

Table I. Extent of Racemization during Peptide Bond Formation<sup>a</sup>

No.	Coupling reagent	Additional component	Solvent	Tertiary amine	Reaction time, hr	Reaction temp, °C	Yield of tripeptide I, %	Extent of racemization
1 <sup>b</sup>	Isobutyl chloroformate		THF	TEA	15	25	87	9.5
2 <sup>b</sup>			THF	NMM	15	25	91	2.4
3 <sup>c</sup>		HOSu	THF	TEA	2	25	55 <sup>d</sup>	1.1
4 <sup>c</sup>		HOSu	THF	NMM	2	25	63 <sup>d</sup>	0.2
5	DCC		THF	TEA	48	0	73	22
6			THF	NMM	48	0	77	21
7 <sup>e</sup>		HOSu	THF	TEA	48	0	98	0.0
8 <sup>c</sup>	NEPIS		CH <sub>3</sub> CN	TEA	24	25	95	1.8
9			CH <sub>3</sub> CN	NMM	24	25	72	1.7
10 <sup>c</sup>	EEDQ		THF	TEA	7	25	97	0.2
11			THF	NMM	7	25	91	0.2

<sup>a</sup> All components (II, IV, coupling reagent, HOSu, and tertiary amine) in the coupling were of equivalent weight. NMM, N-methylmorpholine. <sup>b</sup> The procedure following that in the literature<sup>9</sup> was noted in detail in this text. <sup>c</sup> The procedure was similar to that described in the literatures: MA,<sup>10</sup> NEPIS,<sup>14</sup> and EEDQ.<sup>15</sup> <sup>d</sup> The lower yields compared with that using the MA method without HOSu may be due to the extraction operation with isopropyl ether<sup>10</sup> of the reaction mixture of Z-Gly-L-Ala-OH, isobutyl chloroformate, and HOSu. <sup>e</sup> The procedure reported<sup>11</sup> was slightly modified; the components were of equivalent weight and the temperature was 0° during the entire reaction.

a load of up to 6  $\mu$ mol. The result agreed with the fact that the azide procedure has been considered to be safe to avoid racemization.<sup>7</sup>

We have now employed this procedure to examine the influence of racemization of several coupling reagents. A typical procedure was as follows. The reaction conditions (temperatures and reaction times) were similar, as described in the literature.<sup>8</sup> To Z-Gly-L-Ala-OH<sup>9</sup> (IV; 1 mmol) (mp 133°) was added isobutyl chloroformate (1 mmol). After the solution was left standing at -15° for 12 min, II (1 mmol) in THF (5 ml) and TEA (1 mmol) was added, and the mixture was left at 25° for 15 hr. After evaporation, ethyl acetate was added to the residue. It was washed with dilute HCl and then NaHCO<sub>3</sub> solution, dried with Na<sub>2</sub>SO<sub>4</sub>, and evaporated; yield of crude solid (V), 474 mg. Part (47.4 mg) of V was hydrogenated in 90% acetic acid, and the filtrate was evaporated. The residue was dissolved in 0.2 M citrate buffer at pH 4.25 (10 ml), and part (0.7 ml) of the solution was submitted to the analyzer; the yield of I (L,L plus D,L) from IV was calculated as 87%, and the extent of racemization,<sup>3</sup> which is defined as  $\{100[I(D,L)]\} / \{[I(L,L)] + [I(D,L)]\}$ , was calculated as 9.5.

The experiments are summarized in Table I. The results shown confirm the observation of Anderson, *et al.*,<sup>8</sup> on the role of tertiary bases in the racemization on the mixed anhydride (MA) method. The results also indicate that the addition of N-hydroxysuccinimide (HOSu) on the MA<sup>10</sup> and dicyclohexylcarbodiimide (DCC) method<sup>11,12</sup> decreased the racemization remarkably, and the use of N-ethyl-5-phenylisoxazolium-3'-sulfonate (NEPIS)<sup>13,14</sup> and N-ethoxycarbonyl-2-eth-

oxy-1,2-dihydroquinoline (EEDQ)<sup>15</sup> caused only slight racemization. An easy and straightforward procedure such as the racemization test described in this paper is useful to detect possible racemization when a new coupling method will be developed in future.

