

stirred for 2 hr. at 45~48°. The separated crystals were filtered and washed with dil. NaOH and H₂O. Recrystallization from Me₂CO gave 1.0 g. of pale yellow rhombics, m.p. 146~148°. Rf 0.82. IR cm⁻¹: $\nu_{C=O}$ 1728, 1710 (Nujol). Anal. Calcd. for C₂₂H₂₆O₅N₄S: C, 57.63; H, 5.72; N, 12.22. Found: C, 57.86; H, 5.97; N, 11.98.

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Summary

O-(2-Tetrahydropyranyl)thiamine (II) and O-tritylthiamine (III) were prepared from O-(2-tetrahydropyranyl)SB₁ (V) and O-trityl SB₁ (VII), respectively. II and III were converted into S-alkoxycarbonyl or S-acyl derivatives, and removal of the trityl group gave S-acylthiamine. S-Alkoxycarbonyl and S-acylthiamine reacted with phosgene to give O-chlorocarbonyl derivatives, which were converted into O-alkoxycarbonyl- and O-carbamoylthiamine. These compounds were also obtained from S-alkoxycarbonyl- and S-carbamoylthiamine by S→O rearrangement. The combination of these reactions gave various kinds of thiol type thiamine derivatives.

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79. Masaichiro Masui and Keiko Hotta: *n*-Butyraldoxime Complexes of Copper (II), Nickel (II), Cobalt (II), and Manganese (II).

(Faculty of Pharmaceutical Sciences, Osaka University*¹)

A simple aldoxime, except formaldoxime,¹⁾ and a ketoxime are said to react with copper, nickel and cobalt salts to form an addition compound, [X₂M(←HON=CH-R)_n],²⁾ where *n* is 2 or 4, but in the simple aliphatic series, only acetaldoxime,²⁾ acetoxime³⁾ and isobutyraldoxime²⁾ are the examples reported, and only very little have been studied on the compounds. We found that *n*-butyraldoxime reacts with not only copper (II), nickel (II) and cobalt (II) chlorides, but also with manganese (II) chloride under an exothermic reaction, and forms a crystalline complex with relatively low melting point. The color and the solubility of the complexes, which are non-electrolytes, are quite similar to those described,²⁾ and the value of *n* in the above equation is 4. Further has been studied spectroscopically.

Experimental

Reagents—*n*-Butyraldoxime was prepared by usual method and purified by repeating distillation. Extra pure grade Cu (II), Ni (II), Co (II) and Mn (II) chlorides with crystalline water were dehydrated by gentle heating in a casserole with a small flame, and used as soon as possible after being cool.

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1) M. Bartusec, A. Okac: Collection Czech. Chem. Commun., 26, 52, 883, 2174 (1961).

2) W. Hieber, F. Leutert: Ber., 60B, 2296 (1927).

3) *Idem*: *Ibid.*, 60B, 2310 (1927).

Apparatus—A Hitachi EPI-2 double beam IR spectrophotometer with NaCl prisms was used. For dilute solutions in CCl_4 a cell with a light pass of 20.0 mm. was used. The wave lengths were corrected by using polystyrene film. A Hitachi automatic recording spectrophotometer EPS-2 was used for UV and visible region spectra.

Preparation of $[\text{CuCl}_2(n\text{-C}_4\text{H}_9\text{NOH})_4]$ —Dried CuCl_2 was added in small portions to n -butyraldoxime so as not to raise the temperature above 5° . After all the chloride was dissolved on warming the mixture up to 25° for a while, it was filtered and left at 5° or below. Dark blue prisms were obtained. After filtration, the crystals were kept in a evacuated desiccator ($<10^{-2}$ mm.Hg) for one or two days to make the compound free from the adsorbed aldoxime. Recrystallization from EtOH, BuOH or light petroleum gave rather labile crystals. *Anal.* Calcd. for $\text{CuCl}_2(\text{C}_4\text{H}_9\text{NOH})_4$: C, 39.8; H, 7.52; N, 11.6; Cl, 14.7. Found: C, 39.7; H, 7.48; N, 11.6; Cl, 15.1.

