Synthesis of 5,6-Dihydropyrrolo[1,2-*a*][3,1,6]thiadiazocines

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The title compounds **15-18** and **26** are prepared by intramolecular cyclisation of the pyrrolylthiols derived from sodium borohydride reduction of *N*-aryl-2-thiocyanatopyrroles **11-14** and **25**.

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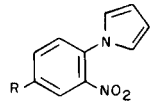
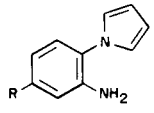
In a recent paper, we reported the thiocyanation of a series of *N*-arylpyrroles and the transformation of the resulting 2-thiocyanatopyrroles by sodium borohydride reduction to the corresponding pyrrolylthiols [1]. In the present investigation, we have prepared a series of novel pyrrolobenzothiadiazocines by a route which involves the generation of a pyrrolylthiol by this method and subsequent ring closure by nucleophilic displacement of halogen from a suitably constructed benzenoid side-chain by the intermediate thiol.

The starting materials **1-3** for these experiments were prepared by the reaction of an *o*-nitroaniline with 2,5-dimethoxytetrahydrofuran [2] and the reduction of the derived *N*-(2-nitrophenyl)pyrroles to the corresponding amines **4-6**. Compounds **4** and **5** were prepared by catalytic reduction but the chloroamine **6** could not be obtained satisfactorily by this method. This was readily prepared by reduction with zinc and formic acid.



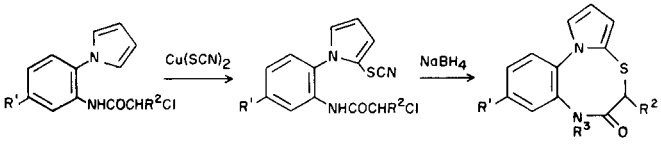
1, R = H
2, R = CH_3
3, R = Cl



4, R = H
5, R = CH_3
6, R = Cl

The amines **4-6** were smoothly chloroacetylated by reaction with chloroacetic anhydride and compound **4** was also reacted with α-chloropropionyl chloride and *p*-toluenesulphonyl chloride to give compounds **10** and **23**, respectively. The sodium salt of compound **23** was converted into the bromoethyl derivative **24** by reaction with 1,2-dibromoethane [3]. The thiocyanation of compounds **7-10** and **24** was effected with copper(II) thiocyanate and the reduction of the resulting 2-thiocyanatopyrroles **11-14** and **25** was carried out with sodium borohydride. The pyrrolyl-2-thiols so formed were not isolated since intramolecular nucleophilic displacement of side-chain halogen occurred with the formation of the thiadiazocines **15-18** and **26**.

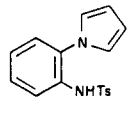
Literature precedents for thiadiazocine ring formation include the preparation of 1,4,5-benzothiadiazocines from *N*-chloroacetyl-2-mercaptobenzohydrazides [4] and 3,1,6-benzothiadiazocines from 2-isothiocyanato-*N*-tosyl-*N*-bromoethylanilines [5]. As far as we are aware, there are no previous reports of the preparation of pyrrolo[1,2-*a*]-[3,1,6]benzothiadiazocines.



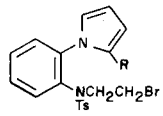
7, $R^1 = R^2 = H$
8, $R^1 = CH_3$, $R^2 = H$
9, $R^1 = Cl$, $R^2 = H$
10, $R^1 = H$, $R^2 = CH_3$

11, $R^1 = R^2 = H$
12, $R^1 = CH_3$, $R^2 = H$
13, $R^1 = Cl$, $R^2 = H$
14, $R^1 = H$, $R^2 = CH_3$

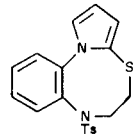
15, $R^1 = R^2 = R^3 = H$
16, $R^1 = CH_3$, $R^2 = R^3 = H$
17, $R^1 = Cl$, $R^2 = R^3 = H$
18, $R^1 = H$, $R^2 = CH_3$, $R^3 = H$
19, $R^1 = R^2 = H$, $R^3 = CH_3$
20, $R^1 = CH_3$, $R^2 = H$, $R^3 = CH_3$
21, $R^1 = Cl$, $R^2 = H$, $R^3 = CH_3$
22, $R^1 = H$, $R^2 = R^3 = CH_3$



