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The reaction of various potassium salts [RNHC(=S)SK, R = $N(CH_3)_2$, morpholino, piperidino, and hexahydro-1-(1*H*)-azepinyl] with 3-chloro-2,4-pentanedione in ethanol at 25-30° afforded the 1-acetylacetonyl substitutedaminodithiocarbamates **1-4** [RNHC(=S)SCH$(COCH_3)_2$]. Under refluxing conditions, the same reactants gave the heterocyclic compounds **5-8**. Possible mechanism and supporting ir, nmr and mass spectral data are discussed.

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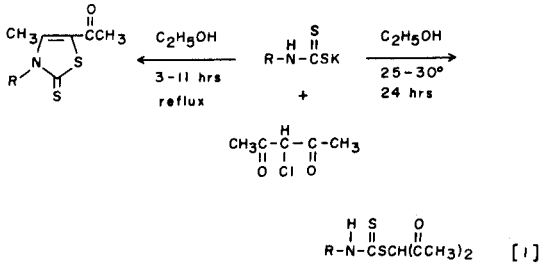
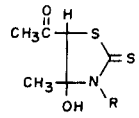
Mathes [2] and Sandström [3] reported the synthesis of mercaptothiadiazines and *N*-aminothiazolethiones by reaction of potassium or ammonium dithiocarbazates with various electrophiles such as chloroacetone, ethyl α-chloroacetoacetate and sodium chloroacetate. We [4] reported the preparation of alkenyl, cycloalkenyl and chlorobenzyl esters of dithiocarbazic acids by the reaction of potassium or ammonium dithiocarbazates with allyl chloride, 3-bromocyclohexene, 1,3-dichloro-2-butene, 1,1,2,3-tetrachloro-1-propene and a variety of chlorobenzyl chlorides.

The reaction of potassium salts [RNHC(=S)SK], R = $-N(CH_3)_2$, morpholino, piperidino, or hexahydro-1-(1*H*)-azepinyl] in ethanol with 3-chloro-2,4-pentanedione [5] at 25-30° afforded 1-acetylacetonyl]dimethylaminodithiocarbamate (**1**), 1-acetylacetonyl 4-morpholinodithiocarbamate (**2**), 1-acetylacetonyl 1-piperidinodithiocarbamate (**3**), 1-acetylacetonyl hexahydro-1(1*H*)azepinedithiocarbamate (**4**), respectively (Table 1). However, under refluxing temperatures (78-80°), the same reactants gave the heterocyclic compounds, 3-dimethylamino-4-methyl-5-acetyl-4-thiazoline-2-thione (**5**), 3-morpholino-4-methyl-5-acetyl-4-thiazoline-2-thione (**6**), 3-piperidino-4-methyl-5-acetyl-4-thiazoline-2-thione (**7**) and 3-(hexahydro-1-(1*H*)azepinyl)-4-methyl-5-acetyl-4-thiazoline-2-thione (**8**), respectively (Table 2).



[1]

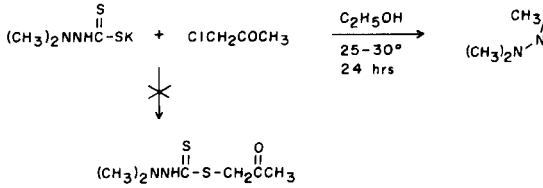
Based on elemental analysis and molecular weight determinations, the cyclic structures, **A**, had to be considered for compounds **1-4**.



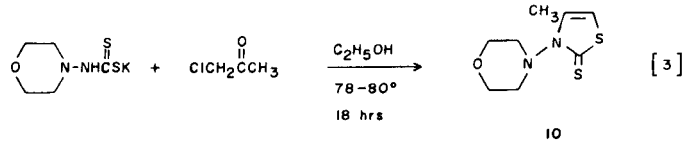
A

However, the absence of the OH absorption band at 3500-3100 cm^{-1} and the presence of the NH absorption band at 3168 cm^{-1} in the infrared spectrum for **2** ruled out structure **A**. In addition, the proton nmr spectra revealed the presence of the NH proton at δ 8.75 to 9.37 (Table 1) and the absence of OH protons. Thus, the spectral data confirm the non-cyclic structure for compounds **1-4** and rule out structure **A**.

