REACTION OF 5,5-DIMETHYL-4-CYANOMETHYLENE-1,3-OXATHIOLAN-2-ONE WITH AMINES AND AMMONIA

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A simple method for the synthesis of 5,5-dimethyl-4-cyanomethylene-2-cyanomethyl-2-[1-methyl-1-(carbamoyloxy)ethyl]-1,3-dithiolanes was developed on the basis of the reaction of 5,5-dimethyl-4-cyanomethylene-1,3-oxathiolan-2-one with amines (primary and secondary) and ammonia.

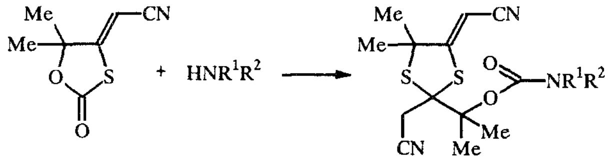
It is known [1-3] that 1,3-oxathiolan-2-one is converted to 2-mercaptoethyl carbamates on treatment with primary amines in dioxane. When excess amine is present, these carbamates are cleaved to give ethylene sulfide, which enters into the 2-mercaptoethylation of amines. In toluene this process also terminates with the formation of 2-mercaptoethylamines [1]. Carrying out the reaction in aqueous methanol leads to oligoethylene sulfides [3].

We recently [4] published a brief communication regarding an unexpected pathway of the reaction of a cyclic thiocarbonate — 5,5-dimethyl-4-cyanomethylene-1,3-oxathiolan-2-one (I) — with secondary amines, which leads to the formation of the previously unknown 5,5-dimethyl-4-cyanomethylene-2-cyanomethyl-2-[1-methyl-1-(N,N-dialkylcarbamoyloxy)ethyl]-1,3-dithiolanes II. This reaction is a new method for obtaining 1,3-dithiolanes.

The most widely used method for the synthesis of 1,3-dithiolanes is based on the addition of ethane-1,2-dithiol to acetylenic ketones [5]. The reaction of acetylenedicarboxylic acid esters with vinylene-1,1-dithiol [6] is also used for this purpose. Patent data on the high insecticidal and herbicidal activity of substituted dithiolanes have been published [7, 8].

The present paper is devoted to a study of the general principles of the reaction of 5,5-dimethyl-4-cyanomethylene-1,3-oxathiolan-2-one (I), which has now become accessible, with amines (primary and secondary) and ammonia in order to develop a new general method for the synthesis of functionally substituted 1,3-dithiolanes.

It was found that ammonia and primary amines react just as readily as secondary amines with 1,3-oxathiolan-2-one I to give substituted 1,3-dithiolanes II in 72-98% yields.



I

IIa - e

II a R^1=R^2=H; b R^1=H, R^2=*i*-C_4H_9;c R_1=R_2=C_2H_5;d R_1=R_2=C_3H_7; e R_1=R_2=C_4H_9

Opening of the 1,3-oxathiolane ring to give 2-mercapto carbamate III, the subsequent dimerization of which via the addition of the mercapto group of one molecule to the double bond of another molecule leads to intermediate IV, evidently occurs in the first step under the influence of the amine. This is followed by intramolecular substitution of the carbamoyl grouping with the formation of a 1,3-dithiolane ring.

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TABLE 1. Bond Angles in the 5,5-Dimethyl-4-cyanomethylene-2-cyanomethyl-2-[1-methyl-1-(N,N-diethylcarbamoyloxy)ethyl]-1,3-dithiolane (IIc) Molecule

