SYNTHESIS AND SOME PROPERTIES OF NEW COMPLEXING AND CHELATE COMPOUNDS OF THE FURAN SERIES

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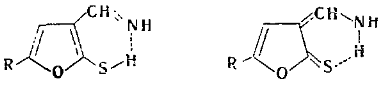
Some difunctional compounds of the furan series of the mercaptoaldimine type were synthesized, their polarographic behavior was studied, and Ni(II), Co(II), ZN(II), and Cu(I) chelates of these ligands were obtained.

Continuing our research on the synthesis and investigation of the properties of complexing compounds and complexes of the thiophene series and condensed thiophene systems [1], it seemed of interest to obtain and study within a definite plan the properties of the analogous compounds of the furan series. Systems including a thiophene ring contain sulfur and nitrogen atoms as coordinating centers. An investigation of their properties showed, in particular, that the complexes formed by them are effective inhibitors of the oxidation of aliphatic hydrocarbons [2] and, in addition, have a certain amount of activity against deep-seated mycoses [3].

The fundamental possibility of the preparation of difunctional furan derivatives of structure A was demonstrated by one of us and Ya. L. Danyushevskii [4]. A study of the PMR spectra of these derivatives [5] in solution showed that they include a relatively strong intramolecular hydrogen bond and should preferably be assigned to the 5-alkyl-3-(aminomethylene)-4-oxolene-2-thione series (Ab):



a A b

The tasks that we presented ourselves within undertaking the present research were, first of all, to obtain, with the available ligands, a number of chelates that could be compared with respect to their properties with their thiophene analogs and thus to a certain degree ascertain the effect of replacement of a ring heteroatom, and, second, to find a method for increasing the solubility of the ligands and the chelates of the series under consideration. We were able to solve the second of these tasks to a certain degree by introduction of a tert-butyl group in place of the methyl or ethyl group in the 5 position of the ring.

Derivative II (see Table 1) was synthesized by the method previously described for the analogous compounds by the action of sodium in liquid ammonia on 5-tert-butyl-2-ethylmercapto-3-formylfuran diethylacetal. On reaction with amines, I and II form derivatives that, in one of their tautomeric forms, are mercapto-substituted Schiff bases (III-VI). The data pertaining to these compounds are presented in Table 1. A number of chelates, which are characterized in Table 2, were obtained by the action of equimolecular amounts of metal acetates on derivatives I-VI in alcohol or aqueous alcohol solutions.

It is interesting to note that zinc and cadmium chelates X, XII, and XIV lose nitrogen on refluxing with 50% acetic acid or even on brief heating with dilute (1:1) hydrochloric acid to give XXVI-XXVIII, which, at least with respect to their composition, correspond to chelates of the B type.

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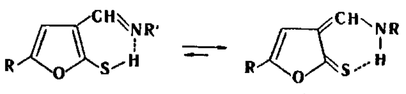
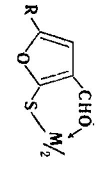
TABLE 1



Compound	R	R′	mp, deg C	Purification method: R = reprecipitation and C = crystallization	Color	Solubility	Empirical formula	Found, %				Calc., %				Yield, %
								C	H	N	S	C	H	N	S	
I[4]	CH_3	H	168—170° (dec.)	C (ethanol)	Green	Ethanol, acetone, and dioxane (partially)										85
II	$(CH_3)_3C$—	H	102—104,5°	R (from benzene-heptane	Yellow-brown	Ethanol, acetone, and benzene (very good)	$C_9H_{13}NOS$	59,0	7,3	7,4	17,3	59,0	7,1	7,6	17,5	80,5
III	CH_3	C_6H_5	83—85°	C (ethanol)	Bright-red	Ethanol, acetone, and benzene	$C_{12}H_{11}NOS$	66,2	4,8	6,3		66,7	4,6	6,5		97
IV	$(CH_3)_3C$—	C_6H_5	111—112°	C (ethanol)	Red	Ethanol, acetone, and benzene	$C_{15}H_{17}NOS$	69,8	6,4	5,4	12,3	69,5	6,6	5,4	12,4	82
V	$(CH_3)_3C$—	β-$C_{10}H_7$	169,5—171°	C (ethanol)	Red	Ethanol, acetone, and benzene	$C_{19}H_{19}NOS$	73,9	6,3	4,6	10,4	73,8	6,1	4,5	10,4	90
VI	$(CH_3)_3C$—	C_6H_{11}	117—119°	C (ethanol)	Bright-yellow	Ethanol, acetone, and benzene	$C_{15}H_{23}NOS$	67,4	8,5	4,8	12,4	67,9	8,7	5,3	12,1	90



