1,3,4-Thiadiazole-2-carboxylate esters: new synthetic methodology for the preparation of an elusive family of self-organizing materials

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A series of alkyl 5-(4-octyloxyphenyl)-1,3,4-thiadiazole-2-carboxylates has been prepared *via* a novel chemoselective ring-closure of appropriate tricarbonyl precursors. This paper represents the first report of a general and reproducible synthetic methodology for the preparation of 1,3,4-thiadiazole-2-carboxylate esters. The 1,3,4-thiadiazole esters synthesized were designed to evaluate the feasibility of this new core unit for potential ferroelectric applications. The core unit was found to promote strongly the formation of tilted smectic phases (the smectic C phase in particular). The 1,3,4-thiadiazole ester was found to be a stronger promoter of the smectic C phase than its phenyl-based counterpart.

Introduction

1,3,4-Thiadiazoles are relatively common in the liquid crystal (LC) literature although the variety of structural modifications that have been studied are actually very limited. The majority of systems have the 1,3,4-thiadiazole core substituted at the 2 and 5-positions by aryl units or a combination of aryl and alkyl/cycloalkyl units.[1–7] Typically, these materials (**4**) are prepared *via* sulfurization of appropriately substituted *N*,*N*′-diacyldiazanes **3** that are, in turn, prepared by the reaction of hydrazides **1** with acid chlorides **2** (Fig. 1). Early reports utilized phosphorus pentasulfide as the sulfurization reagent although Lawesson's reagent soon emerged as the most reliable and reproducible reagent for this task.[8,9]

In 1995, Tschierske *et al.* reported a novel synthesis of a 2-alkylsulfanyl-5-aryl-1,3,4-thiadiazole for nonlinear optical (NLO) applications.[10] However, this appears to be the only compound of this type in the LC literature.

A significant body of work has been reported on the synthesis of 1,3,4-thiadiazoles that are attached to aromatic systems by amide, azo, and imine linking groups.[11–16] These compounds were synthesized by the dehydration of thiosemicarbazides (or cyclization of thiosemicarbazones) to give 2-amino-5-aryl-1,3,4-thiadiazoles that were then subjected to standard amine transformations. To our knowledge, these compounds constitute the only 1,3,4-thiadiazole-linked mesogens in the LC literature prior to our work.

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For some time, we have been interested in the synthesis of new heterocyclic materials for ferroelectric and antiferroelectric applications. As part of this program, we have focused on ester-linked materials, since the ester linkage is well known to be an excellent promoter of tilted smectics such as the smectic C (SmC) phase.[17] 1,3,4-Thiadiazoles have also been noted to be exceptionally good promoters of the SmC phase.[18–20] We have identified 1,3,4-thiadiazole-2-carboxylates as worthy targets with potentially low viscosities, high dielectric biaxialities (due to the large heterocyclic dipole of 3.0 D),[21] and more linear structures than other common five-membered heterocycles (thus leading to higher mesophase thermal stabilities). Recently, we reported our preliminary results in this area with the synthesis of the first 1,3,4-thiadiazole-2-carboxylate ester; the synthesis reported was low-yielding and reaction conditions were not optimized.[22] Subsequently, we decided to target a number of 1,3,4-thiadiazole-2-carboxylate esters (**14**–**17**) that would allow us to assess the feasibility of this new core as a promoter of SmC phase behavior and to fully optimize the synthetic methodology that was used to prepare this new class of materials.

Synthetic studies

A survey of the organic literature reveals that 1,3,4-thiadiazole-2-carboxylate esters with a carbon-based group at the 5-position are extremely rare. The synthesis of such esters has been reported only once (from an *ortho* ester)[23] and the methodology used was limited to a methyl chain being attached to the ethereal oxygen. Unfortunately this procedure is not amenable to large scale synthesis or to the preparation of liquid crystalline precursors.

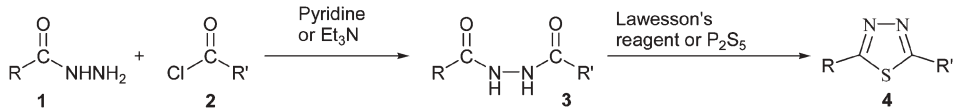


Fig. 1 Typical synthesis of 2,5-disubstituted-1,3,4-thiadiazoles.

