Summary

Nineteen kinds of sodium thiohydroxamate (I) were synthesized from hydroxylamine and esters of thionic acids or dithioacids in the presence of sodium methylate with about 40% yields for the aliphatic compounds and above 70% yields for the aromatic ones with some exceptions. A number of sodium O-methylthiohydroxamate (II) were also obtained by the analogous method using O-methylhydroxylamine. On long standing, I were apt to rearrange to the 1,3-disubstituted thiourea while II were very stable. Some crystalline thiohydroxamic acid and O-methylthiohydroxamic acids were prepared from I and II.

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171. Kōichi Nagata and Satoshi Mizukami: Studies on Thiohydroxamic Acids and Their Metal Chelates. II.[*1] Structures of Thiohydroxamic Acids.

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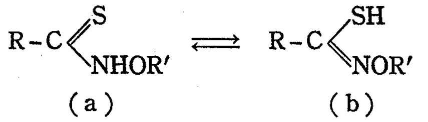
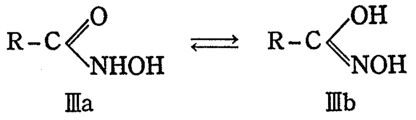
For hydroxamic acids which are capable of tautomeric changes (IIIa, b) it has been established[1~4)] that the keto-form exists predominantly both in the solid state and in solution, whereas there is no such reports of the structures and thiolthione tautomerisms of thiohydroxamic acids (Ia, b). In this paper some thiohydroxamic acids and O-methyl thiohydroxamic acids (IIa, b) which are reported in Part I[*1] were examined by physical methods and their probable structures were discussed.



(a) (b)

I: $R'=H$ II: $R'=CH_3$



IIIa IIIb

A) Infrared Spectra

Some typical infrared spectra of II are shown in Fig. 1. No marked differences of the spectra are found between in carbon tetrachloride solution and in the solid or as the liquid film. The SH stretching frequencies at $2578\pm8\,cm^{-1}$ are in a satisfactory agreement with those found for ordinary thiol group, $2600\sim2550\,cm^{-1}$,[5)] so that any hydrogen-bonding associated with thiol group is less likely. Furthermore, NH stretching bands are not found under any circumstances in the region $3400\sim3550\,cm^{-1}$ (monomer) or $3300\sim3140\,cm^{-1}$ (dimeric), in which those of secondary thioamides or

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[*1] Part I: This Bulletin, **14**, 1249 (1966).

[*2] Sagisukami, Fukushima-ku, Oaska (永田耕一, 水上 聰).

1) D. Hadži, D. Prevoršek: Spectrochim. Acta, **10**, 38 (1957).

2) H. Lenormant: Bull. soc. chim. France, **1948**, 33.

3) F. Mathis: Compt. rend., **232**, 505 (1951).

4) W. J. Orville-Thomas, A. E. Parsons: J. Mol. Spectroscopy, **2**, 203 (1958).

N-substituted thioureas[6~9] appear. These observations lead us to the conclusion that II exists in the only one structure, namely in thiol-form (IIb), in the solid or liquid and in the solution.

On the contrary, the infrared spectrum of I in solution differ from those in solid as shown in Fig. 2. In the solution, SH stretching vibration appears and furthermore three bands exist in the high frequency region over 3200 cm^{-1}. All these three bands move on deuteration to smaller wave-numbers at which the wave-number ratio are near 1.40, and the intensity of the broad band at 3220~3230 cm^{-1}, among the three bands, is reduced with dilution of the carbon tetrachloride solution while the intensities of the other two sharp bands at 3580±5 cm^{-1} and 3405±15 cm^{-1} are increased slightly, so that the former is due to the intermolecularly associated bonds and the latter two bands result from non-associated vibrations. Although the appearance of the SH band shows the existence of the thiol isomer (Ib), it is improbable that two non-associated bands occur from only the thiol isomer, because the oxime group should give only one non-associated band in the region 3500~3650 cm^{-1}.[10~12] These observations can be elucidated only by assuming the presence of both thiol and thione tautomers in equilibrium in the solution. Then SH stretching vibration is due to the thiol-form, and the two non-associated bands at 3580±5 cm^{-1} and 3405±15 cm^{-1} should be assigned respectively to the OH and the NH stretching vibration which result from the -NHOH group in Ia and the =NOH group in Ib. These frequencies are in fair agreement with the OH frequencies in oximes or amidoximes[13] (3610~3650 cm^{-1}) and the NH frequencies in secondary amides (3400~3460 cm^{-1})[5] or the secondary thioamides or N-substituted thioureas (3350~3430 cm^{-1}).[6~9]

