Formation of *N*-heterocycles by the reaction of thiols with glyoxamides: exploring a connective Pummerer-type cyclisation†

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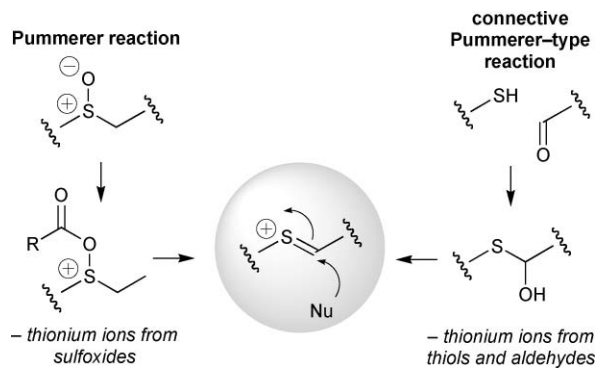
The reaction of thiols with glyoxamides provides a convenient method for the generation of thionium ions and the initiation of Pummerer-type reactions. When the glyoxamides contain tethered aromatic nucleophiles, *N*-heterocycles are formed by a thionium ion cyclisation. The scope and mechanism of the connective Pummerer-type process has been investigated using a range of thiols, Lewis acids and both mono- and bis-glyoxamides. The utility of the process has been illustrated in a synthesis of the indoloquinoline natural product, neocryptolepine.

Introduction

Pummerer reactions,[1] involving nucleophilic additions to thionium ions, are a useful tool for the synthesis of heterocyclic compounds.[2] We have recently developed a fluorous approach to *N*-heterocycles that utilises a Pummerer-type process to introduce the fluorous tag and construct the heterocyclic scaffold in a single step,[3] thus a higher synthetic return is gained from the introduction of a phase tag. The *cyclative–capture* step involves the reaction of a fluorous thiol with glyoxamide substrates in a 'connective' Pummerer-type reaction.[3] The classical Pummerer reaction of sulfoxides and the connective Pummerer reaction are compared in Scheme 1.



Scheme 1 Comparison of the Pummerer reaction of sulfoxides and a connective Pummerer-type reaction.

In the classical Pummerer reaction, sulfoxides are activated by acylation of the sulfoxide oxygen. Elimination then generates a thionium ion that is trapped by an external or internal nucleophile. In the connective variant, thiol addition to an aldehyde generates a hemithioacetal that upon activation, for example, by acylation, generates a thionium ion. The connective route to thionium ions has several advantages over its traditional counterpart: the process utilises widely available thiol and aldehyde starting materials, negating the need to prepare sulfoxide or sulfide starting materials (sulfides are essentially prepared *in situ*). In addition, the properties or structural features of the thiol and aldehyde substituents are united in a single synthetic operation, with concomitant addition of a nucleophile. Reactive aldehydes such as glyoxylates[4] and glyoxamides[3] are ideal substrates and the use of an internal nucleophile allows heterocycles to be constructed.[3] Attractively, the residual organosulfanyl group can impart specific properties to the Pummerer adducts or can be used as a synthetic handle for further manipulation.

Here we report in full[5] our studies on the potential of this new Pummerer-type process for the synthesis of heterocycles. Our studies have concentrated on the mechanism of the cyclisation, the role of the thiol component, the Lewis acid, and the feasibility of two–directional Pummerer cyclisations to form extended heterocyclic systems. The products of the Pummerer-type cyclisations possess heterocyclic motifs that are widespread amongst natural products and compounds of pharmaceutical significance. A concise synthesis of the indoloquinoline natural product neocryptolepine has been carried out to illustrate the utility of the connective Pummerer-type cyclisation.

Results and discussion

Generality and mechanism of the connective Pummerer-type cyclisation

We began by examining the reaction of functionalised alkyl and aryl thiols with glyoxamides **9–12** derived from secondary anilines containing neutral, electron-withdrawing and electron-releasing substituents. The glyoxamides were prepared from secondary anilines **1–4** using the approach of Bartlett *et al.*:[6] coupling with acetoxyacetic acid gave amides **5–8** that were deprotected and oxidised under Swern conditions (Scheme 2).[7] The purification of intermediates by column chromatography was typically not required. Glyoxamides **9–12** were isolated as a mixture of aldehyde

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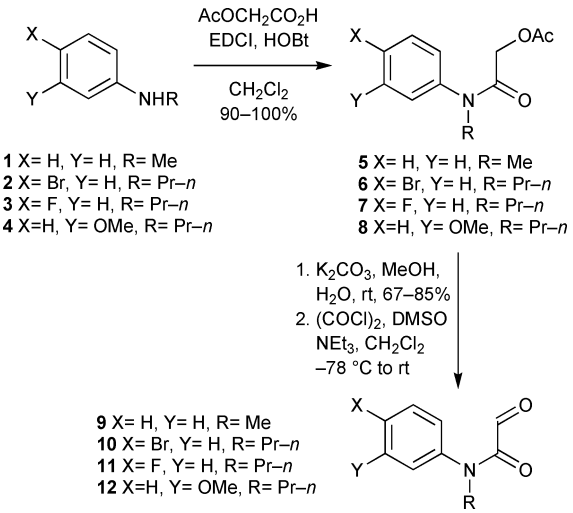


Scheme 2 Synthesis of glyoxamides from anilines.

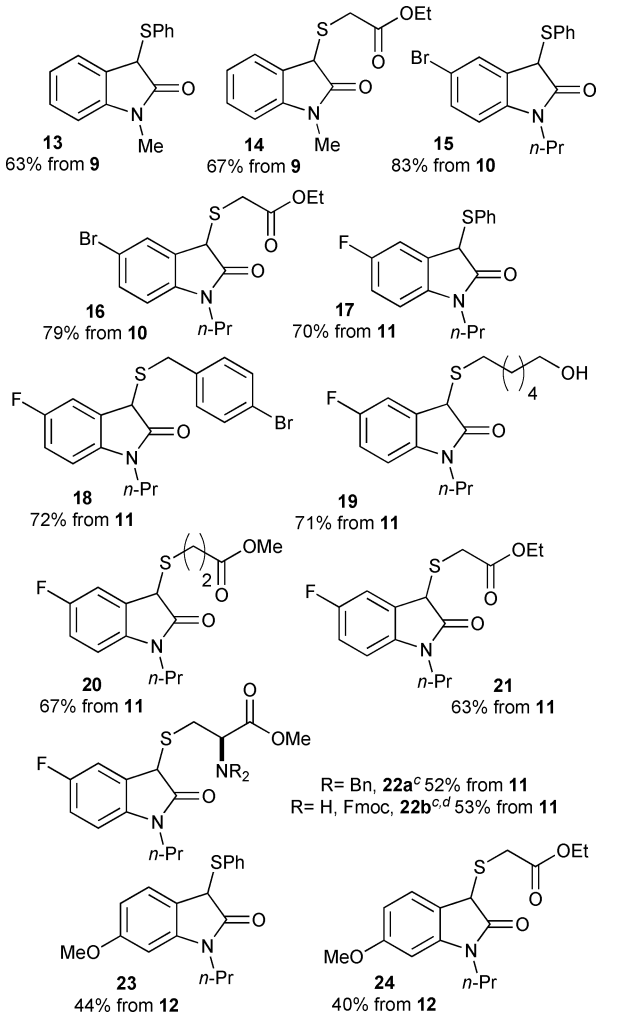
and the corresponding hydrate[8] and were used without further purification (*vide infra*).

Pummerer-type cyclisations were carried out by stirring thiol with glyoxamide, followed by addition of trifluoroacetic anhydride (TFAA), then $BF_3{\cdot}OEt_2$. Omitting either TFAA or the Lewis acid led to the observation of hemithioacetal or trifluoroacetylated hemithioacetal intermediates (*vide infra*). We have found that at least two equivalents of $BF_3{\cdot}OEt_2$ and four equivalents of TFAA are required before a significant degree of cyclisation is seen (Table 1).

