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The Syntheses of 3-(Carboxyalkyl)salicylaldehyde Derivatives and Their Copper Chelates[1]

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In order to study the influence of the side-chain carboxylic acid groups on the formation of the metal chelates, 5-bromo-3-carboxymethyl-, 5-methyl-3-β-carboxyethyl-, and 5-chloro-3-β-carboxyethyl-salicylaldehyde (**2a, b c**) were synthesized. The green binuclear copper chelates of these aldehydes, di-μ-aquo-bis-(5-bromo-3-carboxymethylsalicylaldehyde)-, di-μ-aquo-bis-(5-methyl-3-β-carboxyethylsalicylaldehyde)-, and di-μ-aquo-bis-(5-chloro-3-β-carboxyethylsalicylaldehyde)-dicopper (**11a, b, c**) yielded the green binuclear bis-ethylenediimine chelates (**12a, b, c**), while bis-(5-bromo-3-carboxymethylsalicylaldehyde)-, bis-(5-methyl-3-β-carboxyethylsalicylaldehyde)-, and bis-(5-chloro-3-β-carboxyethylsalicylaldehyde)-ethylenediimine (**14a, b, c**) gave a brown (**13a**) and gray-purple (**13b, c**) mononuclear copper chelates. The reduction of **14a, b, c** with sodium borohydride yielded the hexadentate ligands *N,N'*-bis-(5-bromo-2-hydroxy-3-carboxymethylbenzyl)-, *N,N'*-bis-(5-methyl-2-hydroxy-3-β-carboxyethylbenzyl)-, and *N,N'*-bis-(5-chloro-2-hydroxy-3-β-carboxyethylbenzyl)-ethylenediamine (**15a, b, c**), which proved useful for the spectrophotometric determination of the copper (II) ion from solutions containing copper (II) and nickel (II) ions, and the iron (II) ion from solutions containing iron (II) and nickel (II) ions.

Since the isolation of purple penta-coordinate addition compounds of bis-salicylaldehyde-ethylenediimine-copper with the carboxylic acids and the phenols,[2] many penta-coordinate copper chelates have been reported.[3] In view of the role of carboxylic acid groups in the penta-coordination as well as in the formation of the ethylenediamine conjugates,[4] the aldehydes **2a,b,c**, their ethylenediimine derivatives **14a,b,c**, and their copper chelates were synthesized for a study of the physical properties and chemical behaviors of the ligands as well as their chelates.

A binuclear structure of the copper chelate of **2a** was deduced from the analyses, IR spectrum and mass spectrum of the copper chelate. The mass spectrum[5] of **11a** is illustrated in Fig. 2. Ions having values of M/e 474 ($-CO_2$, $-2Br$, $+2H$), 429 ($-2CO_2$, $-2Br$, $+H$) and others with values of M/e higher than 337 of the ion of monomeric form (**20**) were observed in the spectrum. The ions are considered to originate from the dimeric chelate **11a**. Four sets of twin peaks (240, 242), (228, 230), (200, 202), and (184, 186) represent those of the bromine containing fragments.

The carboxylate, the coordinated aldehyde and the phenoxide structures of **11a** were assigned on the basis of the 1580 and 1400 cm^{-1} IR peaks due to the antisymmetric and the symmetric vibration of the carboxylate ions,[6,4] the 1611 cm^{-1} IR peak due to the shifted C=O stretching vibration of the aldehyde groups and the 1535 cm^{-1} absorption, respectively (Table 2 (B)).

Lower magnetic moments of binuclear copper chelates were summarized.[7] The magnetic moments of the penta-coordinate copper chelates were normal.[8] The

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[1] Part X of "Some addition compounds of bis-salicylaldehyde-ethylenediimine-copper". Preliminary communication: T. Tanaka, This Bulletin, **41**, 1277 (1968).

[2] a) T. Tanaka, *ibid.*, **29**, 93 (1956). b) T. Tanaka, Proceedings of IX I.C.C. C., St. Moritz-Bad, Switzerland, 1966, p. 71.

[3] Reviews are available: E. L. Muetterties and R. A. Schun, *Quart. Revs.*, **20**, 245 (1966). L. Sacconi, Coordination chemistry (plenary lectures of X I. C. C. C., Butterworth, London, 1968, p. 95.

[4] T. Tanaka, This Bulletin, **39**, 2558 (1966).

[5] H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Interpretation of mass spectra of organic compounds." Holden-Day, San Francisco, 1964, p. 162. M. Tsutsui, "Characterization of organometallic compounds." Part I, Interscience publishers, New York, 1969, p. 137—203.

[6] L. J. Bellamy, "The infrared spectra of complex molecules," Methuen, London, 1964, p. 140. K. Nakamoto and P. J. McCarthy, "Spectroscopy and structure of metal chelate compounds," John-Wiley and Sons, New York 1968, p. 269—281.

[7] M. Kato and H. B. Jonassen, *Chem. Rev.*, **64**, 104 (1964).

[8] The measured magnetic moments of the penta-coordinate addition compounds were 1.74 Bohr magneton (at 256.2°K, $\Delta = -1°$) for the addition compound of bis-(5-methylsalicylaldehyde)-ethylenediimine-copper with propionic acid and 1.68 Bohr magneton (at 219°K, $\Delta = 0°$) for the addition compound of the same chelate with hydroquinone of the composition $(C_{18}H_{18}N_2O_2Cu)_2$-$C_6H_4(OH)_2$. The magnetic moments were measured by K. Hirakawa and his collaborators on their instrument. K. Hirakawa, K. Hirakawa, and S. Yoneyama, *Japan J. Appl. Phys.*, **2**, 816 (1963).

