ppm confirm the ethyl ester group in the compound. Three multiplets at 1.78-1.81, 1.42-1.50 and 1.25-1.38 ppm and a triplet at 0.88 ppm refer to the aliphatic protons from the \(n\)-nonyloxy chain. Compound 14 is a liquid crystal molecule with a phase sequence of Cr-Col\(_{h2}\)-I. The
melting and clearing temperatures of this compound are 69.1 and 88.0°C, respectively. On heating, the DSC peak can be observed at 68.93°C (Colh2 phase) and at 87.84°C (isotropic liquid). Figure 5.6 shows representative texture of compound 14.

Figure 5.6: POM photographs of 14 on cooling (I- Colh2-Cr); Colh2 texture at 45.3 °C (magnification: 10 × 10).

Compound 15, ethyl 5-(4-(nonyloxy)phenyl)-1,3,4-oxadiazole-2-carboxylate is the cyclization product of compound 14. It shows the same pattern of the NMR protons but without two small singlets of bishydrazide protons above the aromatic region. Compound 15 with a 1,3,4-oxadiazole ring is not a liquid crystal molecule and has a melting point of 64.0°C. A suppression of mesomorphic behavior observed in this compound may be due to the 1,3,4-oxadiazole ring, which deviates from the co-linear 180 degree configuration.

A series of novel fluorophores, dicyanomethylenedihydrofuran (DCDHF) dyes with an olefin link (Figure 5.7) have been intensively studied also in Twieg’s group.31-36
Studies showed that these molecules also provide a rich class of chromophores for photorefractive applications.

![Diagram of DCDHF chromophores](image)

Figure 5.7: Retrosynthesis of DCDHF chromophores.

The DCDHF chromophore contains a dialkylamine donor group, a linking $\pi$-system with or without an olefin link and an acceptor group of 2-dicyanomethylene-3-cyano-2,5-dihydrofuran (DCDHF). Different combinations of aromatic units, alkene length and various amine donor structures have been used to synthesize novel compounds in this class. A tremendous amount of work has been done in order to understand how the $\pi$-conjugated system relates with the systematic changes in the fluorescence activity. These polar fluorescent dyes, which contain both electron-donating and electron-withdrawing groups, have been modified and functionalized in various locations with a wide variety of groups. So far, most of the chromophores that have been synthesized did not exhibit any liquid crystalline behavior. A common retrosynthesis route of these DCDHF precursors is as shown in Figure 5.7. Compound 19 is the condensation of commercially available 2-hydroxy-3-methyl-2-butanone with malononitrile. We are interested to synthesize some of the main precursors for a new type of DCDHF chromophores. These precursors could later be transformed into intermediate 18 of the benzene-oxadiazole unit together with an amine donor, such as piperidine. By attaching this intermediate to compound 19, a new
type of DCDHF dye, which can be used for possible biological labelling can be obtained. Figure 5.8 shows the proposed synthesis route to produce the target compound 20.

![Figure 5.8: Proposed synthesis routes for DCDHF chromophore, 20.](image)

Synthetic studies and characterization of intermediates 17, 2-(4-fluorobenzoyl)-5-(chloromethyl)-1,3,4-oxadiazole have already been done. Precursor 2 can be prepared using three different routes, as shown in Scheme 5.4. The first route involves transformation of 4-fluorobenzonitrile to 5-(4-fluorophenyl) tetrazole,\(^19\) which is then transformed into a variety of substituted 1,3,4-oxadiazoles by reaction with the appropriate acid chlorides to yield the expected compound 2. The second route is a common synthesis pathway which involves 1,2-diacylhydrazine, followed by cyclization with phosphorus oxychloride.\(^5,37\) The third route involves the cyclization of an acyl hydrazide with chloroacetyl chloride\(^38\) to give the expected precursor 2.
Scheme 5.4: Three possible synthesis routes to obtain chloromethyl precursor 2.

The compound \( N'-(2\text{-chloroacetyl})-4\text{-fluorobenzoyl hydrazine} \) from the second synthesis route in Scheme 4 shows two bishydrazide protons at 9.29 and 8.91 ppm in the \( ^1\text{H} \) NMR spectrum. The aromatic protons show a multiplet at 7.83-7.89 ppm and a triplet at 7.14 ppm. There is also a singlet for methylene proton peak at 4.18 ppm. This compound is not mesogenic and has a melting point of 160.1°C. The \( ^1\text{H} \) NMR for precursor 2 shows two singlets of bishydrazide protons. The aromatic protons are multiplet (8.07-8.12 ppm) and a triplet (7.23 ppm) with a singlet at 4.78 ppm for the methylene protons.

A series of intermediates to obtain compound 17 have been synthesized and characterized. As shown in Scheme 5.5, the reaction of chloromethyl precursor 2 produced azide compound 16, 2-(4-fluorobenzoyl)-5-(azidomethyl)-1,3,4-oxadiazole in good yield (82%), which is obtained by nucleophilic replacement of the halogen atom by the azido group under conditions of phase-transfer catalysis using benzyltrimethylammonium chloride, BTMAC\(^{39}\). Decomposition of the resulting azido
compound in concentrated sulfuric acid\textsuperscript{39} afforded the expected aldehyde 17, 5-(4-fluorophenyl)-1,3,4-oxadiazole-2-carbaldehyde, also in moderate yield.

\[
\begin{array}{c}
\text{F-} \quad \text{O} \\
\text{N} \quad \text{N} \quad \text{Cl} \quad \text{Cl} \\
\text{H} \quad \text{H} \\
\text{F} \quad \text{F} \\
\end{array}
\quad \xrightarrow{\text{NaN}_3, \text{BTMAC, H}_2\text{O}}
\quad \begin{array}{c}
\text{C} \quad \text{N} \quad \text{N} \\
\text{H} \quad \text{H} \quad \text{H} \\
\end{array}
\quad \xrightarrow{\text{H}_2\text{SO}_4 (\text{conc.})}
\quad \begin{array}{c}
\text{F} \quad \text{O} \\
\text{N} \quad \text{N} \\
\end{array}
\quad \text{BTMAC} = \text{Benzyltrimethylammonium chloride, 98%}
\]

Scheme 5.5: Synthesis routes of intermediates to produce compound 17.

The $^1$H NMR peaks for 16 show the aromatic multiplet (8.06-8.11 ppm) and a triplet (7.23 ppm) with a singlet at 4.63 ppm. In $^{13}$C NMR spectrums, the methylene carbon for precursor 2 is at $\delta$ 32.97 ppm while for compound 16, it is at $\delta$ 44.36 ppm. The IR spectrum confirms the absorption band at 2100 cm\textsuperscript{-1} which is typical for azido group in compound 16. Both compounds 2 and 16 are not liquid crystal molecules and have melting temperatures of 80.8 and 85.4°C, respectively. Further reaction of compound 16 in concentrated sulfuric acid at 0°C for 8 h transformed the azide to the aldehyde in quite good yield (70%)\textsuperscript{39}. The $^1$H NMR peaks for compound 17 confirms the expected product 5-(4-fluorophenyl)-1,3,4-oxadiazole-2-carbaldehyde. A singlet at 10.05 ppm refers to the aldehyde proton while the aromatic protons show a multiplet (8.20-8.23 ppm) and a triplet (7.27 ppm). In $^{13}$C NMR, there is an intense peak at 176.09 ppm for the aldehyde carbon which is slightly upfield compared to the normal aldehyde position. This might be due to the electron deficient 1,3,4-oxadiazole ring, which is attached directly to the carbonyl. The carbonyl band for the aldehyde is at 1705 cm\textsuperscript{-1} in the IR spectrum.
An alternative route to transform precursor 2 to compound 17 which involves a microwave version of a typical Kornblum oxidation\(^{40}\) was also investigated. In the past few years, microwave-assisted synthesis in organic reactions has been of growing interest due to the remarkable decrease in reaction time, better yields and more convenient procedure. We are interested to adopt this one step oxidation of precursor 2 to compound 17 using the method proposed by Xu et al.\(^{40}\) It is a straightforward and environmentally-friendly method for the oxidation of organic halides to the corresponding aldehydes using DMSO as oxidation reagent (Scheme 5.6), followed by a direct workup procedure in basic aqueous solution to form the corresponding aldehyde.\(^{41-43}\)

![Scheme 5.6: Synthesis routes (microwave-assisted) to obtain compound 17.](image)

The reaction was performed using a CEM Discover microwave (P: 250W, T: 250 °C). Different bases such as NaHCO\(_3\) and Et\(_3\)N were used to find the optimal reaction conditions and the reactions were run in different time frames (5, 20 and 30 mins). So far, most of the reactions produce mixtures of the product and its starting material. The postulated mechanism for Kornblum oxidation is as illustrated in Figure 5.9. Reaction of DMSO with the substituted halide, 2 creates an alkoxy sulphonium ion which in the presence of base will eliminate to form the desired aldehydes, 17.
Another interesting area to explore is the investigation of some other potential reactions of different functional groups on the benzene-oxadiazole system. We are interested to look further into the structure-property relationship of these benzene-oxadiazole systems. Specifically, we are interested in the potential reaction between the cyano group of precursor 3, 5-(4-fluorophenyl)-1,3,4-oxadiazole-2-carbonitrile (page 117) and 1,2-aminothiols such as is found in derivatives of HSCH₂CH₂NH₂ where one or more H on -CH₂- is replaced by something other than hydrogen.

Precursor 3 can be prepared according to the synthesis route shown in Scheme 5.7. Oxamic hydrazide reacts with 4-fluorobenzoyl chloride in two different solvents via two different methods to produce the oxoacetamide derivative, 21, 2-(2-(4-fluorobenzoyl)hydrazinyl)-2-oxoacetamide which then undergoes cyclodehydration with phosphorus oxychloride to give precursor 3, in moderate yield.³⁰
Scheme 5.7: Synthesis routes for precursor 3.

Compound 21, 2-(2-(4-fluorobenzoyl)hydrazinyl)-2-oxoacetamide is identified based on the $^1$H NMR spectrum of two singlets for bishydrazide protons at 10.62 and 10.48 ppm and two singlets at 8.19 and 7.91 ppm due to the primary amides. The aromatic protons show a multiplet at 7.91-7.97 ppm and a triplet at 7.35 ppm. Compound 21 is not a liquid crystal molecule and has a melting point of 270.1°C. The $^1$HNMR of precursor 3 shows the aromatic protons of a multiplet (8.12-8.16 ppm) and a triplet (7.28 ppm). In the $^{13}$C NMR spectrum, there is a peak at δ 106.19 ppm that is due to the nitrile carbon. Further confirmation in the IR spectrum shows a band at 2260-2220 cm$^{-1}$ region for the C≡N functional group.

Several synthetic studies to evaluate the reactivity of intermediate 3 have been pursued. Several different reactions using intermediate 1, as illustrated in Scheme 5.8 produce different target materials.
Scheme 5.8: Proposed synthesis routes for different target compounds.

Reaction of precursor 3 with piperidine in DMSO, in the presence of Hunig’s base at room temperature yielded amide derivative 13 in good yield (87%). $^1$H NMR spectrum shows the aromatic protons of a multiplet at 8.09-8.16 ppm and a triplet at 7.23 ppm. The multiplets at 3.50-3.62 and 1.62-1.76 ppm integrate as four and six protons, respectively for the piperidine. The reaction of precursor 3 with piperidine (ratio of 1:3) without any base under reflux conditions produced compound 12 in low yield (15%). $^1$H NMR spectrum shows two doublets at 6.93 and 7.97 ppm for the aromatic protons. Two multiplets at 4.03-4.09 and 3.73-3.80 ppm which integrate two protons each, refers to the piperidine ring at the fluorine position. One multiplet at 3.31-3.38 ppm which integrates for four protons is due to the piperidine ring at the amide position. Another multiplet at
1.63-1.76 ppm integrates for twelve protons and is due to the rest of the protons in both piperidine rings.

Nitrogen-containing five-membered heterocyclic compounds such as 2-thiazolines are of great interest due to their importance as building blocks in pharmaceutical agents and possess interesting bioactivities in natural products and biomedical applications. In this case, the preparation of the thiazoline segment was accomplished by the cyclo-condensation of the nitrile derivatives with aminothiol. Reaction of precursor 3 with 2-mercaptoethylamine hydrochloride or cysteamine hydrochloride in ethanol in the presence of Hunig base under nitrogen atmosphere afforded compound 22, 2-(4,5-dihydrothiazol-2-yl)-5-(4-fluorophenyl)-1,3,4-oxadiazole in low yield (18%). The pure compound could be isolated after separation using silica gel column chromatography. $^1$HNMR spectrum shows the aromatic protons of a multiplet (8.18 ppm) and a triplet (7.22 ppm). Two triplets at 4.59 and 3.56 ppm refer to the methylene protons in the thiazoline ring. Compound 22 is not a liquid crystal molecule and has a melting point of 194.5°C.

When L-cysteine ethyl ester hydrochloride was used in the same reaction, the expected compound 23, (S)-ethyl-2-(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl)-4,5-dihydrothiazole-4-carboxylate could not be isolated as pure product. The reactions were repeated several times but no pure compounds could be isolated. The reaction using cysteamine hydrochloride occurs mainly at the –NH$_2$ position to give the expected compound 22 whereas for L-cysteine ethyl ester hydrochloride, the reaction might occur at the –SH group, presumably for steric reasons. The presence of –COOEt group, alpha to
the –NH₂ promote a reaction at the less sterically hindered –SH group. This might lead to a more complex or mixture of components in the reaction product. In any case, this result is only preliminary and further study is warranted.

5.4 Conclusion

This chapter contains a variety of related synthesis efforts, which focused mainly on three different oxadiazole precursors as the starting materials. Laboratory work on some of these components is incomplete and there are various synthetic suggestions for further work in these areas.

5.5 References


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Chapter 6

Optimization of Flexoelectric and Blue Phase Bimesogens
6.1 Introduction

6.1.1 Blue Phase Liquid Crystals (BPLCs)

Blue phases are liquid crystal phases that may appear between a cholesteric phase and an isotropic liquid and usually with a very narrow temperature range of only a few degrees Kelvin. In this phase, the molecular directors rotate in a helical fashion perpendicular to lines that form a number of helical axes in different directions. It is sometimes called a double twist structure even though an unlimited number of axes are present and is more stable than the single twist structure found in cholesteric molecules. The double twist structures are limited in all directions to the distance from the center line where the twist amounts to 45° and a double twist cylinder results. Such a cylinder is more stable because of its small radius compared to the same volume filled with only one single twist of cholesteric liquid crystal (Figure 6.1).

![Figure 6.1:](image)

Figure 6.1: (a) Perspective view of a double twist structure with two helical axes, h₁ and h₂; (b) Top view of a double twist cylinder with three helical axes; (c) Perspective view of a double twist cylinder (outside lines indicate a 45° rotation of the director).
Blue phases have a regular three-dimensional cubic structure of defects. If the spacing between the defects is in the range of the wavelength of light, interference occurs in a certain wavelength range for light reflected from the lattice (especially blue colored light). These double twist cylinders form a cubic lattice wherein the defects occur at the contact point of the cylinders\(^3\) (Figure 6.2).

![Figure 6.2: (a) A cylindrical region of double twist structure; (b) Intersection of three double twist cylinders which form a defect; Arrangement of double twist cylinders which may exist in (c) BPI and (d) BPII.\(^4\)](image)

Liquid crystals are typically rodlike anisotropic materials with parallel orientation and limited positional order, forming one or several mesophases between the solid crystal and isotropic liquid phase. The refractive index and the static dielectric constant depend on the orientation of the director and the electric field which cause the birefringence and dielectric anisotropy, respectively. This phenomenon is exceptional for blue phases materials which appear in chiral systems in the temperature range just below the isotropic liquid phase.\(^5\) These phases are optically isotropic and they are not birefringent.\(^6\)
However, they may show colors due to the selective reflection of circularly polarized light. Three different thermodynamically stable blue phases, BPI, BPII and BPIII have been observed on cooling from the isotropic phase to the chiral nematic phase. They are the colorful BPI and BPII and the misty blue BPIII which are separated by first order transitions. Both BPI and BPII have long-range orientational order with 3-D cubic symmetry that is the body-centered cubic (BPI) and simple cubic (BPII) while BPIII is only isotropic (Figure 6.3).

Figure 6.3: Schematic representation of the defect line and cubic lattice formed by double twist cylinders (left), defect lines (middle) and POM photographs for (a) BPI and (b) BPII.

It was reported that some new materials possess blue phases with enhanced thermal stability from 1°C range to 30°C range and the flexoelectricity effects observed in them are profound. This report is of interest as most any practical application of some electro-
optical phenomenon in a blue phase will require an operating temperature regime well in excess of the few degree range characteristic of conventional materials. Coles reported that the stabilization of these blue phases over a wide temperature range of 60°C in a mixture of three homologous dimers mixed in equal proportion with a small amount of chiral dopant.

6.1.2 Flexoelectric effects in liquid crystals

Flexoelectricity is described as an in-plane rotation of the short pitch chiral nematic material’s optic axis (one-dimensional helices) when an electric field is applied perpendicular to the helix axis. The flexoelectric liquid crystals have short response times (in the microsecond range). The flexoelectric effect arises when a liquid crystal develops a spontaneous polarization due to the deformation of the directors. These deformations (curvature strains) do not have a center of symmetry and they can be categorized into three types: splay, twist and bend. The twist deformation is not connected to the local polarization because there is always an axis of rotation perpendicular to the helix axis of the twist, whereby any polarization along the twist axis averages out to zero. To display the flexoelectric effect, the molecules should adopt certain shapes such as are found in wedge-, pear- or banana-shaped molecules now known to possess flexoelectricity. Wedge-shaped molecules can efficiently pack to show a splay formation and banana-shaped molecules show a bend formation. A combination of splay and bend deformations leads to a preferred direction of orientation of the
molecular dipole moments and hence a flexoelectric polarization of a nematic phase.\textsuperscript{15,16}

Examples are as shown in Figure 6.4.

Blue phase materials possess a cubic symmetry and have a double twist cylinder (two-dimensional helix) structure. In spite of having a very narrow temperature range, the study of the flexoelectric effect in these blue phase materials has resulted in the research work initiated in this chapter. Most of the molecules examined for the flexoelectric materials are not exactly a rod-like but instead they adopt features of permanently bent molecules, such as the banana-shaped molecules or at least have structures of bent
conformation available, such as in the bimesogens. Quite a number of bimesogen materials have been developed for this purpose.18-23

6.1.3 Arene-perfluoroarene interactions

Supramolecular systems based on arene perfluoroarene interactions have attracted much attention due to their noncovalent intermolecular interactions.24 The body of work reported about this electrostatic interaction between arenes and perfluoroarenes or their derivatives is a subset of what had been described as “charge-transfer complexes”.25-28 It has been known for some time that benzene and hexafluorobenzene undergo a favorable interaction of face-to-face stacking in a co-crystal structure.25 Hexafluorobenzene has a quadrupole moment that is about equal in magnitude but opposite in sign to that of benzene. The regions of negative electrostatic potential in benzene are regions of positive electrostatic potential in hexafluorobenzene, and likewise the regions of positive electrostatic potential in benzene are regions of negative electrostatic potential in hexafluorobenzene. This is because the H is less electronegative than an sp² C while F is more electronegative than an sp² C. Due to these differences, benzene and hexafluorobenzene experience a favorable face-to-face stacking interaction or a quadrupole-quadrupole interaction29 (Figure 6.5).
Figure 6.5: Schematic representation of the $\pi-\pi$ stacking geometries: (a) T-shaped or edge-to-face; (b) displaced or slip stacking (c) face-to-face stacking.\(^{29}\)

6.2 Research Proposal

We propose examination of a particular class of locally perfluorinated bimesogens having potential flexoelectric and blue phase properties. Blue phases which occur in chiral liquid crystals are very interesting three dimensional self-organized structures with unusual cubic symmetry.\(^{30,31}\) We are interested to learn whether flexoelectricity is related to the stability of these wide temperature range blue phase liquid crystals and further investigation will examine whether the electrostatic interactions involving arene-perfluoroarene systems may further enhance this blue phase stability and flexoelectric behavior.

In our earlier work, we have synthesized and characterized again the three homologous dimers originally proposed by Coles.\(^{7}\) These dimers which we have prepared are currently under examination at the Liquid Crystal Institute. In our follow-up work, we now focus on the preparation of a new class of bimesogens with more highly fluorinated systems, as illustrated in Figure 6.6. In these cases, the ArF unit is a highly fluorinated ring which has the opposite electrostatic properties compared to the ArH ring. These ArH
and ArH (or ArF and ArF) have mutual cofacial repulsion while the ArH and ArF have mutual cofacial attraction. We will prepare a variety of different combinations of number and relative location of fluorinated rings in these bimesogens and examine the impact on the phase behavior and any possible influence on flexoelectric phenomena.

<table>
<thead>
<tr>
<th>Compounds (n = 7, 9, 11)</th>
<th>Abbreviation</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Compound 2" /></td>
<td>H-H—H-H</td>
</tr>
<tr>
<td><img src="image" alt="Compound 3" /></td>
<td>F-F—F-F</td>
</tr>
<tr>
<td><img src="image" alt="Compound 4" /></td>
<td>H-F—F-H</td>
</tr>
<tr>
<td><img src="image" alt="Compound 5" /></td>
<td>F-H—H-F</td>
</tr>
<tr>
<td><img src="image" alt="Compound 6" /></td>
<td>H-F—H-F (or F-H—F-H)</td>
</tr>
</tbody>
</table>

Figure 6.6: New bimesogen materials with potential Blue Phase/ Flexoelectric properties.

Rings bearing an “F” are fully fluorinated.

The first part of the study covers the understanding of several different dimers with a single heptyloxy linkage between the two conjugated end sections. Our work
involves the study on the synthesis and mesomorphic behavior of these types of dimers, 1-6. We hope to complete synthesis and characterization of at least one full series of compounds in Figure 6.6, with a common bridge size perhaps with n=7.

6.3 Synthesis

The three homologues dimers, 1a-c were synthesized and characterized according to Scheme 6.1. First, 4-Bromo-3-fluorophenol and 4-fluorophenyl boronic acid undergo Suzuki coupling to produce the fluorinated 4-phenylphenol. Next this precursor reacts with some α,ω-diols in a Mitsunobu reaction to form the expected dimers.

\[
\begin{align*}
\text{Br} & \quad \text{F} \\
\text{O} & \quad \text{F} \\
\text{OH} & \quad \text{B(OH)}_2 \\
+ & \quad + \\
\text{Pd(PPh}_3)_4 \ (0.05 \text{ eq}) & \quad 2\text{N aq K}_2\text{CO}_3 \\
\text{Benzene-EtOH} & \\
\text{Br} & \quad \text{F} \\
\text{F} & \quad \text{OH} \\
\text{O} & \quad \text{F} \\
\text{OH} & \quad \text{B(OH)}_2 \\
\text{PPh}_3, \text{DIAD} & \quad \text{THF, rt} \\
\text{48 h, N}_2 & \\
\text{n} & = 7, 9, 11 \\
1a-c & 
\end{align*}
\]

Scheme 6.1: The synthesis routes of three homologous dimers, 1a-c.

There are four biphenols needed for the preparation of the target dimers in Figure 6.6. The synthesis routes for these biphenol intermediates are as shown in Scheme 6.2. Decafluorobiphenyl readily undergoes nucleophilic substitution at the 4- and 4’-positions. When refluxed in t-BuOH in the presence of potassium hydroxide, the fluoro substituents at the active positions are replaced by the hydroxyl groups to afford the
mono-, 7 and/or biphenol compounds depending on the exact reaction conditions.\textsuperscript{33} Phenylboronic acid reacts with iodopentafluorobenzene in the Suzuki coupling to produce precursor 8, which undergoes nucleophilic substitution reaction with hydroxide to give precursor 9. Irradiation of phenol and iodopentafluorobenzene in acetonitrile using a photochemical reactor (Rayonet photochemical reactor - Southern New England Ultraviolet company: clear glass 254 nm low-pressure mercury lamp) afforded the target compound 10 but in low yield (20%).

\[
\begin{align*}
&\text{F} \quad \text{F} \quad \text{KOH, } t-\text{BuOH} \quad \text{reflux, 24 h} \quad \text{F} \quad \text{F} \quad \text{OH} \\
&\text{B(OH)}_2 + \text{F} \quad \text{I} \quad \text{Pd(PPh}_3)_4 \quad \text{(0.05 eq)} \quad \text{2N aq K}_2\text{CO}_3 \\
&\text{DME, reflux, 24 h} \quad \text{F} \quad \text{OH} \\
&\text{F} \quad \text{I} + \text{OH} \quad \text{CH}_3\text{CN} \quad \text{Irradiation} \quad \text{F} \quad \text{OH}
\end{align*}
\]

Scheme 6.2: The synthesis routes of the intermediates 7-10.

