Synthesis of some Pyrrolobenzothiadiazonines

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Received July 22, 1987

Four pyrrolobenzothiadiazonines, compounds **6**, **10**, **16** and **24**, have been prepared from 1-substituted-2-thiocyanatopyrrole intermediates.

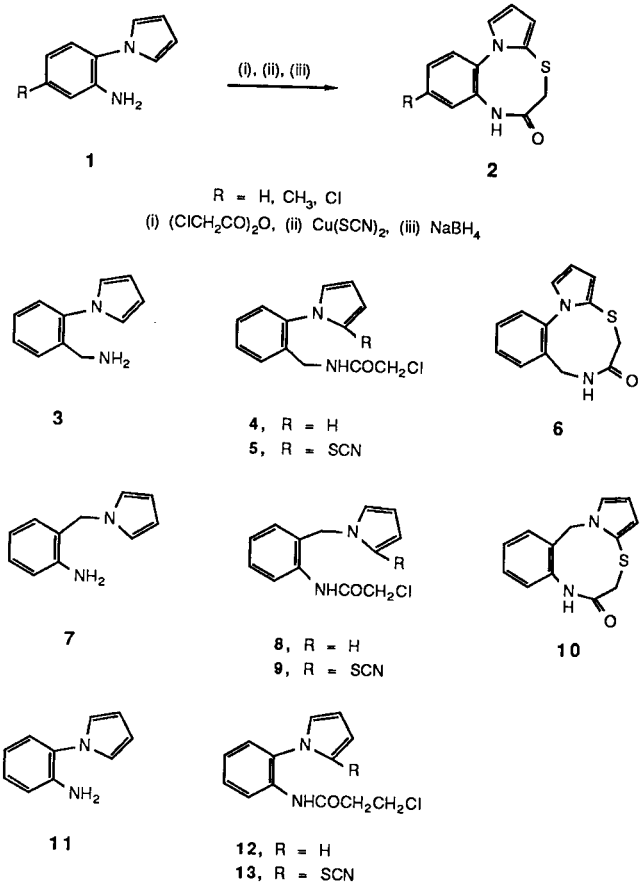
J. Heterocyclic Chem., **25**, 431 (1988).

In our earlier work we showed that pyrrolobenzothiadiazocines of type **2** could be prepared from 1-(2-aminophenyl)pyrroles **1** by a three step synthesis involving chloroacetylation, thiocyanation and reductive ring closure of the resulting 2-thiocyanatopyrrole [1]. In the final step, reduction with sodium borohydride caused cleavage of the thiocyanate to give a pyrrolylthiol which then underwent ring closure by intramolecular nucleophilic displacement of chlorine.

We now report that our method can be applied to the synthesis of the novel structurally related pyrrolobenzothiadiazonines **6** and **10**. Compound **6** was prepared from 1-(2-aminomethylphenyl)pyrrole **3** [2] by chloroacetylation, thiocyanation of the resulting chloroacetyl derivative **4** with copper(II) thiocyanate and finally treatment of the 2-thiocyanatopyrrole **5** with sodium borohydride. A similar sequence of reactions based on 1-(2-aminobenzyl)pyrrole **7** [3] gave the thiadiazonine **10** *via* the intermediates **8** and **9**. In the light of these observations we had anticipated that reductive ring closure of the thiocyanate **13** derived from the 3-chloropropionyl derivative **12** of 1-(2-aminophenyl)pyrrole **11** would yield the thiadiazonine **16**. However when this reaction was attempted only amorphous material was obtained. This difficulty was circumvented by the use of the thiocyanate **14** [4] as starting material. The latter compound underwent both cleavage of its thiocyanate and amide groups on treatment with sodium borohydride [5] so that subsequent reaction of the resulting 2-aminophenylpyrrolyl thiol with ethyl 3-bromopropionate gave the amino ester **15**. The required lactam **16** was smoothly formed when the amino ester was treated with trimethylaluminium [6].

Two additional routes to thiadiazonines were explored using 1-(2-*p*-toluenesulphonylaminophenyl)pyrrole **17** as starting material. Reaction of the sodium salt of this compound with 3-chloropropionyl chloride gave mainly the vinyl amide **18** rather than the expected chloropropionyl derivative. It was subsequently found that the vinylamide was conveniently prepared by interaction of the sodium salt of **17** and 2-propenoyl chloride. Thiocyanation of **18** furnished the 2-thiocyanatopyrrole **19** but treatment of the latter compound with sodium borohydride yielded an intractable reaction mixture from which it was not possible to isolate the hoped-for thiadiazonine **20**. We do not know if our difficulties arise from our failure to achieve selective reduction of the thiocyanato group of **19** or from reluctance of the intermediate pyrrolyl thiol to undergo intramolecular nucleophilic addition to the adjacent α,β-unsaturated carbonyl system.