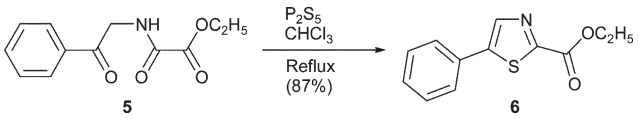


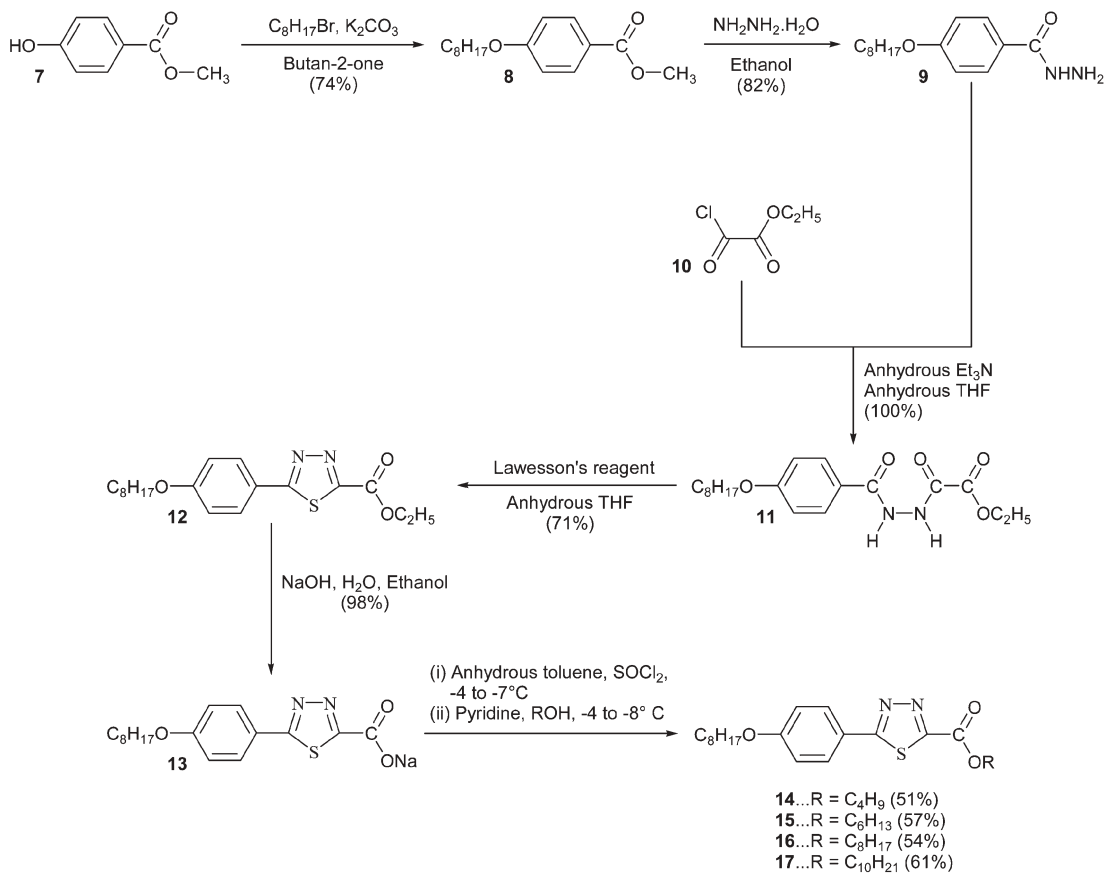
Fig. 2 Tanaka's chemoselective synthesis of 1,3-thiazole-2-carboxylate ester **6**.

Tanaka *et al.* have reported the chemoselective reaction of ethoxalylaminoacetophenone **5** with phosphorus pentasulfide to give ethyl 5-phenyl-1,3-thiazole-2-carboxylate **6** (Fig. 2).[24]

We reasoned that the analogous diacyldiazane derivative (**11**, Scheme 1) might be similarly cyclized to a 1,3,4-thiadiazole-2-carboxylate ester using a suitable sulfurization agent. Further precedent for the chemoselective sulfurization of an amide carbonyl in the presence of an ester carbonyl was reported in the same year by Scheibye *et al.* using Lawesson's reagent.[25] With this knowledge in hand, we targeted the key diazane **11** as a suitable 1,3,4-thiadiazole precursor (Scheme 1).