The preparation of compounds 2-6 adopts the same Mitsunobu reaction as shown in Scheme 6.1. In this chapter, only compound 2 has been synthesized thus far, as shown in Scheme 6.3.
6.4 Results and Discussion

Precursor 7 was identified based on the $^{19}$F NMR spectrum which shows two fluorine atoms at -130.1, -132.1, -150.4 and -153.1 ppm and one fluorine atom at -142.8 ppm. These nine (five equivalent signals) fluorine atoms and a broad peak of –OH in the IR spectrum confirms precursor 7. Precursor 8 shows five (three equivalent signals) aromatic protons in the $^1$H NMR spectrum and three equivalent fluorine signals in the $^{19}$F NMR spectrum, at -135.3 (2F), -147.0 (1F) and -153.2 (2F) ppm. Nucleophilic substitution reaction of precursor 8 gave precursor 9 with five (three equivalent signals) aromatic protons in the $^1$H NMR spectrum but only two equivalent fluorine signals in the $^{19}$F NMR spectrum that are at -133.2 (2H) and -151.3 (2H). $^1$H NMR spectrum for precursor 10 shows two doublets in the aromatic region at 7.32 and 6.95 ppm. $^{19}$F NMR confirms five (three equivalent signals) fluorine atoms in the molecule that are at -135.3 (2F), -146.9 (1F) and -153.2 (2F) ppm.

A method for the synthesis of all the precursors, 7-10 required for the synthesis of all the different dimers has been developed and tested. A series of different dimers, 1-6, with a single heptyloxy bridge between the two conjugated end sections, have been
synthesized. Characterization of dimer 2 shows a clean product of 1,7-bis(4-phenylphenoxy)heptane with moderate yield (58%). Synthesis of dimer 3 using the Mitsunobu reaction did not show the expected product, 1,7-bis(perfluorobiphenyl-4-yloxy)heptane. The same reaction was repeated but dimer 3 could not be obtained. Only the starting material, 2,3,5,6-tetrafluoro-4(pentafluorophenyl)phenol was detected while examples of conversion of a mono-\(o\)-fluorinated phenol to the corresponding ether are known using the Mitsunobu reaction.\(^{34,35}\) Reports of the conversion of a difluorinated-\(o, o'\)-phenol (or still higher fluorinated phenols) to the corresponding \(o, o'\)-difluorinated ether using the Mitsunobu reaction are much less common, but do exist.\(^{36}\)

The research work accomplished thus far in this project is very preliminary. In order to get a clearer picture in this study a more comparable set of reactions needs to be done.

6.5 Conclusion

This chapter consists of some preliminary work which focused mainly on the preparation of precursors for the synthesis of a new class of highly fluorinated bimesogens. Laboratory work on the entire set of bimesogens is incomplete.

6.6 References

3. "http://www.lassp.cornell.edu/sethna/LiquidCrystals/BluePhase/BluePhases.html."
4. Cohen, J.


Appendix - Experimental Details
1. General Instrumentation and Techniques

1.1. Materials.

Chemicals were purchased from Aldrich and Acros Chemical Co. and were used without any further purification. THF was distilled from sodium and benzophenone. Anhydrous DMF was purchased from Aldrich.

1.2. Methods.

The progress of the reactions was monitored using thin-layer chromatography (TLC, Uniplate silica gel HLF with organic binder, 250 microns). Products were dried in a Napco Vacuum Oven Model 5831 at 60°C. Structure confirmation of the products was obtained by $^1$H NMR (400 MHz) and $^{13}$C NMR spectroscopy using a Bruker DMX 400 spectrometer. $^{19}$F NMR spectra were recorded using at 300 MHz. IR spectroscopy was performed on Bruker Vector 33 Fourier-transform infra-red spectrometer (FTIR) using a zinc selenide ATR and spectra are reported as neat in the unit of cm$^{-1}$.

The mesomorphic behavior was studied by thermal analysis (DSC, differential scanning calorimetry) and polarized optical microscopy (POM). The transition temperatures (°C) and latent heats were determined using DSC Standard Cell – 2920 MDSC. Samples of 5-10 mg were placed in aluminum pans and heated in a static nitrogen atmosphere. The DSC was operated at the heating and cooling rates of 5 °C min$^{-1}$ and 10 °C min$^{-1}$, respectively. The mesophases were characterized using a Mettler Toledo FP 82 HT hot stage control unit with a Nikon E600 POL polarizing optical microscope (POM).
1.3 NMR spectra

All the samples are prepared as solutions in the solvents indicated. Data for $^1$H NMR spectra are reported as follows: chemical shift, multiplicity ($s =$ singlet, $d =$ doublet, $dd =$ doublet of doublet, $t =$ triplet, $q =$ quintet, and $m =$ multiplet), coupling constant (Hz), and integration. For the semifluorinated compounds in Chapters 2 and 3, the carbons bearing fluorine atoms in the aliphatic chains show very small peaks in the NMR spectra due to multiple splittings. For these compounds, the chemical shifts for carbon-13 are recorded as: chemical shift, multiplicity (doublet, triplet or multiplet), coupling constant, $J$ (values are given in Hz) and the fluorinated carbons.$^{1,2}$ For fluorinated compounds in Chapters 5 and 6, the chemical shifts for carbon-13 are recorded as: chemical shift, multiplicity (doublet, triplet or multiplet), coupling constant (Hz).
2. Experimental procedures for Chapter-2

Synthesis of methyl 4-(n-alkyloxy)benzoates (n = 9, 10, 12). Methyl p-
hydroxybenzoate (5.00 g, 32.86 mmol) and potassium carbonate (13.60 g, 0.10 mmol)
were combined in 20.0 ml of DMF under nitrogen atmosphere and then 1-bromononane
(7.49 g, 36.15 mmol) was added and the mixture was refluxed. The reaction was
monitored by TLC. After 20 h the reaction mixture was cooled to room temperature and
poured into 200 ml of ice water. After acidification, the product was collected by vacuum
filtration, recrystallized from methanol/water and dried in the oven at 60°C to give the
expected product.

Methyl 4-(n-nonyloxy)benzoate.

![Chemical structure]

Yield = 92%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.97 (dd, J=6.8, 2.0 Hz, 2H), 6.89 (dd,
J=6.8, 2.0 Hz, 2H), 4.00 (t, J=6.6 Hz, 2H), 3.87 (s, 3H), 1.79 (q, J=6.8 Hz, 2H), 1.40-1.50
(m, 2H), 1.22–1.38 (m, 10H), 0.88 (t, J=7.0 Hz, 3H). $^{13}$C NMR (CDCl$_3$) $\delta$ 14.09, 22.66,
25.98, 29.12, 29.24, 29.36, 29.51, 31.86, 51.80, 68.22, 114.08, 122.32, 131.56, 162.98,
166.93. IR (cm$^{-1}$) 2800, 1724, 1607, 1510, 1257, 1170, 1106, 1020.

Methyl 4-(n-decyloxy)benzoate.

![Chemical structure]
Yield = 96%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.96 (dd, J=6.8, 2.0 Hz, 2H), 6.88 (dd, J=6.8, 2.0 Hz, 2H), 3.98 (t, J=6.4 Hz, 2H), 3.86 (s, 3H), 1.76-1.80 (m, 2H), 1.42-1.46 (m, 2H), 1.26–1.33 (m, 12H), 0.87 (t, J=6.8 Hz, 3H). $^{13}$C NMR (CDCl$_3$) $\delta$ 14.12, 22.69, 25.99, 29.12, 29.32, 29.37, 29.55, 29.56, 31.90, 51.81, 68.21, 114.06, 122.31, 131.56, 162.97, 166.92. IR (cm$^{-1}$) 2800, 1723, 1607, 1510, 1257, 1169, 1106, 1020.

Methyl 4-(n-dodecyloxy)benzoate.

\[
\text{C}_{12}\text{H}_{25}\text{O} \quad \bigg\|_{OCH_3}
\]

Yield = 98%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.96 (dd, J=7.2, 2.0 Hz, 2H), 6.88 (dd, J=6.8, 2.0 Hz, 2H), 3.98 (t, J=6.6 Hz, 2H), 3.86 (s, 3H), 1.76-1.79 (m, 2H), 1.42-1.46 (m, 2H), 1.25–1.35 (m, 16H), 0.87 (t, J=6.8 Hz, 3H). $^{13}$C NMR (CDCl$_3$) $\delta$ 14.12, 22.70, 25.99, 29.12, 29.36, 29.57, 29.59, 29.60, 29.64, 29.66, 31.93, 51.81, 68.20, 114.06, 122.30, 131.56, 162.97, 166.92. IR (cm$^{-1}$) 2802, 1723, 1607, 1510, 1257, 1169, 1108, 1021.

Synthesis of 4-(n-alkyloxy)benzoic acids, 1a-c. The preparation of 4-(n-nonyloxy)benzoic acid 1a is provided as a general example: A mixture of methyl 4-(n-nonyloxy) benzoate (3.00 g, 10.0 mmol) in 10 N aqueous KOH (20.0 ml), 95% EtOH (80.0 ml) and THF (20.0 ml) in a round bottom flask was refluxed. A white solid forms but dissolves when the mixture is heated. Upon completion (TLC), the mixture was cooled to room temperature and acidified. The product was collected by vacuum
filtration, recrystallized from methanol/water and dried in the oven at 60°C to give the white flakes.

4-(n-nonyloxy)benzoic acid, 1a.

\[
\begin{align*}
\text{\text{C}}_{9}\text{H}_{19}\text{O} & \quad \text{OH} \\
\text{Yield = 95\%}. \quad \text{\textsuperscript{1}H NMR (400 MHz, CDCl}_3\text{) \text{\textdelta} 8.06 (d, J=8.4 Hz, 2H), 6.94 (d, J=8.4 Hz, 2H), 4.03 (t, J=6.6 Hz, 2H), 1.82 (q, J=6.8 Hz, 2H), 1.44-1.51 (m, 2H), 1.21–1.39 (m, 10H), 0.90 (t, J=6.8 Hz, 3H).} \\
\text{\textsuperscript{13}C NMR (CDCl}_3\text{) \text{\textdelta} 14.11, 22.68, 25.99, 29.10, 29.26, 29.37, 29.52, 31.88, 68.31, 114.20, 121.40, 132.35, 163.72, 172.06.} \\
\text{IR (cm}\text{\textsuperscript{-1}) 3433-3015, 2920, 2850, 1734, 1558, 1508, 1177, 1124, 1018, 940, 846.}
\end{align*}
\]

4-(n-decyloxy)benzoic acid, 1b.

\[
\begin{align*}
\text{\text{C}}_{10}\text{H}_{21}\text{O} & \quad \text{OH} \\
\text{Yield = 91\%}. \quad \text{\textsuperscript{1}H NMR (400 MHz, CDCl}_3\text{) \text{\textdelta} 8.05 (dd, J=6.8, 2.0 Hz, 2H), 6.92 (dd, J=6.8, 2.0 Hz, 2H), 4.02 (t, J=6.6 Hz, 2H), 1.76-1.84 (m, 2H), 1.41-1.50 (m, 2H), 1.22–1.38 (m, 12H), 0.88 (t, J=6.8 Hz, 3H).} \\
\text{\textsuperscript{13}C NMR (CDCl}_3\text{) \text{\textdelta} 14.12, 22.69, 25.99, 29.10, 29.32, 29.36, 29.55, 29.56, 31.90, 68.30, 114.20, 121.36, 132.35, 163.72, 171.90.} \\
\text{IR (cm}\text{\textsuperscript{-1}) 3430-3010, 2916, 2820, 1683, 1605, 1469, 1305, 1256, 1167, 936, 845, 771.}
\end{align*}
\]
4-(n-dodecyloxy)benzoic acid, 1c.

\[
\text{C}_{12}\text{H}_{25}\text{O} - \text{O} \quad \text{OH}
\]

Yield = 94%. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.05 (dd, \(J=7.0, 2.2\) Hz, 2H), 6.93 (dd, \(J=6.8, 2.0\) Hz, 2H), 4.02 (t, \(J=6.6\) Hz, 2H), 1.76-1.85 (m, 2H), 1.41-1.51 (m, 2H), 1.22–1.39 (m, 16H), 0.88 (t, \(J=6.8\) Hz, 3H). \(^13\)C NMR (400 MHz, CDCl\(_3\)) \(\delta\) 14.13, 22.70, 25.98, 29.09, 29.36, 29.56, 29.59, 29.63, 29.64, 29.66, 31.92, 68.30, 114.21, 121.00, 132.34, 164.00, 171.40. IR (cm\(^{-1}\)) 3450-3040, 2914, 2847, 1672, 1606, 1513, 1469, 1306, 1257, 1172, 939, 845, 771.

**Synthesis of 4-n-(fluoroalkyloxy)benzoic acids, 1d-h.** All these semifluorinated benzoic acids were synthesized for earlier studies by an established method.\(^4\)-\(^8\)

4-n-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluorononyloxy)benzoic acid, 1d.

\[
\text{F}(\text{F}_2\text{C})_6(\text{H}_2\text{C})_3 - \text{O} - \text{OH}
\]

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.07 (dd, \(J=11.4, 2.6\) Hz, 2H), 6.96 (dd, \(J=8.8, 2.8\) Hz, 2H), 4.14 (t, \(J=6.0\) Hz, 2H), 2.28-2.41 (m, 2H), 2.12-2.19 (m, 2H). \(^13\)C NMR (400 MHz, CDCl\(_3\)) \(\delta\) 20.64, 28.04 (d, \(J=22.1\) Hz, CF\(_2\)CH\(_2\)-), 66.68 (-C\(_2\)H\(_2\)O-), 110-120 (m, CF\(_3\)(CF\(_2\))\(_3\)), 114.28, 122.16, 132.34, 163.0 (aromatic), 170.1 (PhCOOH). IR (cm\(^{-1}\)) 3430-3020, 2980, 2890, 1672, 1606, 1515, 1450, 1252, 1175, 1140, 1025.
4-\textit{n}-\textit{(7,7,8,8,9,10,10,10)-nonafluorodecyloxy}benzoic acid, 1e.

\[
\text{F}(\text{F}_2\text{C})_4(\text{H}_2\text{C})_6\text{O} \begin{array}{c}
\text{O} \\
\end{array} \begin{array}{c}
\text{OH} \\
\end{array}
\]

\(^1\)H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 8.06 (dd, \(J=6.8, 2.0\) Hz, 2H), 6.94 (dd, \(J=7.0, 1.8\) Hz, 2H), 4.04 (t, \(J=6.4\) Hz, 2H), 2.01-2.16 (m, 2H), 1.81-1.88 (m, 2H), 1.62-1.70 (m, 2H), 1.44-1.58 (m, 4H). \(^{13}\)C NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 20.08, 25.73, 28.82, 29.00, 34.10 (d, \(J=22.1\) Hz, CF\textsubscript{2}CH\textsubscript{2}-), 67.95 (-CH\textsubscript{2}O-), 110-120 (m, CF\textsubscript{3}(CF\textsubscript{2})\textsubscript{3}), 114.18, 125.50, 132.36, 163.50 (aromatic), 172.00 (PhCOOH). IR (\text{cm}^{-1}) 3320-3030, 2980, 2895, 1667, 1605, 1514, 1434, 1214, 1173, 1130.

4-\textit{n}-\textit{(4,4,5,5,6,6,7,7,8,8,9,9,10,10-pentadecafluorodecyloxy}benzoic acid, 1f.

\[
\text{F}(\text{F}_2\text{C})_7(\text{H}_2\text{C})_3\text{O} \begin{array}{c}
\text{O} \\
\end{array} \begin{array}{c}
\text{OH} \\
\end{array}
\]

\(^1\)H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 8.06 (d, \(J=8.8\) Hz, 2H), 6.95 (d, \(J=8.8\) Hz, 2H), 4.13 (t, \(J=6.0\) Hz, 2H), 2.27-2.41 (m, 2H), 2.12-2.19 (m, 2H). \(^{13}\)C NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 20.80, 32.05 (d, \(J=22.1\) Hz, CF\textsubscript{2}CH\textsubscript{2}-), 66.68 (-CH\textsubscript{2}O-), 109-120 (m, CF\textsubscript{3}(CF\textsubscript{2})\textsubscript{3}), 114.29, 120.20, 132.32, 155.20 (aromatic), 161.90 (PhCOOH). IR (\text{cm}^{-1}) 3400-3020, 2970, 2890, 1694, 1606, 1516, 1431, 1322, 1206, 1176, 1145, 1026.

4-\textit{n}-\textit{(7,7,8,8,9,10,11,11,12,12,12-tridecafluorododecyloxy}benzoic acid, 1g.

\[
\text{F}(\text{F}_2\text{C})_8(\text{H}_2\text{C})_6\text{O} \begin{array}{c}
\text{O} \\
\end{array} \begin{array}{c}
\text{OH} \\
\end{array}
\]

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.03 (d, J=8.8 Hz, 2H), 6.91 (dd, J=8.8, 2H), 4.02 (t, J=6.2 Hz, 2H), 1.99-2.15 (m, 2H), 1.78-1.86 (m, 2H), 1.61-1.68 (m, 2H), 1.44-1.55 (m, 4H).

$^{13}$C NMR (400 MHz, CDCl$_3$) $\delta$ 20.05, 25.73, 28.82, 30.80, 31.50 (d, J=22.1 Hz, CF$_2$CH$_2$-), 67.94 (-CH$_2$O-), 111-120 (m, CF$_3$(CF$_2$)$_5$), 114.18, 118.0, 132.36, 158.50 (aromatic), 171.50 (PhCOOH). IR (cm$^{-1}$) 3390-3020, 2970, 2870, 1673, 1606, 1514, 1428, 1262, 1184, 1144, 1072.

4-n-(5,5,6,6,7,7,8,8,9,9,10,10,11,11,12,12-heptadecafluorododecyloxy)benzoic acid, 1h.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.04 (dd, J=9.2, 2.4 Hz, 2H), 6.94 (dd, J=9.2, 2.4 Hz, 2H), 4.09 (t, J=6.0 Hz, 2H), 2.13-2.26 (m, 2H), 1.82-1.97 (m, 4H). $^{13}$C NMR (400 MHz, CDCl$_3$) $\delta$ 25.30, 28.75, 33.55 (d, J$_{C-F}$=22.1 Hz, CF$_2$CH$_2$), 67.53 (-CH$_2$O-), 110-120 (m, CF$_3$(CF$_2$)$_7$), 114.28, 121.30, 132.28, 154.10 (aromatic), 170.80 (PhCOOH). IR (cm$^{-1}$) 3380-3010, 2980, 2880, 1690, 1606, 1515, 1255, 1147, 956.

**Synthesis of 4-(n-alkyloxy)benzoyl hydrazides, 2a-c.** The preparation of 4-(n-nonyloxy)benzoyl hydrazide 2a is provided as a general example: A mixture of methyl $p$-(n-nonyloxy)benzoate (25.31 g, 0.09 mol) and an excess of a solution of hydrazine monohydrate, NH$_2$NH$_2$.H$_2$O (10.43 g, 0.21 mol) in 40.0 ml of ethanol was refluxed for 12 h. The reaction was monitored by TLC. After the reaction was complete, the mixture was cooled to room temperature and the white solid obtained was filtered off and washed with
water. The product was collected by vacuum filtration, recrystallized from methanol/water and dried in the oven at 60°C.

**4-(n-nonyloxy)benzoyl hydrazine, 2a.**

![Chemical structure of 4-(n-nonyloxy)benzoyl hydrazine]

Yield = 96%, mp = 99.6 °C. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.75 (s, br, 2H), 8.13 (s, br, 1H), 7.69 (d, J=12.0 Hz, 2H), 6.88 (d, J=12.0 Hz, 2H), 3.96 (t, J=6.4 Hz, 2H), 1.77 (q, J=6.8 Hz, 2H), 1.40-1.45 (m, 2H), 1.21–1.35 (m, 10H), 0.88 (t, J=6.8 Hz, 3H). $^{13}$C NMR (400 MHz, CDCl$_3$) δ 14.10, 22.66, 25.97, 29.11, 29.24, 29.36, 29.50, 31.86, 68.22, 114.39, 124.60, 128.65, 162.09, 168.42. IR (cm$^{-1}$) 3335, 2917, 2852, 1644, 1616, 1576, 1504, 1303, 1252, 980.

**4-(n-decyloxy)benzoyl hydrazine, 2b.**

![Chemical structure of 4-(n-decyloxy)benzoyl hydrazine]

Yield = 88%, mp = 101.2 °C. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.79 (s, br, 2H), 8.15 (s, br, 1H), 7.69 (d, J=8.8 Hz, 2H), 6.83 (dd, J=9.2, 2.4 Hz, 2H), 3.91 (t, J=6.4 Hz, 2H), 1.69-1.77 (m, 2H), 1.37-1.41 (m, 2H), 1.15–1.30 (m, 12H), 0.88 (t, J=6.8 Hz, 3H). $^{13}$C NMR (400 MHz, CDCl$_3$) δ 14.11, 22.66, 25.50, 25.97, 29.11, 29.30, 29.36, 29.54, 31.87, 68.17, 114.25, 124.67, 128.74, 161.99, 168.10. IR (cm$^{-1}$) 3380, 2917, 2852, 1644, 1616, 1576, 1504, 1303, 1252, 980.
4-(\(n\)-dodecyloxy)benzoyl hydrazine, 2c.

\[
\text{C}_{12}\text{H}_{25}\text{O} \quad \text{NH-NH}_2
\]

Yield = 79%, mp = 102.9 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.81 (s, br, 2H), 8.17 (s, br, 1H), 7.70 (d, \(J=8.0\) Hz, 2H), 6.86 (d, \(J=8.4\) Hz, 2H), 3.94 (t, \(J=6.4\) Hz, 2H), 1.74-1.78 (m, 2H), 1.41-1.44 (m, 2H), 1.21–1.30 (m, 16H), 0.86 (t, \(J=6.8\) Hz, 3H). \(^1^3\)C NMR (400 MHz, CDCl\(_3\)) \(\delta\) 14.11, 22.68, 25.99, 29.13, 29.35, 29.38, 29.56, 29.59, 29.63, 29.66, 31.91, 68.21, 114.37, 124.54, 128.73, 162.12, 168.37. IR (cm\(^{-1}\)) 3330, 2916, 2852, 1646, 1621, 1577, 1507, 1478, 1352, 1304, 1251, 1114, 1048, 982.

Synthesis of 4-(\(n\)-fluoroalkyloxybenzoyl) hydrazines, 2d-h.\(^{10}\) The preparation of 2d is provided as a general example: A solution of 4-\(n\)-(7,7,8,8,9,9,10,10,10-nonafluorodecyloxy)benzoic acid (0.90 g, 2.04 mmol) in methanol (5.0 ml) containing a few drops of concentrated sulfuric acid was refluxed for 12 h. Hydrazine monohydrate (0.51 g, 10.22 mmol) was added and the reflux was continued for 8 h. The reaction was monitored by TLC. Excess methanol was removed under reduced pressure and the reaction mixture was poured into ice cold water. The crude product obtained was recrystallized from methanol/water and dried in the oven at 60°C.

4-\(n\)-(4,4,5,5,6,6,7,7,8,8,9,9-tridecafluorononyloxy)benzoyl hydrazine, 2d.

\[
\text{F(F}_2\text{C})_6\text{(H}_2\text{C})_3\text{O} \quad \text{NH-NH}_2
\]
Yield = 48%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 9.02 (s, br, 2H), 8.38 (s, br, 1H), 7.84 (d, J=8.8 Hz, 2H), 6.95 (d, J=5.2, 2H), 4.12 (t, J=6.0 Hz, 2H), 2.27-2.40 (m, 2H), 2.15-2.19 (m, 2H). $^{13}$C NMR (400 MHz, CDCl$_3$) $\delta$ 19.74, 35.30 (d, J=22.4 Hz, CF$_2$CH$_2$-), 67.00 (-CH$_2$O-), 110-120 (m, CF$_3$(CF$_2$)$_7$), 114.64, 128.40, 129.09, 162.10 (aromatic), 168.90 (PhCONHNH$_2$). IR (cm$^{-1}$) 3190, 2940, 2860, 1611, 1593, 1564, 1453, 1254, 1254, 1192, 1141, 1030.

4-n-(7,7,8,8,9,9,10,10,10-nonafluorodecyloxy)benzoyl hydrazine, 2e.

\[
\text{F(F}_2\text{C)}_4(\text{H}_2\text{C})_6-\text{O} \rightarrow \begin{array}{c}
\text{O} \\
\text{NH-NH}_2
\end{array}
\]

Yield = 73%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.96 (s, br,2H), 8.31 (s, br, 1H), 7.68 (d, J=8.8 Hz, 2H), 6.89 (d, J=8.8, 2H), 3.98 (t, J=6.4 Hz, 2H), 1.98-2.13 (m, 2H), 1.75-1.84 (m, 2H), 1.59-1.66 (m, 2H), 1.41-1.53 (m, 4H). $^{13}$C NMR (400 MHz, CDCl$_3$) $\delta$ 20.06, 25.73, 28.82, 28.88, 30.70 (d, J=22.4 Hz, CF$_2$CH$_2$-), 67.88 (-CH$_2$O-), 110-120 (m, CF$_3$(CF$_2$)$_3$), 114.41, 124.74, 128.64, 161.99 (aromatic), 168.34 (PhCONHNH$_2$). IR (cm$^{-1}$) 3269, 2944, 2869, 1605, 1504, 1223, 1172, 1130, 1006.

