Table V. Relative Gd^{III}-Induced Longitudinal ^{13}C Relaxation Rate Enhancements (s^{-1}) in EGDS at pH 7 and 25 °C

nuclei	meso-EGDS	rac-EGDS	nuclei	meso-EGDS	rac-EGDS
C(1), C(1′)	1.00[a]	1.00[a]	C(4), C(4′)	0.82	0.76
C(2), C(2′)	0.46	0.59	C(5), C(5′)	0.40	0.55
C(3), C(3′)	0.25	0.54			

[a] The absolute relaxation rate enhancements are 10.7×10^3 and 9.9×10^3 s^{-1} for *meso*-EGDS and *rac*-EGDS, respectively.

The Dy^{III}-induced ^{17}O shifts (see Table II) show that the Dy^{III}–EGDS complex contains two water ligands in the first coordination sphere. So if it is assumed that the coordination number is 8 or 9, then this suggests a hexadentate coordination of EGDS.

The Gd^{III}-induced RRE's are very similar to those observed for EGMS.[52] It can be inferred that EGDS is bound to Gd^{III} analogously to EGMS, thus in a hexadentate fashion with the carboxylates and the ether oxygens as donor sites. The small differences in the RRE's between the two diastereomers can be ascribed to small differences in the conformation of the bound ligands. The largest differences occur in C(3) and C(3′). With the use of eq 5 it can be calculated that the differences observed for these nuclei correspond with only a 13% difference in the Gd^{III}–C distance. These nuclei are part of six-membered chelate rings, and an inspection of molecular models shows that these rings are rather flexible.

Conclusions

Multinuclear NMR techniques have been proven to be very valuable for the establishment of the structures of species occurring in the reaction mixture of the lanthanide-catalyzed O-alkylation of EG with MAL. Ln^{III} cations have a preference for the coordination of EG over that of water, which is in agreement with the observation made previously[2] that water does not interfere in the O-alkylation reaction as long as it is not present in a large amount. The Cl^- ion is not in the first coordination sphere of the Ln^{III} cation, whereas MAL is able to compete with EG for coordination. The products of the first and the second O-alkylation steps (EGMS and EGDS, respectively) are strong chelators for the Ln^{III} ions. Therefore, the water addition is not an important side reaction in the second O-alkylation step (EGMS → EGDS), and product inhibition plays a role in the O-alkylation reactions.

Deprotonation of the Ln^{III}-coordinated hydroxyl groups of EG and EGMS could not be observed, in contrast to that of the previously studied glycolate, for which the pK_a was determined to be about 8.[10] Mixed-ligand complexes with deprotonated hydroxyl groups are supposed to be the key intermediates in the O-alkylation of hydroxy compounds with MAL. The observations on EG and EGMS, suggesting a relatively high pK_a of the Ln^{III}-coordinated hydroxyl group of these compounds, are therefore in agreement with the relatively low reaction rates in the O-alkylation reaction of EG with MAL in comparison with the corresponding reaction with glycolate.[10,24]

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(52) The assignments of the peaks in the ^{13}C NMR spectrum were made previously[2] with the use of a chiral shift reagent, except for the peaks of the carboxylate groups, which almost coincided. The relative relaxation rate enhancements of the carboxylate carbons were 1.0 and 0.8, which is very similar to the values observed for the related nuclei in EGMS. On the basis of the comparison of the magnitudes of the relative relaxation rates the signal with a RRE of 1.0 is assigned to C(1) and C(1′).

Contribution from the Nuclear Research Centre Negev, Beer-Sheva, Israel,
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Oxidation of Copper(II) Bis(glycinate) by Methyl Free Radicals in Aqueous Solutions. A Pulse-Radiolysis Study

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The reaction of $^{\bullet}CH_3$ free radicals with $Cu^{II}(NH_2CH_2CO_2^-)_2$ in aqueous solutions was studied. The formation of the unstable intermediate $(NH_2CH_2CO_2^-)_2Cu^{III}–CH_3(aq)$ in this reaction was observed. This intermediate decomposes into $Cu^{III}(NH_2CH_2CO_2^-)_2^+(aq) + CH_4$. The formation of $Cu^{III}(NH_2CH_2CO_2^-)_2^+(aq)$ is not observed, as this complex is short-lived under these conditions and decomposes via ligand oxidation. The $^{\bullet}CH_3$ free radicals react with the transient complex $(NH_2CH_2CO_2^-)_2Cu^{III}–CH_3(aq)$ to form ethane and $Cu^{II}(NH_2CH_2CO_2^-)_2$; the specific rate of this reaction approaches the diffusion-controlled limit. The results thus point out that aliphatic free radicals can oxidize copper(II) complexes to copper(III) complexes. The results suggest that the reactions of aliphatic free radicals with copper complexes might cause the reported radiosensitization by copper compounds.

In a recent study it was reported that *N*-benzylglycine is formed quantitatively when an alkaline aqueous solution containing $Cu^{II}(NH_2CH_2CO_2^-)_2$ and $ClCH_2C_5H_6$ is sonolyzed.[2] No plausible mechanisms for this process were proposed.