The thiadiazonine **24** was successfully synthesised from the sodium salt of **17**. Our attempts to bromopropylate this compound by reaction with 1,3-dibromopropane did not yield the required product but the chloropropyl derivative



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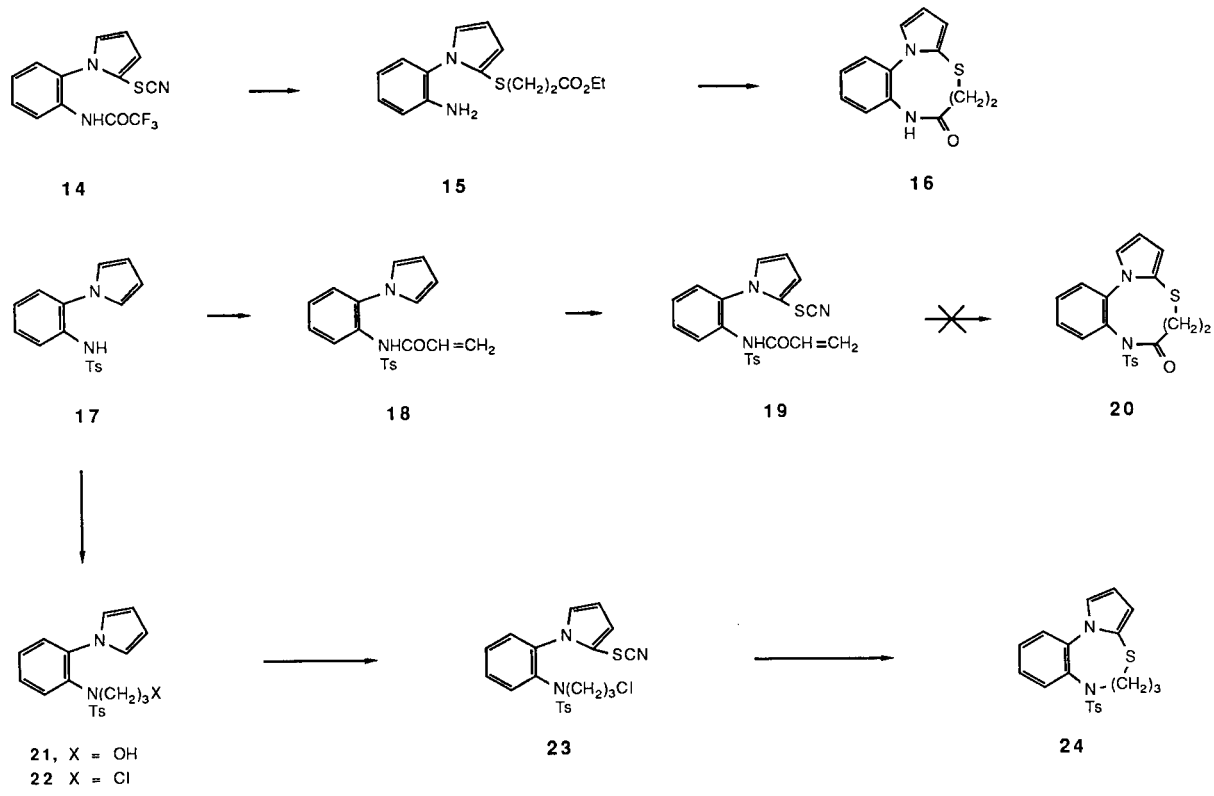

22 was obtained by chlorination of the hydroxypropyl compound **21** isolated from reaction of the sodium salt with 3-bromopropan-1-ol. Chlorination was carried out using carbon tetrachloride and triphenylphosphine, but phosphorus trichloride could not be used to effect this conversion. Thiocyanation of **22** gave the expected 2-thiocyanatopyrrole **23** and this on sodium borohydride reduction gave the thiadiazonine **24**. In the four successful ring-closure reactions cited, those leading to compounds **6**, **10**, **16** and **24**, the yields of thiadiazonines varied from 56 to 79%. It thus appears that the nine-membered ring in these compounds is formed with comparable ease to the eight-membered ring in the analogous pyrrolobenzothiadiazocines **2**.

