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Thionation reactions of 2-pyrrole carboxylates†

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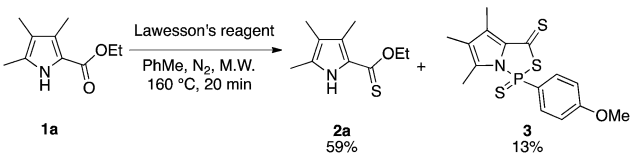
Reaction of 2-pyrrole carboxylates with Lawesson's reagent at elevated temperatures results in the corresponding thionoesters, concurrent with the production of a new class of pyrrole annulated with the (1,3,2)-thiazaphospholidine unit. X-ray crystallography was used to identify the pyrrolic thiazaphospholidine, which was found to have unique structural features compared to literature analogues. Addition of $BF_3{\cdot}OEt_2$ to the thionation procedure was found to produce the corresponding F-BODIPY, constituting a four-step reaction in one-pot. The scope and limitations of these reactions involving the promiscuous Lawesson's reagent are discussed herein.

Introduction

Pyrroles decorated with sulfur-containing functionalities are a rarity. Examples bearing thioesters (*S*-alkyl, $R^1C(O)SR^2$) are amongst the best known, courtesy of the critical role that thioesterase-appended pyrroles play in the biosynthesis of secondary metabolites containing pyrroles.[1,2] In contrast, examples of small molecule pyrroles bearing thioesters in the 2-position are seemingly confined to a brief foray into the use of this functionality as a protecting group,[3–5] a study regarding the reactivity of $PhSCF_2Br$[6] and the reactivity of trialkyl trithioorthocarboxylates.[7] Reports of pyrroles appended with thionoesters (*O*-alkyl, $R^1C(S)OR^2$) appear to be limited to examples of mono- and di-pyrroles reacting with dithiocarbonate[8] and methanolic solutions of thiophosgene.[9,10] Against this backdrop, and with the knowledge that thionoesters are more electrophilic than their all-oxygen counterparts,[11,12] we became interested in the synthesis of pyrroles substituted with thionoesters at the 2-position. Cognisant that the use of Lawesson's reagent usually offers a reasonable route into thionoesters, we herein report the reactivity of *O*-alkyl 2-pyrrole carboxylates with this thionation agent.

Results and discussion

Our work began with ethyl 2-pyrrole carboxylate **1a**, a representative example readily available *via* Knorr-type condensation. Rather than endure the long reaction times often reported for successful thionation using Lawesson's reagent,[13] we achieved the necessary high temperature using microwave-assisted heating: 160 °C for 20 minutes was initially examined (Scheme 1).



Scheme 1 Generation of thionoester **2a** and (1,3,2)-thiazaphospholidine **3**.

Complete consumption of starting material was accompanied by the generation of two new compounds. Upon isolation, one of these compounds was identified as the desired product **2a**, isolated in 59% yield. The structure of **2a** was confirmed using X-ray crystallography,‡ and compares favourably to the only other reported example of this type.[10] The second, more polar, isolated compound featured enhanced structural complexity with ^1H and ^{13}C NMR signals that derived from both starting materials, and with a ^{31}P signal that evidently originated from Lawesson's reagent. Fortunately, crystals suitable for X-ray crystallography were obtained,§ enabling this material to be unequivocally identified as thiazaphospholidine **3** (Fig. 1).

Although the (1,3,2)-thiazaphosphole functional group (N–P–S)[14] is well described, we were unable to find pyrrolic

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‡ Crystal data for **2a**: $C_{10}H_{15}NOS$, MM = 197.30 g mol^{-1}. Light-yellow plate crystal, dimensions 0.29 × 0.28 × 0.08 mm; triclinic space group, $P\bar{1}$ (#2); a = 7.215(2) Å, b = 8.581(3), c = 9.903(2) Å, α = 103.094(9)°, β = 93.3290(16)°, γ = 112.892(9)°, V = 542.8(3) Å^3; d = 1.207 g cm^{-3}, μ(Mo-Kα) = 2.609 cm^{-1}, 12 478 reflections (4181 unique, R_{int} = 0.073), R = 0.0446, R_w = 0.0404, GOF = 1.062. CCDC deposition number: 1455753.