23



24, R = H
25, R = SCN

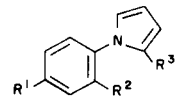


26

All new compounds were characterised by C, H and N microanalysis and by appropriate spectroscopic measurements (Tables I to IV). However two of the thiocyanates, compounds **14** and **25**, were non-crystalline and they were converted without characterisation by microanalysis into the corresponding crystalline pyrrolobenzothiadiazocines **18** and **26**. All of the thiocyanates showed infrared absorption at about 2150 cm^{-1} due to C≡N stretching and a pmr spectrum typical of an α-substituted pyrrole [1]. The methylene protons of the thiocyanates **11-13** gave rise to singlet absorption at about δ 3.9. In the derived thiadiazocines **15-17** the methylene protons are no longer equivalent and a typical AB pattern of absorption centred at about δ 3.0 and 3.4 ($J_{gem} \cong 11$ Hz) was observed. Also consistent with the displacement of side-chain chlorine was the overall up-

Table I

N-Arylpyrroles

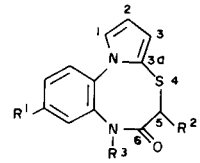


Compound	R¹	R²	R³	Mp°	Yield %	Recrystallisation Solvent	Molecular Formula	Elemental Analysis Calcd. C	H	(Found) N
7	H	$NHCOCH_2Cl$	H	152-154	88	petroleum ether (bp 80-100°)	$C_{12}H_{11}ClN_2O$	61.41 (61.40)	4.72 (4.70)	11.95 (12.05)
8	CH_3	$NHCOCH_2Cl$	H	125-127	94	petroleum ether (bp 80-100°)	$C_{13}H_{13}ClN_2O$	62.78 (62.93)	5.27 (5.21)	11.27 (11.27)
9	Cl	$NHCOCH_2Cl$	H	111-112	92	ethyl acetate-petroleum ether (bp 60-80°)	$C_{12}H_{10}Cl_2N_2O$	53.55 (53.79)	3.75 (3.70)	10.41 (10.25)
10	H	$NHCOCHCH_3Cl$	H	84-85	73	petroleum ether (bp 60-80°)	$C_{13}H_{13}ClN_2O$	62.78 (62.77)	5.27 (5.27)	11.27 (11.22)
11	H	$NHCOCH_2Cl$	SCN	113-115	80	ethyl acetate-petroleum ether (bp 60-80°)	$C_{13}H_{10}ClN_3OS$ [b]	—	—	—
12	CH_3	$NHCOCH_2Cl$	SCN	112-113	81	ethyl acetate-petroleum ether (bp 60-80°)	$C_{14}H_{12}ClN_3OS$	54.99 (54.75)	3.96 (3.86)	13.74 (13.62)
13	Cl	$NHCOCH_2Cl$	SCN	120-121	72	ethyl acetate-petroleum ether (bp 60-80°)	$C_{13}H_9Cl_2N_3OS$	47.87 (47.60)	2.78 (2.82)	12.88 (12.55)
14	H	$NHCOCHCH_3Cl$	SCN	oil	84 [a]	—	—	—	—	—

[a] The crude product was dried over phosphorus pentoxide and used as such for the preparation of thiadiazocine **18**. [b] See reference [1].