In previous studies[3,4] we have shown that aliphatic free radicals, $^{\bullet}R$, react with Cu^{II}(peptidate), where peptidate = tri- or tetraglycinate, to form transient complexes of the type (peptidate)-Cu^{III}–R. As sonochemistry in aqueous solutions stems from the formation of free radicals,[5] it seems reasonable to suggest that

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(1) (a) Chemistry Department, Ben-Gurion University of the Negev. (b) Nuclear Research Centre Negev. (c) R. Bloch Coal Research Center.

(2) Reddy, G. S.; Smith, G. G. *Inorg. Chim. Acta* **1987**, *133*, 1.

(3) Mulac, W. A.; Meyerstein, D. *J. Chem. Soc., Chem. Comm.* **1979**, 823.

(4) Kirschenbaum, L. J.; Meyerstein, D. *Inorg. Chem.* **1980**, *19*, 1373.

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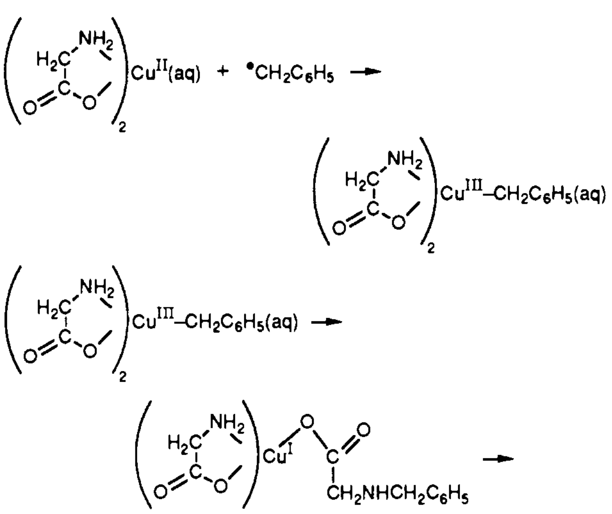
the *N*-benzylglycine observed in the sonochemical experiments was formed via the following reactions:



(1)

$$Cu^+(aq) + {}^+NH_3CH_2CO_2^- + {}^+NH_2(CH_2C_6H_5)CH_2CO_2^- + {}^+OH^-(aq) \quad (2)$$

It was decided to check whether this is indeed the mechanism of reaction, as it could explain the fact that copper ions are known to be radiosensitizers. As benzyl radicals are not good models for the free radicals formed in biological systems, we decided to study the reaction of methyl free radicals with $Cu^{II}(NH_2CH_2CO_2^-)_2$ with the expectation of observing the transient complex $(NH_2CH_2CO_2^-)_2Cu^{III}-CH_3(aq)$ and to obtain $^+NH_2(CH_3)CH_2CO_2^-$ as one of the final products. The results indicate that indeed $(NH_2CH_2CO_2^-)_2Cu^{III}-CH_3(aq)$ is formed under these conditions but that it decomposes into $Cu^{III}(NH_2CH_2CO_2^-)_2^+$ + CH_4.

Experimental Section

Reagents. All chemicals used were of analytical grade and were used as received. The pH was adjusted with $HClO_4$ and NaOH. All solutions were prepared with distilled water that was further purified by using a Millipore setup. The N_2O used to saturate the solutions was purified from traces of dioxygen by bubbling it through two washing bottles containing VSO_4 in dilute H_2SO_4 over a Zn amalgam followed by a washing bottle containing distilled water.

Irradiations. Pulse-radiolysis experiments were carried out with a Varian 7715 linear electron accelerator at the Hebrew University of Jerusalem. The pulse duration was 0.05–1.5 μs with a 200-mA current of 5-Mev electrons. Irradiations were done in a 4-cm Spectrosil cell by using three light passes. All other experimental details were identical with those described previously in detail.[6]

Each rate constant is the average of at least six kinetic runs using at least two independently prepared stock solutions. The dependence of the rate constants on solute concentrations was checked by changing the concentrations of the solutes by at least a factor of 5. When a dependence on concentration was observed, the kinetics were determined at least at four different concentrations.

A N_2O-saturated solution containing 1 mM KSCN was used for dosimetry. The yield of $(SCN)_2^{\bullet-}$ was measured by taking $\epsilon_{475} = 7600$ M^{-1} cm^{-1} and assuming $G[(SCN)_2^{\bullet-}] = 6.0$. The accuracy of the dose per pulse thus determined is ±10%.

Large doses of irradiation for product analysis have been delivered into small cylindrical glass bulbs (12-mL volume) filled with 10 mL of N_2O-saturated solutions and sealed with rubber septa. In this case the modified Fricke dosimeter for high doses was used to determine the total concentration of free radicals by taking $G(Fe^{3+}) = 1.6$ and $\epsilon_{302} = 2197$ M^{-1} cm^{-1}.

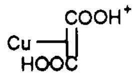
A ^{60}Co γ source (Noratom) with a dose rate of 3.0 krads/min was used for low-dose-rate experiments and product analysis. Samples identical to those in the high-dose-rate experiments were used.

Analysis. The yield of methane and ethane was determined by GC analysis by using a Varian 3700 chromatograph. ^{13}C NMR experiments were performed by using a Bruker WP200 (sy) 200-MHz spectrometer. High-voltage electrophoresis was carried out with a Gilson Model D machine.