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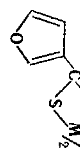


C

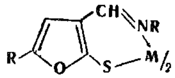
XXVI R = $(CH_3)_3C$, M = Zn; XXVII R = CH_3, M = Cd; XXVIII R = $(CH_3)_3C$, M = Cd

The fact that the ring opening that, generally speaking, is peculiar to furan compounds under similar conditions and subsequent recyclization to favor system C do not occur in this case follows from the PMR data for the newly formed zinc compounds. The PMR spectra (in dichloroethane) contain singlets for XXVII (R = CH_3) at δ 9.05 (CHO), 6.10 (β-H), and 2.17 ppm (CH_3) and at 9.05 (CHO), 6.03 (β-H), and 1.22 [$(CH_3)_3C$] for XXVI and XXVIII [R = $(CH_3)_3C$]. In addition, this is also confirmed by other facts. For instance, the reaction of the product of hydrolysis of XXVI (see the experimental section) with aniline gives the same chelate that is obtained as a result of the reaction of starting chelate XIV with this amine. This sort of stabilizing effect of chelate formation on the extremely labile difunctional chelate-forming compound is of undoubted interest. However, the mechanism of the transformation of chelates X, XII, and XIV to compounds of the B type remains unclear. The analogous copper and nickel chelates do not lose nitrogen on refluxing with acetic acid.

The presence of different substituents in the 5 position of the furan ring and attached to the extracyclic nitrogen atom of ligands I-VI has made it possible to follow the effect of the nature of the substituents on the polarographic behavior of these compounds. In this connection, let us point out that we have previously made a similar polarographic analysis [7] for the analogous compounds of the thiophene series.

The transition from I to II causes appreciable difficulty in the reduction, probably because of the effect of two factors — an increase in the electron-donor effect of the substituent in the 5 position of the furan ring and an increase in the solubility (see Table 3). The significance of the first of these factors by itself is small, inasmuch as the reduced group is in the meta position relative to the alkyl substituent; it is more likely that the effect of this substituent is manifested in a reduction of the acidity of the group that acts as the proton donor (see [7]). The increase in the solubility entails a decrease in the adsorbability, and, consequently, a decrease in the near-electrode concentration of the depolarizer, all other things being equal.

In dimethylformamide (DMFA), where the adsorption of the depolarizer is appreciably less (as attested to by the slope of the waves), the $E_{1/2}$ values are shifted markedly to more negative potentials. When the proton-donor activity of the medium