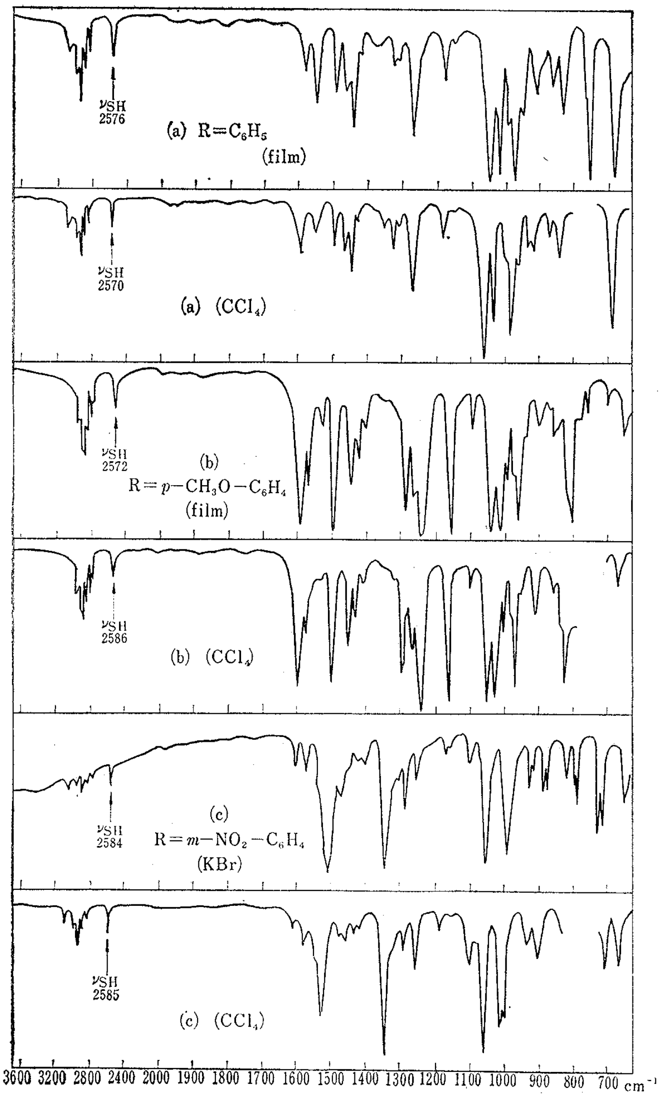

Fig. 1. Infrared Spectra of $R-C\langle^{SH}_{NOCH_3}$ (II)

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5) L. J. Bellamy : "The Infrared Spectra of Complex Molecules," 2nd Ed. (1958), Methuen & Co., Ltd., London.

6) D. Hadži : J. Chem. Soc., **1957**, 847.

7) E. Spinner : *Ibid.*, **1960**, 1237.

8) B. Milligan, E. Spinner, J. M. Swan : *Ibid.*, **1961**, 1919.

9) I. Suzuki : Bull. Chem. Soc. Japan, **35**, 1456 (1962).

10) A. Palm, H. Werbin : Can. J. Chem., **31**, 1004 (1953).

11) Y. Matsui : Nippon Kagaku Zasshi, **83**, 985, 990 (1962).

12) S. Califano, W. Lüttke : Z. Physik. Chem. (Frankfurt) [N. F.], **6**, 83 (1956).

13) J. Barrans, T. Marty, R. Mathis : Compt. rend., **254**, 2736 (1962).