§ Crystal data for compound **3**: $C_{15}H_{16}NPS_3O$, MM = 353.46 g mol^{-1}. Orange plate crystal, dimensions 0.27 × 0.26 × 0.09 mm; monoclinic space group, $P21/n$; a = 7.4515(15) Å, b = 11.579(2), c = 19.631(3) Å, α = 90°, β = 97.168(6)°, γ = 90°, V = 1680.5(5) Å^3; d = 1.397 g cm^{-3}, μ(Mo-Kα) = 5.33 cm^{-1}, 21 248 reflections (5767 unique, R_{int} = 0.048), R = 0.0292, R_w = 0.0357, GOF = 1.096. CCDC deposition number: 1455752.

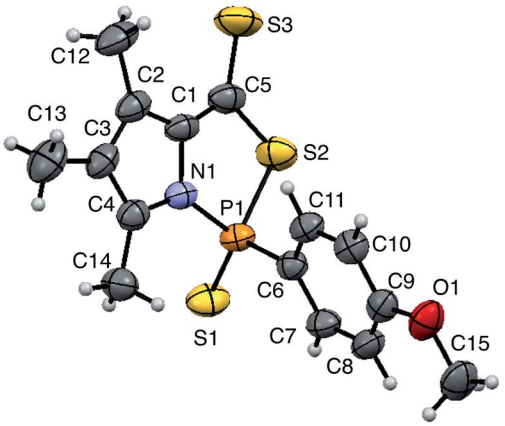
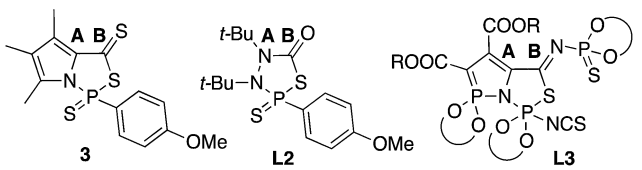


Fig. 1 ORTEP view of (1,3,2)-thiazaphospholidine **3**; thermal ellipsoids shown at 50%.

examples bearing this functionality. Four-, five- and six-membered cyclic thiazaphospholes are well studied, and many related crystal structures are readily available from the Cambridge Crystallographic Data Centre (CCDC). When limiting the fourth and fifth atoms of the ring to main group elements, and Lawesson's reagent as the sulfur source, dozens of known compounds can be found in the literature. Of these, the X-ray structure of only one compound (**L2**) is reported.[15] Table 2 contains selected geometric parameters for **3** and **L2**, as well as for **L3** which contains an analogous (1,3,2)-thiazaphospholidine ring.[16]

The bond parameters of **3** are within expected ranges for the thiazaphospholidine system (Table 1). The N–P bonds in **3** and **L2**, both compounds derived from Lawesson's reagent, are identical. These values are quite long for bonds of the type X_2–P(=X)–NX_2, which are typically near 165 pm for compounds bearing sp^2 nitrogen atoms.[17] The presence of the nitrogen atom adjacent to the phosphorous-bound nitrogen in **L2** does not appear to have a large effect on the length of the N–P bond, relative to molecules **3** and **L3** bearing carbon at that position.

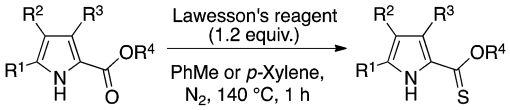
Table 1 Selected geometric parameters of compounds bearing thiazaphospholidines[a]



Compound	N–P (pm)	P–S (pm)	N–P–S (°)	N–P–S–C^B (°)
3	170.94(13)	211.15(6)	92.81(5)	3.50
L2	170.8	210.8	94.93	30.93
L3	177.2(4)	210.1(2)	90.41	20.03

[a] Bond distances and angles derived using raw coordinate data for **L2** and **L3**.[15,16]

Table 2 Substrate scope of thionation



Entry	Pyrrole	R^1	R^2	R^3	R^4	**2a–l**[a] (%)
1	**1a**	Me	Me	Me	Et	72
2	**1b**	Me	Me	Me	Bn	49
3	**1c**	Me	H	Me	Et	72
4	**1d**	Me	H	Me	Bn	50
5	**1e**	Me	Me	Et	Et	59
6	**1f**	Me	Me	Et	Bn	47
7	**1g**	H	Me	Me	Et	58
8	**1h**	Me	$(CH_2)_4CH_3$	Me	Et	64
9	**1i**	Me	$(CH_2)_2CH_3$	$(CH_2)_2CH_3$	Et	68
10	**1j**	Me	CO_2Et	Me	Et	52[b,c]
11	**1k**	Me	Ph	Me	Bn	55[b]
12	**1l**	Me	Ac	Me	Et	61[d]

[a] Isolated yield. [b] Reaction time of 4 h. [c] Di-thio product **2jS** also obtained (7% yield). [d] Thionation occurred at the acyl position.