Angle	deg	Angle	deg	angle	deg
$C_{(1)}$-$S_{(1)}$-$C_{(3)}$	98,2(2)	$S_{(2)}$-$C_{(2)}$-$C_{(3)}$	107,2(3)	$N_{(2)}$-$C_{(9)}$-$C_{(8)}$	179,0(5)
$C_{(1)}$-$S_{(2)}$-$C_{(2)}$	101,3(2)	$S_{(2)}$-$C_{(2)}$-$C_{(4)}$	110,1(4)	$O_{(1)}$-$C_{(10)}$-$C_{(1)}$	101,4(3)
$C_{(10)}$-$O_{(1)}$-$C_{(13)}$	120,2(3)	$C_{(3)}$-$C_{(2)}$-$C_{(4)}$	109,3(4)	$O_{(1)}$-$C_{(10)}$-$C_{(11)}$	110,6(4)
$C_{(13)}$-$N_{(3)}$-$C_{(14)}$	122,8(4)	$S_{(2)}$-$C_{(2)}$-$C_{(5)}$	107,8(4)	$O_{(1)}$-$C_{(10)}$-$C_{(12)}$	110,3(4)
$C_{(13)}$-$N_{(3)}$-$C_{(16)}$	117,8(4)	$C_{(3)}$-$C_{(2)}$-$C_{(5)}$	113,5(4)	$C_{(1)}$-$C_{(10)}$-$C_{(11)}$	111,0(4)
$C_{(14)}$-$N_{(3)}$-$C_{(16)}$	119,2(4)	$C_{(4)}$-$C_{(2)}$-$C_{(5)}$	109,7(4)	$C_{(1)}$-$C_{(10)}$-$C_{(12)}$	111,9(4)
$S_{(1)}$-$C_{(1)}$-$S_{(2)}$	107,7(2)	$S_{(1)}$-$C_{(3)}$-$C_{(2)}$	115,9(3)	$C_{(11)}$-$C_{(10)}$-$C_{(12)}$	111,3(4)
$S_{(1)}$-$C_{(1)}$-$C_{(8)}$	106,2(3)	$S_{(1)}$-$C_{(3)}$-$C_{(6)}$	122,2(3)	$O_{(1)}$-$C_{(13)}$-$O_{(2)}$	123,8(4)
$S_{(2)}$-$C_{(1)}$-$C_{(8)}$	109,8(3)	$C_{(2)}$-$C_{(3)}$-$C_{(6)}$	121,6(4)	$O_{(1)}$-$C_{(13)}$-$N_{(3)}$	111,6(4)
$S_{(1)}$-$C_{(1)}$-$C_{(10)}$	111,4(3)	$C_{(3)}$-$C_{(6)}$-$C_{(7)}$	121,5(5)	$O_{(2)}$-$C_{(13)}$-$N_{(3)}$	124,6(4)
$S_{(2)}$-$C_{(1)}$-$C_{(10)}$	110,4(2)	$N_{(1)}$-$C_{(7)}$-$C_{(6)}$	178,8(7)	$N_{(3)}$-$C_{(14)}$-$C_{(15)}$	112,5(5)
$C_{(8)}$-$C_{(1)}$-$C_{(10)}$	111,3(3)	$C_{(1)}$-$C_{(8)}$-$C_{(9)}$	113,2(4)	$N_{(3)}$-$C_{(16)}$-$C_{(17)}$	112,7(6)

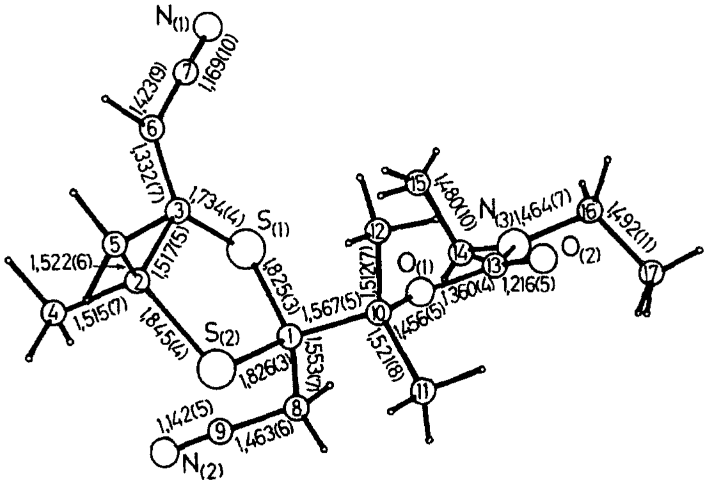
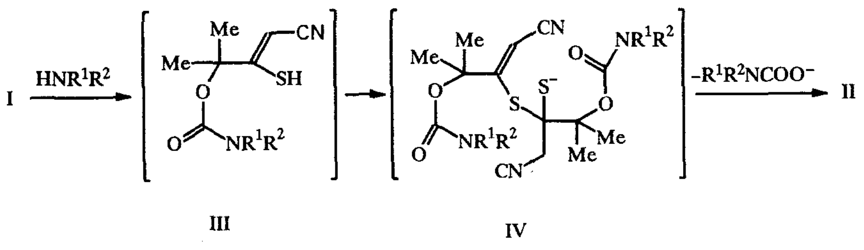


Fig. 1. Structure of the 5,5-dimethyl-4-cyanomethylene-2-cyanomethyl-2-(1-methyl-1-(N,N-diethylcarbamoyloxy)ethyl]-1,3-dithiolane (IIc) molecule. The numbering of the atoms and the bond lengths (Å) are presented.



The nature of the amine does not have a substantial effect on the yields of 1,3-dithiolanes IIa-e. Thus the yields for secondary and primary amines are 90% and 98%, respectively. At the same time, the yield of IIa is 72% when ammonia (both liquid ammonia and 25% ammonium hydroxide) is used.

The synthesized 1,3-dithiolanes IIa-e are crystalline substances or oily liquids that are soluble in most organic solvents. Absorption bands at 1560-1590, 3040-3070 (C=CH), 2200-2210 (=CHCN), and 2240-2250 cm^{-1} (CH_2CN) are present in their IR spectra; the spectra of IIa, b contain absorption bands at 1620-1630 and 3215-3420 cm^{-1}, which are related to stretching and deformation vibrations of NH and NH_2 groups.

