Transmetalation and Adduct Formation as Routes to Heterobimetallic [(DABP)M–MCl_2] Complexes [DABP = the Dinegative Anion of (1,2-Dimethyl-1,2-ethanediylidene)bis(hydrazinecarbothiopiperidinamide)]

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Abstract

By employing the simple reaction of a mononuclear complex, [(DABP)Pd], and a homobinuclear complex [(DABP)Zn]$_2$, [DABP = the dinegative anion of (1,2-dimethyl-1,2-ethanediylidene)bis(hydrazinecarbothiopiperidinamide)] with an anhydrous metal(II) chloride in 1:1 and 1:2 molar ratios, respectively, we were able to prepare a number of heterobimetallic complexes [(DABP)M–M′Cl_2] (M,M′ = Pd,Ni; Pd,Cu; Pd,Zn; Ni,Zn or Cu,Zn). Reaction of [(DABP)Pd] with MCl_2 proceeds with simple adduct formation while reaction of [(DABP)Zn]$_2$ with MCl_2 takes place initially by substitution of zinc in [(DABP)Zn]$_2$ with M in MCl_2 (transmetalation) followed by adduct formation. The driving force for the transmetalation reaction is the high affinity of the DABP ligand to Pd, Cu and Ni ions relative to the Zn ion. The spectral properties (IR, UV–Vis, ^{1}H NMR and ESR) of these new heterobimetallic products are discussed.

Introduction

Thiosemicarbazones have been found to possess a broad spectrum of chemotherapeutic properties, among them antibacterial [1], antiviral [2], antimalarial [3] and antitumor [4] activities. In the case of, for instance, 3-ethoxy-2-oxobutyraldehyde bis(thiosemicarbazone) the presence of copper(II) or zinc(II) ion enhances the antineoplastic activity in both *in vitro* and *in vivo* systems [5]. Similarly, the presence of copper ion augments the antitubercular activity of *p*-acetamidebenzaldehyde thiosemicarbazone [6]. The ligand hexa-2,5-dione bis(4-phenylthiosemicarbazone) possesses *in vitro* activity against *E. coli*; the nickel chelate shows a four-fold increase in this activity [7]. In certain instances palladium has also been seen to increase the activity of thiosemicarbazone ligands [8].

The activity of these ligands can also be modified by derivatization [3]. Since small changes to the ligand have been shown, in some instances, to markedly alter antiviral or carcinostatic activity [8–12] of the metal chelates, many chelates of thiosemicarbazone derivatives have been studied as potential antitumor agents.

The recent development of interest in binuclear complexes owes much to their potential as models for that group of metalloproteins for which the biological function is known, or believed, to be associated with the occurrence of the metal centers in pairs [13]. These data provided the original basis of our interest in binuclear metal(II) complexes of thiosemicarbazone.

This paper discusses the synthesis and coordination chemistry of binuclear complexes prepared through adduct formation and for transmetalation [14, 15] of bis(thiosemicarbazone) complexes namely (1,2-dimethyl-1,2-ethanediylidene)bis(hydrazinecarbothiopiperidinamido)palladium(II) and zinc(II) with MCl_2 salts (M = Pd(II), Ni(II), Cu(II) and Zn(II)).

Experimental

Materials

The synthesis of [(DABP)Pd] and [(DABP)Zn]$_2$ complexes followed literature procedures [16]. Methods for purification of all reactants and solvents have been described previously [14, 16]. Anhydrous metal(II) chlorides were obtained from the hydrate (Aldrich) by heating overnight at 130 °C under vacuum.

Preparation of [(DABP)Pd–MCl_2] Complexes, (M = Pd(II), Ni(II), Cu(II) or Zn(II))

A clear green solution of [(DABP)Pd] complex (5 mmol) in methylene chloride (30 ml) was treated with a solution of the appropriate metal(II) chloride (5 mmol) in methanol (20 ml). The reaction mixture was stirred vigorously at room temperature for 12 h,

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after which the product solution was filtered into hexane (100 ml). The precipitated complex was filtered off and dried in a vacuum desiccator over P_4O_{10}.