A standard Williamson etherification was used for the preparation of ether **8** from phenol **7**.[26] Benzohydrazide **9** was obtained by the reaction of a large excess of hydrazine hydrate with ester **8**.[27] The key tricarbonyl intermediate **11** was prepared by the reaction of ethyl oxalyl chloride (**10**) with benzohydrazide **9**. These materials are extremely polar, difficult to purify by chromatography, and were used crude in the subsequent cyclization step. Sulfurization and ring-closure of **11** was carried out using Lawesson's reagent in anhydrous THF.[28] The use of fresh Lawesson's reagent was found to be very important with older reagent giving reduced yields (in some cases a 25% reduction in yield was noted). Careful monitoring of the reaction was also found to be important as extended reaction times were found to lead to the production of significant quantities of unidentified byproducts.

At this point we had intended to hydrolyze the resulting ester **12** to the carboxylic acid derivative and subsequently to esterify with appropriate alcohols.[29] Unfortunately, the 1,3,4-thiadiazole-2-carboxylic acid proved to be unstable in solution and underwent spontaneous decarboxylation (the solid carboxylic acids also underwent decarboxylation over several days). Attempted esterification of 5-(4-methoxyphenyl)-1,3,4-thiadiazole-2-carboxylic acid with *p*-cresol using DCC/DMAP gave an unsatisfactory yield (25%) of the ester with the remainder of the material being lost to decarboxylation. Decarboxylation has been observed previously in 5-amino-1,3,4-thiadiazole-2-carboxylic acids.[30–33] We therefore decided to isolate the sodium salt of the carboxylic acid (**13**, a stable molecule unless heated in solution upon which decarboxylation was observed). Direct conversion of **13** into the corresponding acid chloride derivative followed by *in situ* esterification with the desired alcohols was expected to afford the desired ester adducts. However, this reaction proved to be extremely sensitive to temperature and competitive decarboxylation was again observed unless the reaction temperature was carefully maintained at −6 to −8 °C. For example, reaction temperatures of −10 to −17 °C gave >20%



Scheme 1 Synthesis of alkyl 1,3,4-thiadiazole-2-carboxylates **14–17**.

decarboxylation byproduct while temperatures of −4 to −7 °C gave 5–17% decarboxylation (determined from ^{1}H NMR analyses of the crude products). Reaction temperatures of −6 to −8 °C gave only 0–4% decarboxylation and yields of the purified final esterification products **14–17** were good (51–61%).

Our initial attempts to purify these obtained esters using silica chromatography proved to be slow and difficult due to acid–base interactions involving the thiadiazole nitrogens; however, pre-treatment of the silica with a triethylamine-containing solvent mixture alleviated this problem and led to efficient purification. It is interesting to note that attempted chromatography using basic alumina led to complete loss of the product.

Mesophase properties

The transition temperatures for the alkyl 1,3,4-thiadiazole-2-carboxylates (**14–17**) are given in Table 1, and the transition temperatures for the analogous phenyl carboxylates **18–21** (synthesized by Gray and Goodby)[34,35] are presented in Table 2.

The melting points of the thiadiazole derivatives are all higher than the corresponding phenyl derivatives whereas the mesophase thermal stabilities of the thiadiazoles are higher than the phenyl analogs. Compounds **15**, **16**, and **17** exhibit SmC phases at temperatures of 71.3 °C, 82.5 °C, and 84.5 °C respectively. The phenyl analog of **15** (compound **19**) does not exhibit a smectic C phase but a virtual LC phase was measured at 15.3 °C lower than the thiadiazole derivative.

When a compound does not exhibit a LC phase, virtual LC phase values can be obtained by dissolving known quantities of the compound under examination into a host material that displays the phase in question (a SmC phase in this case). The mixture obtained is examined by polarizing optical microscopy and the phase transition temperature is measured as usual (the value will be modulated by the dopant). By making several mixtures with different concentrations of the compound under examination in the host, one can obtain a number of concentration-dependent transition temperatures and extrapolate to 100% of the compound under investigation. The phase transition temperature so obtained is known as a virtual LC phase transition temperature.

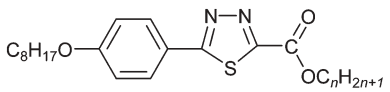
The C8 (**20**) and C10 (**21**) phenyl analogs do not exhibit SmC phases and virtual LC phase values were not recorded by the authors. Fortunately, Gray's original paper also gives details of the degree of cooling of the SmA phases of **20** and **21**, with recrystallization occurring at 80 °C and 69 °C respectively, without the observation of a SmC phase. Compounds **20** and **21** recrystallize at 2.5 °C and 15.5 °C below the observed SmC phases in compounds **16** and **17** respectively.

