

# Inorganic Chemistry

including bioinorganic chemistry

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**Supplementary Material:**

**Boc-Ile-Ser-OMe (1):** Boc-Ile (248 mg; 1.072 mmol) and Serinemethylester hydrochloride (200 mg; 1.286 mmol) were dissolved on 2 ml dry DMF. At  $-4^{\circ}\text{C}$ , DPPA (354 mg; 1.286 mmol) and dry triethylamine (260 mmol; 2.572 mmol) were added. The mixture was stirred for 3 days at  $-4^{\circ}\text{C}$  and then for 4h at room temperature. After evaporation of the solvent, the mixture was dissolved in ethylacetate and washed with 1 N aqueous  $\text{KHSO}_4$ , 1 N aqueous  $\text{KHCO}_3$  and water. The solution was dried over  $\text{Na}_2\text{SO}_4$ , filtered and the solvent evaporated. The crude product was then purified with a column of silica gel, solvent: pentane : ethylacetate = 3:7. Yield: 85%.  $^1\text{H-NMR}$ :  $\delta_{\text{H}}$ : ( $\text{CDCl}_3$ , 200 MHz): 0.86 (t, 3H,  $\gamma\text{-CH}_3$  Ile,  $^3J_{\text{HH}}$ : 7.4 Hz); 0.95 (d, 3H,  $\delta\text{-CH}_3$  Ile,  $^3J_{\text{HH}}$ : 6.7 Hz); 1.15 (m, 2H,  $\delta\text{-CH}_2$  Ile); 1.40 (s, 9H,  $\text{CH}_3\text{-Boc}$ ); 1.80 (m, 1H,  $\beta\text{-CH-Ile}$ ); 3.76 ( $\text{OCH}_3$ ); 3.85-4.13 (m, 2H,  $\alpha\text{-CH-Ser}$ ,  $\alpha\text{-CH-Ile}$ ); 4.67 (m,  $\beta\text{-CH}_2\text{-Ser}$ ); 5.34 (d, 1H,  $\text{NH-Ser}$ ,  $^3J_{\text{HH}}$ : 8.4 Hz); 7.17 (d, 1H,  $\text{NH-Ile}$ ,  $^3J_{\text{HH}}$ : 8.0 Hz);  $\delta_{\text{C}}$ : ( $\text{CDCl}_3$ , 75.47 MHz): 11.26 ( $\gamma\text{-CH}_3$  Ile); 15.43 ( $\delta\text{-CH}_3$  Ile); 24.86 ( $\delta\text{-CH}_2$  Ile); 28.34 ( $\text{CH}_3\text{-Boc}$ ); 37.29 ( $\beta\text{-CH-Ile}$ ); 50.54 ( $\text{OCH}_3$ ); 54.72 ( $\alpha\text{-CH-Ser}$ ); 59.48 ( $\alpha\text{-CH-Ile}$ ); 62.70 ( $\beta\text{-CH}_2\text{-Ser}$ ); 80.22 ( $\text{C}(\text{CH}_3)_3\text{-Boc}$ ); 156.32 ( $\text{CO-Boc}$ ); 170.85, 172.27 (2 CO).

**Boc-Ile-Thr-OMe (2):** analogous (1). Yield: 85%.  $^1\text{H-NMR}$ :  $\delta_{\text{H}}$ : ( $\text{CDCl}_3$ , 200 MHz): 0.91 (t, 3H,  $\gamma\text{-CH}_3$  Ile,  $^3J_{\text{HH}}$ : 7.3 Hz); 0.94 (d, 3H,  $\delta\text{-CH}_3$  Ile,  $^3J_{\text{HH}}$ : 6.6 Hz); 1.15 (m, 2H,  $\delta\text{-CH}_2$  Ile); 1.20 (d, 3H,  $\text{CH}_3\text{-Thr}$ ,  $^3J_{\text{HH}}$ : 6.2 Hz); 1.40 (s, 9H,  $\text{CH}_3\text{-Boc}$ ); 1.80 (m, 1H,  $\beta\text{-CH-Ile}$ ); 3.76 ( $\text{OCH}_3$ ); 3.90-4.40 (m, 2H,  $\beta\text{-CH-Thr}$ ,  $\alpha\text{-CH-Ile}$ ); 4.63 (d von d,  $\alpha\text{-CH-Thr}$ ,  $^3J_{\text{HH}}$ : 8.8 Hz und 9.1 Hz); 5.23 (d, 1H,  $\text{NH-Thr}$ ,  $^3J_{\text{HH}}$ : 9.1 Hz); 6.95 (d, 1H,  $\text{NH-Ile}$ ,  $^3J_{\text{HH}}$ : 8.41 Hz);  $\delta_{\text{C}}$ : ( $\text{CDCl}_3$ , 75.47 MHz): 11.23 ( $\gamma\text{-CH}_3$  Ile); 15.41 ( $\delta\text{-CH}_3$