Preparation of [(DABP)M–ZnCl$_2$] Complexes (M = Pd(II), Ni(II) or Cu(II))

The title complexes were prepared by the same method as above except 2.5 mmol of the dimeric $[(DABP)Zn]_2$ complex were used instead of 5 mmol of the monomeric [(DABP)Pd] complex.

Analytical Procedures

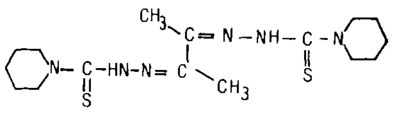
Elemental analyses of nickel, copper, zinc and palladium were performed by Dr T. R. Gilbert with an inductively coupled plasma spectrometer at Northeastern University, Boston, MA. Nitrogen and sulphur analyses were made by Galbraith Laboratories, Knoxville, TN.

Physical Measurements

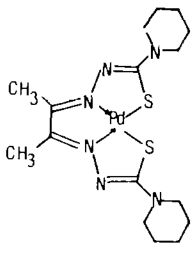
Solution electronic spectral measurements were made with a Perkin-Elmer 552 spectrophotometer in matched quartz cells at room temperature. The solvent nitromethane was used as reference. Infrared spectra (KBr disks) were obtained with a Pye Unicam SP 2000 spectrophotometer calibrated with the 906.5 or 3026.3 cm^{-1} absorption of polystyrene. ^{1}H NMR spectra were recorded with a Varian T60A spectrometer at 37 °C using TMS ($\delta = 0$) as internal standard. Merck DMSO-d^6 was used as solvent. ESR spectra were recorded at 100 KHz modulation and 10 G modulation amplitude on a Varian E-9 spectrometer. 10 mW incident power was used and resonance conditions were at *c.* 9.75 GHz (X-band) at room temperature and *c.* 9.10 GHz at 16 K. Spectra at low temperature was obtained with an Air Products LTD-3-110 Heli-Tran liquid helium transfer refrigerator. The field was calibrated with a powder sample of DPPH ($g = 2.0037$) [17].

Results and Discussion

The reaction of the *trans*-(1,2-dimethyl-1,2-ethylidene)bis(hydrazinecarbothiopiperidinamide) ligand (I) [18], with metal(II) salts in a 1:1 ligand-to-metal molar ratio gave the neutral metal(II) chelates in which the dinegative anion of **I** present in the *cis* form behaves as a dibasic tetradentate ligand chelated to the central metal ion via the two imino nitrogen and the two deprotonated thiol sulphur. Although, the palladium complex of **I** is the monomeric square planar complex **II**, the corresponding zinc complex, **III**, exists as a dimer [16, 18] to obviate an unfavourable square planar zinc coordination geometry [14, 19].



I



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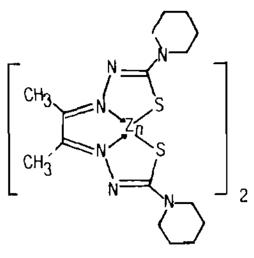

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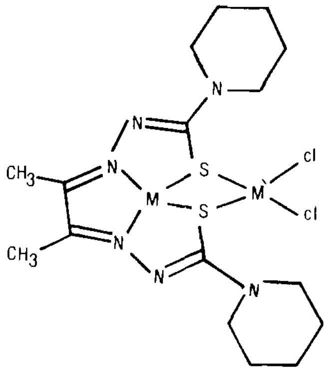

IV

The binuclear metal(II) complexes, **IV**, (M,M′ = Pd,Ni; Pd,Cu; Pd,Zn or Pd,Pd) were prepared by adding an alcoholic solution of anhydrous metal(II) chloride to the methylene chloride solution of **II** at room temperature. The nucleophilicity of the thiolate sulphur atoms in **II** is responsible for this simple adduct formation.

Bearing in mind the fact that the thermodynamic stability order of MN_2S_2 complexes [20] is $PdN_2S_2 > CuN_2S_2 > NiN_2S_2 > ZnN_2S_2$ and our recently discovered transmetalation phenomenon [14, 15], we were able to prepare the heterobimetallic complexes **IV** (M,M′ = Pd,Zn; Ni,Zn or Cu,Zn), by transmetalating the zinc ion in **III** with the palladium, copper and nickel ions in their metal chlorides, then adduct formation takes place. The complexes that we were able to isolate in reasonably pure form are stable indefinitely at 25 °C and are given in Table 1.