Preparation of (i) $[\text{NiCl}_2(n\text{-C}_4\text{H}_9\text{NOH})_4]$ —The procedure used for (i), (ii), and (iii) were the same as described above. *Anal.* Calcd. for $\text{NiCl}_2(\text{C}_4\text{H}_9\text{NOH})_4$: C, 40.2; H, 7.61; N, 11.7; Cl, 14.8. Found: C, 40.4; H, 7.65; N, 12.4; Cl, 14.5.*²

(ii) $[\text{CoCl}_2(n\text{-C}_4\text{H}_9\text{NOH})_4]$ —*Anal.* Calcd. for $\text{CoCl}_2(\text{C}_4\text{H}_9\text{NOH})_4$: C, 40.2; H, 7.61; N, 11.7; Cl, 14.8. Found: C, 40.25; H, 7.51; N, 12.2; Cl, 14.4.*²

(iii) $[\text{MnCl}_2(n\text{-C}_4\text{H}_9\text{NOH})_4]$ —*Anal.* Calcd. for $\text{MnCl}_2(\text{C}_4\text{H}_9\text{NOH})_4$: C, 40.5; H, 7.67; N, 11.8; Cl, 14.9. Found: C, 39.3; H, 7.47; N, 11.3; Cl, 15.8.*²

Results and Discussion

The physical properties are shown in Table I. In crystalline state the copper complex is the most labile and decomposed to brown black solid even in an evacuated desiccator in about ten days, producing brown black tar and volatile products by further decomposition.

TABLE I. Physical Properties of the Complexes

	m.p. ($^\circ\text{C}$)	Color	$\nu \times 10^{-13} \text{ sec}^{-1} (\log \epsilon)$
$[\text{CuCl}_2(n\text{-C}_4\text{H}_9\text{NOH})_4]$	57	dark blue	41.4 (1.72), 101 (4.54), 116 (4.48)
$[\text{NiCl}_2(n\text{-C}_4\text{H}_9\text{NOH})_4]$	85	light blue	46.9 (0.82), 76.9 (1.08)
$[\text{CoCl}_2(n\text{-C}_4\text{H}_9\text{NOH})_4]$	75	red purple	57.2 (1.09)
$[\text{MnCl}_2(n\text{-C}_4\text{H}_9\text{NOH})_4]$	54	colorless	—

Measured at $33.3 \sim 136 \times 10^{13} \text{ sec}^{-1}$ on a dilute solution ($<0.01 M$) in hexane.

These complexes are easily soluble but not stable in ethanol. Non polar organic solvents are good solvent for these compounds, but manganese complex react with the compounds containing chlorine, *e.g.* chloroform, 1,1,2,2-tetrachloroethane, even with carbon tetrachloride. They are all insoluble in water and easily decomposed by it. Copper complex is somewhat different from the others, and changed to another form by contacting with the aqueous solution containing carbonate, acetate, phosphate or hydroxy ions, and the resulted form shows a maximum absorption at about $47 \times 10^{13} \text{ sec}^{-1}$ in not a strongly acidic medium.

When copper (II) ion is extracted from neutral or alkaline aqueous solution by n -butyraldoxime to an organic layer, the absorption maximum of the green organic layer is also near $47 \times 10^{13} \text{ sec}^{-1}$, irrespective of the kind of an anion present, though the intensity depends on them.⁴⁾ The green substance was failed to isolate from the solution. The green organic layer is again able to be converted to the original blue color of the complex, if the layer is treated with a proper amount of hydrogen chloride; but in this case, as the color fades rapidly, because of the acidified medium, the absorption spectrum was not measured. This color change was not observed with sulfuric

*² Values were obtained by titration (Volhard method) with 0.1N AgNO_3 on a sample dissolved in aqueous ethanol and nitric acid.