Ile); 19.87 (CH<sub>3</sub>-Thr); 24.88 ( $\delta$ -CH<sub>2</sub> Ile); 28.32 (CH<sub>3</sub>-Boc); 37.08 ( $\beta$ -CH-Ile); 52.47 (OCH<sub>3</sub>); 57.32 ( $\beta$ -CH-Thr); 59.43 ( $\alpha$ -CH-Ile); 68.13 ( $\alpha$ -CH-Thr); 80.06 (C(CH<sub>3</sub>)<sub>3</sub>-Boc); 156.08 (CO-Boc); 171.23, 172.48 (2 CO).

**Boc-Ile-Ser-OH (3):** Boc-Ile-Ser-OMe (1.0 g; 3 mmol) was dissolved in methanol. After addition of 1 drop of phenolphthalein, the solution was titrated with 1 N aqueous NaOH solution (ca. 3 ml). The methanol was evaporated and the aqueous phase washed with diethylether. The aqueous phase was then, at 0°C, carefully acidified (to approximately pH 2). The free acid was extracted with methylenechloride, dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated. Yield: 81%. <sup>1</sup>H-NMR:  $\delta_H$ : (CDCl<sub>3</sub>, 200 MHz): 0.86 (t, 3H,  $\gamma$ -CH<sub>3</sub> Ile, <sup>3</sup>J<sub>HH</sub>: 7.3 Hz); 0.93 (d, 3H,  $\delta$ -CH<sub>3</sub> Ile, <sup>3</sup>J<sub>HH</sub>: 6.6 Hz); 1.15 (m, 2H,  $\delta$ -CH<sub>2</sub> Ile); 1.42 (s, 9H, CH<sub>3</sub>-Boc); 1.80 (m, 1H,  $\beta$ -CH-Ile); 3.85-4.20 (m, 2H,  $\alpha$ -CH-Ser,  $\alpha$ -CH-Ile); 4.67 (m,  $\beta$ -CH<sub>2</sub>-Ser); 5.52 (d, 1H, NH-Ser, <sup>3</sup>J<sub>HH</sub>: 8.0 Hz); 7.52 (d, 1H, NH-Ile, <sup>3</sup>J<sub>HH</sub>: 7.3 Hz).

**Boc-Ile-Thr-OH (4):** analogous (3). Yield: 83%. <sup>1</sup>H-NMR:  $\delta_H$ : (CDCl<sub>3</sub>, 200 MHz): 0.91 (t, 3H,  $\gamma$ -CH<sub>3</sub> Ile, <sup>3</sup>J<sub>HH</sub>: 7.3 Hz); 0.96 (d, 3H,  $\delta$ -CH<sub>3</sub> Ile, <sup>3</sup>J<sub>HH</sub>: 6.6 Hz); 1.19 (m, 2H,  $\delta$ -CH<sub>2</sub> Ile); 1.21 (d, 3H, CH<sub>3</sub>-Thr, <sup>3</sup>J<sub>HH</sub>: 6.2 Hz); 1.43 (s, 9H, CH<sub>3</sub>-Boc); 1.80 (m, 1H,  $\beta$ -CH-Ile); 4.15 und 4.49 (2m, 2H,  $\beta$ -CH-Thr,  $\alpha$ -CH-Ile); 4.65 (m, 1H,  $\alpha$ -CH-Thr); 5.31 (m, 1H, NH-Thr); 7.35 (m, 1H, NH-Ile).