The introduction of disubstituted 5-membered heterocycles as replacements for 1,4-disubstituted benzene core units in mesogenic structures has, until now, always resulted in a reduction of mesophase thermal stability.[36–40] This is due to the introduction of a bend to the molecular structure that invariably results in a reduced packing ability. This observation is likely to be due to the interplay of polarity/conformational issues; ongoing studies will attempt to elucidate the factors responsible for this phenomenon. It should be noted, however, that prior to this work Joachimi *et al.*[18] and Zab *et al.*[19] had independently reported that 1,3,4-thiadiazoles had higher SmC phase transitions than the analogous linear 2,5-disubstituted pyrimidine derivatives. Our observation is therefore not altogether unexpected.

Thiadiazoles **14–17** also possess SmA phases and compounds **15**, **16**, and **17** have phase transitions 13.4 °C, 12.5 °C, and 9.8 °C higher than those of phenyl analogs **19**, **20**, and **21**, respectively. The SmA phases of thiadiazole **14** and phenyl analog **18** are comparable (85.5 °C and 86 °C, respectively).

Esters **14–17** have been exposed to bright sunlight for over six months and have not shown any changes in color or mesophase transitions, thus indicating very good photochemical and thermal stability.

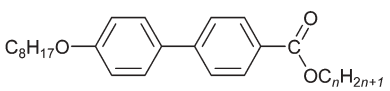
Table 1 Transition temperatures of alkyl 1,3,4-thiadiazole-2-carboxylates **14–17**[a]



n	Compound number	Cryst	SmC	SmA	Iso Liq
4	**14**	· 99.4 —		(· 85.5)	·
6	**15**	· 79.3 (·	71.3)	· 95.4	·
8	**16**	· 87.0 (·	82.5)	· 92.5	·
10	**17**	· 91.8 (·	84.5	· 88.8)	·

[a] () indicates a monotropic transition.

Table 2 Transition temperatures of phenyl carboxylates **18–21** synthesized by Gray and Goodby[a]



n	Compound number	Cryst	SmC	SmA	Iso Liq
4	**18**	· 56 (·	56)	· 86	·
6	**19**	· 72 [·	56]	· 82	·
8	**20**	· 80 —		(· 80)	·
10	**21**	· 75 —		· 79	·

[a] () indicates a monotropic transition, [] indicates a virtual transition.

Experimental

Confirmation of the structures of intermediates and products was obtained by ^{1}H (400 MHz, Bruker Avance 400 MHz spectrometer using Topspin version 1.3 software; tetramethylsilane was used as internal standard) and ^{13}C (100 MHz) NMR spectroscopy in $CDCl_3$, unless another solvent is stated. Elemental analyses were performed by Atlantic Microlabs Inc. (Norcross, GA).

The progress of reactions was monitored using either TLC [aluminium backed silica gel plates (Sigma-Aldrich, 200 μm layer thickness, 2–25 μm particle size and 60 Å pore size)] or GC [Shimadzu gas chromatograph GC-14A with a Restek™ RTX-5 capillary column (30 m) and Shimadzu class VP software].

Transition temperatures of the final products were measured using a Mettler FP82HT hot-stage and FP90 control unit in conjunction with a Leica Laborlux 12PolS polarizing microscope. All transitions are quoted from microscopic measurements and are given upon cooling at a rate of 5 °C per minute. For all compounds melting points were recorded using the same apparatus at a heating rate of 5 °C per minute. The control unit was calibrated with three Merck standards (benzophenone, benzoic acid and caffeine). Differential scanning calorimetry (DSC) measurements were performed using a TA Instruments Differential Scanning Calorimeter 2920 at heating and cooling rates of 5 °C per minute (unless otherwise stated) with indium as internal standard.

Triethylamine was dried by distillation over calcium hydride under dry argon, and was stored over potassium hydroxide. Anhydrous tetrahydrofuran was obtained by distillation from benzophenone ketyl. Butan-1-ol, octan-1-ol, and decan-1-ol were dried by distillation from anhydrous potassium carbonate under dry nitrogen and were stored over anhydrous potassium carbonate. Petroleum ether was freshly distilled and stored in amber bottles. Toluene was dried over sodium metal.

All chromatographic separations were performed using flash column chromatography on silica gel [Fisher Davisil® silica gel (60 Å, 55–75 μm particle size, grade 1740)] unless otherwise stated.

Sonication was carried out using a Fisher Scientific sonic bath (model number FS20H).

Syntheses of compounds **8**[41] and **9**[42] have been previously reported.

