ACTION OF AMINES ON N,N-DISUBSTITUTED 5-ALKYL-3-AMINOMETHYLENE-4-THIOLEN-2-ONES

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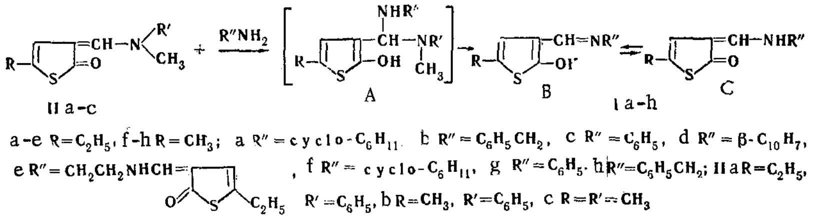
The corresponding N-monosubstituted 5-alkyl-3-aminomethylene-4-thiolen-2-ones, which are oxygen analogs of mercaptoaldimines of the thiophene series, were obtained by the action of primary amines on N,N-disubstituted 5-alkyl-3-aminomethylene-4-thiolen-2-ones.

In a previous communication [1] it was shown that the action of several monosubstituted formamides on 5-methoxy-2-alkylthiophenes yields N-monosubstituted 5-alkyl-3-aminomethylene-4-thiolen-2-ones (I), which are oxygen analogs of mercaptoaldimines of the thiophene series and may be of interest as ligands for the preparation of chelates. However, this method for the synthesis of I is limited to a certain degree since the monosubstituted formamides needed in this case are not always readily accessible. It was, therefore, expedient to use another route for this purpose, viz., the action of primary amines on N,N-disubstituted 5-alkyl-3-aminomethylene-4-thiolen-2-ones (II) (see the reaction scheme), which we previously [1] obtained from 5-methoxy-2-alkylthiophenes. The presence of an α, β-unsaturated ketone grouping in molecules of II could be manifested in their ability to add nucleophiles, particularly amines, and to give the necessary compounds in a subsequent step.

Experiments fully confirmed this assumption, and we obtained up to 80% yields of N-monosubstituted aminomethylene-4-thiolen-2-ones (Ia-h) by the reaction of II with primary amines or diamines.

This transformation can be explained, for example, as 1,4-addition of the amine to the O=C−C=C fragment of the molecule with the development of intermediate gem-diamine A (see scheme), which is then converted to the corresponding Schiff base.



a-e $R=C_2H_5$, f-h $R=CH_3$; a $R''=\text{cyclo-}C_6H_{11}$, b $R''=C_6H_5CH_2$, c $R''=C_6H_5$, d $R''=\beta\text{-}C_{10}H_7$, e $R''=CH_2CH_2NHCH=$, f $R''=\text{cyclo-}C_6H_{11}$, g $R''=C_6H_5$, h $R''=C_6H_5CH_2$; IIa $R=C_2H_5$, $R'=C_6H_5$, b $R=CH_3$, $R'=C_6H_5$, c $R=R'=CH_3$

According to the results of an investigation of the NMR spectra currently available to us, the I obtained exist in solution primarily in the ketoamine form.* The IR spectra of Ia-d, obtained with a UR-20 spectrophotometer with KBr pellets, also do not contradict their existence in the ketoamine form. The intense bands at 1530-1575 cm^{-1}, which are also displayed in the spectra of II (1560 cm^{-1}) which have an authentic keto form, indicate the presence of a dihydrothiophene ring; the absorption is of low intensity in this region in the spectra of substituted thiophenes. The bands at 1645-1660 cm^{-1} are close to the ν_{CO} frequencies of IIa and IIc (1660 and 1650 cm^{-1}, respectively). Finally, III and IV have a broad band at 3200 cm^{-1} which can be ascribed to the vibrations of an associated NH group.

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* The problem of the structure of I will be examined in greater detail in our next communication.