Samples for the NMR experiments were prepared as follows: 100-mL portions of N_2O-saturated solutions containing 0.1 M DMSO and the required concentrations of $CuSO_4$ and glycine were irradiated in the cobalt-60 γ source by a dose of 200 000 rads. The solution was acidified to pH 1.0 by HCl and passed through a cation-exchange column (Dowex 50 W-X8(H)). The column was then rinsed with 1 M HCl, and the amino acids were extracted by 1 M NH_3. The solution thus obtained was dried by vacuum evaporation, and the solid was dissolved in 2 mL of D_2O for analysis.

Samples for the electrophoresis experiments were prepared as follows: 100 mL of the irradiated solution was dried by vacuum evaporation, and the solid was dissolved in 2 mL of H_2O. An aliquot of the solution thus prepared was placed on the paper and placed in a bath containing a 6.8% formic acid solution and petroleum ether. Detection of the amino acids was carried out with ninhydrin.

In order to determine whether $Cu^+(aq)$ is being formed, a deaerated solution containing fumaric acid was added to the irradiated solution. The plausible formation of the known d → π complex



was checked spectrophotometrically. It is known that this complex has an absorption band with $\lambda_{max} = 335$ nm and $\epsilon_{max} = 3000$ M^{-1} cm^{-1}.[7]

Preparation of Methyl Free Radicals. The radiolysis of water may be summed up by the equation

$$H_2O \xrightarrow{\gamma, e^-} e_{aq}^- \ (2.65),\ {}^{\bullet}OH\ (2.65),\ {}^{\bullet}H\ (0.60),\ H_2\ (0.45),\ H_2O_2\ (0.75) \quad (3)$$

The numbers in parentheses are *G* values, which represent the number of molecules of a product formed/100 eV of energy absorbed in the solution.[8] The precise values of the *G*'s are slightly dependent on solute concentration. At high concentration the yield of the free radicals increases and that of H_2 and H_2O_2 decreases.[8] The free radicals formed are homogeneously distributed within less than 100 ns after the radiation is absorbed.[8]

In N_2O-saturated solution ($[N_2O] = 0.022$ M), e_{aq}^- reacts with N_2O according to reaction 4. After completion of reaction 4 over 90% of all the primary radicals are present as $^{\bullet}OH$ free radicals, $G(^{\bullet}OH) = 6.0$,[8] the rest being $H^{\bullet}$ atoms.

$$e_{aq}^- + N_2O \xrightarrow{H_2O} N_2 + OH^- + {}^{\bullet}OH \qquad k_4 = 8.7 \times 10^9\ M^{-1}\ s^{-1}\ {}^{9} \quad (4)$$

The $^{\bullet}OH$ free radicals react with $(CH_3)_2SO$ according to reaction 5, which is followed by reaction 6.[10] Thus, over 90% of the primary radicals are transformed, within less than 1 μs, into methyl free radicals in N_2O-saturated solutions containing $(CH_3)_2SO$.

$$^{\bullet}OH + (CH_3)_2SO \rightarrow (CH_3)_2\dot{S}(O)OH \qquad k = 7.0 \times 10^9\ M^{-1}\ s^{-1} \quad (5)$$

$$(CH_3)_2\dot{S}(O)OH \rightarrow CH_3S(O)OH + {}^{\bullet}CH_3 \qquad k = 1.5 \times 10^7\ s^{-1} \quad (6)$$

The change in the concentration of $Cu^{II}(NH_2CH_2CO_2^-)_2$ was determined spectrophotometrically in 6-cm-long cells by using an HP 8452 diode-array spectrophotometer.

Results

Kinetics. N_2O-saturated solutions containing (2–30) × 10^{-4} M $CuSO_4$, {2[$CuSO_4$] + 1.0 × 10^{-4}} M glycine, 0.1–0.2 M $(CH_3)_2SO$, and 1.0 × 10^{-2} M KH_2PO_4 at pH 6–10 were irradiated by short electron pulses. Three consecutive chemical processes, well separated in time, were observed in these experiments; see Figure 1. It should be pointed out that none of these processes was observed in the absence of copper ions.

In the first process the formation of an unstable intermediate within 50 μs is observed. The spectrum of this intermediate is plotted in Figure 2a. The apparent absorption coefficient at 360 ± 5 nm, where the maximal absorption is observed, as a function of dose per pulse is summed up in Table I. (The error limit in

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(5) Henglein, A. *Ultrasonics* **1987**, *25*, 6.

(6) Goldstein, S.; Czapski, G.; Cohen, H.; Meyerstein, D. *Inorg. Chem.* **1988**, *27*, 4130.

(7) Meyerstein, D. *Inorg. Chem.* **1975**, *14*, 1716.

(8) Matheson, M. S.; Dorfman, L. M. *Pulse Radiolysis*; MIT Press: Cambridge, MA, 1969.

(9) Buxton, G. V.; Greenstock, C. L.; Helman, W. P.; Ross, A. B. *J. Phys. Chem. Ref. Data* **1988**, *17*, 513.

(10) Veitwisch, D.; Janata, E.; Asmus, K. D. *J. Chem. Soc., Perkin Trans.* **1980**, 146.