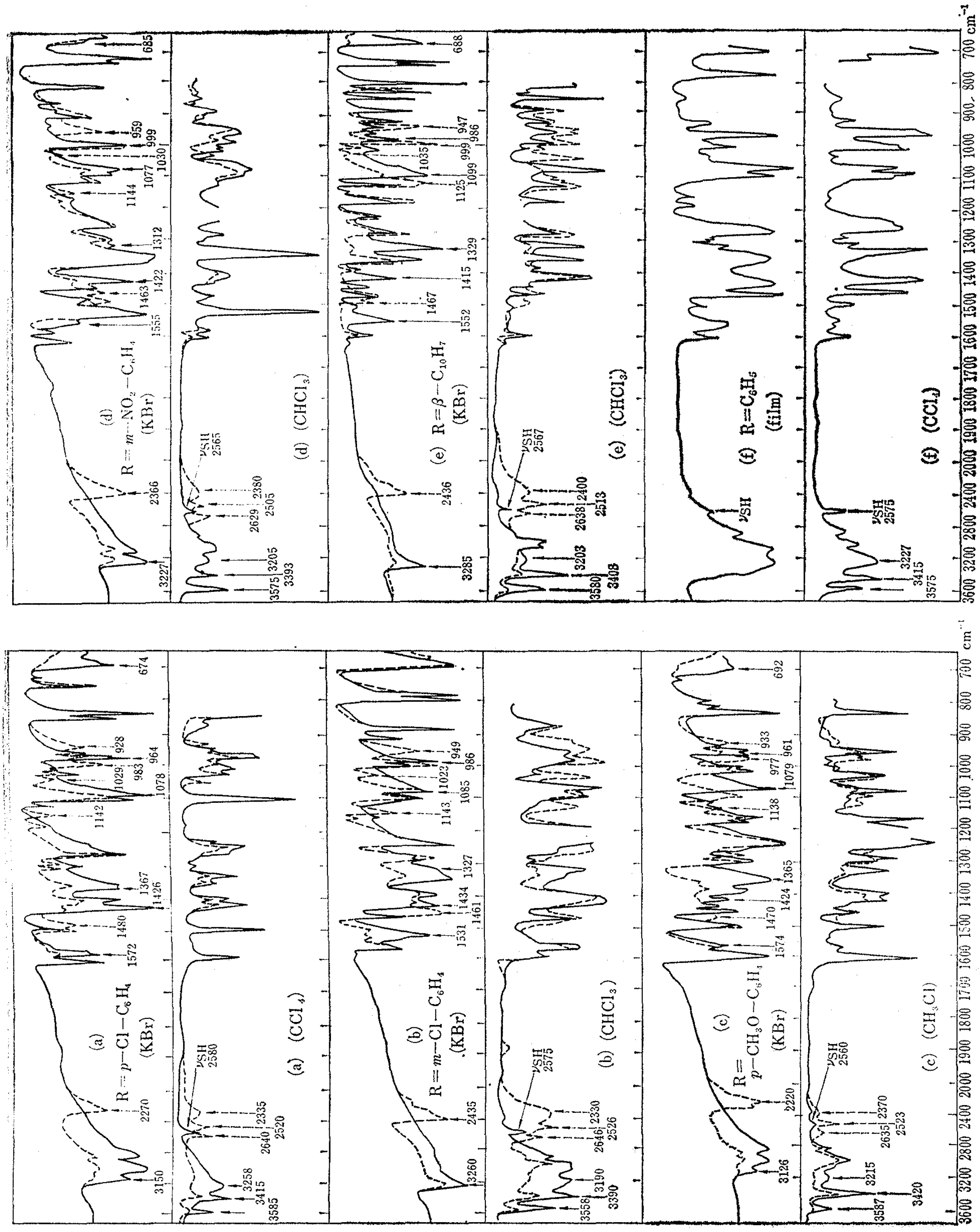

Fig. 2. Infrared Spectra of $R-C(=S)NHOH$ (Ia) $\rightleftarrows$ $R-C(SH)=NOH$ (Ia)

—— simple ------ deuterated

On the one hand, the absence of SH band in the solid state suggests that the structures of the crystalline thiohydroxamic acids may be the thione-form (Ia). Additional supports for this probable structures are obtained by investigating the spectral changes with deuteration summarized as follows: (i) in the high-frequency region the associated NH and OH stretching vibrations move to lower frequencies at which wave-number ratio are near 1.40, (ii) five bands at 1550±20, 1425±10, 1340±30, 1085±5 and 680±10 cm^{-1} disappear or decrease their intensity remarkably and new four bands appear at 1470±10, 1135±10, 1035±5, 945±15 cm^{-1} after deuteration, (iii) a band at near 970 cm^{-1} is sensitive to deuteration, though it is obscure in some cases.

It may be mentioned here that somewhat similar results have been obtained for thioamides or thioureas. Rao[14] has recently suggested that the compounds including

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[14] C. N. R. Rao, R. Venkataraghavan: Spectrochim. Acta, **18**, 541 (1962).

