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Novel pyrrolo[1,2-*a*][3.1.6]benzothiadiazocine ring synthesis. Unusual Truce–Smiles type rearrangement of 1-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]sulfonyl(or sulfinyl)}acetone

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Abstract—Reaction of 1-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]sulfonyl}acetone with sodium hydroxide with or without zinc gave 1-(2-nitrophenyl)(1*H*-pyrrol-2-ylsulfonyl)methane by a Truce–Smiles type of transformation and 1-(2-nitrophenyl)-2-methylsulfonylpyrrole by deacetylation. Similar treatment of 1-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]sulfinyl}acetone gave only 1-(2-nitro-phenyl)(1*H*-pyrrol-2-ylsulfinyl)methane. 1-{[1-(2-Nitrophenyl)-1*H*-pyrrol-2-yl]sulfanyl}acetone, 2-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]sulfanyl}-1-phenyl-ethan-1-one or 2-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]sulfanyl}acetonitrile were reductively cyclised with sodium borohydride and 5% palladium-on-carbon into 6-methyl(or phenyl)-5,6-dihydro-7*H*-pyrrolo[1,2-*a*][3.1.6]benzothiadiazocin-7-ol or 6-amino-5*H*-pyrrolo[1,2-*a*][3.1.6]benzothiadiazocine-7-oxide, respectively.

1. Introduction

Diaryl and arylheterocyclic sulfones are an emerging class of non-nucleoside HIV-1 reverse transcriptase inhibitors.[1–10] Compounds with the sulfonyl group not part of a ring seem to be the most potent, although related cyclic counterparts such as 5*H*-pyrrolo[1,2-*b*][1.2.5]pyrrolobenzothiadiazepin-11(10*H*)-one-5,5-dioxides[6] are important members of these bioactive compounds. Artico and coworkers have recently synthesised 9*H*-pyrrolo[2,1-*b*][1.3.6]benzothiadiazocin-10-(11*H*)-one-4,4-dioxide[4] as a potential anti-HIV-1 agent. The compound was prepared by reacting 2-aminothiophenol with ethyl 2-(1*H*-pyrrol-1-yl) acetate, hydrolysing ethyl 2-{2-[(2-amino-phenyl)sulfanyl]-1*H*-pyrrol-1-yl}acetate, cyclising 2-{2-[(2-aminophenyl)-sulfanyl]-1*H*-pyrrol-1-yl}acetic acid and oxidising 9*H*-pyrrolo[2,1-*b*][1.3.6]benzothiadiazocin-10-(11*H*)-one. The synthesis of 10*H*-pyrrolo[1,2-*b*][1.2.5]benzothiadiazocine-5,5-dioxide[11] has been carried out by intramolecular cyclisation of *N*-[2-(1*H*-pyrrol-1-ylsulfonyl)benzyl]methanamide, prepared from the reaction of [2-(1*H*-pyrrol-1-ylsulfonyl)phenyl]methanamine with ethyl chloroformate, followed by treatment with triphosgene. An isomer, 10*H*-pyrrolo[1,2-*b*][1.2.6]benzothiadiazocin-11-(12*H*)-one-5,5-dioxide,[12] was prepared by intramolecular cyclisation of 2-{1-[(2-aminophenyl)sulfonyl]-1*H*-pyrrol-2-yl}acetic acid. Fifteen years ago Cheeseman et al. reported the synthesis of the 5,6-dihydropyrrolo[1,2-*a*]-[3.1.6]benzothiadiazocine ring system.[13,14] Two routes were employed that utilized 1-(2-aminophenyl)-1*H*-pyrroles as starting materials. These compounds were derived from the reaction between 2-nitroanilines and 2,5-dimethoxytetrahydrofuran followed by reduction of the resulting 1-(2-nitrophenyl)-1*H*-pyrroles. The first route involved reaction of 1-(2-aminophenyl)-1*H*-pyrroles with chloroacetic anhydride or α-chloropropionyl chloride, thiocyanation of the *N*1-[2-(1*H*-pyrrol-1-yl)-phenyl]-2-chloroacetamides with copper(II) thiocyanate and reductive cyclisation of the resulting *N*1-[2-(2-thiocyanato-1*H*-pyrrol-1-yl)phenyl)-2-chloroacetamides in the presence of sodium borohydride.[13] The second route involved treatment of 1-(2-aminophenyl)-1*H*-pyrrole with trifluoroacetic anhydride, thiocyanation of *N*1-[2-(1*H*-pyrrol-1-yl)-phenyl]-2,2,2-trifluoroacetamide, reductive alkylation of *N*1-[2-(2-thiocyanato-1*H*-pyrrol-1-yl)-phenyl]-2,2,2-trifluoroacetamide with ethyl bromoacetate and concomitant cleavage of the amide group in the presence of sodium borohydride, followed by cyclisation of the resulting ethyl 2-{[1-(2-aminophenyl)-1*H*-pyrrol-2-yl]sulfanyl}acetate in the presence of trimethylaluminium.[14]

Keywords: Pyrroles; Pyrrolobenzothiadiazocines; Cyclisation; Reduction; Truce–Smiles rearrangement.
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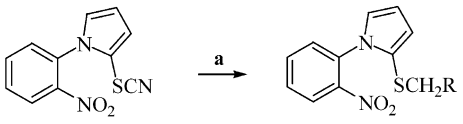
2. Results and discussion

With an extension of this work in mind, we decided to exploit the intramolecular capture of in situ generated nitroso species by carbanions and the intramolecular addition of hydroxyl-amines to carbonyl groups or nitriles in order to effect ring closure by carbon–nitrogen bond formation. To this end, we prepared ketones **2** and **3**,[14] ester **4** and nitrile **5**[15] by selectively reducing 1-(2-nitrophenyl)-2-thiocyanato-1*H*-pyrrole **1**[15] with sodium borohydride and then treating the resulting thiol, that was not isolated, with 2-chloroacetone, phenacyl bromide, ethyl bromoacetate or chloroacetonitrile, respectively (Scheme 1).

A few examples, where intramolecular capture of in situ generated nitroso species is used for the synthesis of fused heterocycles, are given below. Reductive cyclisation of *N*1-(alkyl or aryl)-2-nitrobenzamides into 2-(alkyl or aryl)-2,3-dihydro-1*H*-3-indazolones has been accomplished via treatment with zinc dust and sodium hydroxide.[16] Milder reaction conditions, zinc dust and ammonium chloride, have been used for the cyclisation of substituted 3-(2-nitrophenoxy)phenols to 3*H*-phenoxazin-3-ones[17] and of ethyl 2-nitrophenylacetate to 4-hydroxy-1,4-benzoxazine-3(4*H*)-one.[18] Recently, we reported the reductive cyclisation of (2-nitrophenyl)(1*H*-pyrrol-2-yl)methanone with zinc and ammonium chloride or sodium hydroxide which gave 5,10-dihydropyrrolo[1,2-*b*]cinnolin-10-one.[19]

Selective reduction of compounds **2**, **3** and **4** with zinc dust and ammonium chloride in aqueous ethanol from 0 °C to room temperature respectively afforded mixtures of the corresponding amines **7**, **9**[14] and **11**,[14] and hydroxylamines **8**, **10** and **12** (Scheme 2). No trace of the anticipated pyrrolobenzothiadiazepines **6** was detected. This could be due to the weakly basic reaction conditions that were ineffective in deprotonating the methylene group in the intermediate nitroso compounds. On the other hand when compounds **2** and **3** were subjected to selective reduction using zinc dust and sodium hydroxide in refluxing aqueous ethanol, a complex mixture was produced in each case that appeared as a streak on TLC. All attempts to separate the components of these mixtures proved unsuccessful.