Structural assignments for all new compounds were supported by measurement of their elemental composition, mass spectra and ^1H and ^{13}C nmr spectra. A characteristic loss of 74 a.m.u. was noted from the molecular ions of the thiadiazonines **6** and **10** and 88 a.m.u. from the thiadiazonine **16**, presumably due to the cleavage of the fragments -S-CH_2-CO- and -S-CH_2-CH_2-CO-, respectively. Proton-decoupled ^{13}C nmr spectra were used to confirm carbon content and DEPT routines employed as an additional check on carbon content and classification. For example, compound **16** was found to contain two methylene carbons at 36.6 and 37.8 ppm, seven methine carbons at 110.5, 119.3, 125.6, 129.3, 129.4, 129.5 and 130.2 ppm and four quaternary carbon atoms at 123.3, 136.0, 140.3 and 175.0 ppm. A detailed account of our nmr measurements and assignments will be published in a further paper.

EXPERIMENTAL

All melting points are uncorrected. The ir spectra of solids were taken as Nujol mulls and liquids as thin films between sodium chloride discs. The ^1H nmr spectra were measured on either a Perkin Elmer R 32 or Brucker WM 250 spectrometer, ^{13}C nmr spectra were measured on either a Brucker WP 60 or WM 250 spectrometer. Deuteriochloroform (unless otherwise stated) was used as solvent and TMS as an internal standard. All signals integrated for the expected number of protons. Mass spectral measurements were recorded on a Kratos MS 25 machine equipped with a DS 55 data system. Column chromatography was carried out using Merck 7734 silica gel.

1-[2-(2-Chloroacetylaminomethyl)phenyl]pyrrole **4**.

To a stirred solution of the aminomethylphenylpyrrole **3** [2] [14.0 g, 0.08 mole) in glacial acetic (85 ml) at 40°, chloroacetic anhydride (14.7 g, 0.086 mole) was added in portions. Stirring was continued for 1.5 hours and then the reaction mixture was poured into ice-water (300 ml). The crystalline product was filtered off, washed with water, dried and then recrystallised from ethanol-water (5:3) to give the chloroacetylaminomethylphenylpyrrole **4** (18.01 g, 89%) as colourless needles, mp 91-92°; ir: 3225 cm^{-1} (NH), 1660 (C = O); nmr: δ 3.91 (s, CH_2Cl), 4.36 (d, J = 6 Hz, CH_2N), 6.33 (t, H-3, H-4), 6.65 (s, br, NH, deuterium oxide exchangeable), 6.83 (t, H-2, H-5), 7.25-7.60 (m, benzenoid); ms: 248 (M^+), 212 (248 -HCl), 155 (248 -NH_2COCH_2Cl).

Anal. Calcd. for $C_{13}H_{13}ClN_2O$: C, 62.78; H, 5.27; N, 11.26. Found: C, 62.79; H, 5.32; N, 11.23.

5,6-Dihydro-8*H*-6-oxopyrrolo[1,2-*a*][3,1,6]benzothiadiazonine **6**.

To a stirred suspension of 1-[(2-chloroacetylaminomethyl)phenyl]-

pyrrole **4** (8.95 g, 0.036 mole) in absolute ethanol (250 ml) under nitrogen at 4°, was added in portions copper(II) thiocyanate (19.4 g, 0.10 mole). The mixture was stirred at 7° for 60 hours, copper(I) thiocyanate was then filtered off, washed several times with hot ethanol and the combined filtrates reduced in volume to 50 ml by vacuum distillation, before pouring into ice-water (250 ml). The oil which separated was extracted with chloroform (3 x 20 ml) dried (magnesium sulphate) and after evaporation of the solvent the residue was absorbed onto a silica gel column. Elution with a 1:1-mixture of ethyl acetate and petroleum ether (bp 60-80°) gave an eluant from which the thiocyanate **5** was obtained as an oil (8.61 g, 78%); ir: 3280 cm^{-1} (NH), 2140 (SCN), 1650 (C=O). A portion (5.8 g, 0.019 mole) was redissolved in ethanol (150 ml) and the solution stirred and kept in an atmosphere of nitrogen while sodium borohydride (1.6 g, 0.04 mole) was added in portions over 0.5 hours. Stirring was continued for 3 hours, the suspension was then reduced in volume to 40 ml by vacuum distillation, poured into ice-water (150 ml), acidified to *p*H 5 with glacial acetic acid and then filtered, washed well with water and dried. Recrystallisation form ethanol-water (5:1) gave clusters of colourless needles of the thiadiazonine **6** (2.96 g, 64%), mp 205-206°; ir: 3180 cm^{-1} (NH), 1650 (C=O); nmr (DMSO-d_6): δ 3.39 (d, H-5a, J_{gem} = 14.3 Hz), 3.57 (d, H-5b, J_{gem} = 14.3 Hz), 3.76 (dd, H-8a, J_{gem} = 10.3 Hz), 4.00 (dd, H-8b, J_{gem} = 10.3 Hz), 6.34 (dd, H-2), 6.65 (dd, H-3), 7.11 (dd, H-1), 7.18-7.77 (m, benzenoid), 8.34 (q, NH, deuterium oxide exchangeable); ms: 244 (M^+), 170 (244 -SCH_2CO).