4-n-(4,4,5,5,6,6,7,7,8,8,9,9,10,10-pentadecafluorodecyloxy)benzoyl hydrazine, 2f.

\[
\text{F(F}_2\text{C)}_7(\text{H}_2\text{C})_3-\text{O} \rightarrow \begin{array}{c}
\text{O} \\
\text{NH-NH}_2
\end{array}
\]

Yield = 60%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 9.15 (s, br, 1H), 8.51 (s, br 1H), 8.06 (d, J=8.8 Hz, 2H), 6.94 (d, J=8.8 Hz, 2H), 4.12 (t, J=6.0 Hz, 2H), 2.28-2.40 (m, 2H), 2.10-2.19 (m, 2H). $^{13}$C NMR (400 MHz, CDCl$_3$) $\delta$ 20.62, 28.00 (d, J=22.4 Hz, CF$_2$CH$_2$-),
66.63 (–$\text{CH}_2\text{O}$–), 110-120 (m, CF$_3$(CF$_2$)$_5$), 114.24, 128.90, 132.33, 157.50 (aromatic), 170.10 (PhCONHNH$_2$). IR (cm$^{-1}$) 3270, 2941, 2862, 1610, 1506, 1253, 1178, 1135, 1023.

$4-n$-(7,7,8,8,9,10,11,12,12-tridecafluorododecyloxy)benzoyl hydrazine, 2g.

\[
\text{F(F}_2\text{C})_6(\text{H}_2\text{C})_6-\text{O} \quad \text{NH-NH}_2
\]

Yield = 74%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.98 (s, br, 2H), 8.33 (s, br, 1H), 7.70 (dd, J=6.8, 2.0 Hz, 2H), 6.92 (dd, J=6.8, 2.0 Hz, 2H), 4.00 (t, J=6.2 Hz, 2H), 2.01-2.15 (m, 2H), 1.79-1.86 (m, 2H), 1.61-1.69 (m, 2H), 1.44-1.52 (m, 4H). $^{13}$C NMR (400 MHz, CDCl$_3$) $\delta$ 20.10, 26.00, 28.75, 28.90 31.50 (d, J=22.4 Hz, CF$_2$CH$_2$–), 68.20 (–$\text{CH}_2\text{O}$–), 110-120 (m, CF$_3$(CF$_2$)$_3$), 114.43, 124.10, 128.63, 163.50 (aromatic), 166.50 (PhCONHNH$_2$). IR (cm$^{-1}$) 3275, 2948, 2869, 1605, 1505, 1249, 1186, 1140, 1048.

$4-n$-(5,5,6,6,7,7,8,8,9,9,10,10,11,11,12,12-heptadecafluorododecyloxy)benzoyl hydrazine, 2h.

\[
\text{F(F}_2\text{C})_8(\text{H}_2\text{C})_4-\text{O} \quad \text{NH-NH}_2
\]

Yield = 71%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.97 (s, br, 2H), 8.32 (s, br, 1H), 7.69 (d, J=8.8 Hz, 2H), 6.90 (d, J=8.4 Hz, 2H), 4.02 (t, J=5.6 Hz, 2H), 2.08-2.22 (m, 2H), 1.78-1.92 (m, 4H). $^{13}$C NMR (400 MHz, CDCl$_3$) $\delta$ 17.5, 20.4, 28.8 (d, J=22.4 Hz, CF$_2$CH$_2$–), 67.7 (–$\text{CH}_2\text{O}$–), 110-120 (m, CF$_3$(CF$_2$)$_7$), 114.51, 125.80, 128.62, 163.9 (aromatic), 174.3 (PhCONHNH$_2$). IR (cm$^{-1}$) 3273, 2947, 2880, 1589, 1504, 1251, 1198, 1144, 1013, 844.
Synthesis of $N,N'$-bis(4-$n$-alkyloxy)benzoyl hydrazines, 3a-c or $N$-$[4-(n$-nonyloxybenzoyl)]-$N'$-$[4-$(n$-fluoroalkyloxybenzoyl)] hydrazines, 3d-h or $N,N'$-bis(4-$n$-fluoroalkyloxy)benzoyl hydrazines, 3i-m.$^{11}$

The preparation of 3a is provided as a general example: A mixture of 4-$(n$-nonyloxy)benzoic acid (0.40 g, 1.52 mmol) and oxalyl chloride (0.96 g, 7.60 mmol) was heated at 40°C in methylene chloride (3.0 ml) for 8 h. Excess oxalyl chloride was evaporated and the residue was mixed with 4-$(n$-nonyloxybenzoyl) hydrazine (0.39 g, 1.42 mmol) in dichloromethane (15.0 ml). Triethylamine (0.2 ml, 1.42 mmol) was added and the mixture stirred at room temperature. The reaction was monitored by TLC. The crude product was collected by filtration, recrystallized from methanol/water and dried in the oven at 60°C.

$N,N'$-bis(4-$n$-nonyloxy)benzoyl hydrazine, 3a.

Yield = 51%. $^1$H NMR (400 MHz, CDCl₃) $\delta$ 9.20 (s, 2H), 7.81 (d, J=8.8 Hz, 4H), 6.92 (d, J=8.8 Hz, 4H), 3.99 (t, J=6.6 Hz, 4H), 1.75-1.82 (m, 4H), 1.41-1.49 (m, 4H), 1.22–1.38 (m, 20H), 0.89 (t, J=6.8 Hz, 6H). $^{13}$C NMR (CDCl₃) $\delta$ 14.12, 22.68, 25.99, 29.12, 29.26, 29.38, 29.52, 31.88, 68.29, 114.52, 123.33, 129.05, 162.56, 163.71. IR (cm$^{-1}$) 3271, 2917, 2848, 1684, 1604, 1540, 1465, 1434, 1308, 1295, 1254, 1174, 844, 771.
N-(4-n-nonyloxybenzoyl)-N’-(4-n-decyloxybenzoyl) hydrazine, 3b.

\[
\text{C}_{9}\text{H}_{19}\text{O} \quad \text{O} \quad \text{O} \quad \text{OC}_{10}\text{H}_{21}
\]

Yield = 72%. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 9.21 (s, br, 2H), 7.80 (d, J=8.4 Hz, 4H), 6.91 (d, J=8.4 Hz, 4H), 3.99 (t, J=6.6 Hz, 4H), 1.75-1.83 (m, 4H), 1.41-1.50 (m, 4H), 1.25-1.37 (m, 22H), 0.88 (t, J=6.6 Hz, 6H). \(^13\)C NMR (CDCl\(_3\)) \(\delta\) 13.97 (2C), 22.60 (2C), 25.96 (2C), 29.11 (2C), 29.18 (2C), 29.24 (2C), 29.31 (2C), 29.49 (1C), 31.82 (2C), 68.33 (2C), 114.56 (2C), 123.52 (2C), 129.04 (2C), 162.58 (2C), 163.80 (2C). IR (cm\(^{-1}\)) 3224, 2954, 2919, 2851, 1639, 1605, 1577, 1508, 1454, 1248, 1174, 1016.

N-(4-n-nonyloxybenzoyl)-N’-(4-n-dodecyloxybenzoyl) hydrazine, 3c.

\[
\text{C}_{9}\text{H}_{19}\text{O} \quad \text{O} \quad \text{O} \quad \text{OC}_{12}\text{H}_{25}
\]

Yield = 69%. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 9.36 (s, br, 2H), 7.82 (d, J=8.8 Hz, 4H), 6.91 (d, J=7.6 Hz, 4H), 3.99 (t, J=6.6 Hz, 4H), 1.76-1.84 (m, 4H), 1.41-1.51 (m, 4H), 1.24-1.38 (m, 26H), 0.88 (t, J=6.8 Hz, 6H). \(^13\)C NMR (CDCl\(_3\)) \(\delta\) 14.08 (2C), 22.66 (2C), 25.99 (2C), 29.12 (2C), 29.24 (2C), 29.37 (2C), 29.51 (2C), 29.59 (2C), 29.63 (1C), 31.86 (1C), 31.91 (1C), 68.28 (2C), 114.47 (2C), 123.42 (2C), 129.10 (2C), 162.51 (2C), 168.90 (2C). IR (cm\(^{-1}\)) 3220, 2920, 2849, 1609, 1597, 1566, 1456, 1251, 1177, 1108, 1033.
N-[4-n-(nonyloxybenzoyl)]-N’-[4-n-(4,4,5,6,6,7,7,8,8,9,9,9-
tridecafluorononyloxybenzoyl)] hydrazine, 3d.

\[
\text{C}_9\text{H}_{19}\text{O}_\text{O} \quad \text{HN} \quad \text{O} \quad \text{NH} \quad \text{O} \quad \text{-(CH}_2)_3\text{(CF}_2)_9\text{F}
\]

Yield = 55%. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 9.55 (s, br, 1H), 9.46 (s, br, 1H), 7.83 (t, J=8.6 Hz, 4H), 6.90 (d, J=8.8 Hz, 4H), 4.08 (t, J=6.0 Hz, 2H), 3.98 (t, J=6.6 Hz, 2H), 2.24-2.40 (m, 2H), 2.08-2.17 (m, 2H), 1.74-1.85 (m, 2H), 1.41-1.49 (m, 2H), 1.22-1.37 (m, 10H), 0.88 (t, J=6.6 Hz, 3H). \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\) 14.10, 20.51, 22.67, 25.99, 29.26 (2C), 29.38, 29.52 (2C), 31.88 (d, J=22.4 Hz, CF\(_3\text{CH}_2\)-), 66.50, 68.28 (-CH\(_2\text{O}-\)), 110-120 (m, CF\(_3\text{(CF}_2)_3\)), 114.38, 114.46, 123.24, 124.02, 129.19, 129.30, 161.81, 162.58 (aromatic, 8C), 163.99, 164.22 (-CONH-). IR (cm\(^{-1}\)) 3320, 2961, 2855, 1731, 1687, 1642, 1511, 1255, 1185, 1141, 1069.

N-[4-n-(nonyloxybenzoyl)]-N’-[4-n-(7,7,8,8,9,9,10,10-
nonafluorodecyloxybenzoyl)] hydrazine, 3e.

\[
\text{C}_9\text{H}_{19}\text{O}_\text{O} \quad \text{HN} \quad \text{O} \quad \text{NH} \quad \text{O} \quad \text{-(CH}_2)_6\text{(CF}_2)_4\text{F}
\]

Yield = 86%. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 9.10 (s, br, 2H), 7.81 (dd, J=8.8, 2.4 Hz, 4H), 6.93 (dd, J=9.0, 1.0 Hz, 4H), 4.01 (m, 4H), 2.00-2.14 (m, 2H), 1.75-1.85 (m, 4H), 1.61-1.68 (m, 2H), 1.41-1.53 (m, 6H), 1.24-1.37 (m, 10H), 0.87 (t, J=6.8 Hz, 3H). \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\) 14.17, 20.08, 22.69, 25.73, 26.00, 28.83, 28.87, 29.12, 29.26, 29.37, 29.53, 31.89, 32.00 (d, J22.4 Hz, CF\(_3\text{CH}_2\)-), 67.94, 68.30 (-CH\(_2\text{O}-\)), 110-120 (m, CF\(_3\text{(CF}_2)_3\)), 114.51, 114.55, 126.20 (2C), 129.01, 129.05, 162.00, 162.80 (aromatic, 8C),
N-[4-n-(nonyloxybenzoyl)]-N'[4-n-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-pentadecafluorodecyloxybenzoyl)] hydrazine, 3f.

\[
\text{C}_{9}\text{H}_{19}\text{O} - \text{O} - \text{HN} - \text{NH} - \text{O} - (\text{CH}_2)_3(\text{CF}_2)_7\text{F}
\]

Yield = 69%. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 9.36 (d, \(J=6.4\) Hz, 1H), 9.28 (d, \(J=6.0\) Hz, 1H), 7.82 (t, \(J=8.8\) Hz, 4H), 6.91 (dd, \(J=8.8, 1.2\) Hz, 4H), 4.08 (t, \(J=5.8\) Hz, 2H), 3.98 (t, \(J=6.6\) Hz, 2H), 2.23-2.40 (m, 2H), 2.08-2.17 (m, 2H), 1.74-1.84 (m, 2H), 1.40-1.49 (m, 2H), 1.23-1.36 (m, 10H), 0.87 (t, \(J=7.0\) Hz, 3H). \(^{13}\)C NMR (400 MHz, CDCl\(_3\)) \(\delta\) 14.11, 20.47, 22.68, 25.99, 27.90, 29.11, 29.26, 29.38, 29.52, 31.87 (d, \(J=22.4\) Hz, CF\(_2\)CH\(_2\)-), 66.51, 68.29 (\(-\text{CH}_2\text{O}-\)), 109-120 (m, CF\(_3\)(CF\(_2\))\(_6\)), 114.42, 114.50, 123.28, 124.05, 129.10, 129.21, 161.81, 162.58 (aromatic, 8C), 163.71, 163.93 (\(-\text{CONH}-\)). IR (cm\(^{-1}\)) 3294, 3248, 2922, 2853, 1668, 1642, 1612, 1510, 1195, 1142, 1017, 837.

N-[4-n-(nonyloxybenzoyl)]-N'[4-n-(7,7,8,8,9,9,10,10,11,11,12,12-tridecafluorododecyloxybenzoyl)] hydrazine, 3g.

\[
\text{C}_{9}\text{H}_{19}\text{O} - \text{O} - \text{HN} - \text{NH} - \text{O} - (\text{CH}_2)_6(\text{CF}_2)_6\text{F}
\]

Yield = 98%. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 9.37 (s, br, 2H), 7.82 (d, \(J=6.8\) Hz, 4H), 6.91 (d, \(J=8.0\) Hz, 4H), 4.00 (dd, \(J=6.4, 6.0\) Hz, 4H), 2.01-2.16 (m, 2H), 1.75-1.88 (m, 4H), 1.61-1.71 (m, 2H), 1.42-1.57 (m, 6H), 1.25-1.36 (m, 10H), 0.89 (t, \(J=7.0\) Hz, 3H). \(^{13}\)C
NMR (400 MHz, CDCl₃) δ 14.11, 20.10, 22.68, 25.75 (2C), 25.99, 28.85, 29.12, 29.26, 29.38, 29.52, 30.60, 31.88 (d, J=22.4 Hz, CF₂CH₂-), 67.93, 68.28 (-CH₂O-), 109-120 (m, CF₃(CF₂)₃), 114.43, 114.47, 123.50, 123.52, 129.13, 129.15, 162.36, 162.54 (aromatic, 8C), 163.80, 164.0 (-CONH-). IR (cm⁻¹) 3210, 2930, 2840, 1737, 1642, 1611, 1530, 1509, 1380, 1233, 1217, 1143.

N-[4-n-(nonyloxybenzoyl)]-N'-[4-n-(5,5,6,6,7,8,8,9,9,10,10,11,11,12,12,12-heptadecafluorododecyloxybenzoyl)] hydrazine, 3h.

N,N'-bis[4-n-(4,4,5,5,6,6,7,8,8,9,9,9-tridecafluorononyloxybenzoyl)] hydrazine, 3i.
Yield = 72%. \( ^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 8.99 (d, J=4.4 Hz, 2H), 7.84 (dd, J=6.8, 2.0 Hz, 4H), 6.97 (d, J=8.8 Hz, 4H), 4.12 (t, J=6.0 Hz, 4H), 2.26-2.42 (m, 4H), 2.10-2.22 (m, 4H). \( ^{13}\)C NMR (400 MHz, CDCl\(_3\)) \( \delta \) 28.00, 30.40 (d, J=22.4 Hz, CF\(_2\)C\(_2\)H\(_2\)), 66.70 (-CH\(_2\)O-), 110-120 (m, CF\(_3\)(CF\(_2\))\(_3\)), 114.63, 127.50, 129.08, 138.10 (aromatic, 4C), 162.10 (-CONH-). IR (cm\(^{-1}\)) 3200, 2954, 2891, 1610, 1594, 1518, 1470, 1455, 1243, 1191, 1140, 1043.

\(N,N'\)-bis[4-n-(7,7,8,8,9,9,10,10,10-nonafluorodecyloxybenzoyl)] hydrazine, 3j.

\[
\begin{align*}
F(F_2C)_4(H_2C)_6\text{O} & - \overset{\text{HN}}{\text{O}} \overset{\text{O}}{\text{O}} \overset{\text{NH}}{\text{O}} \overset{\text{H}}{\text{N}} \overset{\text{N}}{\text{N}} \overset{\text{O}}{\text{O}} \overset{\text{CH}_2}{\text{H}_6} \overset{\text{CF}_2}{\text{F}} \\
\end{align*}
\]

Yield = 77%. \( ^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 9.19 (s, br, 2H), 7.83 (d, J=8.8 Hz, 4H), 6.94 (d, J=8.0 Hz, 4H), 4.06 (t, J=10.8 Hz, 4H), 2.01-2.17 (m, 4H), 1.79-1.88 (m, 4H), 1.63-1.71 (m, 8H), 1.44-1.56 (m, 4H). \( ^{13}\)C NMR (400 MHz, CDCl\(_3\)) \( \delta \) 20.05, 20.10, 25.73, 28.83, 30.71 (d, J=22.4 Hz, CF\(_2\)C\(_2\)H\(_2\)), 67.94 (-CH\(_2\)O-), 110-120 (m, CF\(_3\)(CF\(_2\))\(_3\)), 114.50, 118.05, 129.07, 163.80 (aromatic), 172.70 (-CONH-). IR (cm\(^{-1}\)) 3251, 2944, 2871, 1609, 1572, 1461, 1219, 1187, 1130.

\(N,N'\)-bis[4-n-(4,4,5,5,6,6,7,7,8,8,9,9,10,10-pentadecafluorodecyloxybenzoyl)] hydrazine, 3k.

\[
\begin{align*}
F(F_2C)_7(H_2C)_3\text{O} & - \overset{\text{HN}}{\text{O}} \overset{\text{O}}{\text{O}} \overset{\text{NH}}{\text{O}} \overset{\text{H}}{\text{N}} \overset{\text{N}}{\text{N}} \overset{\text{O}}{\text{O}} \overset{\text{CH}_2}{\text{H}_3} \overset{\text{CF}_2}{\text{F}} \\
\end{align*}
\]

Yield = 68%. \( ^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 9.12 (s, br, 2H), 7.69 (d, J=12.0 Hz, 4H), 6.88 (d, J=12.0 Hz, 4H), 3.96 (t, J=6.4 Hz, 4H), 2.26-2.41 (m, 4H), 2.11-2.19 (m, 4H).
$^{13}$C NMR (400 MHz, CDCl$_3$) $\delta$ 20.80, 28.10 (d, J=22.4 Hz, CF$_2$CH$_2$-), 66.64 (-CH$_2$O-), 110-120 (m, CF$_3$(CF$_2$)$_6$), 114.25, 129.50, 132.34, 139.10 (aromatic), 162.20 (-CONH-). IR (cm$^{-1}$) 3260, 2921, 2851, 1686, 1642, 1614, 1580, 1511, 1256, 1196, 1022.

$N,N'$-bis[4-n-(7,7,8,8,9,10,10,11,11,12,12,12-tridecafluorododecyloxybenzoyl)] hydrazine, 3l.

\[
\begin{array}{c}
\text{F(F}_2\text{C)}_6\text{(H}_2\text{C)}_6\text{O} \quad \text{O} \\
\text{HN=NH}\end{array}
\]

Yield = 18%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 9.15 (s, br, 2H), 8.04 (d, J=8.8 Hz, 4H), 7.84 (d, J=8.8 Hz, 4H), 6.94 (t, J=8.6 Hz, 4H), 4.02-4.07 (m, 4H), 2.01-2.18 (m, 4H), 1.79-1.89 (m, 4H), 1.62-1.72 (m, 4H), 1.45-1.60 (m, 4H). $^{13}$C NMR (400 MHz, CDCl$_3$) $\delta$ 20.12, 25.64, 28.76, 28.83, 30.99 (d, J=22.4 Hz, CF$_2$CH$_2$-), 68.02 (-CH$_2$O-), 110-120 (m, CF$_3$(CF$_2$)$_5$), 114.64, 129.06, 132.22, 162.52 (aromatic), 171.50 (-CONH-). IR (cm$^{-1}$) 3270, 2920, 2850, 1607, 1575, 1440, 1240, 1176, 1136, 1030.

$N,N'$-bis[4-n-(5,5,6,6,7,7,8,8,9,9,10,10,11,11,12,12-heptadecafluorododecyloxybenzoyl)] hydrazine, 3m.

\[
\begin{array}{c}
\text{F(F}_2\text{C)}_5\text{(H}_2\text{C)}_4\text{O} \quad \text{O} \\
\text{HN=NH}\end{array}
\]

Yield = 38%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 9.16 (s, br, 2H), 8.04 (d, J=8.8 Hz, 4H), 7.72 (d, J=9.2 Hz, 4H), 6.93 (d, J=8.8 Hz, 4H), 4.04-4.09 (m, 4H), 2.11-2.25 (m, 4H), 1.81-1.95 (m, 4H). $^{13}$C NMR (400 MHz, CDCl$_3$) $\delta$ 17.28, 28.59, 30.67 (d, J=22.4 Hz, CF$_2$CH$_2$-), 67.38 (-CH$_2$O-), 110-120 (m, CF$_3$(CF$_2$)$_7$), 114.42, 129.34, 132.28, 161.75 (aromatic),
168.27 (-CONH-). IR (cm$^{-1}$) 3270, 2920, 2850, 1607, 1575, 1440, 1240, 1176, 1136, 1030.

2-Fluoro-4-(n-dodecyloxy)benzonitrile, 4.$^{12}$

![Structural formula of 2-Fluoro-4-(n-dodecyloxy)benzonitrile](image)

2-Fluoro-4-hydroxybenzonitrile (6.00 g, 43.76 mmol) and potassium carbonate (15.12 g, 109.40 mmol) were mixed with 70.0 ml of DMF under a nitrogen atmosphere. Next, 1-bromododecane (13.09 g, 52.51 mmol) was added and the mixture was refluxed and monitored by TLC. After 48 h, the reaction mixture was cooled to room temperature and poured into 300 ml of ice water. After acidification, the product was collected by vacuum filtration and dried. Purification using silica chromatography (10% ethyl acetate in hexane) afforded the product as a white solid. Yield = 8.62 g (64%). mp = 47.2 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.47 (t, J=8.0 Hz, 1H), 6.73 (dd, J=8.8, 2.4 Hz, 1H), 6.67 (dd, J=11.0, 2.2 Hz, 1H), 3.97 (t, J=6.4 Hz, 2H), 1.74-1.82 (m, 2H), 1.39-1.47 (m, 2H), 1.22–1.32 (m, 16H), 0.86 (t, J=7.0 Hz, 3H). $^{13}$C NMR (CDCl$_3$) $\delta$ 14.11, 22.70, 25.86, 28.82, 29.28, 29.36, 29.53, 29.58 (2C), 29.65, 31.93, 69.07 (-CH$_2$O-), 102.62 (d, J=92.0 Hz), 111.68 (d, J=8.0 Hz), 114.49 (-CN), 134.10 (d, J=8.0 Hz), 163.32, 164.42 (d, J=44.0 Hz), 165.88 (=C-O-, Ar). IR (cm$^{-1}$) 2916, 2852, 2232, 1621, 1507, 1472, 1305, 1172, 1112.
2-Fluoro-4-(n-dodecyloxy)benzoic acid, 5.12

\[
\text{C}_{12}\text{H}_{25}\text{O}^\cdot
\]

A solution of 2-fluoro-4-(n-dodecyloxy)benzonitrile (5.57 g, 18.26 mmol), concentrated sulfuric acid (6.0 ml), water (6.0 ml) and acetic acid (60.0 ml) was refluxed. The reaction was monitored by TLC. After 72 h, the solution was cooled and poured onto water (200 ml). The resulting precipitate was filtered off, washed with water. The product was recrystallized from methanol/water and dried in the oven at 60°C. Yield = 4.73 g (80%).

\(^1\text{H}\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 10.98 (s, br, 1H), 7.96 (t, J=8.6 Hz, 1H), 6.72 (dd, J=9.0, 2.6 Hz, 1H), 6.63 (dd, J=12.8, 2.4 Hz, 1H), 3.99 (t, J=6.4 Hz, 2H), 1.74-1.83 (m, 2H), 1.40-1.48 (m, 2H), 1.23–1.34 (m, 16H), 0.87 (t, J=6.8 Hz, 3H). \(^{13}\text{C}\) NMR (CDCl\(_3\)) \(\delta\) 14.13, 22.70, 25.91, 28.92, 29.14, 29.32, 29.36, 29.54, 29.58, 29.65, 31.93, 68.82 (-\(\text{CH}_2\text{O}\)-), 102.77 (d, J=104.0 Hz), 110.82 (2C), 134.06, 162.98, 165.10 (d, J=44.0 Hz), 165.58 (-\(\text{COOH}\)). IR (cm\(^{-1}\)) 3300-2500 (O-H stretch), 2917, 2851, 1682, 1618, 1592, 1469, 1285, 1136, 1101.