Table II

Pyrrolo[1,2-*a*][3,1,6]benzothiadiazocines



Compound	R¹	R²	R³	Mp°	Yield %	Recrystallisation Solvent	Molecular Formula	Elemental Analysis Calcd. C	H	(Found) N
15	H	H	H	193-196 (dec)	55	toluene	$C_{12}H_{10}N_2OS$	62.58 (62.49)	4.38 (4.49)	12.16 (12.30)
16	CH_3	H	H	207-208 (dec)	70	toluene	$C_{13}H_{12}N_2OS$	63.91 (63.90)	4.95 (5.20)	11.47 (11.38)
17	Cl	H	H	216-218 (dec)	62	toluene	$C_{12}H_9ClN_2OS$	54.44 (54.57)	3.43 (3.45)	10.58 (10.60)
18	H	CH_3	H	180-181	53	toluene	$C_{13}H_{12}N_2OS$	63.91 (64.23)	4.95 (4.92)	11.47 (11.48)
19	H	H	CH_3	182-184	53	ethanol-water	$C_{13}H_{12}N_2OS$	63.91 (63.68)	4.95 (4.91)	11.47 (11.60)
20	CH_3	H	CH_3	175-176	70	ethanol-water	$C_{14}H_{14}N_2OS$	64.98 (65.09)	5.45 (5.51)	10.83 (10.99)
21	Cl	H	CH_3	185-187	66	propan-2-ol	$C_{13}H_{11}ClN_2OS$	56.01 (56.28)	3.98 (4.04)	10.05 (9.90)
22	H	CH_3	CH_3	170-172	90	ethanol-water	$C_{14}N_{14}N_2OS$	64.98 (64.93)	5.45 (5.48)	10.83 (10.82)

field shift of the methylene proton absorptions. The cmr absorption spectra of the thiadiazocines are fully in accord with their proposed structures. Thus the appropriate number of signals were located in the fully decoupled spectra. On the basis of signal intensity and off-resonance measurements, individual signals could be assigned to protonated and non-protonated carbon atoms. The methylene carbon signals in compounds **15-17** appeared at about δ 34 (*cf.* methylene carbon absorption in thiocyanate precursors at about δ 43) and the low-field, low-intensity, carbonyl-carbon signals were at about δ 169. Selective decoupling of the pyrrolic protons indicated that the signals close to δ 110 were due to C-2, those close to δ 118 were due to C-3 and those near to δ 127 were due to C-1. The pyrrolic quaternary carbon C-3a, gave a low-intensity signal at about δ 119 and the signals from the benzenoid carbons appeared in the range δ 127-139 [6].

Table III

PMR of Pyrrolo[1,2-*a*][3,1,6]benzothiadiazocines

Compound	
15	3.03 (d, H-5a, J_{gem} = 9.9 Hz), 3.42 (d, H-5b, J_{gem} = 9.9 Hz), 6.18 (dd, H-2), 6.40 (dd, H-3), 7.00 (dd, H-1), 7.30-7.60 (m, benzenoid), 9.31 (s, NH)
16	2.37 (s, CH_3), 3.03 (d, H-5a, J_{gem} = 10.8 Hz), 3.46 (d, H-5b, J_{gem} = 10.8 Hz), 6.20 (dd, H-2), 6.40 (dd, H-3), 6.96 (dd, H-1), 7.07-7.52 (m, benzenoid), 9.38 (s, NH)
17	2.88 (d, H-5a, J_{gem} = 11.7 Hz), 3.30 (d, H-5b, J_{gem} = 11.7 Hz), 6.00 (dd, H-2), 6.23 (dd, H-3), 6.83 (dd, H-1), 7.22-7.48 (m, benzenoid), 9.18 (s, NH)
18	1.40 (d, CH_3, J = 7.0 Hz), 3.75 (q, H-5, J = 7.0 Hz), 6.40 (dd, H-2), 6.56 (dd, H-3), 7.06 (dd, H-1), 7.38-7.80 (m, benzenoid), 9.50 (s, NH)
19	2.83 (s, NCH_3), 3.21 (d, H-5a, J_{gem} = 9.9 Hz), 3.54 (d, H-5b, J_{gem} = 9.9 Hz), 6.25 (dd, H-2), 6.54 (dd, H-3), 6.86 (dd, H-1), 7.24-7.64 (m, benzenoid)
20	2.48 (s, CH_3), 2.84 (s, NCH_3), 3.21 (d, H-5a, J_{gem} = 10.0 Hz), 3.57 (d, H-5b, J_{gem} = 10.0 Hz), 6.23 (dd, H-2), 6.52 (dd, H-3), 6.85 (dd, H-1), 7.17-7.48 (m, benzenoid)
21	2.69 (s, NCH_3), 3.09 (d, H-5a, J_{gem} = 10.8 Hz), 3.40 (d, H-5b, J_{gem} = 10.8 Hz), 6.12 (dd, H-2), 6.39 (dd, H-3), 6.70 (dd, H-1), 7.20-7.45 (m, benzenoid)
22	1.36 (d, CH_3, J = 6.0 Hz), 2.81 (s, NCH_3), 3.87 (q, CH, J = 6.0 Hz), 6.23 (dd, H-2), 6.47 (dd, H-3), 6.85 (dd, H-1), 7.25-7.65 (m, benzenoid)