The reaction of potassium dimethylaminodithiocarbamate with chloroacetone at only 25-30° gave none of the expected ester **B**, but instead furnished the cyclized product, 3-dimethylamino-4-methyl-4-thiazoline-2-thione (**9**) in 78% yield (Table 3). The reaction of chloroacetone with potassium 4-morpholinodithiocarbamate in refluxing ethanol gave the expected 3-morphilino-4-methyl-4-thiazoline-2-thione (**10**).

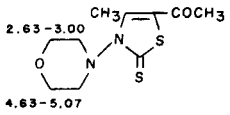


[2]

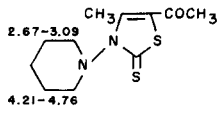


[3]

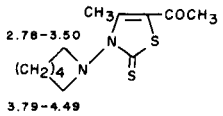
Confirmation of the cyclic structure for **5-10** was afforded by the elemental analysis, ir, nmr and mass spectral data. The nmr spectra of these compounds show a large difference (1-2 ppm) in chemical shift for two of the methylene protons of the morpholine, piperidine and azepine rings.



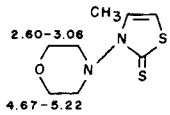
6



7



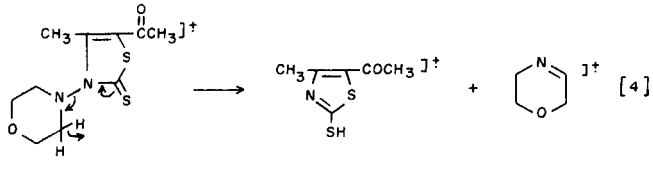
8



10

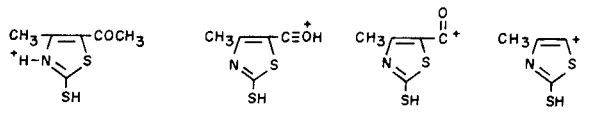
The large downfield shift of two of these protons is attributed to the deshielding effect of the thiocarbonyl group.

The electron impact mass spectrum for **6** furnished the molecular weight in form of M^{+} 258. The dominant breakdown pattern of the molecular ion for **6** is explained by the following McLafferty rearrangement:

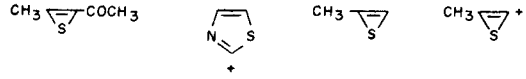


M^{+}, m/e 258(15) m/e 173(58) m/e 85(70)

In addition of this process, the N-N bond is cleaved to give the morpholine radical cation [C_4H_8NO, 86 (10)] as the base peak. Other fragments confirm this initial cleavage. The thiazole ring gives rise to the following ions which are expected.



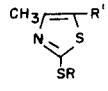
m/e 174(15) m/e 159(6) m/e 158(53) m/e 130(9)



m/e 114(6) m/e 84(3) m/e 72(7) m/e 71(18)

The ir spectrum for **6** exhibited absorption bands at 1322-1306 and 1172 cm^{-1} attributed to the thiazoline-2-thione ring and the thiocarbonyl group, respectively to afford additional confirming evidence for the structures of **5-10**.

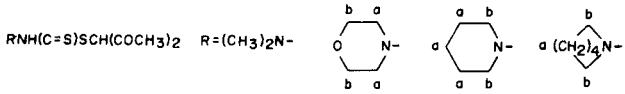
The proposed mechanism for formation of compounds **1-10** is depicted in Scheme 1. Although the analytical data were in agreement with the proposed structures for **5-10**, there still remained the possibility that the products obtained in reactions 1-3 could be the isomeric structure **C**.



C

In order to rule out that possibility, the corresponding isomer of **8** was prepared by the oxidative condensation of hexamethylenimine with 5-acetyl-4-methyl-2-thiazolethiol [6,7] to give **11**, and the nmr spectral data of compounds **8** and **11** were compared.