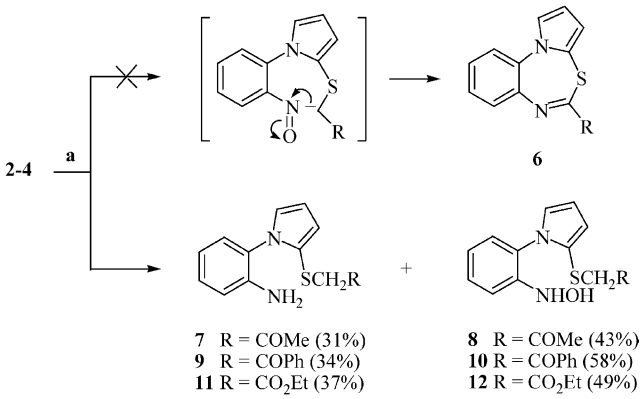
Oxidation of **2** and **3** to their sulfones would increase the acidity of the methylene hydrogens in these compounds. Thus, compounds **2** and **3** were oxidized smoothly into their corresponding sulfones **13** and **15** by 2-chloroperbenzoic acid (Scheme 3). However, the required reductive cyclisation of **13** and **15** by treatment with zinc and ammonium



1

2 R = COMe (72%)
3 R = COPh (76%)
4 R = CO_2Et (49%)
5 R = CN (62%)

Scheme 1. Reagents: (a) (i) $NaBH_4$, EtOH, NaOH, (ii) $ClCH_2COMe$, $BrCH_2COPh$, $BrCH_2CO_2Et$ or $ClCH_2CN$.



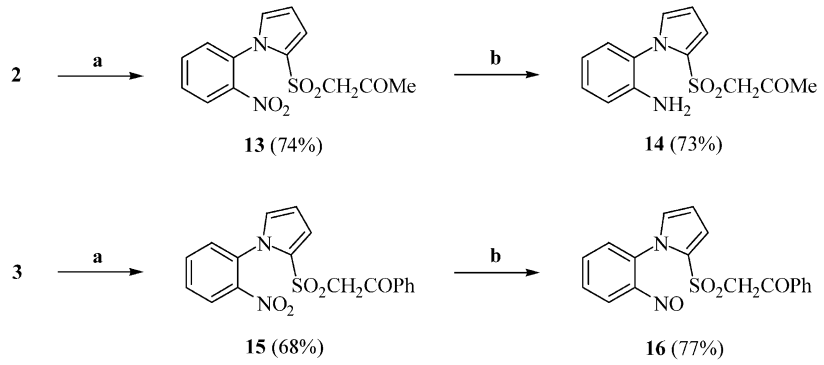
7 R = COMe (31%)
9 R = COPh (34%)
11 R = CO_2Et (37%)

8 R = COMe (43%)
10 R = COPh (58%)
12 R = CO_2Et (49%)

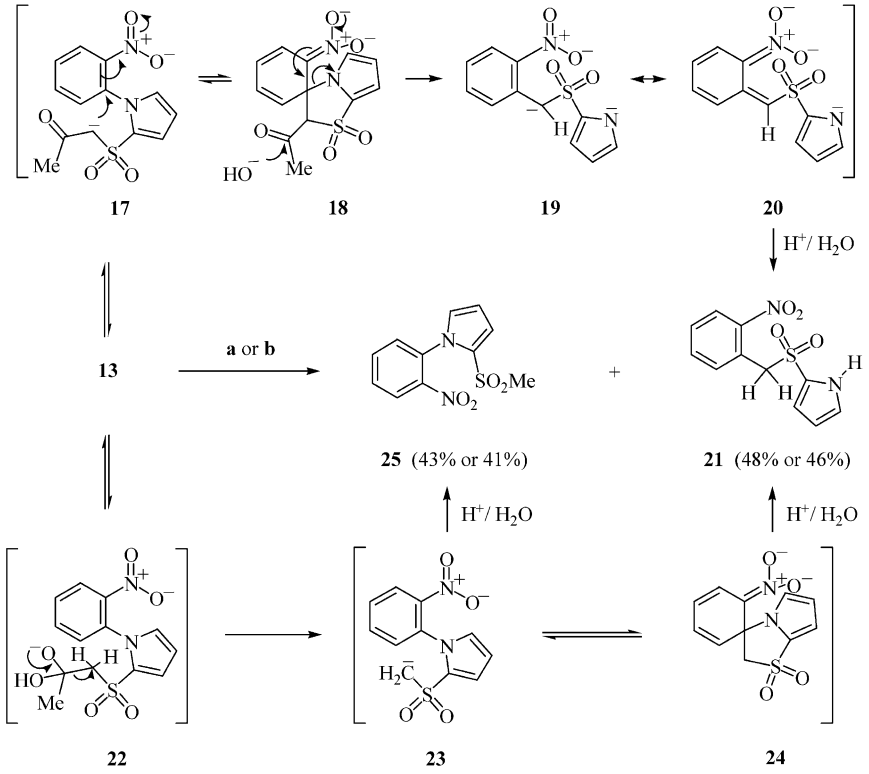
Scheme 2. Reagents: (a) Zn, NH_4Cl, H_2O, EtOH, 0–22 °C.

chloride failed, yielding instead the amine **14** and nitroso compound **16**, respectively.

We anticipated that by using a stronger base such as sodium hydroxide in the reduction of sulfone **13**, the abstraction of the relatively acidic methylene proton should be accelerated according to the mechanism of Scheme 2, and would lead to the sulfone derivative of pyrrolobenzothiadiazepine **6** (R = COMe). However, heating **13** in aqueous ethanolic sodium hydroxide containing zinc dust yielded a mixture of two new compounds, **21** and **25**, in 48 and 43% yield, respectively. A speculative mechanism for this reaction is shown in Scheme 4. In line with the proposed mechanism, hydroxide ion could react on compound **13** both as a base and as a nucleophile. Intramolecular nucleophilic attack on the benzene ring by carbanion **17** would give the Meisenheimer-type intermediate **18** that could ring-open prior or after addition of hydroxide anion to the acetyl group to give, after loss of acetate anion, pyrrolyl dianion **19**. On the other hand, addition of hydroxide ion to the acetyl group of **13** would give intermediate **22** from which loss of acetate anion would lead to carbanion **23**. After acidification, the reaction would lead to products **21** and **25**. The formation of **21** is considered to be an unusual case of a Truce–Smiles rearrangement. The reason that the nitro groups of compounds **21** and **25** are not reduced by the reductive reaction conditions is probably due to the rapid interconversion between **19** and **21** and **23** and **25**, before acidification. The structure of **25** was confirmed by its unambiguous synthesis from thiocyanate **1**. The latter was alkylated with methyl iodide in the presence of sodium borohydride to give 1-(2-nitrophenyl)-2-methylthio-1*H*-pyrrole, which was then oxidised directly to sulfone **25** by reaction with oxone® in acetone at room temperature. Heating compound **13** in aqueous ethanolic sodium hydroxide gave a mixture of **21** and **25** in 46 and 41% yield, respectively. Furthermore when compounds **21** and **25** were heated in aqueous sodium hydroxide with or without the presence of zinc dust, starting material was recovered unchanged. These results confirm beyond doubt that zinc dust plays no role in the reaction and that the formation of **21** and **25** occurs independently from **13**. Cheeseman and Hawi have proposed a mechanism similar in some respects to that of Scheme 4 to explain the rearrangement of methyl 2-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]thio}acetate into 2,3-dihydro-2-(2-nitrophenyl)-3-oxo-pyrrolo[2,1-*b*]thiazole. The reaction took place in dimethyl sulfoxide with potassium *t*-butoxide as base.[15]



Scheme 3. Reagents: (a) 3-chloroperbenzoic acid, CH_2Cl_2, reflux; (b) Zn, NH_4Cl, H_2O, EtOH, 0–22 °C.