[a] Spectra of compounds **15-18** measured in DMSO-d_6, spectra of compounds **19-22** measured in deuteriochloroform. [b] Values of $J_{1,2} \cong 2.9$ Hz, $J_{2,3} \cong 3.8$ Hz and $J_{1,3} \cong 1.7$ Hz were observed. [c] All signals integrated for the correct number of protons.

The mass spectra of all new compounds showed the expected molecular ions, fragmentation of the molecular ions from the pyrrolobenzothiadiazocines **15-18** and **26** occurred not unexpectedly by rupture of the eight-membered ring. Thus fragment ions resulting from the loss of CHO, $COCH_2$, and $CHOCH_2$ from the molecular ion of the parent thiadiazocine **15** were observed.

Table IV

CMR of Pyrrolo[1,2-*a*][3,1,6]benzothiadiazocines

Compound	
15	34.1 (C-5), 109.5 (C-2), 117.5 (C-3), 119.4 (C-3a), 126.7 (C-1), 127.3 [b], 128.8 [b], 129.4 [b,c], 135.0 [d], 139.0 [d], 168.4 (C=O)
16	34.0 (C-5), 109.3 (C-2), 117.3 (C-3), 119.3 (C-3a), 126.6 (C-1), 126.9 [b], 129.3 [b], 129.6 [b], 134.6 [d], 136.3 [d], 139.3 [d], 168.4 (C=O), 20.4 (C-CH_3)
17	34.2 (C-5), 109.8 (C-2), 117.9 (C-3), 119.3 (C-3a), 126.8 (C-1), 128.6 [b], 128.9 [b], 129.3 [b], 133.1 [c], 136.2 [c], 137.9 [c], 168.2 (C=O)
18	39.7 (C-5), 109.5 (C-2), 117.3 (C-3), 120.4 (C-3a), 126.5 (C-1), 127.0 [b], 129.0 [b], 129.4 [b], 129.8 [b], 134.5 [d], 139.3 [d], 170.6 (C=O), 17.0 (C-CH_3)
19	35.7 (C-5), 110.4 (C-2), 119.1 (C-3), 120.4 (C-3a), 125.7 (C-1), 128.0 [b], 128.6 [b], 129.7 [b], 130.1 [b], 139.1 [d], 141.5 [d], 167.4 (C=O), 37.0 (N-CH_3)
20	35.7 (C-5), 110.3 (C-2), 118.8 (C-3), 120.4 (C-3a), 125.7 (C-1), 127.7 [b], 128.9 [b], 130.4 [b], 136.4 [d], 140.6 [d], 141.2 [d], 167.5 (C=O), 21.2 (C-CH_3), 37.0 (N-CH_3)
21	35.6 (C-5), 110.8 (C-2), 119.4 (C-3), 120.3 (C-3a), 125.6 (C-1), 128.9 [b,c], 130.0 [b], 135.3 [d], 137.8 [d], 142.4 [d] 167.1 (C=O), 37.0 (N-CH_3)
22	41.8 (C-5), 110.4 (C-2), 118.7 (C-3), 122.0 (C-3a), 125.3 (C-1), 127.7 [b], 129.0 [b], 129.7 [b], 130.1 [b], 139.3 [d], 141.1 [d], 169.8 (C=O), 17.2 (C-CH_3), 37.0 (N-CH_3)

