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Reaction of *sym*-Tetracyanoethane with Isothiocyanates. Synthesis of Bis(2-Amino-1-aryl-3,4-dicyanopyrrol-5-yl)disulphide

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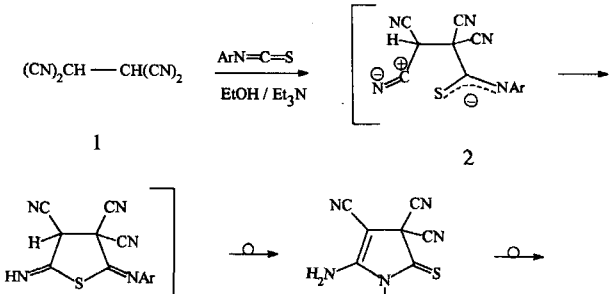
Owing to high toxicity and preparation difficulty, 1,1,2,2-tetracyanoethane has had over years a rather limited use in organic synthesis. Its possible applicability to heterocyclization reactions was noticed first by Middleton [1, 2] who obtained thiophene derivatives in the reaction of tetracyanoethylene with hydrogen sulphide and thiols. *sym*-Tetracyanoethane formed by hydrogenation of the C=C bond in the substrate was postulated as having been the actual active intermediate [1, 2]. This view got much support in the research on tetracyanoethylene hydrogenation with hydrogen sulphide or mercaptoacetic acid [3].

An extensive research on the use of *sym*-tetracyanoethane in the synthesis of carbo- and heterocyclic compounds was initiated by Nasakin [4] only a few decades later. The same author developed also a simple and efficient method for preparing this compound by hydrogenation of tetracyanoethylene with dialkylphosphine [5, 6].

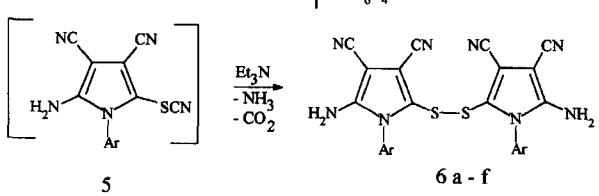
As a continuation of our research on the synthesis [7] and structure [8, 9] of thioamides as well as on the use of thioamides in the synthesis of heterocyclic systems [10] we present now results concerning the reaction of *sym*-tetracyanoethane with aromatic isothiocyanates.

The reaction of *sym*-tetracyanoethane with aromatic isothiocyanates, carried out in ethanol or acetonitrile in the presence of catalytic amounts of triethylamine, yielded bis(2-amino-1-aryl-3,4-dicyanopyrrol-5-yl)disulphides (**6**). With aliphatic isothiocyanates, decomposition of the reaction products occurred under similar conditions. When the reaction with aromatic isothiocyanates was carried out in isopropanol-water 2:1 under mild conditions (60 °C), in absence of triethylamine, the intermediate 2-amino-1-aryl-3,4,4-tricyano-4,5-dihydropyrrol-5-thione (**4a,b**) were isolated.

The reaction seems to follow the mechanism outlined in Scheme 1. In the first step, the thioamide **2** is formed, which is resonance-stabilised by the aromatic substituent. This explains the failure noted with aliphatic isothiocyanates. Similar reactions of isothiocyanates with other CH-acidic compounds were reported earlier [11]. The thioamides **2** cyclize to the unstable 2-amino-3,4,4-tricyano-4,5-dihydro-thiophenes (**3**) which undergo Dimroth rearrangement to **4**. These products, can be isolated in the absence of strong base. However, in the presence of bases such as triethylamine or pyridine, compounds **4** undergo aromatization to the unstable 2-amino-1-aryl-3,4-dicyano-5-thiocyanopyrrole (**5**) which are oxidised to the disulphides **6**. An analogous conversion of aromatic thiocyanantes into disulphides promoted by triethylamine – or pyridine – was described by Hoggarth [12]. In our case, migration of CN to the sulphur atom results in the formation of the aromatic pyrrole derivative **5**. The conversion of **4** into **6** can be also effected by heating with acetic acid in the presence of triethylamine, i.e. under the conditions reported by Hoggarth [12].



4	Ar	% Yield
a	C_6H_5	53
b	4-ClC_6H_4	60



6	Ar	% Yield		Ar	% Yield
a	4-Cl-C_6H_4	29	d	4-Me-C_6H_4	28
b	4-Me-C_6H_4	27	e	4-MeO-C_6H_4	26
c	4-Br-C_6H_4	28	f	a-naphthyl	31

In addition to routine spectral identification, the structures of **4a** and **6a** were confirmed by X-ray analyses (Figure 1, 2).