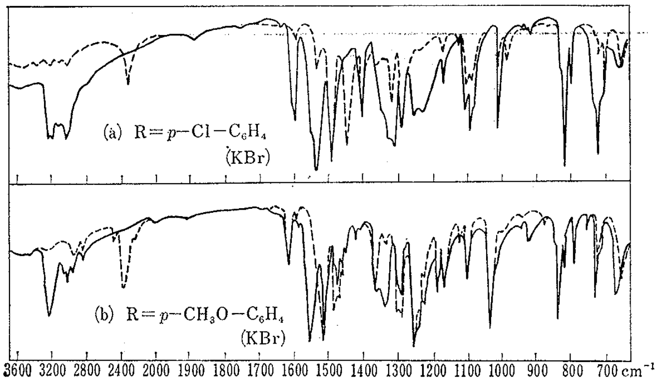
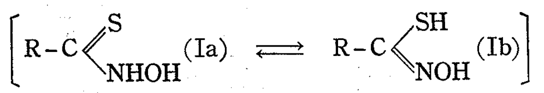


Fig. 3. Infrared Spectra of $RNH-\underset{\underset{S}{\|}}{C}-NH-R$

——— simple - - - - - deuterated

-N-C=S group show consistently characteristic bands which were tentatively designated by him as the "N-C=S I, II and III bands" in the region 1395~1570, 1260~1420 and 940~1140 cm^{-1}, and these bands are probably due to the strongly coupled vibration among the C-N and C=S stretching and NH deformation vibration. Then these characteristic bands must be more or less affected by deuteration because of the large shift of the NH deformation mode to lower frequencies. For example the spectra of

Table I. Band Assignments for Tautomers of Thiohydroxamic Acid



$$\left[R-C\begin{matrix}\nearrow S\\ \searrow NHOH\end{matrix}(Ia) \rightleftarrows R-C\begin{matrix}\nearrow SH\\ \searrow NOH\end{matrix}(Ib)\right]$$

R		ν_{OH} (monomer)		ν_{NH} (monomer)		ν_{OH}, ν_{NH} (dimer-)		ν_{SH} cm^{-1}	δ_{OH}	
		cm^{-1}	Ratio	cm^{-1}	Ratio	cm^{-1}	Ratio		cm^{-1}	Ratio
p-Cl-C_6H_4	H-Comp.	3585	1.36	3415	1.36	3258	1.40	2580	1426	1.39
	D-Comp.	2640		2520		2335			1029 w	
m-Cl-C_6H_4	H-Comp.	3558	1.34	3390	1.34	3190	1.37	2575	1434	1.40
	D-Comp.	2646		2526		2330			1023 w	
p-$CH_3OC_6H_4$	H-Comp.	3587	1.36	3420	1.36	3215	1.36	2560	1424	
	D-Comp.	2635		2523		2370			n. i.	
m-NO_2-C_6H_4	H-Comp.	3575	1.36	3393	1.35	3205	1.35	2565	1422	1.38
	D-Comp.	2629		2505		2380			1030 w	
β-$C_{10}H_7$	H-Comp.	3580	1.36	3408	1.36	3203	1.33	2567	1415	1.37
	D-Comp.	2638		2513		2406			1035 w	

R		$>N-\overset{\mid}{C}=S$ band (cm^{-1})								γ_{NH} and/or γ_{OH} (cm^{-1})
		I		II		III				
p-Cl-C_6H_4	H-Comp.	1572	—	1367	—	1078	—	964	—	674
	D-Comp.	—	1480	—	1142 w	—	983	—	928	—
m-Cl-C_6H_4	H-Comp.	1531	—	1327	—	1085br	—	986sp	—	n.i.
	D-Comp.	—	1461	—	1143 w	1077sp	994br, s	—	949	
p-$CH_3OC_6H_4$	H-Comp.	1574	—	1365	—	1079	—	961	—	692
	D-Comp.	—	1470	—	1138 w	—	977	—	933	—
m-NO_2-C_6H_4	H-Comp.	1555	—	1312	—	1079	—	999sp	—	685
	D-Comp.	—	1463	—	1144 w	—	1002br, s	—	959	—
β-$C_{10}H_7$	H-Comp.	1552	—	1324	—	1090	—	986	—	688
	D-Comp.	—	1467	—	1125 w	—	999	—	947	—

ν_{OH}, ν_{NH} and ν_{SH} bands were obtained in $CHCl_3$ (R=p-Cl-C_6H_4; in CCl_4), and other bands in KBr disks.
H-Comp., D-Comp.; simple and deuterated thiohydroxamic acid
w: weak s: strong sp: sharp br: broad n.i.: not investigated

some 1,3-disubstituted-2-thioureas and their deuterated compounds prepared by authors are shown in Fig. 3. Similar spectra have been recorded for the secondary thioamides⁶⁾ and N-methylthioformamide.⁹⁾ Since there is no doubt that as a whole the spectra of solid I are closely analogous to those of these compounds including -N-C=S group, the above mentioned three bands of I, at about 1550, 1340, and 1085 cm^{-1}, which move after deuteration must be assigned to the "-N-C=S I, II, III bands," respectively.