A preliminary survey of other Lewis acids showed that $Sc(OTf)_3$ gave comparable results to $BF_3{\cdot}OEt_2$ when used in the cyclisation, while $Yb(OTf)_3$ also promoted the Pummerer-type reaction but gave lower yields. Reaction conditions involving the use of $Sc(OTf)_3$ provide a useful, milder alternative to the use of $BF_3{\cdot}OEt_2$. In all cases, the connective Pummerer-type cyclisation occurred to give the corresponding oxindole products in moderate to good isolated yields (over two steps) indicating that the process is compatible with thiols bearing a range of functional groups (aryl rings, ester, bromide, amino and hydroxyl groups). The reaction of **11** with thiols derived from cysteine proceeded to give the expected products **22a** and **22b** (Table 1). Milder conditions using $Sc(OTf)_3$ were required for the cyclisation of Fmoc-protected cysteine methyl ester. The use of cysteine derivatives in connective Pummerer reactions suggest that the process could form the basis of a method for chemical ligation:[9] hemithioacetal formation through the reaction of a carbonyl compound, or a masked derivative, with a cysteine residue could be followed by cyclisation to make the attachment permanent.

A complementary approach to glyoxamide substrates involves the *N*-arylation of amines. For example, *N*-arylation of (*S*)-α-methylbenzylamine **25**[10] and coupling with acetoxyacetic acid gave amide **26** that upon deprotection and Swern oxidation[7] gave **27**. Consistent with our previous observations, glyoxamide **27** was obtained as a mixture of hydrate and aldehyde, as evident from the complex ^{1}H NMR of crude **27**. After moderate heating under vacuum, the ^{1}H NMR of glyoxamide **27** simplified and could be assigned. Pummerer-type cyclisation of **27** with ethylthioglycolate, TFAA and $Sc(OTf)_3$ gave oxindole **28** in 64% yield (over 2 steps)

Table 1 Reaction of thiols with glyoxamides derived from secondary anilines[a]

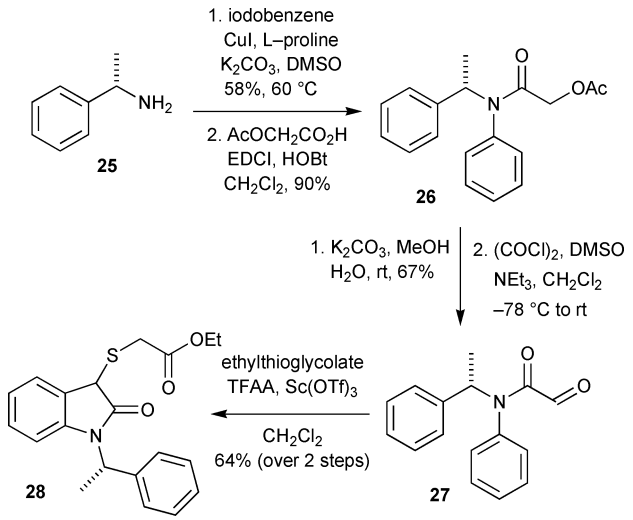


[a] RSH (1 eq), TFAA (9 eq), $BF_3{\cdot}OEt_2$ (4 eq), CH_2Cl_2. [b] Yields are for 2 steps as glyoxamides are not purified. [c] 1 : 1 mixture of diastereoisomers. [d] RSH (1 eq), TFAA (6 eq), $Sc(OTf)_3$ (2 eq), CH_2Cl_2.

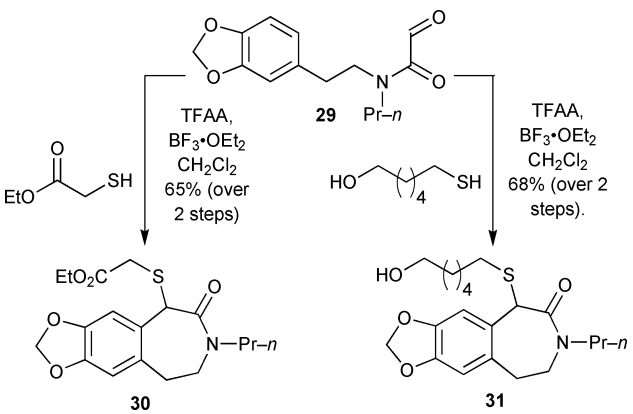
as a 1 : 1 mixture of diastereoisomers (Scheme 3). In this case, higher yields were obtained when the crude glyoxamide was *dried* in the manner described above.

Functionalised thiols can also be used in connective Pummerer-type cyclisations with glyoxamide substrates derived from phenethylamines. For example, glyoxamide **29** underwent cyclisation upon treatment with ethylthioglycolate or 6-hydroxyhexanethiol to give **30** and **31**, respectively, in good overall yield (Scheme 4).

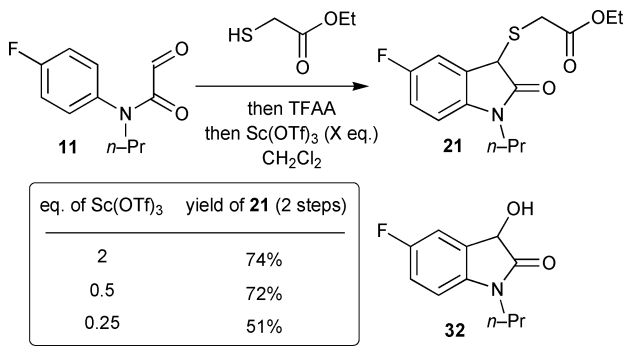
We have also examined the feasibility of a connective, Pummerer process that is catalytic in Lewis acid. Varying the amount of $Sc(OTf)_3$ used in the reaction between glyoxamide **11** and ethylthioglycolate showed that the yield of **21** decreases as the loading of Lewis acid is reduced, although significant conversion is still seen when sub-stoichiometric amounts of Lewis acid are used. *'Drying'* of the glyoxamide (*vide supra*) proved necessary when using lower quantities of Lewis acid to prevent the formation of the hydroxyoxindole by-product **32** (Scheme 5).



Scheme 3 *N*-Arylation in an approach to glyoxamide substrates.



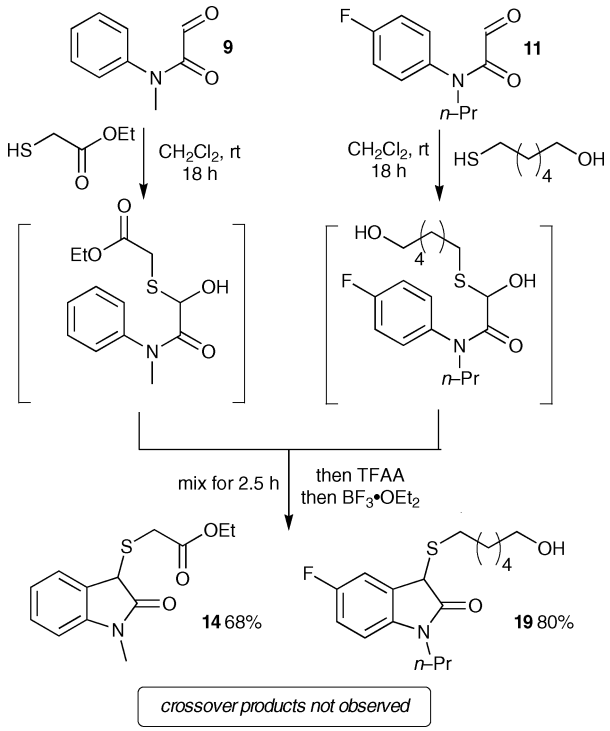
Scheme 4 Functionalised thiols in the synthesis of benzazepinones.



eq. of $Sc(OTf)_3$	yield of **21** (2 steps)
2	74%
0.5	72%
0.25	51%

Scheme 5 The use of sub-stoichiometric amounts of Lewis acid in the connective Pummerer-type cyclisation.

