On the Reaction of Methylthio- and Methoxythiophenes with Tetracyanoethylene Oxide

SALO GRONOWITZ and BENGT UPPSTRÖM *

Division of Organic Chemistry, University of Lund, Chemical Center, P.O. Box 740, S-220 07 Lund 7, Sweden

The reaction between methoxythiophenes or methylthiothiophenes and tetracyanoethylene oxides gives methoxy- or methylthiosubstituted thenoyl cyanides in low yields. A probable reaction mechanism for the formation of the thenoyl cyanides is given.

The mass spectra of the thenoyl cyanides are briefly discussed.

In connection with our work [1] on the effect of substituents on the cycloaddition of tetracyanoethylene oxide (I) to thiophene (II) [2] we used methoxy- and methylthiothiophenes as substrates. However, in these cases the normal substituted 1,1,3,3-tetracyano-1,3,3a,6a-tetrahydrothieno[2,3-c]furans (III) [2] were not obtained. Reacting for instance 2-methoxythiophene with I in benzene at 150° gave a crystalline compound, m.p. 68°C, which elemental analysis and mass spectrum showed to have the composition $C_7H_5NO_2S$. The IR spectrum indicated the presence of $C\equiv N$ (2230 cm^{-1}) and $C=O$ stretchings (1675, 1640 cm^{-1}) and the NMR spectrum showed aromatic methoxyl at δ 4.05 and two doublets at δ 6.44 and δ 7.87 with couplings of 4.5 Hz characteristic of a disubstituted thiophene. All these facts clearly show that the compound obtained is 5-methoxy-2-thenoyl cyanide (IV). 2-Thenoyl cyanide has

recently been studied by Roques and Robba.[3] Using their substituent shifts in the proton NMR spectra and those earlier obtained by Gronowitz and Hoffman [4] for 2-methoxythiophene and assuming additivity, shifts of δ 7.67 and δ 6.34 for the 3- and 4-hydrogen were calculated for 5-methoxy-2-thenoyl cyanide, which are in good accordance with the observed values. Roques and Robba [3] also observed two carbonyl stretching frequencies at 1661 and 1683 cm^{-1} which they assigned to the presence of s-cis and s-trans conformers. This may also be the case in the 5-methoxy-substituted derivative, the somewhat lower frequencies being due to higher single bond character due to through-conjugation between the methoxy and the carbonyl cyanide group.[5]

2-Methylthiothiophene reacted in the same way, although the yield of 5-methylthio-2-thenoyl cyanide (V) was only 6 %. Also in this case the structure followed from spectroscopic data and good accordance between the experimental chemical shifts ($\delta_3 = 8.03$ ppm, $\delta_4 = 7.20$ ppm) and those calculated by assuming additivity of
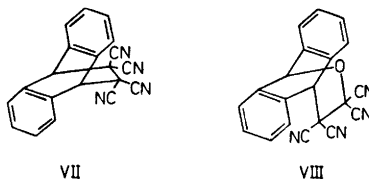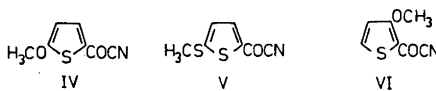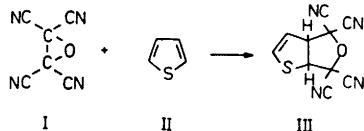
substituent shifts ($\delta_3 = 7.92$ ppm, $\delta_4 = 7.25$ ppm) was observed.

In the reaction of I with 3-methoxythiophene, 12 % of 3-methoxy-2-thenoyl cyanide (VI) was obtained. In this case larger deviations of the shifts from additivity were obtained. The observed shifts were 7.22 and 8.20 for the 4- and 5-hydrogen resonance, while the calculated values were δ 6.90 and δ 7.77, respectively. The deviation is probably due to steric interaction between the substituents.