4) This will be reported elsewhere.

or nitric acid or with sodium chloride. This result suggests that the copper in the center of a square planar can fix the fifth and the sixth ligands fairly tightly, if the anion is a chloride ion and the system is in a non-polar medium, and the anion exchange takes place rapidly in the acidic condition. The ν_{\max} at $41.4 \times 10^{13} \text{ sec}^{-1}$ of the complex and at $47 \times 10^{13} \text{ sec}^{-1}$ of the green solution are for a six-co-ordinate⁵⁾ and a square planar^{5,6)} cupric complex respectively. But because the similar blue color is developed when anhydrous copper sulfate is dissolved in *n*-butyraldioxime, the necessary conditions for the six-co-ordinate complex appear to be the low polarity of the solvent molecule and a sufficient amount of the aldoxime though chloride is the more favourable than sulfate. From the results shown above, the cobalt complex is also clearly six-co-ordinate cobalt (II) complex.⁶⁾ For the other two complexes the similar configuration may be concluded.

Some of the infrared spectra and the characteristic absorption bands are shown in Fig. 1 and Table II. The peaks are assigned by comparing them with those reported.⁷⁾ The spectra for the four complexes are, as a whole, all quite similar with each other, except the peaks only for $\nu(\text{O-H})$ of the copper complex and $\nu(\text{C=N})$ of the manganese complex, but, of course, significantly different from the spectrum of *n*-butyraldioxime. The copper complex shows two very strong and rather broad $\nu(\text{O-H})$ bands with comparable intensity at somewhat lower frequencies, but the other three complexes show one very strong peak near 3300 cm^{-1} . Only the manganese complex has a distinct $\nu(\text{C=N})$ peak at 1613 cm^{-1} , but a very weak absorption is noticed at a higher frequency. The other three complexes show a very weak absorption band at $1660 \sim 1670 \text{ cm}^{-1}$ for $\nu(\text{C=N})$. The frequency difference between the $\nu(\text{C=N})$ at the higher frequency and that of *n*-butyraldioxime is about $15 \pm 5 \text{ cm}^{-1}$.

TABLE II. Characteristic Infrared Absorption Bands of the Complexes (Wave number, cm^{-1})

		$\nu(\text{O-H})_{\text{free}}$	$\nu(\text{O-H})_{\text{assoc.}}$	$\nu(\text{C=N})$	$\delta(\text{O-H})$	$\gamma(\text{O-H})$ or $\nu(\text{N-O})$
<i>n</i> -Butyraldioxime	liquid		3250 v s	1650 m		
	in CCl_4	3560 m	3310 s	1650 w	1436 sh	932 m
Cu-complex	KBr disk		3165 v s	1669 v w	1456 s	951 s
	in CCl_4		3153 v s		1456 s	961 s
Ni-complex	KBr disk		3315 v s	1669 v w	1432 s	938 s
	in CCl_4		3310 v s		1431 s	946 s
Co-complex	KBr disk		3320 v s	1664 v w	1431 s	936 s
	in CCl_4		3320 v s	(1658 v w)	1429 s	943 s
Mn-complex	KBr disk		3330 v s	1661 w	1429 s	931 s
				1613 m		

Abbreviations: v, very; s, strong; w, weak; sh, shoulder

In the relatively simple spectra, there are three strong bands at about 3300 , 1440 , and 950 cm^{-1} . The relative intensity of the bands, particularly in nickel, cobalt and manganese complexes, is even larger than that for $\nu(\text{C-H})$, though $\nu(\text{C-H})$ shows the strongest absorption in the spectrum of *n*-butyraldioxime. The former two are clearly

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6) R. Tsuchida, S. Yamada: "Muki Kagaku Zensho," XV-2, Maruzen Co., Ltd. (1959), p. 260.