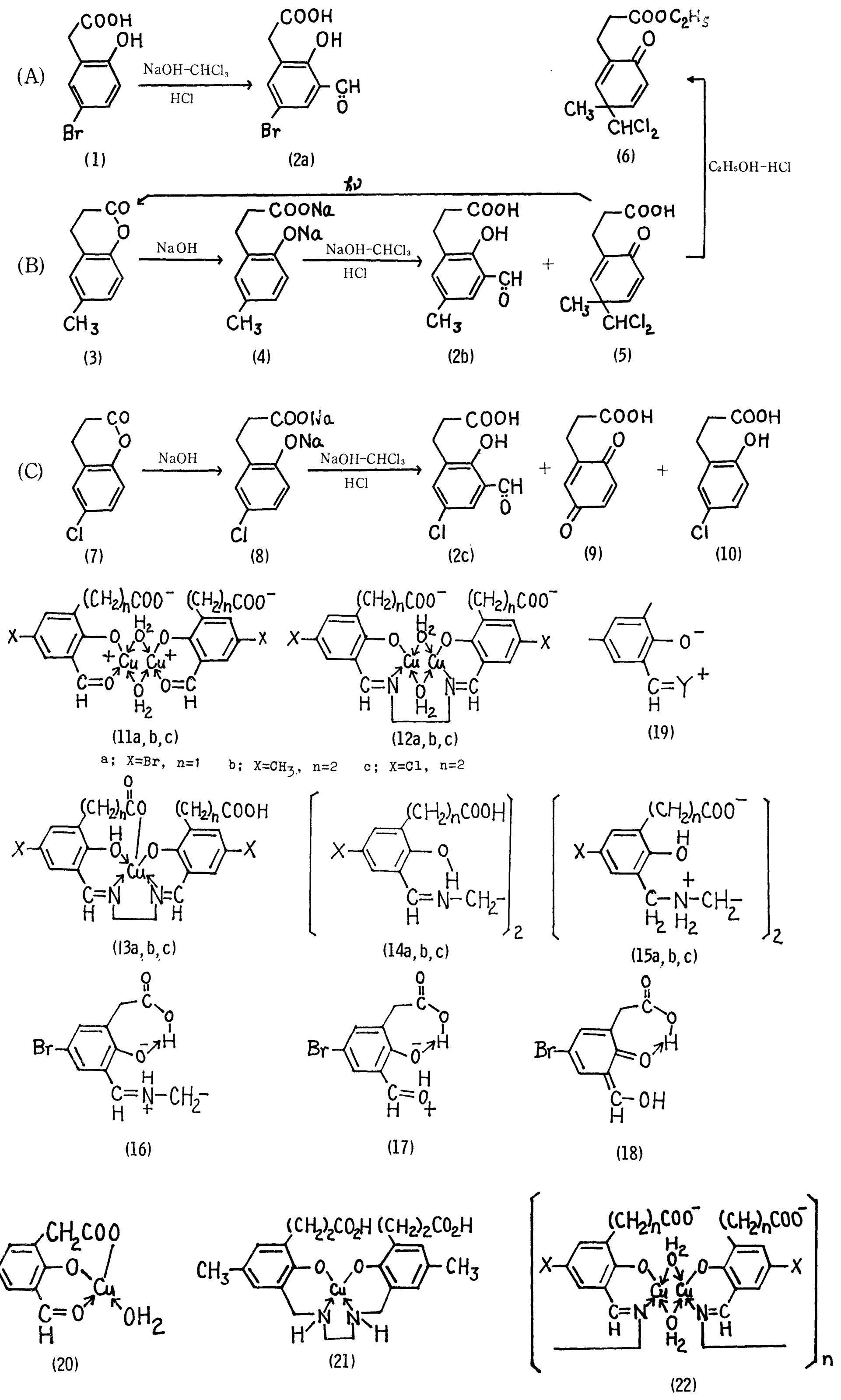

Fig. 1.

magnetic moments of **11a,b,c** were 1.90 Bohr magneton (273°K,Δ = −70°), 1.77 Bohr magneton (272°K,Δ = −52°), and 1.73 Bohr magneton (273°K,Δ = −77°), respectively, and a deviation from the Curie-Weiss law was observed for **11c** at low temperatures (Fig. 3).

In the mass spectrum of **11b**, 345 (−2 $CH_2CH_2CO_2$, −2 CH_3, −2 CO, +H) and 317 were observed for *M/e* indicating a dimeric structure. The structure of **11c** was deduced from the similarity of results of its analysis, IR and UV spectra to those of **11a,b**.

The reaction of **11a,b,c** with ethylenediamine gave deep green ethylenediimine chelates which were considered to be either **12a,b,c** or the polymer **22a,b,c**. On the other hand, the Schiff base **14a,b,c** yielded

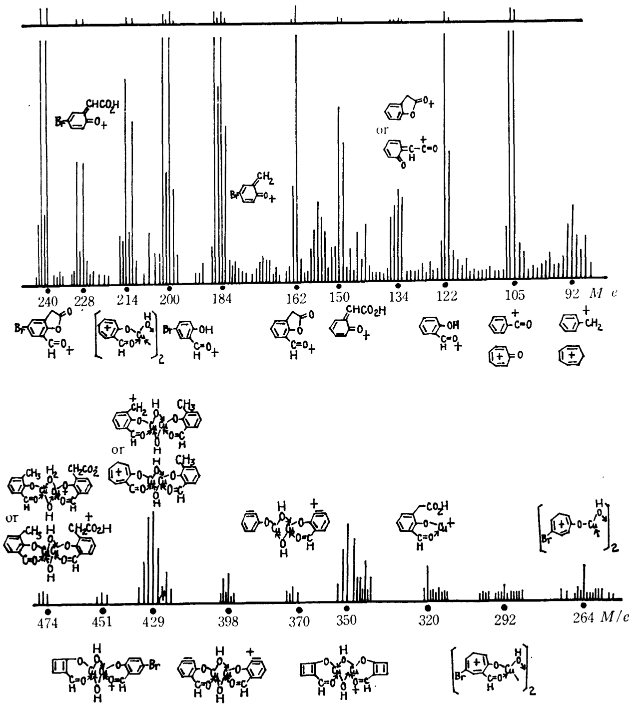

Fig. 2. Mass spectrum of **11a**. Ionizing voltage, 75 eV; ionizing current, 200 μA; sample temperature, 240°C; chamber temperature, 280°C. The formulae are possible ionic species.

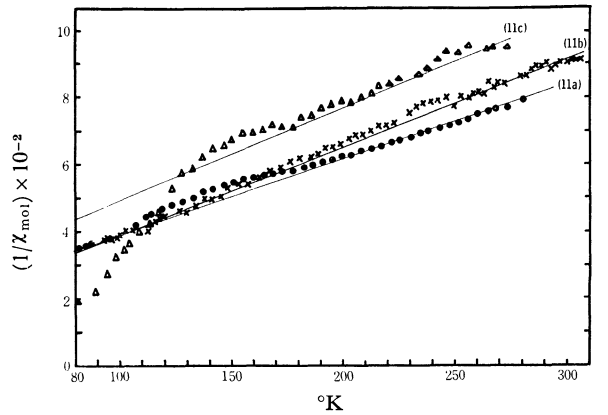

Fig. 3. Magnetic susceptibilities of **11a**, **b**, **c**.

mononuclear chelates **13a**,**b**,**c** respectively. The penta-coordinated structure of the mononuclear chelates is discussed with reference to absorption spectra.