It is known [3,6] that electron-rich olefins do not give normal adducts with I. Thus 2,3-dimethylbutene and I gave 2,3-dimethyl-2-butene epoxide. Anthracene and I gave a complex mixture of anthrone, anthraquinone, and bianthrone in addition to the anomalous adducts VII and VIII.[6] The side-reaction observed by us is most probably of another type. It has been found that I reacts with dimethyl sulphide to give dimethylsulphonium dicyanomethylide and carbonyl cyanide.[7] The corresponding reaction with dibutyl sulphide is indeed one of the most convenient methods for the preparation of carbonyl cyanide.[8] This reaction also occurs with aromatic sulphides. Thus p-anisyl methyl sulphide gave p-anisylmethylsulphonium dicyanomethylide in 67 % yield.[9]

It therefore seems likely that 2-methylthiothiophene first reacts with I to give the sulphonium dicyanomethylide and carbonyl cyanide, and the latter then reacts with excess of 2-methylthiothiophene to give V (*cf.* Formula Scheme).
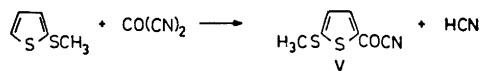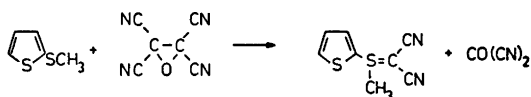
Fig. 1. Mass spectral fragmentation pattern for 5-methyl-2-thenoyl cyanide.

in this reaction could be due to the decomposition of the ylides.

The hypothesis that methylthio- and methoxythiophenes react with carbonyl cyanide at 130° to give thenoyl cyanides was confirmed with 2-methylthiothiophene and 3-methoxythiophene, which gave 33 % and 55 % yield of V and VI, respectively. Also less activated thiophenes such as 2-methylthiophene reacted with carbonyl cyanide to give the thenoyl cyanide, albeit in lower yield.

This way of introducing the COCN group into thiophenes appears to be more convenient than the AlCl$_3$-catalyzed reaction utilized earlier.[10]

We have also studied the mass spectral fragmentation of the thenoyl cyanides to some extent. The structures and mechanisms which are suggested should be considered as tentative. The simplest pattern is obtained for 5-methyl-2-thenoyl cyanide, Fig. 1. The molecular ion (a) loses a cyanogen radical to give the stable acylium ion (b) which further loses CO to give the ion (d). As with other methylthiophenes the molecular ion also loses hydrogen to give the thiopyrylium ion (c).[11]

Also in the mass spectra of the two methoxy-substituted thenoyl cyanides, the molecular ion is the most intense (Figs. 2 – 3). Fragmentation then occurs for IV by loss of either a cyanogen or a methyl radical to give the ion (f) (48 %) and (g) (60 %) of about equal intensity. For VI the loss of methyl is of much less importance, as the ion (o) has only an intensity of 5 %. The suggestion that the ions (g) (Fig. 2) and (o) (Fig. 3) lose the ring-carbonyl group as C = O

An analogous route for the formation of IV and VI could be possible. However, the corresponding carbonyl ylide must be much less stable and more reactive than the sulphur analogue due to the absence of d-orbital stabilization. The formation of large amount of tars
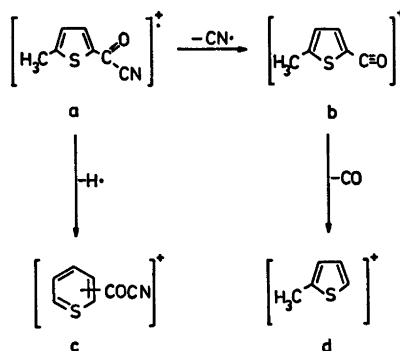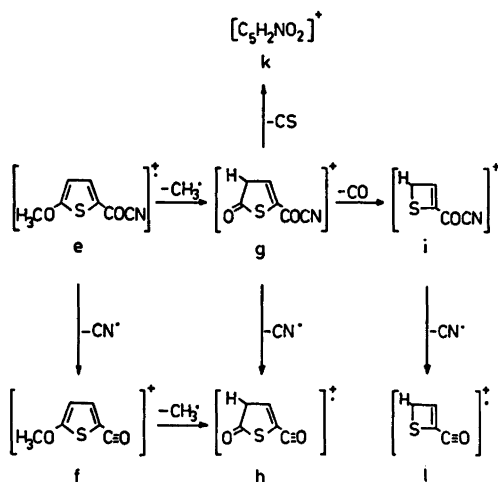
Fig. 2. Mass spectral fragmentation pattern for 5-methoxy-2-thenoyl cyanide.