2-Fluoro-4-(n-dodecyloxybenzoyl) hydrazine, 6.10

\[
\text{C}_{12}\text{H}_{25}\text{O}^\cdot
\]

A solution of 2-fluoro-4-(n-dodecyloxy)benzoic acid (0.20 g, 0.62 mmol) in methanol (5.0 ml) containing few drops of concentrated sulfuric acid was refluxed for 8 h. Hydrazine monohydrate (0.06 g, 0.06 ml, 1.85 mmol) was added and the reaction was
continued to reflux for 10 h. The reaction was monitored by TLC. Excess methanol was removed under reduced pressure and the reaction mixture was poured into ice cold water. The crude material obtained was recrystallized from ethanol/water and dried in the oven at 60°C to give the expected product as a white solid. Yield = 0.14 g (74%) 1H NMR (400 MHz, CDCl3) δ 9.64 (d, J=10.4 Hz, 1H), 8.07 (t, J=9.0 Hz, 1H), 6.81 (dd, J=9.4, 2.2 Hz, 1H), 6.67 (dd, J=14.0, 2.4 Hz, 1H), 5.35 (s, br, 2H), 4.00 (t, J=6.6 Hz, 2H), 1.76-1.85 (m, 2H), 1.42-1.50 (m, 2H), 1.25-1.35 (m, 16H), 0.88 (t, J=6.8 Hz, 3H). 13C NMR (CDCl3) δ 14.13, 22.70, 25.92, 28.94, 29.32, 29.35, 29.54, 29.58, 29.64, 29.65, 31.92, 68.85 (-C\(\text{H}_2\text{O}-\), 102.04 (d, J=112.0 Hz), 111.54 (2C), 132.94, 158.99, 163.07, 164.00 (-CONH-). IR (cm\(^{-1}\)) 3328, 2918, 2854, 1645, 1620, 1575, 1504, 1472, 1352, 1302, 1250, 1112, 1043.

\(N,N'\)-bis(4-dodecyloxy)benzoyl hydrazine, 7.\(^{11}\)

\[
\text{C}_{12}\text{H}_{25}\text{O} \begin{array}{c} \text{O} \\ \text{HN-\text{NH}} \\ \text{O} \end{array} \text{O} \text{C}_{12}\text{H}_{25}
\]

A mixture of 4-(\(n\)-dodecyloxy)benzoic acid (0.80 g, 2.61 mmol) and oxalyl chloride (1.66 g, 13.06 mmol) was heated at 40°C in methylene chloride (4.0 ml) for 8 h. Excess oxalyl chloride was evaporated and the residue was mixed with 4-(\(n\)-dodecyloxybenzoyl) hydrazine (0.79 g, 2.46 mmol) in dichloromethane (15.0 ml). Triethylamine (0.34 ml, 2.46 mmol) was added and the mixture stirred at room temperature. The reaction was monitored by TLC. After 8 h, it was precipitated and the crude product was collected by filtration. The product was recrystallized from methanol/water and dried in the oven at
60°C. Yield = 0.58 g (40%). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 9.24 (s, 2H), 7.82 (d, J=8.8 Hz, 4H), 6.93 (d, J=8.8 Hz, 4H), 4.00 (t, J=6.6 Hz, 4H), 1.76-1.85 (m, 4H), 1.42-1.50 (m, 4H), 1.25-1.37 (m, 32H), 0.88 (t, J=6.8Hz, 6H). \(^1^3\)C NMR (CDCl\(_3\)) \(\delta\) 14.13, 22.70, 25.99,29.12, 29.36, 29.38, 29.57, 29.60, 29.64, 29.67, 31.93, 68.30 (-C\(\text{H}_2\text{O}-), 114.52, 123.32, 129.06, 162.56 (aromatic), 163.60 (-\text{CONH}-). IR (cm\(^{-1}\)) 3212, 2919, 2850, 1597, 1566, 1456, 1248, 1174.

4-(dodecyloxy)-N'-(4-(dodecyloxy)benzoyl)-2-fluorobenzoyl hydrazine, 8.\(^{11}\)

![Chemical Structure](image)

A mixture of 2-fluoro-4-(\(n\)-dodecyloxy)benzoic acid, 5 (0.76 g, 2.34 mmol) and oxalyl chloride (1.49 g, 11.72 mmol) was heated at 40°C in methylene chloride (5.0 ml) for 8 h. The excess of oxalyl chloride was evaporated and the residue was mixed with 4-(\(n\)-dodecyloxybenzoyl) hydrazine (0.71 g, 2.22 mmol) in dichloromethane (14.0 ml). Triethylamine (0.31 ml, 2.22 mmol) was added and the mixture stirred at room temperature. The reaction was monitored by TLC. After 8 h, the crude product was collected by filtration, recrystallized from methanol/water and dried in the oven at 60°C. Yield = 0.90 g (65%). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 9.54 (s, 1H), 9.18 (s, 1H), 8.04 (t, J=9.0 Hz, 1H), 7.82 (d, J=8.8 Hz, 2H), 6.94 (d, J=8.8 Hz, 2H), 6.81 (dd, J=2.4, 8.8 Hz, 1H), 6.67 (dd, J=2.4, 14.0 Hz, 1H), 4.01 (t, J=6.8 Hz, 4H), 1.76-1.85 (m, 4H), 1.42-1.51 (m, 4H), 1.25-1.38 (m, 32H), 0.89 (t, J=6.8 Hz, 6H). \(^1^3\)C NMR (CDCl\(_3\)) \(\delta\) 14.00 (2C), 22.62 (2C), 25.89, 25.96, 28.94 (2C), 29.11 (2C), 29.28 (2C), 29.32 (2C), 29.48 (2C),
29.52 (2C), 29.58 (2C), 31.87 (2C), 68.33, 68.88, 102.09 (d, J=108.0 Hz), 110.52, 114.58 (2C), 123.48, 132.84, 129.02 (2C), 129.82, 132.84 (d, J=16.0 Hz), 159.46, 162.59, 163.16 (d, J=16.0 Hz), 163.93 (d, J=48.0 Hz). IR (cm⁻¹) 3226, 2920, 2851, 1599, 1566, 1459, 1251, 1176, 1107.

**N,N'-Bis(4-(dodecyloxy)-2-fluorobenzoyl) hydrazine, 9.**

![Chemical structure of N,N'-Bis(4-(dodecyloxy)-2-fluorobenzoyl) hydrazine, 9.](image)

A mixture of 2-fluoro-4-(n-dodecyloxy)benzoic acid, 5 (0.50 g, 1.54 mmol) and oxalyl chloride (0.98 g, 7.71 mmol) was heated at 40ºC in methylene chloride (5.0 ml) for 8 h. The excess of oxalyl chloride was evaporated and the residue was mixed with 2-fluoro-4-(n-dodecyloxybenzoyl) hydrazine, 6 (0.49 g, 1.46 mmol) in dichloromethane (10.0 ml) Triethylamine (0.20 ml, 1.46 mmol) was added and the mixture stirred at room temperature. The reaction was monitored by TLC. After 8 h, the crude product was collected by filtration, recrystallized from methanol/water and dried in the oven at 60ºC. Yield = 0.50 g (53%).

**1H NMR (400 MHz, CDCl₃)** δ 9.60 (d, J=9.6 Hz, 2H), 8.06 (t, J=9.0 Hz, 2H), 6.81 (dd, J=2.2, 9.0 Hz, 2H), 6.67(dd, J=2.0, 14.0 Hz, 2H), 4.01 (t, J=6.4 Hz, 4H), 1.76-1.86 (m, 4H), 1.42-1.52 (m, 4H), 1.26-1.39 (m, 32H), 0.89 (t, J=6.8 Hz, 6H).

**13C NMR (CDCl₃)** δ 14.13, 22.70, 25.92, 28.95, 29.32, 29.36, 29.54, 29.58, 29.65, 29.67, 31.93, 68.85 (-CH₂O-), 102.04 (d, J=112.0 Hz), 110.32 (d, J=52.0 Hz), 111.54, 132.92 (d, J=16.0 Hz), 158.98, 163.93 (d, J=48.0 Hz). IR (cm⁻¹) 3419, 2918, 2850, 1620, 1464, 1338, 1245, 1085.
3. Experimental procedures for Chapter 3

General Procedure for the Synthesis of Oxadiazoles: \(2,5\)-bis[(4-alkyloxy)phenyl]- or \(2\)-[(4-alkyloxy)phenyl]-5-[(4-fluoroalkyloxy)phenyl]- or \(2,5\)-bis[(4-fluoroalkyloxy)phenyl]-1,3,4-oxadiazole, 1a-m.\(^{13}\) The preparation of 1a is provided as a general example: A mixture of \(N,N'\)-bis(4-nonyloxybenzoyl) hydrazine (0.05 g, 0.10 mmol), which was prepared and reported earlier\(^{11}\) and phosphorus oxychloride, POCl\(_3\) (0.07 g, 0.04 ml, 0.48 mmol) was heated gently under reflux in dried toluene (2.0 ml) for 12 h. The reaction was monitored by TLC. After cooling the solvent and excess POCl\(_3\) were evaporated off under reduced pressure. Product was purified using silica gel column chromatography (15% of ethyl acetate in hexane), recrystallized from methanol/water and dried in the oven at 60°C.

\(2,5\)-Bis(4-\(n\)-nonyloxybenzoyl)-1,3,4-oxadiazole, 1a.

\[
\text{C}_9\text{H}_{19}\text{O}^\text{N}^\text{N}^\text{O} \text{C}_9\text{H}_{19}
\]

Yield = 98%, mp = 127.3°C. \(^1\text{H}\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.14 (d, \(J=8.8\) Hz, 4H), 7.10 (d, \(J=8.8\) Hz, 4H), 4.08 (t, \(J=6.4\) Hz, 4H), 1.79-1.86 (m, 4H), 1.43-1.49 (m, 4H), 1.24–1.36 (m, 20H), 0.88 (t, \(J=6.4\) Hz, 6H). \(^{13}\text{C}\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 14.12, 22.68, 25.94, 28.98, 29.25, 29.35, 29.51, 31.88, 68.88, 110.77, 115.96, 130.47, 163.90, 164.82. IR (cm\(^{-1}\)) 2940, 2924, 2850, 1610, 1495, 1474, 1255, 1177, 1035.
2-(4-\textit{n}-nonyloxyphenyl)-5-(4-\textit{n}-decyloxyphenyl)-1,3,4-oxadiazole, 1b.

\[ \text{C}_9\text{H}_{19}\text{O} \quad \text{O} \quad \text{C}_{10}\text{H}_{21} \]

Yield = 53\%, mp = 127.8 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.04 (d, J=8.8 Hz, 4H), 7.01 (d, J=8.8 Hz, 4H), 4.03 (t, J=6.6 Hz, 4H), 1.78-1.85 (m, 4H), 1.44-1.51 (m, 4H), 1.25-1.36 (m, 20H), 0.88 (t, J=6.8 Hz, 6H). $^{13}$C NMR (400 MHz, CDCl$_3$) $\delta$ 14.15 (2C), 22.71(2C), 26.02 (2C), 29.16(2C), 29.29 (2C), 29.35 (2C), 29.40 (2C), 29.58, 31.90 (2C), 68.27 (2C), 114.93 (2C), 116.36 (2C), 128.55 (2C), 161.81 (2C), 164.13 (2C). IR (cm$^{-1}$) 2942, 2920, 2852, 1611, 1496, 1473, 1256, 1175, 1034.

2-(4-\textit{n}-nonyloxyphenyl)-5-(4-\textit{n}-dodecyloxyphenyl)-1,3,4-oxadiazole, 1c.

\[ \text{C}_9\text{H}_{19}\text{O} \quad \text{O} \quad \text{C}_{12}\text{H}_{25} \]

Yield = 69\%, mp = 118.5°C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.02 (d, J=8.8 Hz, 4H), 7.00 (d, J=8.8 Hz, 4H), 4.02 (t, J=6.6 Hz, 4H), 1.77-1.84 (m, 4H), 1.42-1.50 (m, 4H), 1.21-1.39 (m, 26H), 0.87 (t, J=6.8 Hz, 6H). $^{13}$C NMR (400 MHz, CDCl$_3$) $\delta$ 14.13 (2C), 22.70 (2C), 26.02 (2C), 29.16 (2C), 29.27 (2C), 29.39 (2C), 29.53 (2C), 29.57, 29.60, 29.65, 31.93 (2C), 68.28 (2C), 114.94 (2C), 116.40 (2C), 128.55 (2C), 161.81 (2C), 164.60 (2C). IR (cm$^{-1}$) 2942, 2920, 2853, 1611, 1496, 1473, 1256, 1175, 1022.
2-[4-\(n\)-(nonyloxyphenyl)]-5-[4-\(n\)-(4,4,5,6,7,7,8,8,9,9,9-tridecafluorononyloxyphenyl)]-1,3,4-oxadiazole, 1d.

Yield = 41%. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.05 (t, J=8.4 Hz, 4H), 7.00 (dd, J=9.0, 3.4 Hz, 4H), 4.11 (t, J=6.0 Hz, 2H), 4.02 (t, J=6.6 Hz, 2H), 2.25-2.41 (m, 2H), 2.14-2.16 (m, 2H), 1.77-1.82 (m, 2H), 1.40-1.51 (m, 2H), 1.22-1.39 (m, 10H), 0.88 (t, J=6.8 Hz, 3H).

\(^{13}\)C NMR (400 MHz, CDCl\(_3\)) \(\delta\) 14.11, 20.50, 22.68, 26.01, 29.26 (2C), 29.38 (2C), 29.53 (d, J= 22.4 Hz, CF\(_2\)CH\(_2\)-), 31.88, 66.52, 68.29, 110-120 (m, CF\(_3\)(CF\(_2\))\(_5\)), 114.90, 114.96, 116.20 (2C), 128.58, 128.64, 152.10 (2C), 161.50 (2C). IR (cm\(^{-1}\)) 2965, 2927, 2863, 1613, 1498, 1475, 1258, 1230, 1188, 1146, 1031.

2-[4-\(n\)-(nonyloxyphenyl)]-5-[4-\(n\)-(7,7,8,8,9,9,10,10,10-nonafluorodecyloxyphenyl)]-1,3,4-oxadiazole, 1e.

Yield = 62%. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.05 (dd, J=8.8, 2.4 Hz, 4H), 7.01 (d, J=8.4 Hz, 4H), 4.02-4.06 (m, 4H), 2.01-2.17 (m, 2H), 1.78-1.89 (m, 2H), 1.69-1.71 (m, 2H), 1.44-1.58 (m, 4H), 1.26-1.41 (m, 14H), 0.89 (t, J=6.8 Hz, 3H). \(^{13}\)C NMR (400 MHz, CDCl\(_3\)) \(\delta\) 14.12, 20.07, 22.68, 25.76, 26.01, 28.84, 28.91, 29.15, 29.26, 29.39, 29.53, 30.72, 31.88 (d, J= 22.4 Hz, CF\(_2\)CH\(_2\)-), 67.92, 68.28, 110-121 (m, CF\(_3\)(CF\(_2\))\(_3\)), 114.91, 114.94, 116.36, 116.56, 128.53, 128.55, 161.66, 161.82, 164.12, 164.17. IR (cm\(^{-1}\)) 2935, 2923, 2855, 1612, 1497, 1476, 1256, 1227, 1176.
2-[4-\(n\)-(nonyloxyphenyl)]-5-[4-\(n\)-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-pentadecafluorodecyloxyphenyl)]-1,3,4-oxadiazole, 1f.

Yield = 49%. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.04 (t, \(J=7.4\) Hz, 4H), 7.00 (dd, \(J=8.6, 3.6\) Hz, 4H), 4.11 (t, \(J=6.0\) Hz, 2H), 4.02 (t, \(J=6.6\) Hz, 2H), 2.26-2.40 (m, 2H), 2.11-2.18 (m, 2H), 1.77-1.84 (m, 2H), 1.43-1.50 (m, 2H), 1.25-1.37 (m, 10H), 0.89 (t, \(J=6.8\) Hz, 3H).

\(^{13}\)C NMR (400 MHz, CDCl\(_3\)) \(\delta\) 14.12, 20.54, 22.68, 26.01, 27.93, 29.15, 29.26, 29.39, 29.53, 31.88 (CF\(_2\)CH\(_2\)-, \(J_{C-F} = 22.4\) Hz), 66.52, 68.29, 110-120 (m, CF\(_3\)(CF\(_2\))\(_6\)), 114.89, 114.96, 116.30, 117.10, 128.58, 128.64, 161.20, 161.88, 164.00, 164.40. IR (cm\(^{-1}\)) 2925, 2858, 1497, 1258, 1221, 1197, 1151, 1031.

2-[4-\(n\)-(nonyloxyphenyl)]-5-[4-\(n\)-(7,7,8,8,9,9,10,10,11,11,12,12-tridecafluorododecyloxyphenyl)]-1,3,4-oxadiazole, 1g.

Yield = 61%. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.04, (dd, \(J=8.8, 2.0\) Hz, 4H), 7.01 (d, \(J=8.4\) Hz, 4H), 4.01-4.06 (m, 4H), 2.01-2.17 (m, 2H), 1.80-1.86 (m, 4H), 1.64-1.68 (m, 2H), 1.42-1.59 (m, 6H), 1.24-1.38 (m, 10H), 0.89 (t, \(J=6.8\) Hz, 3H). \(^{13}\)C NMR (400 MHz, CDCl\(_3\)) \(\delta\) 14.12, 20.10, 22.68, 25.76, 26.01, 28.85, 28.91, 29.15 (2C), 29.27, 29.39, 29.53, 31.88 (CF\(_2\)CH\(_2\)-, \(J_{C-F} = 22.4\) Hz), 67.92, 68.28, 110-120 (m, CF\(_3\)(CF\(_2\))\(_5\)), 114.90,
2-[4-n-(nonyloxyphenyl)]-5-[4-n-(5,5,6,6,7,7,8,8,9,9,10,10,11,11,12,12,12-
heptadecafluorododecyloxyphenyl)]-1,3,4-oxadiazole, 1h.

\[ \text{C}_{9}\text{H}_{19}\text{O} - \text{O(CH}_2\text{)}_4\text{(CF}_2\text{)}_8\text{F} \]

Yield = 71%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.03 (dd, J=8.8, 6.5 Hz, 4H), 6.99 (d, J=8.8 Hz, 4H), 4.06 (t, J=5.8 Hz, 2H), 4.01 (t, J=6.6 Hz, 2H), 2.10-2.23 (m, 2H), 1.76-1.94 (m, 6H), 1.42-1.49 (m, 2H), 1.23-1.37 (m, 10H), 0.88 (t, J=6.8 Hz, 3H). $^{13}$C NMR (400 MHz, CDCl$_3$) $\delta$ 14.12, 17.31, 22.68, 26.01, 28.62, 29.15 (2C), 29.26, 29.39, 29.53, 31.88 (CF$_2$CH$_2$-, $J_{C-F} = 22.4$ Hz), 67.43, 68.29, 110-120 (m, CF$_3$(CF$_2$)$_7$), 114.89, 114.95, 126.30 (2C), 128.57, 128.61, 161.87 (2C), 167.60 (2C). IR (cm$^{-1}$) 2940, 2918, 2849, 1611, 1495, 1476, 1256, 1232, 1175, 1140.

2,5-Bis[4-n-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluorononyloxyphenyl)]-1,3,4-oxadiazole, 1i.

\[ \text{F(F}_2\text{C})_6\text{(H}_2\text{O)}_3\text{O} - \text{O(CH}_2\text{)}_3\text{(CF}_2\text{)}_8\text{F} \]

Yield = 79%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.83 (d, J=8.8 Hz, 4H), 6.96 (d, J=8.8 Hz, 4H), 4.11 (t, J=6.0 Hz, 4H), 2.25-2.41 (m, 4H), 2.10-2.19 (m, 4H). $^{13}$C NMR (400 MHz, CDCl$_3$) $\delta$ 28.00, 28.69 (CF$_2$CH$_2$-, $J_{C-F} = 22.4$ Hz), 66.68 (-CH$_2$O-), 110-120 (m,
CF$_3$(CF$_2$)$_3$, 114.64, 124.50, 129.09, 141.30, 174.20. IR (cm$^{-1}$) 2959, 2950, 2885, 1614, 1497, 1244, 1225, 1202, 1142, 1027.

2,5-Bis[4-\textit{n}-(7,7,8,8,9,9,10,10,10-nonafluorodecyloxyphenyl)]-1,3,4-oxadiazole, 1j.

\[
\text{F(F}_2\text{C)}_4(\text{H}_2\text{C})_6\text{O}^\text{N}\text{N}\text{O(CH}_2\text{)}_6(\text{CF}_2)_4\text{F}
\]

Yield = 44 %. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.03, (d, J=9.2 Hz, 4H), 6.99 (d, J=9.2 Hz, 4H), 4.03 (t, J=6.4 Hz, 4H), 1.99-2.14 (m, 4H), 1.79-1.87 (m, 4H), 1.60-1.68 (m, 4H), 1.44-1.52 (m, 8H). $^{13}$C NMR (400 MHz, CDCl$_3$) $\delta$ 20.80, 24.80, 25.76, 28.92, 30.73 (CF$_2$CH$_2$-, $J_{C-F}$ = 22.4 Hz), 68.20 (-CH$_2$O-), 110-120 (m, CF$_3$(CF$_2$)$_3$), 114.91, 116.60, 128.59, 158.80, 171.80. IR (cm$^{-1}$) 2942, 2869, 1617, 1496, 1254, 1223, 1176, 1132, 1003.

2,5-Bis[4-\textit{n}-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-pentadecafluorodecyloxyphenyl)]-1,3,4-oxadiazole, 1k.

\[
\text{F(F}_2\text{C)}_7(\text{H}_2\text{C})_3\text{O}^\text{N}\text{N}\text{O(CH}_2\text{)}_3(\text{CF}_2)_7\text{F}
\]

Yield = 62%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.06 (d, J=8.8 Hz, 4H), 6.95 (d, J=8.8 Hz, 4H), 4.11-4.16 (m, 4H), 2.26-2.42 (m, 4H), 2.11-2.20 (m, 4H). $^{13}$C NMR (400 MHz, CDCl$_3$) $\delta$ 29.00, 31.90 (CF$_2$CH$_2$-, $J_{C-F}$ = 22.4 Hz), 66.64 (-CH$_2$O-), 110-120 (m, CF$_3$(CF$_2$)$_6$), 114.26, 120.30, 132.34, 154.90, 172.10. IR (cm$^{-1}$) 2972, 2963, 2889, 1673, 1607, 1251, 1206, 1175, 1145, 1026.
2,5-Bis[4-\textit{n}-(7,7,8,8,9,10,11,11,12,12,12-tridecafluorododecyloxyphenyl)]-1,3,4-oxadiazole, 1l.

![Chemical Structure]

Yield = 0.12 g (58%). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.05 (d, J=8.8 Hz, 4H), 7.01 (d, J=8.8 Hz, 4H), 4.06 (t, J=6.2 Hz, 4H), 2.02-2.19 (m, 4H), 1.81-1.91 (m, 4H), 1.64-1.73 (m, 4H), 1.48-1.60 (m, 8H). $^{13}$C NMR (400 MHz, CDCl$_3$) $\delta$ 20.12, 25.69, 28.80, 28.89, 30.71 (CF$_2$CH$_2$-, JC-F = 22.4 Hz), 68.00 (-CH$_2$O-), 110-120 (m, CF$_3$(CF$_2$)$_5$), 115.00, 116.76, 128.56, 161.73, 164.10. IR (cm$^{-1}$) 2942, 2868, 1612, 1496, 1255, 1234, 1177, 1145, 1048.

2,5-Bis[4-\textit{n}-(5,5,6,6,7,7,8,8,9,9,10,10,11,11,12,12,12-heptadecafluorododecyloxyphenyl)]-1,3,4-oxadiazole, 1m.

![Chemical Structure]

Yield = 51%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.06 (d, J=8.8 Hz, 4H), 6.97 (d, J=9.2 Hz, 4H), 4.05-4.10 (m, 4H), 2.15-2.22 (m, 4H), 1.91-1.96 (m, 4H), 1.82-1.87 (m, 4H). $^{13}$C NMR (400 MHz, CDCl$_3$) $\delta$ 28.54, 29.71, 30.66 (CF$_2$CH$_2$-, JC-F = 22.4 Hz), 67.63 (-CH$_2$O-), 110-120 (m, CF$_3$(CF$_2$)$_5$), 114.57, 115.13, 128.15, 133.80, 163.75. IR (cm$^{-1}$) 2956, 2925, 2854, 1596, 1508, 1309, 1203, 1146, 1015.
General Procedure for the Synthesis of Thiadiazoles: 2,5-Bis[(4-alkyloxy)phenyl]- or 2-(4-alkyloxyphenyl)-5-[(4-fluoroalkyloxy)phenyl]- or 2,5-bis[(4-fluoroalkyloxy)phenyl]-1,3,4-thiadiazole, 2a–m. The preparation 2a is provided as a general example: A mixture of bis(4-nonyloxybenzoyl) hydrazine (0.05 g, 0.10 mmol) and Lawesson’s reagent (0.03 g, 0.07 mmol) was heated at gentle reflux in dried toluene (5.0 ml) for 12 h. The reaction was monitored by TLC. Excess solvent was evaporated under reduced pressure. Purification using silica gel column chromatography (15% of ethyl acetate in hexane) and recrystallization from methanol/water yield the expected product.

2,5-Bis(4-n-nonyloxyphenyl)-1,3,4-thiadiazole, 2a.

Yield = 80%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.92 (d, J=8.8 Hz, 4H), 6.98 (d, J=8.8 Hz, 4H), 4.02 (t, J=6.6 Hz, 4H), 1.80-1.83 (m, 4H), 1.46-1.49 (m, 4H), 1.29–1.38 (m, 20H), 0.89 (t, J=6.8 Hz, 6H). $^{13}$C NMR (CDCl$_3$) $\delta$ 14.12, 22.68, 26.01, 29.16, 29.27, 29.39, 29.54, 31.88, 68.28, 115.01, 122.79, 129.36, 161.41, 167.17. IR (cm$^{-1}$) 2918, 2849, 1609, 1520, 1444, 1306, 1179, 1057, 1041.