The ligand **15a** formed a colorless stable chelate with Ni(II) ion in aqueous buffer solution of pH 10, and revealed the purple color of murexide on addition to a solution of nickel-murexide complex. Thus, the quantitative determination of nickel(II) ion was attained by chelatometric titration by use of M/100 aqueous solution of the disodium salt of **15a** and murexide in a buffer solution of pH 10.[9] Ligands **15b**,**c**, which, were colorless, formed no stable chelate with Ni(II), but formed green copper(II) and red iron(II) chelates in buffer solutions of pH 10 and pH 7, respectively. Spectrophotometric determinations were achieved for the copper(II) ion from the solutions containing Cu(II) and Ni(II) ions, and for the iron(II) ion from those containing Fe(II) and Ni(II)[10] as illustrated in Fig. 8. Of the Mg, Ca, Sr, Ba, Hg, Zn, Cd, Pb, Sn, Ni, Fe(II), Co(III) and Cu(II) ions, Co(III) (green), Cu(II) (green), and Fe(II) (red) ions formed colored chelates with **15a**,**b**,**c** in the aqueous solutions of pH 10 and 7.

Structure of the Abnormal Product of the Reimer-Tiemann Reaction[11]

Formation of dienone (**5**) as the main product of reaction B (Fig. 1), was deduced from the following experiments. 1. In the NMR spectrum of the product **Q** (see Experimental), a singlet CH_3 proton peak of 8.60 τ[12] and a singlet $HCCl_2$ proton peak of 4.40 τ were observed. 2. In the IR spectrum of **Q**, clear doublet dienone peaks of 1663 and 1640 cm^{-1} were observed together with the 1705 cm^{-1} peak of the carboxylic acid group. 3. In the mass spectrum, the ions with *M/e* values of 262, 244, 227, 216, 208,[13] 190, 180 and others with the value 262 corresponding to the molecular weight of **5** were observed. 4. Esterification of **Q** with ethanol and hydrogen chloride gave a fairly good yield of **6**. The semicarbazone of **6** was also obtained. 5. Distillation of **Q** after irradiation with sunlight for 20 hrs gave 69% of the lactone **3**,[14] while ditillation without irradiation resulted in polymerization into a resinous substance.

Structure of 6. Comparison of the UV absorption maxima of **6**, 202 mμ (log ε 3.58), 233 mμ (log ε 3.99), 267 mμ (shoulder, log ε 3.47), and 332 mμ (log ε 2.82) with those of its semicarbazone, 201 mμ (log ε 3.62), 251 mμ (log ε 3.84), and 301 mμ (log ε 4.25) suggested the cyclohexadienone structure of **6**, because on the formation of the semicarbazone, the 233 mμ absorption band of **6** disappeared and a 301 mμ band appeared as is usually the case with a dienone.[15] In the NMR spectrum of **6**, the singlet methyl protons

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9) Buffer solution: H. A. Flaschka, EDTA titration, Pergamon, Oxford, 1964, p. 72. Titration: *ibid.*, p. 83. The results of titration were reported in the preliminary communication. It should be added that the reagent solution separated white precipitate when stored for more than four or five days.

10) Spectrophotometric determination of iron: W. Nielsch and G. Böltz, *Microdhim. Acta*, 481 (1954); *Z. Anal. Chem.*, **144**, 401 (1954). P. Schneider and J. Janko, *Chem. Listy*, **50**, 899 (1956). Of copper: W. Nielsch and G. Böltz, *Z. Anal. Chem.*, **142**, 406 (1954); *ibid.*, **143**, 1 (1954). Reviews are available: K. Ueno and B. Sakaguchi, The metal chelates (Japanese) Vol. II, Nankodo, Tokyo, 1966, p. 208—228.

11) H. Wynberg, *Chem. Rev.*, **60**, 169 (1960).

12) L. M. Jackmann, "Application of nuclear magnetic resonance spectroscopy in organic chemistry," Pergamon, New York 1959, pp. 53, 58.

13) Since the *M/e* value 208, corresponding to the molecular weight of **2b**, was observed in the mass spectrum of **Q**, part of it was treated with an aqueous alcoholic solution of potassium acetate and semicarbazide hydrochloride. Semicarbazone of mp 207°C was obtained in 8.83% yield. The yield of **2a** in the reaction B preliminary reported should be revised to 9.48%.

14) H. E. Zimmermann, *J. Amer. Chem. Soc.*, **84**, 4527 (1962); *ibid.*, **88**, 4895 (1966). J. S. Swenton, E. Sauerborn, R. Srinivasan, and F. I. Sonntag, *ibid.*, **90**, 2990 (1968). D. I. Schuster, and D. J. Patel, *ibid.*, **87**, 2516 (1965).

15) A. I. Scott, "Interpretation of the ultraviolet spectra of natural products." Pergamon, Oxford, 1964, p. 78.

of 8.55 τ, the triplet methylene protons adjascent to the double bond (4H) of 7.5 τ (J=7.7 cps), a singlet $HCCl_2$ proton (1H) of 4.20 τ, a doublet vinyl proton (1H) of 3.72 τ (J_1=9.4 cps), a quartet vinyl proton (1H) of 3.17 τ (J_1=9.4 cps, J_2=2.6 cps), and a doublet vinyl proton (1H) of 3.32 τ (J_2=2.6 cps) were observed corresponding to **6**, as illustrated in Fig. 4. The 1735 cm^{-1} IR peak of the ester carbonyl group together with the clear doublet peaks 1663 and 1640 cm^{-1} of the dienone indicated the structure **6**. Of the mass spectrum (Fig. 5), the triplet sets of ions with M/e values such as 290, 292, 294, and 240, 242, 244 whose intensity ratio was approximately 1.0: 0.65: 0.15, seemed to be those of the dichloro fragments, while the doublet sets (254, 256), (181, 183), and (155, 157), whose intensity ratio was approximately 1.0: 0.4, seemed to be the monochloro fragments. Structures of **6** and **5** were confirmed by these physical measurements and chemical transformations.

Absorption Spectra

The O–H stretching IR peak of 3400 cm^{-1} of **2a** was considered from its similarity to those of hydroxyacids **1a** and **9** to be due to the hydrogen bond between the carboxyl and the hydroxyl groups and not to that between the hydroxyl and the aldehyde groups.