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(15) B. Belleau and G. Malek, *J. Am. Chem. Soc.*, **90**, 1651 (1968). We thank Dr. Belleau for the generous gift of EEDQ.

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### Chemical Information from Forbidden Hyperfine Lines in Electron Paramagnetic Resonance. Copper Complexes

Sir:

The allowed transitions ( $\Delta M_S = \pm 1$ ,  $\Delta M_I = 0$ ) in electron paramagnetic resonance yield useful information on spin density distribution, and this has been much used in chemical studies of bonding. In contrast, although the intensities and positions of the so-called forbidden transitions (particularly those where  $\Delta M_S = \pm 1$ , but  $\Delta M_I = 0$ ) usually carry information about the over-all charge distribution (namely, the nuclear quadrupole coupling constants and thus the electric field gradient at the magnetic nucleus), these transitions have not been much exploited by chemists.

The forbidden hyperfine lines are made allowed and are shifted and split by a combination of nuclear Zeeman interaction and nuclear electric quadrupole coupling with the molecular electric field gradient.<sup>1</sup> In general, the nuclear gyromagnetic ratio is well known, and an analysis of the forbidden lines gives the nuclear quadrupole coupling constant as well as some information as to the relative signs of the parameters in the spin Hamiltonian.<sup>1</sup> Lyons and Kedzie<sup>2</sup> recently demonstrated for the case of Mn<sup>2+</sup> in an axial site that the complete diagonalization of the spin Hamiltonian is

(1) B. Bleaney, *Phil. Mag.*, **42**, 441 (1951).

(2) D. H. Lyons and R. W. Kedzie, *Phys. Rev.*, **145**, 148 (1966).

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(8) G. W. Anderson, J. E. Zimmerman, and F. M. Callahan, *J. Am. Chem. Soc.*, **89**, 5012 (1967).

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(11) F. Weygand, D. Hoffmann, and E. Wunsch, *Z. Naturforsch.*, **21b**, 426 (1966).

(12) J. E. Zimmerman and G. W. Anderson, *J. Am. Chem. Soc.*, **89**, 7151 (1967).

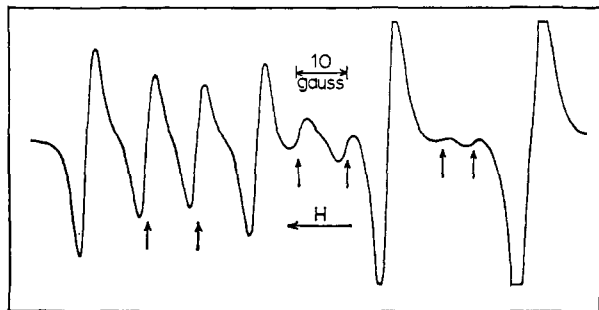


Figure 1. The Q-band spectrum of  $\text{Cu}(\text{acac})_2$  at  $\theta = 87^\circ$ . Forbidden lines are indicated by arrows. The medium-field pair is made allowed by the nuclear Zeeman effect; the high-field pair, by cooperative nuclear Zeeman and quadrupole coupling effects; the low-field pair, by opposing nuclear Zeeman and quadrupole coupling effects.

necessary, and that the conventional perturbation treatment fails for large angles ( $\theta$ ) between the magnetic field and the symmetry axis. This has been our experience with copper and vanadyl systems.

An accurate analysis can be made from the epr spectra of a magnetically dilute crystal for the entire range of  $\theta$ . Here we report these data and their analyses for bis(2,4-pentanedionato)copper [ $\text{Cu}(\text{acac})_2$ ,  $\text{Cu}(\text{CH}_3\text{COCHCOCH}_3)_2$ ], bis(1-phenyl-1,3-butanediolato)copper [ $\text{Cu}(\text{bzac})_2$ ,  $\text{Cu}(\text{C}_6\text{H}_5\text{COCHCOCH}_3)_2$ ], and bis(diethylthiocarbamato)copper [ $\text{Cu}(\text{dte})_2$ ,  $\text{Cu}[(\text{C}_2\text{H}_5)_2\text{NCS}_2]_2$ ].