is supported by the fact that the ion (x) does not lose CO but CS to give (y) (Fig. 4) and that ion (a) (Fig. 1) does not lose CO. The fragmentation with loss of ring-carbonyl groups is also observed in methoxythiophenes, which show step-wise loss of CH₃ and CO from the molecular
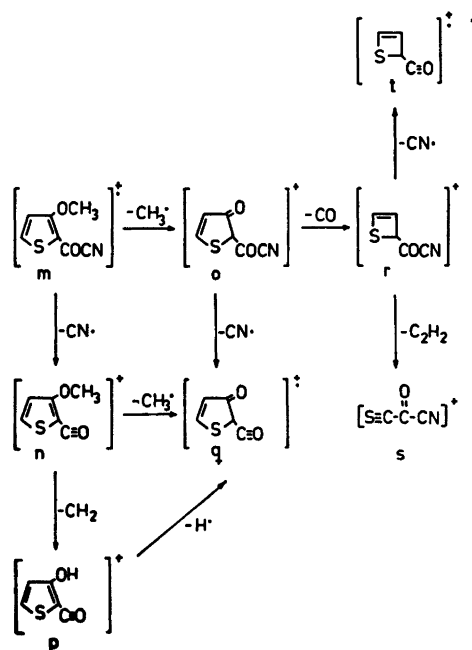

Fig. 3. Mass spectral fragmentation pattern for 3-methoxy-2-thenoyl cyanide.

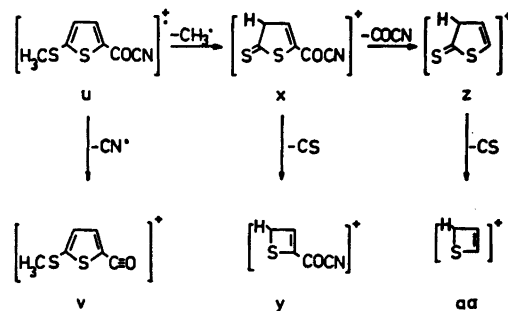Fig. 4. Mass spectral fragmentation pattern for 5-methylthio-2-thenoyl cyanide.

ions.[13] The ion (i) (m/e 124) loses a fragment with mass 26 which could indicate loss of either a cyanogen radical or acetylene or both. High-resolution mass spectroscopy showed that the ion (l) had the composition C_4H_2OS. Thus the ion (i) loses only a cyanogen radical. On the other hand, the ion (r) (Fig. 3) loses both cyanogen and acetylene as with high-resolution mass spectroscopy both ion (s) and (t) could be observed. They had approximately the same intensity. Also the composition of ions (e), (g), (h), (i), (m), (n), (p), (q), and (r) was determined by high-resolution mass spectrometry. Further fragmentation is indicated in Figs. 2 – 3.

The mass spectrum of anisole shows the elimination of formaldehyde from the molecular ion.[12] This fragmentation path was not observed for IV and VI.

The fragmentation pattern of 5-methylthio-2-thenoyl cyanide is shown in Fig. 4. The loss of the cyanogen radical from the molecular ion is more important than the loss of methyl. No elimination of SH or CH_2S, which is characteristic for 2-fluoro-5-methylthiothiophene,[13] was observed. Neither was any intermediate ion observed on the path from the ion (x) to the ion (z) which might indicate the direct elimination of COCN.

EXPERIMENTAL

Reaction of methoxythiophenes with tetracyanoethylene oxide. 11.4 g (0.10 mol) of 2-methoxythiophene,[14] and 5.0 g (0.035 mol) of tetracyanoethylene oxide [15] in 100 ml of anhydrous benzene were heated in a glass ampoule at 150°C for 5 h. The mixture was filtered hot and evaporated to a volume of 20 ml. This

solution was chromatographed on silica gel, using benzene as eluent, and yielding 1.4 g (24 %) of 5-methoxy-2-thenoyl cyanide after recrystallization from 1,2-dichloroethane, m.p. 67−69°C. NMR (CDCl$_3$) $\delta_3 = 6.44$ ppm, $\delta_4 = 7.87$ ppm, $\delta_{CH_3} = 4.05$ ppm, $J_{3,4} = 4.5$ Hz. IR (KBr) C≡N: 2230 cm^{-1}, C=O: 1675, 1640 cm^{-1}. Mass spectrum (m/e, %): 169, 5; 168, 10; 167, 100; 153, 20; 152, 60; 141, 48; 126, 5; 124, 10; 108, 65; 98, 70; 96, 12; 70, 48; 69, 35; 64, 8; 57, 6; 54, 10; 53, 8; 45, 14; 38, 11; 37, 9. [Found: C 51.30; H 3.15; N 8.21; O 18.58; S 18.74. Calc. for C$_7$H$_5$NO$_2$S (167.2): C 50.29; H 3.01; N 8.38; O 19.14; S 19.18].