**Z-Aminoacetonitrile (5):** Aminoacetonitrile hydrogensulfate (10 g; 64.9 mmol) was dissolved in dioxane/water 1:1. After addition of 2.5 equivalents NaHCO<sub>3</sub> (13.6 g; 162.2 mmol), the solution was cooled to 0°C. After addition of 1.1 equivalents of chloroformicacidbenzylester (10.2 ml; 12.2 g; 71.4 mmol), the solution was stirred

for 2 days. The solution was evaporated and dried *in vacuo*. Yield: 97%.  $^1\text{H}$ -NMR:  $\delta_{\text{H}}$  : ( $\text{CDCl}_3$ , 200 MHz): 4.06 (d, 2H,  $\text{CH}_2\text{CN}$ ,  $^3J_{\text{HH}}$ : 5.5 Hz); 5.16 (s, 2H,  $\text{CH}_2\text{C}_6\text{H}_5$ ); 5.5 (breites s, 1H, NH); 7.37 (s, 5H,  $\text{C}_6\text{H}_5$ ).

**Z-Glycinethioamide (6):**  $\text{H}_2\text{S}$  was purged into a solution of Z-aminoacetonitrile (12.3 g; 64.4 mmol) and triethanolamine (1.9 g; 12.9 mmol) in 65 ml dry ethanol for 24 h. The solvent was then evaporated and the residue dissolved in ethylacetate. The organic phase was washed with water and dried over  $\text{MgSO}_4$ , filtered and evaporated. Yield: 85%.  $^1\text{H}$ -NMR:  $\delta_{\text{H}}$  : ( $\text{CDCl}_3$ , 200 MHz): 4.20 (d, 2H,  $\text{CH}_2\text{CN}$ ,  $^3J_{\text{HH}}$ : 6.1 Hz); 5.15 (s, 2H,  $\text{CH}_2\text{C}_6\text{H}_5$ ); 5.5 (breites s, 1H, NH); 7.3 (breites s, 2H,  $\text{NH}_2$ ); 7.37 (s, 5H,  $\text{C}_6\text{H}_5$ ).

**Z-(Gly)Thz-OEt (7):** Z-Glycinethioamide (5 g; 22.3 mmol) and ethyl-brompyruvate (4.35 g; 22.3 mmol) were dissolved in 30 ml dry ethanol and the water which was generated during the reaction was captured using a molecular sieve 3 Å. The mixture was refluxed for 7 h and cooled to room temperature over night. The molecular sieve was filtered off and washed with hot ethanol. After evaporation of the solvent, the crude product was purified with flash chromatography (silica gel; pentane : ethalacetate = 1:1). Yield: 70%.  $^1\text{H}$ -NMR:  $\delta_{\text{H}}$  : ( $\text{CDCl}_3$ , 300 MHz): 1.42 (t, 3H,  $\text{CH}_2\text{CH}_3$ ,  $^3J_{\text{HH}}$ : 9.9 Hz); 4.39 (q, 2H,  $\text{CH}_2\text{CH}_3$ ,  $^3J_{\text{HH}}$ : 7.7 Hz); 4.65 (m, 2H,  $\text{CH}_2\text{-Gly}$ ); 5.15 (s, 2H,  $\text{CH}_2\text{C}_6\text{H}_5$ ); 5.8 (breites s, 1H, NH); 7.35 (s, 5H,  $\text{C}_6\text{H}_5$ ); 8.10 (s, 1H, CH-Thz);  $\delta_{\text{C}}$  : ( $\text{CDCl}_3$ , 75.47 MHz): 14.35 ( $\text{CH}_2\text{CH}_3$ ); 42.74 ( $\text{CH}_2\text{CH}_3$ ); 61.52, 67.34 ( $\text{CH}_2\text{-C}_6\text{H}_5$  und  $\text{CH}_2\text{-Gly}$ ); 128.56, 128.29, 128.14 ( $\text{C}_6\text{H}_5$ ); 136.08, 147.06, 156.36 (3 C-Thz); 161.22, 169.19 (2 CO).

**Z-(Gly)Thz-OMe (8):** LiBr (dried over  $P_4O_{10}$ ) (680 mg; 7.8 mmol) and Z-(Gly)Thz-OEt (500 mg; 1.6 mmol) were dissolved in dry methanol under argon. After addition of DBU (119 mg; 0.78 mmol) at room temperature, the mixture was stirred until thin layer chromatography showed the reaction had come to an end. The solvent was evaporated, the residue dissolved in ethylacetate and washed with 1 N aqueous  $KHSO_4$ , 1 N aqueous  $KHCO_3$ , and water, then dried over  $Na_2SO_4$ , filtered and the solvent evaporated. Yield: 65%.  $^1H$ -NMR:  $\delta_H$  : ( $CDCl_3$ , 300 MHz): 3.81 (s, 3H,  $OCH_3$ ); 4.65 (m, 2H,  $CH_2$ -Gly); 5.15 (s, 2H,  $CH_2C_6H_5$ ); 5.7 (breites s, 1H, NH); 7.35 (s, 5H,  $C_6H_5$ ); 8.10 (s, 1H, CH-Thz);  $\delta_C$  : ( $CDCl_3$ , 75.47 MHz): 52.18 ( $OCH_3$ ); 61.52, 67.34 ( $CH_2-C_6H_5$  und  $CH_2$ -Gly); 128.56, 128.29, 128.14 ( $C_6H_5$ ); 136.08, 147.06, 156.36 (3 C-Thz); 161.22, 169.19 (2 CO).