[a] Spectra of compounds **15-18** were measured in DMSO-d_6; spectra of compounds **19-22** were measured in deuteriochloroform. [b] Protonated benzenoid carbon. [c] Overlapping signals. [d] Quaternary benzenoid carbon.

A preliminary study has been made of the chemistry of the thiadiazocines. As would be expected of cyclic amides such as compounds **15-18**, treatment with methyl iodide and sodium methoxide furnished the corresponding *N*-methyl derivatives **19-22**. The eight-membered ring was stable to oxidation with sodium *meta*-periodate and peracids. Thus the sulphoxide of compound **19** was obtained by oxidation with sodium metaperiodate and the corresponding sulphone by oxidation with excess of *m*-chloroperbenzoic acid [4].

Experiments in progress are aimed at synthesising derivatives of related 5,6,7- and 5,6,9-ring systems, also a fuller exploration of the chemistry of these novel compounds is being carried out.

EXPERIMENTAL

The ir spectra of solids were taken as Nujol mulls and liquids as thin films between sodium chloride discs. Nmr spectra were measured in deuteriochloroform unless otherwise stated. Mass spectral measurements were recorded on a Kratos MS 25 machine equipped with a DS 50 S data system. The compounds listed in Tables I and II all gave the expected molecular ions.

N-(2-Nitrophenyl)pyrrole (**1**) and *N*-(2-aminophenyl)pyrrole (**4**) were prepared by the published procedure [2].

N-(2-Amino-4-methylphenyl)pyrrole (**5**).

A mixture of 4-methyl-2-nitroaniline (30 g, 0.20 mole), 2,5-dimethoxytetrahydrofuran (26 g, 0.20 mole) and glacial acetic acid (140 ml) was heated under reflux for 30 minutes. After removal of solvent, the residue was vacuum-distilled to give *N*-(4-methyl-2-nitrophenyl)pyrrole (**2**) (22.3 g), bp 146-152°/0.2 mm as an orange oil which crystallised on cooling. The distillate was used without further purification and dissolved in ethanol (300 ml). The solution was hydrogenated at 3 atmospheres for 6 hours over 10% palladium-on-charcoal (0.5 g). After removal of the catalyst by filtration, the filtrate was evaporated to dryness. Crystallisation of the residue from light petroleum (bp 60-80°) gave *N*-(2-amino-4-methylphenyl)pyrrole (13.6 g, 72%) as colourless needles, mp 89-90°; ir: 3390, 3300 cm^{-1} (NH_2).

Anal. Calcd. for $C_{11}H_{12}N_2$: C, 76.71; H, 7.03; N, 16.27. Found: C, 76.79; H, 6.92; N, 16.24.

N-(2-Amino-4-chlorophenyl)pyrrole (**6**).

N-(4-Chloro-2-nitrophenyl)pyrrole (**3**) (bp 152-154/0.2 mm, mp 53-54°) was prepared in a similar manner to compound **2** above from 4-chloro-2-nitroaniline and 2,5-dimethoxytetrahydrofuran. The distilled product was used without further purification and a 15 g portion was dissolved in methanol (850 ml) and 90% formic acid (30 ml) and powdered zinc (45 g) added to the vigorously stirred solution. After 5 minutes, the warm reaction mixture was filtered and the residue washed with hot methanol (100 ml). The combined filtrate and washings were reduced in volume to *ca.* 25 ml by distillation under reduced pressure (bath temperature <45°) Water (100 ml) was added and the precipitate of *N*-(2-amino-4-chlorophenyl)pyrrole filtered off. Crystallisation from light petroleum (bp 60-80°) gave colourless needles, (10.25 g, 79%), mp 88-90°; ir: 3380, 3310 cm^{-1} (NH_2).