TABLE 2. Compounds of the Composition 

Compound	R	R′	Metal	mp, deg C	Purification method: C = crystallization, R = refluxing	Color	Solubility	Empirical formula	Found, %				Calc., %			
									C	H	S	M	C	H	S	M
VII	CH_3	H	Ni	Does not melt up to 300°	R (water)	Yellow	Partially in acetone, ethanol, and chloroform	$C_{12}H_{12}N_2NiO_2S_2$	42,4	3,9	19,3	16,8	42,5	3,5	18,9	17,3
VIII	CH_3	H	Zn	260—263° (dec.)	C (acetone)	Yellow-green	Acetone	$C_{12}H_{12}N_2O_2S_2Zn$	41,8	3,6	—	19,5	41,7	3,5	—	18,9
IX	CH_3	H	Cu	Does not melt at 300° (dec.)	R (methanol)	The same	DMFA	C_6H_6CuNOS	35,3	3,1	—	31,6	35,4	3,0	—	31,2
X	CH_3	H	Cd		C (ethanol)	Yellow	Ethanol	$C_{12}H_{12}CdN_2O_2S_2$	36,5	3,1	16,1	28,2	36,7	3,1	16,3	28,6
XI	$(CH_3)_3C$	H	Cu	240—246° (dec.)	R (methanol)	Green		$C_9H_{12}CuNOS$	44,4	4,9	—		44,0	4,9		
XII	$(CH_3)_3C$	H	Cd	237—240° (dec.)	C (ethanol)	Yellow	Ethanol	$C_{18}H_{24}CdN_2O_2S_2$	45,1	4,8	13,5	23,8	45,4	5,0	13,4	28,5
XIII	$(CH_3)_3C$	H	Ni	Above 200° (dec.)	R (water and methanol)	The same		$C_{18}H_{24}N_2NiO_2S_2$	51,1	5,7	—	15,5	51,1	5,7	—	15,7
XIV	$(CH_3)_3C$	H	Zn	217—222° (dec.)	C (ethanol)	" "	Ethanol	$C_{18}H_{24}N_2O_2S_2Zn$	50,3	5,7	—	15,3	50,3	5,6	—	15,2
XV	CH_3	C_6H_5	Ni[a]	217—220,5°	C (ethanol)	Black	Ethanol, acetone, benz.	$C_{24}H_{20}N_2NiO_2S_2$	58,7	4,2	13,4	11,9	58,7	4,1	13,1	11,9
XVI	$(CH_3)_3C$	C_6H_{11}	Ni	216—219°	C (ethanol)	Green-yellow	"	$C_{30}H_{44}N_2NiO_2S_2$	61,7	7,4	10,7	10,0	61,4	7,5	10,9	10,0
XVII	CH_3	C_6H_5	Co[b]	232—235°	C (ethanol + acetone)	Dark-red	"	$C_{24}H_{20}CoN_2O_2S_2$	58,4	4,1	—	—	58,7	4,1	—	—
XVIII	$(CH_3)_3C$	C_6H_{11}	Zn[c]	243—245,5°	C (acetone)	Yellow	"	$C_{30}H_{44}N_2O_2S_2Zn$	60,6	7,3	11,1	11,3	60,7	7,4	10,8	11,0
XIX	$(CH_3)_3C$	C_6H_5	Zn[d]	201—203°	C (ethanol + acetone)	The same	The same	$C_{30}H_{32}N_2S_2Zn$	62,0	5,7	11,0	11,6	61,9	5,5	11,0	11,2
XX	CH_3	C_6H_5	Zn	221—224°	C (acetone)	Yellow	Ethanol, acetone, benz.	$C_{24}H_{20}N_2O_2S_2Zn$	57,7	4,1	12,9	13,5	57,9	4,0	12,9	13,1
XXI	$(CH_3)_3C$	C_6H_5	Cd	212—217,5°	C (ethanol)	The same	Ethanol, acetone	$C_{30}H_{32}CdN_2O_2S_2$	57,1	5,1	4,3d	—	57,3	5,1	4,4	—
XXII	$(CH_3)_3C$	β-$C_{10}H_7$	Zn	180—183°	C (ethanol + acetone)	Yellow	Acetone, ethanol	$C_{28}H_{36}N_2O_2S_2Zn$	66,6	5,3	8,9	10,7	66,9	5,3	9,4	9,6
XXIII	$(CH_3)_3C$	β-$C_{10}H_7$	Cu	214—230°	C (acetone + ethanol)	The same	Ethanol, acetone	$C_{14}H_{18}CuNOS$	61,0	5,0	—	—	61,4	4,8	—	—

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a–e) The molecular weights were determined ebullioscopically in benzene in a precision ebulliometer [6]. The following corresponding molecular weights of the "monomers" were obtained under these conditions: a) found 476, calculated 491; b) found 489.6, calculated 491.3; c) found 595.8, calculated 583.3; d) found 577.6, calculated 581.8; e) analysis for N: found 4.33, 4.17%, calculated 4.45%.

TABLE 3. $E_{1/2}$ Values and Slopes of the Polarographic Graphs of the Waves of Mercaptoaldimines of the Furan Series

Compound	In 50% ethanol with a 0.1 N KCl base electrolyte		In 30% ethanol with a 0.1 N KCl base electrolyte		In 99.97% DMFA with a 0.1 N LiCl base electrolyte		In 90% DMFA with a 0.1 N acetate buffer base electrolyte ($CH_3COOH/CH_3COOLi = 1$)	
	$E_{1/2}$, V	$\frac{bb'}{b'-b}$*, mV	$E_{1/2}$, V	$\frac{bb'}{b'-b}$, mV	$E_{1/2}$, V	$\frac{bb'}{b'-b}$, mV	$E_{1/2}$, V	$\frac{bb'}{b'-b}$, mV
I	−1,57	65	−1,54	69	−1,72	57	−1,68	99
II	−1,60	70	−1,57	87	−1,76	64	−1,69	98
III	−1,39	99	−1,30	71	−1,41	88	−1,39	98
IV	−1,40	97	−1,35	123	−1,39	72	−1,40	87
V	Precipitates				−1,36	95	−1,33	76
VI	−1,69	56	−1,63	88	−1,76	51	−1,70	82

*The bb'/b'-b value is the pre-exponential factor in the equation of the area of the kinetic wave (see [9]).