The pentacoordinate phosphorous atom in **L3** has a longer P–N bond, at 177.2(4) pm, but is in a significantly different chemical environment compared to the P–N bond found in **3**. The length of the ring P–S bond in the three compounds is relatively consistent, considering the significant differences in their surrounding environments, and is within expected values. The bond angle of the N–P–S functionality of **3** also appears reasonable, falling midway between that of **L2** and **L3**.

Contrary to literature examples, the (1,3,2)-thiazaphospholidine ring of **3** approaches planar geometry. This is reflected by the size of the dihedral angles of the N–P–S–C^B unit of the three compounds. Whilst **3** shows only a mild deviation from planarity (3.50°), the other two systems differ significantly, adopting non-planar puckered conformations in their crystal structures. This planarity is likely due to the forced sp^2 geometry of the binding nitrogen atom in the pyrrole ring, which is not present in **L2** and is significantly reduced by the sp^3 nature of the neighbouring phosphorous atom in **L3**. Indeed, the bond angles surrounding the nitrogen and X^A atoms of **3** are closer to ideal for sp^2 hybridised atoms than in either **L2** or **L3**. The sum of the interior bond angles for the (1,3,2)-thiazaphospholidine ring of **3** is within error of 540°, the expected value for a planar five-membered ring system. The pyrrole ring and the thiazaphospholidine rings are almost coplanar, with dihedral angles of no more than 3.5° between their atoms. The structural features of the pyrrole ring in **3** compare well with those found in the crystal structure of **2a**.

Returning to thionoesters, brief efforts to optimise the synthesis of **2a** included variation of the solvents used, as well as of the temperature of the reaction using both microwave-promoted and conventional heating. Although we were unable to significantly improve the yield of **2a** (72% being the maximum), we did discover that extended reaction times lead to

decomposition. Furthermore, reactions performed using conventional heating generally provide higher yields than those performed in the microwave. Substrate scope of the thionation reaction was then explored using pyrroles bearing a variety of substituents (Table 2).

The thionation reaction proceeded in moderate-to-good yield. As a general trend, pyrroles bearing ethyl esters in the 2-position offered higher yields than analogous benzyl esters (compare entries 1 *vs.* 2, entries 3 *vs.* 4, entries 5 *vs.* 6). The presence of an unsubstituted α-position (entry 7) or β-position (entries 3 and 4) on the pyrrole was tolerated. Where a second ester was present at the distal β-position, a 7% yield of the dithionated species **2jS** was obtained (entry 10), in addition to the expected product **2j** (52%). The presence of a phenyl group at the distal β-position did not affect the yield of reaction (entry 11), relative to the analogous methyl-substituted result (entry 2). Thionation of a pyrrole bearing an acyl group left the ester untouched, and instead yielded only the thioketone **2l** (entry 12).

Having expanded the substrate scope of the thionation process, attention was focused on the generation of thiazaphospholidine **3**. Lawesson's-derived five- and six-membered 1,3,2-thiazaphosphinanes (compounds **L4** [18] and **L5**,[19] Fig. 2) are known. Five-membered derivatives can be generated *via* reaction of 2-amino alcohols or 2-amino phenols with Lawesson's reagent,[18] while the six-membered rings are often produced from pyrano[2,3-*d*]pyrimidine-2,4-(1*H*,3*H*)-diones,[20] although generation from other sources has also been reported.[21]

Intriguingly, (1,3,2)-thiazaphospholes of the type **L6** displayed some herbicidal and viruicidal activity during preliminary biological screens.[17] This bioactivity prompted our further interest in heterocycle **3**, with the hope being to optimise the synthesis at the expense of thionoester **2a**. Efforts focused on the effects of temperature, time and concentration on the reaction of **2a** with an increased stoichiometry of Lawesson's reagent (Scheme 2), as this led to higher yields of **3** than did conversion from ester **1a**.