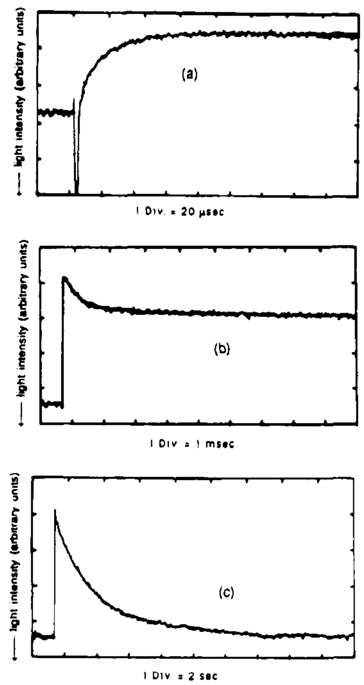

Figure 1. Computer output of the time dependence of the three chemical processes observed after a pulse is absorbed in the sample: (a) first process; (b) second process; (c) third process. Solution composition: N_2O saturated, $[Cu^{2+}] = 1 \times 10^{-3}$ M, [glycine] = 2.1×10^{-3} M, [DMSO] = 0.1 M, $[KH_2PO_4] = 1 \times 10^{-2}$ M, pH 7.0, pulse intensity 1000 rads/pulse, and measured at 360 nm.

Table I. Dependence of the Apparent Absorption Coefficient of $(NH_2CH_2CO_2^-)_2Cu^{III}-CH_3(aq)$ on Pulse Intensity[a]

$10^4[Cu^{2+}]$, M	pulse intensity, rads	ϵ_{360}, M^{-1} cm^{-1}	$10^4[Cu^{2+}]$, M	pulse intensity, rads	ϵ_{360}, M^{-1} cm^{-1}
2.5	350	750	6.5	1500	550
2.5	550	450	10.0	350	800
2.5	1500	300	10.0	550	650
6.5	350	750	10.0	1500	550
6.5	550	650			

[a] Solution composition: N_2O saturated, [glycine] = $\{2[Cu^{2+}] + 1 \times 10^{-4}\}$ M, [DMSO] = 0.1 M, $[KH_2PO_4] = 1 \times 10^{-2}$ M, pH 7.0, measured at 360 nm, and accuracy ±15%. Each value is the average of at least three independent experiments.

determining λ_{max} is due to the slit widths of the monochromator and the accuracy in determining absorption coefficients.) The kinetics of formation of this transient obey a first-order rate law. The rate of the formation reaction depends linearly on the $Cu^{II}(H_2NCH_2CO_2^-)_2$ concentration (Figure 3) and is independent of the concentrations of the other solutes and the wavelength at which the measurement is performed. However, the observed rate increases considerably with the pulse intensity (Figure 3).

From Figure 3 the apparent specific rate of formation of the intermediate complex, as observed at the low dose per pulse experiments, is calculated to be $(2.5 \pm 0.3) \times 10^7$ M^{-1} s^{-1}, whereas at the high dose per pulse it is $(7.0 \pm 0.7) \times 10^7$ M^{-1} s^{-1}.

In the second process observed the spectrum observed changes slightly (Figure 2). It should be noted that though the maximum of absorption remains at 360 ± 5 nm and the apparent absorption coefficients decrease throughout the spectral range measured, the shape of the absorption band changes slightly, thus indicating that the second product differs from the first one. The second process obeys a first-order rate law with $k = (1.0 \pm 0.3) \times 10^3$ s^{-1}. This rate is independent of the concentrations of the different components of the solution, the pulse intensity, and the wavelength at which the experiment is carried out.

In the third process the absorption due to the second intermediate disappears (Figure 1c). This process also obeys a first-order rate law, with a specific rate of 0.10 ± 0.02 s^{-1}. It should be noted that this rate increases somewhat when the concentration of free glycine in the solution is increased, i.e. to ~0.3 s^{-1} when [excess glycine] = 1×10^{-3} M. The rate also increases somewhat upon repetitive pulsing and with increasing pulse intensity; these effects were not studied in detail.

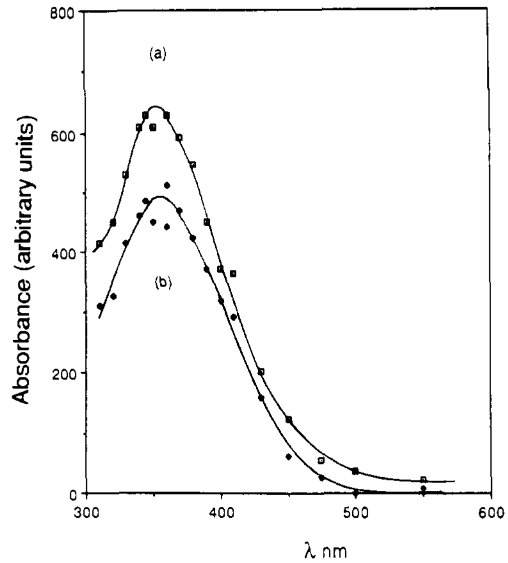

Figure 2. Absorption spectra of the transients observed: (a) transient formed in the first process; (b) transient formed in the second process. Solution composition: N_2O saturated, $[Cu^{2+}] = 1 \times 10^{-3}$ M, [glycine] = 2.1×10^{-3} M, [DMSO] = 0.1 M, $[KH_2PO_4] = 1 \times 10^{-2}$ M, pH 7.0, and pulse intensity 1000 rads/pulse. An arbitrary absorption scale is used, as the absorption coefficients depend on the pulse intensity (Table I).