Anal. Calcd. for $C_{10}H_9ClN_2$: C, 62.34; H, 4.71; N, 14.54. Found: C, 62.38; H, 4.72; N, 14.55.

Chloroacetylation of *N*-(2-Aminophenyl)pyrroles.

To a warm stirred solution of the aminophenylpyrrole (0.05 mole) in glacial acetic acid (45 ml), chloroacetic anhydride (0.056 mole) was added in portions. Stirring was continued for 1.5 hours and then the reaction mixture was poured into ice-water (150 ml). The crystalline product was filtered off, washed with water, air dried and purified by recrystallisation. The chloroacetamido pyrroles **7-9** prepared by this procedure are listed in Table I.

N-[2-(2'-Chloropropionamido)phenyl]pyrrole (**10**).

A solution of 2-chloropropionyl chloride (5.95 g, 0.047 mole) in dry dioxane (20 ml) was added dropwise, at room temperature, to a stirred solution of *N*-(2-aminophenyl)pyrrole (7.40 g, 0.047 mole) in dry dioxane (50 ml). A stream of nitrogen gas was bubbled continuously through the stirred reaction mixture and after 12 hours it was poured into ice-water (200 ml). The solid was filtered off, washed with water, air dried, and purified by crystallisation (Table I).

Thiocyanation of *N*-Arylpyrroles.

The 2-thiocyanatopyrroles **11-14** were prepared by the published procedure [1] using copper(II) thiocyanate and are listed in Table I. The reaction was monitored by tlc, reaction times of up to 30 hours were necessary until all of the starting material had been consumed [7].

Synthesis of Pyrrolobenzothiadiazacines **15-18**.

To a stirred suspension of the appropriate *N*-(2-chloroacetamidophenyl) 2-thiocyanatopyrrole **11**, **12** or **13** (0.013 mole) in ethanol (150 ml), kept under a continuous stream of nitrogen, was added in portions sodium borohydride (0.032 mole). Stirring was continued for 3 hours at room temperature and then the reaction mixture was reduced in volume to 20 ml by vacuum-distillation. Water (100 ml) was added followed by 10% aqueous acetic acid to adjust the *p*H to 6. The precipitated product was either isolated by filtration or by extraction with chloroform. The pyrrolothiadiazocines **15-17** were purified by crystallisation (see Table II).

N-[2-(2-chloropropionamido)phenyl]2-thiocyanatopyrrole (**14**) was converted into the pyrrolobenzothiadiazocine **18** by a similar procedure. In this case the starting material (0.016 mole) was dissolved in ethanol (200 ml) and treated with sodium borohydride (0.040 mole).

N-(2-Toluene-*p*-sulphonamidophenyl)pyrrole (**23**).

To a stirred solution of *N*-(2-aminophenyl)pyrrole (**4**) (15 g, 0.095 mole) in dry pyridine (70 ml), freshly recrystallised *p*-toluenesulphonyl chloride (18.30 g, 0.096 mole) was added in portions. The reaction mixture was heated under reflux for 6 hours in an atmosphere of dry nitrogen, then cooled, and diluted with water (50 ml). After adjusting the *p*H to 1.5 by addition of 10% hydrochloric acid, the product was extracted into chloroform (3 × 30 ml). The combined extracts were treated with charcoal, dried (magnesium sulphate) and solvent removed by vacuum distillation. The pale-yellow crystalline residue was recrystallised from chloroform:-petroleum ether (bp 60-80°) (1:4) to give the product (22.92 g, 78%), mp 110-112°; ir: 3300 cm^{-1} (NH), 1320 (unsym SO_2), 1150 (sym SO_2); nmr: δ 2.35 (s, CH_3), 6.28-7.87 (m, pyrrolic, benzenoid and NH); ms: 312 (M^+).