The IR spectra of complexes **IV** are consistent with dimeric molecules in which the organic ligand is acting as a dianionic tetradentate to the endogenous metal ion and bridging the exogenous metal ion via its two thiolato sulphur atoms. This is evident from the disappearance of ν(N–H) and the negative shift in ν(C=N) bands, as compared to the spectrum of the

TABLE 1. Analytical data for [(DABP)M–M′Cl_2] complexes[a]

Compound	Colour	N (%)	S (%)	Pd (%)	Ni (%)	Cu (%)	Zn (%)
[(DABP)Pd–PdCl_2]	red	12.66 (12.92)	9.73 (9.85)	32.11 (32.74)			
[(DABP)Pd–NiCl_2]	bright red	13.62 (13.94)	10.53 (10.62)	18.04 (17.66)	9.56 (9.79)		
[(DABP)Pd–CuCl_2]	brown	13.71 (13.84)	10.13 (10.54)	17.23 (17.53)		10.37 (10.46)	
[(DABP)Pd–ZnCl_2]	greenish brown	13.55 (13.79)	10.28 (10.46)	17.08 (17.47)			10.51 (10.74)
[(DABP)Ni–ZnCl_2]	brown	14.76 (14.97)	11.13 (11.41)		10.44 (10.52)		11.34 (11.66)
[(DABP)Cu–ZnCl_2]	reddish brown	14.39 (14.84)	10.98 (11.30)			11.05 (11.23)	11.17 (11.55)

[a]Calculated values are given in parentheses.

parent ligand **I** and the large shift ($\Delta\nu = 40$ cm^{-1}) in ν(C–S) as compared to the IR spectrum of the monomeric palladium complex **II**. The medium intensity bands centered at *c.* 280 and 365 cm^{-1}, Table 2, proposed for ν(M–S) and ν(M–Cl), respectively, is another evidence for the bridging structure **IV**.

The measured chemical shifts, δ, of the methyl and the piperidyl hydrogen atoms in the organic ligand, **I**, its monomeric palladium, **II**, and dimeric zinc **III** reactants, as well as, those in their diamagnetic binuclear metal(II) complexes **IV** are listed in Table 2. The ^{1}H NMR spectrum of the ligand **I** shows a downfield signal at 8.95 ppm due to the N-H proton, which disappears either upon deuteration or upon complex formation. It also shows a broad signal at 3.92 ppm due to α-CH_2 protons of the piperidyl moiety, while the β- and γ-CH_2 protons appear in a single broad peak at 1.66 ppm. The chemical shift of α- and β-, γ-CH_2 protons in the binuclear metal (II) complexes are more or less the same as for the parent ligand and the reactants **II** and **III**.

The sharp signal that appeared at *c.* 1.80–2.15 ppm for **IV** complexes (Table 2) can be assigned to the two methyl groups of the diacetyl residue indicating that they are magnetically equivalent as in the case of the free ligand.

The electronic spectra of the prepared complexes are summarized in Table 2. The main contribution to these spectra in the near-UV region is due to intraligand transitions within the conjugated N_2S_2 ligand and it is exemplified here by the spectrum of the zinc complex **III** [16].

Since the d^{10}Zn(II) ion is spectroscopically inactive over the visible region, the electronic spectral features of these binuclear metal ion units containing Zn(II), **III** (M,M′ = Pd,Zn; Ni,Zn; Cu,Zn) are essentially those of the MN_2S_2 portion. The weak coupling of the M(II) and Zn(II) ions via the thiolato sulphur bridge is not expected to appreciably perturb the electronic spectroscopic features of the M(II) site. Besides the ligand absorptions, additional contributions due to ligand-to-metal charge transfer (LMCT) transitions from filled orbitals on the donor groups to the metal(II) d vacancy are expected to occur down to 500 nm.