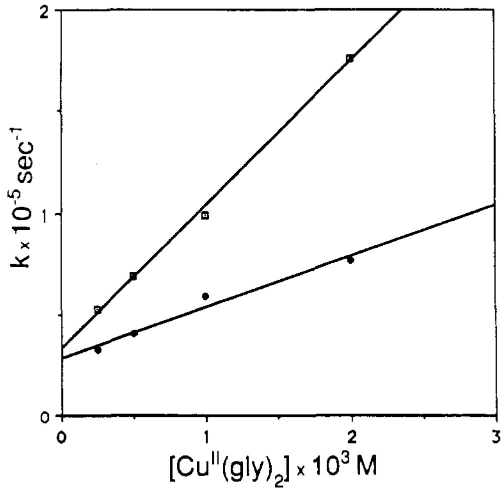

Figure 3. Dependence of the observed first-order rate of the first process observed on $[Cu^{2+}]$: (lower curve) pulse intensity 350 rads/pulse; (upper curve) pulse intensity 1500 rads/pulse. Solution composition: N_2O saturated, $[Cu^{2+}] = (5-30) \times 10^{-4}$ M, [glycine] = $\{2[CuSO_4] + 1.0 \times 10^{-4}\}$ M, [DMSO] = 0.1 M, $[KH_2PO_4] = 1 \times 10^{-2}$ M, and pH 7.0.

Analysis of Final Products. N_2O-saturated solutions containing 1.0×10^{-3} M $CuSO_4$, 2.1×10^{-3} M $^+H_3NCH_2CO_2^-$, 0.1 M $(CH_3)_2SO$, and 0.01 M KH_2PO_4 at pH 7.0 were irradiated in the ^{60}Co γ source by doses of 15 000–90 000 rads, and the following analyses were carried out:

1. The yield of $Cu^+(aq)$ was determined to be smaller than $G(Cu^+) < 0.3$.

2. The concentration of the $Cu^{II}(NH_2CH_2CO_2^-)_2$ complex was determined spectrophotometrically. The concentration changes at most by $G(-Cu^{II}(NH_2CH_2CO_2^-)_2) \leq 0.5$.

3. Experiments to determine whether $NH(CH_3)CH_2CO_2H$ is a product of irradiation were performed as described in the Experimental Section. No $NH(CH_3)CH_2CO_2H$ was detected by ^{13}C NMR spectroscopy and high-voltage electrophoresis though when amounts of $NH(CH_3)CH_2CO_2H$ equivalent to $G = 1.0$ of this product were added to unirradiated or to irradiated solutions,

Table II. Yields of CH_4 and C_2H_6

type of sample[a]	$G(C_2H_6)$	$G(CH_4)$	$G(C_2H_6)/G(CH_4)$	$G_T = 2G(C_2H_6) + G(CH_4)$
1[c]	2.5	1.1	2.3	6.1
1[d]	1.8	1.7	1.0	5.3
2[b]	1.6	1.4	1.1	4.6
2[c]	2.8	0.8	3.5	6.4
2[d]	2.0	1.6	1.2	5.6

[a] Solution composition: N_2O saturated, $[Cu^{2+}] = 1 \times 10^{-3}$ M, [glycine] $= 2.1 \times 10^{-3}$ M, [DMSO] = 0.1 M, $[KH_2PO_4] = 1 \times 10^{-2}$ M, pH 7.0, and accuracy ±15%. Each value is the average of at least four independent samples. Sample key: (1) solution contained no copper; (2) solution contained copper. [b] 30 pulses from the linear accelerator; dose per pulse 500 rads. [c] 10 pulses from the linear accelerator; dose per pulse 2000 rads. [d] Irradiation by the cobalt source; total dose 15 000–30 000 rads.

Table III. Specific Rates of Reaction of the Primary Free Radicals with the Solutes

reaction	k, $M^{-1}\ s^{-1}$
$e_{aq}^- + N_2O \xrightarrow{H_2O} N_2 + OH^- + {}^\bullet OH$	8.7×10^{9} [9]
$e_{aq}^- + Cu^{II}(NH_2CH_2CO_2^-)_2 \rightarrow Cu^{I}(NH_2CH_2CO_2^-)_2^-$	1.4×10^{10} [9]
$e_{aq}^- + {}^+NH_3CH_2CO_2^- \rightarrow NH_2CH_2CO_2^- + H^\bullet$	1.0×10^{7} [9]
$e_{aq}^- + (CH_3)_2SO \rightarrow$ products	1.7×10^{6} [9]
${}^\bullet OH + (CH_3)_2SO \rightarrow CH_3SOOH + {}^\bullet CH_3$	7.0×10^{9} [10]
${}^\bullet OH + Cu^{II}(NH_2CH_2CO_2^-)_2 \rightarrow Cu^{III}(NH_2CH_2CO_2^-)_2^+$	1.5×10^{9} [11]
${}^\bullet OH + {}^+NH_3CH_2CO_2^- \rightarrow {}^+NH_3CHCO_2^- + H_2O$	2.8×10^{9} [9]

they were detected. It has to be concluded that *N*-methylglycine is not the product, or at least a major product, of the reactions observed.