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TABLE 1. N-Monosubstituted 5-Alkyl-3-aminomethylene-4-thiolen-2-ones (Ia-h)

Compound	mp, °C	Empirical formula	Found, %			Calculated, %			Yield, %
			C	H	S	C	H	S	
Ia	136—137[a]	$C_{13}H_{19}NOS$	65,5; 65,4	8,0; 7,8	13,6; 13,6	65,8	8,1	13,5	80
Ib	96—97[b]	$C_{14}H_{15}NOS$	68,22; 68,41	6,31; 6,12	12,94; 12,96	68,54	6,16	13,07	67
Ic	99,5—100,5[a,c]	$C_{13}H_{13}NOS$[d]	—	—	—	—	—	—	43
Id	164—165[a]	$C_{17}H_{15}NOS$	72,6; 72,4	5,3; 5,2	11,4; 11,6	72,6	5,4	11,4	50
Ie	231—232[e]	$C_{16}H_{20}N_2O_2S_2$	57,3; 57,5	6,2; 6,1	18,8; 18,9	57,1	6,0	19,1	67
If	152,5—153,5[a]	$C_{12}H_{17}NOS$	64,5; 64,5	7,8; 7,6	14,4; 14,2	64,5	7,7	14,4	65
Ig	159—160[a,c]	$C_{12}H_{11}NOS$	—	—	—	—	—	—	52
Ih	125—125,5[a]	$C_{13}H_{13}NOS$	67,6; 67,8	6,1; 5,9	13,8; 14,0	67,5	5,7	13,9	70

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[a] From alcohol.

[b] From alcohol and heptane.

[c] A sample did not depress the melting point of the sample obtained in [1].

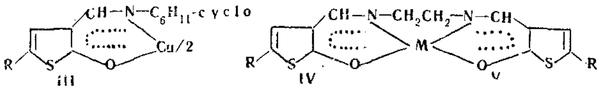
[d] Perchlorate mp 147-158 deg (dec., from acetic acid containing $HClO_4$). Found %: C 47.2, 47.1; H 4.0, 3.9; Cl 10.9, 10.7; N 4.3, 4.6; S 9.9, 9.7. $C_{13}H_{13}NOS \cdot HClO_4$. Calc. %: C 47.1; H 4.2; Cl 10.7; N 4.2; S 9.7.

[e] With decomposition, from dimethylformamide–alcohol.

One of the Schiff bases obtained by us, viz., 5-methyl-3-(N-phenylaminomethylene)-4-thiolen-2-one (Ig), was, according to [2], synthesized by the action of dimethylformamide and phosphorus oxychloride on 5-hydroxy-2-methylthiophene with subsequent treatment of the aldehyde thus formed with aniline. However, our attempt to accomplish the synthesis of the starting 5-methyl-2-hydroxy-3-formylthiophene in a similar manner resulted in N,N-dimethylaminomethylene derivative IIc rather than the aldehyde. It is possible that the difference in the results is due to the different conditions used to carry out the experiment or in the workup, since a description of the experiment and the data of elementary analysis are not given in [2]. In addition, the formation of IIc during the formylation of 5-hydroxy-2-methylthiophene becomes understandable if one considers that, as established in [3], it has the 5-methyl-4-thiolen-2-one structure and, consequently, is capable of reacting with the Vilsmeier complex, as a compound with an active methylene group, to give a derivative of the II type [4].

Compound IIc reacts with aniline to give Schiff base Ig with mp 159-160 deg; the melting point could not be raised by repeated recrystallization (according to [2] the melting point is 165 deg). Judging from thin-layer chromatography on Al_2O_3 [hexane–ether (4:1)] and gas-liquid chromatography, our compound does not contain impurities. Unfortunately, we were deprived of the possibility of performing a mixed melting-point determination with the compound obtained by the French investigators [2].

It was of interest to obtain complexes with metal ions from the synthesized ketoamines in order to study their properties as compared to their sulfur analogs. However, in contrast to the corresponding mercaptothienylideneimines which readily give chelates with copper, zinc, and nickel ions [5], we were able to obtain only copper complex III from 5-ethyl-3-(N-cyclohexylaminomethylene)-4-thiolen-2-one (Ia).



