

Complexes of Thiazoles. Part IV.¹ Acetamido-thiazoles as Ambidentate Ligands

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Some complexes of 2-acetamidothiazole and 2-acetamidobenzothiazole with Ni^{II} and Cu^{II} have been prepared and three types of co-ordination behaviour distinguished on the basis of their i.r. spectra. The organic ligand donor atoms may be (a) carbonyl oxygen and thiazole nitrogen, (b) amide nitrogen and thiazole nitrogen, or (c) carbonyl oxygen, amide nitrogen, and thiazole nitrogen. Types (b) and (c) are of interest as examples of co-ordination via a non-deprotonated amide nitrogen atom.

As part of our work on thiazoles as ligands¹ we have prepared the compounds 2-acetamidothiazole (acam) and 2-acetamidobenzothiazole (acamb) and have examined their co-ordination behaviour. This was of

RESULTS

The complexes fall into three groups in terms of the behaviour of the ligand as indicated by a study of their i.r. spectra (Table 1). Details of electronic spectra,

TABLE 1
Far-infrared spectra (660—222 cm⁻¹) and $\nu(\text{C}=\text{O})$ frequencies (cm⁻¹)

Complex	* $\nu(\text{C}=\text{O})$	Ligand modes	$\nu(\text{M}-\text{O})$	$\nu(\text{M}-\text{N})$	Others
Ni(acamb) ₂ Cl ₂	1659s	429s, 412sh	352s, 315sh		$\nu(\text{Ni}-\text{Cl})$ ca. 230br
Ni(acamb) ₂ Br ₂	1675m	429s, 412sh	352s, 314m		
Ni(acamb) ₂ I ₂	1658m	430m	350s		
[Ni(acamb) ₂ (H ₂ O) ₂] ₂ I ₂	1661m	429m	351s		$\nu(\text{Ni}-\text{OH}_2)$ 463m
Ni(acam) ₂ Cl ₂ ·2H ₂ O	1660m	355s, 319m	392m	269s, 233s	
[Ni(acam) ₂ (H ₂ O) ₂] ₂ Br ₂	1660m	355s, 317m	394m		$\nu(\text{Ni}-\text{OH}_2)$ 463m
Ni(acam) ₂ (NO ₃) ₂	1668m	355s, 321m	392m	260m, 226m	
Cu(acamb) ₂ Cl ₂	1710m	429m			292s, 282s
Cu(acam)Br	1708m	433m			278m, 267m
Cu(acamb) ₂ (ClO ₄) ₂	1653m	427s, 415sh	351m, 318m		279m, 245m
Cu(acam) ₂ Cl ₂	1714m	320w		288s, 247m	
Cu(acam)Cl ₂	1658m	370m, 311w	405m	278m, 246m	$\nu(\text{Cu}-\text{Cl})$ 331s
Cu(acam) ₂ Br ₂	1648m	368s, 318m	408s	276s, 245m	
Cu(acam)Br ₂	1652m	370m, 310w	405m	280m	$\nu(\text{CuBr})$ 260s
Cu(acam) ₂ (NO ₃) ₂	1663m	374s, 319w	412m	282s	
Cu(acam) ₂ (ClO ₄) ₂	1640m	377s, 320m	410s	286s, 249m	309m

* $\nu(\text{C}=\text{O})$ in acamb = 1704 cm⁻¹, acam = 1708 cm⁻¹.

TABLE 2
Magnetic moments, conductances, and electronic spectra

Complex	(Ω^{-1})	μ_{eff} (B.M.)	Absorption maxima (m μ)
Ni(acamb) ₂ Cl ₂	18.7 *	3.27	25.8s, 24.2sh, 14.5m, ca. 13.0sh, ca. 9.8sh, 8.0m
Ni(acamb) ₂ Br ₂	14.2 *	3.19	25.6s, 23.6sh, 14.4m, ca. 12.8sh, ca. 9.3w, 7.5m
Ni(acamb) ₂ I ₂	21.6 *	3.06	25.5s, 19.8sh, 14.5m, ca. 12.8sh, 10.3w, 7.3m
Ni(acamb) ₂ I ₂ ·2H ₂ O	139 *		ca. 26.6sh, 15.5m, ca. 14.0sh, 9.6m
Ni(acam) ₂ Cl ₂ ·2H ₂ O	74.1	3.16	ca. 26.5sh, 16.5m, 10.5m, ca. 8.9sh
Ni(acam) ₂ Br ₂ ·2H ₂ O	75.8	3.08	16.6m, 10.7m, ca. 9.4sh
Ni(acam) ₂ (NO ₃) ₂	76.3	2.87	ca. 26.5sh, 16.2m, 10.4m, ca. 8.1sh
Cu(acamb) ₂ Cl ₂	11.1 *	1.86	13.0s, br
Cu(acamb)Br	47.6 *	Diamagnetic	
Cu(acamb) ₂ (ClO ₄) ₂	14.8 *	1.83	
Cu(acam) ₂ Cl ₂	22.3	1.90	ca. 24.0sh, 14.6m
Cu(acam)Cl ₂	16.3	1.84	24.1s, br, 9.4s, br
Cu(acam) ₂ Br ₂	46.9	1.92	ca. 26.0sh, 14.7m, ca. 10.8sh
Cu(acam)Br ₂	14.4	1.87	18.9s, 16.7s, 9.5s
Cu(acam) ₂ (NO ₃) ₂	72.3	1.94	15.2s
Cu(acam) ₂ (ClO ₄) ₂	76.4	1.91	15.9s