Anal. Calcd. for $C_{13}H_{12}N_2OS$: C, 63.91; H, 4.95; N, 11.46. Found: C, 63.66; H, 4.97; N, 11.36.

1-(2-Chloroacetylamino)benzylpyrrole **8**.

The chloroacetylation of 1-(2-aminobenzyl)pyrrole **7** [3] was carried out in an identical manner to the chloroacetylation of the aminomethylphenylpyrrole **3** above. The recrystallised product was obtained as colourless needles in 64% yield and had mp 116-118°; ir: 3250 cm^{-1} (NH), 1650 (C=O); nmr: δ 4.07 (s, CH_2N), 5.02 (s, CH_2Cl), 6.19 (t, H-3, H-4), 6.61 (t, H-2, H-5), 7.0-7.81 (m, benzenoid), 7.98 (s, br, NH, deuterium oxide exchangeable); ms: 248 (M^+).

Anal. Calcd. for $C_{13}H_{13}ClN_2O$: C, 62.78; H, 5.27; N, 11.26. Found: C, 62.48; H, 5.25; N, 11.12.

1-(2-Chloroacetylamino)benzyl-2-thiocyanatopyrrole **9**.

To a suspension of 1-benzylpyrrole **8** (3.5 g, 0.014 mole) in absolute ethanol (150 ml) under nitrogen and at 2°, copper(II) thiocyanate (7.6 g, 0.042 mole) was added portionwise. Stirring was continued at 7° for 36 hours, white copper(I) thiocyanate was filtered off, washed with hot ethanol several times and then the combined alcohol extracts were reduced in volume to 60 ml before pouring into ice-water (200 ml). The solid which separated was filtered off and air dried. Crystallisation from ethanol-water (1:1) afforded the product **9** (3.38 g, 78%) as colourless needles, mp 113-115°; ir: 3290 cm^{-1} (NH), 2155 (SCN), 1680 (C=O); nmr: δ 4.15 (s, CH_2N), 5.24 (s, CH_2Cl), 6.26 (dd, H-4), 6.76 (dd, H-3), 6.80-7.60 (H-5 and benzenoid), 8.17 (s, br, NH, deuterium oxide exchangeable); ms: 305 (M^+), 256 (305 -CH_2Cl), 182 (305 -$C_4H_3N.SCN$).

Anal. Calcd. for $C_{14}H_{12}ClN_3OS$: C, 54.99; H, 3.96; N, 13.74. Found: C, 54.65; H, 3.92; N, 13.78.

5,6-Dihydro-12*H*-6-oxopyrrolo[2,1-*e*][4,1,6]benzothiadiazonine **10**.

To a stirred suspension of 1-benzylpyrrole **9** (2.5 g, 0.0082 mole) in absolute ethanol (80 ml) under nitrogen was added sodium borohydride (0.77 g, 0.02 mole) over a period of 0.5 hours. The mixture was stirred for 3 hours at room temperature and then the volume reduced to 15 ml before pouring into ice-water (50 ml). The suspension was acidified to *p*H 5 with glacial acetic acid then cooled for several hours. The solid was filterd off washed with water and air-dried. It was crystallised from toluene to give colourless microneedles of the thiadiazonine **10** (1.58 g, 79%) mp 203-204°; ir : 3150 cm^{-1} (NH), 1655 (C=O); nmr (DMSO-d_6): δ 3.01 (d, H-12a, J_{gem} = 11 Hz), 3.33 (d, H-12b, J_{gem} = 11 Hz), 4.74 (d, H-5a, J_{gem} = 14 Hz), 5.47 (d, H-5b, J_{gem} = 14 Hz), 6.04 (dd, H-2), 6.36 (dd, H-3), 6.74 (dd, H-1), 6.90-7.72 (m, benzenoid), 9.09 (s, NH, deuterium oxide exchangeable); ms: 244 (M^+), 170 (244 -SCH_2CO).