Table 1

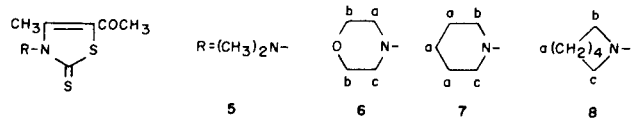


1 2 3 4

No.	Mp °C	% Yield	NMR δ, ppm CDCl$_3$-(Me$_4$Si)	Empirical Formula	%C Calcd.	%C Found	%H Calcd.	%H Found	%N Calcd.	%N Found	%S Calcd.	%S Found
1	160-161 [1]	85	2.28 (s, 6, 2COCH$_3$) 2.72 (s, 6, -N(CH$_3$)$_2$) 3.00 (s, 1, CH) 9.30 (br s, 1, NH)	$C_8H_{14}N_2O_2S_2$	41.00	41.12	6.02	6.07	11.96	11.94	27.37	27.12
2 [3]	177-178 [2]	77	2.13 (s, 6, 2COCH$_3$) 2.62-2.92 (m, 4, a) 3.56-3.80 (m, 4, b) 8.75 (br s, 1, NH)	$C_{10}H_{16}N_2O_3S_2$	43.46	43.68	5.84	5.80	10.14	9.87	23.24	22.95
3	170-171 [2]	88	1.28-2.10 (m, 6, a) 2.22 and 2.30 (2s, 6, 2COCH$_3$) 2.41-3.42 (m, 4, b) 8.87 (br s, 1, NH)	$C_{11}H_{18}NO_2S_2$	48.14	48.32	6.61	6.86	10.21	10.41	23.37	23.20
4	163-164 [2]	77	1.50-2.10 (m, 8, a) 2.21 and 2.30 (2s, 6, 2COCH$_3$) 2.81-3.55 (m, 4, b) 9.37 (br s, 1, NH)	$C_{12}H_{20}N_2O_2S_2$	49.97	49.97	6.99	7.09	9.71	9.81	22.24	22.32

[1] Recrystallization from ethanol. [2] Recrystallization from ethyl acetate. [3] ir (potassium bromide) 3168 (H bonded NH), 2800-3000 (CH$_2$ morpholino + CH$_3$ of diketone), 1570 (C=O of 1,3-diketone in enol form, 1100, 1074, 1030 (morpholine bonds) and 1020 (C=S) cm^{-1}.

Table 2

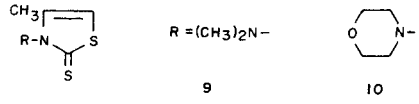


5 6 7 8

No.	Reflux Hours	Mp °C	% Yield	NMR δ, ppm $CDCl_3$-(Me_4Si)	Empirical Formula	%C Calcd.	%C Found	%H Calcd.	%H Found	%N Calcd.	%N Found	%S Calcd.	%S Found
5	3	118-119 [1]	89	2.33 (s, 3, CH_3C=) 2.56 (s, 3, $COCH_3$) 3.22 (s, 6, -$N(CH_3)_2$)	$C_8H_{12}N_2OS_2$	44.51	44.51	5.59	5.77	12.95	12.85	29.65	29.40
6 [3,4,5]		126-127 [2]	77	2.38 (s, 3, CH_3C=) 2.62 (s, 3, $COCH_3$) 2.63-3.00 (m, 2, a) 3.40-4.09 (m, 4, b) 4.63-5.07 (m, 2, c)	$C_{10}H_{14}N_2O_2S_2$	46.49	46.62	5.46	5.66	10.84	10.74	24.82	24.60
7 [3]	11	134-135 [2]	78	1.09-2.09 (m, 6, a) 2.30 (s, 3, CH_3C=) 2.55 (s, 3, -$COCH_3$) 2.67-3.09 (m, 2, b) 4.21-4.76 (m, 2, c)	$C_{11}H_{16}N_2OS_2$	51.53	51.78	6.29	6.26	10.93	11.02	25.01	24.85
8 [3]	3	105-106 [1]	80	1.46-1.99 (m, 8, a) 2.36 (s, 3, CH_3C=) 2.62 (s, 3, $COCH_3$) 2.78-3.50 (m, 2, b) 3.79-4.49 (m, 2, c)	$C_{12}H_{18}N_2OS_2$	53.30	53.37	6.71	6.90	10.36	10.20	23.72	23.4

[1] Recrystallization from ethanol. [2] Recrystallization heptane. [3] The methyl hydrogens shown as [c] in **6, 7** and **8** are adjacent to the C=S group and the large downfield shift of these methylene protons is due to the deshielding effect of the thiocarbonyl moiety. [4] Electron impact mass spectrum m/e (relative intensity) M+ 258 (15), 174 (15), 173 (58), 159 (6), 158 (53), 130 (9), 114 (6), 86 (100), 85 (70), 84 (3), 72 (7), 71 (8). [5] ir (potassium bromide) 2800-3000 (CH_2 of morpholino), 1680 (C=C), 1640 (C=O), 1586 (mode of the thiazoline-2-thione ring), 1420 (CH_3 asym), 1380 (CH_3 sym), 1322 and 1306 NC(=S)S- mode of thiazoline ring), 1240 (morpholine) and 1172 (C=S) cm^{-1}.