III IV V

III $R = C_2H_5$; IV $M = Cu$; V $M = Ni$

A nickel chelate could not be obtained by heating for many hours in dimethylformamide or in the presence of sodium acetate, sodium methoxide, or alkali. It is possible that this is explained by the low stability of the β-ketoamine complexes to the action of oxygen and moisture, which was noted for analogous compounds of the aliphatic series [6] and several others [7]. The complexes of tetradentate ligand Ie, which form a system of condensed chelate rings (IV and V), were more stable and can be isolated in good yields by the reaction of Ie with copper and nickel acetates.

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EXPERIMENTAL

N-Monosubstituted 5-Alkyl-3-aminomethylene-4-thiolen-2-ones (Ia-h) (see Table 1). A mixture of 0.001 mole of N,N-disubstituted 5-alkyl-3-aminomethylene-4-thiolen-2-one (IIa-c) and 0.0012 mole of freshly distilled or recrystallized amine in 1-2 ml of alcohol was heated for several minutes on a water bath and cooled. The precipitate was filtered (in some cases heptane was added or the solvent was partially evaporated to initiate crystallization), washed with ether or heptane, and recrystallized from suitable solvents.

Action of Dimethylformamide and Phosphorus Oxychloride on 5-Hydroxy-2-methylthiophene. Phosphorus oxychloride [2.7 g (0.018 mole)] was added with stirring to 2 g (0.018 mole) of 5-hydroxy-2-methylthiophene [3] in 2.5 ml of dimethylformamide at 0-5 deg. The mixture was held at 0-5 deg for 2 h, allowed to stand overnight, and then hydrolyzed at 0-5 deg with a saturated solution of sodium acetate and extracted with benzene. The extract was washed with water, dried with $MgSO_4$, and the benzene was removed by distillation to give 1.60 g (54%) of 5-methyl-3-(N,N-dimethylaminomethylene)-4-thiolen-2-one (IIc) with mp 131-132 deg (from benzene–petroleum ether and from alcohol). The product did not depress the melting point of a sample of IIc obtained in [1].

Copper Chelate of 5-Ethyl-3-(N-cyclohexylaminomethylene)-4-thiolen-2-one (III). An aqueous solution of 0.15 g of copper acetate was added to a hot methanol solution of 0.36 g of Ia, and the mixture was heated for several minutes. The resulting precipitate was filtered, washed with methanol, and reprecipitated twice from chloroform with methanol to give 0.15 g (37%) of violet crystals of copper chelate III with mp 152.5-153.5 deg (dec.). Found %: C 57.8, 58.1; H 6.7, 6.7; S 11.7, 11.8; Cu 12.4, 12.4. $C_{26}H_{36}N_2O_2S_2Cu$. Calc. %: C 58.2; H 6.8; S 12.0; Cu 11.8. About 30% of starting Ia was isolated from the filtrate.

Copper Chelate of N,N'-Bis[(2-oxo-5-ethyl-3-thienylidene)methyl]ethylenediamine (IV). A solution of 0.15 g of copper acetate in dimethylformamide–water was added to a solution of 0.2 g of Ie in 4 ml of dimethylformamide. Shiny crystals of the chelate began to precipitate immediately. Methanol was added to the mixture, and the precipitate was filtered and reprecipitated twice from $CHCl_3$ with methanol to give 0.2 g of IV with mp 302.5-303.5 deg (dec.). Found %: C 48.5, 48.7; H 4.7, 4.6; S 16.5, 16.3; Cu 16.2, 16.3. $C_{16}H_{18}N_2O_2S_2Cu$. Calc. %: C 48.3; H 4.6; S 16.1; Cu 16.0.

Nickel Chelate of N,N-Bis[(2-oxo-5-ethyl-3-thienylidene)methyl]ethylenediamine (V). This compound was obtained in the same way as IV from 0.2 g of Ie in dimethylformamide and a methanol solution of 0.15 g of nickel acetate. Two reprecipitations from $CHCl_3$ with methanol gave 0.2 g (85%) of a product with mp 327-328 deg (dec.). Found %: C 48.8, 48.6; H 4.5, 4.7; S 16.1, 16.5; Ni 15.0, 15.0. $C_{16}H_{18}N_2O_2S_2Ni$. Calc. %: C 48.9; H 4.6; S 16.3; Ni 14.9.

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