From 11.4 g (0.10 mol) of 3-methoxythio-phene,[16] 5.0 g (0.035 mol) of tetracyanoethylene oxide and 100 ml of benzene, 0.70 g (12 %) of the title compound, m.p. 134−135°C after recrystallization from 1,2-dichloroethane/cyclohexane, was obtained in the same way as described above. NMR (CD$_3$COCD$_3$): $\delta_5 = 8.20$ ppm, $\delta_4 = 7.22$ ppm, $\delta_{CH_3} = 4.13$ ppm, $J_{45} = 5.5$ Hz. IR (KBr) C≡N: 2210 cm^{-1}, C=O: 1610 cm^{-1}. Mass spectrum (m/e, %): 169, 5; 168, 10; 167, 100; 152, 5; 150, 12; 142, 5; 141, 60; 140, 25; 139, 6; 138, 12; 137, 5; 128, 5; 127, 60; 126, 45; 124, 12; 113, 8; 112, 25; 111, 60; 110, 10; 109, 25; 98, 30; 96, 12; 85, 6; 84, 5; 83, 12; 82, 10; 81, 5; 73, 13; 69, 12; 64, 5; 58, 7; 56, 5; 54, 28; 53, 9; 45, 35; 44, 10; 41, 10; 39, 12; 38, 7; 37, 2. [Found: C 51.34; H 3.13; N 8.19; O 18.72; S 18.67. Calc. for C$_7$H$_5$NO$_2$S (167.2): C 50.29; H 3.01; N 8.38; O 19.14; S 19.18].

2-Methylthiothiophene. This compound was prepared in a manner analogous to that described for 3-methylthiothiophene.[17] To 42.0 g (0.50 mol) of thiophene in 450 ml of anhydrous ether, 0.55 mol of 1.64 N butyllithium in hexane was added dropwise. The solution was cooled to −70°C and 47.1 g (0.50 mol) of dimethyl disulphide was added dropwise. The mixture was left over night at room temperature and then poured into ice-water. The ether phase was separated, the aqueous layer extracted with ether and the combined organic phases washed with water, sodium hydroxide solution and water. The organic layer was dried over magnesium sulphate, the ether and hexane evaporated and the residue distilled in vacuo to yield 50.0 g (77 %) of 2-methylthiothiophene, b.p. 65−70°/15 mmHg. Literature value[18] b.p. 80−82°/22 mmHg.

Reaction of 2-methylthiothiophene with tetracyanoethylene oxide. From 13.0 g (0.10 mol) of 2-methylthiothiophene, 5.0 g (0.035 mol) of tetracyanoethylene oxide and 100 ml of anhydrous benzene, 0.40 g (6 %) of the title compound, m.p. 69−70°C after recrystallization from 1,2-dichloroethane/cyclohexane mixture was obtained in the same way as described above. NMR ((CD$_3$)$_2$CO): $\delta_3 = 8.03$ ppm, $\delta_4 = 7.20$ ppm, $\delta_{CH_3} = 2.75$ ppm, $J_{34} = 4.4$ Hz. IR (KBr) CN: 2220 cm^{-1}, C=O: 1640 cm^{-1}. Mass spectrum (m/e, %): 185, 7; 184, 8; 183, 100; 168, 15; 159, 6; 158, 5; 157, 90; 124, 5; 114, 62; 108, 5; 96, 5;

88, 5; 85, 28; 82, 9; 81, 7; 70, 30; 69, 55; 57, 10; 54, 8; 53, 5; 45, 52; 41, 5; 38, 10; 37, 5. [Found: C 45.97; H 3.12; N 7.54; O 8.38; S 35.10. Calc. for C$_7$H$_5$NOS$_2$ (183.2): C 45.88; H 2.75; N 7.64; O 8.73; S 34.99].

3-Methoxy-2-thenoyl cyanide. To a solution of 2.6 g (0.033 mol) of carbonyl cyanide,[8] in 50 ml of anhydrous benzene, 9.5 g (0.083 mol) of 3-methoxythiophene was added, and the solution heated to 130°C for 2 h in a glass ampoule. The reaction mixture was worked up as described in method A yielding 1.8 g (33 %) of the title compound, m.p. 133−134°C and with the same spectroscopic data as the sample described above.