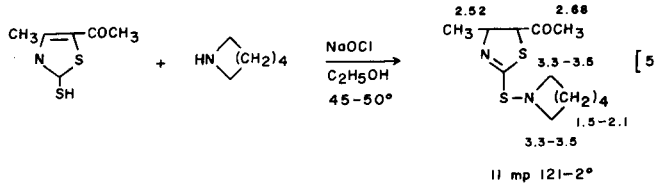
Table 3



9 10

No.	Reaction Temp °C	Mp °C	% Yield	NMR δ, ppm $CDCl_3$-(Me_4Si)	Empirical Formula	%C Calcd.	%C Found	%H Calcd.	%H Found	%N Calcd.	%N Found	%S Calcd.	%S Found
9	25-30 24 hrs	66.0-66.5 [1]	78	2.17 (s, 3, CH_3C=) 3.25 (s, 6, -$N(CH_3)_2$) 6.15 (s, 1, =CH)	$C_6H_{10}N_2S_2$	41.35	41.28	5.78	5.83	16.07	16.08	36.80	36.59
10 [3]	78-80 18 hrs	150-151 [2]	75	2.19 (s, 3, CH_3C=) 2.60-3.06 (m, 2, a), 3.31-4.17 (m, 4, b), 4.67-5.22 (m, 2, c) 6.17 (s, 1, =CH)	$C_8H_{12}N_2S_2$	44.41	44.70	5.59	5.63	12.95	13.01	29.65	29.74

[1] Recrystallization from heptane. [2] Recrystallization ethanol. [3] The methylene shown as [c] in **10** are adjacent to the C=S group and the large downfield shift (4.67-5.22 δ) is due to the deshielding effect of the thiocarbonyl moiety.



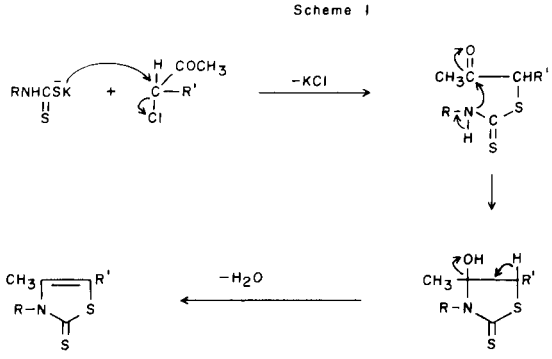
11 mp 121-2°

[5]

The nmr spectrum of compound **11** did not show the large downfield shift (δ 3.79-4.49) for any of the azepine ring protons as also exhibited by spectra for **8, 6, 7** and **10** which was attributed to the thiocarbonyl group deshielding effect. Thus, sufficient evidence was obtained to rule

out the isomeric structures such as **11** and additional support for the original proposed structures **5-10** was afforded.

Scheme I



R = $-N(CH_3)_2$, morpholino, piperidino and hexahydro-1-(1H)azepinyl, R' = $COCH_3$.

R = $-N(CH_3)_2$, morpholino. R' = H.

EXPERIMENTAL

The nmr spectra were obtained with a Varian T-60 nmr spectrometer. The chemical shifts are reported in ppm δ, using tetramethylsilane as reference. All melting points were taken upon a Fisher-Johns block and are uncorrected. The infrared spectra for 2 and 6 were obtained with a Perkin-Elmer Model 21 spectrophotometer with a sodium chloride prism. The electron impact mass spectrum for **6** was determined with a Varian-MAT CH-7A mass spectrometer operating at an ionizing potential of 70 eV using a direct insertion probe technique with a source temperature at 250°.

1-Acetylacetonyl Dimethylaminodithiocarbamate (**1**). 1-Acetylacetonyl 4-Morpholinodithiocarbamate (**2**). 1-Acetylacetonyl 1-Piperidinodithiocarbamate (**3**). 1-Acetylacetonylhexahydro-1(1*H*)-azepinedithiocarbamate (**4**).