4. GC analyses of the gaseous products were performed. Methane and ethane were observed as products. The sum of their yields accounts for the total yield of methyl radicals formed by the radiation. These experiments were repeated also for samples irradiated by short high-dose-rate pulses from the linear electron accelerator; the results are summed up in Table II.

Discussion

When neutral N_2O-saturated solutions containing 1×10^{-3} M $CuSO_4$, 2.1×10^{-3} M ${}^+NH_3CH_2CO_2^-$, and 0.1 M $(CH_3)_2SO$ are irradiated, nearly all the primarily formed e_{aq}^- and ${}^\bullet OH$ radicals are transformed into ${}^\bullet CH_3$ radicals (Table III) within less than 1 μs from the pulse. Thus, the first intermediate being observed (Figure 1a) is clearly formed by a reaction between the ${}^\bullet CH_3$ radicals and $Cu^{II}(NH_2CH_2CO_2^-)_2$. It is suggested that the reaction observed is

$$
{}^\bullet CH_3 + Cu^{II}(NH_2CH_2CO_2^-)_2 \rightarrow (NH_2CH_2CO_2^-)_2\,Cu^{III}\text{–}CH_3 \quad (7)
$$

due to the following reasons:

1. The reaction is first order in ${}^\bullet CH_3$ and in $Cu^{II}(NH_2CH_2CO_2^-)_2$.

2. The observed intermediate is clearly not $Cu^{III}(NH_2CH_2CO_2^-)_2^+(aq)$, as its spectrum and lifetime differ considerably from those reported for the latter intermediate.[11]

3. The observed intermediate is also clearly not $Cu^{I}(NH_2CH_2CO_2^-)_2$, as Cu^{I}(amino acid)$_n$ complexes do not absorb in this spectral range[3,4,11] and as CH_4 and not CH_3OH is the final product observed.

4. The spectrum of the intermediate and its rate of decomposition are similar to those earlier reported for (peptidate)Cu^{III}–R (where R = $CH_2CO_2^-$ or $CH_2(CH_3)_2OH$).[3,4]

The second process observed obeys a first-order rate law and causes only slight changes in the spectral features of the intermediate. Due to these reasons and to the fact that the rate is independent of pulse intensity, we conclude that this process is due to a rearrangement in the transient complex, most probably in the coordination geometry, i.e.

$$
(NH_2CH_2CO_2^-)_2Cu^{III}\text{–}CH_3(aq) \rightarrow [(NH_2CH_2CO_2^-)_2Cu^{III}\text{–}CH_3(aq)]_R \quad (8)
$$

$$
k = 1.0 \times 10^3\ s^{-1}
$$

where the R indicates that this is a rearranged complex. A similar rearrangement was previously reported for the analogous (tetraglycinate)$Cu^{III}CH_2CO_2^-$ complex.[4]

The third process observed leads to the formation of the final products. It is suggested therefore that the reaction observed is

$$
[(NH_2CH_2CO_2^-)_2Cu^{III}\text{–}CH_3(aq)]_R + H_2O \rightarrow Cu^{III}(NH_2CH_2CO_2^-)_2^+(aq) + CH_4 + OH^- \quad (9)
$$

$$
k = 0.10\ s^{-1}
$$

It is evident that this process cannot explain the formation of ethane (Table II), as any plausible mechanism leading from $[(NH_2CH_2CO_2^-)_2Cu^{III}\text{–}CH_3(aq)]_R$ to ethane has to obey a second-order rate law and not a first-order rate law as observed.

The ethane is also clearly not formed in reaction 10, as this reaction cannot compete with reaction 7 under the low-dose-rate conditions of the irradiation by the ^{60}Co γ source (Table II). We

$$
2{}^\bullet CH_3 \rightarrow C_2H_6 \qquad 2k = 3.2 \times 10^9\ M^{-1}\,s^{-1}\ {}^{12} \quad (10)
$$

therefore propose that the ethane is formed via reaction 11.

$$
[(NH_2CH_2CO_2^-)_2Cu^{III}\text{–}CH_3(aq)]_R + {}^\bullet CH_3 \rightarrow Cu^{II}(NH_2CH_2CO_2^-)_2 + C_2H_6 \quad (11)
$$

This suggestion is supported by the following observations:

1. The yield of ethane increases with the dose rate (Table II). The yield is considerably larger than that due to the competition between reactions 10 and 7, as can be deduced from the magnitude of the intercept in Figure 3.

2. The apparent absorption coefficient decreases with increasing dose per pulse (Table I). This observation can only be explained if reaction 11 competes with reaction 7, as the effect is considerably larger than that due to the competition between reactions 10 and 7, as can be deduced from Figure 3.