The UV spectra of **2a,b,c** in the ethanolic solutions as well as in the 0.5% aqueous sodium hydroxide solutions were nearly the same. However, in the hexane solutions in which acid exerts strong action, the 344 mμ n-π^* transition band[16] of **2a** disappeared while those of **2b,c** remained (Table 1).

Table 1. Absorption maxima of **2a,b,c** measured in hexane solutions and their relative intensities[a]

2a		**2b**		**2c**	
mμ	(intensity)	mμ	(intensity)	mμ	(intensity)
217.5	(2.50)				
219	(2.41)	218.5	(0.58)	219	(1.26)
229	(0.60)			229	sh. (0.58)
234	(0.80)				
239	(1.21)			239	(0.42)
245	(1.41)			244	(0.59)
				248	sh. (0.49)
251	(1.55)			250	(0.63)
255	sh. (1.51)			254	sh. (0.57)
258	sh. (1.39)			256	(0.64)
261	(1.30)	260	(1.70)	260	sh. (0.54)
		265	(1.88)	262	(0.61)
269	(0.73)			269	(0.20)
342	(0.01)	345	(0.57)	347	(0.08)

a) Absorbance of their saturated solutions. sh. Shoulder.

The results suggest a dipolar ion such as **17**, with the following structure: — phenoxide and the protonated + carbonyl groups. A shoulder of 248 mμ ascribed to the phenoxide ion, was observed in the spectrum of **14a** but not in those of **14b,c** in the ethanolic solutions and the intensity of 347 mμ n–π^* band of the former decreased. A strong absorption peak of 1543 cm^{-1} was observed in the IR spectrum of the ligand **14a** but not in those of **14b,c**.

The absorption peak 1540 cm^{-1} of the salicylaldehyde Schiff base chelates was discussed and its assignment based on three different views. 1. the C=N stretching vibration.[17] 2. the C–O$^-$ stretching vibtation of the phenoxide ion endowed with a double bond character.[18] 3. the skeletal vibration of the aromatic ring loosened by ctoss resonance between the aromatic and the chelate ring.[19] It was recognized that the IR as well as the UV spectra of **14a** were closely related to those of the Schiff base chelates. It was thus considered that the proton shifted from the phenol oxygen atom toward the nitrogen atom to form a dipolar structure such as **19**. The structure **16** was introduced in place of **14a** on this basis.

In contrast to those of **11a,b,c**, and **12 a,b,c**, the IR absorption peaks of the carboxylic acid groups of **13a,b,c**, were observed between 1703 and 1710 cm^{-1} together with the shoulders appearing between 1725 and 1730 cm^{-1} as illustrated in Fig. 6 and in Table 2 (B). The shoulders were ascribed to the C=O stretching vibration

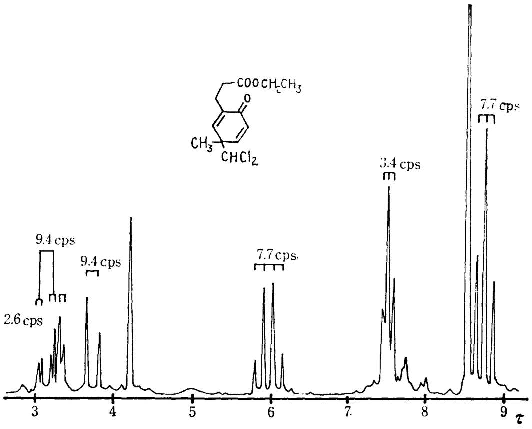

Fig. 4. NMR spectrum of **6** ($CDCl_3$).

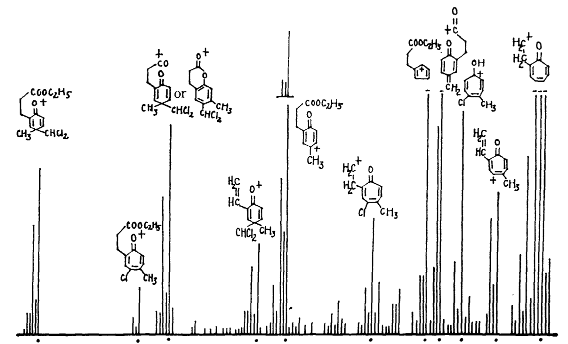

Fig. 5. Mass spectrum of **6**. Ionizing voltage, 75 eV; ionizing current, 200 μA; Sample temperature, 75°C; chamber temperature, 80°C. The formulae are possible ionic species.

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16) Ref. 15, p. 103.

17) K. Ueno and A. E. Martell, *J. Phys. Chem.*, **59**, 998 (1955); *ibid.*, **60**, 1270 (1956).

18) P. L. Teyssie and J. J. Charette, *Spectrochim. Acta*, **19**, 1403 (1963). G. E. Batley and D. P. Graddon, *Aust. J. Chem.*, **20**, 877 (1967).

19) R. C. Burrows and J. C. Bailar. Jr., *J. Amer. Chem. Soc.*, **88**, 4150 (1966).

of the COO–Cu/2 bond,[20] in analogy with those of the penta-coordinate addition compounds of bissalicylaldehyde-ethylenediimine-copper derivatives with propionic acid. The broad first bands of binuclear chelates **11a,b,c** and **12a,b,c** were observed between 690 and 750 mμ and between 624 and 700 mμ (blue shift), respectively, while the distinct first bands of **13a,b,c** were observed between 553 and 560 mμ as shown in Fig. 7 and Table 2 (A). The wave lengths of the absorption maxima of **13a,b,c** were nearly the same as those of the addition compounds of bis-salicylaldehyde-ethylene-diimine-copper derivatives with propionic acid. This indicates that one of the side chain carboxylic acid groups form the addition compound of the chelate itself to make the pentacoordinate structure such as **13a,b,c**.

The absorption peaks of 1610—1645 cm^{-1} due to the carboxylate ions of the ligands **15a,b,c** and the $-\overset{+}{N}H_2-$ peaks of 1550—1565 cm^{-1} indicate their dipolar structure.