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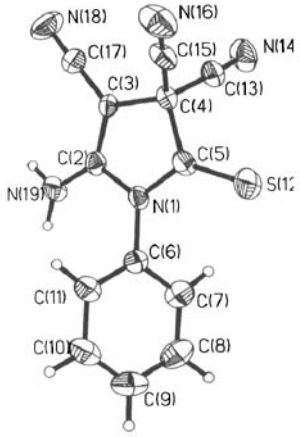

Fig. 1 Molecular structure of **4a**.
Selected bond lengths [Å]: N(1)-C(2) 1.407(3), N(1)-C(5) 1.363(3), N(1)-C(6) 1.443(3), C(2)-C(3) 1.352(4), C(4)-C(5) 1.552(4), C(3)-C(4) 1.506(3), C(5)-S(12) 1.619(2); selected bond angles [^{0}]: C(5)-N(1)-C(2) 111.5(2), C(5)-N(1)-C(6) 124.1(2), C(2)-N(1)-C(6) 124.2(2), N(1)-C(5)-S(12) 128.8(2).

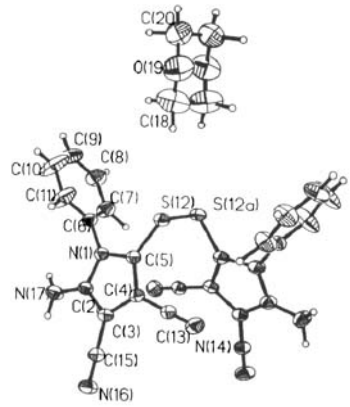

Fig. 2 Molecular structure of **6a**
Selected bond lengths [Å]: N(1)-C(2) 1.364(2), N(1)-C(5) 1.390(2), N(1)-C(6) 1.442(2), C(2)-C(3) 1.394(2), C(4)-C(5)1.380(2), C(5)-S(12) 1.715(2), S(12)-S(12a) 2.117(1); selected bond angles [^{0}]: C(2)-N(1)-C(5) 109.9(1), N(1)-C(2)-C(3) 107.8(2), C(2)-C(3)-C(4) 107.1(2), N(1)-C(5)-S(12) 125.7(1), C(5)-S(12)-S(12a) 102.57(6).

Experimental

Melting points: uncorrected. Infrared spectra: Specord M80; KBr pellets. ^{1}H and ^{13}C NMR: Bruker DPX - 400 spectrometer; DMSO-d_6 with TMS as internal standard.
Crystallographic measurements: KM-4 difrractometer with MoK_α radiation for **4a** (71.033pm) and CuK_α for **6a** (154.178pm). Two reflections were used as standards and remeasured during the data collections; no crystal decomposition was observed. The structures were solved by direct methods using the programs SHELXS-86 [13] and refined on F^2 by the full-matrix last-squares method (SHELL-93) [14], initially isotropically. The positions of all H atoms were found from Δp maps at the and of the anisotropic refinement. They were refined isotrophically.
Crystal data for **4a** [13]: $C_{13}H_7N_5S$, mol.mass 265.30, T=293(2)K, crystal size: 0.03×0.035×0.045 cm, monoclinic, $P2_1/n$ space group, a = 1096.5(2) pm, b = 1262.8(3) pm, c = 1090.9(2) pm, b = 118.40(3)°, Z = 4, d_x = 1.326 g×cm^{-3}, $\mu(MoK_\alpha)$ = 2.36cm^{-1}, F(000) = 544, final R = 0.045 for 1686 reflections with $F^2 > 4\delta(F^2)$.
Crystal data for **6a** [14]: $C_{24}H_{14}N_8S_2 \cdot C_4H_8O_2$, mol.mass 566.66, T = 293(2)K, crystal size: 0.02×0.02×0.04 cm, monoclinic, C2/c space group, a = 1388.2(3)pm, b = 1632.8(3)pm, c = 1279.2(2)pm, ß = 101.33(2)°, Z = 4, d_x=1.324 g×cm^{-3}, $\mu(CuK_\alpha)$ = 20.35cm^{-1}, F(000) = 1176, final R = 0.033 for 2157 reflectionswith $F^2 > 4\delta(F^2)$.
Further information on the X-ray structure determination may be obtained from the Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaflich - technische Information mbH, D - 76344 Eggenstein - Leopoldshafen, on quoting the registration number CSD -59255 the name of the authors and the journal citation.