We have carried out preliminary studies to probe the mechanism of the Pummerer-type cyclisations. As previously stated, omitting either TFAA or the Lewis acid led to the observation of hemithioacetal or trifluoroacetylated hemithioacetal intermediates. Only electron-rich glyoxamide **12** underwent cyclisation to give a hydroxyoxindole on treatment with $BF_3{\cdot}OEt_2$. To investigate the importance of hemithioacetal formation in the cyclisations, a cross-over experiment was conducted: glyoxamides **9** and **11** were stirred with ethylthioglycolate and 6-hydroxyhexanethiol, respectively, in separate reaction flasks. After 18 h, hemithioacetal formation was complete by TLC and the two solutions were mixed. After 2 h, TFAA and then $BF_3{\cdot}OEt_2$ were added to complete the cyclisation process. Oxindoles **14** (68%) and **19** (80%) were isolated with no cross-over products observed in the crude ^{1}H NMR (Scheme 6).



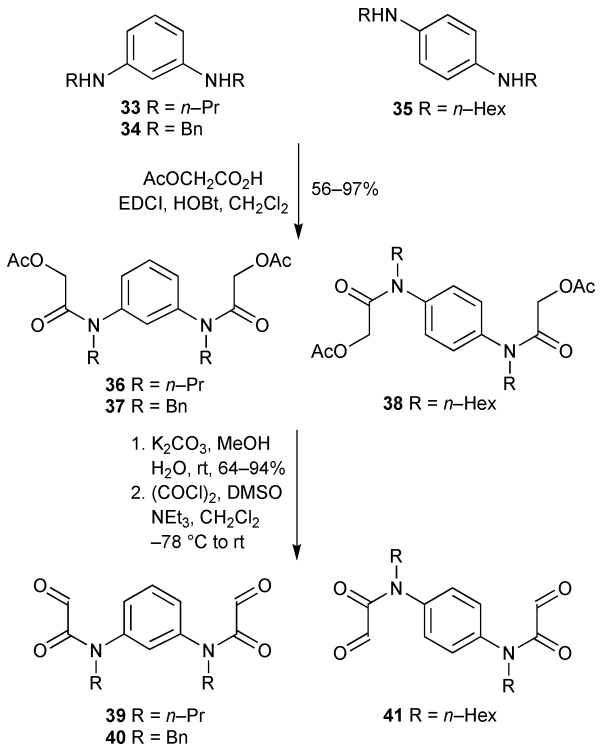
Scheme 6 Investigating the mechanism of the Pummerer-type cyclisations.

This experiment confirms that equilibria between thiols and glyoxamides lie well over to the side of the hemithioacetal as no thiol-exchange is observed upon mixing. In addition, the lack of cross-over products would appear to rule out alternative mechanisms involving breakdown of hemithioacetals and addition of thiols to the 3-position of oxindoles formed by cyclisations of 'free' glyoxamides. Our current understanding of the reaction mechanism therefore remains consistent with that proposed in Scheme 1: hemithioacetal formation, activation of the hemithioacetal intermediate by trifluoroacetylation, elimination to give a thionium ion, and intramolecular addition of a nucleophile.

The connective Pummerer-type cyclisations of bis-glyoxamides

We have also examined the reaction of bis-1,3-glyoxamides and bis-1,4-glyoxamides with thiols. Bis-1,3-glyoxamides **39–41** were conveniently prepared, in two-directional fashion, from diaminobenzenes **33–35** (Scheme 7).

Although the overall yields for the two-directional Pummerer-type cyclisations of bis-glyoxamides are somewhat lower than

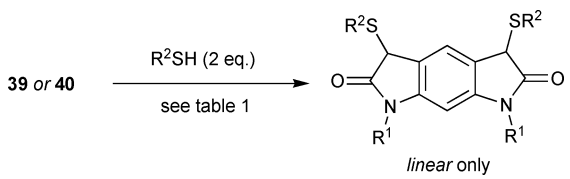


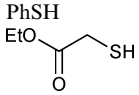
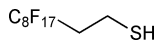
Scheme 7 Two-directional synthesis of bis-glyoxamide substrates.

those obtained with simple glyoxamides, the expected products are obtained in acceptable yields and good purity. To the best of our knowledge these represent the first examples of two–directional thionium ion cyclisations (Table 2 and Table 3). In the case of bis-1,3-glyoxamides, the oxindole products were obtained as single, *linear* regioisomers and inseparable ~1 : 1 mixtures of *cis* and *trans* diastereoisomers.

The analogous reactions of a 1,4-bis-glyoxamide proceeded to give oxindoles with the *linear* regioisomers predominating

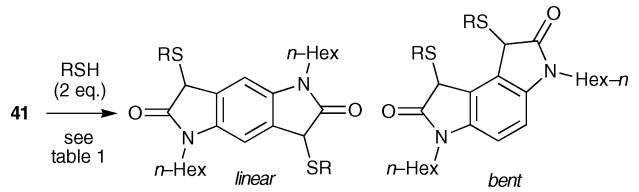
Table 2 Connective Pummerer cyclisations of bis-1,3-glyoxamides[a,b]

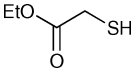
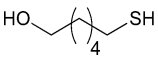
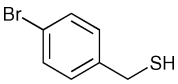
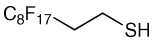


R^2SH	R^1	Isolated yield[b]	Product
BnSH	*n*-Pr	51%	**42**[c]
PhSH	*n*-Pr	47%	**43**[c]
	*n*-Pr	45%	**44**[c]
	*n*-Pr	56%	**45**[c]
BnSH	Bn	62%	**46**[c]
PhSH	Bn	45%	**47**[c]

[a] See Table 1 for reagents and conditions. [b] Yields are for 2 steps as glyoxamides are not purified. [c] 1 : 1 to 1 : 1.5 mixture of diastereoisomers.

Table 3 Connective Pummerer cyclisations of a 1,4 bis-glyoxamide[a,b]



RSH	Isolated yield[b]	Product	*linear* : *bent*[c,d]
PhSH	55%	**48**	>5 : 1
	54%	**49**	5 : 1
	61%	**50**	~3 : 1
	55%	**51**	>5 : 1
	57%	**52**	2 : 1

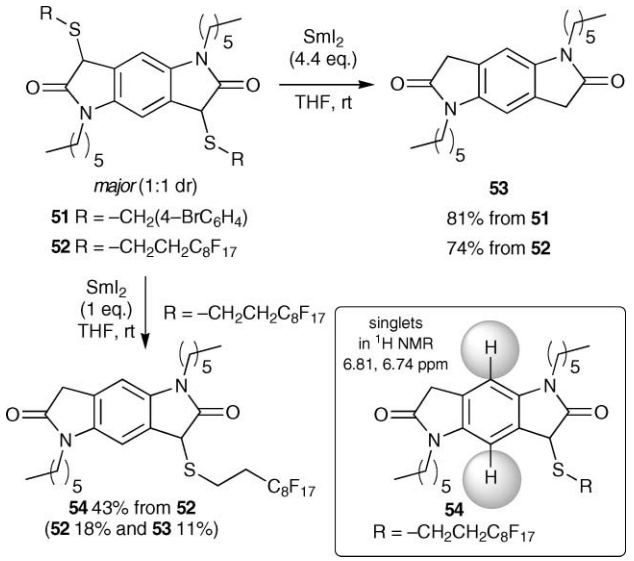
[a] See Table 1 for reagents and conditions. [b] Yields are for 2 steps as glyoxamides are not purified. [c] Regioisomeric ratios are obtained from ^{1}H NMR. [d] Each regioisomer is a 1 : 1 mixture of diastereoisomers.

(approximately 2 : 1 to >5 : 1). The use of bulkier thiols such as thiophenol and *p*-bromobenzylthiol gave more *linear* isomer presumably due to unfavourable steric interactions involved in the formation of the *bent* isomers. Both the *linear* and *bent* regioisomers were obtained as ~1 : 1 mixtures of *cis* and *trans* diastereoisomers. In most cases regioisomeric bis-oxindole products could be separated by chromatography (*e.g.* **52**) or recrystallisation (*e.g.* **49**) (Table 3).