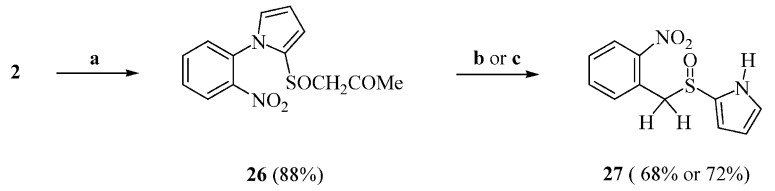


Scheme 4. Reagents: (a) Zn, NaOH, H_2O, EtOH, reflux; (b) NaOH, H_2O, EtOH, reflux.

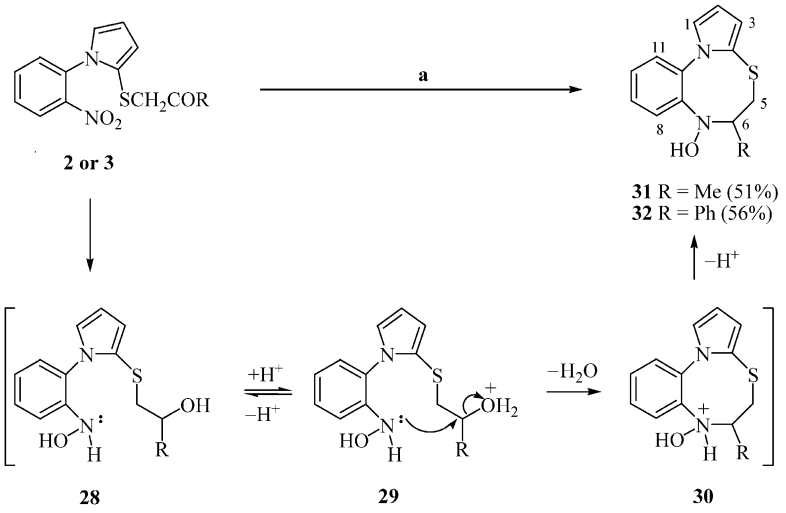
In order to acquire further insight into the reaction of Scheme 4 it was decided to prepare sulfoxide **26**. The first attempt involved the oxidation of sulfide **2** by 3-chloroperbenzoic acid at room temperature for several days. This however resulted in a mixture of starting material and sulfoxide **26** but reaction of **2** with oxone® in acetone at ambient temperature afforded sulfoxide **26** as a single product in 88% yield (Scheme 5). When **26** was heated in aqueous ethanolic sodium hydroxide containing zinc dust pyrrolylsulfinylmethane **27** was obtained in 68% yield. Repeating the reaction without zinc dust gave **27** in 72% yield. An analogous mechanism to that described for the transformation of **13** to **21** in Scheme 4 is proposed. A likely explanation for 1-(2-nitrophenyl)-2-methylsulphinylpyrrole not being formed is that the sulfoxide analogue of carbanion **23** (Scheme 4) is less stabilised than **23** itself and is therefore not formed.

Compounds **2**, **3** and **5** were found to be useful precursors to the novel pyrrolo[1,2-*a*][3.1.6]benzothiadiazocin-7-ols **31** and **32**, and, pyrrolo[1,2-*a*][3.1.6]benzothiadiazocine-7-oxide **36**, respectively. Thus ketones **2** or **3** were reductively cyclised in the presence of sodium borohydride and 5% palladium-on-carbon to give the corresponding tricycles **31** and **32** in 51 and 56% yield respectively (Scheme 6). It is proposed that the initial step in this reaction is reduction of both nitro and keto groups of compounds **2** or **3** leading intermediate **28**. After addition of ethanolic hydrogen chloride, protonation of **28** gives intermediate **29**. The latter may deprotonate back to **28** or intramolecularly cyclise to **30** by displacement of water. Loss of a proton from intermediate **30** gives either **31** or **32**.

In the ^{1}H NMR spectrum of **31** at 24 °C, the broad signal at 2.24 ppm contains the upfield signal of the methylene



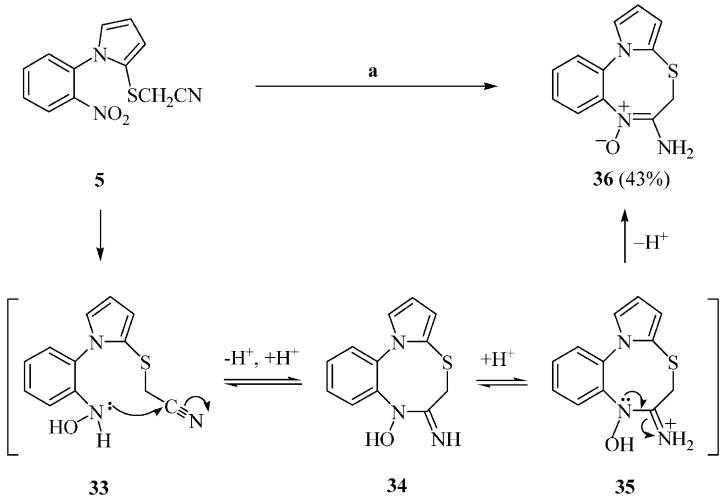
Scheme 5. Reagents: (a) oxone®, $(Me)_2CO$, 30 min; (b) Zn, NaOH, H_2O, EtOH, reflux; (c) NaOH, H_2O, EtOH, reflux.



Scheme 6. Reagents: (a) (i) $NaBH_4$, 10% Pd–C, H_2O, 1,4-dioxane, 2% aq. NaOH, (ii) EtOH–HCl, pH = 5–6.

group, assigned to H-5a, overlapping with the hydroxyl group. This was verified by D_2O addition which showed a remaining broad signal at 2.24 ppm. H-5b appears as a doublet at 2.48 ppm and H-6 appears as a multiplet in the region 3.65–3.70. Line narrowing is known to occur when the conformational equilibrium of a methylene group is fast on the NMR time-scale.[20] The fine structure of these signals was revealed by recording the spectrum at 60 °C. At this temperature the OH signal shifted upfield by 0.22 ppm, H-5a and H-5b are double doublets at 2.35 and 2.51 ppm, respectively, and H-6 is a double doublet of a quartet at 3.69 ppm. In the ^1H NMR spectrum of **32** at 24 °C, the broad signal at 2.50 ppm, assigned to H-5a, overlaps with the hydroxyl group. After D_2O addition the remaining signal at 2.50 ppm is broad. H-5b and H-6 appear as double doublets at 2.69 and 4.57 ppm, respectively. In the spectrum of **32** at 60 °C, H-5a has sharpened to a double doublet at 2.55 ppm whereas the OH signal is so broad that its chemical shift cannot be recorded.