After considerable effort, the optimal conditions for producing **3** emerged as 140 °C and a reaction time of 1.5 hours to provide 33% yield, a modest improvement upon the original yield of 13% from **1a** (Scheme 1). The starting material **2a** was reclaimed (46%). Purification and isolation of **3** was difficult, whereby the product proved to be unstable on both basic and neutral alumina and moderately unstable on silica, resulting in rapid decomposition. Other 1,3,2-thiazaphosphinanes (Fig. 2, structures **L4** and **L5**) are reported to survive purification on

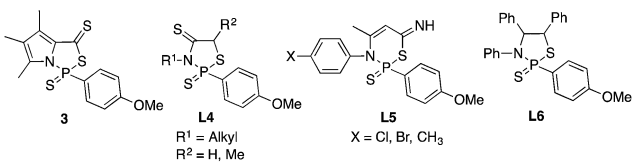
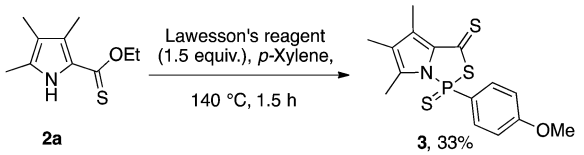


Fig. 2 The structure of novel heterocycle **3** alongside three known compounds.



Scheme 2 Synthesis of thiazaphosphole **3**.

silica, not undergoing decomposition to the degree seen when attempting to isolate the pyrrole-containing derivative **3**. As such, the relative instability of **3** appears to be inherent to the presence of the pyrrole moiety, placing it within the many types of pyrrole-containing species that are intolerant to purification under even mildly acidic conditions. Despite these difficulties, a pure sample of compound **3** was found to be stable when stored in the freezer. Reducing the concentration of the reaction from 0.5 M to 0.25 M was found to be detrimental, resulting in 86% recovery of thionoester **2a** and only trace amounts of **3**. Increasing the concentration to 1.0 M returned a comparable yield of **3** (27%). The addition of an acid or a base to the reaction brought little reward. For example, the use of catalytic amounts of DMAP (0.2 equiv.) or a stoichiometric amount of NaHMDS only resulted in trace amounts of **3**. The addition of a catalytic amount of 4 M HCl in dioxane (0.1 equiv.) did not serve to improve the yield of the desired compound **3**, while use of a stoichiometric amount of HCl was detrimental and led to the formation of trace amounts of an unidentifiable product.

Moving to a Lewis acid, the addition of $BF_3 \cdot Et_2O$ resulted in the isolation of a fluorescent material, alongside decomposition products. Cognisant of the rich chemistry offered by pyrroles, we were excited to identify the fluorescent material as F-BODIPY **4a**.¶ The 4,4-difluoro-4-bora-3*a*,4*a*-diaza-*s*-indacene (F-BODIPY) framework has enjoyed a considerable rise in interest from the chemical community in the last twenty years. Due primarily to the strong absorption and fluorescence properties that F-BODIPYs exhibit,[22] these compounds have found extensive use, especially as laser dyes,[23] luminescent probes,[24] functional materials[25] and chemical indicators.[26] However, methods to synthesise F-BODIPYs have remained largely unchanged throughout the past four decades:[27] addition of excess tertiary amine (usually 6 equiv. NEt_3 or Hünig's base) to a dipyrrin salt generates the free-base dipyrrin, followed by, or concurrent with, addition of excess BF_3 (typically 9 equiv. in the form of $BF_3 \cdot Et_2O$). There are very few exceptions to this methodology; the most notable perhaps being the use of NaHMDS for prior deprotonation, allowing for stoichiometric use of $BF_3 \cdot Et_2O$ to generate the F-BODIPY.[28] The isolation of F-BODIPY **4a** from the reaction of **1a** with Lawesson's reagent necessitates the execution of four synthetic steps in a one-pot process: ester hydrolysis, partial decarboxylation,[29,30] self-condensation of

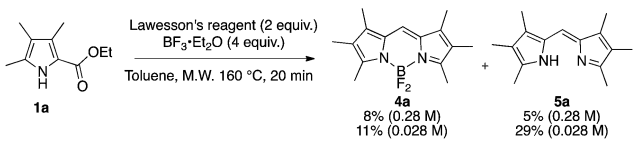
¶ Crystal data for compound **4a**: $C_{15}H_{19}N_2BF_2$, MM = 197.30 g mol^{-1}. Deep-red needle crystal, dimensions 0.42 × 0.19 × 0.08 mm; monoclinic space group, $P2_1/n$; a = 7.2351(6) Å, b = 16.6785(14), c = 11.8701(10) Å, α = 90°, β = 98.682(4)°, γ = 90°, V = 1416.0(2) Å^3; d = 1.295 g cm^{-3}, μ(Mo-Kα) = 0.940 cm^{-1}, 12 329 reflections (3788 unique, R_{int} = 0.025), R = 0.0485, R_w = 0.0576, GOF = 1.089. CCDC deposition number: 1468172.

a decarboxylated pyrrole with one still bearing the α-acid to form a dipyrrin, and complexation to boron.