Anal. Calcd. for $C_{17}H_{16}N_2O_2S$: C, 65.36; H, 5.16; N, 8.97. Found: C, 64.99; H, 5.22; N, 9.11.

Bromoethylation of *N*-(2-Toluene-*p*-sulphonamidophenyl)pyrrole (**23**).

The pyrrole **23** (14 g, 0.045 mole) was added to a solution of sodium ethoxide [prepared from sodium (0.98 g, 0.045 g-atom) and ethanol (150 ml)]. The mixture was heated under reflux for 30 minutes then concentrated to 20 ml and diluted with ether (40 ml). The crystalline sodium salt (11.22 g, 0.0335 mole, 75%) was filtered off and dissolved in *N,N*-dimethylformamide (60 ml), 1,2-dibromoethane (6.31 g, 0.0335 mole) was added and the mixture stirred and heated at 110° for 3 hours. After cooling, the product was precipitated by pouring into a solution of sodium hydroxide (5.38 g, 0.013 mole) in water (120 ml). Crystallisation (charcoal) from propan-2-ol gave the bromoethyl compound **24** (10.75 g, 77%), mp 130-131°. The analytical sample, prepared by recrystallisation from the same solvent, was obtained as colourless needles, mp 131-132°; nmr: δ 2.50 (s, CH_3), 3.04 (t, CH_2N), 3.54 (t, CH_2Br), 6.34 (t, H-3 and H-4), 6.97 (t, H-2 and H-5), 7.01-7.51 and 7.68-7.85 (m, benzenoid); ms: 419 (M^+).

Anal. Calcd. for $C_{19}H_{19}BrN_2O_2S$: C, 54.52; H, 4.57; N, 6.68. Found: C, 54.57; H, 4.50; N, 6.69.

5,6-Dihydro-7-toluene-*p*-sulphonylpyrrolo[1,2-*a*][3,1,6]benzothiadiazocine (**26**).

A suspension of the pyrrole **24** (8 g, 0.019 mole) in ethanol (500 ml) was cooled to 0-2° and kept under a continuous stream of nitrogen while copper(II) thiocyanate (17.05 g, 0.095 mole) was added portionwise. The reaction mixture was then stirred at 7° for a further 72 hours in an atmosphere of nitrogen, filtered, and solvent removed by vacuum-distillation. The viscous, orange, oily residue of the thiocyanate **25** showed ir absorption at 2150 cm^{-1} (SC≡N). A portion (4.0 g, 0.009 mole) was redissolved in ethanol (150 ml) and the solution stirred and kept in an atmosphere of nitrogen while sodium borohydride (0.8 g, 0.02 mole) was added gradually. Stirring was continued at room temperature for 7 hours, the mixture was then left overnight, concentrated to about 20 ml, and diluted with water (60 ml). The product was extracted into chloroform (3 × 20 ml), and evaporation of the combined and dried extracts gave a crude solid (3.49 g) which on crystallisation from propan-2-ol gave the thiadiazocine **26** (2.38 g, 34%), mp 147-149°. Tan needles of mp 149-150° were obtained by recrystallisation from the same solvent; pmr: δ 2.39 (s, CH_3), 2.53-3.52 and 4.29-4.56 (m, NCH_2CH_2S), 6.32 (dd, H-2), 6.59 (dd, H-3), 6.94 (dd, H-1), 7.02-7.59 (m, benzenoid); cmr: δ 21.5 (CH_3), 38.3 (CH_2-S), 54.5 (CH_2-N), 109.6 (C-2), 119.1 (C-3), 122.9 (C-3a), 125.9 (C-1), 127.8, 128.9, 129.5, 129.8, 129.9, 136.6, 137.8, 140.9, 143.6 [8]; ms: 370 (M^+).

Anal. Calcd. for $C_{19}H_{18}N_2O_2S$: C, 61.60; H, 4.90; N, 7.56. Found: C, 61.48; H, 4.84; N, 7.27.

Methylation of Thiadiazocines **15-18**.