Methyl 4-octyloxybenzoate (8)

A waxy white solid was obtained. Yield 38.72 g (74%). ^{1}H NMR ($CDCl_3$) δ 0.91 (t, 3H, J = 7.1 Hz), 1.25–1.53 (m, 10H), 1.82 (quint, 2H, J = 7.1 Hz), 3.91 (s, 3H), 4.03 (t, 2H, J = 6.6 Hz), 6.92 (d, 2H, J = 8.8 Hz), 8.00 (d, 2H, J = 8.8 Hz). ^{13}C NMR ($CDCl_3$) δ 166.70, 163.02, 131.58, 122.36, 114.02, 68.15, 51.66, 31.93, 29.48, 29.36, 29.24, 26.10, 22.76, 14.14.

4-Octyloxybenzohydrazide (9)

A white solid was obtained. Yield 31.72 g (82%), mp 90–91 °C (lit.[42] 82–84 °C). ^{1}H NMR ($CDCl_3$) δ 0.91 (t, 3H, J = 6.8 Hz), 1.26–1.52 (m, 10H), 1.82 (quint, 2H, J = 6.8 Hz), 2.06 (br s, 2H), 4.01 (t, 2H, J = 6.4 Hz), 6.94 (d, 2H, J = 8.8 Hz), 7.72 (d, 2H, J = 8.8 Hz), 7.78 (br s, 1H). ^{13}C NMR ($CDCl_3$) δ 168.34, 162.03, 128.62, 124.54, 114.32, 68.16, 31.74, 29.26, 29.15, 29.06, 25.93, 22.59, 14.03.

1-(Ethyl oxalyl)-2-(4-octyloxybenzoyl)diazane (11)

Anhydrous triethylamine (6.1 mL, 44 mmol, d. 0.726 g mL^{-1}) was added to a solution of **9** (8.0 g, 29 mmol) in anhydrous THF (200 mL) under dry nitrogen. The reaction mixture was stirred for 10 min at room temperature before ethyl oxalyl chloride (**10**) (3.9 mL, 35 mmol, d. 1.22 g mL^{-1}) was added dropwise to the mixture at room temperature over approximately 15 min. The reaction mixture was stirred at room temperature for a further 20 h (TLC analysis revealed the completion of the reaction). The reaction mixture was filtered and an excess of ethanol (53 mL) was added to the filtrate with stirring. The solvent was removed *in vacuo* and the crude product was dried *in vacuo* (P_2O_5) overnight to afford an off-white solid (97–98% pure by NMR analysis) that was used in the next step without purification. Yield 10.42 g (100%). ^{1}H NMR ($CDCl_3$) δ 0.91 (t, 3H, J = 7.0 Hz), 1.29–1.52 (m, 10H), 1.44 (t, 3H, J = 7.0 Hz), 1.83 (quint, 2H, J = 7.4 Hz), 4.03 (t, 2H, J = 6.6 Hz), 4.44 (q, 2H, J = 7.2 Hz), 6.97 (d, 2H, J = 8.8 Hz), 7.82 (d, 2H, J = 8.8 Hz), 8.86 (1H, br d, J = 6.2 Hz), 9.87 (1H, br d, J = 6.2 Hz). ^{13}C NMR ($CDCl_3$) δ 164.18, 163.02, 158.65, 152.97, 129.51, 122.59, 114.67, 68.46, 63.86, 31.95, 29.47, 29.37, 29.22, 26.12, 22.81, 14.26, 14.12.

Ethyl 5-(4-octyloxyphenyl)-1,3,4-thiadiazole-2-carboxylate (12)

Lawesson's reagent (7.01 g, 17.3 mmol) was added to a solution of **11** (10.00 g, 27.44 mmol) in anhydrous THF (200 mL) under dry nitrogen. The reaction mixture was stirred for 29 h at room temperature (NMR and TLC analysis revealed a near completion of the reaction) before the crude product was purified by column chromatography [silica gel/ethyl acetate : petroleum ether, 1 : 3] to afford a white solid. Yield 7.07 g (71%), mp 105.3 °C. ^{1}H NMR ($CDCl_3$) δ 0.91 (t, 3H, J = 7.1 Hz), 1.26–1.43 (m, 10H), 1.49 (t, 3H, J = 7.1 Hz), 1.84 (quint, 2H, J = 7.2 Hz), 4.05 (t, 2H, J = 6.6 Hz), 4.55 (q, 2H, J = 7.2 Hz), 7.01 (d, 2H, J = 8.8 Hz), 7.98 (d, 2H, J = 8.8 Hz). ^{13}C NMR ($CDCl_3$) δ 172.49, 162.44, 158.95, 158.68, 130.05, 121.77, 115.27, 68.44, 63.20, 31.91, 29.44, 29.33, 29.20, 26.08, 22.76, 14.30, 14.21. Anal. Calcd for $C_{19}H_{26}N_2O_3S$: C, 62.96; H, 7.23; N 7.73; S 8.85. Found: C, 62.50; H, 7.27; N, 7.82; S, 8.90%.