The symmetry present in the *linear* and *bent* isomers of **48**–**52** does not allow the isomers to be distinguished by NMR. The nature of the isomers obtained from the cyclisation of bis-1,4-glyoxamides was determined by the following experiments: after the isolation of the major pair of isomers from the reactions to form **51** and **52**, independent treatment of each mixture with SmI_2[11] gave a single product **53** in good yield after reductive removal of the sulfanyl groups[12] (Scheme 8). Thus, the major isomer pairings from each reaction are diastereoisomers and the major isomer pairs for **51** and **52** belong to the same regioisomeric family. The identity of the major regioisomers was confirmed by partial SmI_2 reduction of **52** to break the symmetry and provide **54**. The presence of two singlets in the ^{1}H NMR spectrum for the aromatic protons in **54** confirmed the major products of cyclisation to be *linear* isomers (Scheme 8).

Application in a synthesis of neocryptolepine

We have utilised the connective Pummerer-type cyclisation in a synthesis of the indoloquinoline natural product neocryptolepine **65**. Neocryptolepine was isolated from *Cryptolepis sanguinolenta*[13] and has been shown to display cytotoxicity through the inhibition of DNA topoisomerase II activity.[14] Neocryptolepine and its analogues have also been shown to be sequence-selective



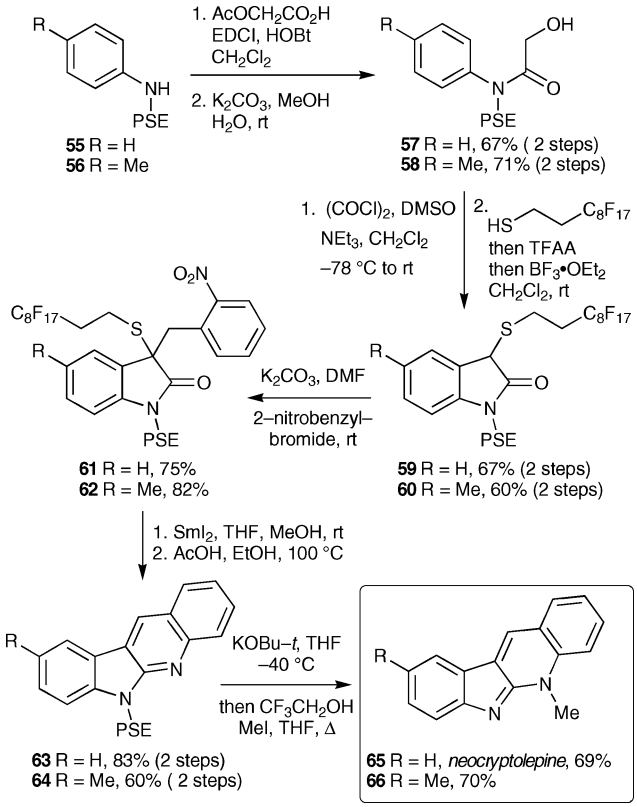
Scheme 8 Determining the regioselectivity of the cyclisation of 1,4-bis-glyoxamides.

DNA intercalators.[15] Our synthesis began with the protection of phenylamine with the 2-phenylsulfonylethyl (PSE) group[16] (phenylvinylsulfone, MeOH, MW 20 min, 76%) and straightforward conversion of **55** to the corresponding hydroxyamide **57**. After oxidation to the glyoxamide, the connective Pummerer-type cyclisation was carried out by treatment with the fluorous thiol $C_8F_{17}CH_2CH_2SH$, under our standard conditions, to give **59** in 67% after two steps. As the resultant oxindole contains a fluorous tag, conventional chromatography can be avoided and fluorous solid-phase extraction (FSPE)[17] can be used for rapid purification, as we have previously shown.[3] Alkylation of the oxindole skeleton with 2-nitrobenzylbromide is facilitated by the alkylsulfanyl group introduced in the Pummerer-type cyclisation and gave **61** in 75% after FSPE. Sequential reductive removal of the fluorous tag[18] and nitro group reduction, using SmI_2, according to our recently reported procedure,[3d] and cyclisation with acid, gave **63** in 83% yield. Finally, one-pot removal of the PSE group and *N*-methylation gave neocryptolepine **65** in 69% yield (Scheme 9).

Our route to neocryptolepine illustrates the utility of the connective Pummerer-type cyclisation of substrates having a protecting group on nitrogen. The route to the indoloquinoline ring system can easily be modified to allow analogues of the natural product to be prepared for biological evaluation, for example, the approach has been used to convert protected 4-methylphenylamine **56** to neocryptolepine analogue **66**.

Conclusions

We have begun to assess the scope of a connective Pummerer-type process in which thionium ions are generated by the coupling of thiols with reactive aldehydes. The use of glyoxamides bearing an aromatic nucleophile as the reactive aldehyde component, allows *N*-heterocycles to be prepared by intramolecular additions to the thionium ion. Extension of this method has allowed us to carry out the first, two-directional Pummerer cyclisations. During our



Scheme 9 Synthesis of neocryptolepine and an analogue (PSE = $CH_2CH_2SO_2Ph$).

studies, we have varied the thiol and glyoxamide components and also the choice of Lewis acid, and have made observations regarding the mechanism of the process. We have utilised the connective Pummerer-type cyclisation in a synthesis of the indolquinoline ring system and the natural product neocryptolepine. We continue to explore the utility of the connective Pummerer process.

Experimental

General Procedure A for the connective Pummerer cyclisation reactions

1-Methyl-3-phenylsulfanyl-1,3-dihydroindol-2-one 13[19]

To a solution of **9** (105 mg, 0.64 mmol, 1 eq) in CH_2Cl_2 (10 ml) was added thiophenol (66 µl, 0.64 mmol, 1 eq) at room temperature. After 18 h, TFAA (823 µl, 5.82 mmol, 9 eq) was added. After a further 1 h, $BF_3{\cdot}OEt_2$ (398 µl, 3.20 mmol, 5 eq) was added. After 1 h, the reaction was quenched with aqueous $NaHCO_3$ (25 ml), the organic layer was washed with aqueous $NaHCO_3$ (2 × 20 ml), dried ($MgSO_4$), filtered and concentrated *in vacuo* to give an orange oil. Purification by column chromatography using 30% EtOAc in petroleum ether as eluant, gave **13** (103 mg, 0.40 mmol, 63% from hydroxyamide, 2 steps) as an oil. δ_H (500 MHz, $CDCl_3$) 2.85 (3H, s, NCH_3), 4.39 (1H, s, C*H*S), 6.47 (1H, d, J = 7.8 Hz, Ar*H*), 6.90 (1H, t, J = 7.8 Hz, Ar*H*), 7.00 (2H, t, J = 7.8 Hz, 2 × Ar*H*), 7.05–7.10 (3H, m, 3 × Ar*H*) and 7.19–7.22 (2H, m, 2 × Ar*H*). δ_C (75 MHz, $CDCl_3$) 26.5 (CH_3), 49.4 (*C*HS), 108.3 (Ar*C*H), 123.0 (Ar*C*H), 125.5 (Ar*C*H), 126.5 (Ar*C*H), 128.8 (Ar*C*H), 128.9

(ArCH), 129.3 (ArCH), 131.2 (ArC), 129.9 (ArC), 133.9 (ArCH), 134.4 (ArCH), 144.2 (ArC) and 174.6 (C=O). ν_{max}/(cm^{-1}) 3054, 2916, 1697 (C=O), 1465, 1350, 1085 and 725. *m/z* (EI$^+$ mode) 255 (M$^+$, 24%), 218 (14%), 146 (100%), 118 (10%) and 91 (6%). *m/z* (M + H) 256.0783, $C_{15}H_{14}NOS$ requires 256.0791.