Treatment of nitrile **5** with sodium borohydride and 5% palladium-on-carbon gave tricyclic-*N*-oxide **36** in 43% yield (Scheme 7). The proposed mechanism for this transformation involves reduction of **5** to intermediate hydroxylamine **33**, intramolecular nucleophilic addition to the nitrile group, protonation of resulting imine **34** to iminium cation **35** and conversion of the later to *N*-oxide **36** by lone pair electron delocalisation and deprotonation. The



Scheme 7. Reagents: (a) (i) $NaBH_4$, 10% Pd–C, H_2O, 1,4-dioxane, 2% aq. NaOH, (ii) EtOH/HCl, pH = 5–6.

carbon and proton atoms of compounds **31**, **32** and **36** were fully characterised with the aid of DQF-COSY, DEPT, HMQC and HMBC spectra.

In summary, it has been shown that substituted pyrroles such as 1-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]sulfanyl}acetone are reduced by zinc and ammonium chloride to the corresponding hydroxylamine and amine derivatives, without the observation of any intramolecular interaction. A similar result was obtained with 1-{[1-(2-nitro-phenyl)-1*H*-pyrrol-2-yl]sulfonyl}acetone where only the corresponding amine was isolated. However, treatment of 1-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]sulfonyl}acetone with zinc and sodium hydroxide gave a mixture of two products resulting from a Truce–Smiles type of transformation and a simple deacetylation. Remarkably, no reduction of the nitro group in these compounds had occurred. Reduction of 1-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]sulfonyl}acetone or -1-phenylethan-1-one with sodium borohydride and 5% palladium-on-carbon, lead to two novel pyrrolo[1,2-*a*]-[3.1.6]benzothiadiazocine derivatives. The N-oxide function of these compounds suggests transient hydroxyl-amine intermediates This novel synthetic method was successfully applied.

3. Experimental

3.1. General methods

Melting points were taken on a Büchi 510 apparatus and are uncorrected. Infrared spectra were recorded on a Perkin–Elmer 257 spectrometer, as Nujol mulls and liquids between sodium chloride discs. Elemental analyses were performed on a Carlo Erba 1106 elemental analyser. Nuclear magnetic resonance spectra were measured at 360 MHz on a Brüker AM 360 spectrometer or at 400 MHz on a Brüker AMX 400 spectrometer using tetramethylsilane as internal standard. Mass spectra were obtained using a JEOL JMS-AX 505W high resolution instrument under EI or CI conditions, or a Bruker Apex III high resolution instrument under ESI conditions. Analytical TLC was carried out on Fluka silica gel 60 F_{254}. Preparative flash chromatography was carried out using Merck 9385 silica gel. Solvents and reagents were used as received from the manufacturers except for dichloromethane, ethanol, ethyl acetate, light petroleum (bp 40–60 °C) and methanol that were purified and dried according to recommended procedures.[21]

3.2. Alkylation of 1-(2-nitrophenyl)-1*H*-pyrrol-2-ylthiocyanate. General procedure A

To a stirred solution of **1** (1.22 g, 5 mmol) in dry ethanol (50 mL), kept under a continuous stream of argon, sodium borohydride (0.28 g, 7.5 mmol) was added in portions and the mixture stirred at room temperature for 45 min. A solution of sodium hydroxide (0.42 g, 7.5 mmol) in dry ethanol (10 mL) was then added followed by chloroacetone, phenacyl bromide, ethyl chloroacetate or chloroacetonitrile (7.5 mmol). The mixture was stirred at 60–65 °C for 1.5 h and at room temperature for 12 h. The solvent was removed in vacuo up to 15 mL and to this oily residue, water (45 mL) was added and extracted with dichloromethane (3×15 mL). The combined organic extracts were dried (Na_2SO_4) and the solvent was evaporated under reduced pressure. The residue was purified by flash chromatography (12, 25% ethyl acetate/light petroleum) to give 1-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]sulfanyl}acetone **2**, 2-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]sulfanyl}-1-phenylethan-1-one **3**, ethyl 2-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]sulfanyl}acetate **4** or [1-(2-nitrophenyl)-1*H*-pyrrol-2-ylsulfanyl]acetonitrile **5**, respectively.

3.2.1. 1-{[1-(2-Nitrophenyl)-1*H*-pyrrol-2-yl]sulfanyl}-acetone (2). (0.5 g, 72%) as pale yellow oil, bp 112–114 °C/12 mm Hg; ν_{max}(liquid film) 1720, 1540, 1360 cm^{-1}; δ_H (360 MHz; $CDCl_3$) 2.07 (3H, s, Me), 3.12 (1H, s, br, CH_2), 6.33 (1H, dd, J=3.6, 3.1 Hz, H-4), 6.59 (1H, dd, J=3.6, 1.7 Hz, H-3), 6.88 (1H, dd, J=3.1, 1.7 Hz, H-5), 7.50 (1H, dd, J=7.9, 1.3 Hz, H-6′), 7.61 (1H, ddd, J=9.0, 8.0, 1.3 Hz, H-4′), 7.74 (1H, ddd, J=9.0, 7.9, 1.6 Hz, H-5′), 8.05 (1H, dd, J=8.0, 1.6 Hz, H-3′); δ_C (90.5 MHz; $CDCl_3$) 28.3, 47.3, 110.9, 120.3, 120.8, 125.1, 125.9, 129.3, 131.2, 132.9, 133.5, 146.6, 202.9; *m/z* (EI) 276 (65, M^+), 260 (10) 187 (33), 171 (38), 143 (12), 83 (100%); HRMS (EI): (M^+), found 276.0563. $C_{13}H_{12}N_2O_3S$ requires 276.0569.

3.2.2. 2-{[1-(2-Nitrophenyl)-1*H*-pyrrol-2-yl]sulfanyl}-1-phenylethan-1-one (3). (1.27 g, 76%) as yellow needles (ethanol); mp=96–97 °C; (lit.[14] mp=97–98 °C), identical in all respects to an authentic sample.

3.2.3. Ethyl 2-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]sulfanyl}acetate (4). (0.68 g, 49%) as a yellow oil, bp 123–128 °C/12 mm Hg; ν_{max} (liquid film) 1740, 1540, 1350 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 1.20 (3H, t, J=7.0 Hz, Me), 3.03 (2H, d, J=7.8, Hz, SCH_2), 4.01–4.12 (2H, m, CH_2), 6.35 (1H, dd, J=3.3, 3.0 Hz, H-4), 6.67 (1H, dd, J=3.3, 1.7 Hz, H-3), 6.89 (1H, dd, J=3.0, 1.7 Hz, H-5), 7.48 (1H, dd, J=7.8, 1.4 Hz, H-6′), 7.60 (1H, ddd, J=8.1, 7.9, 1.5 Hz, H-4′), 7.71 (1H, ddd, J=7.9, 7.8, 1.5 Hz, H-5′), 8.04 (1H, dd, J=8.1, 1.5 Hz, H-3′); δ_C (100 MHz; $CDCl_3$) 12.8, 33.8, 60.3, 106.3, 115.9, 117.7, 119.0, 124.4, 125.3, 126.5, 128.0, 131.2, 142.8, 171.4; *m/z* (EI) 306 (35, M^+), 275 (68), 173 (100), 140 (25%); HRMS (EI): (M^+), found 306.0671 $C_{14}H_{14}N_2O_4S$ requires 306.0674.

3.2.4. [1-(2-Nitro-phenyl)-1*H*-pyrrol-2-ylsulfanyl]acetonitrile (5). (0.76 g, 62%) as pale yellow oil; (lit.[15]), identical in all respects to an authentic sample.