Conductances in Me₂SO (1 : 1 = 40 Ω^{-1} , 1 : 2 = 80 Ω^{-1}) or nitromethane * (1 : 1 = 80 Ω^{-1} , 1 : 2 = 130 Ω^{-1}).

interest partly because of their close similarity to the anti-parasitic compound² Aminotrozal (2-acetamido-5-nitrothiazole). We now report a study of the complexes of these ligands with nickel(II) and copper(II) halides, nitrates, and perchlorates. A number of different types of ligand behaviour have been observed.

¹ Part III, M. N. Hughes and K. J. Rutt, *J. Chem. Soc. (A)*, 1970, 3015.

magnetic moments, and molar conductances are given in Table 2.

The co-ordination behaviour of the ligands may be related to that of amides and peptides, although one familiar form of co-ordination in peptides, involving deprotonated amide nitrogen atoms is clearly not

² E. F. Elslager, Reviews in *Ann. Rep. Medicin. Chem.*, 1965, 1966.

involved in our complexes. We must, however, consider the possibility that the ligand is co-ordinated in the enol form.

The free ligand exists in the keto-form [$\nu_{\text{C=O}}$ at 1708 cm^{-1} for acam and at 1704 cm^{-1} for acamb, $\nu(\text{N-H})$ at 3240 and 3237 cm^{-1} respectively]. On complex formation the spectrum is largely unaffected apart from shifts in certain bands and intensity changes which can be rationalised in terms of co-ordination. These changes occur in regions associated with the $\nu_{\text{C=O}}$ and $\nu_{\text{N-H}}$ bands of the free ligand.

Type a. We include here the complexes of acam and acamb with Ni^{II} halides and copper bromide and a complex of acam with copper chloride, of stoichiometry $\text{Ni}(\text{acamb})_2\text{X}_2$ ($\text{X} = \text{Cl}, \text{Br}, \text{or I}$), $\text{Ni}(\text{acamb})_2\text{I}_2 \cdot 2\text{H}_2\text{O}$, $\text{Ni}(\text{acam})_2\text{Cl}_2 \cdot \text{H}_2\text{O}$, $\text{Ni}(\text{acam})_2\text{Br}_2 \cdot \text{H}_2\text{O}$, $\text{Cu}(\text{acam})_2\text{Br}_2$, and $\text{Cu}(\text{acam})\text{X}_2$ ($\text{X} = \text{Cl or Br}$). The magnetic moments and electronic spectra of the 1 : 2 complexes are characteristic of distorted octahedral structures. Conductance data suggest that the aquo-complexes in nitromethane or dimethyl sulphoxide solution have unco-ordinated anions, while in the solid state the i.r. spectra indicate that the water molecules are probably co-ordinated. The conductance of $\text{Cu}(\text{acam})_2\text{Br}_2$ is fairly high but we attribute this to dissociation since the solution spectrum indicates considerable decomposition of the complex. The remainder of the complexes were non-electrolytes in nitromethane or dimethyl sulphoxide.

The electronic spectrum of $\text{Cu}(\text{acam})\text{Cl}_2$ is consistent with a tetrahedral geometry, whereas the corresponding bromo-complex has a more complicated spectrum which we are unable to account for by any single structure. This spectrum shows strong bands at 18.9, 16.7, and 9.5 kK which might be due to a mixture of planar and tetrahedral species; however, adjustments to the conditions of preparation of $\text{Cu}(\text{acam})\text{Br}_2$ did not alter the intensities of the bands in its electronic spectrum. The far-i.r. spectra of the chloro- and bromo-complexes each show only one metal-halogen stretching frequency (331 cm^{-1} in chloro, 260 cm^{-1} in bromo) instead of the doublet expected for a tetrahedral species and multiplet for a mixture.