1,1,2,2-Tetracyanoethane

Tetracyanoethylene (10 g) was added portionwise below 25 °C to the stirred mixture of 25 ml of diethylphosphine and 15 ml of acetic acid. Stirring was continued until the color reaction with hydroquinone was negative. Alternatively, the mixture was stirred 1h at 23 °C and then left at 5 °C for 12h. Dilution with H_2O (100 ml) afforded a precipitate which was filtered off, washed with H_2O, dried *in vacuo* over H_2SO_4 and recrystallized from dioxane (30 ml).
Yield: 9.0 g (89%) of colorless crystals; m.p. 168–169 °C (dec.), (Lit.[13]: 166–168 °C).

2-Amino-1-aryl-3,4,4-tricyano-4,5-dihydropyrrole-5-thione (4) (General Procedure)

The aryl isothiocyanate (0.01 mole) and then tetracyanoethane (1.3 g, 10 mmole) were added at 50 °C with stirring to isopropanol–H_2O (2:1, 30 ml). In the case of solid isothiocyanates (*e.g.* 4-chloro-phenyl isothiocyanate) tetracyanoethane should not be added until the isothiocyanate is completely melted and well dispersed in the solvent. Stirring was continued at 50 °C for 15 min. After 12h at 23 °C a yellow powder was filtered off, washed with dilute ethanol and recrystallized from dioxane (20 – 25 ml). Column chromatography on silica with $CHCl_3$–THF (1:1) as eluent followed by crystallization from dioxane (20 ml) gave the pure product.
2-Amino-1-phenyl-3,4,4-tricyano-4,5-dihydropyrrole-5-thione (**4a**). Yield: 1.4 g (53%), m.p. 215–217 °C (dec.), yellow crystals. – IR (KBr): ν = 3420, 3290, 3220, 3140 (NH_2), 2200 (C=N), 1670 (C=N) cm^{-1}. – ^{1}H-NMR (DMSO - d_6): δ = 7.50–7.62 (m, 5H, aryl), 8.28 (br., NH_2). – ^{13}C-NMR (DMSO-d_6): δ = 50.7, 51.8 (C-3, C-4), 111.5 (4-CN), 114.4

(3-CN), 160.1 (C-2), 187.8 (C-5), 126.4, 130.0, 130.6, 132.7 (aryl).

2-Amino-1- (4-chlorophenyl)-3,4,4-tricyano-4,5-dihydropyrrole-5-thione (**4b**). Yield: 1.8 g (60%), m.p. 230–232 °C (dec.), yellow crystals. – IR (KBr): ν = 3390, 3280, 3220, 3170 (NH_2), 2200 (C=N), 1670 (C=N) cm^{-1}. – ^{1}H-NMR (DMSO-d_6): δ = 7.62 (2H, aryl), 7.68 (2H, aryl), 8.3 (br., NH_2). – ^{13}C-NMR (DMSO-d_6): δ = 50.7, 51.8 (C-3, C-4), 111.4 (4-CN), 114.4 (3-CN), 160.1 (C-2), 187.8 (C-5), 130.1, 130.6, 131.7, 135.4 (aryl).

Bis-(2-amino-1-aryl-3,4-dicyanopyrrol-5-yl) disulphides (6) (General procedures)

a) Tetracyanoethane (1.3 g, 0.01 mole) and the isothiocyanate (10 mmol) were dissolved in ethanol (20 ml) at 60 °C. Triethylamine (1 ml) was added under stirring.The mixture was left at 23 °C for 1–2h. Filtration and recrystallization from nitromethane furnished the pure compounds.

b) A solution or suspension of **4** (10 mmole) in ethanol (20 ml) was treated under stirring with 1–2 ml of triethylamine. The solution, which turned dark, was stirred at 60 °C for 1 min and then left for 1h at 23 °C. Filtration and recrystallization from nitromethane afforded the orange product.

Bis-(2-amino-1-phenyl-3,4-dicyanopyrrol-5-yl) disulphide (**6a**). Yield:0.69 g (29%) of orange crystals, m.p. 275–276 °C (dec.). – IR (KBr): ν = 3450, 3330, 3190 (NH_2), 2216 (C=N), 1640 (C=N) cm^{-1}. – ^{1}H-NMR (DMSO-d_6): δ = 7.0(br., 4H, aryl), 7.51–7.61 (m, 6H, aryl). 7.33 (br., 4H, NH_2). – ^{13}C-NMR (DMSO-d_6): δ = 151.8 (C-2), 73.3(C-3), 107.3(C-4), 120.2(C-5), 112.4 and 113.7(3-CN, 4-CN), 128.4, 129.5, 129.6, 132.7 (aryl).