Maki and McGarvey<sup>3</sup> originally determined parameters for  $\text{Cu}(\text{acac})_2$  doped into  $\text{Pd}(\text{acac})_2$ . However, probably as a result of improved instrumentation and a more complete analysis, we obtain a quadrupole coupling constant,  $Q'$ , drastically different from their reported value of  $7 \times 10^{-4} \text{ cm}^{-1}$ . For  $^{63}\text{Cu}^{2+}$  doped into  $\text{Pd}(\text{acac})_2$ , we find three pairs of lines for  $\Delta M_I = \pm 1$  over a wide range of angles and some lines for  $\Delta M_I = \pm 2$  near the coordination plane. Around  $\theta = 86^\circ$ , some "forbidden" lines are 40% as intense as a normal allowed one; see Figure 1.

By computer diagonalization of the  $8 \times 8$  spin-Hamiltonian matrix, we were able to fit all spacing and intensity data by the usual spin-Hamiltonian.

$$\mathcal{H} = \beta[g_{\parallel}H_zS_z + g_{\perp}(H_xS_x + H_yS_y)] + AS_zI_z + B(S_xI_x + S_yI_y) + Q'[I_z^2 - \frac{1}{3}I(I+1)] - g_I\beta_N H \cdot I$$

We used the reported values<sup>3,4</sup> for all parameters except  $Q'$ , which was varied to produce the best fit to the data.  $Q' = (3.4 \pm 0.2) \times 10^{-4} \text{ cm}^{-1}$  explains all the data from both Q-band and X-band spectra. (Note that for  $I = 3/2$ ,  $4Q'$  is the usual parameter  $eqQ$ .)

The spacing between each pair in the Q-band spectra as a function of  $\theta$  is shown in Figure 2. The nuclear quadrupole interaction affects the "medium field" pair very slightly. Therefore, the good fit between experimental and calculated values for this particular pair is evidence that the anisotropic part of the nuclear Zeeman term is very small.<sup>5</sup> The nuclear quadrupole interaction either increases or decreases the spacing and intensity of the other two pairs, bringing about

(3) A. H. Maki and B. R. McGarvey, *J. Chem. Phys.*, **29**, 31 (1958).

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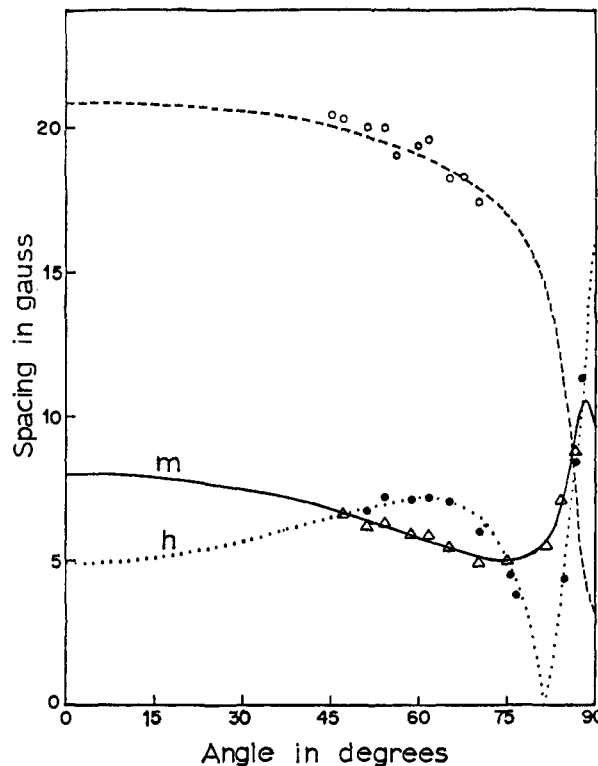


Figure 2. Angular dependence of the spacing between each pair of forbidden lines ( $\Delta M_I = \pm 1$ ) in the Q-band spectra of  $\text{Cu}(\text{acac})_2$ . The curves are calculated values using  $Q' = 3.4 \times 10^{-4} \text{ cm}^{-1}$  and the symbols are experimental values. The letters l, m, and h represent low-field, medium-field, and high-field pairs, respectively.