The thiadiazocine (0.008 mole) followed by methyl iodide (0.032 mole) were added to methanolic sodium methoxide (prepared from 0.008 g atom of sodium and 40 ml of methanol). The reaction mixture was stirred at room temperature for 24 hours and then concentrated to 20 ml before dilution with ice-water (50 ml). The precipitate of 7-methylthiadiazocine **19-22** was filtered off and purified by crystallisation (Table II).

Oxidation of 5,6-Dihydro-7-methyl-6-oxopyrrolo[1,2-*a*][3,1,6]benzothiadiazocine (**19**). (a) With Sodium Metaperiodate.

A solution of sodium metaperiodate (1.29 g, 0.006 mole) in water (10 ml) was added to the thiadiazocine **19** (1.50 g, 0.006 mole) in ethanol (75 ml). The mixture was heated at 80° for 12 hours and then a further portion of sodium metaperiodate (0.6 g, 0.0028 mole) in water (5 ml) was added. After continued heating at 80° for 12 hours, the precipitate was filtered off and the filtrate concentrated to 20 ml. Water (20 ml) was added and the product collected by filtration. Crystallisation from toluene gave the *S*-oxide (1.34 g, 84%), mp 230-232°. The mp was raised to 231-232° by recrystallisation from the same solvent; ir: 1655 cm^{-1} (C=O); nmr: δ 2.99 (s, NCH_3), 3.63 (d, H-5a, J_{gem} = 11.7 Hz), 4.41 (d, H-5b, J_{gem} = 11.7 Hz), 6.35 (dd, H-2), 6.90-7.00 (m, H-1 and H-3), 7.10-7.80 (m, benzenoid); ms: 260 (M^+).

Anal. Calcd. for $C_{13}H_{12}N_2O_2S$: C, 59.98; H, 4.65; N, 10.76. Found: C, 60.17; H, 4.59; N, 10.42.

(b) With *m*-Chloroperbenzoic Acid.

A mixture of the thiadiazocine **19** (1.0 g, 0.004 mole) and *m*-chloroperbenzoic acid (0.875 g, 0.004 mole) in dichloromethane (50 ml) was heated under reflux for 12 hours. During the next 10 hours, 0.1 g portions of *m*-chloroperbenzoic acid were added at 1 hourly intervals to the refluxing mixture. After cooling, excess of aqueous sodium hydrogen carbonate was added, the organic layer was separated, washed with water, dried (magnesium sulphate), and concentrated to about 5 ml. The product was filtered off and crystallisation from acetonitrile:water (1:1) gave the *S,S*-dioxide (0.72 g, 64%), mp 263-264°; ir: 1670 cm^{-1} (C=O), 1315 (unsym SO_2), 1120 (sym SO_2); nmr (DMSO-d_6): δ 2.99 (s, NCH_3), 4.03 (d, H-5a, J_{gem} = 12.6 Hz), 4.32 (d, H-5b, J_{gem} = 12.6 Hz), 6.45 (dd, H-2), 7.06 (dd, H-3), 7.37 (dd, H-1), 7.62-7.82 (m, benzenoid); ms: 276 (M^+).

Anal. Calcd. for $C_{13}H_{12}N_2O_3S$: C, 56.51; H, 4.38; N, 10.14. Found: C, 56.81; H, 4.40; N, 10.34.

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[6] These assignments are also supported by some unpublished work on the cmr of pyrrolo[1,2-*a*]quinoxalines by G. W. H. Cheeseman and J. Cobb.

[7] A recent paper by M. Kakushima and R. Frenette, *J. Org. Chem.*, **49**, 2025 (1984) reports the preparation of *N*-tosyl-2-thiocyanatopyrrole using thiocyanogen chloride as the thiocyanating agent.

[8] The signals from the four quaternary benzenoid carbons appeared at δ 136.6, 137.8, 140.9 and 143.6. The signals from the remaining eight protonated benzenoid carbons were not fully resolved.