7) Y. Matsui, T. Kubota: J. Chem. Soc. Japan, Pure Chem. Sec. (Nippon Kagaku Zasshi), **83**, 985 (1962); Y. Kuroda, M. Kimura: Bull. Chem. Soc. Japan, **36**, 464 (1963); H. E. Ungnade, L. W. Kissinger, A. Narath, D. C. Barham: J. Org. Chem., **28**, 134 (1963); L. J. Bellamy: "The IR Spectra of Complex Molecules," Methun & Co., Ltd., London (1958), p. 98, 268, 271, 297; R. Blinc, D. Hadzi: J. Chem. Soc., **1958**, 4536.

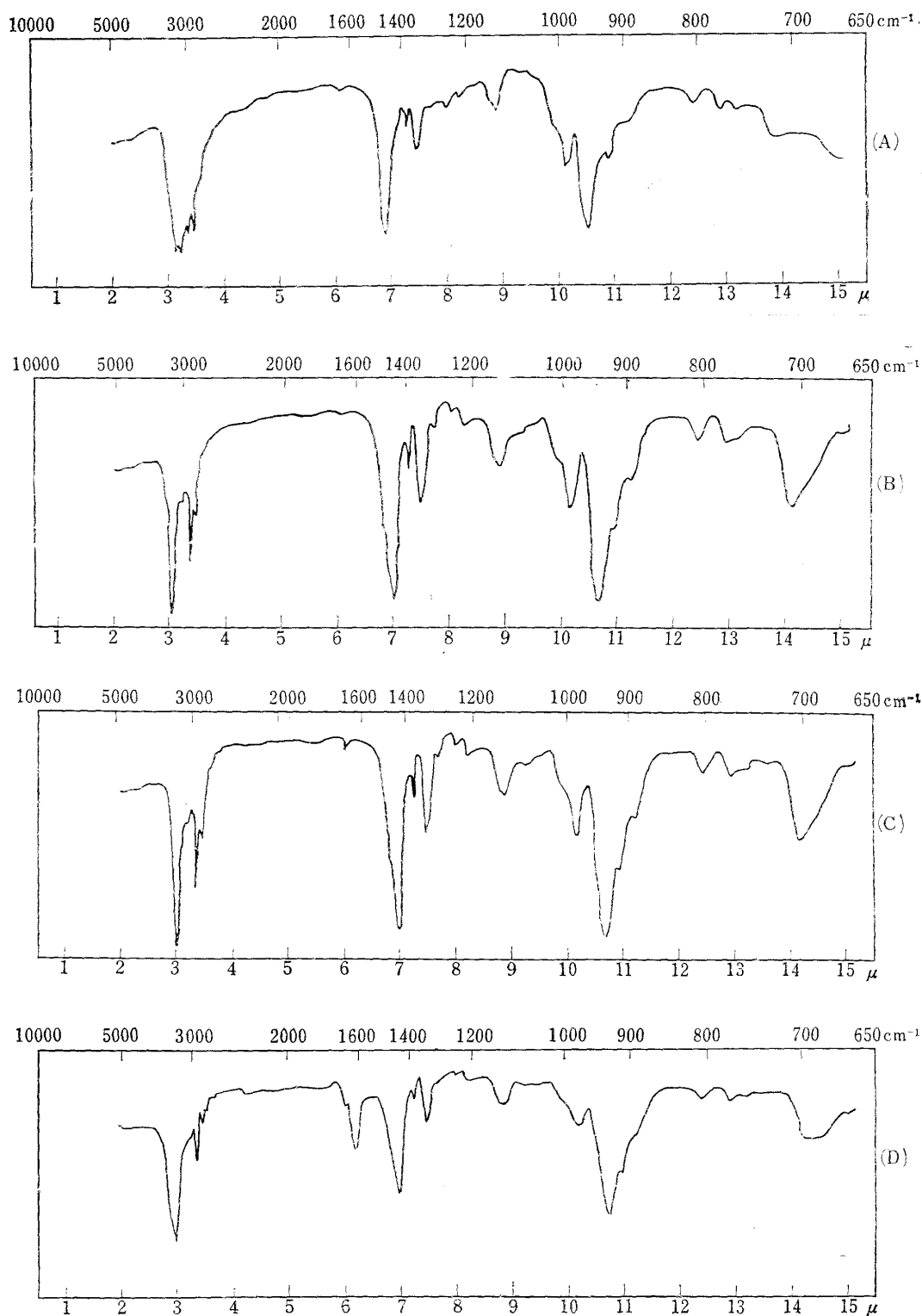


Fig. 1. Infrared Absorption Spectra of (A) $[\text{CuCl}_2(n\text{-C}_4\text{H}_9\text{NOH})_4]$, (B) $[\text{NiCl}_2(n\text{-C}_4\text{H}_9\text{NOH})_4]$, (C) $[\text{CoCl}_2(n\text{-C}_4\text{H}_9\text{NOH})_4]$, (D) $[\text{MnCl}_2(n\text{-C}_4\text{H}_9\text{NOH})_4]$ in KBr Disk

derived from the O-H mode, and the third may probably be partly contributed from the same mode.⁷⁾ The associated O-H stretching frequencies of the complexes are nearly in the reverse order of the electronegativity of the metals, $\text{Cu} > \text{Ni} > \text{Co} > \text{Mn}$,⁸⁾ and

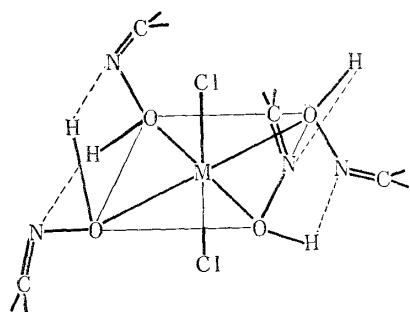
8) Y. Kuroda, K. Ito : J. Chem. Soc. Japan, Pure Chem. Sec. (Nippon Kagaku Zasshi), **76**, 766 (1955).

the association is completely intramolecular as clearly indicated by the dilution method carried out between 10^{-2} and $5 \times 10^{-5} M$ on the nickel and cobalt complexes in carbon tetrachloride. As the frequency of $\nu(\text{O-H})_{\text{assoc.}}$ of *n*-butyraldoxime is ascribed mostly to that of simple cyclic structure or dimeric form,⁹⁾ the absorption is somewhat affected