2-(4-n-nonyloxyphenyl)-5-(4-n-decyloxyphenyl)-1,3,4-thiadiazole, 2b.
Yield = 41%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.03 (d, J=8.8 Hz, 2H), 7.90 (d, J=8.8 Hz, 2H), 6.99 (dd, J=12.4, 8.8 Hz, 4H), 3.99-4.03 (m, 4H), 1.76-1.83 (m, 4H), 1.42-1.48 (m, 4H), 1.21-1.39 (m, 22H), 0.87 (t, J=6.4 Hz, 6H). $^{13}$C NMR (CDCl$_3$) $\delta$ 14.15, 22.70, 26.02 (2C), 29.16 (2C), 29.28 (2C), 29.34 (2C), 29.40 (2C), 29.58, 31.92 (2C), 68.27 (2C), 114.93, 114.99, 122.80 (2C), 128.55, 129.35, 161.38, 161.84, 167.15, 170.93. IR (cm$^{-1}$) 2954, 2919, 2851, 1607, 1520, 1496, 1499, 1256, 1175.

2-(4-$n$-nonyloxyphenyl)-5-(4-$n$-dodecyloxyphenyl)-1,3,4-thiadiazole, 2c.

Yield = 50%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.90 (d, J=8.8 Hz, 4H), 6.96 (d, J=8.8 Hz, 4H), 4.01 (t, J=6.4 Hz, 4H), 1.76-1.84 (m, 4H), 1.41-1.50 (m, 4H), 1.24-1.37 (m, 26H), 0.87 (t, J=6.8 Hz, 6H). $^{13}$C NMR (CDCl$_3$) $\delta$ 14.11 (2C), 22.72 (2C), 26.01 (2C), 29.16 (2C), 29.26(2C), 29.39 (2C), 29.53 (2C), 29.58, 29.60, 29.65, 31.88 (2C), 68.28 (2C), 115.00 (2C), 122.90 (2C), 129.35 (2C), 161.40 (2C), 173.20 (2C). IR (cm$^{-1}$) 2919, 2849, 1606, 1519, 1447, 1302, 1251, 1173, 1022.

2-[4-$n$-(nonyloxyphenyl)]-5-[4-$n$-(4,4,5,6,6,7,7,8,8,9,9,9-tridecafluorononyloxyphenyl)]-1,3,4-thiadiazole, 2d.

Yield = 50%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.91(t, J=8.0 Hz, 4H), 6.97 (dd, J=9.0, 3.0 Hz, 4H), 4.10 (t, J=5.8 Hz, 2H), 4.01 (t, J=6.6 Hz, 2H), 2.26-2.41 (m, 2H), 2.10-2.18 (m,
2H), 1.76-1.84 (m, 2H), 1.42-1.49 (m, 2H), 1.25-1.37 (m, 10H), 0.87 (t, J=6.6 Hz, 3H).

$^{13}$C NMR (CDCl$_3$) δ 14.13, 20.60, 22.69, 26.02, 29.27 (2C), 29.39 (2C), 29.54, 31.89 (CF$_2$CH$_2$-, JC-F = 22.4 Hz), 66.52, 68.29, 110-120 (m, CF$_3$(CF$_2$)$_5$), 114.95, 115.02, 122.50, 123.47, 129.38, 129.44, 160.60, 160.80, 170.70, 171.20. IR (cm$^{-1}$) 2936, 2925, 2854, 1607, 1520, 1448, 1249, 1231, 1184, 1175, 1142, 1028.

2-[4-n-(nonyloxyphenyl)]-5-[4-n-(7,7,8,8,9,9,10,10,10-nonfluorodecyloxyphenyl)]-1,3,4-thiadiazole, 2e.

![Structure of 2e](image)

Yield = 69 %. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.92 (dd, J=8.8, 2.0 Hz, 4H), 6.98 (d, J=8.0 Hz, 4H), 4.01-4.06 (m, 4H), 2.01-2.16 (m, 2H), 1.78-1.88 (m, 4H), 1.62-1.71 (m, 2H), 1.44-1.57 (m, 6H), 1.26-1.39 (m, 10H), 0.89 (t, J=7.0 Hz, 3H). $^{13}$C NMR (CDCl$_3$) δ 14.12, 20.08, 22.68, 25.75, 26.01, 28.84, 29.16, 29.26, 29.39, 29.53, 30.72, 31.88 (CF$_2$CH$_2$-, JC-F = 22.4 Hz), 67.92, 68.28, 110-120 (m, CF$_3$(CF$_2$)$_5$), 114.96, 115.01, 122.79, 122.97, 128.56, 129.36, 161.23, 161.42, 167.08, 167.21. IR (cm$^{-1}$) 2938, 2922, 2853, 1607, 1520, 1258, 1224, 1175, 1132.

2-[4-n-(nonyloxyphenyl)]-5-[4-n-(4,4,5,6,7,7,8,8,9,9,10,10,10-pentadecafluorodecyloxyphenyl)]-1,3,4-thiadiazole, 2f.

![Structure of 2f](image)

Yield = 70 %. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.93 (t, J=8.2 Hz, 4H), 6.99 (dd, J=9.0, 3.0 Hz, 4H), 4.12 (t, J=5.8 Hz, 2H), 4.02 (t, J=6.6 Hz, 2H), 2.28-2.41 (m, 2H), 2.12-2.19 (m,
2H), 1.78-1.87 (m, 2H), 1.44-1.51 (m, 2H), 1.27-1.39 (m, 10H), 0.89 (t, J=6.8 Hz, 3H).

$^{13}$C NMR (CDCl$_3$) $\delta$ 14.12, 19.89, 22.70, 26.01, 27.93, 29.16, 29.26, 29.39, 29.53, 31.90 (CF$_2$CH$_2$-, J$_{C-F}$ = 22.4 Hz), 66.52, 68.29, 110-120 (m, CF$_3$(CF$_2$)$_6$), 114.96, 115.02, 128.58, 128.65, 129.38, 129.44, 161.55, 167.43, 174.67, 176.70. IR (cm$^{-1}$) 2921, 2852, 1607, 1519, 1448, 1247, 1202, 1174, 1145, 1028.

2-[4-n-(nonyloxyphenyl)]-5-[4-n-(7,7,8,8,9,9,10,10,11,11,12,12-tridecafluorododecyloxyphenyl)]-1,3,4-thiadiazole, 2g.

Yield = 60%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.90 (dd, J=8.8, 2.0 Hz, 4H), 6.95 (d, J=7.6 Hz, 4H), 3.98-4.02 (m, 4H), 1.99-2.14 (m, 2H), 1.75-1.85 (m, 4H), 1.60-1.68 (m, 2H), 1.41-1.56 (m, 6H), 1.24-1.36 (m, 10H), 0.86 (t, J=6.8 Hz, 3H). $^{13}$C NMR (CDCl$_3$) $\delta$ 14.12, 20.10, 22.68, 25.76, 26.01, 28.86, 28.93, 29.16, 29.27, 29.39 (2C), 29.54, 31.88 (CF$_2$CH$_2$-, J$_{C-F}$ = 22.4 Hz), 67.92, 68.28, 110-120 (m, CF$_3$(CF$_2$)$_5$), 114.96, 115.01, 122.78, 123.01, 128.58, 129.37, 161.24, 161.42, 167.09, 167.20. IR (cm$^{-1}$) 2939, 2921, 2853, 1608, 1521, 1446, 1263, 1240, 1175, 1140, 1048.

2-[4-n-(nonyloxyphenyl)]-5-[4-n-(5,5,6,6,7,7,8,8,9,9,10,10,11,11,12,12-heptadecafluorododecyloxyphenyl)]-1,3,4-thiadiazole, 2h.
Yield = 38%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.92 (dd, J=8.8, 4.8 Hz, 4H), 6.98 (d, J=8.8 Hz, 4H), 4.07 (t, J=5.4 Hz, 2H), 4.02 (t, J=6.6 Hz, 2H), 2.11-2.25 (m, 2H), 1.78-1.95 (m, 6H), 1.43-1.51 (m, 2H), 1.25-1.38 (m, 10H), 0.88 (t, J=6.8 Hz, 3H). $^{13}$C NMR (CDCl$_3$) $\delta$ 14.12, 17.31, 22.69, 26.01, 28.62, 29.16, 29.27, 29.39 (2C), 29.54, 31.89 (CF$_2$CH$_2$-, $J_{C-F} = 22.4$ Hz), 67.42, 68.28, 110-120 (m, CF$_3$(CF$_2$)$_2$), 114.95, 115.01, 128.62 (2C), 129.30, 129.41, 161.50 (2C), 171.0 (2C). IR (cm$^{-1}$) 2932, 2858, 1603, 1510, 1447, 1246, 1205, 1175, 1148, 1020.

2,5-Bis[4-n-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluorononyloxyphenyl)]-1,3,4-thiadiazole, 2i.

Yield = 50%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.06 (d, J=8.8 Hz, 2H), 7.94 (d, J=8.8 Hz, 2H), 6.99 (d, J=8.8 Hz, 4H), 4.12 (t, J=5.6 Hz, 4H), 2.26-2.41 (m, 4H), 2.12-2.20 (m, 4H). $^{13}$C NMR (CDCl$_3$) $\delta$ 27.30, 32.90 (CF$_2$CH$_2$-, $J_{C-F} = 22.4$ Hz), 66.70 (-CH$_2$O-), 110-120 (m, CF$_3$(CF$_2$)$_2$), 115.00, 122.90, 129.47, 145.6, 172.8. IR (cm$^{-1}$) 2961, 2925, 2891, 1615, 1585, 1498, 1233, 1187, 1176, 1143, 1026.

2,5-Bis[4-n-(7,7,8,8,9,9,10,10,10-nonafluorodecyloxyphenyl)]-1,3,4-thiadiazole, 2j.

Yield = 43%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.05 (d, J=8.8 Hz, 2H), 7.92 (d, J=8.8 Hz, 2H), 6.99 (dd, J=12.0, 9.2 Hz, 4H), 4.02-4.06 (m, 4H), 2.01-2.16 (m, 4H), 1.81-1.87 (m,
4H), 1.64-1.71 (m, 4H), 1.45-1.58 (m, 8H). $^{13}$C NMR (CDCl$_3$) δ 20.08, 24.50, 25.76, 28.91, 31.50 (CF$_2$CH$_2$-, J$_{C-F}$ = 22.4 Hz), 67.93 (-CH$_2$O-), 110-120 (m, CF$_3$(CF$_2$)$_3$), 114.98, 128.59, 129.39, 161.50, 176.50. IR (cm$^{-1}$) 2943, 2870, 1610, 1496, 1253, 1219, 1176, 1131.

2,5-Bis[4-n-(4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-pentacafluorodecyloxyphenyl)]-1,3,4-thiadiazole, 2k.

![Chemical structure](image)

Yield = 50%. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.05 (d, J=8.8 Hz, 4H), 6.96 (d, J=9.2 Hz, 4H), 4.12 (t, J=6.0 Hz, 4H), 2.25-2.40 (m, 4H), 2.10-2.19 (m, 4H). $^{13}$C NMR (CDCl$_3$) δ 27.60, 31.50 (CF$_2$CH$_2$-, J$_{C-F}$ = 22.4 Hz), 66.90 (-CH$_2$O-), 110-120 (m, CF$_3$(CF$_2$)$_6$), 114.58, 117.60, 130.56, 156.2, 177.4. IR (cm$^{-1}$) 2940, 2871, 1608, 1501, 1252, 1210, 1175, 1135.

2,5-Bis[4-n-(7,7,8,8,9,9,10,10,11,11,12,12-tridecafluorododecyloxyphenyl)]-1,3,4-thiadiazole, 2l.

![Chemical structure](image)

Yield = 60%. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.92 (d, J=8.8 Hz, 4H), 6.98 (d, J=8.8 Hz, 4H), 4.05 (t, J=6.2 Hz, 4H), 2.03-2.18 (m, 4H), 1.81-1.90 (m, 4H), 1.64-1.72 (m, 4H), 1.45-1.59 (m, 8H). $^{13}$C NMR (CDCl$_3$) δ 20.12, 25.72, 28.82, 29.65, 31.12 (CF$_2$CH$_2$-, J$_{C-F}$
= 22.4 Hz), 67.98 (-CH$_2$O-), 110-120 (m, CF$_3$(CF$_2$)$_3$), 115.04, 123.08, 129.37, 161.30, 167.06. IR (cm$^{-1}$) 2942, 2868, 1609, 1447, 1239, 1175, 1140, 1072.

2,5-Bis[4-n-(5,5,6,7,8,8,9,9,10,10,11,11,12,12,12-
heptadecafluorododecyloxyphenyl)]-1,3,4-thiadiazole, 2m.

Yield = 48%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.05 (t, J=8.0 Hz, 2H), 7.94 (d, J=8.4 Hz, 2H), 7.00 (dd, J=8.8, 12.0 Hz, 2H), 6.93 (d, J=8.8 Hz, 2H), 4.07-4.11 (m, 4H), 2.13-2.27 (m, 4H), 1.90-1.96 (m, 4H), 1.83-1.89 (m, 4H). $^{13}$C NMR (CDCl$_3$) $\delta$ 22.60, 28.64, 31.01 (CF$_2$CH$_2$-, J$_{C-F}$ = 22.4 Hz), 67.50 (-CH$_2$O-), 110-120 (m, CF$_3$(CF$_2$)$_7$), 114.22, 129.42, 132.30, 161.48, 164.12. IR (cm$^{-1}$) 2956, 2925, 2854, 1596, 1508, 1309, 1203, 1146, 1015.

2,5-Bis(4-(dodecyloxy)phenyl)-1,3,4-oxadiazole, 3.$^{13}$

A mixture of N,N’-bis(4-n-nonyloxy)benzoyl hydrazine (0.21 g, 0.34 mmol), which was prepared and reported earlier$^{15}$ and phosphorus oxychloride, POCl$_3$ (0.26 g, 0.16 ml, 1.73 mmol) was heated gently under reflux in dried toluene (5.0 ml) for 12 h. The reaction was monitored by TLC. After cooling the solvent and excess POCl$_3$ were evaporated off under reduced pressure. The product was purified using silica gel column chromatography (15% of ethyl acetate in hexane), recrystallized from methanol/water.
and dried in the oven at 60°C. Yield = 83%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.04 (d, J=8.8 Hz, 4H), 7.01 (d, J=8.8 Hz, 4H), 4.03 (t, J=6.6 Hz, 4H), 1.76-1.89 (m, 4H), 1.42-1.52 (m, 4H), 1.25–1.38 (m, 32H), 0.88 (t, J=6.6 Hz, 6H). $^{13}$C NMR (CDCl$_3$) $\delta$ 14.14, 22.71, 26.02, 29.16, 29.37, 29.39, 29.55, 29.58, 29.61, 29.67, 31.93, 68.28, 114.94, 116.40, 128.55, 161.82, 164.13. IR (cm$^{-1}$) 2918, 2852, 1611, 1496, 1471, 1253, 1175, 1023.

2-(4-dodecyloxy-2-fluorophenyl)-5-(4-(dodecyloxy)phenyl)-1,3,4-oxadiazole, 4.$^{13}$

A mixture of 4-(dodecyloxy)-N’-(4-(dodecyloxy)benzoyl)-2-fluorobenzoyl hydrazine (0.30 g, 0.48 mmol), which was prepared and reported earlier$^{15}$ and phosphorus oxychloride, POCl$_3$ (0.37 g, 0.22 ml, 2.40 mmol) was heated gently under reflux in dried toluene (5.0 ml) for 12 h. The reaction was monitored by TLC. After cooling the solvent and excess POCl$_3$ were evaporated off under reduced pressure. The product was purified using silica gel column chromatography (15% of ethyl acetate in hexane), recrystallized from methanol/water and dried in the oven at 60°C. Yield = 89%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.00-8.08 (m, 3H), 7.01 (d, J=8.8 Hz, 2H), 6.83 (dd, J=2.4, 8.8 Hz, 1H), 6.76 (dd, J=2.2, 12.6 Hz, 1H), 3.99-4.06 (m, 4H), 1.78-1.86 (m, 4H), 1.44-1.51 (m, 4H), 1.24-1.38 (m, 32H), 0.88 (t, J=6.8 Hz, 6H). $^{13}$C NMR (CDCl$_3$) $\delta$ 14.14 (2C), 22.70 (2C), 25.94, 26.01, 28.98 (2C), 29.15 (2C), 29.36 (2C), 29.39 (2C), 29.55 (2C), 29.59 (2C), 29.65 (2C), 31.93 (2C), 68.28, 68.79, 102.85 (d, J=176 Hz, 2C), 111.45 (2C), 114.95,
116.22, 128.68, 130.43, 162.22 (d, J=176.0 Hz, 2C), 162.44, 163.13. IR (cm\(^{-1}\)) 2917, 2852, 1625, 1612, 1497, 1472, 1292, 1252, 1171, 1136, 1024.

2,5-Bis(4-dodecyloxy-2-fluorophenyl)-1,3,4-oxadiazole, 5.\(^{13}\)

A mixture of \(N,N'\)-bis(4-dodecyloxy-2-fluorobenzoyl) hydrazine (0.10 g, 0.16 mmol), which was prepared and reported earlier\(^{15}\) and phosphorus oxychloride, POCl\(_3\) (0.12 g, 0.07 ml, 0.78 mmol) was heated gently under reflux in dried toluene (5.0 ml) for 12 h. The reaction was monitored by TLC. After cooling the solvent and excess POCl\(_3\) were evaporated off under reduced pressure. The product was purified using silica gel column chromatography (15% of ethyl acetate in hexane), recrystallized from methanol/water and dried in the oven at 60\(^{\circ}\)C. Yield = 69 %. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.02 (t, J=8.6 Hz, 2H), 6.82 (dd, J=2.0, 8.8 Hz, 2H), 6.75 (dd, J=2.4, 12.4 Hz, 2H), 4.01 (t, J=6.4 Hz, 4H), 1.77-1.86 (m, 4H), 1.42-1.51 (m, 4H), 1.25-1.37 (m, 32H), 0.88 (t, J=6.8 Hz, 6H). \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\) 14.13, 22.70, 25.94, 28.98, 29.34, 29.38, 29.55, 29.59, 29.62, 29.65, 31.93, 68.79, 102.86 (d, J=96.0 Hz), 104.70, 111.47, 130.48, 159.97, 161.32 (d, J=20.0 Hz), 163.28 (d, J=40.0Hz). IR (cm\(^{-1}\)) 2918, 2853, 1626, 1593, 1472, 1291, 1170, 1129, 1024.
2,5-Bis(4-(dodecyloxy)phenyl)-1,3,4-thiadiazole, 6.  

C\text{_{12}H_{25}O}OC\text{_{12}H_{25}}

A mixture of 4-(dodecyloxy)-N'-(4-(dodecyloxy)benzoyl)benzoyl hydrazine (0.20 g, 0.33 mmol), which was prepared and reported earlier 15 and Lawesson’s reagent (0.09 g, 0.23 mmol) was heated gently under reflux in dried toluene (5.0 ml) for 12 h. The reaction was monitored by TLC. The excess solvent was evaporated under reduced pressure. The product was purified using silica gel column chromatography (15% of ethyl acetate in hexane), recrystallized from methanol/water and dried in the oven at 60°C. Yield = 80%.

\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) δ 7.91 (d, J=8.8 Hz, 4H), 6.97 (d, J=8.4 Hz, 4H), 4.02 (t, J=6.4 Hz, 4H), 1.75-1.88 (m, 4H), 1.42-1.51 (m, 4H), 1.23–1.37 (m, 32H), 0.88 (t, J=6.6 Hz, 6H). \textsuperscript{13}C NMR (CDCl\textsubscript{3}) δ 14.14, 22.71, 26.02, 29.17, 29.37, 29.39, 29.59, 29.61, 29.66, 29.68, 31.94, 68.28, 115.00, 122.81, 128.55, 161.40, 167.14. IR (cm\textsuperscript{-1}) 2917, 2850, 1610, 1520, 1410, 1305, 1255, 1179, 1035, 1028.

2-(4-dodecyloxy-2-fluorophenyl)-5-(4-dodecyloxyphenyl)-1,3,4-thiadiazole, 7.  

C\text{_{12}H_{25}O}OC\text{_{12}H_{25}}

A mixture of 4-(dodecyloxy)-N'-(4-(dodecyloxy)benzoyl)-2-fluorobenzoyl hydrazine (0.29 g, 0.463 mmol) and Lawesson’s reagent (0.13 g, 0.324 mmol), which was prepared and reported earlier 15 was heated gently under reflux in dried toluene (5.0 ml) for 12 h. The reaction was monitored by TLC. The excess solvent was evaporated under reduced...
pressure. The product was purified using silica gel column chromatography (15% of ethyl acetate in hexane), recrystallized from methanol/water and dried in the oven at 60°C. Yield = 80%. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.32 (t, J=8.6 Hz, 1H), 7.95 (d, J=8.8 Hz, 2H), 6.98 (d, J=8.8 Hz, 2H), 6.84 (dd, J=2.2, 9.0 Hz, 1H), 6.73 (dd, J=2.4, 12.8 Hz, 1H), 3.99-5.05 (m, 2H), 1.77-1.86 (m, 4H), 1.43-1.51 (m, 4H), 1.25-1.38 (m, 32H), 0.88 (t, J=6.8 Hz, 6H). $^{13}$C NMR (CDCl$_3$) δ 14.14 (2C), 22.71 (2C), 25.95, 26.02, 29.01 (2C), 29.17 (2C), 29.36 (2C), 29.57 (2C), 29.60 (2C), 29.65 (2C), 29.67 (2C), 31.93 (2C), 68.27, 68.75, 102.06 (d, J=100.0 Hz), 110.84 (d, J=52.0 Hz), 111.71, 115.03, 122.69, 128.68, 129.31, 129.62 (d, J=12.0 Hz), 159.39 (d, J=152.0 Hz), 159.66, 161.43, 168.25 (d, J=16.0 Hz). IR (cm$^{-1}$) 2918, 2851, 1621, 1604, 1518, 1470, 1443, 1415, 1293, 1256, 1164, 1120, 1025.

2,5-Bis(4-dodecyloxy-2-fluorophenyl)-1,3,4-thiadiazole, 8.$^{14}$

A mixture of $N,N'$-bis(4-dodecyloxy-2-fluorobenzoyl) hydrazine (0.15, 0.233 mmol), which was prepared and reported earlier $^{15}$ and Lawesson’s reagent (0.056 g, 0.140 mmol) was heated gently under reflux in dried toluene (5.0 ml) for 12 h. The reaction was monitored by TLC. The excess solvent was evaporated under reduced pressure. The product was purified using silica gel column chromatography (15% of ethyl acetate in hexane), recrystallized from methanol/water and dried in the oven at 60°C. Yield = 60%. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.35 (t, J=8.4 Hz, 2H), 6.85 (dd, J=2.4, 8.8 Hz, 2H), 6.75
(dd, J=2.0, 12.8 Hz, 2H), 4.02 (t, J=6.4 Hz, 4H), 1.77-1.87 (m, 4H), 1.42-1.51 (m, 4H),
1.25-1.36 (m, 32H), 0.88 (t, J=6.6 Hz, 6H). $^{13}$C NMR (CDCl$_3$) $\delta$ 14.13, 22.70, 25.95,
29.01, 29.32, 29.35, 29.37, 29.56, 29.59, 29.65, 31.93, 68.75, 102.06 (d, J=100.0 Hz),
110.79 (d, J=48.0 Hz), 115.03, 129.66 (d, J=16.0 Hz), 159.28, 161.34 (d, J=276.0 Hz),
162.57 (d, J=48.0 Hz). IR (cm$^{-1}$) 2918, 2850, 1622, 1578, 1513, 1468, 1419, 1289, 1263,
1161, 1121, 1110.
4. Experimental procedures for Chapter-4

**Synthesis of monomers and precursors.** Methyl 3,4,5-tris(\(n\)-alkyloxy)benzoate, 3,4,5-tris(\(n\)-alkyloxy)benzoic acid, the \(N\)-(2,3-dihydroxypropyl)-3,4,5-tris(\(n\)-alkyloxy)benzamides and other amino alcohol benzamides were prepared by literature procedures.\(^{16,3}\)

**Syntheses of Monomers and precursors.**

**Synthesis of methyl 3,4,5-tris(\(n\)-alkyloxy)benzoate, 1a,b.**\(^3\) A mixture of methyl gallate (16.04 g, 0.09 mol), potassium carbonate (42.07 g, 0.30 mol) and 1-bromononane (75.98 g, 0.30 mol) in 50.0 ml of DMF was heated to 80\(^\circ\)C. The reaction was monitored by TLC. After 72 h, the mixture was cooled to room temperature and poured into 200 ml of ice water. An oily layer was formed. The mixture was extracted using ethyl acetate (3 \(\times\) 100 ml). The combined organic layers were dried with anhydrous magnesium sulfate and filtered. The solvent was evaporated and the crude product was purified using silica gel column chromatography (15% of ethyl acetate in hexane) to give the expected product.