increases (transition to a buffer in DMFA, data in the last column of Table 3) reduction is somewhat facilitated, and (which is extremely surprising) the difference in the $E_{1/2}$ values of I and II is reduced to practically zero. A similar but less pronounced effect is observed on comparison of III and IV. As compared with I and II, their reduction is considerably facilitated because of the introduction of a phenyl group, which not only lowers the electron density on the reduced group and causes expansion of the π-electron system but also increases the adsorbability. This latter circumstance apparently explains the large slope of the waves of III and IV (compare this result with the data for I and II). For the same reasons, V, which has a β-naphthyl grouping attached to the nitrogen atom, is reduced even more readily.

Compound VI, which contains an electron-donor cyclohexyl substituent, which, moreover, owing to its noncoplanar conformation, reduces the adsorbability of VI, is reduced with the greatest difficulty of all. An increase in the alcohol concentration therefore had practically no effect on the $E_{1/2}$ value of VI, and $E_{1/2}$ is shifted to more negative potential by 70 mV only on passing to DMFA, whereas in the case of I and II their $E_{1/2}$ values become appreciably more negative as the alcohol concentration increases and becomes particularly sharply more negative (by 180 mV) on passing to DMFA.

EXPERIMENTAL

The PMR spectra of dichloroethane solutions of the compounds (0.4-0.6 mole/liter) were recorded with a Varian DA-60 spectrometer. The chemical shifts are presented relative to tetramethylsilane.

Polarography was carried out in a thermostatted cell at 25 ± 0.5°. Silver chloride and aqueous saturated calomel electrodes served as the anode. The curves were recorded by means of a PÉ-312 polarograph with potentiometric monitoring of the potentials with respect to an external saturated aqueous calomel electrode, which in the case of DMFA was separated from the test solution by a bridge filled with a solution of the same composition as that in the cell. The dropping electrode has a spatula for forced detachment of the drop; the dropping electrode characteristics were m = 0.89 mg/sec, and t = 0.47 sec. The curves of the base electrolyte for each test solution were recorded in order to introduce a correction for the residual current. The solvents were 30 and 50% ethanol and 90% and practically anhydrous DMFA (99.97%). The following solutions were used as the base electrolytes: 0.1 N KCl in 50% ethanol, 0.1 N LiCl in 99.97% DMFA, and an acetate buffer (0.05 N CH_3COOH + 0.05 N CH_3COOLi + 0.1 LiCl in 90% DMFA).

2-Ethylmercapto-5-tert-butyl-3-formylfuran Diethylacetal (XXV). A 39-ml (0.042 mole) sample of phosphorus oxychloride was added with stirring in the course of 10 min at 0° to a mixture of 11 ml of DMFA and 6 g (0.033 mole) of 5-tert-butyl-2-ethylmercaptofuran [8], after which the mixture was held at this temperature for 1 h, at room temperature for 2 h, and at 60-70° for 5 h. It was then allowed to stand overnight, and the resulting viscous mass was poured over ice. The aqueous mixture was neutralized with sodium carbonate, the organic layer was separated, and the aqueous layer was extracted with ether. The combined ether solutions were washed with water and dried with magnesium sulfate. The solvent was removed by vacuum distillation, and the residue was fractionated to give 4 g (74.5%) of formylfuran XXIV with bp 102-106° (1-2 mm) and n_D^{21} 1.5198. A 10-g (0.048 mole) sample of this aldehyde, 11 ml (0.067 mole) of ethyl orthoformate, 6 ml of absolute ethanol, and a few drops of concentrated HCl were mixed, during which a small amount of heating was observed and the solution became cherry-red. After 20 h, this solution was made alkaline with sodium ethoxide to give an almost neutral solution, and the precipitated NaCl was removed by filtration. The solvent was removed by distillation, and the residue was vacuum distilled to give 11.3 g of acetal XXV (85%) with bp 120-123° (3 mm) and n_D^{23} 1.4800. Found: C 63.0, H 9.2, S 11.2%. $C_{15}H_{26}O_3S$. Calculated: C 62.9, H 9.1, S 11.2%.