by dilution. If a cyclic dimer $\text{>C=N} \begin{array}{c} \text{O-H} \cdots \\ \text{H-O} \cdots \end{array} \text{N=C<} \text{ could act as a unit, this would be a very promising ligand for these complexes.}$

It is interesting to note that the O-H stretching frequencies of the aldoxime and the complexes are not very different. From this, it may be assumed that the distance of the hydroxyl oxygen and the hydrogen-bond acceptor in the complexes, except for the copper complex, is not very different from that in a simple cyclic or dimeric form of the oxime, if the acceptor is identical.

Now the present discussion is concentrated on the nickel and cobalt complexes for the simplicity. From the simplicity of the spectrum, the four ligand oximes are assumed to be co-ordinated with the metal symmetrically, that is, they should take planar structure. If the ligand oxime would be co-ordinated with metals through the nitrogen atom as usual oxime complexes,⁷⁾ the proton acceptor of the intramolecular hydrogen-bond should be oxygen, chlorine or the π electron system of the C=N double bond. The two chlorines can accept two hydrogens, then in this case, the other two hydrogen-bonds must be linked with the other acceptors, and should appear as a separate peak. If not, because the chlorine is not so ionic as it causes such a large frequency shift¹⁰⁾ from the free O-H stretching frequency of the oxime (3560 cm^{-1} in carbon tetrachloride), this idea must be abandoned. The intramolecular hydrogen-bond from a hydroxyl to a π electron system is also too weak as an acceptor¹¹⁾ to cause such a large frequency shift.