Sodium 5-(4-octyloxyphenyl)-1,3,4-thiadiazole-2-carboxylate (13)

A mixture of **12** (7.00 g, 19.3 mmol), ethanol (140 mL), water (47 mL) and sodium hydroxide (1.62 g, 40.5 mmol) was stirred for 24 h at room temperature (TLC analysis revealed completion of the reaction). The product was filtered off, washed with diethyl ether, and dried *in vacuo* (P_2O_5). The product was used in the next step without purification. Yield 6.72 g (98%). ^{1}H NMR (DMSO-d_6) δ 0.87 (t, 3H, J = 6.7 Hz), 1.21–1.38 (m, 8H), 1.42 (quint, 2H, J = 6.7 Hz), 1.73 (quint, 2H, J = 6.7 Hz), 4.04 (t, 2H, J = 6.5 Hz), 7.06 (d, 2H, J = 8.9 Hz), 7.87 (d, 2H, J = 8.9 Hz). ^{13}C NMR ($CDCl_3$) δ 171.95, 169.93, 161.25, 159.74, 129.52 (2C), 123.24, 115.59 (2C), 68.22, 31.69, 29.21, 29.18, 29.02, 25.93, 22.61, 14.43.

Butyl 5-(4-octyloxyphenyl)-1,3,4-thiadiazole-2-carboxylate (14)

A suspension of **13** (0.50 g, 1.4 mmol) in anhydrous toluene (5 mL) under dry nitrogen was subjected to sonication for 30 min. The mixture was cooled to −6 °C before thionyl chloride (0.17 mL 2.3 mmol, d. 1.63 g mL^{-1}) was added dropwise at −6 °C. The reaction mixture was allowed to stir for 1½ h at −6 °C before anhydrous toluene (7.5 mL) was added at −4 to −6 °C and the reaction mixture was allowed to stir for 1 h at −4 to −7 °C. Anhydrous pyridine (0.2 mL, 2 mmol, d. 0.9700 g mL^{-1}) was added dropwise at −4 to −5 °C. Anhydrous butan-1-ol (0.34 mL, 3.7 mmol, d. 0.8100 g mL^{-1})

in anhydrous toluene (2 mL) was added dropwise at −4 to−5 °C and the reaction mixture was allowed to slowly warm to room temperature before being stirred overnight. The mixture was sequentially washed with saturated sodium bicarbonate (2 × 100 mL) and deionized water (2 × 75 mL) before being dried ($MgSO_4$). The mixture was concentrated *in vacuo* followed by purification using column chromatography (the silica column was pre-treated with a mixture of 5% triethylamine, 10% ethyl acetate, and 85% petroleum ether) [silica gel/petroleum ether : ethyl acetate, 1 : 9]. The product was crystallized from petroleum ether and dried *in vacuo* (P_2O_5) to afford a white solid. Yield 0.28 g (51%). Transitions (°C) Cryst 99.4 (SmA 85.5) Iso Liq [recrystallized (Rec.) 80.7]. ^{1}H NMR ($CDCl_3$) δ 0.92 (t, 3H, J = 7.0 Hz), 1.02 (t, 3H, J = 7.4 Hz), 1.29–1.57 (m, 14H), 1.84 (quint, 2H, J = 7.2 Hz), 4.05 (t, 2H, J = 6.6 Hz), 4.49 (t, 2H, J = 6.8 Hz), 7.01 (d, 2H, J = 8.3 Hz), 7.98 (d, 2H, J = 8.8 Hz). ^{13}C NMR ($CDCl_3$) δ 172.46, 162.37, 159.04, 158.62, 130.03 (2C), 121.77, 115.22 (2C), 68.39, 66.95, 31.81, 30.53, 29.33, 29.23, 29.10, 25.99, 22.66, 19.10, 14.11, 13.69. Anal. Calcd for $C_{21}H_{30}N_2O_3S$: C, 64.58; H, 7.74; N, 7.17; S, 8.21. Found: C, 64.84; H, 7.80; N, 7.22; S, 8.21%.