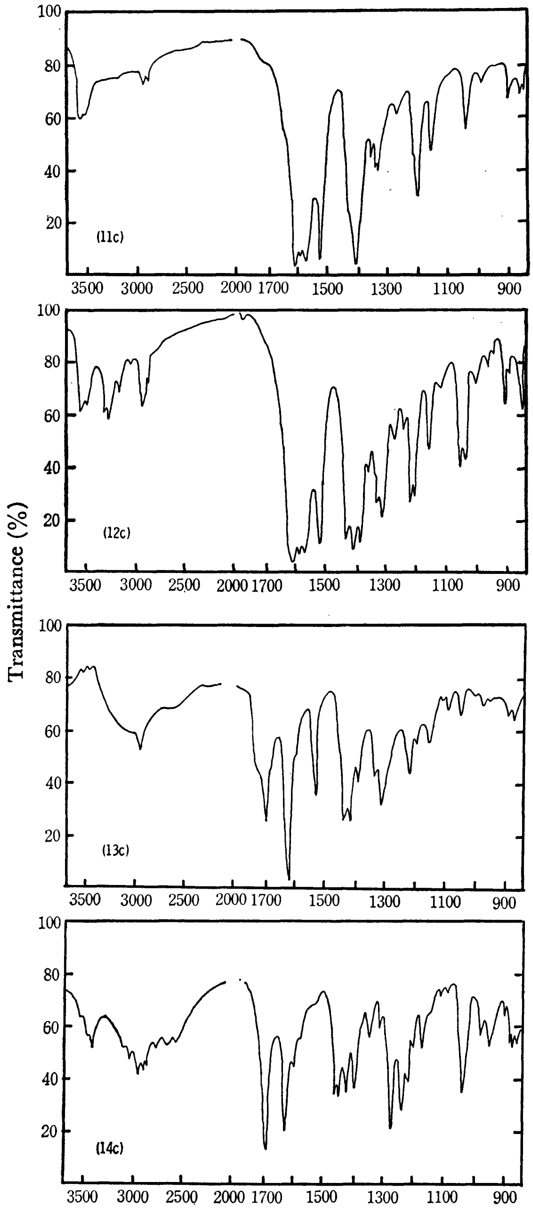

Fig. 6. Infrared spectra of **11c**, **12c**, **13c**, and **14c**. (KBr disc)

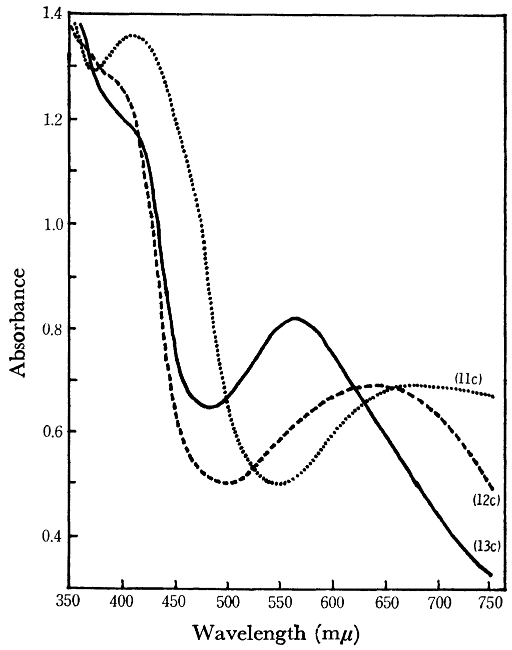

Fig. 7. Reflectance spectra of **11c**, **12c**, and **13c**.

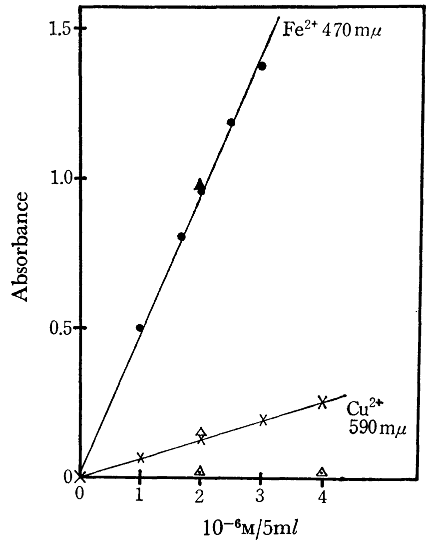

Fig. 8. Spectrophotometric determination of Cu(II) and Fe(II). Measurements were made of 5 ml of aqueous solutions containing 0.5 ml of 1/100 M solution of disodium salt of (15c), 0.1 ml of pH 10 and 7 buffer solutions respectively and; ×, moles of copper acetate; ●, moles of ferrous chloride; △̸, moles of nickel acetate; △, ▲, mixtures of each moles of Cu(II)-Ni (II) and Fe (II)-Ni (II) respectively. Cell depth 1 cm and pure water as reference.

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[20] Most of the copper carboxylates are of the symmetric carboxylate ion coordination type (ref. 5) and references are not available for the asymmetric copper carboxylate of this structure. Assignment of the structure, nevertheless, was based on the steric hindrance studies: T. Tanaka, *Nippon Kagaku Zasshi*, **79**, 942 (1958) and the IR spectra: T. Tanaka, *ibid.*, **81**, 1013 (1960).

TABLE 2. (A). UV AND VISIBLE ABSORPTION SPECTRA

Compound	Solvent	mμ (log ε)			
2a	Ethanol	200.5 (4.10),	223 (4.30),	260.5 (3.86),	344 (3.48)
2b	Ethanol	200 (4.09),	218 (4.25),	264 (4.06),	348 (3.49)
2c	Ethanol	198 (4.09),	222 (4.36),	260.5 (4.00),	345 (3.68)
2a	0.5% aq. NaOH		237 (4.23),	275 sh(3.65),	399 (3.75)
2b	0.5% aq. NaOH		231 (4.20),	276 (3.83),	400 (3.82)
2c	0.5% aq. NaOH		237 (4.30),	275 sh(3.72),	398 (3.84)
14a	Etahnol	200.5 (3.79), 347 (3.08),	226 (3.93), 430 (ref)	248 sh(3.67),	264sh(3.47),
14b	Ethanol	200.5 (5.07), 424 (2.60)	220 (4.89),	267 (4.61),	336 (4.16),
14c	Ethanol	198.5 (4.58), 412 (2.66)	224 (4.68),	260 (4.22),	334 (3.77),
11a	Ethanol	200.5 (*), 750 (ref)	224 (*),	256 (*),	420 (ref),
11b	Ethanol	200.5 (3.55), 432 (2.83),	228sh(3.51), 412 (ref),	269sh(3.13), 710 (ref)	285sh(3.08),
11c	Ethanol	200 (3.54), 406 (2.92),	228 (3.72), 410 (ref),	248sh(3.50), 690 (ref)	277sh(3.28),
12a	Pyridine	305 (3.15), 700 (ref)	386 (3.23),	496 (2.67),	406 (ref),
12b	Ethanol	200.5 (3.38), 624 (ref)	228sh(3.32),	256sh(2.98),	388 (ref),
12c	Ethanol	200.5 (*), 370 sh(ref),	231sh(*), 400sh(ref),	256sh(*), 640 (ref)	426 (*),
13a	Pyridine	280 sh(3.39), 553 (ref)	302 (3.53),	380 (3.83),	416sh(ref),
13b	Ethanol	202 (4.41), 416 sh(ref),	235 (4.42), 560 (ref)	280 (4.21),	377 (3.81),
13c	Ethanol	200.5 (3.70), 415 sh(ref),	232 (3.61), 560 (ref)	282sh(3.39),	378 (3.18),
15b	Ethanol	202.5 (3.97),	223sh(3.22),	287 (2.63)	
21b	Ethanol	203 (4.85), 410 (3.01),	241 (4.04), 600 (2.35)	285 (3.88),	340sh(2.98),