As F-BODIPYs represent an important class of fluorophore, new methodologies for synthesis are desirable, especially those that operate in a succinct manner from simple starting materials. Our efforts thus turned to the synthesis of **4a** from **1a** (Scheme 3). Following the reaction, a relatively large amount of tarry precipitate was found to have adhered to the walls of the microwave vial. Furthermore, the previously pale-white slurry had formed a black, sticky suspension. The precipitate was insoluble in most common solvents (toluene, hexane, ethyl acetate, dichloromethane, methanol), but could be dissolved in acetone. Analysis of the corresponding ^{1}H-NMR spectrum revealed that the precipitate consisted of a complex mixture of materials originating with Lawesson's reagent, but featured none of the characteristic signals of the starting material pyrrole (**1a**).

Despite the ruinous nature[31] of the product mixture, analysis of the filtrate using TLC revealed the presence of the desired, highly fluorescent, F-BODIPY **4a** as well as dipyrrin **5a**. To isolate these materials, the reaction mixture was diluted with ethyl acetate, sonicated for 5 minutes to ensure fragmentation of the precipitate and consequent dissolution of any residual F-BODIPY, then poured into ethyl acetate : hexanes (3 : 7) and filtered over neutral alumina. Purification of the filtrate was performed using column chromatography over neutral alumina, using an eluent gradient consisting of dichloromethane : hexanes (5 : 95 → 20 : 80). Two impurities eluted closely to the F-BODIPY, thus several chromatographic runs were required to obtain satisfactorily pure product **4a** in an 8% yield. 1D and 2D NMR techniques and mass spectrometry were used in an attempt to elucidate the structure of the impurities, to no avail. The impurities bore structural features of Lawesson's reagent and $BF_3 \cdot Et_2O$ but not the original pyrrole, for which the methyl groups are diagnostic. Attempts to recreate the impurities through combination of Lawesson's reagent with $BF_3 \cdot Et_2O$, in the absence of pyrrole, proved fruitless. Following the elution of all mobile substrates in the dichloromethane : hexane system, the solvent was changed to ethyl acetate : hexanes (1 : 19), and a small amount of the intermediate product dipyrrin was isolated (5% yield). Performing the same reaction at ten-fold dilution allowed for isolation of the symmetric free-base dipyrrin **5a** in 29% yield. Unfortunately, the increase in isolable dipyrrin did not correlate to a significant increase in the yield of the desired F-BODIPY **4a** (11%).

During examination of the scope of F-BODIPY formation, it was discovered that pyrroles bearing a *t*-butyl ester in the 2-position reacted more cleanly and the product mixture contained fewer insoluble, black side-products. Rather, a sticky, red, insoluble film formed on the walls of the vessel, while the solution was vibrant red and transparent. Unfortunately, the impurities described previously were persistent. As reactions containing the *t*-butyl ester were more easily handled and purified, *t*-butyl 3,4,5-trimethylpyrrole-2-carboxylate, **1m**, was used to optimise the reaction conditions (Table 3).

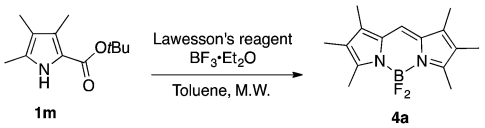


Scheme 3 Generation of F-BODIPY **4a** and dipyrrin **5a** using Lawesson's reagent.