M : Ni, Co

Chart 1. Proposed Structure for the Aldoxime Complexes

Any model which contains four N-metal links and four O-H...O hydrogen-bonds can not be composed without a considerable distortion, or taking an unreasonable configuration. Out of several other models, which include four identical intramolecular hydrogen-bonds or two N-metal and two O-metal co-ordinations, one model as shown in Chart 1 is left after excluding those which can not explain the experimental results or/and contain an unreasonable steric structure.

This model will also be supported by the following.

Assuming that the similar effect of a N-metal link in an amine complex on the N-H stretching frequency and its intensity¹²⁾ is also applicable to an O-metal link, and considering that the intramolecular hydrogen-bond of OH...O or OH...N causes only a small increase in the over-all integrated intensity,¹³⁾ and that O-metal co-ordination in a certain oxime complex makes the $\nu(\text{C=N})$ peak shift to a higher frequency ($\Delta 22 \text{ cm}^{-1}$),¹⁴⁾ the aldoxime may also be thought to be co-ordinated through its oxygen atom to the metal.

9) L. J. Bellamy, H. E. Hallam : *Trans. Faraday Soc.*, **55**, 220 (1959).

10) A. Allerhand, P. R. Schleyer : *J. Am. Chem. Soc.*, **85**, 1233 (1963).

11) P. R. Schleyer, D. S. Trifan, R. Backskai : *Ibid.*, **80**, 6991 (1958).

12) G. F. Svatos, C. Curran, J. V. Quagliano : *Ibid.*, **77**, 6159 (1955).

13) H. M. Fales, W. C. Wildman : *Ibid.*, **85**, 784 (1963).

14) H. Nakamura, Y. Shimura, R. Tsuchida : *Bull. Chem. Soc. Japan*, **36**, 296 (1963).

Therefore, the link between the metal and the ligand is believed to be O-metal, and the above considerations favour the structure.

The simple cyclic form of the oxime acts as a unit in the complex formation, being stabilized in turn by the interaction with the metal halide. From another point of view, MCl_2 is thought to be sandwiched with two cyclic dimers of the oxime.

For the copper and manganese complexes, further study must be necessary to deduce their structure. But, of course, the precise structure for any of the complexes must not be decided until X-ray study will be carried out.

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Summary

n-Butyraldoxime complexes of copper (II), nickel (II), cobalt (II), and manganese (II) were prepared by a direct reaction between the metal halides and the oxime. From their chemical and physical properties, a octahedral structure is deduced. Further, the infrared absorption spectra suggest for the complexes that the oxime is co-ordinated through its oxygen atom in the simple cyclic structure of the oxime to the metal.

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80. Yoshio Ota, Nobuo Endo, and Midori Hirasawa : Antitussive Activity of Narcotine Derivatives.*¹

(Kowa Chemical Laboratories, Kowa Co., Ltd.*²)

The naturally occurring *l*- α -narcotine (Noscapine) is an alkaloid widely known as a non-narcotic antitussive agent. Takagi, *et al.*¹⁾ studied the pharmacological properties

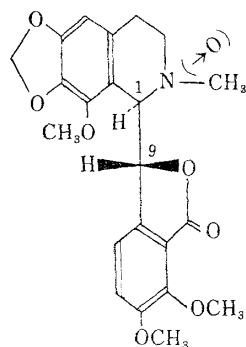


Chart 1. Chemical Structure of *l*- α -Narcotine and its N-Oxide (1R:9S)

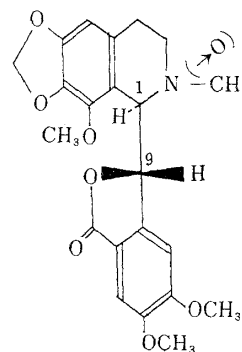


Chart 2. Chemical Structure of *l*- β -Narcotine and its N-Oxide (1R:9R)

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1) K. Takagi, H. Fukuda, *et al.* : Yakugaku Zasshi, 81, 266 (1960).