3.3. Reduction of 1-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-sulfanyl}acetone, 2-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-sulfanyl}-1-phenylethan-1-one and ethyl 2-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]sulfanyl}acetate with zinc dust and ammonium chloride in aqueous ethanol. General procedure B

To a stirred solution of compounds **2**, **3** or **4** (1.2 mmol) in ethanol (15 mL) at 0 °C was added zinc dust (0.24 g, 3.6 mmol) followed by a solution of ammonium chloride (0.38 g, 7.2 mmol) in water (8 mL). The reaction mixture was left to stir at room temperature for 1.5 h, filtered the residue washed with hot ethanol (15 mL). The solvents were evaporated in vacuo to near dryness, water (35 mL) was added and extracted with dichloromethane (3×10 mL). The

combined organic extracts were dried (Na_2SO_4) and the solvent removed under reduced pressure. The oily residue was purified by flash chromatography (12% ethyl acetate/light petroleum) to give two fractions. The first fraction gave 1-{[1-(2-aminophenyl)-1*H*-pyrrol-2-yl]sulfanyl}acetone **7**, 2-{[1-(2-aminophenyl)-1*H*-pyrrol-2-yl]-sulfanyl}-1-phenylethan-1-one **9** or ethyl 2-{[1-(2-aminophenyl)-1*H*-pyrrol-2-yl]sulfanyl}acetate **11** and the second fraction gave 1-{[1-(2-hydroxylaminophenyl)-1*H*-pyrrol-2-yl]sulfanyl}acetone **8**, 2-{[1-(2-hydroxylaminophenyl)-1*H*-pyrrol-2-yl]sulfanyl}-1-phenylethan-1-one **10** or ethyl 2-{[1-(2-hydroxylaminophenyl)-1*H*-pyrrol-2-yl]sulfanyl}acetate **12**, respectively.

3.3.1. 1-{[1-(2-Aminophenyl)-1*H*-pyrrol-2-yl]sulfanyl}acetone (7). (90 mg, 31%) as pale yellow oil, bp 152–155 °C/12 mm Hg; ν_{max} (liquid film) 3525, 3420, 1685 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 2.29 (3H, s, Me), 3.69 (2H, s, br, NH_2), 3.71 (2H, d, $J=13$ Hz, SCH_2), 6.27 (1H, t, $J=3.6$ Hz, H-4), 6.81 (1H, dd, $J=3.6$, 1.8 Hz, H-3), 6.91 (1H, dd, $J=7.9$, 1.4 Hz, H-3′), 7.11 (1H, dd, $J=3.6$, 1.8 Hz, H-5), 7.29 (1H, ddd, $J=9.0$, 7.9, 1.4 Hz, H-5′), 7.48 (1H, ddd, $J=7.9$, 1.3 Hz, H-4′), 7.52 (1H, dd, $J=9.0$, 1.3 Hz, H-6′); δ_C (100 MHz; $CDCl_3$) 28.8, 41.7, 106.2, 115.6, 116.5, 116.8 (2C), 126.4 (2C), 128.7, 129.5, 202.2; *m/z* (EI) 246 (63, M^+), 229 (18) 153 (75), 69 (100%); HRMS (EI): (M^+), found 246.0826. $C_{13}H_{14}N_2OS$ requires 246.0833.

3.3.2. 1-{[1-(2-Hydroxylaminophenyl)-1*H*-pyrrol-2-yl]sulfanyl}acetone (8). (0.13 g, 43%) as pale yellow oil, bp 143–145 °C/12 mm Hg; ν_{max} (liquid film) 3380, 1710 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 2.07 (3H, s, Me), 3.18 (2H, s, SCH_2), 5.62 (2H, s, br, NHOH), 6.28 (1H, t, $J=3.1$ Hz, H-4), 6.48 (1H, dd, $J=3.1$, 1.4 Hz, H-3), 6.87 (1H, dd, $J=3.1$, 1.4 Hz, H-5), 6.97 (1H, ddd, $J=8.0$, 7.2, 2.4 Hz, H-5′), 7.16 (1H, dd, $J=7.8$, 2.4 Hz, H-3′), 7.52 (1H, ddd, $J=7.8$, 7.2, 1.4 Hz, H-4′), 7.79 (1H, dd, $J=8.0$, 1.4 Hz, H-6′); δ_C (100 MHz; $CDCl_3$) 28.7, 41.8, 106.3, 110.7, 117.1, 118.3, 122.2, 126.5, 128.2, 129.0, 140.1, 202.1; *m/z* (EI) 263 (45, M^+), 188 (58) 169 (65), 83 (100%); HRMS (EI): (M^+), found 263.0854. $C_{13}H_{14}N_2O_2S$ requires 263.0845.

3.3.3. 2-{[1-(2-Aminophenyl)-1*H*-pyrrol-2-yl]sulfanyl}-1-phenylethan-1-one (9). (0.12 g, 34%) as an oil (lit.[14]), identical in all respects to an authentic sample.

3.3.4. 2-{[1-(2-Hydroxylaminophenyl)-1*H*-pyrrol-2-yl]-sulfanyl}-1-phenylethan-1-one (10). (0.22 g, 58%) as a pale yellow oil, bp 168–172 °C/12 mm Hg; ν_{max} (liquid film) 3400, 1680 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 3.53 (1H, d, $J=12.4$ Hz, *H*CH), 3.69 (1H, d, $J=12.4$ Hz, HC*H*), 5.83 (2H, s, br, NHOH), 6.26 (1H, t, $J=3.3$ Hz, H-4), 6.38 (1H, dd, $J=3.3$, 1.4 Hz, H-3), 6.86 (1H, dd, $J=3.3$, 1.4 Hz, H-5), 6.98 (1H, dd, $J=7.1$, 2.4 Hz, benzenoid), 7.15 (1H, d, $J=7.6$ Hz, benzenoid), 7.37–7.44 (5H, m, benzenoid), 7.55 (1H, d, $J=7.5$ Hz, benzenoid), 7.82 (1H, dd, $J=7.6$, 1.4 Hz, benzenoid); δ_C (100 MHz; $CDCl_3$) 37.8, 115.8, 116.1, 116.9, 118.4, 119.2, 122.4, 126.7 (2C), 128.6 (2C), 130.4 (2C), 131.8, 132.2, 134.6, 142.2, 193.5; *m/z* (EI) 324 (3, M^+), 281 (39), 267 (22), 221 (49), 187 (67), 147 (100), 133 (21%); HRMS (EI): (M^+), found 324.0937. $C_{18}H_{16}N_2O_2S$ requires 324.0932.

3.3.5. Ethyl 2-{[1-(2-aminophenyl)-1*H*-pyrrol-2-yl]sulfanyl}acetate (11). (0.12 g, 37%) as an oil (lit.[14]), identical in all respects to an authentic sample.

3.3.6. Ethyl 2-{[1-(2-hydroxylaminophenyl)-1*H*-pyrrol-2-yl]sulfanyl}acetate (12). (0.17 g, 49%) as pale yellow oil, bp 151–154 °C/12 mm Hg; ν_{max} (liquid film) 2430, 1760 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 1.19 (3H, t, $J=7.1$ Hz, Me) 3.04 (2H, d, $J=7.8$ Hz, SCH_2), 4.02 (2H, q, CH_2), 5.5 (2H, s, br, NHOH), 6.29 (1H, t, $J=3.3$ Hz, H-4), 6.57 (1H, dd, $J=3.3$, 1.8 Hz, H-3), 6.86 (1H, dd, $J=3.3$, 1.8 Hz, H-5), 7.03 (1H, ddd, $J=8.0$, 7.0, 2.2 Hz, H-5′), 7.17 (1H, dd, $J=7.8$, 2.2 Hz, H-3′), 7.38–7.42 (2H, m, H-4′, H-6′); δ_C (100 MHz; $CDCl_3$) 12.9, 33.7, 60.3, 105.1, 115.1, 116.2, 116.5, 118.5, 122.3, 126.9, 128.0, 129.5, 140.4, 171.4; *m/z* (EI) 292 (14, M^+), 276 (67), 187 (57), 173 (100), 156 (70), 140 (20), 119 (10%); HRMS (EI): (M^+), found 292.0888. $C_{14}H_{16}N_2O_3S$ requires 292.0882.