Abbreviations: sh···shoulder, *···saturated solution, ref···reflective measurement.

TABLE 2 (B). INFRARED SPECTRA (BETWEEN 1500 AND 1800 cm^{-1})

Compound/Group	Wave number cm^{-1}						
	COO-Cu/2	COOH	HC=O	HC=N	aromatic ring	COO^-	structure **19**
2a		1701s	1660s		1605m		
2b		1710s	1645s		(1620sh) 1600m		
2c		1705s	1650s		1606m		
14a		1703m		1625s	1593w		1543s
14b	(1722sh)	1705s		1632s	1605m		
14c		1703s		1635s	1603sh		
11a			1611vs			1580s	1535m
11b		(1640sh)	1603s			1580s	1535s
11c			1612s		1595m	1578s	1530s
12a			(1645sh)	1610vs		1580vs	1535s
12b			(1630s)	1610vs		1575s	1530s
12c				1620vs	1595s	1578s	1528s
13a	1725sh	1710m		1630vs	1595w		1540m
13b	1725s	1705s		1620s			1542s
13c	1730sh	1703s		1625vs	1600sh		1540s

Abbreviations: s ··· strong, m ··· medium, w ··· weak, v ··· very, ( ) ··· not assigned.

Experimental

The melting points were uncorrected. The spectra were taken on a Hitachi EPS-3T ultraviolet and visible spectrophotometer, Hitachi EPI-G2 infrared spectrophotometer, Hitachi H-60 NMR spectrometer and Nihon-Densi JMS-01S-G mass spectrometer. The infrared spectra were measured over 400—4000 cm^{-1} in Nujol mull and a potassium bromide disk. The wave numbers of the observed absorption bands were calibrated with polystyrene. The samples for magnetic measurements were purified by washing twice with hot ethanol, three times with hot water and four times with 70% (v/v) aqueous ethanol in an amount from which **11a**, **b**, **c** could be recrystallized.

*5-Methyl-3-β-carboxyethylsalicylaldehyde (**2b**).* Forty grams of 6-methyldihydrocoumarin[21] was dissolved in an aqueous sodium hydroxide solution (110 g of sodium hydroxide in 650 m*l* of water) at 65—70°C. To the solution was added 90 g of chloroform for an hour at the same temperature under thorough stirring which was continued for 7 hr and a half. The reaction mixture was cooled, acidified with hydrochloric acid and extracted twice with ether. The combined ether solution was washed with water and extracted twice with a saturated aqueous solution of sodium bisulfite (30 g of sodium bisulfite was used). The ether layer (A) and the sodium bisulfite solution were separated. The combined sodium bisulfite solution was acidified with hydrochloric acid and extracted with ether (B). The ethereal extract (B) was washed with water, dried over sodium sulfate. A grease-like residue obtained after the evaporation of ether was extracted with hot petroleum ether. Crystals obtained from the petroleum ether solution were recrystallized from the same solvent. Pale yellow crystal, mp 93°C. Yield 332 mg.[22] In another run, extraction with an aqueous solution of 50 g of sodium bisulfite yielded 956 mg of the aldehyde.

*4-Methyl-4-dichloromethyl-2-β-carboxyethyl-cyclohexa-2,5-dien-1-one (**5**).* The ether layer (A) obtained as above was washed with water and dried over sodium sulfate. Evaporation of ether in a vacuum at room temperature yielded 31 g of residual dark red oil **Q**. Examination of the mass spectrum and thin layer chromatogram of **Q** indicated that it consisted of **5** (main fraction), **2b** (minor fraction) and a small amount of other compounds.

*Separation of **2b** in **Q** as Semicarbazone.* Three grams of semicarbazide hydrochloride and 3 g of potassium acetate were dissolved in 9 m*l* of water. To the solution was added 5.9 g of **Q** dissolved in 8 m*l* of ethanol. The semicarbazone of **2b** separated immediately after the addition was recrystallized from ethanol. Mp 207°C. Yield 1.1 g. This was identified by both the mixed melting point and a comparison of the IR spectra with those of the authentic sample.

Found: C, 53.40; H, 5.75; N, 15.39%. Calcd for $C_{12}H_{15}O_4N_3$: C, 54.33; H, 5.70; N, 15.84%.

*Conversion of **5** into 6-Methyldihydrocoumarin (**3**).* Thirty grams of **Q** dissolved in 100 m*l* of dioxane was irradiated with sunlight for twenty hours. The solution was dried over sodium sulfate and distilled. A distillate of bp 120—150°C/4 mmHg was obtained and solidified by the seeding. Recrystallization of the distillate from aqueous alcohol (alcohol 7: water 3) gave 12.68 g of 6-methyldihydrocoumarin. Distillation without any irradiation gave a resinous polymerizate.

*The Ethyl Ester **6**.* Fifteen grams of **Q** was dissolved in 100 m*l* of ethanol (in which 3 g of dry hydrogen chloride was contained), warmed in a water bath at 60°C for 3 hr and left to stand overnight. The solution was treated with 50 m*l* of benzene, washed with water, dried over sodium sulfate and distilled. Fraction I. bp —153°C/6 mmHg, 1.4 g; Fraction II. bp 135—155°C/5 mmHg, 1.8 g; Fraction III. bp 155—168°C/5 mmHg, 9.1 g. Redistillation of Fraction III gave slightly yellow colored distillate of bp 158—162°C/5 mmHg (tlc, $R_f=0.58$, silica gel; benzene 8: ethyl acetate 2) which was proved to be the ester **6** as discussed above. Fractions I and II contained a compound of $R_f=0.72$ as the major component and **6** as a minor component.