Pummerer-type cyclisation with Fmoc-protected cysteine derivative using Sc(OTf)$_3$-2-(9*H*-fluoren-9-ylmethoxycarbonylamino)-3-(5-fluoro-2-oxo-1-propyl-2,3-dihydro-1*H*-indol-3-ylsulfanyl)-propionic acid methyl ester 22b

To a solution of glyoxamide **11** (70 mg, 0.33 mmol, 1 eq) in CH_2Cl_2 (3 ml) was added 2-(9*H*-fluoren-9-ylmethoxycarbonylamino)-3-mercaptopropionic acid methyl ester (116 mg, 0.33 mmol, 1 eq) at room temperature. After 18 h, TFAA (284 µl, 2.00 mmol, 6 eq) was added and, after a further 1 h, Sc(OTf)$_3$ (329 mg, 0.67 mmol, 2 eq) was added. After 1 h, the reaction was quenched with $NaHCO_3$ (15 ml) and CH_2Cl_2 (15 ml) added, the organic layer was washed with $NaHCO_3$(aq) (2 × 15 ml), dried (Na_2SO_4), filtered and concentrated *in vacuo* to give a clear oil. Purification by column chromatography using 30% EtOAc in petroleum ether as eluant to give **22b** (93 mg, 0.17 mmol, 53% from hydroxyamide, 2 steps) as a clear oil (1 : 1 mixture of diastereoisomers). $[\alpha]_D$ = 8.0 (*c* = 1.75, CH_2Cl_2). δ_H (500 MHz, $CDCl_3$) 0.84 (3H, t, *J* = 7.3 Hz, C*H*$_3$), 0.88 (3H, t, *J* = 7.3 Hz, C*H*$_3$), 1.56–1.63 (4H, m, 2 × C*H*$_2$), 2.89 (1H, d, *J* = 7.3 and 13.9 Hz, 1H of C*H*$_2$CHS one isomer), 2.97 (1H, d, *J* = 4.1 and 14.2 Hz, 1H of C*H*$_2$CHS one isomer), 3.34 (1H, d, *J* = 4.1 and 14.2 Hz, 1H of C*H*$_2$CHS one isomer), 3.39 (1H, d, *J* = 6 and 14.2 Hz, 1H of C*H*$_2$CHS one isomer), 3.54–3.60 (4H, m, 2 × C*H*$_2$N), 3.69 (3H, s, C*H*$_3$OC=O one isomer), 3.69 (3H, s, C*H*$_3$OC=O one isomer), 4.12–4.19 (2H, m, 2 × C*H*CH$_2$OC=O), 4.22 (1H, s, C*H*S one isomer), 4.25–4.35 (5H, m, 2 × C=OOC*H*$_2$CH and C*H*S one isomer), 4.57–4.64 (2H, m, 2 × C*H*CH$_2$S), 6.00 (1H, d, *J* = 7.9 Hz, 1 × N*H* one isomer), 6.64–6.68, (2H, m, 2 × Ar*H* both isomers), 6.72 (1H, d, *J* = 8.5 Hz, 1 × N*H* one isomer), 6.89–6.93 (2H, m, 2 × Ar*H* both isomers), 6.98–7.06 (2H, m, 2 × Ar*H* both isomers), 7.16–7.23 (4H, m, 4 × Ar*H* both isomers), 7.27–7.32 (4H, m, 4 × Ar*H* both isomers), 7.54–7.58 (4H, m, 4 × Ar*H* both isomers) and 7.63–7.67 (4H, m, 4 × Ar*H* both isomers). δ_C (125 MHz, $CDCl_3$) 11.3 (*C*H$_3$), 11.4 (*C*H$_3$), 20.7 (*C*H$_2$ one isomer), 20.7 (*C*H$_2$), 32.5 (*C*H$_2$S), 32.9 (*C*H$_2$S), 42.0 (*C*H$_2$N), 42.1 (*C*H$_2$N), 44.1 (*C*HS), 45.4 (*C*HS), 47.1 (*C*HCH$_2$OC=O), 47.2 (*C*HCH$_2$OC=O), 52.8 (*C*H$_3$O), 52.9 (*C*H$_3$O), 53.4 (*C*HCH$_2$S), 54.5 (*C*HCH$_2$S), 67.1 (C=OO*C*H$_2$CH), 67.3 (C=OO*C*H$_2$CH), 109.2 (Ar*C*H, d, *J* = 8.8 Hz), 109.3 (Ar*C*H, d, *J* = 8.8 Hz), 113.4 (Ar*C*H, d, *J* = 25 Hz), 113.6 (Ar*C*H, d, *J* = 25 Hz), 115.7 (Ar*C*H, d, *J* = 23.75 Hz), 115.8 (Ar*C*H, d, *J* = 23.75 Hz), 119.9 (2 × Ar*C*H), 120.0 (2 × Ar*C*H), 125.2 (2 × Ar*C*H), 125.3 (2 × Ar*C*H), 127.0 (Ar*C*H), 127.1 (Ar*C*H), 127.1 (Ar*C*H), 127.2 (Ar*C*H), 127.3 (Ar*C*H), 127.4 (Ar*C*H), 127.7 (Ar*C*H), 127.7 (Ar*C*H), 139.0 (Ar*C*), 139.5 (Ar*C*), 141.3 (Ar*C*), 141.3 (Ar*C*), 143.7 (Ar*C*), 143.9 (Ar*C*), 144.0 (2 × Ar*C*), 156.1 (2 × Ar*C*), 159.2 (Ar*C*F, d, *J* = 240 Hz), 159.2 (Ar*C*F, d, *J* = 240 Hz), 170.9 (*C*=O amide), 171.0 (*C*=O amide), 175.4 (*C*=O ester) and 175.4 (*C*=O ester). ν_{max}/(cm^{-1}) 3337, 3064, 2962, 1717 (C=O), 1612, 1489, 1452, 1342, 1266, 1135, 1051 and 815. *m/z* (ES+ mode) 607 (22%), 571 ((M + Na)$^+$ 100%), 566 (40%) and 549 (14%). *m/z* (M + NH$_4^+$) 566.2121, $C_{30}H_{33}FN_3O_5S$ requires 566.2119.

General procedure B for the Pummerer-type cyclisation to give benzazepinones

1-(Ethoxycarbonylmethoxysulfanyl)-3,4-methylenedioxy-3-propyl-1,3,4,5-tetrahydro-benzo[*d*]azepin-2-one 30

To a stirred solution of glyoxamide **29** (69 mg, 0.26 mmol, 1 eq) in CH_2Cl_2 (3 ml) was added ethylthioglycolate (29 µl, 0.26 mmol, 1 eq) and the reaction mixture stirred at room temperature for 18 h. TFAA (335 µl, 2.37 mmol, 9 eq) was added followed by $BF_3{\cdot}OEt_2$ (162 µl, 1.32 mmol, 5 eq) after a further 1 h. After 1 h, the reaction was quenched with aqueous saturated $NaHCO_3$ (5 ml), and the organic layer washed with aqueous saturated $NaHCO_3$ (2 × 5 ml). The organic layer was dried (Na_2SO_4), filtered and concentrated *in vacuo.* Purification by column chromatography using 15% EtOAc in petroleum ether as eluant gave **30** (61 mg, 0.17 mmol, 65% from hydroxyamide, 2 steps) as a yellow oil. δ_H (500 MHz, $CDCl_3$) 0.84 (3H, t, *J* = 7.6 Hz, C*H*$_3$), 1.24 (3H, t, *J* = 7.1 Hz, C*H*$_3$), 1.50–1.57 (2H, m, C*H*$_2$CH$_2$N), 2.90–2.99 (2H, m, C*H*$_2$), 3.19–3.27 (2H, m, 1H of CH$_3$CH$_2$C*H*$_2$N and 1H of NC*H*$_2$CH$_2$ArC), 3.27 (1H, d, *J* = 16.0 Hz, 1H of C*H*$_2$S), 3.41–3.47 (1H, m, 1H of CH$_3$CH$_2$C*H*$_2$N), 3.55 (1H, d, *J* = 16.0 Hz, 1H of C*H*$_2$S), 4.16 (2H, q, *J* = 7.1 Hz, C*H*$_2$CH$_3$), 4.45–4.51 (1H, m, 1H of NC*H*$_2$CH$_2$ArC), 4.86 (1H, s, C*H*S), 5.84 (1H, d, *J* = 1.25 Hz, 1H of OC*H*$_2$O), 5.86 (1H, d, *J* = 1.25 Hz, 1H of OC*H*$_2$O), 6.44 (1H, s, ArC*H*) and 6.73 (1H, s, ArC*H*). δ_C (125 MHz, $CDCl_3$) 11.3 (*C*H$_3$), 14.2 (*C*H$_3$), 21.2 (*C*H$_2$), 33.8 (*C*H$_2$), 34.5 (*C*H$_2$S), 45.7 (*C*H$_2$N), 50.3 (*C*H$_2$N), 55.5 (*C*HS), 61.6 (*C*H$_2$CH$_3$), 101.3 (*C*H$_2$), 109.7 (Ar*C*H), 111.6 (Ar*C*H), 124.7 (Ar*C*), 131.2 (Ar*C*), 146.6 (Ar*C*), 147.7 (Ar*C*), 169.1 (*C*=O amide) and 169.8 (*C*=O ester). ν_{max}/(cm^{-1}) 2864, 2920, 1733, 1643, 1504, 1486, 1386, 1268, 1226, 1153, 1036 and 867. *m/z* (ES+ mode) 388 ((M + Na)$^+$ 100%) and 366 ((M + H)$^+$ 23%). *m/z* (M + Na) 388.1184, $C_{18}H_{23}NNaO_5S$ requires 388.1189.