Anal. Calcd. for $C_{13}H_{12}N_2OS$: C,63.91; H, 4.95; N, 11.46. Found: C, 64.04; H, 4.90; N, 11.42.

1-[2-(3-Chloropropionylamino)phenyl]pyrrole **12**.

To a stirred solution of 1-(2-aminophenyl)pyrrole **11** [2] (6.0 g, 0.038 mole) in dry dioxan (30 ml) under nitrogen at room temperature, was added dropwise a solution of 3-chloropropionylchloride (3.62 ml, 0.038 mole) in dry dioxan (15 ml). After the addition was complete, the mixture was stirred for 2.5 hours at ambient temperature. Water (80 ml) was then added and the resulting crystalline material filtered off, washed with water and air-dried. Recrystallisation from petroleum ether (bp 60-80°) gave colourless needles of the product **12** (5.18 g, 55%), mp 101-102°; ir: 3200 cm^{-1} (NH), 1665 (C=O); nmr: δ 2.63 (t, $COCH_2$), 3.77 (t, CH_2Cl), 6.38 (t, H-3, H-4), 6.77 (t, H-2, H-5), 7.03-7.52 (m, 3H, benzenoid and NH, deuterium oxide exchangeable), 8.23-8.44 (m, 1H, benzenoid); ms: 248 (M^+), 185 (248 -CH_2CH_2Cl), 157 (185 -CO).

Anal. Calcd. for $C_{13}H_{13}ClN_2O$: C, 62.78; H, 5.27; N, 11.26. Found: C, 62.75; H, 5.23; N, 11.31.

1-[2-(3-Chloropropionylamino)phenyl]-2-thiocyanatopyrrole **13**.

The thiocyanation of the chloropionylaminophenylpyrrole **12** was carried out in essentially the same way as for the chloroacetylaminomethylphenylpyrrole **4**, except that an oil was obtained after evaporation of the chloroform extracts. Trituration of this oil with diethyl ether at −30° gave a pale yellow solid which crystallised (charcoal) from cyclohexane to give the thiocyanate **13** as clusters of colourless needless, yield 56%, mp 87.5-88.5°; ir: 3220 cm^{-1} (NH), 2175 (SCN), 1680 (C=O); nmr: δ 2.59 (t, $COCH_2$), 3.68 (t, CH_2Cl), 6.42 (dd, H-4), 6.58 (dd, H-3), 6.92 (s, NH, deuterium oxide exchangeable), 6.97 (dd, H-5), 7.17-7.62 (m, 3H, benzenoid), 8.15-8.33 (m, 1H, benzenoid); ms: 305 (M^+), 247 (305 -SCN).

Anal. Calcd. for $C_{14}H_{12}ClN_3OS$: C, 54.99; H, 3.96; N, 13.74. Found: C, 54.70; H, 3.77; N, 13.56.

Ethyl 3-[1-(2-Aminophenyl)-2-pyrrolylthio]propionate **15**.

To a stirred solution of 1-(2-trifluoroacetylaminophenyl)-2-thiocyanatopyrrole **14** [4] (1.5 g, 0.005 mole) in absolute ethanol (50 ml), kept under nitrogen, sodium borohydride (0.79 g, 0.021 mole) was added in portions over a period of 25 minutes. The mixture was stirred at room temperature for another hour and then acetone (25 ml) was added slowly and stirring continued for a further hour. To the resulting stirred, dark reaction mixture, ethyl 3-bromopropionate (0.99 g, 0.0055 mole) in absolute ethanol (10 ml) was added. The mixture was heated under reflux for one hour and then concentrated to 20 ml. Aqueous sodium chloride solution (25 ml) was added and the crude product was extracted with dichloromethane (3 x 15 ml). The combined extracts were dried (magnesium sulphate) and evaporated. The residual oil was absorbed on a silica gel column. Two minor impurities were removed by elution with a 1:2-mixture of ethyl acetate and petroleum ether (bp 60-80°). Continued elution with the same solvent mixture gave an eluate which after evaporation and crystallisation of the residue from petroleum ether (bp 60-80°) yielded the product **15** as yellow needles (0.93 g, 64%), mp 64-65°; ir: 3450, 3360 cm^{-1} (NH_2), 1720 (ester C=O); nmr: δ 1.21 (t, CH_3), 2.30-2.80 (m, CH_2CH_2), 3.46 (s, br, NH_2, deuterium oxide exchangeable), 4.08 (q, OCH_2), 6.28 (dd, H-4), 6.54 (dd, H-3), 6.63-7.35 (m, H-5 and benzenoid); ms: 290 (M^+), 245 (290 -OC_2H_5), 189 (290 -$CH_2CH_2CO_2C_2H_5$), 157 (290 -$SCH_2CH_2CO_2C_2H_5$).