5-Methylthio-2-thenoyl cyanide. To a solution of 2.3 g (0.029 mol) of carbonyl cyanide[8] in 50 ml of anhydrous benzene 12.0 g (0.092 mol) of 2-methylthiothiophene was added and the solution heated in a glass ampoule to 130°C for 2 h. The reaction mixture was worked up as described above yielding 3.0 g (55 %) of the title compound, m.p. 68−69°C, having the same spectroscopic properties as the sample described above.

5-Methyl-2-thenoyl cyanide. To a solution of 1.8 g (0.023 mol) of carbonyl cyanide[8] in 50 ml of anhydrous benzene, 13.0 g (0.13 mol) of 2-methylthiophene[19] was added and the solution heated in a glass ampoule to 130°C for 3 h. The reaction mixture was filtered, evaporated almost to dryness and the residue chromatographed on silica gel using benzene as eluent. The product was recrystallized from carbon tetrachloride, yielding 0.6 g (17 %) of the title compound, m.p. 73−74°. NMR ((CD$_3$)$_2$CO): $\delta_3 = 8.03$ ppm, $\delta_4 = 7.12$ ppm, $\delta_{CH_3} = 2.68$ ppm, $J_{34} = 4.0$ Hz, $J_{CH_3-4} = 1.0$ Hz, $J_{CH_3-3} = 0.6$ Hz. IR (KBr) CN: 2220 cm^{-1}, C=O: 1640 cm^{-1} (broad). Mass spectrum (m/e, %): 153, 5; 152, 10; 151, 100; 150, 15; 127, 5; 126, 8; 125, 95; 122, 8; 98, 5; 97, 58; 96, 8; 95, 8; 93, 5; 82, 5; 71, 8; 70, 10; 68, 22; 63, 5; 59, 7; 58, 7; 57, 12; 54, 30; 53, 40; 52, 5; 51, 12; 50, 10; 45, 32; 39, 18; 38, 13; 37, 10. [Found: C 54.81; H 3.36; N 9.10; S 20.94. Calc. for C$_7$H$_5$NOS (151.2): C 55.61; H 3.33; N 9.26; S 21.21].

IR spectra were recorded on a Perkin-Elmer 257 Grating Infrared Spectrophotometer, NMR spectra on a Varian A-60 spectrometer and mass spectra on an LKB 9000 mass spectrometer. The compounds were injected through a direct inlet at approximately 25°C. The energy of the ion beam was 70 eV and the electron current was set to 60 μA. High-resolution mass spectra were obtained with an MS 902 AEI spectrometer.

REFERENCES

1. Gronowitz, S. and Uppström, B. *To be published.*
2. Linn, W. J. and Benson, R. E. *J. Amer. Chem. Soc. 87* (1965) 3657.
3. Roques, B. and Robba, M. *Bull. Soc. Chim. Fr.* (1969) 4032.
4. Gronowitz, S. and Hoffman, R. A. *Ark. Kemi 16* (1960) 539.
5. Gronowitz, S. *Ark. Kemi 13* (1958) 295.
6. Brown, P. and Cookson, R. C. *Tetrahedron 24* (1968) 2551.
7. Linn, W. J., Webster, O. W. and Benson, R. E. *J. Amer. Chem. Soc. 87* (1965) 3651.
8. Martin, E. L. *Org. Syn. 51* (1971) 70.
9. Middleton, W. J., Buhle, E. L., McNally, Jr., J. G. and Zanger, M. *J. Org. Chem. 30* (1965) 2384.
10. Achmatowicz, O. and Achmatowicz, Jr., O. *Rocz. Chem. 35* (1961) 813.
11. Hanuš, V. and Čermak, V. *Collect. Czech. Chem. Commun. 24* (1959) 1602.
12. Barnes, C. S. and Occolowitz, J. L. *Aust. J. Chem. 16* (1963) 219.
13. Rosén, U. *Ph. D. Thesis,* University of Lund 1972.
14. Sicé, J. *J. Amer. Chem. Soc. 75* (1953) 3697.
15. Linn, W. J. *Org. Syn. 49* (1969) 103.
16. Gronowitz, S. *Ark. Kemi 12* (1958) 239.
17. Gronowitz, S. *Ark. Kemi 13* (1958) 269.
18. Cymerman-Craig, J. and Loder, J. W. *Org. Syn. Coll. Vol. 4* (1963) 667.
19. King, W. J. and Nord, F. F. *J. Org. Chem. 14* (1949) 638.

Received December 4, 1973.