3.4. Oxidation of 1-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]sulfanyl}acetone and 2-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]sulfanyl}-1-phenylethan-1-one with 2-chloroperbenzoic acid. General procedure C

To a solution of compound **2** or **3** (1.45 mmol) in dichloromethane (30 mL) was added 2-chloroperbenzoic acid (0.25 g, 1.45 mmol) and the resulting mixture was heated under reflux for 12 h. Heating was continued for 10 h during which time 2-chloroperbenzoic acid (0.03 g, 0.15 mmol) was added at hourly intervals. The solvent was evaporated under reduced pressure and to the oily residue water (30 mL) was added and the mixture extracted with dichloromethane (3×10 mL). The combined organic extracts were dried (Na_2SO_4) and the solvent removed in vacuo. Purification of the oily residue by flash chromatography (11%, 50% ethyl acetate/light petroleum) afforded 1-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]sulfonyl}acetone **13** or 2-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]sulfonyl}-1-phenylethan-1-one **15**.

3.4.1. 1-{[1-(2-Nitrophenyl)-1*H*-pyrrol-2-yl]sulfonyl}-acetone (13). (0.33 g, 74%) as a yellow oil, bp 159–162 °C/12 mm Hg; ν_{max} (liquid film) 1710, 1545, 1340, 1290, 1140 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 2.30 (3H, s, Me), 3.84 (1H, d, $J=13.2$ Hz, *H*CH), 4.06 (1H, d, $J=13.2$ Hz, HC*H*) 6.45 (1H, dd, $J=3.9$, 2.8 Hz, H-4), 6.96 (1H, dd, $J=3.9$, 2.2 Hz, H-3), 7.14 (1H, dd, $J=3.9$, 2.2 Hz, H-5), 7.63 (1H, dd, $J=7.6$, 1.5 Hz, H-6′), 7.70 (1H, ddd, $J=8.0$, 7.6, 1.5 Hz, H-4′), 7.75 (1H, ddd, $J=8.0$, 7.6, 1.6 Hz, H-5′), 8.14 (1H, dd, $J=8.0$, 1.6 Hz, H-3′); δ_C (100 MHz; $CDCl_3$) 31.0, 65.7, 111.4, 114.5, 125.3, 128.0, 130.5, 131.3, 131.5, 133.8, 134.2, 146.4, 199.3; *m/z* (EI) 308 (1, M^+), 279 (10) 235 (3), 210 (13), 188 (42), 168 (53), 143 (40), 129 (47), 102 (63), 83 (100%); HRMS (EI): (M^+), found 308.0454. $C_{13}H_{12}N_2O_5S$ requires 308.0466).

3.4.2. 2-{[1-(2-Nitrophenyl)-1*H*-pyrrol-2-yl]sulfonyl}-1-phenylethan-1-one (15). (0.36 g, 68%) as colourless plates (ethyl acetate); mp 143–144 °C [Found: C, 58.31; H, 3.85; N, 7.61. $C_{18}H_{14}N_2O_5S$ requires C, 58.37; H, 3.81; N, 7.57%]; ν_{max} (liquid film) 1680, 1540, 1340, 1325, 1240 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 3.84 (1H, d, $J=13.1$ Hz, *H*CH), 4.28 (1H, d, $J=13.1$ Hz, HC*H*), 6.32 (1H,

t, J=3.3 Hz, H-4), 6.81–6.84 (2H, m, H-3, benzenoid), 7.15 (1H, dd, J=3.3, 1.8 Hz, H-5), 7.35–7.39 (5H, m, benzenoid), 7.52 (1H, d, J=7.4 Hz, benzenoid), 7.72 (2H, m, benzenoid); δ_C (100 MHz; $CDCl_3$) 47.8, 117.2, 117.9, 119.8, 120.9, 124.1, 128.0, 130.0, 130.3 (2C), 130.6, 131.1 (2C), 133.2, 134.9, 135.3, 144.8, 180.7; *m/z* (EI) 370 (14, M^+), 317 (18), 267 (26), 198 (100), 155 (60), 113 (72%).

3.5. Reduction of 1-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]sulfonyl}acetone and 2-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]sulfonyl}-1-phenylethan-1-one with zinc dust and ammonium chloride in aqueous ethanol

Compound **13** or **15** (0.9 mmol) was dissolved in ethanol (10 mL), the solution cooled to 0 °C and treated with zinc dust (0.18 g, 2.7 mmol) and ammonium chloride (0.29 g, 5.4 mmol) according to General procedure B. The oily residue after work-up was purified by column chromatography (33% ethyl acetate/light petroleum) to give 1-{[1-(2-aminophenyl)-1*H*-2-pyrrol-2-yl]sulfonyl}acetone **14** or 2-{[1-(2-nitrosophenyl)-1*H*-pyrrol-2-yl]-sulfonyl}-1-phenylethan-1-one **16**.

3.5.1. 1-{[1-(2-Aminophenyl)-1*H*-2-pyrrol-2-yl]sulfonyl}acetone (14). (0.18 g, 73%) as colourless needles (ethanol); mp 100–101 °C; [Found: C, 56.16; H, 4.99; N, 10.02. $C_{13}H_{14}N_2O_3S$ requires C, 56.10; H, 5.07; N, 10.07%]; ν_{max} (Nujol) 3460, 3360, 1705, 1320, 1125 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 2.29 (3H, s, Me), 3.91 (2H, s, br, NH2), 4.14 (2H, s, CH2), 6.33 (1H, dd, J=3.9, 2.6 Hz, H-4), 6.87 (1H, dd, J=2.6, 1.8 Hz, H-3), 6.91 (1H, dd, J=7.9, 1.4 Hz, H-3′), 7.11 (1H, dd, J=3.9, 1.8 Hz, H-5), 7.28 (1H, ddd, J=8.8, 7.9, 1.4 Hz, H-5′), 7.47 (1H, ddd, J=8.8, 7.7, 1.3 Hz, H-4′), 7.52 (1H, dd, J=7.9, 1.3 Hz, H-6′); δ_C (100 MHz; $CDCl_3$) 31.0, 57.8, 109.3, 112.7, 113.3, 116.9, 117.6, 125.49, 126.2, 128.1, 131.4, 140.1, 197.1; *m/z* (EI) 278 (75, M^+), 221 (62), 169 (100), 142 (35%).