**HBr-(Gly)Thz-OMe (9):** At 0°C 1.2 ml 33% HBr in glacial acetic acid were added to Z-(Gly)Thz-OMe. The mixture was stirred over night. After adding a large amount of diethylether, the hydrobromide was filtered off and washed several times with diethylether and dried. The crude product was recrystallized from ethanol/diethylether. Yield: 75%.  $^1H$ -NMR:  $\delta_H$  : ( $d_6$ -DMSO, 200 MHz): 3.83 (s, 3H,  $OCH_3$ ); 4.50 (s, 2H,  $CH_2$ -Gly); 8.62 (s, 1H, CH-Thz); 8.64 (breites s,  $NH_3^+$ );  $\delta_C$  : ( $d_6$ -DMSO, 50.32 MHz): 52.22 ( $OCH_3$ ); 39.38 ( $CH_2$ -Gly); 131.38, 145.19, 160.94 (3 C-Thz); 163.06 (CO).

**Boc-Ile-Ser-(Gly)Thz-OMe (10):** Boc-Ile-Ser-OH (239 mg; 0.75 mmol) and HBr-(Gly)Thz-OMe (228 mg; 0.90 mmol) were suspended in methylenechloride and cooled to 0°C. Then TBTU (253 mg; 0.79 mmol) and DBU (0.28 ml; 290 mg; 1.9 mmol) were added and the mixture was stirred for 3 days at room temperature. A yellow-orange solution was formed. The mixture was diluted with methylenechloride

and washed with 1 N aqueous  $\text{KHSO}_4$ , 1 N aqueous  $\text{KHCO}_3$ , and water, then dried over  $\text{Na}_2\text{SO}_4$ , filtered and the solvent evaporated. The crude product was purified with flash chromatography (silica gel;  $\text{CH}_2\text{Cl}_2$  :  $\text{MeOH}$  = 9:1). Yield: 85%.  $^1\text{H-NMR}$ :  $\delta_{\text{H}}$  : ( $\text{d}_6$ -DMSO, 200 MHz): 0.80 (t, 3H,  $\gamma$ - $\text{CH}_3$ -Ile,  $^3J_{\text{HH}}$ : 7.2 Hz); 0.83 (d, 3H,  $\delta$ - $\text{CH}_3$ -Ile,  $^3J_{\text{HH}}$ : 6.3 Hz); 1.20 (m, 2H,  $\delta$ - $\text{CH}_2$ -Ile); 1.41 (s, 9H,  $\text{CH}_3$ -Boc); 1.75 (m, 1H,  $\beta$ -CH-Ile); 3.82 (s, 3H,  $\text{OCH}_3$ ); 3.20-5.20 (mehrere m, 6H,  $\text{CH}_2$ -Gly,  $\alpha$ -CH-Ser,  $\alpha$ -CH-Ile,  $\beta$ - $\text{CH}_2$ -Ser); 8.40 (s, 1H, CH-Thz); 6.90, 7.90, 8.85 (3m, 3H, NH-Ile, NH-Ser, NH-Gly);  $\delta_{\text{C}}$  : ( $\text{d}_6$ -DMSO, 50.32 MHz): 11.16 ( $\gamma$ - $\text{CH}_3$ -Ile); 15.42 ( $\delta$ - $\text{CH}_3$ -Ile); 24.33 ( $\delta$ - $\text{CH}_2$ -Ile); 28.19 ( $\text{CH}_3$ -Boc); 36.62 ( $\beta$ -CH-Ile); 38.26 ( $\text{CH}_2$ -Gly); 51.91 ( $\text{OCH}_3$ ); 55.01 ( $\alpha$ -CH-Ile); 59.0 ( $\alpha$ -CH-Ser); 61.62 ( $\beta$ - $\text{CH}_2$ -Ser); 78.22 ( $\text{C}(\text{CH}_3)_3$ -Boc); 129.0, 146.5, 162.08 (3 C-Thz); 155.67 (CO-Boc); 170.2, 170.64, 171.31 (3 CO).