Found: C, 53.98; H, 5.53; Cl, 22.60%. Calcd for $C_{13}H_{16}O_3Cl_2$: C, 53.62; H, 5.54; Cl, 24.35%.

*The Semicarbazone of **6**.* To a solution of 600 mg of semicarbazide hydrochloride and 600 mg of potassium acetate in 1.8 m*l* of water was added 920 mg of **6** and a small amount of ethanol. The solution was left to stand for 4 days at room temperature. The crystals separated were recrystallized from ethanol. Mp 153°C. Yield 586 mg.

Found: C, 48.34; H, 5.49; N, 12.07; Cl, 20.21%. Calcd for $C_{14}H_{20}O_3N_3Cl_2$: C, 48.14; H, 5.77; N, 12.03; Cl, 20.29%.

*5-Chloro-3-β-carboxyethylsalicylaldehyde (**2c**) and 2-β-carboxyethyl-1,4-benzoquinone (**9**).* The same procedure as for the Reimer-Tiemann reaction by use of 30 g of 6-chlorodihydrocoumarin,[21] 72.6 g of sodium hydroxide in 220 m*l* of water and 62 g of chloroform followed by bisulfite extraction yielded a mixture of compounds. On recrystallization of the mixture from benzene, a compound with very small solubility 2-β-carboxyethyl-1,4-benzoquinone, mp 160°C, separated out. Yield 232 mg (after recrystallization from benzene). IR spectrum, 1703 cm^{-1} (COOH), 1650, 1586 cm^{-1} (quinonoid enone). NMR spectrum ($(CD_3)_2SO$), 1H (COOH) 0.25 τ; 3H (quinone ring) 1H doublet 3.06 τ ($J_1=9$ cps), 1H doublet 2.38 τ ($J_2=2$ cps), 1H quartet 2.41 τ ($J_1=9$ cps, $J_2=2$ cps).

Found: C, 60.64; H, 5.25%. Calcd for $C_9H_8O_3$: C, 60.00, H, 4.48%.

From the mother liquor of recrystallization, **2c** of mp 118°C was obtained. Yield 2.15 g (after recrystallization from benzene).[22]

As a non-carbonyl fraction (not removed by bisulfite extraction) 19.5 g of crystal was obtained which after recrystallization from benzene melted at 136°C and was identified to be **10** by melting point, analysis and the superimposable IR spectra.

*5-Bromo-2-hydroxyphenylacetic acid (**1**).* To a vigorously stirred mixture of 30.2 g of 2-hydroxyphenylacetic acid[23] in 200 m*l* of carbon disulfide cooled in an ice-salt bath, was added a solution of 32 g of bromine in 80 m*l* of carbon disulfide for two hours. Stirring was continued for 2 hr, and left to stand overnight at room temperature. The precipitate separated was filtered and recrystallized from benzene. Mp 151°C, yield 23.7 g.[22]

*5-Bromo-3-carboxymethylsalicylaldehyde (**2a**).* 1.60 g of **2a** was obtained by the same Reimer-Tiemann procedure, starting with 11.6 g of 5-bromo-2-hydroxyphenylacetic acid, 22 g of sodium hydroxide in 120 m*l* of water and 18 g of chloroform. Recrystallized from benzene. Pale yellow crystal. Mp 204°C.[22]

*Bis-(5-bromo-3-carboxymethylsalicylaldehyde)-ethylenediimine (**14a**).* To a solution of 1.036 g of **2a** in 50 m*l* of ethanol heated on a water bath was added a solution of 0.156 g of ethylenediamine in 10 m*l* of ethanol and the mixture was heated for 30 min on the water bath. The precipitate with a small solubility in ethanol separated immediately, and was filtered (1.1 g) and recrystallized from a large amount of ethanol. Yellow crystal. Mp 242°C.[22]

*Bis-(5-methyl-3-β-carboxyethylsalicylaldehyde)-ethylenediimine (**14b**).* To a hot solution of 51 mg of ethylenediamine in 4 m*l* of ethanol were added crystals of 312 mg of **2b** and the mixture was heated on a water bath for 30 min. On

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[21] K. Sato, T. Amakasu, and S. Abe, *J. Org. Chem.*, **29**, 2971 (1964).

[22] Analytical values were given in a preliminary report. This Bulletin, **41**, 1277 (1968).

[23] J. Levine, T. E. Eble, and H. Fischbach, *J. Amer. Chem. Soc.*, **60**, 1930 (1948).

cooling and scratching the wall of the flask with a glass rod, yellow crystals separated; readily soluble in ethanol and recrystallized from ethanol, mp 195°C, yield 276 mg.[22]

Bis-(5-chloro-3-β-carboxyethylsalicylaldehyde)-ethylenediimine (14c). Prepared in the same way as **14b**, from 457 mg of **2c** and 65 mg of ethylenediamine in 6 m*l* of ethanol. Yellow crystal. Mp 204°C. Yield 226 mg.[22]

N,N′*-bis-(5-chloro-2-hydroxy-3-β-carboxyethylbenzyl)-ethylenediamine (15c).* To a suspension of 150 mg of the Schiff base **14c** in 18 m*l* of absolute methanol heated to 48—50°C in an oil bath, was gradually added 100 mg of crystals of sodium borohydride after the frothing subsided.[24] When the addition was over, the temperature of the reaction mixture was gradually raised to 90°C, and then cooled and filtered. To the filtrate was added 15 m*l* of water and then a dilute aqueous acetic acid solution until turbidity appeared. In a few minutes white crystals separated out and which were filtered and dried. For further purification, the product was dissolved in 15 m*l* of a dilute aqueous sodium hydroxide solution (*ca.* 1/10 N), to which was added 18 m*l* of methanol and a dilute aqueous acetic acid solution until turbidity ensued. Crystals which separated out in a few minutes were filtered, washed with water and dried. Colorless crystals. Mp (dec.) 280—300°C, yield 128 mg.

Found: C, 53.55; H, 5.70; N, 5.19%. Calcd for $C_{22}H_{26}O_6N_2Cl_2$: C, 54.43; H, 5.40; N, 5.79%.