The complexes Pd,Zn; Ni,Zn and Cu,Zn exhibit an absorption of somewhat broadened d–d bands due to their relatively low intensity (Table 2) which is typical for square planar complexes [21]. The d–d transition of complexes **IV** (M,M′ = Pd,Ni and Pd,Cu) are quite intense, suggesting that the geometry at the MS_2Cl_2 position could be distorted from square planar [21].

The X-band ESR spectra of copper(II) containing complexes, **IV**, (M,M′ = Pd,Cu and Cu,Zn) were measured in nitromethane solution at ambient and liquid helium temperature (16 K). The results for room temperature ESR spectra ($g_0 = 2.1$, $A_0 = 43.7 \times 10^{-4}$ cm^{-1} for the Pd,Cu complex; $g_0 = 2.08$, $A_0 = 42.2 \times 10^{-4}$ cm^{-1} for the Cu,Zn complex) are typical of isotropic spectra observed for mononuclear Cu(II) complexes [22], suggesting that there is no magnetic interaction between the Cu(II) center in **IV** and each of the diamagnetic Pd(II) and Zn(II) centres.

The frozen nitromethane solution spectrum of **IV** (M,M′ = Cu,Zn) is of the axial type ($g_\parallel = 2.16$, $A_\parallel = 174 \times 10^{-4}$ cm^{-1}, $g_\perp = 2.036$) with a partially resolved structure (≈ 13 G) in the perpendicular component of the signal, probably due to superhyperfine coupling with the nitrogen donor of the ligand, and also indicative of a $d_{x^2-y^2}$ ground state with square planar stereochemistry ($g_\parallel > g_\perp$, large $A_\parallel$ value).

The frozen solution spectrum of **IV** (M,M′ = Pd, Cu) is also of the axial type and indicates a $d_{x^2-y^2}$

TABLE 2. Electronic[a], infrared[b] and ^{1}H NMR[c] spectral data for [(DABP)M–M′

Compounds	Band maxima (nm) (log ε (mol^{-1} cm^{-1}))					IR spectral bands (cm^{-1})					δ (ppm)		
						ν(C=N)	ν(M–N)	ν(M–S)	ν(M–S)	ν(M–Cl)	–CH$_3$	α-CH$_2$	β,γ-CH$_2$
[(DABP)Pd–PdCl$_2$]	380 (4.66)	420 (4.35)	435(sh) (4.23)	570 (3.95)		1590	410	265	260	340	1.94	4.10	1.53
[(DABP)Pd–NiCl$_2$]	400 (4.73)	425(sh) (4.53)	435 (4.64)	610 (3.88)	705 (3.72)	1590	410	270	295	375	1.92	4.09	1.53
[(DABP)Pd–CuCl$_2$]	395 (4.80)	440(sh) (4.37)	490 (4.62)	550(sh) (3.97)	620 (3.10)	1590	405	270	290	370			
[(DABP)Pd–ZnCl$_2$]	420 (4.12)	435(sh) (4.41)	605 (3.52)	630(sh) (3.40)		1585	410	270	275	365	1.91	4.05	1.53
[(DABP)Ni–ZnCl$_2$]	440 (4.73)	465 (4.37)	625(sh) (3.20)	690 (2.83)		1595	420	310	270	365	1.85	3.90	1.49
[(DABP)Cu–ZnCl$_2$]	370 (4.25)	495 (4.03)	545(sh) (2.36)			1590	490	280	270	365			
H$_2$DABP[d]											2.00	3.86	1.63
[(DABP)Pd][d]	330 (3.95)	400(sh)	415 (4.20)	590 (3.43)	610(sh)						1.90	3.95	1.51
[(DABP)Zn]$_2$[d]	270 (3.98)	320 (4.04)	450 (4.14)	465(sh)							2.16	3.91	1.40

[a] Electronic spectra were examined in nitromethane as solvent. [b] Infrared spectra were examined as KBr discs. [c] ^{1}H NMR spectra were examined in DMSO-d^6. [d] Ref. 16.

ground state ($g_{\parallel} = 2.14$, $A_{\parallel} = 145 \times 10^4$ cm^{-1}, $g_{\perp} = 2.06$). The $A_{\parallel}$ value is markedly lower than for the other Cu,Zn complex indicating that significant distortion towards a pseudo-tetrahedral arrangement occurs in the present case (CuS_2Cl_2 chromophore). The rather low $g_{\parallel}$ values are typical for Cu(II) chromophores containing sulphur ligands [23–26].