Bis-[2-amino-1-(4-chlorophenyl)-3,4-dicyanopyrrol-5-yl] disulphide (**6b**). Yield: 0.74 g (27%) of orange crystals, m.p. 314–316 °C (dec.). – IR (KBr): ν = 3420, 3330, 3240, 3190 (NH_2), 2216 (C=N), 1634 (C=N) cm^{-1}. – ^{1}H-NMR (DMSO-d_6): δ: = 7.13 (s, 4H, NH_2), 7.38 (4H, aryl), 7.66 (4H, aryl). – ^{13}C-NMR (DMSO-d_6); δ = 152.0 (C-2), 73.2 (C-3), 107.8 (C-4), 119.8 (C-5), 112.4, 113.5 (3-CN, 4-CN), 129.7, 130.4, 131.6, 134.6 (aryl).

Bis-[2-amino-1-(4-bromophenyl)-3,4-dicyanopyrrol-5-yl] disulphide (**6c**). Yield: 0.89 g (28%) of orange crystals, m.p. 294–296 °C (dec.). – IR (KBr): ν = 3430, 3340, 3237, 3180 (NH_2), 2216 (C=N), 1628 (C=N) cm^{-1}. – ^{1}H-NMR (DMSO-d_6): δ = 7.13 (s, 4H, NH_2), 7.31 (4H, aryl), 7.80 (4H, aryl). – ^{13}C-NMR (DMSO-d_6): δ = 152.0 (C-2), 73.2 (C-3), 107.7 (C-4), 119.7 (C-5), 112.3, 113.5 (3-CN, 4-CN), 123.3, 130.7, 132.0, 132.6 (aryl).

Bis-[2-amino-1-(4-methylphenyl)-3,4-dicyanopyrrol-5-yl] disulphide (**6d**). Yield 0.71 g (28%) of orange crystals, m.p. 267–269 °C (dec.). – IR (KBr): ν = 3400, 3340, 3240, 3180 (NH_2), 2216 (C=N), 1640 (C=N). – ^{1}H-NMR (DMSO-d_6): δ = 2.83 (6H, CH_3), 6.95 (4H, NH_2), 7.19(m, 4H, aryl), 7.36 (m, 4H, aryl). – ^{13}C-NMR (DMSO-d_6): δ = 151.8 (C-2), 73.2 (C-3), 107.2 (C-4), 120.2 (C-5), 20.8 (CH_3), 112.5, 113.7 (3-CN, 4-CN), 128.2, 130.0, 130.2, 139.5 (aryl).

Bis-[2-amino-1-(4-methoxyphenyl)-3,4-dicyanopyrrol-5-yl] disulphide (**6e**). Yield: 0.7 g (26%) of orange crystals, m.p. 289–291°C (dec.). – IR (KBr): ν = 3435, 3340, 3240, 3180 (NH_2), 2216 (C=N), 1627 (C=N) cm^{-1}. – ^{1}H-NMR (DMSO-d_6): δ = 3.80 (6H, OCH_3), 6.95 (4H, NH_2), 7.09 (m, 4H, aryl), 7.24 (m, 4H, aryl). – ^{13}C-NMR (DMSO-d_6): δ = 152.0 (C-2), 73.0 (C-3), 107.7 (C-4), 120.7 (C-5), 55.5 (OCH_3), 112.5, 113.8 (3-CN, 4-CN), 114.7, 125.2, 129.8, 159.9 (aryl).

Bis-(2-amino-1-naphthyl-3,4-dicyanopyrrol-5-yl) disulphide (**6f**). Yield: 0.9 g (31%) of yiellow crystals, m.p. 233-234 °C (dec.). – IR (KBr): ν = 3450, 3330, 3237, 3180 (NH_2), 2224 (C=N), 1634 (C=N) cm^{-1}. – ^{1}H-NMR (DMSO-d_6): δ = 7.00–8.10 (m, 18H, NH_2, aryl). – ^{13}C-NMR (DMSO-d_6): δ =152.3 (C-2), 73.5 (C-3), 106.8 (C-4), 121,7 (C-5), 112.7, 113.9 (3-CN, 4-CN), 112.7, 113.9, 125.4, 126.7, 127.5, 128.0, 128.1, 128.2, 129.0, 129.6, 130.6, 133.8 (aryl).

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