Absorption bands due to the OH linkage of the -NHOH group are also expected besides -N-C=S bands for Ia. The bands at 1425±10 and 1030±5 cm^{-1} which have a wave-number ratio of near 1.40 may be ascribed to the OH and OD deformation mode respectively, because these bands had not been found in secondary thioamides by Hadži.⁶⁾ The appropriateness of this assignment is confirmed by the facts that the OH deformation band for oximes is within the range 1300~1500 cm^{-1},10,11,15,16) and some derivatives of I give it at 1430±10 cm^{-1} as shown in Part III.*³ The characteristic bands of I were finally summarized in Table I.

In the oily thiohydroxamic acids such as benzothiohydroxamic acid both thione and thiol tautomers may exist, because the SH band, even though so weak, is found as liquid film and the spectra in carbon tetrachloride solution scarcely differ from those of liquid film as shown in Fig. 2f. It has been well known that both tautomers exist in the liquid for acetylacetone¹⁷⁾ and ethylbenzoylacetate.¹⁸⁾

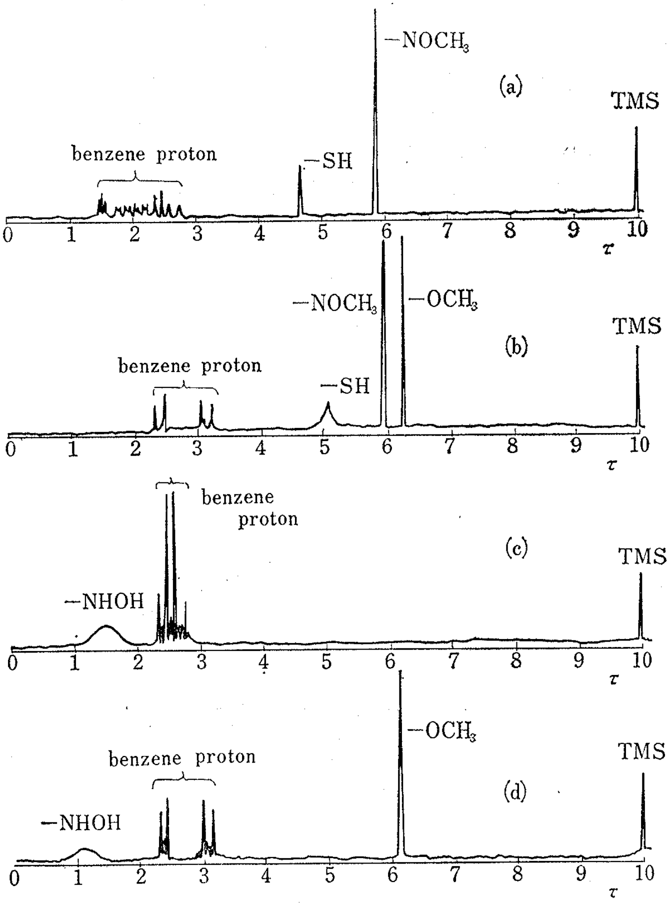
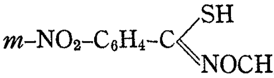
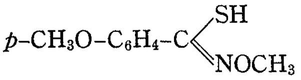


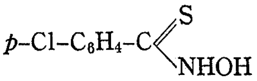
Fig. 4. Nuclear Magnetic Resonance Spectra of Thiohydroxamic Acid (I) and O-Methylthiohydroxamic Aicd (II)

(a)


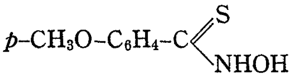
$m\text{-}NO_2\text{-}C_6H_4\text{-}C\begin{cases}SH\\NOCH_3\end{cases}$

(b)


$p\text{-}CH_3O\text{-}C_6H_4\text{-}C\begin{cases}SH\\NOCH_3\end{cases}$

(c)


$p\text{-}Cl\text{-}C_6H_4\text{-}C\begin{cases}S\\NHOH\end{cases}$

(d)


$p\text{-}CH_3O\text{-}C_6H_4\text{-}C\begin{cases}S\\NHOH\end{cases}$

B) Nuclear Magnetic Resonance Spectrum

The difference of structures between I and II in solution are also observed in the nuclear magnetic resonance spectra.