The PMR spectra of II ($CDCl_3$) contain one signal of an olefinic proton at 5.24-5.27 ppm or at 5.95 ppm in the case of dithiolane IIa (recorded in solution in d_6-DMSO). The chemical shifts of the alkyl protons are presented in the experimental section.

The structure of II is also confirmed by data from the x-ray diffraction analysis of a single crystal of 5,5-dimethyl-4-cyanomethylene-2-cyanomethyl-2-[1-methyl-1-(N,N-diethylcarbamoyloxy)ethyl]-1,3-dithiolane (IIc). The geometry of the molecule, the numbering of the atoms in it, the principal bond lengths, and the principal bond angles are shown in Fig. 1 and presented in Table 1.

The molecule has a half-chair conformation: the $C_{(1)}$, $S_{(2)}$, and $C_{(20)}$ atoms are situated in a single plane, and the $C_{(3)}$ and $S_{(1)}$ atoms deviate from the plane by 0.26 Å and −0.27 Å, respectively. The $S_{(1)}$—$C_{(3)}$ bond is somewhat shortened (1.73 Å) as compared with the $S_{(2)}$—$C_{(2)}$ bond (1.845 Å; literature value 1.82 Å [10]); this is evidently due to conjugation of the $S_{(1)}$ atom with the π system of multiple bonds of the cyanomethylene fragment.

The structure of 1,3-dithiolane IIc is also confirmed by the ^{13}C NMR spectrum: 86.1 [$C_{(10}$]; 64.8 [$C_{(2)}$]; 153 [$C_{(3)}$]; 88.7 [$C_{(6)}$]; 116.2, 118.1 [$C_{(7)}$, $C_{(9)}$]; 31.97 [$C_{(8)}$]; 72.4 [$C_{(10)}$]; 173.2 [$C_{(13)}$]; 41.7 [$C_{(14)}$, $C_{(16)}$]; 28.8, 31.7, 13.5 [$C_{(4)}$, $C_{(5)}$, $C_{(11)}$, $C_{(12)}$, $C_{(15)}$, $C_{(17)}$].

Thus 1,3-oxathiolan-2-ones that contain an acceptor group (a cyanomethylene fragment) react with amines and ammonia to give functionally substituted 1,3-dithiolanes.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra of solutions in d_6-DMSO (for IIa) or in $CDCl_3$ (for IIb-e) were recorded with a Tesla BS-567A spectrometer (100 MHz) with hexamethyldisiloxane (HMDS) as the internal standard. The IR spectra of KBr pellets (for IIa-c) or microlayers (for IId, e) were obtained with a Specord 75-IR spectrometer. The progress of the reactions was monitored by TLC on Al_2O_3 in a chloroform—benzene—alcohol (20:4:1) system with development by iodine vapors; the completion of the reaction was judged from the disappearance of the spot of the starting 1,3-oxathiolan-2-one.

X-ray diffraction analysis was carried out with a Nicolet P3 diffractometer (λ_{Mo}, graphite monochromator, $\theta/2\theta$ scanning, $2\theta_{max} = 48°$). The number of independent reflections with $I > 3\sigma$ was 1242. The structure was decoded by the Paterson method and refined within the anisotropically (S, O, N, C) isotropic (H) approximation up to R = 0.028 (R = 0.030). The coordinates of the H atoms were determined from differential synthesis. The parameters of the rhombic cell of IIc were as follows: $a = 17.919(3)$, b = 11.151(1), c = 9.809(1) Å, V = 1959.9(6) Å^3, z = 4, $d_{calc} = 1.25$ g/cm^3, space group PBC 2_1.

5,5-Dimethyl-4-cyanomethylene-1,3-oxathiolan-2-one was obtained in 86% yield as described in [9].

The results of elementary analysis of IIa-e for C, H, N, and S were in agreement with the calculated values.

5,5-Dimethyl-4-cyanomethylene-2-cyanomethyl-(1-methyl-1-carbamoyloxyethyl)-1,3-dithiolane (IIa, $C_{13}H_{17}N_3O_2S_2$). A 5 ml sample of 25% ammonium hydroxide (or 5 ml of liquid ammonia) was added slowly to a stirred solution of 1.18 mmole of 1,3-oxathiolan-2-one I in 5 ml of methanol, after which the reaction mixture was stirred at room temperature for 5 h and then allowed to stand overnight. The solvent and excess ammonia were removed in vacuo, and the resulting crystals of IIa were washed with ether to give a product with mp 258-260°C. IR spectrum: 530, 570, 590, 660, 800, 1030, 1040, 1150, 1160, 1230, 1380, 1400, 1415, 1460, 1470, 1590, 1630, 1740, 2210, 2250, 2950, 2990, 3000, 3070, 3215, 3290, 3350, 3420 cm^{-1}. PMR spectrum: 5.95 (1H, s, =CHCN); 3.66 (2H, m, CH_2CN); 1.84, 1.70, 1.72, 1.61 ppm (12H, s, s, s, s, $4CH_3$). The yield was 0.13 g (72.2%).