Hexyl 5-(4-octyloxyphenyl)-1,3,4-thiadiazole-2-carboxylate (15)

A suspension of **13** (1.00 g, 2.81 mmol) in anhydrous toluene (10 mL) was subjected to sonication under dry nitrogen for 30 min. The mixture was cooled to −6 °C before thionyl chloride (0.34 mL, 4.7 mmol, d. 1.6310 g mL^{-1}) was added dropwise at −3 to −4 °C and the mixture was stirred for 1.05 h at −6 to −7 °C. Anhydrous toluene (14 mL) was added dropwise at −8 °C and the mixture was stirred for 1 h at −6 to −7 °C. Anhydrous pyridine (0.46 mL, 5.6 mmol, d. 0.9700 g mL^{-1}) was added dropwise at −4 to −6 °C. Anhydrous hexan-1-ol (0.93 mL, 7.5 mmol, d. 0.8200 g mL^{-1}) in anhydrous toluene (3 mL) was added dropwise at −6 to −7 °C before the reaction mixture was slowly allowed to warm to room temperature overnight. The pyridinium salt was filtered off and the reaction mixture was washed successively with saturated sodium bicarbonate (2 × 100 mL) and deionized water (2 × 75 mL), and dried ($MgSO_4$). The solution was concentrated *in vacuo* followed by purification using column chromatography (the silica column was pre-treated with 5% triethylamine, 10% ethyl acetate, and 85% petroleum ether) [silica gel/petroleum ether : ethyl acetate, 1 : 9]. The product was crystallized from methanol using a minimum volume of added water. Yield 0.6534 g (57%). Transitions (°C) Cryst 79.3 (SmC 71.3) SmA 95.4 Iso Liq (Rec. 69.0). ^{1}H NMR ($CDCl_3$) δ 0.92 (t, 3H, J = 7.2 Hz), 0.93 (t, 3H, J = 7.2 Hz), 1.29–1.54 (m, 16H), 1.80–1.89 (m, 4H), 4.05 (t, 2H, J = 6.6 Hz), 4.48 (t, 2H, J = 6.8 Hz), 7.01 (d, 2H, J = 8.8 Hz), 7.98 (d, 2H, J = 8.8 Hz). ^{13}C NMR ($CDCl_3$) δ 172.45, 162.37, 159.03, 158.62, 130.02 (2C), 121.77, 115.21 (2C), 68.38, 67.24, 31.80, 31.37, 29.30, 29.22, 29.09, 28.48, 26.00, 25.49, 22.66, 22.51, 14.00, 14.00. Anal. Calcd for $C_{23}H_{34}N_2O_3S$: C, 65.99; H, 8.19; N, 6.69; S, 7.66. Found: C, 65.75; H, 8.07; N, 6.84; S, 7.81%.

Octyl 5-(4-octyloxyphenyl)-1,3,4-thiadiazole-2-carboxylate (16)

A suspension of **13** (1.00 g, 2.81 mmol) in anhydrous toluene (10 mL) under dry nitrogen was subjected to sonication for 30 min. The mixture was cooled to −4 °C before thionyl chloride (0.35 mL, 4.8 mmol, d. 1.6310 g mL^{-1}) was added dropwise at −4 °C and the reaction mixture was stirred for 1.05 h at −3 to −4 °C. Anhydrous toluene (15 mL) was added dropwise at −6 to −7 °C. The mixture was stirred for 1 h at −6 to −8 °C. Anhydrous pyridine (0.46 mL, 5.6 mmol, d. 0.9700 g mL^{-1}) was added dropwise at −6 °C. Anhydrous octan-1-ol (1.20 mL, 7.62 mmol, d. 0.8270 g mL^{-1}) in anhydrous toluene (3 mL) was added dropwise at −6 to −9 °C before the reaction mixture was slowly allowed to warm to room temperature overnight. The pyridinium salt was filtered off and the filtrate was washed successively with saturated sodium bicarbonate (2 × 100 mL) and deionized water (2 × 75 mL) before being dried ($MgSO_4$). The solution was concentrated *in vacuo* followed by purification using column chromatography (the column was pre-treated with a mixture of 5% triethylamine, 10% ethyl acetate, and 85% petroleum ether) [silica gel/petroleum ether : ethyl acetate, 1 : 9]. The product was crystallized from methanol using a minimum volume of added water. Yield 0.6688 g (54%). Transitions (°C) Cryst 87.0 (SmC 82.5) SmA 92.5 Iso Liq (Rec. 81.6). ^{1}H NMR ($CDCl_3$) δ 0.91 (t, 3H, J = 7.0 Hz), 0.92 (t, 3H, J = 7.0 Hz), 1.28–1.54 (m, 20H), 1.79–1.89 (m, 4H), 4.04 (t, 2H, J = 6.6 Hz), 4.46 (t, 2H, J = 6.8 Hz), 7.00 (d, 2H, J = 8.8 Hz), 7.97 (d, 2H, J = 9.2 Hz). ^{13}C NMR ($CDCl_3$) δ 172.46, 162.37, 159.04, 158.64, 130.03 (2C), 121.78, 115.22 (2C), 68.39, 67.26, 31.81, 31.77, 29.33, 29.23, 29.17, 29.15, 29.10, 28.52, 25.99, 25.83, 22.66, 22.64, 14.11, 14.10. Anal. Calcd for $C_{25}H_{38}N_2O_3S$: C, 67.23; H, 8.58; N, 6.27; S, 7.18. Found: C, 67.21; H, 8.62; N, 6.35; S, 7.31%.