3. The dependence of the rate of formation of $(NH_2CH_2CO_2^-)_2Cu^{III}\text{–}CH_3(aq)$ on the pulse intensity (Figure 3) can be explained only by this mechanism. The contribution of reaction 10 is included in the intercept in Figure 3, which indeed increases with pulse intensity. According to the suggested mechanism the rate of formation of $(NH_2CH_2CO_2^-)_2Cu^{III}\text{–}CH_3(aq)$ should be

$$
d([(NH_2CH_2CO_2^-)_2Cu^{III}\text{–}CH_3(aq)])/dt = k_7[Cu^{II}(NH_2CH_2CO_2^-)_2][{}^\bullet CH_3] + k_{11}[(NH_2CH_2CO_2^-)_2Cu^{III}\text{–}CH_3(aq)][{}^\bullet CH_3]
$$

(This is the rate law as $d([(NH_2CH_2CO_2^-)_2Cu^{III}\text{–}CH_3])/dt = -d([{}^\bullet CH_3])/dt$). As $[(NH_2CH_2CO_2^-)_2Cu^{III}\text{–}CH_3(aq)]$, depends on $[Cu^{II}(NH_2CH_2CO_2^-)_2]$, the observed rate of reaction increases with the pulse intensity.

4. Analogous reactions have been recently observed for other transient complexes of the type $LM^{III}\text{–}CH_3$.[13-16] In all these cases the specific rate of this reaction is very high.

The specific rate of reaction 11 can be roughly estimated from the yield of ethane in the low-dose-rate irradiation experiments as follows: The dose rate of the γ source is 50 rads/s; i.e., the rate of formation of the ${}^\bullet CH_3$ radicals is $50 \times 6 \times 10^{-9} = 3 \times 10^{-7}$ Ms^{-1}. (The absorption of 1 rad produces 1×10^{-9} M of a product for which the *G* value is 1.[8]) The specific rate of de-

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[11] Meyerstein, D. *Inorg. Chem.* **1971**, *10*, 2244.

[12] Ross, A. B.; Neta, P. *Natl. Stand. Ref. Data Ser. (Natl. Bur. Stand. U.S.), NSRDS-NBS 70*, 1982.

[13] Meyerstein, D.; Schwarz, H. A. *J. Chem. Soc., Faraday Trans.* **1988**, *84*, 2933.

[14] Cohen, H.; Meyerstein, D. *Inorg. Chem.* **1988**, *27*, 3429.

[15] Sauer, A.; Cohen, H.; Meyerstein, D. *Inorg. Chem.* **1988**, *27*, 4578.

[16] Sauer, A.; Cohen, H.; Meyerstein, D. *Inorg. Chem.* **1989**, *28*, 2511.

composition of $[(NH_2CH_2CO_2^-)_2Cu^{III}-CH_3(aq)]_R$ is 0.1 s^{-1}. Therefore, the steady-state concentration of this complex is $[[NH_2CH_2CO_2^-)_2Cu^{III}-CH_3]_R]_{ss} \approx 3 \times 10^{-7}/0.1 \approx 3 \times 10^{-6}$ M. Under these conditions, in solutions containing 1.0×10^{-3} M $Cu^{II}(NH_2CH_2CO_2^-)_2$, the yield of ethane is 2.0 and that of methane is 1.6 (Table II). This means that of the methyl radicals $(2.0 + 1.6)/(2 \times 2.0 + 1.6) = 3.6/5.6$ react via reaction 7 whereas 2.0/5.6 react via reaction 11. Therefore, $1.0 \times 10^{-3} \times k_7/3 \times 10^{-6} \times k_{11} = 3.6/2.0$; i.e., $k_7/k_{11} = 5.4 \times 10^{-3}$. Assuming that $k_7 = 2.5 \times 10^7$ M^{-1} s^{-1}, the value obtained at the low-dose-rate experiments, one obtains therefore $k_{11} = 2.5 \times 10^7/5.4 \times 10^{-3} \approx 5 \times 10^9$ M^{-1} s^{-1}. However, clearly this value of k_7 contains a contribution of reaction 11, and therefore, the calculated k_{11} is an upper limit. The conclusion that k_{11} approaches the diffusion-controlled limit is not surprising, as similar rates were recently reported for analogous reactions.[13-16]

The spectra of $[(NH_2CH_2CO_2^-)_2Cu^{III}-CH_3]$ and $[(NH_2CH_2CO_2^-)_2Cu^{III}-CH_3(aq)]_R$ should be compared with those of (peptidate)Cu^{III}-R, where R = alkyl. The results clearly indicate a significant blue shift when the amino acid is replaced by its peptides. This result is in accord with the assignment of these bands to ligand to metal charge-transfer bands, taking into account that the redox potential of the peptide complexes is considerably lower than that of the glycine complex.[17] The reason for the dependence of the apparent absorption coefficient on the dose per pulse (Table I) is the competition between reactions 7 and 11.