**Methyl 3,4,5-tris-(\(n\)-dodecyloxy)benzoate, 1a.**

![Chemical Structure](attachment:image.png)
Yield = 40.65 g (68%), mp = 52.7-53.8 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.25 (s, 2H), 3.99-4.03 (m, 6H), 3.89 (s, 3H), 1.71-1.85 (m, 6H), 1.43-1.51 (m, 6H), 1.24–1.37 (m, 48H), 0.88 (t, J=6.8 Hz, 9H). $^{13}$C NMR (CDCl$_3$) $\delta$ 14.13 (2C), 22.71 (2C), 26.09 (2C), 29.31 (2C), 29.38 (2C), 29.41 (2C), 29.58 (2C), 29.65 (2C), 29.71 (2C), 30.34 (2C), 31.94 (2C), 69.16 (2C), 73.50, 107.97, 124.65, 142.35, 152.83, 166.96 (-COO-). IR (cm$^{-1}$) 2954, 2917, 2848, 1716, 1589, 1504, 1467, 1432, 1336, 1220, 1130.

**Methyl 3,4,5-tris-(n-nonyloxy)benzoate, 1b.**

![Methyl 3,4,5-tris-(n-nonyloxy)benzoate](image)

This ester was synthesized from methyl gallate (12.50 g, 0.07 mol), potassium carbonate (42.15 g, 0.30 mol) and 1-bromononane (63.28 g, 0.30 mol) in 40.0 ml of DMF. The product was purified using column chromatography (10% EtOAc in hexane). Yield = 38.15 g (55 %), mp = 49.3-50.5 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.24 (s, 2H), 3.98-4.02 (m, 6H), 3.86 (s, 3H), 1.71-1.81 (m, 6H), 1.42-1.48 (m, 6H), 1.21–1.36 (m, 30H), 0.88 (t, J=7.0 Hz, 9H). $^{13}$C NMR (CDCl$_3$) $\delta$ 14.07 (2C), 22.69 (2C), 26.09 (2C), 29.30, 29.32, 29.41, 29.53, 29.60, 29.69, 30.35 (2C), 31.91, 31.95, 69.12, 73.42, 107.97, 124.65, 142.37, 152.82, 166.85. IR (cm$^{-1}$) 2958, 2919, 2850, 1718, 1590, 1500, 1465, 1433, 1335, 1219, 1125.
Synthesis of 3,4,5-tris(\(n\)-alkyloxy)benzoic acid, 2a,b.\(^3\) Methyl 3,4,5-tris(\(n\)-nonyloxy)benzoate (20.00 g, 29.07 mmol) was dissolved in a refluxing mixture of absolute ethanol (40.0 ml) and THF (20.0 ml). 10N KOH (30.0 ml) was added to this solution. The reaction progress was monitored by TLC. After 12 h, the mixture was cooled to room temperature and the solvent was evaporated and then the mixture was acidified and precipitated into ice water (200.0 ml). After filtration, the product was recrystallized from methanol/water and dried in the oven at 60°C.

3,4,5-Tris-\((n\)-dodecyloxy\)benzoic acid, 2a.

\[
\begin{align*}
\text{ Yield } &= 16.07 \text{ g (82\%), } \\
\text{ mp } &= 57.9-58.2 \degree C. \quad ^1\text{H NMR (400 MHz, CDCl}_3\text{)} \delta 10.12 \text{ (s, br, 1H), } 7.31 \text{ (s, 2H), } 4.01-4.06 \text{ (m, 6H), } 1.71-1.86 \text{ (m, 6H), } 1.43-1.52 \text{ (m, 6H), } 1.23-1.38 \text{ (m, 48H), } 0.88 \text{ (t, } J=6.8 \text{ Hz, 9H). } ^{13}\text{C NMR (CDCl}_3\text{)} \delta 14.13 \text{ (2C), } 22.71 \text{ (2C), } 26.09 \text{ (2C), } 29.29 \text{ (2C), } 29.39 \text{ (2C), } 29.41 \text{ (2C), } 29.58 \text{ (2C), } 29.65 \text{ (2C), } 29.68 \text{ (2C), } 29.72 \text{ (2C), } 30.35, 31.95, 69.20, 73.56, 108.56, 123.60, 143.18, 152.86, 171.77. \quad \text{ IR (cm}^{-1}) \quad 3500-2500 \text{ (O-H), } 2954, 2919, 2850, 1683, 1587, 1505, 1468, 1431, 1384, 1334, 1276, 1242, 1121.
\end{align*}
\]

3,4,5-Tris-(\(n\)-nonyloxy)benzoic acid, 2b.

\[
\begin{align*}
\end{align*}
\]
This acid was synthesized from methyl 3,4,5-tris(n-nonyloxy)benzoate (20.61 g, 36.70 mmol) in absolute 40.0 ml ethanol, 20.0 ml THF and 28.0 ml of 10N KOH. The product was recrystallized from methanol/water and dried in the oven at 60°C. Yield = 15.72 g (78%), mp = 46.8-47.5 °C. 1H NMR (400 MHz, CDCl3) δ 10.11 (s, br, 1H), 7.32 (s, 2H), 4.01-4.06 (m, 6H), 1.73-1.84 (m, 6H), 1.44-1.51 (m, 6H), 1.28-1.38 (m, 30H), 0.88 (t, J=6.6 Hz, 9H). 13C NMR (CDCl3) δ 14.11 (2C), 22.70 (2C), 26.05, 26.08, 29.30 (2C), 29.40 (2C), 29.68 (2C), 31.91, 31.95, 69.20, 73.56, 108.57, 123.60, 143.19, 152.86, 171.79. IR (cm⁻¹) 3300-2500 (O-H), 2953, 2921, 2851, 1685, 1587, 1504, 1467, 1431, 1390, 1329, 1275, 1230, 1115.

Synthesis of amides from amino alcohol compounds with different numbers of hydroxy groups. A mixture of 3,4,5-tris(n-dodecyloxy)benzoic acid (0.54 g, 0.80 mmol) and oxalyl chloride (0.41 ml, 4.81 mmol) was refluxed in methylene chloride (2.0 ml). A half drop of DMF was added into the reaction mixture. After 3 h, the excess oxalyl chloride was evaporated and the residue was dissolved in methylene chloride (2.0 ml). The racemic amino alcohol, 3-amino-1-propane-1,2-diol (0.73 g, 8.01 mmol) was dissolved in DMF (2.0 ml) and triethylamine (1.12 ml, 8.01 mmol) was added. To this solution, the acid chloride dissolved in methylene chloride was added dropwise at 5.0°C. The mixture was continued to stir for 1 h at room temperature and then the solvent was removed under reduced pressure. The solid residue was dissolved in ethanol (5.0 ml) and the addition of diethyl ether (10.0 ml) resulted in the formation of a white precipitate of triethylamine hydrochloride which was then filtered off. The solvent was evaporated and
the crude product was recrystallized from ethanol/water and dried in the oven at 60°C to give the expected product.

\[ \text{N-}[3,4,5-\text{Tri}(n\text{-dodecyloxybenzoylamine})]\text{propane-2,3-diol, 3a.} \]

\[
\begin{align*}
&\text{C}_{12}\text{H}_{25}\text{O} \\
&\text{C}_{12}\text{H}_{25}\text{O} \\
&\text{OC}_{12}\text{H}_{25} \\
&\text{N} \\
&\text{H} \\
&\text{OH} \\
&\text{OH} \\
\end{align*}
\]

Yield = 0.41 g (65%) \( ^1H \text{NMR} (400 \text{ MHz, CDCl}_3) \delta 6.96 (s, 2H), 6.48 (t, J=6.1 \text{ Hz, 1H}), 3.97-4.03 (m, 6H), 3.84-3.91 (m, 1H), 3.56-3.67 (m, 4H), 2.96 (s, br, 2H), 1.70-1.85 (m, 6H), 1.43-1.51 (m, 6H), 1.24-1.36 (m, 48H), 0.88 (t, J=7.0 \text{ Hz, 9H}). \]

\( ^{13}\text{C NMR} (\text{CDCl}_3) \delta 14.12 (2\text{C}), 22.71 (2\text{C}), 26.10 (2\text{C}), 29.38 (2\text{C}), 29.52 (2\text{C}), 29.58 (2\text{C}), 29.60 (2\text{C}), 29.66 (2\text{C}), 29.72 (2\text{C}), 30.33 (2\text{C}), 31.94 (2\text{C}), 42.76, 63.61, 69.42, 71.29, 73.56, 105.80, 128.34, 141.59, 153.18, 169.25. \)

\( \text{IR (cm}^{-1}) \text{ 3200-3500 (O-H), 3359, 2918, 2850, 1581, 1505, 1467, 1430, 1338, 1240, 1117, 1015.} \)

\[ \text{N-}[3,4,5-\text{Tri}(n\text{-nonyloxybenzoylamine})]\text{propane-2,3-diol, 3b.} \]

\[
\begin{align*}
&\text{C}_{9}\text{H}_{19}\text{O} \\
&\text{C}_{9}\text{H}_{19}\text{O} \\
&\text{OC}_{9}\text{H}_{19} \\
&\text{N} \\
&\text{H} \\
&\text{OH} \\
&\text{OH} \\
\end{align*}
\]

This amide was synthesized from 3,4,5-tris\( (n\text{-dodecyloxy})\)benzoic acid (0.60 g, 1.10 mmol) and 3-amino-1-propane-1,2-diol (1.00 g, 10.95 mmol). The product was recrystallized twice from ethanol/water and dried in the oven at 60°C. Yield = 0.40 g.
(57%) \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 6.96 (s, 2H), 6.47 (t, \(J=6.1\) Hz, 1H), 3.97-4.04 (m, 6H), 3.84-3.91 (m, 1H), 3.55-3.68 (m, 4H), 2.90-2.97 (m, 2H), 1.70-1.86 (m, 6H), 1.43-1.51 (m, 6H), 1.24–1.37 (m, 30H), 0.88 (t, \(J=6.8\) Hz, 9H). \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\) 14.11 (2C), 22.70 (2C), 26.09 (2C), 29.31 (2C), 29.38 (2C), 29.42 (2C), 29.60, 29.69, 30.33, 31.91, 42.83, 63.66, 69.41, 71.27, 73.56, 105.82, 128.25, 141.58, 153.17, 169.27. IR (cm\(^{-1}\)) 3200-3500 (O-H), 3267, 2954, 2919, 2851, 1636, 1581, 1541, 1500, 1467, 1425, 1343, 1235, 1117.

\(N\)-methyl-(3,4,5-tris(\(n\)-nonyloxy))-\(N\)-((2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl)benzamide, 4.

![Chemical Structure](image)

This amide was synthesized from 3,4,5-tris(\(n\)-nonyloxy)benzoic acid (1.00 g, 1.82 mmol) and \(N\)-methyl-D-glucamine (3.56 g, 18.25 mmol). The product was recrystallized from ethanol/water and dried in the oven at 60°C. Yield = 0.96 g (73%). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 6.58 (s, 2H), 4.57 (s, br, 5H), 4.07-4.14 (m, 4H), 3.89-3.96 (m, 6H), 3.77-3.87 (m, 2H), 3.51-3.60 (m, 2H), 3.03 (s, 3H), 1.68-1.80 (m, 6H), 1.39-1.497 (m, 6H), 1.21–1.34 (m, 30H), 0.84-0.88 (m, 9H). \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\) 14.11 (2C), 22.69 (2C), 26.12, 26.16, 29.32 (2C), 29.42, 29.49, 29.62, 29.71, 30.37 (2C), 31.92, 31.95, 39.50, 51.84, 64.07, 69.31, 70.24, 71.86, 72.23, 73.50, 73.57, 105.84, 130.01, 139.67, 153.10, 173.34.
IR (cm$^{-1}$) 3150-3500 (O-H), 3356, 3262, 2955, 2921, 2853, 1606, 1577, 1493, 1464, 1446, 1421, 1410, 1332, 1239, 1129, 1119, 1089, 1031.

$N$-(3-hydroxypropyl)-3,4,5-tris(n-nonyloxy)benzamide, 5.

![Chemical Structure](image)

This amide was synthesized from 3,4,5-tris(n-nonyloxy)benzoic acid (0.22 g, 0.40 mmol) and 3-amino-1-propanol (0.30 g, 0.31 ml, 4.01 mmol). The product was recrystallized from methanol/water and dried in the oven at 60°C. Yield = 0.19 g (81%). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 6.96 (s, 2H), 6.54 (t, J=6.1 Hz, 1H), 3.95- 4.03 (m, 6H), 3.70 (t, J=5.4 Hz, 2H), 3.60 (t, J=5.6 Hz, 2H), 2.48 (s, br, 1H), 1.76-1.83 (m, 6H), 1.69-1.75 (m, 2H), 1.42-1.47 (m, 6H), 1.27-1.36 (m, 30H), 0.88 (t, J=3.4 Hz, 9H). $^{13}$C NMR (CDCl$_3$) $\delta$ 14.09 (2C), 22.68 (2C), 26.08 (2C), 29.29 (2C), 29.38 (2C), 29.58 (2C), 29.67 (2C), 30.32, 31.90, 31.94, 37.06, 59.63, 69.42, 73.53, 105.78, 129.00, 141.40, 153.14, 168.52. IR (cm$^{-1}$) 3200-3400 (O-H), 3274, 2920, 2872, 2852, 1633, 1581, 1540, 1500, 1467, 1425, 1387, 1342, 1204, 1117, 1063.

$N$-(1-hydroxypropan-2-yl)-3,4,5-tris(n-nonyloxy)benzamide, 6.

![Chemical Structure](image)
This amide was synthesized from 3,4,5-tris(n-nonyloxy)benzoic acid (0.22 g, 0.40 mmol) and DL-2-amino-1-propanol (DL-alaninol, 0.30 g, 4.01 mmol). The product was recrystallized from methanol/water and dried in the oven at 60°C. Yield = 0.16 g (68%).

\[ ^1H \text{ NMR (400 MHz, CDCl}_3 \] \( \delta \) 6.95 (s, 2H), 6.13 (d, J=6.8 Hz, 1H), 4.22-4.30 (m, 1H), 3.96-4.04 (m, 6H), 3.76-3.82 (m, 1H), 3.62-3.69 (m, 1H), 2.68 (t, J=5.3 Hz, 1H), 1.69-1.85 (m, 6H), 1.42-1.51 (m, 6H), 1.30 (s, 3H), 1.25-1.30 (m, 30H), 0.88 (t, J=6.8 Hz, 9H).

\[ ^13C \text{ NMR (CDCl}_3 \] \( \delta \) 14.11 (2C), 17.17, 22.69 (2C), 26.08 (2C), 29.30 (2C), 29.41 (2C), 29.59 (2C), 29.68, 30.32, 31.90, 31.94, 48.39, 67.35, 69.50, 73.54, 105.91, 129.16, 141.40, 153.13, 168.12. IR (cm\(^{-1}\)) 3200-3400 (O-H), 3565, 3259, 2953, 2920, 2851, 1632, 1582, 1538, 1467, 1424, 1350, 1116, 1038.

\( N-(1\text{-hydroxy-2-methylpropan-2-yl})\text{-3,4,5-tris(n-nonyloxy)benzamide, 7.} \)

This amide was synthesized from 3,4,5-tris(n-nonyloxy)benzoic acid (0.21 g, 0.38 mmol) and 2-amino-2-methyl-1-propanol (0.34 g, 3.83 mmol). The product was recrystallized from methanol/water and dried in the oven at 60°C. Yield = 0.13 g (57%).

\[ ^1H \text{ NMR (400 MHz, CDCl}_3 \] \( \delta \) 7.84 (s, 1H), 6.90 (s, 2H), 6.08 (s, br, 1H), 3.96-4.02 (m, 6H), 3.68 (s, 2H), 1.68-1.86 (m, 6H), 1.44-1.50 (m, 6H), 1.40 (s, 6H), 1.24-1.36 (m, 30H), 0.88 (t, J=6.8 Hz, 9H).

\[ ^13C \text{ NMR (CDCl}_3 \] \( \delta \) 14.12 (2C), 22.69 (2C), 24.82, 26.08 (2C), 29.30 (2C), 29.40 (2C), 29.60 (2C), 29.68 (2C), 31.91, 31.95, 56.55, 69.55, 70.86, 73.55,
(S)-N-(1-hydroxy-3-phenylpropan-2-yl)-3,4,5-tris(nonyloxy)benzamide, 8.

This amide was synthesized from 3,4,5-tris(nonyloxy)benzoic acid (0.22 g, 0.40 mmol) and L-phenylalaninol or (S)-(-)-2-amino-3-phenyl-1-propanol (0.61 g, 4.01 mmol). The product was recrystallized from methanol/water and dried in the oven at 60°C. Yield = 0.20 g (76%). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.31-7.36 (m, 2H), 7.25-7.29 (m, 3H), 6.79 (s, 2H), 6.18 (d, J=7.1 Hz, 1H), 4.31 (m, 1H), 4.27-4.36 (m, 1H), 3.90-4.00 (m, 6H) 3.79-3.85 (m, 1H), 3.69-3.75 (m, 1H), 2.92-3.06 (m, 2H), 1.68-1.84 (m, 6H), 1.41-1.51 (m, 6H), 1.24-1.37 (m, 30H), 0.89 (t, J=6.8 Hz, 9H). $^{13}$C NMR (CDCl$_3$) $\delta$ 14.12 (2C), 22.70 (2C), 26.08 (2C), 29.31, 29.35, 29.41 (2C), 29.60, 29.68, 30.31 (2C), 31.91 (2C), 36.98, 53.72, 64.89, 69.32, 73.51, 105.61, 126.88, 128.82 (2C), 129.12, 129.31, 137.58, 153.07, 168.50. IR (cm$^{-1}$) 3200-3450 (O-H), 3272, 2951, 2919, 2851, 1635, 1582, 1540, 1500, 1466, 1427, 1347, 1233, 1115, 1040.
**N-((1S,2S)-1,3-dihydroxy-1-phenylpropan-2-yl)-3,4,5-tris(n-nonyloxy)benzamide, 9.**

![Chemical structure of 9](image)

This amide was synthesized from 3,4,5-tris(n-nonyloxy)benzoic acid (0.23 g, 0.42 mmol) and (1S, 2S)-(+-)-2-amino-1-phenyl-1,3-propanediol (0.70 g, 4.20 mmol). The product was recrystallized from methanol/water and dried in the oven at 60°C. Yield = 0.20 g (71%). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.39 (d, $J$=7.6 Hz, 2H), 7.32 (t, $J$=7.4 Hz, 2H), 7.23-7.28 (m, 1H), 6.84 (s, 2H), 6.75 (d, $J$=7.2 Hz, 1H), 5.14 (s, 1H), 4.20-4.28 (m, 1H), 3.92-3.99 (m, 6H), 3.81-3.92 (m, 2H), 2.60-3.30 (s, br, 2H), 1.68-1.82 (m, 6H), 1.44-1.47 (m, 6H), 1.25-1.35 (m, 30H), 0.88 (t, $J$=6.8 Hz, 9H). $^{13}$C NMR (CDCl$_3$) $\delta$ 14.10 (2C), 22.68 (2C), 26.09 (2C), 29.30, 29.37, 29.43 (2C), 29.60, 29.68, 30.31(2C), 31.91 (2C), 57.24, 63.82, 69.37, 73.53, 74.00, 105.85, 125.83, 127.90, 128.54, 128.99, 141.17, 141.40, 153.05, 168.62. IR (cm$^{-1}$) 3200-3650 (O-H), 3316, 2953, 2920, 2852, 1634, 1618, 1580, 1530, 1499, 1466, 1427, 1357, 1231, 1116, 1084.

**N-((1R,2R)-1,3-dihydroxy-1-(4-nitrophenyl)propan-2-yl)-3,4,5-tris(n-nonyloxy)benzamide, 10.**

![Chemical structure of 10](image)
This amide was synthesized from 3,4,5-tris(n-nonyloxy)benzoic acid (0.22 g, 0.40 mmol) and (D)-(−)-\textit{threo}-2-amino-1-(4-nitrophenyl)-1,3-propanediol or (1\textit{R},2\textit{R})-2-amino-1-(4-nitrophenyl)propane-1,3-diol (0.85 g, 4.01 mmol). The product was crystallized from methanol/water and dried in the oven at 60°C. Yield = 0.23 g (80%). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.18 (d, $J$=8.8 Hz, 2H), 7.84 (s, 1H), 7.59 (d, $J$=8.4 Hz, 2H), 6.82 (s, 2H), 6.71 (d, $J$=8.0 Hz, 2H), 5.30 (d, $J$=3.2 Hz, 1H), 4.26-4.34 (m, 1H), 3.95-4.03 (m, 6H), 3.83-3.95 (m, 2H), 1.70-1.82 (m, 6H), 1.42-1.45 (m, 6H), 1.20-1.38 (m, 30H), 0.88 (t, $J$=6.8 Hz, 9H). $^{13}$C NMR (CDCl$_3$) $\delta$ 14.12 (2C), 22.69 (2C), 26.09 (2C), 29.30, 29.38, 29.42 (2C), 29.60, 29.68, 30.31 (2C), 31.91 (2C), 56.38, 64.00, 69.50, 73.60, 73.89, 105.85, 123.64, 126.78, 128.46, 141.80, 147.49, 148.54, 153.14, 168.10. IR (cm$^{-1}$) 3200-3500 (O-H), 3321, 2954, 2920, 2852, 1620, 1581, 1528, 1501, 1468, 1427, 1393, 1355, 1344, 1237, 1118, 1043.
5. Experimental procedures for Chapter-5

![Chemical structure](image)

5-(4-fluorophenyl)tetrazole, 4.\(^{17}\) A mixture of 4-fluorobenzonitrile (5.40 g, 44.58 mmol), sodium azide (7.24 g, 111.46 mmol) and glacial acetic acid (6.37 ml, 111.46 mmol) in \(n\)-butanol (25.0 ml) was refluxed under a \(N_2\) atmosphere. The reaction was monitored by TLC. After 32 h, the reaction mixture was cooled to room temperature and diethyl ether (75.0 ml) was added. The mixture was extracted with a NaOH solution (2 × 100.0 ml). The aqueous layer was separated. The combined organic layers were acidified. The precipitate was filtered off, washed with water and dried in the oven at 60°C. Yield = 6.22 g (85 %), mp = 216.0°C. \(^1\)H NMR (400 MHz, DMSO) \(\delta\) 8.09-8.13 (m, 2H), 7.46 (t, \(J=8.8\) Hz, 2H), 3.38 (s, br, 1H). \(^13\)C NMR (CDCl\(_3\)) \(\delta\) 117.06 (d, \(J_{C,F} = 88.0\) Hz), 121.34, 129.98 (d, \(J_{C,F} = 36.0\) Hz), 162.88, 165.36. IR (cm\(^{-1}\)) 1610, 1504, 1443, 1239, 1165, 1057.

![Chemical structure](image)

Ethyl 5-(4-fluorophenyl)-1,3,4-oxadiazole-2-carboxylate, 1.\(^{18}\) A mixture of 4 (5.21 g, 31.74 mmol) and ethyl oxalyl chloride (8.67 g, 7.10 ml, 63.49 mmol) in toluene (25.0 ml)
was stirred at 95-105°C. The reaction was monitored by TLC. After 5 h, the mixture was poured into a saturated solution of sodium bicarbonate (60.0 ml) and stirred. The solution was extracted using ethyl acetate (3 × 50.0 ml). The combined organic layers were dried over anhydrous magnesium sulfate, filtered and evaporated. Yield = 6.82 g (90 %), mp = 104.1°C. 1H NMR (400 MHz, CDCl3) δ 8.16-8.20 (m, 2H), 7.24 (t, J=8.6 Hz, 2H), 4.52-4.58 (q, 2H), 1.48 (t, J=7.2 Hz, 3H). 13C NMR (400 MHz, CDCl3) δ 14.11, 63.59, 116.72 (d, JC-F = 88.0 Hz), 119.12, 130.08 (d, JC-F = 36.0 Hz), 154.37, 156.52, 164.20, 166.74. IR (cm⁻¹) 1752, 1606, 1539, 1492, 1422, 1280, 1241, 1182.