A signal with the magnitude of one proton was found at 4.8~5.1 τ in II as shown in Fig. 4a, b, and it disappears by addition of heavy water. This signal is probably ascribed to the proton of SH group, because it is no doubt that II exists

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*³ Part III: This Bulletin, **14**, 1263 (1966).

15) A. Palm, H. Werbin: Can. J. Chem., **32**, 585 (1954).

16) D. Hadži: J. Chem. Soc., **1956**, 2725.

17) L.W. Reeves: Can. J. Chem., **35**, 1351 (1957).

18) Z. Reyes, R.M. Silverstein: J. Am. Chem. Soc., **80**, 6367 (1958).

in thiol-form and the SH group is not associated as mentioned in section (A). This position is reasonable for non-associated SH proton which are shielded strongly by the large sulfur atom.

In I, a broad absorption band with the magnitude of about two protons was observed at very low field as shown in Fig. 4c, d, and this band also disappears by addition of heavy water. This band is likely to result from the proton of -NHOH group in Ia. Although the comparing of the signal pattern with that of Ⅲ was impossible because of the insolubility of Ⅲ in deutero chloroform, such a broad band at the low field has been found for tautomers of ethylacetoacetate.[19] The absence of SH signal in nuclear magnetic resonance spectra is incompatible with the appearance of the SH band besides NH and OH stretching bands in infrared spectra as shown in section (A), but this fact may be interpreted on the assumption that the thione and thiol tautomers are interconverted rapidly in I, or the concentration of the thiol-form is too low to show the SH signal in nuclear magnetic resonance spectra even though the concentration is enough to show the SH band in the infrared spectra.

C) Dissociation Constant

Dissociation constants of I and Ⅱ were determined as shown in Table Ⅱ by titrating the aqueous solution of their sodium salts with 0.1*N* hydrochloric acid. It is clearly pointed out that both series of I and Ⅱ have nearly the same pKa values and I are the more strong acid as Ⅲ because it has been reported that the pKa values of aceto- and benzo-hydroxamic acid are 9.40 and 8.89, respectively.[20] These observations show that I exist in thiol-form in aqueous solution, as observed for Ⅱ. Furthermore, it is interesting to note that linear relationships have been found between the pKa values and the Hammet's σ constants in a series of the aromatic compounds as shown in Fig. 5, and the correlation coefficients are about 1.0 which are the same value for carboxylic acids. These facts are likely to indicate that the effects of substituted groups in I are similar to them in carboxylic acid, so that the analogous mesomeric structures, (c) and (d), may be proposed.

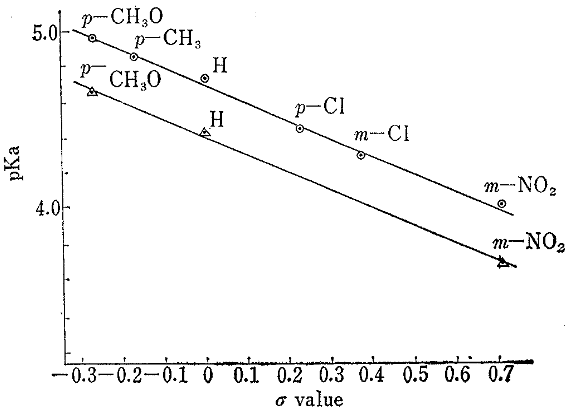
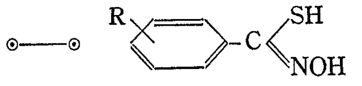
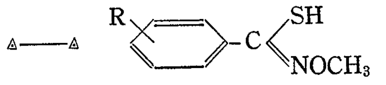


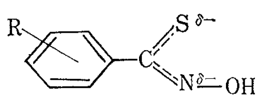
Fig. 5. Correlation of pKa with Hammet's σ Constant



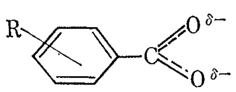
pKa$=-0.98\sigma+4.67$



pKa$=-1.00\sigma+4.41$



(c)



(d)

D) Ultraviolet Spectra

The UV spectra of I and Ⅱ in ethanol are given in Fig. 6. These spectral features are scarcely different from those in cyclohexane. Recent literatures by Jassen[21] have indicated that the aliphatic compounds including -N-C=S group display a n-π^* transition

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[19] J.D. Roberts: "Nuclear Magnetic Resonance, Applications to Organic Chemistry," 67 (1959), McGraw-Hill Book Co., Inc., New York.

