On the Dithiocyanation of Pyrrole

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Some years ago one of us (E.S.) investigated the thiocyanation of aromatic compounds with thiocyanogen, using aluminium chloride as catalyst [1]. It was found that pyrrole reacted smoothly with thiocyanogen in benzene or ether solution even in the absence of aluminium chloride, yielding a dithiocyanopyrrole. At that time it was generally accepted [2] (*cf.* also recent reviews in Refs.[3-5]) that substitution in the pyrrole nucleus occurred in the α-position; hence it was assumed that the compound obtained in these reactions was α,α'-dithiocyanopyrrole.

Later Matteson and Snyder [6,7] succeeded to monothiocyanate pyrrole with thiocyanogen in methanol at $-70°$, or with cupric thiocyanate in methanol at 0°. They gave convincing evidence that the monothiocyanopyrrole of m.p. 41.5–43° was 3-thiocyanopyrrole. This result throws doubt on the structure assigned to the dithiocyanopyrrole and we have therefore reinvestigated this problem.

Treatment of 3-thiocyanopyrrole with thiocyanogen in methanol at $-70°$ or in ether at 0° gave a dithiocyanopyrrole which in all respects (m.p., mixed m.p. and IR-spectra) was identical with that obtained according to Söderbäck [1]. If we assume that no rearrangement of the 3-thiocyano group had occurred under these mild conditions, we can conclude that the product is not the 2,5-isomer.

As the position in which monothiocyanation occurs is rather unexpected, it is difficult to predict the directing effect of the first introduced thiocyano group on further thiocyanation. It should be noted that the effect of the 3-thiocyano group must be different on its two *ortho* positions. Although one can assume that the inductive effect is similar in the 2- and 4-positions, the conjugative effect of this group (+M or −M) can be relayed to the 2-positions (Resonance forms II and III) only, if we assume that resonance structures with long bonds like IV have low weights.

We proved the structure of the dithiocyanopyrrole by investigating its NMR-spectrum. In solvents like acetone and dioxane, the spectrum consists of a broad NH resonance and of a doublet with splitting of 2.6 c/s (Fig. 1). In more basic

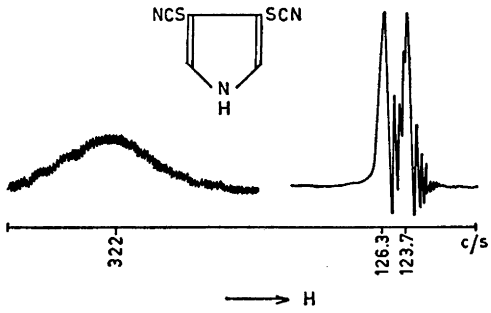
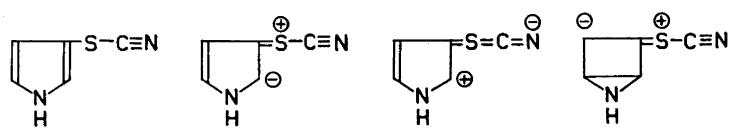


Fig. 1. NMR-spectrum of 3,4-dithiocyanopyrrole in (14 wt %) dioxane solution at 40 Mc/s. The solvent is used as internal reference.

solvents like N,N-dimethyl formamide, one sharp peak is obtained for the ring hydrogens. As it is highly improbable that the chemical shifts for the hydrogens in the 2,3- or 2,4-isomer could coincide in all the solvents investigated, this result shows that the compound obtained is the symmetric 3-4-dithiocyanopyrrole. The splitting in the NMR-spectrum is due to the J_{NH-2} coupling and is of the magnitude found by Abraham and Bernstein [8] in other pyrroles. Additional evidence is obtained



from the NMR-spectrum of the N-methylated dithiocyanopyrrole [1], which also shows a sharp peak for the ring hydrogens.

The reactivity of the β-hydrogens in the thiocyanation reaction is also evident from the ease with which 2,5-dimethylpyrrole is dithiocyanated at −70° to 2,5-dimethyl-3,4-dithiocyanopyrrole.