5,5-Dimethyl-4-cyanomethylene-2-cyanomethyl-2-[1-methyl-1-(N-isobutylcarbamoyloxy)ethyl]-1,3-dithiolan(IIb, $C_{17}H_{25}N_3O_2S_2$). A 0.18-g (98%) sample of IIb was obtained from 1 mmole of 1,3-oxathiolan-2-one I and 1.1 mmole of isobutylamine in 5 ml of methanol after 2 h at room temperature. The product had mp 175-176°C. IR spectrum: 520, 580, 650, 760, 880, 970, 990, 1060, 1140, 1220, 1250, 1360, 1380, 1450, 1520, 1570, 1620, 1705, 2200, 2240, 2870, 2920, 2950, 3040, 3340-3400 cm^{-1}. PMR spectrum: 5.24 (1H, s, =CHCN); 3.48 [1H, q, $CH(CH_3)_2$]; 3.24 (2H, s, CH_2CN); 2.92 [2H, t, $CH_2CH(CH_3)_2$]; 1.83, 1.78 (6H, s, s, $2CH_3$); 1.70 (6H, s, $2CH_3$); 0.83 ppm (6H, d, $2CH_3$).

5,5-Dimethyl-4-cyanomethylene-2-cyanomethyl-2-[1-methyl-1-(N,N-diethylcarbamoyloxy)ethyl]-1,3-dithiolane (IIc, $C_{17}H_{25}N_3O_2S_2$). A 0.17-g (92%) sample of IIc was obtained from 1 mmole of 1,3-oxathiolan-2-one I and 1.5 mmole of diethylamine in 2 ml of methanol after 2 h at room temperature. The product had mp 158-160°C. IR spectrum: 510, 580, 640, 750, 770, 870, 960, 1040, 1080, 1120, 1205, 1260, 1300, 1350, 1360, 1405, 1460, 1465, 1560, 1680, 2200, 2240, 2860, 2930, 2960, 3040 cm^{-1}. PMR spectrum: 5.26 (1H, s, =CHCN), 3.42 (4H, q, 2CH$_2$N), 3.17 (2H, s, CH$_2$CN), 1.84 (6H, s, 2CH$_3$), 1.71 (6H, s, 2CH$_3$), 1.13 ppm (6H, t, 2CH$_3$).

5,5-Dimethyl-4-cyanomethylene-2-cyanomethyl-2-[1-methyl-1-(N,N-dipropylcarbamoyloxy)ethyl]-1,3-dithiolane (IId, $C_{19}H_{29}N_3O_2S_2$). A 0.2-g (92%) sample of IId was obtained in the form of a viscous oil from 1 mmole of 1,3-oxathiolan-2-one I and 3.6 mmole of dipropylamine in 5 ml of methanol after 3 h at room temperature. IR spectrum: 520, 580, 640, 750, 900, 930, 1050, 1120, 1230, 1300, 1350, 1360, 1400, 1450, 1570, 1670, 2200, 2240, 2870, 2920, 2950, 3040 cm^{-1}. PMR spectrum: 5.27 (1H, s, =CHCN), 3.34 (6H, m, 2CH$_3$), 1.84 (6H, s, 2CH$_3$), 1.75 (6H, d, 2CH$_3$), 1.55 (6H, m, 2CH$_3$).

5,5-Dimethyl-4-cyanomethylene-2-cyanomethyl-2-[1-methyl-1-(N,N-dibutylcarbamoyloxy)ethyl]-1,3-dithiolane (IIe, $C_{21}H_{33}N_3O_2S_2$). A 0.2-g (90%) sample of IIe was obtained in the form of a light-yellow viscous oil from 1 mmole of 1,3-oxathiolan-2-one I and 2.8 mmole of dibutylamine in 5 ml of methanol after 3 h at 20°C. IR spectrum: 530, 570, 640, 720, 750, 780, 850, 870, 940, 1060, 1110, 1200, 1250, 1280, 1300, 1360, 1380, 1400, 1570, 1680, 2205, 2240, 2870, 2930, 2950, 3040 cm^{-1}. PMR spectrum: 5.27 (1H, s, =CHCN), 3.29 (4H, q, 2CH$_2$), 3.21 (2H, 1450, m, CH$_2$CN), 1.77 (6H, s, 2CH$_3$), 1.71 (6H, d, 2CH$_3$), 0.94 (6H, m, 2CH$_3$).

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