Anal. Calcd. for $C_{15}H_{18}N_2O_2S$: C, 62.04; H, 6.25; N, 9.65. Found: C, 62.20; H, 6.22; N, 9.69.

6,7-Dihydro-5*H*-6-oxopyrrolo[1,2-*a*][3,1,7]benzothiadiazonine **16**.

To a stirred solution of amino ester **15** (1.29 g, 0.0045 mole) in dry dichloromethane (40 ml) under a continuous stream of nitrogen, was slowly added trimethylaluminium in hexane (3 ml, 0.006 mole, 2*M* solution). The mixture was stirred for 16 hours at room temperature, after which, dilute acetic acid was added dropwise until the *p*H was 5. Water (10 ml) was then added, the aqueous phase separated and extracted with di-

chloromethane (3 x 15 ml). The combined organic extracts were then dried (magnesium sulphate) and evaporated to give an oil which was absorbed on a silica gel column. Two minor impurities were removed by elution with a 1:1-mixture of ethyl acetate and petroleum ether (bp 60-80°). Continued elution with the same solvent mixture gave an eluate which on evaporation and crystallisation of the residue from toluene gave the product **16** as colourless plates (0.61 g, 56%), mp 214-215°; ir: 3030 cm^{-1} (NH), 1660 (C=O); nmr: δ 2.30-2.63 (m, H-5a, H-5b and H-6a), 3.12-3.22 (m, H-6b), 6.32 (dd, H-2), 6.57 (dd, H-3), 6.73 (dd, H-1), 7.26-7.58 (m, benzenoid), 7.82 (s, NH, deuterium oxide exchangeable); ms: 244 (M^+), 227 (244 -OH), 188 (244 $-COCH_2CH_2$), 156 (244 $-COCH_2CH_2S$).

Anal. Calcd. for $C_{13}H_{12}N_2OS$: C, 63.91; H, 4.95; N, 11.46. Found: C, 63.99; H, 5.08; N, 11.42.

1-{2-[*N*-(2-Propenoyl)-*p*-toluenesulphonylamino]phenyl}pyrrole **18**.

Method A.

To a stirred solution of the sodium salt of 1-(2-*p*-toluenesulphonylaminophenyl)pyrrole **17** [1] (4 g, 0.012 mole) in dry *N,N*-dimethylformamide (40 ml) under nitrogen, was added dropwise a solution of 3-chloropropionyl chloride (1.36 ml, 0.014 mole) in dry *N,N*-dimethylformamide (10 ml). The mixture was stirred for 2.5 hours at room temperature and then the solvent evaporated under reduced pressure to dryness. Water (50 ml) was added and the crude material extracted with chloroform (3 x 20 ml), the combined organic extracts were dried (magnesium sulphate) and evaporated to give an oil. The two major components of the oily residue the product **18** (1.55 g, 35%) and starting material **17** (1.64 g, 41%) were separated by column chromatography using silica gel and a 1:2-mixture of ethyl acetate and petroleum ether (bp 60-80°) as eluant. Crystallisation of the product from propan-2-ol gave colourless needles of vinyl amide **18** (1.35 g, 31%), mp 150-151°; ir: 1685 cm^{-1} (C=O), 1615 (C=C), 1360 (unsym SO_2), 1170 (sym SO_2); nmr: δ 2.38 (s, CH_3), 5.56-7.63 (m, vinylic, pyrrolic and benzenoid); ms: 366 (M^+), 311 (366 $-COCH=CH_2$).

Anal. Calcd. for $C_{20}H_{18}N_2O_3S$: C, 65.56; H, 4.95; N, 7.64. Found: C, 65.72; H, 5.11; N, 7.65.

Method B.

To a stirred solution of 2-propenoyl chloride (1.6 ml, 0.020 mole) in dry *N,N*-dimethylformamide (20 ml) under nitrogen, was added dropwise a solution of the sodium salt of amide **17** (6.41 g, 0.019 mole) in dry *N,N*-dimethylformamide (50 ml). Stirring was continued for 12 hours and then the reaction mixture worked up as in Method A, without the need for column chromatography. Instead the oil was dissolved in hot propan-2-ol and then cooled in the refrigerator for several hours to give the product **18** (4.01 g, 57%) indentical in all respects to the vinyl amide prepared by Method A.