In the i.r. spectra of all the complexes in this group the $\nu(\text{C=O})$ mode of the ligand was shifted *ca.* 30 cm^{-1} to lower frequencies, suggesting³ that co-ordination occurs *via* the carbonyl oxygen. We discount the possibility that this band is the ' $\nu(\text{C=N})$ ' band of the enol form as there is no change in the $\nu_{\text{N-H}}$ region. The complexes all show bands at *ca.* 350 cm^{-1} (acamb) or *ca.* 400 cm^{-1} (acam) in their far-i.r. spectra which we assign⁴ as $\nu(\text{M-O})$ (carbonyl). The diaquo-complexes have an additional band in their far-i.r. spectra at 463 cm^{-1} for which a tentative assignment⁵ of $\nu(\text{Ni-OH}_2)$ is made. In the case of acam complexes, bands were observed at *ca.* 260 and 230 cm^{-1} which are probably¹ $\nu(\text{M-N})$

(thiazole) modes, the corresponding bands for acamb complexes being expected⁶ below the limit of our instrument (222 cm^{-1}). We conclude that the acetamido-thiazoles act as bidentate ligands, chelating *via* the carbonyl oxygen and thiazole nitrogen atoms. There is no evidence for co-ordination of the thiazole sulphur atom in these complexes and in other cases¹ thiazoles have been found to co-ordinate preferentially *via* the nitrogen atom.

Attempts were made to dehydrate $\text{Ni}(\text{acam})_2\text{Cl}_2 \cdot \text{H}_2\text{O}$ and $\text{Ni}(\text{acam})_2\text{Br}_2 \cdot 2\text{H}_2\text{O}$ by heating them *in vacuo*, whereupon it was found that the compounds changed colour from blue to green. However neither consistent weight losses were obtained nor reproducible analyses for the products. The analytical figures suggest that the effect of heating is more complicated than the elimination of water.

Another compound which we include here is $\text{Cu}(\text{acamb})\text{Br}$, which is rather different from the others. We were unable to prepare consistently a pure compound from the CuBr_2 -acamb system and obtained a white product analysing only approximately as $\text{Cu}(\text{acamb})\text{Br}$. This diamagnetic species shows no absorptions in its electronic spectrum between 27—5 kK and appears to contain Cu^{I} .

This reduction takes place in the presence of an excess of acamb, but we have not isolated the oxidised species. The $\nu(\text{C=O})$ mode in the i.r. spectrum of this complex is not shifted to lower frequency, and no $\nu(\text{Cu-O})$ modes could be identified in the far-i.r. region. It appears that the carbonyl oxygen is not co-ordinated. Since Cu^{I} is fairly 'soft' it is possible that it complexes with the thiazole sulphur atom in this case.

Type b. Cupric chloride with acetone solutions of acamb gave the compound $\text{Cu}(\text{acamb})_2\text{Cl}_2 \cdot \text{acetone}$. The acetone is readily removed by heating to 100° for a few minutes and the properties of the desolvated complex are very similar to the original compound. The ligand acam gave the compound $\text{Cu}(\text{acam})_2\text{Cl}_2$ with cupric chloride. Both of these complexes are non-electrolytes in nitromethane or Me_2SO . Their electronic spectra are very similar and support their formulation as octahedral Cu^{II} complexes. These complexes differ from the others in that the $\nu(\text{C=O})$ mode in the i.r. spectrum is not shifted down from the free ligand, but by *ca.* 5 cm^{-1} to higher frequencies. This strongly suggests that the carbonyl oxygen is not co-ordinated, corroborative evidence being provided by the far-i.r. spectra which show no bands assignable as $\nu(\text{Cu-O})$ modes. Again the i.r. spectra eliminate the possibility of the ligand being in the enol form. We have assigned $\nu(\text{Cu-N})$ (thiazole) at 288 cm^{-1} in the far-i.r. spectrum of $\text{Cu}(\text{acam})_2\text{Cl}_2$. Another feature of the i.r. spectra is the *ca.* 10-fold enhanced intensity of the $\nu(\text{N-H})$ mode at 3240 cm^{-1} which implicates the amide nitrogen in co-ordination. We suggest that the structures involve the organic ligand

³ E. W. Randall, C. M. Silcox Yoder, and J. J. Zuckerman, *Inorg. Chem.*, 1966, **5**, 2240.

⁴ J. Fujita, A. E. Martell, and K. Nakamoto, *J. Chem. Phys.*, 1962, **36**, 324.

⁵ G. Blyholder and S. Vergez, *J. Phys. Chem.*, 1963, **61**, 2149.