General procedure C for the two-directional Pummerer-type cyclisations of bis-glyoxamides

3,5-Bis-benzylsulfanyl-1,7-dipropyl-5,7-dihydro-1*H*, 3*H*-pyrrolo[3,2-*f*] indole-2,6-dione 42

To a stirred solution of bis-glyoxamide **39** (90 mg, 0.30 mmol, 1 eq) in CH_2Cl_2 (4 ml) was added benzyl thiol (70 µl, 0.60 mmol, 2.0 eq) and the reaction stirred at room temperature for 18 h. TFAA (761 µl, 5.27 mmol, 18 eq) was added and after a further 1 h, $BF_3{\cdot}Et_2O$ (410 µl, 2.93 mmol, 10 eq) was also added. After stirring for 1 h, the reaction was quenched with $NaHCO_3$ (20 ml), the organic layer was washed with $NaHCO_3$ (2 × 30 ml), dried ($MgSO_4$), filtered and concentrated *in vacuo.* Purification by column chromatography using 30% EtOAc in petroleum ether as eluant gave **42** (769 mg, 0.15 mmol, 51% from bis-hydroxyamide, 2 steps) as a dark oil (1 : 1 mixture of diastereoisomers). δ_H (500 MHz, $CDCl_3$) 0.92 (6H, t, *J* = 7.4 Hz, 2 × C*H*$_3$), 1.60–1.66 (4H, m, 2 × C*H*$_2$), 3.53–3.58 (4H, m, 2 × NC*H*$_2$), 3.65 (1H, d, *J* = 13.2 Hz, 1H of C*H*$_2$S), 3.69 (1H, d, *J* = 13.1 Hz, 1H of C*H*$_2$S), 4.01 (1H, s, C*H*S), 4.03 (1H, s, C*H*S), 4.13 (1H, d, *J* = 13.2 Hz, 1H of C*H*$_2$S), 4.14 (1H, d, *J* = 13.1 Hz, 1H of C*H*$_2$S), 6.14 (1H, s, Ar*H*) and 7.14–7.31 (11H, m, 1H of Ar*H* and 10H of benzyl groups). δ_C (75 MHz, $CDCl_3$) 11.7 (2 × *C*H$_3$), 21.2 (2 × *C*H$_2$), 34.6 (2 × *C*H$_2$S), 42.1 (2 × *C*H$_2$N), 43.0 (2 × *C*HS), 91.0 (Ar*C*H), 118.9 (2 × Ar*C*), 122.5 (2 × Ar*C*H), 127.5 (Ar*C*H), 127.6 (Ar*C*H),

128.7 (2 × Ar*C*H), 128.8 (2 × Ar*C*H), 129.5 (2 × Ar*C*H), 129.6 (Ar*C*H), 137.5 (Ar*C*), 137.6 (Ar*C*), 144.8 (Ar*C*), 144.9 (Ar*C*) and 176.3 (2 × *C*=O). ν_{max}/(cm^{-1}) 3410, 3061, 2966, 1714 (C=O), 1614, 1487, 1372, 1208 and 1129. *m*/*z* (EI$^+$ mode) 516 (M$^+$, 7%), 393 (16%), 124 (8%), 91 (100%), 77 (16%) and 65 (43%). *m*/*z* (M + H) 517.1978, $C_{30}H_{33}N_2O_2S_2$ requires 517.1987.

General procedure D for the removal of the organosulfanyl groups using SmI_2

1,5-Dihexyl-5,7-dihydro-1*H*,3*H*-pyrrolo[2,3-*f*]indole-2,6-dione 53 from 52

To a stirred solution of **52** (95 mg, 0.07 mmol, 1eq) in THF (6 ml) was added SmI_2 (3.10 ml of a 0.1 M solution in THF, 4.4 eq) at room temperature. After 14 h, the reaction mixture was opened to air and aqueous saturated $NaHCO_3$ (15 ml) was added. The aqueous layer was extracted with EtOAc (3 × 20 ml), the organic layer dried (Na_2SO_4) and concentrated *in vacuo.* Purification by column chromatography using 40% EtOAc in petroleum ether as eluant gave **53** (19 mg, 0.05 mmol, 74%) as a grey solid. Mp 149.3–151.2 °C (recrystallised from EtOAc and petroleum ether). δ_H (500 MHz, $CDCl_3$) 0.80–0.83 (6H, m, 2 × C*H*$_3$), 1.18–1.31 (12H, m, 2 × C*H*$_2$C*H*$_2$C*H*$_2$CH$_3$), 1.57–1.60 (4H, m, 2 × NCH$_2$C*H*$_2$), 3.48 (4H, s, 2 × (C=O)C*H*$_2$), 3.61 (4H, t, J = 7.4 Hz, 2 × NC*H*$_2$) and 6.71 (2H, s, 2 × Ar*H*). δ_C (75 MHz, $CDCl_3$) 14.3 (2 × *C*H$_3$), 22.8 (2 × *C*H$_2$), 26.9 (2 × *C*H$_2$), 27.7 (2 × NCH$_2$*C*H$_2$), 31.7 (2 × *C*H$_2$), 36.6 (2 × (C=O)*C*H$_2$), 40.4 (2 × N*C*H$_2$), 106.0 (2 × Ar*C*H), 124.2 (2 × Ar*C*), 140.0 (2 × Ar*C*) and 174.6 (2 × *C*=O). ν_{max}/(cm^{-1}) (CH_2Cl_2 evaporated film) 2952, 2929, 2854, 1710 (C=O), 1676, 1478, 1360 and 1128. *m*/*z* (CI$^+$ mode) 357 (M$^+$, 100%), 251 (17%), 242 (20%), 210 (20%), 138 (40%), 122 (25%) and 110 (15%). *m*/*z* (M + H) 357.2547, $C_{22}H_{33}N_2O_2$ requires 357.2537.