[20] W.M. Wise, W.W. Brandt: J. Am. Chem. Soc., **77**, 1058 (1955).

[21] M.J. Janssen: Rec. trav. chim., **79**, 454, 464 (1960).

Table II. Acid Dissociation Constants of Thiohydroxamic Acid (I) and O-Methylthiohydroxamic Acid (II)

	R	*p*-CH_3O-C_6H_4	*p*-CH_3-C_6H_4	C_6H_5	*p*-Cl-C_6H_4	*m*-Cl-C_6H_4	*m*-NO_2-C_6H_4	β-$C_{10}H_7$	α-C_4H_3O	α-C_4H_3S	CH_3
pKa	$R-C\begin{smallmatrix}\nearrow SH\\ \searrow NOH\end{smallmatrix}$	4.94	4.81	4.73	4.41	4.24	4.01	4.64	4.45	4.21	5.58
	$R-C\begin{smallmatrix}\nearrow SH\\ \searrow NOCH_3\end{smallmatrix}$	4.65	—	4.45	—	—	3.69	—	—	—	—
Hammet's σ constant		−0.268	−0.170	0	+0.227	+0.373	+0.710	—	—	—	—

band at wave-lengths between 280 and 365 mμ. Therefore, in the case of aromatic thiohydroxamic acids the n-π* bands due to the -N-C=S group of the thione tautomer, even if it exists, must be overlapped by the more strong benzenoid bands. On the one hand, the pure aliphatic ones were not obtained because of their instability. Hence the UV spectra are not informative to estimate the structure of I in the solution.

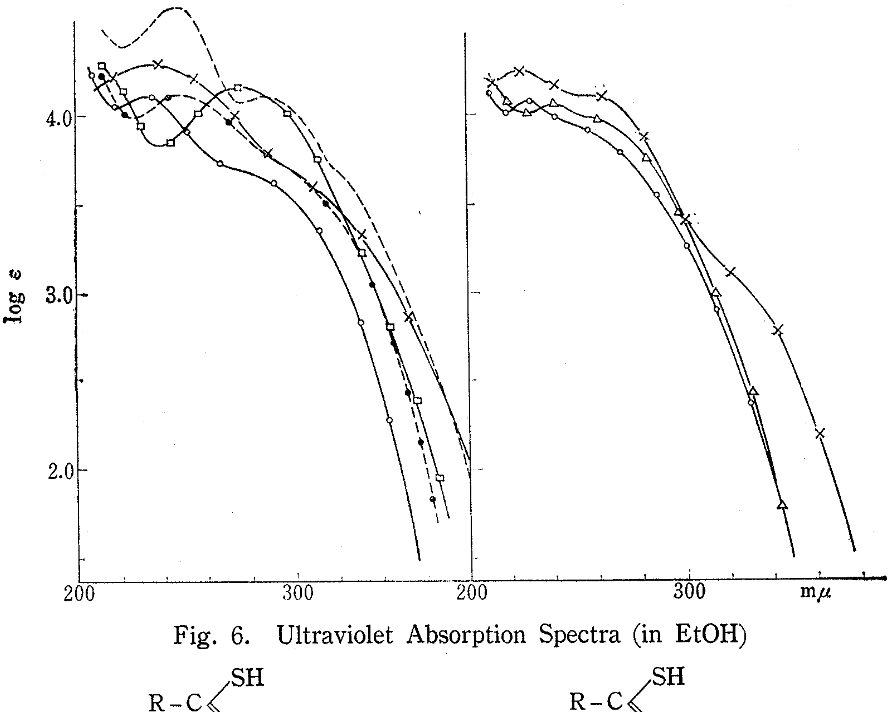

Fig. 6. Ultraviolet Absorption Spectra (in EtOH)

$R-C\begin{smallmatrix}\nearrow SH\\ \searrow NOH\end{smallmatrix}$

○——○ R=C_6H_5
●- - - -● R=*p*-Cl-C_6H_4
□——□ R=*p*-CH_3O-C_6H_4
×——× R=*m*-NO_2-C_6H_4
- - - - - - R=-$C_{10}H_7$

$R-C\begin{smallmatrix}\nearrow SH\\ \searrow NOCH_3\end{smallmatrix}$

○——○ R=C_6H_5
△——△ R=*p*-CH_3-C_6H_4
×——× R=*m*-NO_2-C_6H_4

Conclusion and Discussion

It is evident from the investigations of the infrared spectra that thiohydroxamic acids (I) exist in thione-form (Ia) in the solid state, but thiol and thione tautomers are present in equilibrium in the liquid state or in the solution, whereas O-methyl thiohydroxamic acids (II) occur almost exclusively in the thiol form (IIb) in all the states.