It should be noted that we do not observe the formation of $Cu^{III}(NH_2CH_2CO_2^-)_2^+$ as predicted by reaction 9, as the specific rate of decomposition of the latter complex is considerably faster than k_9.[11]

A comparison of the reaction of $^{\bullet}CH_3$ radicals with $Cu^{2+}(aq)$ and with $Cu^{II}(NH_2CH_2CO_2^-)_2$ sheds some light on the effect of ligands on the mechanism of reaction of copper(II) ions with aliphatic free radicals. In both reactions a transient with a copper(III)-carbon σ bond is formed. However, the rate of reaction with $Cu^{II}(NH_2CH_2CO_2^-)_2$ is faster by about 2 orders of magnitude than that with $Cu^{2+}(aq)$.[18] This effect probably stems from the lowering of the oxidation potential by the amino acid ligand. Furthermore $Cu^{III}-CH_3(aq)$ decomposes into $Cu^+(aq)$ + $HOCH_3$ whereas $(NH_2CH_2CO_2^-)_2Cu^{III}-CH_3(aq)$ decomposes into $Cu^{III}[(NH_2CH_2CO_2^-)_2^+(aq)$ + CH_4, a fact that clearly stems from the effect of the ligands on the redox potential of the central copper ion.

The difference in the mechanism of reaction observed for methyl radicals, this study, and benzyl radicals, reaction described in ref 2, with $Cu^{II}(NH_2CH_2CO_2^-)_2$ is probably due to the fact that methyl radicals are considerably stronger oxidizing agents and that they are less stabilized by resonance.

Finally, we wish to point out that these results indicate that aliphatic free radicals can oxidize copper(II) complexes with available biological ligands under physiological conditions. As it is reasonable to assume that the tervalent copper complexes thus formed have biologically deleterious effects, these observations suggest that this might be another mechanism contributing to the radiosensitization by copper ions, which is usually attributed to a reduction of the copper complexes by the free radicals followed by a Fenton like reaction. Thus, aliphatic free radicals might cause deleterious effects, which are usually attributed to the reaction of hydroxyl free radicals.

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Registry No. $Cu(NH_2CH_2CO_2)_2$, 13479-54-4; CH_3, 2229-07-4; CH_4, 74-82-8; C_2H_6, 74-84-0; $(NH_2CH_2CO_2)_2CuCH_3$, 129916-84-3.

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(17) Bossu, F. P.; Chellappa, K. L.; Margerum, D. W. *J. Am. Chem. Soc.* **1977**, *99*, 2195.

(18) Ferraudi, G. *Inorg. Chem.* **1978**, *17*, 2506.

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Pentacyanoamminechromate(III). Synthesis, Characterization, and Photochemistry

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The $Cr(CN)_5(NH_3)^{2-}$ ion was synthesized by irradiation of $Cr(CN)_6^{3-}$ in methanol and reaction with NH_3, isolated as the potassium salt, and characterized by analysis, chromatography, aquation, absorption spectroscopy (λ_{max} at 397 and 320 nm, as predicted theoretically), and phosphorescence (λ_{max} at 777 nm, $\tau = 32$ μs at 20 °C in Me_2SO). Ligand field excitation causes release of both NH_3 and CN^-. The respective quantum yields are 0.08 and 0.06 in H_2O, 0.05 and 0.007 in Me_2SO, and 0.11 and 0.003 in dimethylformamide. The prevalence of NH_3 loss is in agreement with the angular overlap model but not with previous photolysis theories. The medium markedly affects the absorption spectrum, the emission behavior, the photoreaction efficiencies, and especially the Φ_{NH_3}/Φ_{CN^-} ratio; the changes are interpreted in terms of solvent orientation and hydrogen bonding. The phosphorescence is observed in aprotic solvents but not in H_2O and is quenched by $Co(sep)^{3+}$. In Me_2SO, at least 90% of each photoreaction mode remains unquenched upon complete doublet-state quenching. Both photoprocesses are concluded to proceed from the lowest quartet excited state prior to intersystem crossing. Results for $Cr(CN)_6^{3-}$ photolyzed in Me_2SO in the absence and in the presence of $Co(sep)^{3+}$ are also reported, and the two systems are compared.

Introduction

Pentacyanochromates(III) constitute a potentially rich yet little explored class of anionic complexes that may be regarded as a counterpart of the widely investigated pentaamminechromium(III) cations. Although several $Cr(CN)_5X^{z-}$ species have been mentioned in the literature, their study has probably been limited by difficulties in the isolation of suitable amounts of these compounds. Thus, acid hydrolysis of $Cr(CN)_6^{3-}$ results in solutions of $Cr(CN)_5(H_2O)^{2-}$ mixed with products of subsequent aquation,[1] and Cr(II)-catalyzed CN^- loss in alkaline medium leads to equilibria between $Cr(CN)_6^{3-}$ and $Cr(CN)_5(OH)^{3-}$.[2,3] Similarly, reaction of $Cr(NCS)_6^{3-}$ with KCN yields mixtures of all the $Cr(CN)_{6-n}(NCS)_n^{3-}$ ions, from which the $n = 1$ component can be

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(1) Shaap, W. B.; Krishnamurthy, R.; Wakefield, D. K.; Coleman, W. F. In *Coordination Chemistry*; Kirschner, S., Ed.; Plenum Press: New York, 1969; p 177.

(2) Jeftič, L.; Feldberg, S. W. *J. Am. Chem. Soc.* **1970**, *92*, 5272.

(3) Jeftič, L.; Feldberg, S. W. *J. Phys. Chem.* **1971**, *75*, 2381.

0020-1669/90/1329-5035$02.50/0