1-{2-[*N*-(2-Propenoyl)-*p*-toluenesulphonylamino]phenyl}-2-thiocyanatopyrrole **19**.

To a stirred suspension of vinyl amide **18** (4.42 g, 0.012 mole) in absolute ethanol (200 ml) at 0° and under nitrogen, was added portionwise freshly prepared, dry copper(II) thiocyanate (6.51 g, 0.036 mole) and the mixture was stirred vigorously at 7° for 1 week. Copper(I) thiocyanate was filtered off washed well with hot ethanol and the combined ethanol filtrates concentrated *under vacuo* to 70 ml before pouring into ice-water (250 ml). The crude product (1.32 g) which precipitated was filtered off and air-dried. A further portion of crude product (2.05 g) was obtained by continuous extraction of the copper(I) thiocyanate with ethanol. The combined crude product was dissolved in chloroform and absorbed onto a silica gel column. Elution with a 1:2-mixture of ethyl acetate and petroleum ether (bp 60-80°) gave two main fractions. From the first fraction starting material **18** (0.82 g, 16%) was recovered and from the second fraction thiocyanate **19** (2.07 g, 41%) was obtained as yellow prisms, mp 159-160°, after recrystallisation from ethanol; ir: 2150 cm^{-1} (SCN), 1695 (C=O), 1615 (C=C), 1360 (unsym SO_2), 1170 (sym SO_2); nmr: δ 2.42 (s, CH_3), 5.60-7.80 (m, vinylic, pyrrolic and benzenoid); ms: 423 (M^+), 365 (423 -SCN).

Anal. Calcd. for $C_{21}H_{17}N_3O_3S_2$: C, 59.56; H, 4.05; N, 9.92. Found: C, 59.47, 57.02; H, 3.85, 3.88; N, 9.26, 10.05 [7].

1-{2-[*N*-(3-Hydroxypropyl)-*p*-toluenesulphonylamino]phenyl}pyrrole **21**.

To a stirred solution of sodium (0.85 g, 0.037 mole) in dry methanol (100 ml) was added 1-(2-*p*-toluenesulphonylaminophenyl)pyrrole **17** [1] (11.57 g, 0.037 mole) and the mixture refluxed for 30 minutes before it was concentrated to 25 ml. To the cooled solution, ether was added to the point of precipitation. Colourless needles of the sodium salt of **17** (10.8 g, 87%) were filtered off, washed with ether and dried.

A mixture of the sodium salt (6 g, 0.018 mole), 3-bromopropan-1-ol (2.64 g, 0.0192 mole) and *N,N*-dimethylformamide (40 ml) was stirred and heated at 120° for 12 hours. After cooling, the mixture was poured into a solution of sodium hydroxide (0.3 g, 0.007 mole) in water (60 ml) and then extracted with chloroform (3 x 15 ml). The combined extracts were dried (magnesium sulphate), evaporated and the residue absorbed onto a silica gel column. Elution with a 1:1-mixture of ethyl acetate and chloroform gave two main fractions. From the second the hydroxypropyl derivative **21** (5.03 g, 76%) was obtained as colourless needles, mp 104-105°, after recrystallisation from ethanol-water; ir: 3550 cm^{-1} (OH), 1330 (unsym SO_2), 1150 (sym SO_2); nmr: δ 1.16-1.52 (m, CH_2), 1.83 (s, OH, deuterium oxide exchangeable), 3.17-3.54 (m, NCH_2 and CH_2O), 6.30 (t, H-3 and H-4), 6.87-7.85 (m, H-2, H-5 and benzenoid); ms: 370 (M^+), 215 (370 $-SO_2C_6H_4CH_3$), 197 (215 $-H_2O$).

Anal. Calcd. for $C_{20}H_{22}N_2O_3S$: C, 64.84; H, 5.99; N, 7.56. Found: C, 64.50; H, 5.94; N, 7.40.

1-{2-[*N*-(3-Chloropropyl)-*p*-toluenesulphonylamino]phenyl}pyrrole **22**.