Heptyl 5-(4-fluorophenyl)-1,3,4-oxadiazole-2-carboxylate, 8. A mixture of 1 (0.70 g, 2.94 mmol), 1-heptanol (0.68 g, 0.83 ml, 5.88 mmol), dibutyltin oxide (0.010 g, 0.004 mmol) and toluene (8.0 ml) was placed in a round bottom flask attached to a distillation apparatus. The mixture was heated to 110°C while continuously removing toluene. The reaction was monitored by TLC. The crude was purified using column chromatography (5% ethyl acetate in hexane). Yield = 0.18 g (20 %). 1H NMR (400 MHz, CDCl3) δ 8.16 (dd, J=5.2, 8.8 Hz, 2H), 7.22 (t, J=8.6 Hz, 2H), 4.46 (t, J=6.8 Hz, 2H), 1.77-1.86 (m, 2H), 1.38-1.47 (m, 2H), 1.31-1.38 (m, 2H), 1.23-1.31 (m, 4H), 0.87 (t, J=6.8 Hz, 3H). 13C NMR (400 MHz, CDCl3) δ 14.05, 22.56, 25.70, 28.42, 28.83, 31.65, 67.64, 116.72 (d, JC-.
Compound 1 (0.21 g, 0.88 mmol) was dissolved in a mixture of ethanol (8.0 ml) and THF (3.0 ml). Next, 4.0 ml 10N KOH was added to this solution at 0°C and the mixture was stirred at room temperature. The reaction was monitored by TLC. After 5 h, the reaction mixture was concentrated by rotary evaporation and redissolved in THF. After acidification with HCl, the mixture was poured into 50.0 ml of ice water. An oily layer was formed which was then extracted using ethyl acetate (2 × 50.0 ml). The combined organic layers were dried in anhydrous magnesium sulfate and filtered. The solvent was evaporated and the product was purified using column chromatography (10% ethyl acetate in hexane). Yield = 0.04 g (20%). $^1$H NMR (400 MHz, CDCl$_3$) δ 8.46 (s, 1H), 8.08-8.12 (m, 2H), 7.22 (t, J=8.6 Hz, 2H). $^{13}$C NMR (400 MHz, CDCl$_3$) δ 116.53 (d, $^2$J$_{C-F}$ = 88.0 Hz), 121.23, 129.44 (d, $^2$J$_{C-F}$ = 36.0 Hz), 152.59, 164.32, 166.64. IR (cm$^{-1}$) 3297, 1683, 1651, 1605, 1498, 1238, 1100.
2-(4-(piperidin-1-yl)phenyl)-1,3,4-oxadiazole, 11. A mixture of ethyl 5-(4-fluorophenyl)-1,3,4-oxadiazole-2-carboxylate 1 (0.50 g, 1.68 mmol), piperidine (0.14 g, 0.16 ml, 1.68 mmol) and potassium tert-butoxide (0.23 g, 2.02 mmol) in DMSO (10.0 ml) was stirred at 95°C. The reaction was monitored using TLC. After 24 h, the mixture was cooled to room temperature and poured into concentrated ammonium chloride solution (50.0 ml). The precipitate was filtered and purified using column chromatography (10% ethyl acetate in hexane). Further purification by recrystallization from ethanol:water and dried in the oven at 60°C gave compound 11. Yield = 0.12 g (24%). 

\[ \text{H NMR (400 MHz, CDCl}_3\text{)} \delta 8.36 (s, 1H), 7.92 (d, J= 9.2 Hz, 2H), 6.95 (d, J=8.8 Hz, 2H), 3.34 (t, J=5.4 Hz, 4H), 1.62-1.74 (m, 6H). \]

\[ \text{C NMR 400 MHz, (CDCl}_3\text{)} \delta 24.42, 25.21, 49.59, 112.80, 116.21, 128.72, 149.82, 153.82, 164.52. \]

IR (cm\(^{-1}\)) 3212, 2912, 2887, 1632, 1585, 1498, 1264, 1115, 1024.

A mixture of 1 (0.20 g, 0.85 mmol), piperidine (0.217 g, 0.25 ml, 2.54 mmol) in DMSO (6.0 ml) was stirred at 95°C. The reaction was monitored using TLC. After 24 h, the mixture was cooled and poured into water (50.0 ml). The precipitate was filtered and purified using column chromatography (10% ethyl acetate in hexane). The products were recrystallized from ethanol:water and dried in the oven at 60°C gave to give compounds 11 and 12.
2-(4-(piperidin-1-yl)phenyl)-1,3,4-oxadiazole, 11. Yield = 0.05 g (18%). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.36 (s, 1H), 7.92 (d J= 8.8 Hz, 2H), 6.95 (d, J=9.2 Hz, 2H), 3.33-3.35 (m, 4H), 1.62-1.74 (m, 6H). \(^1\)C NMR (CDCl\(_3\)) \(\delta\) 24.43, 25.22, 49.61, 112.83, 116.23, 128.72, 150.08, 153.82, 164.52. IR (cm\(^{-1}\)) 3218, 2918, 2884, 1628, 1582, 1485, 1265, 1113, 1020.

Piperidin-1-yl(5-(4-(piperidin-1-yl)phenyl)-1,3,4-oxadiazol-2-yl)methanone, 12. Yield = 0.10 g (38%), mp = 131.5°C. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.97 (d, J=9.2 Hz, 2H), 6.94 (d, J=9.2 Hz, 2H), 4.06 (t, J=5.0 Hz, 2H), 3.76 (t, J=5.0 Hz, 2H), 3.34-3.37 (m, 4H), 1.65-1.72 (m, 12H). \(^1\)C NMR (CDCl\(_3\)) \(\delta\) 24.32, 25.40, 25.66, 44.08, 48.16, 114.33, 123.5, 128.96, 154.10, 169.60. IR (cm\(^{-1}\)) 3265, 2932, 2854, 1701, 1620, 1508, 1475, 1318, 1245, 1123, 1098.

A mixture of 1 (0.50 g, 2.10 mmol) and piperidine (0.36 g, 0.41 ml, 4.20 mmol) in DMSO (10.0 ml) was stirred at room temperature. The reaction was monitored using TLC. After 12 h, the mixture was poured into water (50.0 ml). The precipitate was filtered, purified using column chromatography (10% ethyl acetate in hexane) and dried in the oven at 60°C.
Piperidin-1-yl(5-(4-(piperidin-1-yl)phenyl)-1,3,4-oxadiazol-2-yl)methanone, 12. Yield = 0.22 g (30%), mp = 132.0°C. \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 7.96 (d, \(J=9.0\) Hz, 2H), 6.98 (d, \(J=9.0\) Hz, 2H), 4.06 (t, \(J=5.2\) Hz, 2H), 3.76 (t, \(J=5.2\) Hz, 2H), 3.36 (t, \(J=5.2\) Hz, 4H), 1.66-1.72 (m, 12H). \textsuperscript{13}C NMR (CDCl\textsubscript{3}) \(\delta\) 24.31, 25.39, 25.64, 43.98, 47.92, 114.28, 125.51, 128.96, 154.10, 168.80. IR (cm\textsuperscript{-1}) 3262, 2933, 2852, 1705, 1623, 1510, 1478, 1315, 1245, 1125, 1097.

(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl)(piperidin-1-yl)methanone, 13. Yield = 0.20 g (35%), mp = 74.0°C. \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 8.14-8.18 (m, 2H), 7.22 (t, \(J=8.6\) Hz, 2H), 4.05 (t, \(J=5.0\) Hz, 2H), 3.77 (t, \(J=5.2\) Hz, 2H), 1.72-1.76 (m, 6H). \textsuperscript{13}C NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 24.40, 25.64, 44.17, 48.19, 116.57 (d, \(J_{C-F} = 88.0\) Hz), 119.40, 129.83 (d, \(J_{C-F} = 36.0\) Hz), 163.97, 164.45, 166.49. IR (cm\textsuperscript{-1}) 2987, 2872, 2816, 1698, 1602, 1538, 1412, 1253, 1142, 1075.

\[
\begin{array}{c}
\text{F} \\
\text{N-N-O} \\
\text{O} \\
\text{OEt}
\end{array}
\xrightarrow{\text{i-Pr\textsubscript{2}NEt, DMSO}}
\begin{array}{c}
\text{F} \\
\text{N-N-O} \\
\text{O} \\
\text{O}
\end{array}
\]

A mixture of 1 (0.96 g, 4.03 mmol), piperidine (0.34 g, 0.40 ml, 4.03 mmol) and Hunig’s base (0.52g, 0.70 ml, 4.03 mmol) in DMSO (5.0 ml) was stirred at room temperature. The reaction was monitored using TLC. After 24 h, the mixture was poured into water (100.0 ml). The precipitate was filtered, dried and purified using column chromatography (starting with only hexane to 10% ethyl acetate in hexane).
Piperidin-1-yl(5-(4-(piperidin-1-yl)phenyl)-1,3,4-oxadiazol-2-yl)methanone, 12. Yield = 0.10 g (8%), mp = 131.8°C. 1H NMR (400 MHz, CDCl₃) δ 7.96 (d, J=9.2 Hz, 2H), 6.92 (d, J=9.2 Hz, 2H), 4.04 (t, J=5.1 Hz, 2H), 3.74 (t, J=5.0 Hz, 2H), 3.34 (t, J=5.2 Hz, 4H), 1.60-1.75 (m, 12H). 13C NMR (CDCl₃) δ 24.32, 24.46, 25.40, 25.66, 26.67, 44.08, 48.16, 48.73, 114.33, 123.5, 128.96, 154.10, 169.60. IR (cm⁻¹) 3258, 2935, 2850, 1698, 1625, 1510, 1475, 1312, 1243, 1121, 1095.

(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl)(piperidin-1-yl)methanone, 13. Yield = 0.71 g (58%), mp = 73.9°C. 1H NMR (400 MHz, CDCl₃) δ 8.15-8.17 (m, 2H), 7.23 (t, J=8.6 Hz, 2H), 4.05 (t, J=5.0 Hz, 2H), 3.76 (t, J=5.2 Hz, 2H), 1.72-1.76 (m, 6H). 13C NMR (CDCl₃) δ 24.42, 25.64, 44.18, 48.19, 116.47 (d, J_C-F = 88.0 Hz), 119.40, 129.84 (d, J_C-F = 36.0 Hz), 163.97, 166.45, 166.48. IR (cm⁻¹) 2988, 2974, 2874, 1695, 1598, 1502, 1225, 1145, 1069.

A mixture of 1M solution of sodium heptyloxiode in NMP, N-methylpyrrolidinone was prepared by adding n-heptanol (1.20 g, 0.24 ml, 1.68 mmol) to a suspension of sodium hydride (0.04 g, 1.68 mmol) in NMP and the mixture was stirred for 10 mins. This freshly prepared solution was added to a 0.2 M solution of compound 1 (0.40 g, 1.68 mmol) in NMP (6.0 ml). The reaction was heated at 100°C and monitored by TLC. After 24 h, water and ethyl acetate were added and the
aqueous layer was separated. The organic layer was washed with water, dried over anhydrous MgSO₄ and concentrated. The product was purified using column chromatography (10% ethyl acetate in hexane). Yield = 0.51 g (82%). 

1H NMR (400 MHz, CDCl₃) δ 8.46 (s,1H), 8.08-8.12 (m, 2H), 7.22 (t, J=8.6 Hz, 2H). 13C NMR (CDCl₃) δ 116.53 (d, J_C-F = 88.0 Hz), 121.64, 129.46 (d, J_C-F = 36.0 Hz), 152.59, 164.68, 166.64. IR (cm⁻¹) 3297, 1683, 1651, 1605, 1498, 1238, 1100.

\[ \text{C}_9\text{H}_{19}\text{O} \quad \text{NHNNH}_2 \quad \text{O} \quad \text{C}_9\text{H}_{19}\text{O} \quad \text{OCH}_3 \quad \text{O} \quad \text{NHNNH}_2 \text{monohydrate} \]

4-(nonyloxy)benzoylhydrazide. A mixture of methyl \( p-(n\text{-nonyloxy}) \text{benzoate} \) (3.01 g, 9.41 mmol) and an excess of a solution of hydrazine monohydrate, \( \text{NH}_2\text{NH}_2\cdot\text{H}_2\text{O} \) (2.35 g, 47.00 mmol) in 15.0 ml of ethanol was refluxed. The reaction was monitored by TLC. After 24 h, the reaction was complete, the mixture was cooled to room temperature and the white solid obtained was filtered, washed with water, recrystallized from methanol:water and dried in the oven at 60°C. Yield = 2.38 g (79 %), mp = 99.6°C. 

1H NMR (400 MHz, CDCl₃) δ 8.02 (s, 1H), 7.68 (d, J=12.0 Hz, 2H), 6.88 (d, J=12.0 Hz, 2H), 5.25 (s, br, 2H), 3.96 (t, J=6.4 Hz, 2H), 1.73-1.80 (m, 2H), 1.40-1.45 (m, 2H), 1.22–1.35 (m, 10H), 0.88 (t, J=6.8 Hz, 3H). 13C NMR (CDCl₃) δ 14.10, 22.66, 25.97, 29.11, 29.24, 29.36, 29.50, 31.86, 68.22, 114.39, 124.60, 128.65, 162.09, 168.42. IR (cm⁻¹) 3335, 2917, 2852, 1644, 1616, 1576, 1504, 1303, 1252, 1002.
Ethyl 2-(2-(4-(nonyloxy)benzoyl)hydrazinyl)-2-oxoacetate, 14. A mixture of 4-(nonyloxy)benzohydrazide (1.50 g, 5.40 mmol), ethyl oxalyl chloride (0.74 g, 0.60 ml, 5.40 mmol) and triethylamine (0.55 g, 0.75 ml, 5.40 mmol) in dichloromethane (15.0 ml) was stirred at 0°C to room temperature. The reaction was monitored by TLC. After 12 h, the crude product was collected by filtration, recrystallized from ethanol:water and dried in the oven at 60°C. Yield = 1.90 g (93%). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 9.91 (s, br, 1H), 9.07 (s, br, 1H), 7.80 (d, J=9.2 Hz, 2H), 6.92 (d, J=8.8 Hz, 2H), 4.40 (q, J=7.2, 14.0 Hz, 2H), 4.00 (t, J=6.6 Hz, 2H), 1.78-1.81 (m, 2H), 1.42-1.50 (m, 2H), 1.40 (t, J=7.2 Hz, 3H), 1.25-1.38 (m, 10H), 0.88 (t, J=6.8 Hz, 3H). \(^13\)C NMR (CDCl\(_3\)) \(\delta\) 13.99, 14.11, 22.67, 25.97, 29.08, 29.25, 29.36, 29.51, 31.87, 63.70, 68.34, 114.59, 122.49, 129.30, 152.37, 158.51, 162.94, 163.72. IR (cm\(^{-1}\)) 3474, 3208, 2921, 2854, 1756, 1721, 1659, 1513, 1252, 1228, 1186, 1015. DSC: Cr-SmA (68.9°C, \(\Delta\)H=41.0 kJ/mol), SmA-I (87.8°C, \(\Delta\)H=11.6 kJ/mol).

Ethyl 5-(4-(nonyloxy)phenyl)-1,3,4-oxadiazole-2-carboxylate, 15. A mixture of 14 (1.82 g, 4.81 mmol) and phosphorus oxychloride, POCl\(_3\) (7.38 g, 4.37 ml, 48.14 mmol) was heated gently under reflux in dried toluene (15.0 ml). The reaction was monitored by
TLC. After 24 h, excess of POCl₃ was evaporated off under reduced pressure and the residue was purified using silica gel column chromatography (5% ethyl acetate in hexane). Yield = 1.17 g (67%), mp = 64.0°C. ¹H NMR (400 MHz, CDCl₃) δ 8.07 (d, J=8.4 Hz, 2H), 7.00 (d, J=8.4 Hz, 2H), 4.53 (q, J=6.0, 13.6 Hz, 2H), 4.02 (t, J=6.0 Hz, 2H), 1.75-1.86 (m, 2H), 1.42-1.53 (m, 5H), 1.22-1.39 (m, 10H), 0.88 (t, J=6.8 Hz, 3H). ¹³C NMR (CDCl₃) δ 14.12, 22.67, 25.98, 29.08, 29.25, 29.36, 29.51, 31.87, 63.39, 68.39, 114.86, 115.14, 129.51, 154.59, 156.09, 162.87, 164.82, 166.59. IR (cm⁻¹) 2922, 2854, 1741, 1611, 1533, 1264, 1171, 1096, 1019.

2-(chloromethyl)-5-(4-fluorophenyl)-1,3,4-oxadiazole, 2. A mixture of 4 (3.10 g, 18.89 mmol) and chloroacetyl chloride (4.27 g, 3.00 ml, 37.78 mmol) in toluene (40.0 ml) was stirred at 95-105°C. The reaction was monitored by TLC. After 10 h, the mixture was poured into a saturated solution of sodium bicarbonate (150.0 ml) and stirred. The solution was extracted using ethyl acetate (3 x 75.0 ml). The combined organic layers were dried in anhydrous magnesium sulfate, filtered and evaporated. The product was recrystallized from ethanol:water and dried in the oven at 60°C. Yield = 3.63 g (90%), mp = 81.0°C. ¹H NMR (400 MHz, CDCl₃) δ 8.09 (dd, J=5.2, 9.2 Hz, 2H), 7.22 (t, J=8.6 Hz, 2H), 4.78 (s, 2H). ¹³C NMR (CDCl₃) δ 32.97, 116.57 (d, J_C-F = 88.0 Hz), 119.80, 129.44 (d, J_{C,F} = 36.0 Hz), 162.18, 163.84, 166.35. IR (cm⁻¹) 3018, 2962, 1605, 1493, 1258, 1235, 1160, 1099, 1018.
(4-fluorobenzoyl) hydrazine. A solution of 4-fluorobenzoic acid (18.73 g, 0.13 mol) in methanol (60.0 ml) containing 0.5 ml concentrated sulfuric acid was refluxed for 15 h. Hydrazine monohydrate (8.57 g, 8.33 ml, 0.27 mol) was added and the reaction was continued to reflux. The reaction was monitored by TLC. After the additional 10 h, excess methanol was removed under reduced pressure and the reaction mixture was poured into ice cold water (250.0 ml). The crude product obtained was recrystallized from ethyl acetate:hexane and dried in the oven at 40°C. Yield = 12.80 g (62%) \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta \) 7.75 (dd, J= 11.8, 5.0 Hz, 2H), 7.35 (s, br, 1H), 7.12 (t, J= 8.6 Hz, 2H), 3.55 (s, br, 2H). \(^{13}\)C NMR (CDCl\(_3\)) \(\delta \) 115.76 (d, \(J_{C,F} = 88.0\) Hz), 129.18 (d, \(J_{C,F} = 36.0\) Hz), 163.74, 166.40, 167.65. IR (cm\(^{-1}\)) 3280, 2919, 2848, 1689, 1650, 1607, 1519, 1489, 1463, 1321, 1307, 1259, 1236, 1180.

\(N\)-(4-fluorobenzoyl)-\(N'\)-(chloroacetyl)hydrazine. A mixture of (4-fluorobenzoyl) hydrazine (2.20 g, 14.28 mmol), chloroacetyl chloride (1.61 g, 1.14 ml, 14.28 mmol) and triethylamine (1.44 g, 1.99 ml, 14.28 mmol) in dry methylene chloride (35.0 ml) was stirred at room temperature. The reaction was monitored by TLC. After 12 h, the crude product was collected by filtration, recrystallization from ethanol:water and dried in the
oven at 60°C. Yield = 3.12 g (95%), mp = 160.1°C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 9.29 (s, br, 1H), 8.91 (s, br, 1H), 7.83-7.89 (m, 2H), 7.14 (t, $J$=8.4 Hz, 2H), 4.18 (s, 2H). $^{13}$C NMR (CDCl$_3$) $\delta$ 40.94, 116.05 (d, $J_{C-F}$ = 88.0 Hz), 127.20, 129.82 (d, $^2J_{C-F}$ = 36.0 Hz), 163.27, 164.40, 166.69. IR (cm$^{-1}$) 3264, 1695, 1680, 1658, 1603, 1519, 1493, 1238, 1165.

2-(chloromethyl)-5-(4-fluorophenyl)-1,3,4-oxadiazole, 2. A mixture of $N$-(4-fluorobenzoyl)-$N'$-(chloroacetyl)hydrazine (3.00 g, 13.01 mmol) and phosphorus oxychloride, POCl$_3$ (5.99 g, 3.54 ml, 39.04 mmol) was heated gently under reflux in acetonitrile (15.0 ml). The reaction was monitored by TLC. After 24 h, excess POCl$_3$ was evaporated off under reduced pressure and the residue was purified using column chromatography (5% ethyl acetate:hexane) to give the expected product. Yield: 2.18 g (78%), mp = 80.6°C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.07-8.11 (m, 2H), 7.22 (t, $J$=8.8 Hz, 2H), 4.78 (s, 2H). $^{13}$C NMR (CDCl$_3$) $\delta$ 32.97, 116.50 (d, $J_{C-F}$ = 88.0 Hz), 119.64, 129.48 (d, $^2J_{C-F}$ = 36.0 Hz), 162.17, 163.82, 166.35. IR (cm$^{-1}$) 3015, 2965, 1604, 1495, 1257, 1233, 1161, 1085, 1012.

2-(chloromethyl)-5-(4-fluorophenyl)-1,3,4-oxadiazole, 2. A mixture of (4-fluorobenzoyl) hydrazine (0.58 g, 3.76 mmol) and chloroacetyl chloride (0.85 g, 0.60 ml,
7.53 mmol) was heated at 120°C. After 20 minutes, the reaction mixture was cooled and the residue was washed with water, filtered and dried. Purification using column chromatography (5% ethyl acetate in hexane) gave the expected product. Yield = 0.49 g (61%), mp = 80.4°C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.07-8.12 (m, 2H), 7.23 (t, $J$= 8.8 Hz, 2H), 4.78 (s, 2H). $^{13}$C NMR (CDCl$_3$) $\delta$ 32.97, 116.57 (d, $J_{C-F}$ = 88.0 Hz), 119.9, 129.48 (d, $^2J_{C-F}$ = 36.0 Hz), 162.17, 165.06, 166.36. IR (cm$^{-1}$) 3018, 2963, 1605, 1573, 1257, 1233, 1160, 1086, 1009.

$\text{NaN}_3 \rightarrow \text{BTMAC, H}_2\text{O}$

BTMAC = Benzyltrimethylammonium chloride, 98%

2-(4-fluorobenzoyl)-5-(azidomethyl)-1,3,4-oxadiazole, 16. A mixture of 2 (0.26 g, 1.22 mmol), sodium azide (0.16 g, 2.45 mmol), BTMAC (0.04 g, 0.20 mmol) and water (5.0 ml) was vigorously stirred for 24 h at 90-95°C until the solid disappeared. After 24 h, the mixture was cooled to room temperature under continuous stirring and the light brown precipitate was filtered off. Purification using column chromatography (10% ethyl acetate in hexane) gave a white solid. Yield = 0.22 g (82 %), mp = 84.4°C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.06-8.11 (m, 2H), 7.23 (t, $J$= 8.8 Hz, 2H), 4.63 (s, 2H). $^{13}$C NMR (CDCl$_3$) $\delta$ 44.35, 116.59 (d, $J_{C-F}$ = 88.0 Hz), 119.50, 129.44 (d, $^2J_{C-F}$ = 36.0 Hz), 161.40, 163.70, 166.34. IR (cm$^{-1}$) 2093, 1607, 1493, 1233, 1081.
5-(4-fluorophenyl)-1,3,4-oxadiazole-2-carbaldehyde, 17.\textsuperscript{22} Compound 16 (0.20 g, 0.913 mol) was added in portions to concentrated sulfuric acid (5.0 ml) at 0 °C and the solution was allowed to warm from 0 °C to room temperature. The reaction was monitored using TLC. After 48 h, ice-cooled water (50.0 ml) was added and the mixture was extracted with dichloromethane (50.0 ml × 2). The combined organic layers were dried over anhydrous magnesium sulfate, filtered and evaporated to give the expected product. Yield = 0.12 g (70 %), light brown solid. \textsuperscript{1}H NMR (400 MHz, DMSO) \(\delta\) 10.05 (s, 1H), 8.21 (dd, J=5.0, 9.0 Hz, 2H), 7.27 (t, J=8.6 Hz, 2H). \textsuperscript{13}C NMR (CDCl\textsubscript{3}) \(\delta\) 116.92 (d, \(J_{C-F} = 92.0\) Hz), 129.49, 130.46 (d, \(2J_{C-F} = 36.0\) Hz), 158.42, 164.50, 167.04, 176.09. IR (cm\textsuperscript{-1}) 2958, 2924, 2855, 1705, 1604, 1495, 1488, 1422, 1382, 1237, 1163, 1094.

5-(4-fluorophenyl)-1,3,4-oxadiazole-2-carbaldehyde, 17.\textsuperscript{23} A mixture of 2 (0.22 g, 1.03 mmol) and sodium bicarbonate (0.13 g, 1.55 mmol) in DMSO (6.0 ml) was mixed in 100.0 ml round bottom flask attached to a condenser in a microwave (CEM Discover microwave with P: 250W, T: 250 °C). The reaction was run for 10 minutes and monitored by TLC. Water (30.0 ml) was added to the system and the product was extracted with toluene (50.0 ml × 2). The combined organic extracts were washed with
brine and the solvent were dried and evaporated. The crude product was found to be a mixture but no separation was attempted.

**Note:** The reactions were performed using different bases and different reaction conditions. So far, most of the reactions produce mixtures of the product and its starting materials.

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**2-(2-(4-fluorobenzoyl)hydrazinyl)-2-oxoacetamide, 21.**

A mixture of oxamic hydrazide (2.20 g, 21.34 mmol) and 4-fluorobenzoyl chloride (3.38 g, 2.52 ml, 21.34 mmol) in pyridine (25.0 ml) was stirred at room temperature. The reaction was monitored by TLC. After 12 h, the reaction mixture was warmed to 40°C and was continued to stir for another 12 h. The mixture was filtered, recrystallized from methanol and dried in the oven at 60°C. Yield = 2.22 g (46%), mp = 269.0°C. $^1$H NMR (400 MHz, DMSO) $\delta$ 10.62 (s, 1H), 10.48 (s, 1H), 8.19 (s, 2H), 7.95 (dd, J=5.6, 8.8 Hz, 2H), 7.91 (s, 1H), 7.35 (t, J=8.8 Hz, 2H). $^{13}$C NMR (DMSO) $\delta$ 116.01 (d, $J_{C,F} = 88.0$ Hz), 129.21, 130.64 (d, $J_{C,F} = 36.0$ Hz), 160.02, 163.45, 164.50, 165.93. IR (cm$^{-1}$) 3413, 3275, 3226, 1710, 1670, 1603, 1478, 1242, 1231, 1160.
2-(2-(4-fluorobenzoyl)hydrazinyl)-2-oxoacetamide, 21. A mixture of oxamic hydrazide (2.30 g, 22.31 mmol), 4-fluorobenzoyl chloride (3.54 g, 2.64 ml, 22.31 mmol) and triethylamine (0.60 ml) in dry dichloromethane (20.0 ml) was stirred at room temperature. The reaction was monitored by TLC. After 24 h, the reaction mixture was filtered, recrystallization from methanol and dried in the oven at 60°C. Yield = 2.97 g (59%). \(^1\)H NMR (400 MHz, DMSO) \(\delta\) 10.61 (s, 1H), 10.48 (s, 1H), 8.19 (s, 2H), 7.95 (dd, J=5.2, 8.8 Hz, 2H), 7.93 (s, 1H), 7.34 (t, J=8.8 Hz, 2H). \(^13\)C NMR (DMSO) \(\delta\) 116.01 (d, J\textsubscript{C-F} = 88.0 Hz), 129.21, 130.64 (d, J\textsubscript{C-F} = 36.0 Hz), 160.03, 163.46, 164.50, 165.94. IR (cm\(^{-1}\)) 3412, 3273, 3223, 1702, 1670, 1602, 1475, 1381, 1230, 1167.