Decyl 5-(4-octyloxyphenyl)-1,3,4-thiadiazole-2-carboxylate (17)

A suspension of **13** (1.00 g, 2.81 mmol) in anhydrous toluene (10 mL) under dry nitrogen was subjected to sonication for 30 min. The reaction mixture was cooled to −6 °C before thionyl chloride (0.35 mL, 4.8 mmol, d. 1.6310 g mL^{-1}) was added dropwise at −6 °C and the reaction mixture stirred for 1 h 20 min at −4 to −6 °C. Anhydrous toluene (15 mL) was added dropwise at −4 to −6 °C and the reaction mixture was stirred for 1 h at −5 to −6 °C. Anhydrous pyridine (0.46 mL, 5.6 mmol, d. 0.9700 g mL^{-1}) was added dropwise at −5 to −6 °C. Decan-1-ol (1.45 mL, 7.59 mmol, d. 0.8290 g mL^{-1}) in anhydrous toluene (4 mL) was added dropwise at −3 to −6 °C before the reaction mixture was allowed slowly to warm to room temperature overnight. The pyridinium salt was filtered off and the filtrate was washed successively with saturated sodium bicarbonate (2 × 100 mL) and deionized water (2 × 75 mL) before being dried ($MgSO_4$). The solution was concentrated *in vacuo* followed by purification using column chromatography (the column was pre-treated with a mixture of 5% triethylamine, 10% ethyl acetate, and 85% petroleum ether) [silica gel/petroleum ether : ethyl acetate, 1 : 9]. The product was crystallized from methanol using a minimum volume of added water. Yield 0.820 g (61%). Transitions (°C) Cryst 91.8 (SmC 84.5 SmA 88.8) Iso Liq (Rec. 73.5). ^{1}H NMR ($CDCl_3$) δ 0.90 (t, 3H, J = 6.8 Hz), 0.92 (t, 3H, J = 6.8 Hz), 1.25–1.54 (m, 24H), 1.79–1.89 (m, 4H), 4.05 (t, 2H, J = 6.6 Hz), 4.47 (t, 2H, J = 6.8 Hz), 7.01 (d, 2H, J = 8.8 Hz), 7.98 (d, 2H,

J = 8.8 Hz). ^{13}C NMR ($CDCl_3$) δ 172.46, 162.37, 159.03, 158.63, 130.03 (2C), 121.78, 115.22(2C), 68.38, 67.25, 31.89, 31.81, 29.52, 29.49, 29.33, 29.30, 29.23, 29.21, 29.10, 28.52, 25.99, 25.83, 22.68, 22.66, 14.12, 14.11. Anal. Calcd for $C_{27}H_{42}N_2O_3S$: C, 68.31; H, 8.92; N, 5.90; S, 6.76. Found: C, 68.03; H, 8.81; N, 5.91; S, 6.73%.

Conclusions

We have described the novel synthesis of a new family of thiadiazole-2-carboxylate ester-based liquid crystals **14–17** using a chemoselective ring-closing methodology. Further studies designed to investigate the scope of this chemistry are in progress. These novel materials possess remarkably high mesophase thermal stabilities that, surprisingly, exceed those of the analogous phenyl derivatives. The materials have proven to be both thermally and photochemically stable.

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