To a solution of the hydroxypropylpyrrole **21** (1.87 g, 0.005 mole) in dry chloroform (20 ml) was added a solution of triphenylphosphine (2.65 g, 0.01 mole) in dry carbon tetrachloride (25 ml) under an atmosphere of nitrogen. The mixture was refluxed for 12 hours after which it was concentrated to a small volume and the solution passed through a silica gel column. Elution with a 1:1-mixture of ethyl acetate and petroleum ether (bp 60-80°) gave an eluate which on evaporation yielded the chloropropyl derivative **22**. Crystallisation from propan-2-ol furnished (1.05 g, 53%) of colourless needles mp 142-143°; ir: 1330 cm^{-1} (unsym SO_2), 1140 (sym SO_2); nmr: δ 1.40-1.80 (m, CH_2), 2.46 (s, CH_3), 3.03-3.52 (m, NCH_2 and CH_2Cl), 6.31 (t, H-3, H-4), 6.90-7.82 (m, H-2, H-5 and benzenoid): ms: 388 (M^+), 233 (388 $-SO_2C_6H_4CH_3$), 170 (233 $-CH_2CH_2Cl$).

Anal. Calcd. for $C_{20}H_{21}ClN_2O_2S$: C, 61.77; H, 5.44; N, 7.20. Found: C, 61.91; H, 5.41; N, 6.89.

1-{2-[*N*-(3-Chloropropyl)-*p*-toluenesulphonylamino]phenyl}-2-thiocyanatopyrrole **23**.

To a stirred suspension of chloropropylpyrrole **22** (1.05 g, 0.0027 mole) in absolute ethanol (30 ml) at 2° and kept under a continuous stream of nitrogen, was added in portions copper(II) thiocyanate (1.5 g, 0.008 mole). The mixture was stirred at 7° for 14 hours the white copper(I) thiocyanate was then filtered off and washed several times with hot ethanol. The combined filtrates were evaporated to 20 ml and poured into ice-water (50 ml). The white solid was filtered off, air dried and recrystallised from propan-2-ol and water to give the thiocyanatopyrrole **23** (0.73 g, 61%) as clusters of colourless needles mp 117-118°; ir: 2150 cm^{-1} (SCN), 1330 (unsym SO_2), 1140 (sym SO_2); nmr: δ 1.50-1.90 (m, CH_2), 2.46 (s, CH_3), 3.10-3.52 (m, NCH_2 and CH_2Cl), 6.42 (dd, H-4), 6.73-7.78 (m, H-3, H-5 and benzenoid); ms: 445 (M^+), 385 (445 -SCN), 290 (445 $-SO_2C_6H_4CH_3$), 227 (290 $-CH_2CH_2Cl$).

Anal. Calcd. for $C_{21}H_{20}ClN_3O_2S_2.H_2O$: C, 54.35; H, 4.94; N, 9.01. Found: C, 54.36; H, 4.78; N, 9.05.

5,6,7,8-Tetrahydro-8-*p*-toluenesulphonylpyrrolo[1,2-*a*][3,1,7]benzothiadiazonine **24**.

To a suspension of thiacyanatopyrrole **23** (0.58 g, 0.0013 mole) in absolute ethanol (20 ml) under a stream of nitrogen, was added sodium borohydride (0.1 g, 0.003 mole) over 15 minutes. Stirring was continued for 5 hours at room temperature, water (40 ml) was then added and the

mixture acidified to *p*H 6 with glacial acetic acid. The solid was filtered off, air-dried, dissolved in the minimum of chloroform and the solution absorbed on a silica gel column. Elution with a 1:2-mixture of ethyl acetate and petroleum ether (bp 60-80°) gave an eluate which after evaporation and crystallisation of the residue from propan-1-ol, yielded the thiadiazonine **24** (0.28 g, 56%) as colourless clusters of needles, mp 169-171°; ir: 1340 cm^{-1} (unsym SO_2), 1150 (sym SO_2); nmr: δ 1.60-1.80 (m, H-6a), 1.95-2.05 (m, H-6b), 2.30-2.40 (m, H-5a), 2.43 (s, CH_3), 2.48-2.83 (m, H-5b), 3.28-3.43 (m, H-7a and H-7b), 6.35 (dd, H-2), 6.57 (dd, H-3), 7.05 (dd, H-1), 7.12-7.52 (m, benzenoid); ms: 384 (M^+), 229 (384 $-SO_2C_6H_4CH_3$).

Anal. Calcd. for $C_{20}H_{20}N_2O_2S_2$: C, 62.47; H, 5.24; N, 7.29. Found: C, 62.68; H, 5.16; N, 7.39.

Acknowledgements.

We thank the British Council for financial assistance to G. Varvounis; J. Cobb, J. Hawkes and F. Gallway for nmr measurements; W. Gunn and A. Cakebread for mass spectra and S. Denton for microanalytical data.

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[7] Compound **19** gave variable elemental analysis results.