To a stirred slurry at 0° containing 0.25 mole of potassium dimethylaminodithiocarbamate [8] potassium 4-morpholinodithiocarbamate [8] potassium 1-piperidinodithiocarbamate [8] or potassium hexahydro-1-(1*H*)-azepinedithiocarbamate [8] in 400 ml of ethanol, 33.7 g (0.25 mole) of 3-chloro-2,4-pentanedione [5] was added in one portion. An exothermic reaction occurred causing a temperature rise from 0° to 25° over a 1 minute period. By external cooling the temperature of the stirred reaction mixture was never allowed to exceed 30°. The reaction mixture was stirred at 25-30° for 24 hours. After cooling to 0°, 600 g of ice water was added and stirring continued at 0-10° for 30 minutes. The solid was collected by filtration, washed with 500 ml of water and air dried at 25-30°. The data are summarized in Table 1.

3-Dimethylamino-4-methyl-5-acetyl-4-thiazoline-2-thione (**5**), 3-Morpholino-4-methyl-5-acetyl-4-thiazoline-2-thione (**6**), 3-Piperidino-4-methyl-5-acetyl-4-thiazoline-2-thione (**7**) and 3-(Hexahydro-1-(1*H*)-azepinyl)-4-methyl-5-acetyl-4-thiazoline-2-thione (**8**).

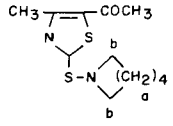
To a stirred slurry at 20° comprising 0.25 mole of the same potassium salts listed above in 300 ml of ethanol, 33.7 g (0.25 mole) of 3-chloro-2,4-pentanedione [5] was added in one portion. An exothermic reaction occurred causing a temperature rise from 20° to 50°. The stirred reaction mixture was then heated at reflux for the time period specified in Table 2 and then stirred at 25-30° for 18 hours. After cooling to 5°, 600 g of ice water was added and stirring continued at 0-10° for 1 hour. The solid was collected by filtration, washed with 1 liter of water and air-dried at 25-30°. The data are summarized in Table 2.

3-Dimethylamino-4-methyl-4-thiazoline-2-thione (**9**) and 3-Morpholino-4-methyl-4-thiazoline-2-thione (**10**).

To a stirred slurry at 20° containing 0.25 mole of potassium dimethyldithiocarbamate or potassium 4-morpholinodithiocarbamate in 400 ml of ethanol, 23.2 g (0.25 mole) of chloroacetone was added in one portion. An exothermic reaction, causing a temperature rise from 20° to 44° and 37°, respectively was observed. The reaction mixture was then stirred at the temperatures and for the time period specified in Table 3. After cooling to 5°, 700 g of ice water was added and stirring continued at 0-10° for 1 hour. The solid was collected by filtration, washed with 500 ml of water and air-dried at 25-30°. The data are summarized in Table 3.

5-Acetyl-2-hexamethyleniminethio-4-methylthiazole (**11**).

A stirred solution containing 43.3 g (0.25 mole) of 5-acetyl-4-methyl-2-thiazolethiol [6], 100 g (1.0 mole) of hexamethylenimine and 300 ml of 2-propanol was heated at 45-50° for 30 minutes. To this stirred solution, at 45-50°, was added, drop by drop, in 2 hours, 121 ml (23.1 g/100 ml) of aqueous sodium hypochlorite. After stirring at 45-50° for additional 30 minutes, the reaction mixture was cooled to 0°. The excess sodium hypochlorite was destroyed by the addition of 5 g of sodium sulfite. To the stirred reaction mixture 500 ml of cold water was added dropwise at 0-10°. After stirring at 0-10° for 30 minutes, the precipitate was filtered, washed with water until free of chloride and air-dried at 25-30°. Crude **11**, mp 118-119°, was obtained in 73% yield. After recrystallization from heptane it melted at 121-122°; nmr (deuteriochloroform) δ 1.50-2.10 (m, 8, a), 2.52 (s, 3, $CH_3C=$), 2.68 (s, 3, $COCH_3$), 3.3-3.5 (m, 4, b).



Anal. Calcd. for $C_{12}H_{18}N_2OS_2$: C, 53.30; H, 6.71; N, 10.36; S, 23.72. Found: C, 53.38; H, 6.72; N, 10.37; S, 23.77.

Acknowledgement.

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