Attempting the reaction at room temperature resulted in complete recovery of starting material (entry 1). At 100 °C, trace amounts of F-BODIPY were produced. The temperature was thus increased in 20 °C increments (Table 3, entries 2–6), with the goal of improving F-BODIPY yield without incurring formation of the problematic tarry precipitates. The yield of **4a** (12%, entry 4) from **1m** at 140 °C was comparable to the initial result from pyrrole **1a** at 160 °C (Scheme 3). However, heating beyond 140 °C did not improve the yield of the reaction and only resulted in thickening and darkening of the reaction mixture. In an effort to reduce the extent of decomposition, the reaction using **1m** was repeated at 160 °C, with ten-fold dilution (entry 7). This resulted in a dramatic decrease in the amount of precipitated side-products. Furthermore, a more facile work-up could be achieved, such that dry loading of the reaction mixture directly onto a neutral alumina column was feasible (mitigating potential loss of F-BODIPY *via* adherence to the precipitates). However, the 10% yield of **4a** was comparable to that obtained under the more concentrated conditions. The addition of 10 equivalents of $BF_3 \cdot Et_2O$ (entry 8), as typically used for synthesis of F-BODIPYs,[28,32] did not enhance the yield. To determine whether the microwave-promoted conditions (160 °C, 20 min) were responsible for formation of **4a**, rather than the sulfur source being a necessary additive, the reaction was repeated in the absence of Lawesson's reagent: **4a** was not isolated after reaction under these conditions. Furthermore, use of only one equivalent of Lawesson's reagent was not beneficial.

The substrate scope of this reaction was probed using a variety of readily available pyrroles (Table 4). F-BODIPY formation occurred in humble yields (9–18%) for the pyrroles

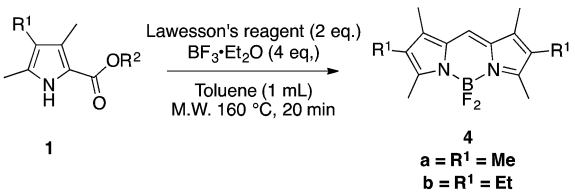
Table 3 Reaction optimization using pyrrole **1m**



Entry	*T* (°C)	*t* (min)	Vol. (mL)	LR (equiv.)	$BF_3 \cdot Et_2O$ (equiv.)	Yield (%)
1	23	24 h	1	2	4	—[a]
2	100	20	1	2	4	<1
3	120	20	1	2	4	5
4	140	20	1	2	4	12
5	160	20	1	2	4	12
6	180	20	1	2	4	10
7	160	20	10	2	4	10
8	160	20	10	2	10	8

[a] Starting material reclaimed without decomposition.

Table 4 Substrate scope of F-BODIPY formation using Lawesson's reagent



1

4
a = R1 = Me
b = R1 = Et

Entry	Pyrrole	R^1	R^2	4[a] (%)
1	**1a**	Me	Et	11
2	**1b**	Me	Bn	11
3	**1m**	Me	*t*-Bu	9
4	**1o**	Et	Et	12
5	**1n**	Et	Bn	15
6	**1p**	Et	*t*-Bu	18
7	**1k**	Ph	Bn	—[b]
8	**1q**	$(CH_2)_7CH_3$	Et	—[b]
9	**1l**	$COCH_3$	*t*-Bu	—[c]
10	**1r**	H	Et	—[d]
11	**1s**	I	*t*-Bu	—[d]
12	**1t**	$(CH_2)_3CH_2OH$	Et	—[d]

[a] Isolated yields. [b] Trace isolable F-BODIPY. [c] Deacylation. [d] No isolable F-BODIPY.

originally bearing short-alkyl chain, ethyl, benzyl and *t*-butyl esters (entries 1–6). The choice of ester substituent did not appear to have any significant effect beyond altering the appearance of the reaction mixture as regards to the extent of precipitation of side-products (reactions utilising *t*Bu were easier to manipulate courtesy of reduced amounts of precipitate). The substrate scope seems limited to short-chain, alkyl-substituted pyrroles. Introduction of an aryl group or longer alkyl chain (entries 7 and 8) resulted in only trace amounts of the required F-BODIPYs. The presence of an acyl group was not tolerated (entry 9).[33] Similarly, pyrroles bearing hydrogen, iodo- and alkyl-alcohol bearing pyrroles (**1r–t**, respectively) were not tolerated.

Conclusions

Pyrroles substituted at the 2-position with thionoesters may be prepared in good yield by reacting Knorr-type pyrrolic esters with Lawesson's reagent. A novel polyheterocyclic construct, of type **3**, is also formed. The formation of F-BODIPYs from alkyl-substituted Knorr-type pyrroles, through reaction with Lawesson's reagent and $BF_3 \cdot Et_2O$, represents a four-step, one-pot process (averaging around 65% yield per step) to form high-value products from simple starting materials. Alternative strategies to prepare symmetrical F-BODIPYs require prior formation of the corresponding dipyrrin, followed by complexation; or prior formation of the corresponding 2-formyl pyrrole.[34] Several questions remain pertaining to mechanism and the fate of the unaccounted-for pyrrolic material. Although pyrrole 2-thionoesters may be readily prepared, researchers using Lawesson's reagent and 2-pyrrole carboxylates should be aware of the potential for adverse interactions between the two moieties, as well as the formation of dipyrrins and their complexation products.