Although the iodimetric titrations were carried out for the estimation of the equilibrium concentrations of the thiol-thione tautomers of I in various solvents, no fair results have been obtained, because I are too unstable, especially in polar solvents, and their reactions with iodine in non-polar solvents are too slow to determine the end-points clearly and to titrate without any side-reactions. It is likely, however, that the increase of the dielectric constants and polarity of solvents favor the thiol-form, because the pKa-values of I were nearly the same as those of II in aqueous solution and a signal of the proton of thiol group was not found in deutero chloroform solution. Although this trend is apparently opposite to that for the keto-enol tautomerism in which the enol-form is more favored in non-polar solvents, this discrepancy may be interpreted by the consideration that the tautomerism occurs between the C=N and the thiol group in the case of I so that the thione tautomers of I still include the polar group, NH group, while in the case of keto-enol tautomerism the keto-form dose not include any polar group.

Experimental

All substances used in this study were prepared by previously reported procedures in Part I,*1 and recrystallized immediately before use. Since liquid thiohydroxamic acids (I) and O-methylthiohydroxamic acids (II) could not be refined by distillation, they were prepared as follows: After addition of diluted hydrochloric acid to aqueous solution of the pure sodium salts of I or II, the separated oil were extracted with ether and washed with water. The extract was dried rapidly over anhydrous Na_2SO_4 followed by addition of a small quantity of P_2O_5, and decanted. After entire evaporation of ether at reduced pressure, the resulting liquid were used for the following experiments.

Deuteration of I was performed as follows: After addition of heavy water to a soluiton of I in a small quantity of dioxane, the mixtures were allowed to stand in a desiccator over P_2O_5 in an air-conditioning room of below 0°, and the solvent was evaporated slowly at reduced pressure. The resulting crystals were collected by filtration and washed with a small quantity of anhydrous petroleum ether and dried for 3 hr. over P_2O_5 at room temperature *in vacuo*. The simple materials used as references were recrystallized in the same manner as deuterated materials by using water in place of heavy water. Although I was somewhat unstable in polar solvent generally, any appreciable decomposition or spectral change which was caused by this procedure were not observed.

The infrared spectra were recorded with a Nippon Bunkō double-beam spectrometer, model DS 201-B. The NMR spectra were obtained on a Varian A-60 spectrometer at 60 Mc.p.s., in $CDCl_3$, with use of $(CH_3)_4Si$ as an internal standard. The ultraviolet spectra were determined by using a Hitachi spectrophotometer model EPS-2U.

The dissociation constants of I and II were determined by conventional potentiometric method from the pH of half titration point which was obtained by titrating the solution of about 0.0005 mole of pure sodium salt in 25 ml. water with standardized 0.1*N* HCl. The titrations were carried out in a closed vessel under a nitrogen atmosphere, with a Yanagimoto potentiometric titrimeter, model KY-6. In the case of β-naphthothiohydroxamic acid and O-methyl-*m*-nitrobenzothiohydroxamic acid, more diluted solution of the sodium salts (0.00025 mole/50 ml. water) was used because the dissociated acid was apt to precipitate before half titration point.

The authors wish to thank Dr. Y. Matsui and Dr. K. Tori of this laboratory for their illuminating discussion on the interpretation of infrared and NMR spectra, and Mr. M. Takasuka and K. Aono for a help in part of the measurement.

Summary

The infrared spectra of some thiohydroxamic acids (I) and their deuterated compounds were investigated and compared with those of some O-methylthiohydroxamic acids (II). It was concluded that I exist in thione-form in the solid state but the both of thiol and thione tautomers exist in the liquid or in the solution, in which state polar solvents favor the former tautomer, whereas II occur in thiol-form in all the states. These facts were more positively confirmed by the NMR spectra and by the determinations of the pKa values. The "N-C=S bands" of the thione-form of I were assigned to the regions 1550±20, 1340±30 and 1085±5 cm^{-1}.

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