References

1 A. S. Dobek. D. L. Klayman, E. J. Dickson, Jr., J. P. Scovill and E. C. Tramont, *Antimicrob. Agents Chemother., 18* (1980) 27.

2 (a) J. C. Logan, M. P. Fox, J. M. Morgan, A. M. Makohon and C. J. Ptau, *J. Gen. Virol., 28* (1975) 271, and refs. therein; (b) C. Shipman, Jr., S. H. Smith, J. C. Drach and D. L. Klayman, *Antimicrob. Agents Chemother., 19* (1981) 682.

3 J. P. Scovill, D. L. Klayman, C. Lambros, G. E. Childs and J. D. Notsch, *J. Med. Chem., 27* (1984) 87, and refs. therein.

4 J. P. Scovill, D. L. Klayman and C. F. Franchiro, *J. Med. Chem., 25* (1982) 1261.

5 (a) A. C. Sartorelli and W. A. Creasey, *Ann. Rev. Pharmacol., 2* (1969) 51; (b) J. A. Gim and H. G. Petering, *Cancer Res., 27* (1967) 1278.

6 K. Leibermeister, *Z. Naturforsch., Teil B, 15* (1950) 79.

7 L. Heilmeyer, *Klin. Wochenschr., 28* (1950) 254; *Chem. Abstr., 71* (1969) 42301.

8 M. Das and S. E. Livingstone, *Inorg. Chim. Acta, 19* (1976) 5.

9 M. A. Ali and S. E. Livingstone, *Coord. Chem. Rev, 13* (1974) 10.

10 S. E. Livingstone and A. E. Mihkelson, *Inorg. Chem., 9* (1970) 2545.

11 M. J. Cleare, *Coord. Chem. Rev., 12* (1974) 349.

12 D. R. Williams, *Chem. Rev., 72* (1972) 203.

13 S. M. Nelson, in K. D. Karlin and J. Zubieta (eds.), *Copper Coordination Chemistry Biochemical and Inorganic Perspectives,* Adenine Press, New York, 1982, p. 331.

14 G. Davies, A. El-Toukhy, K. D. Onan and M. Veidis, *Inorg. Chim. Acta, 84* (1984) 41.

15 A. El-Toukhy, G. Z. Cai, G. Davies, T. R. Gilbert, K. D. Onan and M. Veidis, *J. Am. Chem. Soc., 106* (1984) 4596.

16 M. F. Iskander, L. El-Sayed, A. El-Toukhy and A. K. Chehata, *Inorg. Chim. Acta, 123* (1986) 19.

17 J. E. Wertz and J. R. Bolton, *Electron Spin Resonance,* McGraw Hill, New York, 1972.

18 K. D. Onan, A. El-Toukhy and W. Shomaly, to be published.

19 A. El-Toukhy, M. El-Essawi, M. Tawfik, L. El-Sayed and M. F. Iskander, *Transition Met. Chem., 8* (1983) 116.

20 G. Davies, M. A. El-Sayed, A. El-Toukhy, M. Henary, T. S. Kasem and C. A. Martin, *Inorg. Chem., 25* (1986) 3904.

21 A. B. P. Lever, *Inorganic Electronic Spectroscopy,* Elsevier, Amsterdam, 1968.

22 M. S. Mashuta, R. M. Buchanan and W. Pierce, *Inorg. Chim. Acta, 158* (1989) 227.

23 A. W. Addison, T. N. Rao and E. Sinn, *Inorg. Chem., 23* (1984) 1457.

24 A. W. Addison and E. Sinn, *Inorg. Chem., 22* (1983) 1225.

25 L. Casella, M. Gullotti and R. Vigano, *Inorg. Chim. Acta, 124* (1986) 121.

26 U. Sakaguchi and A. W. Addison, *J. Chem. Soc., Dalton Trans.,* (1979) 600.