asymmetry of the spectrum. From the asymmetry of the spectrum the sign of  $(Kg_I)$ , where  $K$  is the hyperfine splitting, is found to be different from that of  $Q'$ . Since the sign of  $K$  is negative<sup>6,8</sup> and that of  $g_I$  is positive,  $Q'$  should have a positive sign. This result agrees with the previous work.<sup>3</sup>

Using the same method, we obtain  $Q' = (2.6 \pm 0.2) \times 10^{-4} \text{ cm}^{-1}$  for  $^{63}\text{Cu}^{2+}$  in  $\text{Pd}(\text{bzac})_2$  and  $Q' = (0.7 \pm 0.1) \times 10^{-4} \text{ cm}^{-1}$  for  $^{63}\text{Cu}^{2+}$  in  $\text{Ni}(\text{dte})_2$ , for which  $g_{\parallel}$ ,  $g_{\perp}$ ,  $A$ , and  $B$  were reported recently.<sup>7,8</sup>

It is interesting to compare these values with  $Q' = (11 \pm 1) \times 10^{-4} \text{ cm}^{-1}$  for  $\text{Cu}^{2+}$  in  $\text{Zn}(\text{NH}_4)_2(\text{SO}_4)_2 \cdot 6\text{H}_2\text{O}$ .<sup>9</sup> According to our calculation an electron hole localized in the  $d_{x^2-y^2}$  orbital of a free  $\text{Cu}^{2+}$  ion will give  $Q'_{\text{calcd}} \approx 16 \times 10^{-4} \text{ cm}^{-1}$ , close to but larger than the experimental value for  $\text{Cu}^{2+}$  in the Tutton salt. A smaller  $Q'$  value is expected in a covalent than in an ionic cupric complex, the quadrupole coupling constant being a direct measure of the electric field gradient in the direction of the symmetry axis. Also, the smaller  $Q'$  of the complex having sulfur ligands compared with those having oxygen ligands is consistent with higher covalency in the in-plane metal-sulfur  $\sigma$  bonds than

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(8) M. J. Weeks and J. P. Fackler, *Inorg. Chem.*, **7**, 2548 (1968), reported the allowed lines in single crystals but did not observe the forbidden lines which we have obtained and analyzed.

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in the metal-oxygen  $\sigma$  bonds.<sup>10</sup> Although we can account for a considerable reduction in  $Q'$  by taking covalency into account, the experimental values are still much lower than the smallest ones we compute, a fact which suggests that the charge distribution near the copper nucleus in a covalent complex is much closer to spherical than the usual simple crystal field or molecular orbital picture would lead us to expect.

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### Trigonal Prismatic Cobalt(II) in a Polynuclear Complex

Sir:

There are several reports<sup>1-4</sup> in the literature of polynuclear cations containing cobalt and 2-aminoethanol; a trinuclear cation was formulated<sup>1</sup> as a cobalt(II) complex, but has more recently been reported<sup>4</sup> to contain a central cobalt(II) ion coordinated to two tris(2-aminoethoxido)cobalt(III) complexes. A structure with octahedral coordination of the central cobalt(II) through face-sharing of oxygens with the cobalt(III) octahedra was proposed.<sup>4</sup> Analogous trinuclear complexes,  $[M(\text{Co}(\text{chelate})_3)_2]^{m+}$ , with 2-aminoethanethiolate as the chelate ligand and with cobalt(III), zinc(II), and nickel(II) as the central metal, M, have been studied;<sup>5,6</sup> the same structure has been assumed for these complexes.

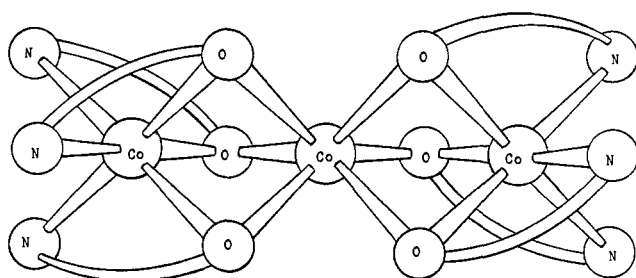


Figure 1.