Experimental

General experimental

All chemicals were purchased and used as received unless otherwise indicated. Hexanes and dichloromethane used for chromatography were obtained crude and purified *via* distillation under atmospheric conditions before use. Anhydrous solvents were used as received. Flash chromatography was performed using Silicycle ultra pure silica (230–400 mesh) or Brockmann III (150 mesh) activated basic or neutral alumina oxide as indicated. TLC was performed using glass-backed silica gel plates or plastic-backed neutral alumina plates. Visualisation of TLC plates was performed using UV light (254 nm) and/or vanillin stain. Moisture sensitive reactions were performed in oven- or flame-dried glassware under a positive pressure of nitrogen. Air- and moisture-sensitive compounds were introduced *via* syringe. NMR spectra were recorded using 500 MHz or 300 MHz spectrometers. ^{1}H and ^{13}C chemical shifts are expressed in parts per million (ppm) using the solvent signal ($CDCl_3$ ^{1}H 7.26; ^{13}C 77.16 ppm) as reference. ^{11}B, ^{19}F and ^{31}P chemical shifts were referenced using the absolute referencing procedure standard for digital spectrometers, with $BF_3 \cdot Et_2O$ (15% in $CDCl_3$), CCl_3F and 85% H_3PO_4 to define the 0 ppm position, respectively. All coupling constants (*J*) are reported in Hertz (Hz). Splitting patterns are indicated as follows: br, broad; s, singlet; d, doublet; t, triplet; at, apparent triplet; q, quartet; m, multiplet; a, apparent. All mass spectra were recorded using ESI TOF ionisation. All microwave-promoted reactions were performed using a Biotage Initiator 8 laboratory microwave apparatus, 0–400 W power, 2.45 GHz. Pyrroles were prepared according to literature procedures, as indicated. All X-ray measurements were made using a Rigaku RAXIS RAPID imaging plate area detector with graphite monochromated Mo-Kα radiation. CCDC reference numbers for compounds used as literature comparisons are as follows: **L1** 667280; **2g** 201149; **L2** 1267621; **L3** 263350.

Experimental procedures

General procedure for pyrrolic thionoesters (GP1)

A suspension of 2-pyrrole carboxylate (0.5 mmol) and Lawesson's reagent (0.3 mmol, 1.2 equiv.) in anhydrous *p*-xylene or anhydrous toluene (0.7 mL, 0.75 M), in a sealed flask under nitrogen, was placed in a sand bath preheated to 140 °C, and then heated with stirring for 1 hour. After this time, the reaction mixture was allowed to cool to room temperature before dilution with ethyl acetate (1 mL). The mixture was then poured into 20% ethyl acetate/hexanes (20 mL), rinsing the flask with ethyl acetate (2 × 1 mL). The combined solution was filtered through a short pad of silica, washing with 20% ethyl acetate/hexanes, and the filtrate concentrated to give the crude product, which was purified using column chromatography over silica, eluting with 5–10% ethyl acetate/hexanes, unless otherwise stated.