Removal of a single organosulfanyl group using SmI_2

3-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluoro-decylsulfanyl)1,5-dihexyl-5,7-dihydro-1*H*,3*H*-pyrrolo[2,3-*f*]-indole-2,6-dione 54

To a stirred solution of **52** (90 mg, 0.07 mmol, 1 eq) in THF (5 ml) was added SmI_2 (0.70 ml of a 0.1 M solution in THF, 1 eq) at room temperature. After 5 min, the reaction was quenched with air and aqueous saturated $NaHCO_3$ (20 ml) added to the reaction mixture. The aqueous layer was extracted with EtOAc (3 × 15 ml), the organic layers dried (Na_2SO_4), and concentrated *in vacuo.* Purification by column chromatography using 20% EtOAc in petroleum ether as eluant gave recovered **52** (17 mg, 0.01 mmol, 18%), **54** (25 mg, 0.03 mmol, 43%) as a yellow oil and **53** (3 mg, 0.009 mmol, 11%). For **54**: δ_H (500 MHz, $CDCl_3$) 0.81 (3H, t, J = 7.2 Hz, C*H*$_3$), 0.82 (3H, t, J = 7.2 Hz, C*H*$_3$), 1.21–1.33 (12H, m, 2 × C*H*$_2$C*H*$_2$C*H*$_2$CH$_3$), 1.51–1.61 (4H, m, 2 × C*H*$_2$ CH$_2$N), 2.32–2.41 (2H, m, C*H*$_2$CF$_2$), 2.72–2.78 (1H, m, 1H of C*H*$_2$S), 2.87–2.93 (1H, m, 1H of C*H*$_2$S), 3.49 (2H, s, C*H*$_2$C=O), 3.55–3.70 (4H, m, 2 × C*H*$_2$N), 4.26 (1H, s, C*H*S), 6.74 (1H, s, ArC*H*) and 6.81 (1H, s, ArC*H*). δ_C (125 MHz, $CDCl_3$) 14.0 (*C*H$_3$), 14.0 (*C*H$_3$), 20.9 (2 × *C*H$_2$), 22.5 (*C*H$_2$), 22.6 (*C*H$_2$), 26.6 (*C*H$_2$), 27.4 (*C*H$_2$), 29.7 (*C*H$_2$), 31.5 (*C*H$_2$CF$_2$), 36.8 (*C*H$_2$), 40.3 (*C*H$_2$N), 40.5 (*C*H$_2$N), 45.2 (*C*HS), 106.1 (Ar*C*H), 106.2 (Ar*C*H), 124.5 (Ar*C*), 125.8 (Ar*C*), 138.5 (Ar*C*), 140.4 (Ar*C*), 174.1 (*C*=O) and 174.3 (*C*=O). ν_{max}/(cm^{-1}) 2930, 2858, 1699, 1475, 1348, 1241, 1211, 1150, 1087 and 956. *m*/*z* (ES+ mode) 857 (M + Na, 100%). *m*/*z* (M + Na) 857.2061, $C_{32}H_{35}F_{17}N_2NaO_2S$ requires 857.2040.

1-(2-Benzenesulfonylethyl)-3-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecylsulfanyl)-1,3-dihydroindol-2-one 59

To a solution of oxalyl chloride (0.66 ml, 7.56 mmol, 1.1 eq) in CH_2Cl_2 (25 ml) was added DMSO (0.98 ml, 13.7 mmol, 2 eq) at –78 °C. After 10 min, **57** (2.19 g, 6.87 mmol, 1 eq.) in CH_2Cl_2 (25 ml) was added. After a further 1 h, Et_3N (4.79 ml, 34.0 mmol, 5 eq) was added and the reaction was allowed to warm to room temperature. After 3.5 h, $NaHCO_3$ (50 ml) was added to the reaction mixture and the organic layer was extracted with CH_2Cl_2 (3 × 50 ml), then the organic layers were dried ($MgSO_4$) and concentrated *in vacuo* to give the crude glyoxamide, which was used without further purification.

To the crude glyoxamide in CH_2Cl_2 (75 ml) was added 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluoro-decane-1-thiol (1.41 ml, 4.81 mmol, 0.7 eq) and the reaction stirred for 18 h at room temperature. Trifluoroacetic anhydride (8.73 ml, 61.8 mmol, 9 eq) was added, stirred for 1 h, then BF_3·OEt_2 (4.24 ml, 34.3 mmol, 5 eq) was added and the reaction mixture was left for 3 h. The reaction mixture was quenched with $NaHCO_3$ (70 ml), extracted with CH_2Cl_2 (3 × 50 ml), and the organic layers dried (Na_2SO_4) and concentrated *in vacuo.* The crude mixture was purified using FSPE to give **59** as a white solid (2.52 g, 3.23 mmol, 67% over 2 steps). Mp 81–83 °C (recrystallised from MeOH). δ_H (400 MHz, $CDCl_3$) 2.32–2.44 (2H, m, C*H*$_2$C$_8$F$_{17}$), 2.77–2.84 (1H, m, SC*H*H), 2.93–3.00 (1H, m, SCH*H*), 3.42–3.49 (1H, m, NC*H*H), 3.53–3.60 (1H, m, NCH*H*), 4.11–4.16 (3H, m, C*H*$_2$SO$_2$ and C*H*C=O), 6.93 (1H, d, J = 8.3 Hz, ArC*H*), 7.13 (1H, dt, J = 7.5 and 1.2 Hz, ArC*H*), 7.34–7.38 (2H, ArC*H*), 7.53–7.57 (2H, m, ArC*H*), 7.67 (1H, tt, J = 7.6 and 1.3 Hz, ArC*H*), 7.88–7.91 (2H, m, ArC*H*). δ_C (100 MHz, $CDCl_3$) 21.2 (*C*H$_2$), 31.8 (*C*H$_2$C$_8$F$_{17}$), 34.4 (S*C*H$_2$), 44.5 (*C*HC=O), 52.3 (N*C*H$_2$), 108.7 (Ar*C*H), 123.5 (Ar*C*H), 124.9 (Ar*C*), 125.5 (Ar*C*H), 127.9 (2 × Ar*C*H), 129.4 (2 × Ar*C*H), 129.7 (Ar*C*H), 134.1 (Ar*C*H), 138.7 (Ar*C*SO$_2$), 142.0 (Ar*C*N), 175.0 (*C*=O). ν_{max}/cm^{-1} 3443 (OH), 3062, 2961, 1716 (C=O), 1612, 1487, 1467, 1359, 1306, 1086 (S=O). *m*/*z*(ES$^+$ mode) 802 ((M + Na)$^+$, 100%), 797 (30%), 441 (15%), 197 (20%), 151 (30%), 101 (20%). *m*/*z* (M + Na)$^+$ 802.0349, $C_{26}H_{18}F_{17}NNaO_3S_2$ requires 802.0343.

1-(2-Benzenesulfonylethyl)-3-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecylsulfanyl)-3-(2-nitrobenzyl)-1,3-dihydroindol-2-one 61

To a solution of **59** (0.69 g, 0.86 mmol, 1 eq) in DMF (15 ml) was added K_2CO_3 (0.60 g, 4.43 mmol, 5 eq) and 2-nitrobenzyl bromide (0.57 g, 2.66 mmol, 3 eq) at room temperature and the reaction mixture was allowed to stir for 18 h. H_2O (15 ml) was added and the mixture extracted with Et_2O (3 × 15 ml). The organic layer was washed with H_2O (5 × 15 ml), dried (Na_2SO_4) and concentrated *in vacuo.* The crude mixture was purified using FSPE to give **61** as a clear, viscous oil (0.60 g, 0.66 mmol, 75%). δ_H (400 MHz, $CDCl_3$) 2.05–2.13 (2H, m, C*H*$_2$C$_8$F$_{17}$), 2.55–2.62 (2H, m, C*H*$_2$SO$_2$), 2.90–2.97 (1H, m, SC*H*H), 3.06–3.14 (1H, m, SCH*H*), 3.64 (1H, d, J = 13.9 Hz, C*H*HAr), 3.76–3.84 (1H, m, C*H*HN), 3.91–3.99 (1H,

m, CH*H*N), 4.02 (1H, d, $J = 13.9$ Hz, CH*H*Ar), 6.66 (1H, d, $J = 7.8$ Hz, ArC*H*), 7.05 (1H, dt, $J = 7.5$ and 1.0 Hz, ArC*H*), 7.13 (1H, dd, $J = 7.6$ and 1.0 Hz, ArC*H*), 7.19–7.26 (3H, m, 3 × ArC*H*), 7.34 (1H, dt, $J = 7.6$ and 1.2 Hz, ArC*H*), 7.54–7.55 (3H, m, 3 × ArC*H*), 7.64–7.69 (1H, m, ArC*H*), 7.87–7.89 (2H, m, 2 × ArC*H*). δ_C (100 MHz, $CDCl_3$) 20.0 (CH_2SO_2), 31.0 ($CH_2C_8F_{17}$), 33.8 (NCH_2), 37.6 (CH_2Ar), 52.3 (SCH_2), 55.0 (*C*), 108.4 (ArCH), 124.1 (ArCH), 124.9 (ArCH), 125.0 (ArCH), 127.4 (Ar*C*), 128.0 (2 × ArCH), 128.5 (ArCH), 129.2 (Ar*C*), 129.6 (2 × ArCH), 130.0 (ArCH), 132.4 (ArCH), 133.5 (ArCH), 134.3 (ArCH), 138.5 (Ar*C*), 140.6 (Ar*C*), 149.8 (Ar*C*), 175.5 (*C*=O). ν_{max}/cm^{-1} 2395, 1716 (C=O), 1682, 1651, 1560, 1505, 1086 (S=O). *m/z* (ES^+ mode) 937 ($(M + Na)^+$, 10%), 179 (50%), 142.2 (50%). *m/z* $(M + Na)^+$ 937.0669 $C_{33}H_{23}F_{17}N_2NaO_5S_2$ requires 937.0660.

