Uncommon Axial Selenium-ligation in Iron–Bleomycin and Hemoglobin

Yukio Sugiura,* June Kuwahara, and Tadashi Suzuki

Faculty of Pharmaceutical Sciences, Kyoto University, Kyoto 606, Japan

Axial S → Se co-ordination replacement in iron(III) complexes of bleomycin and hemoglobin gives a shift in the e.s.r. *g*-values (*ca.* g_{av} = 0.03) towards lower magnetic field.

The presence of thiolate as an axial ligand at the iron–protoporphyrin IX active site of cytochrome P-450 has been believed to be mainly responsible for many of the enzyme's atypical properties.[1,2] However, the presence of the RSe^-–Fe–N ligation mode had not previously been found (even in iron–porphyrins and hemoproteins) because of the remarkably facile redox processes in RSeH–Fe^{III} systems. To avoid this problem, we have applied the rapid freezing e.s.r. technique and obtained the first evidence for axial ligation of RSe^-–Fe–N in the bleomycin–Fe^{III}–$Se[CH_2]_2NMe_2$ adduct complex and in the hemoglobin-Fe^{III}–$Se[CH_2]_2NMe_2$ complex. Indeed, it is known that various spectroscopic parameters are appreciably similar between the iron complexes of bleomycin and porphyrin, except for the CN^- adducts.[3]

Figure 1 shows the comparative e.s.r. spectra for the *N*,*N*-dimethylselenocysteamine and *N*,*N*-dimethylcysteamine adducts of the bleomycin–Fe^{III} complex. Table 1 summarizes the e.s.r. and crystal field parameters for the bleomycin–Fe^{III}–$X[CH_2]_2NMe_2$ and hemoglobin-Fe^{III}–$X[CH_2]_2NMe_2$(X = Se or S) complexes. These adduct complexes were prepared by addition of excess of $HSe[CH_2]_2NMe_2$ (or $HS[CH_2]_2NMe_2$; 50 mM) to the bleomycin–Fe^{III}–OH^- complex (or methemoglobin; 1 mM) at pH 9.0. The crystal field parameters of axial distortion and rhombic distortion at the low-spin iron(III) co-ordination sphere were computed from the three *g*-values according to Bohan's method[4] on the basis of Griffith's model.

Of special interest is the fact that the e.s.r. *g*-values of the Se-adduct complexes are shifted toward lower magnetic field,

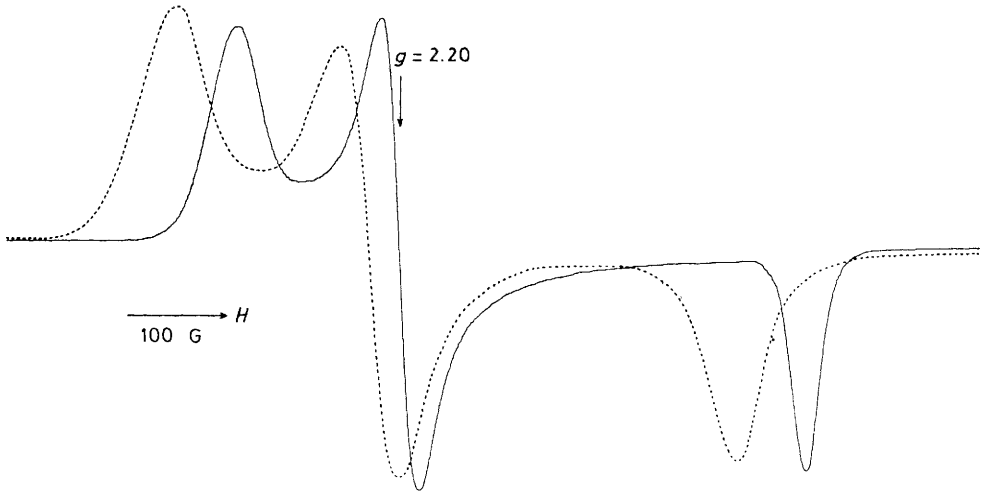

Figure 1. Comparison of the e.s.r. spectra of the bleomycin–Fe^{III}–$Se[CH_2]_2NMe_2$ complex (- - - - - - - -) and the bleomycin–Fe^{III}–$S[CH_2]_2NMe_2$ complex (——) at 77 K.

Table 1. E.s.r. and crystal field parameters for iron(III) complexes of bleomycin and hemoglobin with axial selenium or sulphur co-ordination.

Complex	g_z	g_y	g_x	g_{av}	μ/λ	$\lvert R/\mu \rvert$
Bleomycin–Fe^{III}–$Se[CH_2]_2NMe_2$	1.969	2.218	2.368	2.185	−7.96	0.45
Bleomycin–Fe^{III}–$S[CH_2]_2NMe_2$	1.937	2.203	2.330	2.157	−7.61	0.41
Hemoglobin-Fe^{III}–$Se[CH_2]_2NMe_2$	1.942	2.329	2.411	2.227	−6.01	0.21
Hemoglobin-Fe^{III}–$S[CH_2]_2NMe_2$	1.940	2.260	2.367	2.189	−6.77	0.30

compared with those of the corresponding S-adducts. The similarities in line shapes and apparent g-values are a clear indication of equivalent ground electronic states for these iron complexes. Similar e.s.r. behaviour has also been observed for Se-adrenodoxin ($g_\perp$ = 1.975 and $g_\parallel$ = 2.051)[5] and Se-putidaredoxin (g = 1.93, 1.98, and 2.04),[6] in which selenium is substituted in the bridging positions of native S-adrenodoxin ($g_\perp$ = 1.940 and $g_\parallel$ = 2.027) and S-putidaredoxin ($g_\perp$ = 1.93 and $g_\parallel$ = 2.01). One characteristic feature of the bleomycin–Fe^{III} complexes is large tetragonality and rhombicity in comparison with the hemoglobin complexes. Although the bleomycin–Fe^{III} complex with the axial Se-ligand shows larger rhombicity and tetragonality than the corresponding S-adduct complex, this tendency is reversed in the case of the hemoglobin complexes. Probably, this dissimilarity may be attributed to structural differences in the basal-plane of the peptide and porphyrin skeletons and in the axial *trans*-ligand of the α-amino and imidazole groups, respectively, between iron–bleomycin and hemoglobin.

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