O-Ethyl-3,4,5-trimethyl-1H-pyrrole-2-carbothioate 2a

O-Ethyl-3,4,5-trimethyl-1*H*-pyrrole-2-carbothioate **2a** was synthesised from **1a**[35] using GP1 to give the title compound as a yellow solid (78 mg, 72% yield). Alternatively, a suspension of pyrrolic ester (0.5 mmol) and Lawesson's reagent (0.3 mmol, 1.2 equiv.) in anhydrous toluene (0.7 mL, 0.75 M), in a sealed microwave vial under nitrogen, was placed under microwave heating at 160 °C for 20 min. After this time, the reaction mixture was allowed to cool to room temperature before dilution with ethyl acetate (1 mL). The mixture was then poured into 20% ethyl acetate/hexanes (20 mL), rinsing the flask with ethyl acetate (2 × 1 mL). The combined solution was filtered through a short pad of silica, washing with 20% ethyl acetate/hexanes, and the filtrate concentrated to give the crude product, which was purified using column chromatography over silica, eluting with 5% ethyl acetate/hexanes, to give the title compound as a yellow solid (64 mg, 59% yield). Mp 83–85 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) 9.06 (br s, 1H, NH), 4.66 (q, 2H, J = 7.2 Hz, CH_2CH_3), 2.25 (s, 3H, CH_3), 2.19 (s, 3H, CH_3), 1.91 (s, 3H, CH_3), 1.46 (t, 3H, J = 7.2 Hz, CH_2CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz, UDEFT) 199.5, 134.5, 128.6, 126.1, 119.2, 66.5, 14.3, 12.2, 12.0, 8.8; LRMS: 220.1 $(M + Na)^+$; HRMS: 220.0775 found, 220.0767 calculated for $C_{10}H_{15}NSONa$.

1-(4-Methoxyphenyl)-4,5,6-trimethylpyrrolo[1,2-c][1,3,2] thiazaphosphole-3(1H)-thione-1-sulfide 3

A suspension of thionoester **2a** (50 mg, 0.25 mmol) and Lawesson's reagent (77 mg, 0.19 mmol, 1.5 equiv.) in anhydrous *p*-xylene (0.5 mL), in a sealed flask under nitrogen, was placed in a sand bath preheated to 140 °C and the mixture then heated with stirring for 1.5 hours. After this time, the reaction mixture was allowed to cool to room temperature then poured into 30% ethyl acetate/hexanes (20 mL), rinsing the flask with ethyl acetate. The solution was filtered, washing with 30% ethyl acetate/hexanes, and the filtrate concentrated to give the crude product. The product was purified quickly (to avoid decomposition) using column chromatography over silica eluting with 15% ethyl acetate/hexanes, then again eluting with 45% dichloromethane/hexanes to give the title compound as an orange solid (30 mg, 33% yield). Mp 125–127 °C; λ_{max} CH_2Cl_2 404 (ε 29 000), 279 (ε 20 000); ^{1}H NMR ($CDCl_3$, 500 MHz) 7.82 (dd, 2H, J = 15.2, 9.0 Hz, ArH), 6.99 (dd, 2H, J = 9.0, 3.5 Hz, ArH), 3.88 (s, 3H, OCH_3), 2.43 (s, 3H, CH_3), 2.13 (s, 3H, CH_3), 1.94 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) 194.0, 164.0, 139.5, 138.2 (d), 134.0 (d), 130.2 (d), 124.8, 124.0, 114.7 (d), 55.8, 12.0, 11.3, 9.4; ^{31}P NMR ($CDCl_3$, 202 MHz) 63.4 (t, J = 15.2 Hz); LRMS: 376.0 $(M + Na)^+$; HRMS: 376.0014 found, 376.0024 calculated for $C_{15}H_{16}NPS_3O$.

4,4-Difluoro-1,2,3,5,6,7-hexamethyl-8-H-4-bora-3a,4a-diaza-s-indacene 4a

A mixture of **1a** (100 mg, 0.55 mmol) and Lawesson's reagent (223 mg, 0.55 mmol) was prepared in a 0.5–2.0 mL capacity microwave vial under nitrogen. A suspension was formed upon addition of toluene (1 mL) with vigorous stirring. $BF_3 \cdot Et_2O$ (0.27 mL, 2.2 mmol, 4 equiv.) was then added drop-wise, *via* the septum, and the vial was heated in a microwave reactor at 160 °C for 20 minutes before being allowed to cool to room temperature. The mixture was diluted with ethyl acetate (2 mL) and poured into 20% ethyl acetate/hexanes (30 mL). The solution was filtered through a short pad of silica, washing with 30% ethyl acetate/hexanes, and then concentrated to give the crude product. This was purified over neutral alumina (Brockmann type III), eluting slowly with 5–20% dichloromethane/hexanes to give the title compound as a deep red crystalline solid (8 mg, 11% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) 6.94 (s, 1H, *meso*-H), 2.48 (s, 6H, 2 × CH_3), 2.15 (s, 6H, 2 × CH_3), 1.93 (s, 6H, 2 × CH_3); ^{11}B NMR ($CDCl_3$, 160 MHz) 0.87 (t, J = 33 Hz); ^{19}F NMR ($CDCl_3$, 470 MHz): −146.4 (q, J = 34 Hz); this data matches literature values.[28]

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