⁶ E. J. Duff, M. N. Hughes, and K. J. Rutt, *J. Chem. Soc. (A)*, 1969, 2101.

bridging Cu atoms *via* thiazole and amide nitrogen atoms, with chloride ions in axial positions.

Type c. The metal complexes involving oxy-anions appear to be structurally similar. The compounds prepared were $\text{Ni}(\text{acam})_2(\text{NO}_3)_2$, $\text{Cu}(\text{acam})_2\text{X}_2$ ($\text{X} = \text{NO}_3$ or ClO_4) and $\text{Cu}(\text{acamb})_2(\text{ClO}_4)_2$. Their electronic spectra and magnetic moments are consistent with their formulation as octahedral complexes. The oxy-anions are not co-ordinated, as shown by i.r. and conductance data. The i.r. and far-i.r. spectra of the compounds show that the carbonyl oxygen of the ligand is co-ordinated, while bands assignable¹ as $\nu(\text{M-N})$ (thiazole) are observed for acam complexes. In addition however the ligand $\nu(\text{N-H})$ band at 3240 cm^{-1} shows a much greater intensity in the spectra of the complexes. Again we suggest that its enhanced intensity is due to co-ordination of the amide nitrogen atom. The resulting structure is then one in which the ligand is chelating *via* carbonyl oxygen and thiazole nitrogen, with the amide nitrogen atom linking the unit to an adjacent metal atom. The i.r. evidence in this case is not so clear cut, but in view of the way in which it fits into the pattern shown by type (a) and (b) complexes it is probable that our assignments are correct.

DISCUSSION

The complexes appear to fall into three well-defined categories. The first group has the intuitively expected structure where the ligand chelates *via* the thiazole nitrogen and carbonyl oxygen to form a six-membered ring. Those complexes having oxy-anions are ionic and have terdentate ligands, the third donor atom being the amide nitrogen. Thus it seems that the amide nitrogen is a better donor than the oxy-anions, but poorer than water or halide. The cupric chloride complexes are of interest; there is no ready explanation of why the amide nitrogen appears to co-ordinate in preference to the oxygen atom and the stable chelate ring is not formed.

There have been a number of studies on complexes of peptides, amides, and substituted amides with a range of metal ions. In all cases where crystal structures have been determined⁷ the amide nitrogen is co-ordinated only if deprotonated, while many other papers⁸ cite instances in which a deprotonated amide nitrogen is co-ordinated. In this system the amide nitrogen atom apparently co-ordinates quite readily without deprotonation and in two cases does so at the expense of the carbonyl oxygen.

EXPERIMENTAL

Physical measurements were made as described previously.¹

Preparations.—(Calculated C, H, and N analyses are shown in parentheses after the analytical figures for each complex.) 2-Acetamidothiazole was prepared by warming 2-aminothiazole (Koch-Light) with an excess of acetic anhydride and pouring the mixture into water. The solid formed was filtered off, washed well with water, and then recrystallised

twice from acetone and dried *in vacuo*, m.p. 203° (lit. 203°) [Found: C, 42.4 (42.3); H, 4.43 (4.23); N, 19.7% (19.7)].

2-Acetamidobenzothiazole was prepared as above from 2-aminobenzothiazole; it had m.p. 186° (lit., 186°) [Found: C, 56.1 (56.2); H, 4.33 (4.19); N, 14.6% (14.6)].

$\text{Ni}(\text{acamb})_2\text{X}_2$ ($\text{X} = \text{Cl}$ or Br) and $\text{Ni}(\text{acamb})_2\text{I}_2 \cdot 2\text{H}_2\text{O}$.—A solution of the appropriate hydrated nickel salt (5 mmol) in the minimum volume of ethanol (acetone for NiI_2) was added to an acetone solution of acamb (10 mmol); the mixture was warmed and stirred for 1 h. The green solids which deposited were filtered off and washed with acetone and light petroleum. $\text{Ni}(\text{acamb})_2\text{Cl}_2$ [Found: C, 42.0; (42.0); H, 3.2 (3.1); N, 10.5% (10.9)], $\text{Ni}(\text{acamb})_2\text{Br}_2$ [Found: C, 35.6 (35.8); H, 2.7 (2.65); N, 9.0% (9.28)], $\text{Ni}(\text{acamb})_2\text{I}_2 \cdot 2\text{H}_2\text{O}$ [Found: C, 29.3 (29.5); H, 2.3 (2.2); N, 7.6% (7.65)].

$\text{Ni}(\text{acamb})_2\text{I}_2$.—This compound was prepared as above except that the mixture was refluxed vigorously for 1 h [Found: C, 31.1 (31.0); H, 2.3 (2.3); N, 8.03% (8.05)].