2-Mercapto-5-tert-butyl-3-furfurylideneamine (II). A solution of 42 g (0.147 mole) of formylfuran XXV in 77 ml of absolute ether was added at —65 to —70° to 380 ml of liquid ammonia in a nitrogen atmosphere, after which 6.75 g (0.204 g-atom) of sodium metal was added in small portions with stirring until a persistent blue color was obtained. The mixture was then stirred for another 30 min, after which the cooling bath was removed, and the unchanged sodium was converted to a salt by the addition of ammonium chloride. The ammonia was evaporated, the solution was cooled to —10°, and 125 ml of water and 75 ml of heptane were added. The aqueous layer was extracted with several portions of heptane, after which ammonia was bubbled through it for a certain time. Dilute (1:1) hydrochloric acid was then added to it until the pH was 8. The resulting precipitate was removed by filtration, washed, and dried to give 26.8 g (80.5%) of II with mp 102-104.5° (see Table 1).

(2-Mercapto-5-methyl-3-furfurylidene)aniline (III). A hot solution of 1.27 g (0.014 mole) of aniline in 20 ml of ethanol was added to a hot solution of 2 g (0.014 mole) of I in 40 ml of ethanol, after which the mixture was cooled and evaporated to give 2.98 g (97%) of Anil III with mp 83-84°. Compounds IV-VI were similarly obtained, but the mixtures were refluxed for 1-3 h.

Nickel Chelate of VII. A solution of 2.52 g (0.014 mole) of nickel acetate in 50 ml of methanol was added gradually to a hot solution of 2 g (0.014 mole) of mercaptoaldimine I in 70 ml of methanol, and the resulting yellow precipitate was removed by filtration to give 2.4 g (61%) of product. The remaining data pertaining to this chelate and to the similarly prepared chelates VIII-XXIII are presented in Table 2.

Hydrolysis of Chelate XIV. A 0.3-g (0.7 mmole) sample of the chelate was refluxed with 50% acetic acid for 1 h, during which the color of the solution turned dark-red. The acetic acid was removed by distillation, and the residual 0.22 g (73%) of dark-red XXVI was recrystallized from aqueous alcohol to give a product with mp 75-77°. Found: C 50.3; H 5.1; S 14.9; Zn 14.7%; M (ebullioscopically) 409.2. $C_{18}H_{22}O_4S_2Zn$. Calculated: C 50.1; H 5.1; S 14.9; Zn 15.2%; M 431.2. A similar result was also obtained when XIV was heated for 5 min with dilute (1:1) HCl. A mixture of XXVI (mp 75-77°) and 0.1 g of aniline in ethanol was refluxed for 3 h, after which the solvent was evaporated, and the yellow residue was recrystallized from alcohol to give a product with mp 204-206°. A mixture of this product with chelate XIX also melted at the same temperature.

Zinc Chelate of 2-Mercapto-5-tert-butyl-3-furfurylideneaniline [5-tert-Butyl(3-phenylaminomethylene)-4-oxolene-2-thione] (XIX). A mixture of 0.4 g (0.93 mmole) of XIV, 0.21 g (2.3 mmole) of aniline, and ethanol was refluxed for 3 h. The solvent was then removed by distillation to give 0.56 g of a yellow substance. Two recrystallizations from alcohol gave a product with mp 202-204°. The yield was almost quantitative. No melting-point depression was observed for a mixture of this product with chelate XIX.

Hydrolysis of Chelate X. A mixture of 0.28 g (0.7 mmole) of the chelate with 30 ml of 50% acetic acid was refluxed for 3.5 h. The following day, the green precipitate was removed by filtration and washed with water to give a product with mp 210° (dec.). The product was insoluble in acetone, methylene chloride, and dichloroethane. Found: C 36.5; H 2.7; Cd 28.6; S 15.8%. $C_{12}H_{22}CdO_4S_2$. Calculated: C 36.5; H 2.5; Cd 28.5; S 16.3%.

Hydrolysis of Chelate XII. A 0.3-g (6.3 mmole) sample of chelate XII was refluxed with 50% acetic acid for 3 h, after which the solvent was evaporated to give 0.11 g of a crimson substance with mp 180° (dec., from alcohol). Found: C 45.2; H 4.6; Cd 23.8; S 13.4%. $C_{18}H_{22}CdO_4S_2$. Calculated: C 45.1; H 4.6; Cd 23.5; S 13.4%.

Cadium Chelate of 2-Mercapto-5-tert-butyl-3-furfurylideneaniline (XXI). A solution of 0.3 g (63 mmole) of chelate XII and 0.13 g (1.4 mmole) of aniline in ethanol was refluxed for 3 h, after which the solid was removed by distillation to give 0.4 g (quantitative yield) of a yellow substance with mp 213-222° (from alcohol). No melting-point depression was observed for a mixture of this product with chelate XXI obtained by the general method described above.

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