N,N′*-bis-(5-bromo-2-hydroxy-3-carboxymethylbenzyl)-ethylenediamine (15a).* Prepared in the same way as **15c**, starting with 437 mg of **14a** and 322 mg of sodium borohydride. Colorless crystal. Mp (dec.) 300°C, yield 287 mg.[22]

N,N′*-bis-(5-methyl-2-hydroxy-3-β-carboxyethylbenzyl)-ethylenediamine (15b).* Prepared in the same way as **15c**, starting with 700 mg of **14b** and 500 mg sodium borohydride in 56 m*l* of absolute methanol. Colorless crystal. Mp (dec.) 285°C, yield 559 mg.[22]

Di-μ-aquo-bis-(5-bromo-3-carboxymethylsalicylaldehyde)-dicopper (11a). To a hot solution of 518 mg (1/1000 mol) of **2a** in ethanol was added an aqueous solution of 399 mg (1/1000 mol) of copper acetate and the mixture was heated on a water bath for 20 min. The precipitate separated out immediately was filtered while hot and purified by washing several times with hot ethanol and water; bright green crystal, yield 587 mg. The yield and composition of the chelate were not altered even when twice as much aldehyde was used.

Found: C, 31.70; H, 1.58; Cu, 18.77%. Calcd for $C_{18}H_{14}O_{10}Br_2Cu_2$: C, 31.92; H, 2.08; Cu, 18.77%.

Di-μ-aquo-bis-(5-methyl-3-β-carboxyethylsalicylaldehyde)-dicopper (11b). Prepared in the same way as **11a**, starting with 412 mg of **2b** and 400 mg of copper acetate. Bright green powder. Yield 496 mg.

Found: C, 46.18; H, 4.57; Cu, 21.02%. Calcd for $C_{22}H_{24}O_{10}Cu_2$: C, 45.91; H, 4.20; Cu, 22.08%.

Di-μ-aquo-bis-(5-chloro-3-β-carboxyethylsalicylaldehyde)-dicopper (11c). Prepared in the same way as **11a**, starting with 115 mg of *2c* and 98 mg of copper acetate; bright green powder. Yield 140 mg.

Found: C, 38.51; H, 3.02; Cu, 21.01%. Calcd for $C_{20}H_{18}O_{10}Cl_2Cu_2$: C, 38.97; H, 2.94; Cu, 20.62%.

Di-μ-aquo-bis-(5-chloro-3-β-carboxyethylsalicylaldehyde)-ethylenediimine-dicopper (12c). To a suspension of 100 mg of **11c** in 5 m*l* ethanol was added a solution of 10 mg of ethylenediamine in 3 m*l* of water and the mixture was heated on a water bath for 20 min. Green crystals precipitated which were purified by washing repeatedly with ethanol and water. Yield 91 mg.

Found: C, 41.55; H, 3.64; N, 4.92; Cu, 20.53%. Calcd for $C_{22}H_{22}O_8N_2Cl_2Cu_2$: C, 41.26; H, 3.46; N, 4.37; Cu, 19.84%.

Di-μ-aquo-bis-(5-bromo-3-carboxymethylsalicylaldehyde)-ethylenediimine-dicopper (12a). Prepared by the reaction of 102 mg of **11a** and 10.2 mg of ethylenediamine; green powder, yield 89 mg.

Found: C, 33.63; H, 2.22; N, 4.85; Cu, 18.60%. Calcd for $C_{20}H_{18}O_8N_2Br_2Cu_2$: C, 34.25; H, 2.59; N, 4.01; Cu, 18.12%.

Di-μ-aquo-bis-(5-methyl-3-β-carboxyethylsalicylaldehyde)-ethylenediimine-dicopper (12b). Prepared by the reaction of 87 mg of **11b** in 3 m*l* of ethanol with 10 mg of ethylenediamine in 1 m*l* of water; green powder, yield 85 mg.

Found: C, 47.35; H, 5.13; N, 4.64; Cu, 20.38%. Calcd for $C_{24}H_{28}O_8N_2Cu_2$: C, 48.08; H, 4.70; N, 4.67; Cu, 21.20%.

Bis-(5-chloro-3-β-carboxyethylsalicylaldehyde)-ethylenediimine-copper (13c). To a hot solution of 240 mg of **14c** in 20 m*l* of ethanol was added a solution of 100 mg of copper acetate in 10 m*l* of water. The reaction mixture was heated on a water bath for 30 min and the precipitate was filtered hot. The gray purple product was recrystallized from a large amount of ethanol, yield 239 mg.

Found: C, 47.94; H, 3.73; N, 5.13; Cu, 12.03%. Calcd for $C_{22}H_{20}O_6N_2Cl_2Cu$: C, 48.67; H, 3.71; N, 5.16; Cu, 11.70%.

Bis-(5-methyl-3-β-carboxyethylsalicylaldehyde)-ethylenediimine-copper (13b). Prepared in the same way as **13c** by the reaction of 220 mg of **14b** in 20 m*l* of ethanol with 100 mg of copper acetate in 10 m*l* of water. Gray purple crystal, yield 208 mg.

Found: C, 56.10; H, 5.32; N, 5.59; Cu, 13.12%. Calcd for $C_{24}H_{26}O_6N_2Cu$: C, 57.42; H, 5.22; N, 5.58; Cu, 12.66%.

Bis-(5-bromo-3-carboxymethylsalicylaldehyde)-ethylenediimine-copper (13a). The reaction of 108 mg of **14a** and 40 mg of copper acetate yielded 103 mg of a brown copper chelate. The chelate could not be obtained in a pure state owing to the low solubility of **14a** and the copper chelate; purplish brown powder.

Found: C, 39.13; H, 3.02; N, 5.63; Cu, 9.50%. Calcd for $C_{20}H_{16}O_6N_2Br_2Cu$: C, 39.79; H, 2.67; N, 4.64; Cu, 10.53%.

N,N′*-bis-(5-methyl-2-hydroxy-3-β-carboxyethylbenzyl)-ethylenediamine-copper (21).* A solution of 40.8 mg of copper acetate in 3 m*l* of water was added to a solution of 89.38 mg of **15b** in 5.4 m*l* of 1/10 N aqueous sodium hydroxide (f= 0.744) at room temperature with stirring. Yellow green crystals separated immediately. After stirring for one and a half hour, the precipitate was filtered, washed thoroughly with water and ethanol and recrystalized from 70% aqueous ethanol. Green crystal, yield 88.08 mg.

Found: C, 51.88; H, 6.40; N, 5.01; Cu, 10.91%. Calcd for $C_{24}H_{30}O_6N_2Cu\text{-}3H_2O$: C, 51.46; H, 6.48; N, 5.01; Cu, 11.34%.

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[24] I. L. Finar and K. Utling, *J. Chem. Soc.*, **1959**, 4015.