11-(2-Benzenesulfonylethyl)-11*H*-10,11-diaza-benzo[*b*]fluorene 63

To a solution of SmI_2 in THF (31.0 ml, 0.1 M, 3.10 mmol, 9 eq) was added a degassed solution of **61** (0.31 g, 0.34 mmol, 1 eq) in THF (3 ml) and MeOH (1.5 ml). The solution was allowed to stir for 4 h and then exposed to air. Saturated, aqueous $Na_2S_2O_3$ (30 ml) was added, the aqueous layer extracted with Et_2O (3 × 30 ml), and the combined organic layers dried (Na_2SO_4) and concentrated *in vacuo.* Purification by column chromatography using 50% EtOAc in petroleum ether as eluant gave the aniline intermediate which was then directly dissolved in a MeOH : AcOH (1 : 1) mix (20 ml) and heated to 100 °C for 18 h. K_2CO_3 was added to the mixture until basic pH was reached, the organic layer was extracted with EtOAc (3 × 20 ml), the combined organic layers dried (Na_2SO_4) and concentrated *in vacuo.* The crude mixture was purified by column chromatography using 20% EtOAc in petroleum ether as eluant to give **63** as a white solid (0.11 g, 0.25 mmol, 82%). Mp 103–105 °C (recrystallised from MeOH). δ_H (400 MHz, $CDCl_3$) 3.98 (2H, t, $J = 7.0$ Hz, SCH_2), 4.89 (2H, t, $J = 7.0$ Hz, NCH_2), 7.13–7.17 (2H, m, 2 × ArC*H*), 7.20 (1H, dt, J = 7.2 and 1.0 Hz, ArC*H*), 7.31–7.39 (3H, m, 3 × ArC*H*), 7.48 (1H, ddd, $J = 8.3$, 7.6 and 1.3 Hz, ArC*H*), 7.59–7.64 (3H, m, 3 × ArC*H*), 7.85 (1H, dd, $J = 8.0$ and 1.5 Hz, ArC*H*), 7.92–7.94 (2H, m, 2 × ArC*H*), 8.44 (1H, s, ArC*H*). δ_C (100 MHz, $CDCl_3$) 35.9 (NCH_2), 53.0 (SCH_2), 108.9 (ArCH), 118.0 (Ar*C*), 120.5 (ArCH), 120.6 (Ar*C*), 121.5 (ArCH), 123.3 (ArCH), 124.3 (Ar*C*), 127.3 (ArCH), 127.4 (2 × ArCH), 127.6 (ArCH), 128.3 (ArCH), 128.4 (ArCH), 128.8 (2 × ArCH), 129.0 (ArCH), 133.4 (ArCH), 138.7 (Ar*C*), 141.3 (Ar*C*), 146.5 (Ar*C*), 151.8 (Ar*C*). ν_{max}/cm^{-1} 3334 br, 1650, 1556, 1505, 1455, 1417, 1259, 1123. *m/z* (ES^+ mode) 409 ($(M + Na)^+$, 100%), 284 (20%). *m/z* $(M + Na)^+$ 409.0981 $C_{23}H_{18}N_2NaO_2S$ requires 409.0969.

11*H*-10,11-Diazabenzo[*b*]fluorene[20]

Compound **63** (0.10 g, 0.26 mmol, 1 eq) was suspended in THF (3 ml) and potassium *tert*-butoxide (0.09 g, 0.79 mmol, 3 eq) was added. The reaction was allowed to stir for 4 h. H_2O (5 ml) was added, the organic layer was extracted with EtOAc (3 × 5 ml), the combined organic layers dried (Na_2SO_4) and concentrated *in vacuo.* The crude product was purified by column chromatography using 5% MeOH in CH_2Cl_2 as eluant to give 11*H*-10,11-diazabenzo[*b*]fluorene as a brown solid (0.056 g, 0.26 mmol, 98%). (Analytical data was in agreement with the literature.)[20] δ_H (400 MHz, $CDCl_3$) 7.24–7.30 (1H, m, ArC*H*), 7.46–7.56 (3H, m, 3 × ArC*H*), 7.70–7.75 (1H, m, ArC*H*), 7.98 (1H, d, $J = 8.5$ Hz, ArC*H*), 8.11 (1H, d, $J = 8.3$ Hz, ArC*H*), 8.27 (1H, d, $J = 7.5$ Hz, ArC*H*), 9.06 (1H, s, ArC*H*), 11.7 (1H, s, N*H*). δ_C (75 MHz, $CDCl_3$) 110.9 (ArCH), 117.9 (Ar*C*), 119.7 (ArCH), 120.3 (Ar*C*), 121.8 (ArCH), 122.7 (ArCH), 123.7 (Ar*C*), 127.0 (ArCH), 127.5 (ArCH), 128.2 (2 × ArCH), 128.6 (ArCH), 141.5 (Ar*C*), 144.4 (Ar*C*), 152.9 (Ar*C*). *m/z* (ES^+ mode) 219 ($(M + H)^+$, 10%), 179 (100%), 101 (40%).

Neocryptolepine 65[13,20,21]

11*H*-10,11-Diazabenzo[*b*]fluorene (0.017 g, 0.078 mmol, 1 eq) was suspended in THF (0.5 ml) and methyl iodide was added (0.034 ml, 0.54 mmol, 7 eq). The reaction was heated under reflux for 18 h and then concentrated *in vacuo.* The crude mixture was dissolved in CH_2Cl_2 (3 ml), $NaHCO_3$ (3 ml) was added and the organic layer extracted with CH_2Cl_2 (3 × 3 ml). The combined organic layers were dried (Na_2SO_4), concentrated *in vacuo* and purified by column chromatography using 80% EtOAc in petroleum ether as eluant to give **65** as an orange solid (0.013 g, 0.054 mmol, 70%). (Analytical data was in agreement with the literature.)[13,20,21] Mp 112–114 °C (recrystallised from hexane). δ_H (400 MHz, $CDCl_3$) 4.32 (3H, s, Me), 7.15–7.20 (1H, m, ArC*H*), 7.38–7.42 (1H, m, ArC*H*), 7.49 (1H, t, $J = 7.6$ Hz, ArC*H*), 7.70 (1H, d, $J = 7.9$ Hz, ArC*H*), 7.72 (2H, apparent d, $J = 3.9$ Hz, 2 × ArC*H*), 7.95 (1H, d, $J = 7.6$ Hz, ArC*H*), 8.00 (1H, d, $J = 7.6$ Hz, ArC*H*), 8.49 (1H, s, ArC*H*). δ_C (75 MHz, $CDCl_3$) 32.1 (Me), 113.2 (ArCH), 116.6 (ArCH), 118.9 (ArCH), 119.9 (Ar*C*), 120.0 (ArCH), 121.0 (ArCH), 122.9 (Ar*C*), 127.1 (Ar*C*), 127.2 (ArCH), 128.3 (ArCH), 129.0 (ArCH), 129.5 (ArCH), 135.9 (Ar*C*), 154.0 (Ar*C*), 155.0 (Ar*C*). *m/z* (ES^+ mode) 233 ($(M + H)^+$, 40%), 218 (100%), 107 (90%). *m/z* 233.1069, $C_{16}H_{13}N_2$ requires 233.1073.

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