We prepared the acetate salt of the trinuclear cation,  $[\text{Co}(\text{Co}(\text{OCH}_2\text{CH}_2\text{NH}_2)_3)_2]^{2+}$ ; unlike the previously prepared salts, which were isolated as unstable hydrates, the acetate crystallized from methanol as the anhydrous salt. The compound crystallized as dark red crystals which were roughly octahedral in shape. Precession photographs (Zr-filtered Mo radiation) indicated that the crystals were monoclinic with  $a = 14.98$  (3) Å,  $b = 8.61$  (2) Å,  $c = 11.28$  (3) Å, and

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(3) H. Brintzinger and B. Hesse, *ibid.*, **248**, 345 (1941).

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(5) D. H. Busch and D. C. Jicha, *Inorg. Chem.*, **1**, 884 (1962).

(6) G. R. Brubaker and B. E. Douglas, *ibid.*, **6**, 1562 (1967).

$\beta = 116.7^\circ$  (1);<sup>7</sup> the density calculated for  $Z = 2$ , 1.68 g/cm<sup>3</sup>, agreed well with the experimental value, 1.66 g/cm<sup>3</sup>, obtained by the flotation method. Systematic extinction of the  $hkl$  reflections for  $h + k = 2n + 1$  was consistent with space groups C2 and C2/m. Although both space groups have twofold positions, the  $2/m$  symmetry of the twofold positions of C2/m was not consistent with any reasonable structure for the trimer; C2 was, thus, assumed to be the correct space group and the subsequent refinement was verified this choice.

The same crystal as used for the space group determination was used to collect intensity data on a Picker four-circle automated diffractometer; a total of 830 unique reflections above background were collected in the  $2\theta$  scan mode; unfiltered Mo radiation was used.

Since the origin in the  $y$  direction of space group C2 is not fixed by symmetry, the cobalt of the twofold set (2a) was placed at the origin of the unit cell; from a Patterson synthesis, coordinates for the cobalt of the fourfold general set (4c) were obtained. Successive structure factor and Fourier calculations were used to locate the remaining nonhydrogen atoms of the structure; the oxygen atoms of the acetate appear to be disordered. The present conventional  $R$  value of 0.11 was obtained with all reflections weighted at unity, isotropic temperature factors, and no correction for the  $f''$  component of anomalous dispersion; further refinement is in progress.

The main features of the structure are, however, apparent from the present stage of refinement. As suggested by previous workers,<sup>4</sup> the trimer consists of two tris(2-aminoethoxido)cobalt(III) complexes, each sharing three oxygens with a central cobalt(II); the twofold site symmetry relates the two tris chelates and requires that the two be of the same optical configuration.

The coordination of the central cobalt(II), Figure 1, is unusual; the oxygens are arranged at the corners of an almost perfect trigonal prism with Co-O distances of 2.03 (2), 2.03 (2), and 2.05 (2) Å. The triangular faces are almost perfect equilateral triangles with O-O distances of 2.59 (3), 2.61 (3), and 2.64 (3) Å and angles of 61 (1), 59 (1), and 60° (1); between the triangular faces there are two O-O distances of 2.75 (3) and one of 2.72 (3) Å. The best least-squares plane for the group of four oxygens comprising each rectangular face of the trigonal prism was calculated, the distance of each atom from the plane was calculated, and the dihedral angle between each pair of adjacent faces was calculated; no atom was more than 0.05 Å out of the plane of its face, and the dihedral angles between faces were 117.9° (1.3) for one pair and 120.9° (7) for the other two pairs.

Construction of models of the structure found and the postulated structure with octahedral coordination about cobalt(II) indicates that the hydrogen atoms of the methylene groups adjacent to the oxygens may be responsible for the unusual coordination; hydrogens of the two tris chelates appear to approach to less than the sum of their van der Waals radii in the octahedral complex but are less crowded in the trigonal-prismatic complex. On the basis of models, octahedral coordina-

(7) Figures in parentheses here and elsewhere in this paper represent the estimated error in the least significant digit.