Experimental. 3,4-Dithiocyanopyrrole. A solution of thiocyanogen in ether was prepared from 6.5 g (0.020 mole) of lead thiocyanate and 2.8 g (0.018 mole) of bromine in 30 ml of dry ether at 0°. The light yellow ethereal solution was decanted and the precipitated lead bromide washed with 20 ml of dry ether. 2.0 g (0.016 moles) of 3-thiocyanopyrrole [7] in 15 ml of dry ether was added to the cooled ethereal thiocyanogen and the resulting solution allowed to stand at 0° for 30 min. The ether phase was washed with sodium bicarbonate and water and dried over magnesium sulphate. Evaporation of the ether yielded 2.0 g (69 %) of crude dithiocyanopyrrole. One recrystallization from water yielded 1.4 g (50 %) of pure 3,4-dithiocyanopyrrole, m.p. 113—114°. This compound was identical (IR-spectra and mixed m.p.) with the dithiocyanopyrrole prepared according to Söderbäck [1]. The NMR-spectrum in dioxane solution (14 % by weight) showed the broad NH resonance at 8.1 ppm from the solvent peak, and a doublet due to the α-hydrogens centered at 3.1 ppm from the solvent peak with a splitting of 2.6 c/s. In acetone solution (27 % by weight) the shifts were 9.9 ppm and 4.6 ppm, respectively, and the splitting 2.5 c/s. In N,N-dimethyl formamide solution (33 % by weight) the ring hydrogens give a sharp peak at —1.2 ppm from the hydrogen attached to the carbonyl group of the reference solvent.

2,5-Dimethyl-3,4-dithiocyanopyrrole. Method I. To a solution of thiocyanogen in methanol, prepared at —70° from 20 g (0.21 mole) of potassium thiocyanate in 25 ml of methanol, was added rapidly a precooled (—70°) solution of 4.7 g (0.050 mole) of 2,5-dimethylpyrrole [9] in 12.5 ml of methanol. After 10 min. the cooling-bath was removed and when the temperature had risen to —25°, the reaction mixture was poured into 200 g of ice followed by the addition of 30 g of sodium chloride. After the ice had melted, the precipitated product was filtered off, dissolved in ether and reprecipitated by the addition of petrolether, to give 8.2 g (78 %) of product, m.p. 136—140°. Recrystallization from a benzene-ligroin (2:1) mixture gave 6.0 g (57 %) of pure 2,5-dimethyl-3,4-dithiocyanopyrrole, m.p. 138.5—139.5°. Additional recrystallization did not raise the m.p. (Found: C 46.16; H 3.27; N 19.92; S 30.51. Calc. for $C_8H_7N_3S_2$ (209.3): C 45.91; H 3.37; N 20.08; S 30.64).

Method II. 2,5-Dimethyl-3,4-dithiocyanopyrrole was prepared also according to the description given by Söderbäck [1] for the dithiocyanation of pyrrole. From 70 g (0.22 mole) of lead thiocyanate, 32 g (0.20 mole) of bromine, 300 ml of benzene and 9.5 g (0.10 mole) of 2,5-dimethylpyrrole [9] was obtained 15.5 g (74 %) of 2,5-dimethyl-3,4-dithiocyanopyrrole, m.p. 138—140°. Its IR-spectrum was identical to that of the product obtained by method I.

The melting-points were determined with a hot stage microscope. The NMR-spectra were obtained with a Varian Associates model V-4300-B high-resolution spectrometer operating at 40.00 Mc/s and a flux-stabilized 12 in. magnet equipped with shimcoils from the same company. The magnet sweep was calibrated with the modulation side-band technique using a 50.00 ± 0.05 c/s modulation frequency obtained from the power line.

Note added in proof (February, 21). Recent results obtained in these laboratories seem to indicate that the monothiocyanopyrrole obtained by Snyder *et al.* is, nevertheless, the *2-isomer*. In such a case the present investigation proves the dithiocyanopyrrole to be the 2,5-isomer as originally suggested by Söderbäck.

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