3.5.2. 2-{[1-(2-Nitrosophenyl)-1*H*-pyrrol-2-yl]sulfonyl}-1-phenylethan-1-one (16). (0.25 g, 77%) as pale-yellow solid (ethyl acetate/hexane); mp 49–50 °C; ν_{max} (Nujol) 1670, 1320, 1100 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 4.31 (1H, d, J=13.0 Hz, HCH), 4.44 (1H, d, J=13.0 Hz, HC*H*), 6.33 (1H, t, J=3.4 Hz, H-4), 6.81–6.84 (2H, m, H-3, benzenoid,), 6.96 (1H, s, br, benzenoid), 7.16 (1H, s, br, H-5), 7.35–7.40 (4H, m, benzenoid), 7.52 (1H, t, J=7.3 Hz, benzenoid), 7.71 (2H, s, br, benzenoid); δ_C (100 MHz; $CDCl_3$) 53.7, 112.8, 116.5, 119.6, 120.1, 121.6, 124.3, 127.5, 130.1, 130.3 (2C), 130.7, 131.2 (2C), 134.2, 134.9, 145.8, 188.7; *m/z* (EI) 355 (1, M^++1), 323 (24), 272 (74), 257 (70), 218 (59), 187 (50), 156 (80), 131 (55), 105 (100), 69 (98%); HRMS (EI): (M^++1), found 355.0730. $C_{18}H_{15}N_2O_4S$ requires 355.0752.

3.5.3. Oxidation of 1-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]sulfanyl}acetone with oxone®. To a stirred solution of **2** (0.4 g, 1.4 mmol) in acetone (30 mL) was added dropwise a solution of oxone® (0.87 g, 2.6 mmol) in water (5 mL). The mixture was left stirring for 20 min, water (40 mL) was added and extracted with chloroform (3x30 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated in vacuo to give an oily residue that was purified by column chromatography (ethyl acetate) to give 1-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]sulfinyl}acetone **26** (0.36 g, 88%) as an orange oil, bp 147–152 °C/12 mm Hg; ν_{max} (liquid film) 1710, 1520, 1330, 1220 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 2.15 (3H, s, Me) 3.86 (1H, d, J=14.2 Hz, *H*CH), 3.94 (1H, s, br, HC*H*), 6.39 (1H, t, J=3.3 Hz, H-4), 6.82 (1H, s, H-3), 6.89 (1H, d, J=3.3 Hz, H-5), 7.59–7.72 (3H, m, H-4′, H-5′, H-6′). 7.99 (1H, d, J=8.0 Hz, H-3′); *m/z* (EI) 293 (75, M^++1), 277 (53), 235 (100), 188 (65%); HRMS (EI): (M^+), found 292.0525. $C_{13}H_{12}N_2O_4S$ requires 292.0518.

3.6. Reaction of 1-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-sulfonyl}acetone and 1-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]sulfinyl}acetone with zinc dust and sodium hydroxide in aqueous ethanol. General procedure D

To a stirred solution of **13** or **26** (1.2 mmol) in ethanol (15 mL) was added a solution of sodium hydroxide (0.19 g, 4.8 mmol) in water (8 mL) and zinc dust (0.24 g, 3.6 mmol). The resulting mixture was heated under reflux over a period of 3 h, filtered, washed with hot ethanol and the filtrate evaporated to near dryness. Water (35 mL) was added to the oily residue and then extracted with dichloromethane (3× 10 mL). The combined organic extracts were dried (Na_2SO_4), evaporated in vacuo, and the oily residue was purified by column chromatography (12% ethyl acetate/light petroleum) to give in the first fraction 1-(2-nitrophenyl)(1*H*-pyrrol-2-ylsulfonyl)methane **21** and in the second fraction 1-(2-nitrophenyl)-2-methylsulfonylpyrrole **25** or (ethyl acetate) to give 1-(2-nitrophenyl)(1*H*-pyrrol-2-ylsulfinyl)methane **27**.

3.6.1. 1-(2-Nitrophenyl)(1*H*-pyrrol-2-ylsulfonyl)-methane (21). (0.15 g, 48%) as colourless needles (toluene); mp 116–118 °C; [Found: C, 49.57; H, 3.81; N, 10.57. $C_{11}H_{10}N_2O_4S$ requires C, 49.62; H, 3.79; N, 10.52%]; ν_{max} (Nujol) 3440, 1550, 1365, 1345, 1135 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 4.99 (2H, s, CH_2), 6.26 (1H, dd, J=3.8, 2.8 Hz, H-4), 6.60 (1H, dd, J=3.8, 2.6 Hz, H-3), 6.97 (1H, dd, J=2.8, 2.6 Hz, H-5), 7.39 (1H, dd, J=7.5, 1.6 Hz, H-6′) 7.54 (1H, ddd, J=9.0, 8.0, 1.6 Hz, H-4′), 7.59 (1H, ddd, J=9.0, 7.5, 1.5 Hz, H-5′), 7.99 (1H, dd, J=8.0, 1.5 Hz, H-3′), 9.18 (1H, s, br, NH); δ_C (90.5 MHz; $CDCl_3$) 59.07, 110.4, 116.8, 123.4, 124.1, 124.9, 125.3, 129.8, 133.1, 134.0, 149.4; *m/z* (EI) 266 (28, M^+), 185 (37), 154 (16), 130 (75), 78 (100%); HRMS (EI): (M^+), found 266.0358. $C_{11}H_{10}N_2O_4S$ requires 266.0361.

3.6.2. 1-(2-Nitrophenyl)-2-methylsulfonylpyrrole (25). (0.15 g, 43%) as colourless needles (toluene); mp 90–92 °C; [Found: C, 49.66; H, 3.75; N, 10.59. $C_{11}H_{10}N_2O_4S$ requires C, 49.62; H, 3.79; N, 10.52%]; ν_{max} (Nujol) 1540, 1330, 1310, 1140 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 2.93 (3H, s, Me), 6.43 (1H, dd, J=3.9, 2.8 Hz, H-4), 6.86 (1H, dd, J=2.8, 1.9, Hz, H-3), 7.13 (1H, dd, J=3.9, 1.9 Hz, H-5), 7.63 (1H, dd, J=7.7, 1.5 Hz, H-6′), 7.68 (1H, ddd, J=8.0, 6.3, 1.5 Hz, H-4′), 7.74 (1H, ddd, J=7.7, 6.3, 1.5 Hz, H-5′), 8.09 (1H, dd, J=8.0, 1.5 Hz, H-3′); δ_C (100 MHz; $CDCl_3$) 39.3, 112.9, 117.9, 118.7 (2C), 123.5, 128.1, 129.8, 132.7, 133.7, 143.7; *m/z* (EI) 266 (16, M^+), 185 (23), 136 (64), 82 (100%).

3.6.3. 1-(2-Nitrophenyl)(1*H*-pyrrol-2-ylsulfinyl)methane (27). (0.21 g, 68%) as colourless needles (toluene); mp

143–144.5 °C; [Found: C, 52.76; H, 4.05; N, 11.18. $C_{11}H_{10}N_2O_3S$ requires C, 52.79; H, 4.03; N, 11.20%]; ν_{max} (Nujol) 3450, 1510, 1230, 1040 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 4.79 (1H, d, J=12 Hz, *H*CH), 4.85 (1H, d, J=12 Hz, HC*H*), 6.14 (1H, dd, J=3.7, 2.6 Hz, H-4), 6.43 (1H, dd, J=2.6, 1.7 Hz, H-3), 6.97–7.01 (2H, m, H-5, H-6′), 7.39–7.46 (2H, m, H-4′ και H-5′), 8.06 (1H, dd, J=8.2, 1.7 Hz, H-3′), 11.34 (1H, s, br, NH); δ_C (100 MHz; $CDCl_3$) 59.5, 109.2, 114.7, 124.8, 125.3, 125.7, 125.8, 129.5, 133.5, 134.0, 148.5; *m/z* (CI) 268 (100, $M^+ + NH_3$), 251 (28, M^+), 235 (9), 203 (15).