$\text{Ni}(\text{acam})_2\text{Cl}_2 \cdot \text{H}_2\text{O}$, $\text{Ni}(\text{acam})_2\text{Br}_2 \cdot 2\text{H}_2\text{O}$, and $\text{Ni}(\text{acam})_2(\text{NO}_3)_2$.—These compounds were prepared by a similar method to that for $\text{Ni}(\text{acamb})_2\text{Cl}_2$. $\text{Ni}(\text{acam})_2\text{Cl}_2 \cdot \text{H}_2\text{O}$ [Found: C, 27.8 (27.8); H, 3.3 (3.25); N, 12.8% (12.9)], $\text{Ni}(\text{acam})_2\text{Br}_2 \cdot 2\text{H}_2\text{O}$ [Found: C, 22.6 (22.3); H, 3.3 (2.95); N, 10.3% (10.4)], $\text{Ni}(\text{acam})_2(\text{NO}_3)_2$ [Found: C, 25.4 (25.7); H, 2.70 (2.55); N, 17.6% (18.0)].

$\text{Cu}(\text{acamb})_2\text{Cl}_2$, acetone, $\text{Cu}(\text{acamb})\text{Br}$, $\text{Cu}(\text{acamb})_2(\text{ClO}_4)_2$, $\text{Cu}(\text{acam})_2\text{X}_2$ ($\text{X} = \text{Cl}$, Br , NO_3 , or ClO_4).—A minimum volume solution of the appropriate hydrated metal salt (5 mmol) in ethanol was added to an acetone solution of the ligand (10 mmol) and the mixture was stirred for $\frac{1}{2}$ h. The precipitates formed were filtered off and washed with acetone and light petroleum. $\text{Cu}(\text{acamb})_2\text{Cl}_2$, acetone [Found: C, 43.3 (43.7); H, 3.6 (3.85); N, 10.21% (9.7)], $\text{Cu}(\text{acamb})\text{Br}$ [Found: C, 32.1 (32.2); H, 2.45 (2.4); N, 8.4% (8.35)], $\text{Cu}(\text{acamb})_2(\text{ClO}_4)_2$ [Found: C, 33.2 (33.8); H, 2.55 (2.5); N, 8.7% (8.7)], $\text{Cu}(\text{acam})_2\text{Cl}_2$ [Found: C, 28.7 (28.7); H, 2.5 (2.85); N, 13.4% (13.4)], $\text{Cu}(\text{acam})_2\text{Br}_2$ [Found: C, 23.8 (23.6); H, 2.55 (2.35); N, 11.0% (11.0)], $\text{Cu}(\text{acam})_2(\text{NO}_3)_2$ [Found: C, 25.5 (25.5); H, 2.55 (2.55); N, 17.6% (17.8)], $\text{Cu}(\text{acam})_2(\text{ClO}_4)_2$ [Found: C, 22.3 (22.0); H, 2.35 (2.2); N, 10.2% (10.2)].

$\text{Cu}(\text{acamb})_2\text{Cl}_2$.—The acetone adduct, prepared as above, was heated at 100° for $\frac{1}{2}$ h [Found: C, 41.5 (41.6); H, 3.0 (3.1); N, 10.6% (10.8)].

$\text{Cu}(\text{acam})\text{Cl}_2$.—An acetone solution of acam (5 mmol) was added to a solution of the metal salt (50 mmol) in ethanol (minimum). The mixture was refluxed for $\frac{1}{2}$ h, cooled, and filtered. The product was washed with ethanol and light petroleum [Found: C, 21.7 (21.7); H, 2.25 (2.25); N, 10.0% (10.1)].

$\text{Cu}(\text{acam})\text{Br}_2$.—A solution of CuBr_2 (5 mmol) in ethanol was added to an acetone solution of the ligand and the suspension refluxed for 1 h. The product was filtered off and washed with ethanol and light petroleum [Found: C, 16.5 (16.4); H, 1.6 (1.35); N, 7.55% (7.66)].

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⁷ H. C. Freeman, *Adv. Protein Chem.*, 1968, 257.

⁸ E. g. H. A. O. Hill and K. A. Raspin, *J. Chem. Soc. (A)*, 1968, 3036; R. B. Martin, M. Chamberlin, and J. T. Edsall, *J. Amer. Chem. Soc.*, 1960, **82**, 495; M. F. Kim and A. E. Martell, *ibid.*, 1966, **89**, 914; W. L. Koltun, M. Fried, and F. R. N. Gurd, *ibid.*, 1960, **82**, 233.