Note: The characterization data for compound 21 here matches the same compound from earlier synthesis route.

5-(4-fluorophenyl)-1,3,4-oxadiazole-2-carbonitrile, 3. A mixture of 21 (1.50 g, 6.66 mmol) in POCl\(_3\) (15.0 ml) was stirred and heated at 100°C. The reaction was monitored by TLC. After 12 h, the excess POCl\(_3\) was removed and the remaining product was poured into ice water (60.0 ml). The solution was cooled overnight. The precipitate was filtered and washed with sodium bicarbonate, NaHCO\(_3\) concentrated solution and water.
The product was dissolved in ether (50.0 ml) and then filtered. The ether was evaporated to give a light yellow crude product. The product was purified using column chromatography (5% ethyl acetate in hexane). Yield = 0.26 g (20 %), mp = 122.7°C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.14 (dd, J=5.2, 8.4 Hz, 2H), 7.28 (t, J= 8.4 Hz, 2H). $^{13}$C NMR (CDCl$_3$) $\delta$ 106.19, 117.10 (d, $J_{CF} = 92.0$ Hz), 128.81, 130.35 (d, $^2J_{CF} = 40.0$ Hz), 141.74, 164.61, 167.17. IR (cm$^{-1}$) 3106, 3072, 2959, 2926, 2855, 1730, 1603, 1494, 1421, 1241, 1163, 1086, 1021.

Piperidin-1-yl(5-(4-(piperidin-1-yl)phenyl)-1,3,4-oxadiazol-2-yl)methanone, 12. A mixture of 3 (0.10 g, 0.52 mmol) and piperidine (0.13 g, 0.16 ml, 1.57 mmol) in DMSO (5.0 ml) was refluxed. The reaction was monitored by TLC. After 24 h, the mixture was poured into water (50.0 ml). The solution was extracted with ethyl acetate (2 $\times$ 50.0 ml). The combined organic extracts were dried over anhydrous magnesium sulfate and evaporated to give the crude product. The crude was purified by column chromatography (15% ethyl acetate in hexane). Yield = 0.11 g (82%), mp = 120°C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.97 (d, J=9.2 Hz, 2H), 6.93 (d, J=9.2 Hz, 2H), 4.03-4.09 (m, 2H), 3.73-3.80 (m, 2H), 3.31-3.38 (m, 4H), 1.63-1.76 (m, 12H). $^{13}$C NMR (CDCl$_3$) $\delta$ 24.32 25.40, 26.67, 44.25, 48.73, 114.33, 119.52, 128.96, 153.76, 166.43. IR (cm$^{-1}$) 3262, 2933, 2852, 1702, 1625, 1510, 1473, 1321, 1243, 1120, 1096.
Note: The product is compound 12 because the ratio of the starting material and piperidine used in the reaction is 1:3.

(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl)(piperidin-1-yl)methanone, 13. A mixture of 3 (0.12 g, 0.63 mmol), piperidine (0.05 g, 0.06 ml, 0.63 mmol) and Hunig’s base (0.11 ml, 0.63 mmol) in DMSO (4.0 ml) was stirred at room temperature. The reaction was monitored using TLC. After 18 h, the mixture was poured into water (50.0 ml). The solution was extracted with ethyl acetate (2 × 50.0 ml). The combined organic extracts were dried over anhydrous magnesium sulfate and evaporated to give the crude product. The crude was purified column chromatography (15% ethyl acetate in hexane). Yield = 0.14 g (87 %), mp = 72.8°C. \( ^1 \text{H NMR} \) (400 MHz, CDCl\(_3\)) \( \delta \) 8.11 (t, \( J=6.8 \) Hz, 2H), 7.23 (t, \( J=8.8 \) Hz, 2H), 3.50-3.62 (m, 4H), 1.62-1.76 (m, 6H). \( ^{13} \text{C NMR} \) (CDCl\(_3\)) \( \delta \) 24.56, 25.60, 44.25, 48.77, 116.50 (d, \( J_{C-F} = 88.0 \) Hz), 119.50, 129.32 (d, \( J_{C-F} = 36.0 \) Hz), 152.82, 163.90, 166.43. IR (cm\(^{-1}\)) 2986, 2873, 1701, 1601, 1502, 1221, 1139, 1065.

\[ \text{HCl} \] 2-(4,5-dihydrothiazol-2-yl)-5-(4-fluorophenyl)-1,3,4-oxadiazole, 22.\(^{25}\) A solution of 3 (0.38 g, 1.99 mmol), 2-mercaptopethylamine hydrochloride (0.52 g, 0.06 ml, 4.57 mmol)
and triethylamine (0.27 ml, 1.99 mmol) in ethanol (5.0 ml) was stirred under a nitrogen atmosphere at room temperature. The reaction was monitored using TLC. After 12 h, the solution was poured into water (50.0 ml). The precipitate was filtered, purified by recrystallization from ethanol and dried in the oven at 60°C. Yield = 0.24 g (48 %), mp = 196.0°C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.18 (dd, J=5.2, 9.2 Hz, 2H), 7.22 (t, J=8.6 Hz, 2H), 4.59 (t, J=8.6 Hz, 2H), 3.56 (t, J=8.6 Hz, 2H). $^{13}$C NMR (CDCl$_3$) $\delta$ 33.91, 65.58, 116.61 (d, J$_{C-F}$ = 88.0 Hz), 119.34, 129.94 (d, $^2$J$_{C-F}$ = 36.0 Hz), 154.98, 159.36, 164.04, 166.57. IR (cm$^{-1}$) 3118, 2975, 2882, 1612, 1523, 1434, 1368, 1236, 1128, 1018.

(S)-Ethyl-2-(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl)-4,5-dihydrothiazole-4-carboxylate, 23. A solution of 3 (0.38 g, 1.99 mmol), L-cysteine ethyl ester hydrochloride (0.85 g, 4.57 mmol) and triethylamine (0.28 ml, 1.99 mmol) in ethanol (5.0 ml) was stirred under a nitrogen atmosphere at room temperature. The reaction was monitored using TLC. After 12 h, the solution was poured into water (50.0 ml). The precipitate was filtered and dried. Yield = 0.25 g (44 %). Pure product 23 could not be isolated even after column chromatography.

Note: The reactions were repeated several times but the outcome remained the same.
6. Experimental procedures for Chapter-6

\[
\begin{align*}
\text{Br} & \quad \text{F} & \quad \text{OH} \\
\text{Br} & \quad \text{F} & \quad \text{O} & \quad \text{B(OH)}_2 \\
\text{+} & \quad \text{Pd(PPh}_3)_4 \quad (0.05 \text{ eq}) & \quad \text{Benzene-EtOH} \\
\text{2N aq K}_2\text{CO}_3 & \quad \text{F} & \quad \text{OH} \\
\end{align*}
\]

4-(4’-fluorophenyl)-3-fluoro-1-phenol.\textsuperscript{26} A mixture of 4-bromo-3-fluorophenol (6.00 g, 31.41 mmol) and tetrakis(triphenylphosphine) palladium(0) (0.30 g, 0.26 mmol) was stirred in benzene (52.0 ml) and aqueous potassium carbonate (50.0 ml, 2N, 50.00 mmol). Next, 4-fluorophenylboronic acid (6.00 g, 42.64 mmol) was added, followed by ethanol (40.0 ml). The reaction mixture was heated under reflux for 72 h. The reaction was monitored using TLC. The mixture was cooled, diluted with water (100.0 ml) and extracted with ethyl acetate (2 × 100.0 ml). The combined organic extracts were washed with brine, dried over anhydrous magnesium sulfate and concentrated \textit{in vacuo}. The crude yellow solid was purified using silica gel column chromatography (hexane) to afford the product as white solid. Yield = 4.41 g (68%), mp = 147.9\textdegree C. \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 7.43-7.46 (m, 2H), 7.24-7.28 (m, 1H), 7.08-7.14 (m, 2H), 6.65-6.70 (m, 2H), 5.03 (s, br, 1H). \textsuperscript{13}C NMR (CDCl\textsubscript{3}) \(\delta\) 103.75 (d, \(^2J_{C-F} = 104.0 \text{ Hz}\)), 111.63, 115.36 (d, \(^2J_{C-F} = 88.0 \text{ Hz}\)), 130.40, 131.16 (d, \(^3J_{C-F} = 20.0 \text{ Hz}\)), 131.21 (d, \(^3J_{C-F} = 20.0 \text{ Hz}\)), 131.60, 156.16, 160.50 (d, \(^3J_{C-F} = 44.0 \text{ Hz}\)), 161.36 (d, \(J_{C=\text{C}} = 212.0 \text{ Hz}\)), 163.38. IR (cm\textsuperscript{-1}) 3630-3140, 1625, 1587, 1490, 1456, 1219, 1113, 961, 840, 805.
1,11-undecanediol. A solution of 0.5 M 9-BBN in THF (64.48 g, 70.0 ml, 0.53 mol) was stirred in a 250 ml 2-necked flask under nitrogen at room temperature and 10-undecen-1-ol (6.00 g, 7.1 ml, 0.04 mol) was added dropwise via syringe as the reaction mixture was stirred at room temperature. The reaction was monitored using TLC and stained in an iodine chamber. When the reaction was complete (about 48 h), the hydroboration mixture was oxidized with 40.0 ml hydrogen peroxide, H₂O₂ (30% in water) and 100.0 ml 3M NaOH (aq), followed by stirring at room temperature overnight. The aqueous layer was extracted with diethyl ether (2 x 50.0 ml). The combined organic layers were dried, filtered and concentrated in vacuo. The crude yellow oil was purified using column chromatography on silica gel (10% ethyl acetate in hexane) to afford the product as a white solid. Yield = 3.77 g (57 %), mp = 61.5°C. ¹H NMR (400 MHz, CDCl₃) δ 4.58 (s, br, 2H), 3.63 (t, J=6.6 Hz, 4H), 1.52-1.57 (m, 4H), 1.28-1.36 (m, 14H). ¹³C NMR (CDCl₃) δ 25.72, 29.40, 29.48, 29.56, 32.81, 63.10. IR (cm⁻¹) 3570-3150, 2925, 2854, 1498, 1234, 1016, 821.

Note: Literature data for 1,11-undecanediol: melting point is 60°C.
1,7-bis(2,4’-difluorobiphenyl-4-yloxy)heptane, 1a. A mixture of 4-(4’-fluorophenyl)-3-fluoro-1-phenol (0.78 g, 4.58 mmol), 1,7-heptanediol (0.36 g, 2.75 mmol), triphenylphosphine (1.50 g, 5.73 mmol) and THF (10.0 ml) was stirred in a round-bottomed flask under nitrogen atmosphere. A solution of diisopropyl azodicarboxylate, DIAD (1.16 g, 1.1 ml, 5.73 mmol) in THF (5.0 ml) was added dropwise to the reaction mixture. The reaction was stirred at room temperature and monitored by TLC. After 48 h water (20.0 ml) was added to the mixture and the precipitate was filtered off using a Buchner funnel. The crude product was purified by silica gel column chromatography (hexane only) to yield the expected product. Yield = 1.00 g (50%). ¹H NMR (400 MHz, CDCl₃) δ 7.47 (t, J=6.4 Hz, 4H), 7.30 (t, J=8.8 Hz, 2H), 7.11 (t, J=8.6 Hz, 4H), 6.70-6.78 (m, 4H), 4.01 (t, J=6.2 Hz, 4H), 1.78-1.92 (m, 4H), 1.46-1.64 (m, 6H). ¹³C NMR (CDCl₃) δ 25.93, 29.07, 68.45, 102.71 (d, J_C-F = 104.0 Hz), 110.94, 115.24 (d, J_C-F = 84.0 Hz), 120.36, 130.29, 130.34 (d, J_C-F = 20.0 Hz), 130.78 (d, J_C-F = 20.0 Hz), 131.85, 159.92 (d, J_C-F = 44.0 Hz), 161.22 (d, J_C-F = 212.0 Hz), 163.41. IR (cm⁻¹) 2965, 2936, 2851, 1624, 1494, 1472, 1289, 1220, 1160, 1120, 1037, 841, 800.

1,9-bis(2,4’-difluorobiphenyl-4-yloxy)nonane, 1b. Yield = 1.17 g (52%). ¹H NMR (400 MHz, CDCl₃) δ 7.45-7.47 (m, 4H), 7.29 (t, J=8.8 Hz, 2H), 7.11 (t, J=8.8 Hz, 4H), 6.68-6.77 (m, 4H), 3.98 (t, J=6.4 Hz, 4H), 1.77-1.86 (m, 4H), 1.45-1.53 (m, 4H), 1.36-
1.43 (m, 6H). $^{13}$C NMR (CDCl$_3$) $\delta$ 26.00, 29.13, 29.29, 29.48, 68.42, 102.51 (d, $^2$J$_{C-F}$ = 104.0 Hz), 110.86, 115.34 (d, $^2$J$_{C-F}$ = 84.0 Hz), 120.25, 130.32, 130.38 (d, $^3$J$_{C-F}$ = 20.0 Hz), 130.82 (d, $^3$J$_{C-F}$ = 20.0 Hz), 130.97, 159.82 (d, $^3$J$_{C-F}$ = 44.0 Hz), 161.14 (d, $^1$C$_{F}$ = 212.0 Hz), 163.32. IR (cm$^{-1}$) 2939, 2923, 2856, 1622, 1494, 1475, 1230, 1213, 1157, 1110, 1036, 959, 841, 813.

1,11-bis(2,4'-difluorobiphenyl-4-yl)undecane, 1c. $^{30}$ Yield = 0.67 g (38%). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.43-7.49 (m, 4H), 7.29 (t, J=8.8 Hz, 2H), 7.10 (t, J=8.8 Hz, 4H), 6.67-6.77 (m, 4H), 3.97 (t, J=6.6 Hz, 4H), 1.76-1.84 (m, 4H), 1.43-1.51 (m, 4H), 1.30-1.40 (m, 10H). $^{13}$C NMR (CDCl$_3$) $\delta$ 26.00, 29.35, 29.50, 29.53, 29.72, 68.45, 102.51 (d, $^2$J$_{C-F}$ = 104.0 Hz), 110.89, 115.32 (d, $^2$J$_{C-F}$ = 84.0 Hz), 120.82, 130.36 (d, $^3$J$_{C-F}$ = 20.0 Hz), 130.81 (d, $^3$J$_{C-F}$ = 20.0 Hz), 131.79, 159.89, 161.14 (d, $^1$C$_{F}$ = 212.0 Hz), 163.31. IR (cm$^{-1}$) 2920, 2852, 1624, 1494, 1473, 1290, 1219, 1161, 1121, 1043, 840, 817.

Note: There is some monoadduct and biphenol at the end of the reaction.

$$\begin{array}{c}
\text{F} & \text{F} \\
\text{KOH, t-BuOH} & \text{reflux, 24 h} \\
\text{OH} & \text{F} & \text{F}
\end{array}$$

2,3,5,6-Tetrafluoro-4-(pentafluorophenyl)phenol, 7. $^{31}$ A mixture of decafluorobiphenyl (1.65 g, 4.94 mmol), potassium hydroxide (0.86 g, 21.40 mmol) and t-BuOH (12.0 ml) was refluxed. After 24 h, the reaction mixture was poured into water (50.0 ml) and extracted with diethyl ether. The phenol was then released by acidification with hydrochloric acid and extracted into ether. The extract was dried with anhydrous
magnesium sulfate and after filtration the solvent was removed. The residue was purified using column chromatography and recrystallized from toluene to afford the expected product (light yellow solid). Yield = 0.45 g (32 %), mp = 108.4°C. $^{19}$F NMR (300 MHz, CDCl$_3$, ppm) δ -130.1 (m, 2F), -132.1 (m, 2F), -142.8 (m, 1F), -150.4 (m, 2F), -153.1 (m, 2F). $^{13}$C NMR (CDCl$_3$) δ 116.33 (d, $^2$J$_{C\text{-}F}$ = 16.0 Hz), 127.85 (d, $^2$J$_{C\text{-}F}$ = 56.0 Hz), 128.1, 129.56 (d, J$_{C\text{-}F}$ = 154.0 Hz), 132.18 (d, J$_{C\text{-}F}$ = 156.0 Hz), 142.54 (d, J$_{C\text{-}F}$ = 156.0 Hz), 156.10 (d, J$_{C\text{-}F}$ = 156.0 Hz), 158.21 (d, J$_{C\text{-}F}$ = 156.0 Hz). IR (cm$^{-1}$) 3387-3610 (OH), 2957, 2925, 2856, 1505, 1488, 1082, 994, 965.

Note: Some starting material was recovered at the end of the reaction.

\[ \text{B(OH)}_2 + \text{F} \rightarrow \text{Pd(PPh}_3)_4 (0.05 \text{ eq}) \xrightarrow{2\text{N aq K}_2\text{CO}_3, \text{DME, reflux, 24 h}} \text{8} \]

**2,3,4,5,6-pentafluorobiphenyl, 8.** A mixture of phenylboronic acid (4.02 g, 32.97 mmol), iodopentafluorobenzene (4.84 g, 16.48 mmol), Pd(PPh$_3$)$_4$ (0.19 g), 2N 10.0 ml potassium carbonate in 10.0 ml 1,2-dimethoxyethane, DME was refluxed. The reaction was monitored by TLC. After 24 h, the mixture was cooled, poured into water (50.0 ml) and extracted with ethyl acetate (50.0 ml × 2). The combined organic layers were washed with brine, dried with anhydrous magnesium sulfate and the solvent was evaporated. The crude material was purified using column chromatography (pure hexane) and was isolated as a white solid. Yield = 3.30 g (89 %), mp = 104.3°C. $^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 7.60-7.62 (m, 1H), 7.47-7.51 (m, 2H), 7.42-7.46 (m, 2H). $^{13}$C NMR (CDCl$_3$, ppm) δ 126.41, 127.22 (d, J = 32.0 Hz), 128.74, 129.31(d, J = 34.0 Hz), 139.10
(d, J = 154.0 Hz), 141.44 (d, J_{C-F} = 156.0 Hz), 142.95 (d, J_{C-F} = 156.0 Hz), 145.41 (d, J_{C-F} = 156.0 Hz). \(^1^9\)F NMR (300 MHz, CDCl\(_3\), ppm) \(\delta\) -135.3 (m, 2F), -147.0 (m, 1F), -153.2 (m, 2F). IR (cm\(^{-1}\)) 3060, 3031, 2924, 1524, 1493, 1443, 1061, 978, 853.

\[
\begin{array}{c}
\text{F} \quad \text{KOH, } t-\text{BuOH} \\
\text{reflux, 24 h} \\
\text{OH}
\end{array}
\]

**2,3,5,6-Tetrafluorobiphenyl-4-ol, 9.**\(^{33}\) A mixture of 2,3,4,5,6-pentafluorobiphenyl (2.46 g, 10.08 mmol) and potassium hydroxide (2.02 g, 50.40 mmol) in \(t\)-BuOH (20.0 ml) was refluxed. After 24 h, the reaction mixture was cooled to room temperature, diluted with water (70.0 ml) and acidified with hydrochloric acid. The resulting mixture was extracted with diethyl ether. The organic layers were dried over anhydrous magnesium sulfate and the solvent was removed under reduced pressure. The residue was purified using column chromatography to afford the expected white solid product. Yield = 1.93 g (79%). \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) \(\delta\) 9.01 (s, br, 1H), 7.38-7.55 (m, 5H). \(^{13}\)C NMR (CDCl\(_3\), ppm) \(\delta\) 116.36 (d, \(^2\)J_{C-F} = 8.0 Hz), 126.89, 127.90 (d, J = 20.0 Hz), 129.32 (d, J = 4.0 Hz), 130.85 (d, \(^2\)J_{C-F} = 16.0 Hz), 135.21, 142.67 (d, J_{C-F} = 156.0 Hz), 157.41 (d, J_{C-F} = 156.0 Hz). \(^1^9\)F NMR (300 MHz, CDCl\(_3\), ppm) \(\delta\) -133.2 (m, 2F), -151.3 (m, 2F).

\[
\begin{array}{c}
\text{F} \quad \text{I} \\
\text{OH} \\
\text{Irradiation}
\end{array}
\]

**2',3',4',5',6'-Pentafluorobiphenyl-4-ol, 10.**\(^{34}\) Under a nitrogen atmosphere, a stirred solution of phenol (3.84 g, 40.82 mmol) and iodopentafluorobenzene (3.00 g, 10.20
mmol) in acetonitrile (20.0 ml) was irradiated in a photochemical reactor (Rayonet photochemical reactor - Southern New England Ultraviolet company: clear glass 254 nm low-pressure mercury lamp). After 24 h, acetonitrile and unchanged phenol were evaporated under vacuum and the oily residue was chromatographed on silica gel using pure hexane. Yield = 0.53 g (20%), mp = 62.0°C. $^1$H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 7.32 (d, J=8.8 Hz, 2H), 6.95 (d, J=8.8 Hz, 2H), 4.83 (s, br, 1H). $^{13}$C NMR (CDCl$_3$, ppm) $\delta$ 115.74, 116.02 (d, $^2$J$_{C-F}$ = 20.0 Hz), 130.72, 131.02, 136.78 (d, $^4$J$_{C-F}$ = 48.0 Hz), 148.78 (d, $^4$J$_{C-F}$ = 48.0 Hz), 156.33 (d, $^4$J$_{C-F}$ = 50.0 Hz), 161.02. $^{19}$F NMR (300 MHz, CDCl$_3$, ppm) $\delta$ -135.3 (m, 2F), -146.9 (m, 1F), -153.2 (m, 2F). IR (cm$^{-1}$) 3034-3170 (O-H), 1595, 1524, 1493, 1478, 1430, 1061, 1007, 978.

Note: There was some byproduct at the end of the reaction which was not isolated.

1,7-Bis(4-phenylphenoxy)heptane. A mixture of 4-phenylphenol (3.74 g, 21.90 mmol), 1,7-heptanediol (1.16 g, 8.77 mmol), triphenylphosphine (5.75 g, 21.90 mmol) and THF (20.0 ml) was stirred in a two-necked round-bottomed flask under a nitrogen atmosphere. A solution of diisopropyl azodicarboxylate, DIAD (4.44 g, 21.90 mmol) in THF (11.0 ml) was added dropwise to the reaction mixture. The reaction was stirred at room temperature and monitored by TLC. After 24 h, water (50.0 ml) was added to the mixture and the precipitate was filtered off using a Buchner funnel. The crude product was purified by silica gel column chromatography using 10% of ethyl acetate in hexane to
yield the expected product. Yield = 2.22 g (58%). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.51-7.58 (m, 8H), 7.42 (t, $J$= 7.6 Hz, 4H), 7.30 (t, $J$= 7.6 Hz, 2H), 6.98 (d, $J$= 8.8 Hz, 4H), 4.02 (t, $J$= 6.8 Hz, 4H), 1.79 – 1.88 (m, 4H), 1.47 – 1.55 (m, 6H). $^{13}$C NMR (CDCl$_3$) $\delta$ 25.60, 26.09, 29.6, 68.09, 114.81, 126.63, 126.74, 128.14, 128.37, 128.74, 140.91, 158.75. IR (cm$^{-1}$) 2929.31, 2850.77, 1671.62, 1604.54, 1583.44, 1521.79, 1485.85, 1468.24, 1256.80, 1241.25, 1181.43, 1105.56. 

Note: There is some monoadduct remaining at the end of the reaction.

1,7-bis(perfluorobiphenyl-4-yloxy)heptane, 3.$^{30}$ A mixture of 2,3,5,6-tetrafluoro-4-(pentafluorophenyl)phenol (0.60 g, 1.81 mmol), 1,7-heptanediol (0.14 g, 1.08 mmol), triphenylphosphine (0.47 g, 1.81 mmol) and THF (7.0 ml) was stirred in a round-bottomed flask under nitrogen. A solution of diisopropyl azodicarboxylate, DIAD (0.36 g, 0.36 ml, 1.81 mmol) in THF (3.0 ml) was added dropwise to the reaction mixture. The reaction was stirred at room temperature and was monitored by TLC. After 48 h, water (20.0 ml) was added into the mixture and the precipitate was filtered off using a Buchner funnel. The crude product was purified by silica gel column chromatography (hexane only) to yield the expected product. The product did not appear to contain the expected compound. This Mitsunobu reaction was repeated but none of the desired compound could be obtained.
7. REFERENCES