3.7. Reaction of 1-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]-sulfonyl}acetone and 1-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]sulfinyl}acetone with sodium hydroxide in aqueous ethanol

Compound **13** or **26** (1.2 mmol) was dissolved in ethanol (15 mL) and treated with a solution of sodium hydroxide (0.19 g, 4.8 mmol) in water (8 mL) and heated under reflux over a period of 3 h. After work-up according to General procedure C, compounds **21** (0.14 g, 46%), **25** (0.14 g, 41%) or **27** (0.22 g, 72%), prepared by this method, were identical in all respects to the corresponding compounds obtained by General procedure D.

3.8. Reductive cyclisation of 1-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]sulfanyl}acetone, 2-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]sulfanyl}-1-phenylethan-1-one and 2-{[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]sulfanyl}acetonitrile with sodium borohydride and 5% palladium-on-carbon. General procedure E

A suspension of 5% palladium-on-carbon (0.06 g) in water (3 mL) was added to a stirred solution of sodium borohydride (0.3 g, 7.8 mmol) in water (6 mL) while purging with argon. A solution of **2**, **3** or **5** (1.8 mmol) in 1,4-dioxane (20 mL) was added and the mixture stirred for 30 min. After that time an aqueous solution of 2% sodium hydroxide (18 mL) was added and the mixture was stirred for 20 min. The reaction mixture was then filtered and the pH adjusted to 5–6 by the addition of ethanolic hydrogen chloride. Water (20 mL) was added to the oily solution and then extracted with dichloromethane (3×20 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated in vacuo, and the oily residue was purified by column chromatography (20% ethyl acetate/light petroleum) to give in the first fraction 6-methyl-5,6-dihydro-7*H*-pyrrolo[1,2-*a*][3.1.6]benzothiadiazocin-7-ol **31**, 6-phenyl-5,6-dihydro-7*H*-pyrrolo[1,2-*a*][3.1.6]benzothiadiazocin-7-ol **32** or 6-amino-5*H*-pyrrolo[1,2-*a*][3.1.6]benzothiadiazocine-7-oxide **36**.

3.8.1. (±)-6-Methyl-5,6-dihydro-7*H*-pyrrolo[1,2-*a*]-[3.1.6]benzothiadiazocin-7-ol (31). (0.21 g, 51%) as yellow oil, bp 136–139 °C/12 Torr; ν_{max} (liquid film) 3400 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 1.10 (3H, d, J=6.3 Hz, Me), 2.24 (2H, s, br, OH, H-5a), 2.48 (1H, d, J=12.2 Hz, H-5b), 3.65–3.70 (1H, m, H-6), [at 60 °C: 2.02 (1H, s, br, OH), 2.35 (1H, dd, J=13.2, 8.1 Hz, H-5a), 2.51 (1H, dd, J=13.2, 4.0 Hz, H-5b), 3.69 (1H, ddq, J=8.1, 6.3, 4.0 Hz, H-6)] 6.35 (1H, dd, J=3.6, 3.1 Hz, H-2), 6.58 (1H, dd, J=3.6, 1.7 Hz, H-3), 6.87 (1H, dd, J=3.1, 1.7 Hz, H-1), 7.55 (1H, dd, J=7.9, 1.4 Hz H-8), 7.61 (1H, ddd, J=9.0, 8.0, 1.4 Hz, H-10), 7.73 (1H, ddd, J=9.0, 7.7, 1.6 Hz, H-9), 8.03 (1H, d, J=8.0 Hz, H-11); δ_C (100 MHz; $CDCl_3$) 21.4 (Me), 45.6 (C-5), 65.5 (C-6), 110.1 (C-2), 110.6 (C-3), 115.9 (C-1), 119.8 (C-11), 121.4 (C-3a), 125.0 (C-8), 125.4 (C-10), 129.2 (C-9), 132.9 (C-11a), 146.7 (C-7a); *m/z* (EI) 248 (32, $M^+ + 2$), 246 (5, M^+), 173 (61), 157 (55), 131 (17), 84 (83), 49 (100%); HRMS (EI): (M^+), found 246.0825 $C_{13}H_{14}N_2OS$ requires 246.0827.

3.8.2. (±)-6-Phenyl-5,6-dihydro-7*H*-pyrrolo[1,2-*a*]-[3.1.6]benzothiadiazocin-7-ol (32). (0.33 g, 56%) as yellow oil, bp 141–145 °C/12 Torr; ν_{max} (liquid film) 3420 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 2.50 (2H, s, br, OH, H-5a), [at 60 °C: 2.55 (1H, dd, J=13.5, 9.5 Hz, H-5a), 2.69 (1H, dd, J=13.5, 3.3 Hz, H-5b), 4.57 (1H, dd, J=9.5, 3.3 Hz, H-6)], 6.36 (1H, dd, J=3.3, 3.0 Hz, H-2), 6.64 (1H, dd, J=3.3, 1.7 Hz, H-3), 6.88 (1H, dd, J=3.0, 1.7 Hz, H-1), 7.22–7.75 (9H, m, benzenoid), 8.03 (1H, d, J=7.1 Hz, H-11); δ_C (100 MHz; $CDCl_3$) 46.1 (C-5), 71.3 (C-6), 110.9 (C-2), 120.2 (C-3a), 125.1 (C-3), 125.6 (C-1), 125.9 (4C, benzenoid), 127.8 (1C, benzenoid), 128.5 (3C, benzenoid), 129.2 (1C, benzenoid), 131.2 (1C, benzenoid), 133.3 (1C, benzenoid), 142.2 (C-7a); *m/z* (CI) 343 [18, $(M+NH_4+NH_3)^+$], 340 (100), 272 (20), 221 (20), 187 (57), 171 (24), 107 (21), 83 (39%); HRMS (ESI): ($M^+ + 1$), found 309.1052. $C_{18}H_{17}N_2OS$ requires 309.1056.

3.8.3. 6-Amino-5*H*-pyrrolo[1,2-*a*][3.1.6]benzothiadiazocine-7-oxide (36). (0.21 g, 43%) as yellow powder (ethyl acetate); mp 94–96 °C [Found: C, 58.75; H, 4.53; N, 17.12. $C_{12}H_{11}N_3OS$ requires C, 58.76; H, 4.52; N, 17.14%]; ν_{max} (Nujol) 3430, 1220 cm^{-1}; δ_H (400 MHz; $CDCl_3$) 3.14 (1H, d, J=12.2 Hz, H-5a), 3.56 (1H, d, J=12.2 Hz, H-5b), 3.90 (2H, s, br, NH_2), 6.27 (1H, dd, J=3.6, 3.0 Hz, H-2), 6.57 (1H, dd, J=3.6, 1.7 Hz, H-3), 6.80 (1H, dd, J=3.0, 1.7 Hz, H-1), 7.35–7.55 (3H, m, H-9, H-10 και H-11), 7.61 (1H, d, J=7.7 Hz, H-8); δ_C (100 MHz; $CDCl_3$) 30.7 (C-5), 109.9 (C-2), 118.2 (C-3), 119.1 (C-3a), 124.0 (C-1), 126.3 (C-11), 127.5 (C-10), 128.2 (C-7), 129.0 (C-6), 129.9 (C-8), 130.6 (C-9), 136.3 (C-11a), 139.1 (C-7a); *m/z* (EI) 245 (5, M^+), 229 (38), 156 (100), 113 (30), 70 (9%).

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