**Boc-Ile-Thr-(Gly)Thz-OMe (11):** analogous (10). Yield 87%.  $^1\text{H-NMR}$ :  $\delta_{\text{H}}$  : ( $\text{d}_6$ -DMSO, 200 MHz): 0.81 (m, 6H,  $\gamma$ - $\text{CH}_3$ -Ile und  $\delta$ - $\text{CH}_3$ -Ile); 1.05 (m, 5H,  $\delta$ - $\text{CH}_2$ -Ile und  $\text{CH}_3$ -Thr); 1.38 (s, 9H,  $\text{CH}_3$ -Boc); 1.69 (m, 1H,  $\beta$ -CH-Ile); 3.82 (s, 3H,  $\text{OCH}_3$ ); 3.90-4.95 (mehrere m, 6H,  $\text{CH}_2$ -Gly,  $\alpha$ -CH-Thr,  $\alpha$ -CH-Ile,  $\beta$ -CH-Thr); 8.46 (s, 1H, CH-Thz); 7.59, 8.46, 8.69 (3m, 3H, NH-Ile, NH-Thr, NH-Gly);  $\delta_{\text{C}}$  : ( $\text{d}_6$ -DMSO, 50.32 MHz): 10.95 ( $\gamma$ - $\text{CH}_3$ -Ile); 15.40 ( $\delta$ - $\text{CH}_3$ -Ile); 19.82 ( $\text{CH}_3$ -Thr); 24.37 ( $\delta$ - $\text{CH}_2$ -Ile); 28.12 ( $\text{CH}_3$ -Boc); 36.00 ( $\beta$ -CH-Ile); 38.21 ( $\text{CH}_2$ -Gly); 51.91 ( $\text{OCH}_3$ ); 58.04 ( $\alpha$ -CH-Ile); 59.06 ( $\alpha$ -CH-Thr); 66.46 ( $\beta$ -CH-Thr); 78.22 ( $\text{C}(\text{CH}_3)_3$ -Boc); 129.43, 145.11, 161.11 (3 C-Thz); 155.67 (CO-Boc); 170.21, 170.63, 171.41 (3 CO).

**Boc-Ile-Ser-(Gly)Thz-OH (12):** Boc-Ile-Ser-(Gly)Thz-OMe (620 mg; 1.31 mmol) was dissolved in THF/water and an aqueous solution of  $\text{LiOH}\cdot\text{H}_2\text{O}$  was slowly added dropwise. The reaction was monitored with thin layer chromatography. After

completion, THF was evaporated and the solution was diluted with water and subsequently treated as in (3) after evaporation of methanol (using diluted HCl as an acid). Yield: 83%.  $^1\text{H-NMR}$ :  $\delta_{\text{H}}$  : ( $\text{d}_6$ -DMSO, 200 MHz): 0.80 (m, 6H,  $\gamma$ - $\text{CH}_3$ -Ile und  $\delta$ - $\text{CH}_3$ -Ile); 1.17 (m, 2H,  $\delta$ - $\text{CH}_2$ -Ile); 1.41 (s, 9H,  $\text{CH}_3$ -Boc); 1.75 (m, 1H,  $\beta$ -CH-Ile); 3.30-5.10 (mehrere m, 6H,  $\text{CH}_2$ -Gly,  $\alpha$ -CH-Ser,  $\alpha$ -CH-Ile,  $\beta$ - $\text{CH}_2$ -Ser); 8.40 (s, 1H, CH-Thz); 6.90, 7.85, 8.90 (3m, 3H, NH-Ile, NH-Ser, NH-Gly);  $\delta_{\text{C}}$  : ( $\text{d}_6$ -DMSO, 50.32 MHz): 11.16 ( $\gamma$ - $\text{CH}_3$ -Ile); 15.43 ( $\delta$ - $\text{CH}_3$ -Ile); 24.33 ( $\delta$ - $\text{CH}_2$ -Ile); 28.19 ( $\text{CH}_3$ -Boc); 36.62 ( $\beta$ -CH-Ile); 38.26 ( $\text{CH}_2$ -Gly); 55.01 ( $\alpha$ -CH-Ile); 59.1 ( $\alpha$ -CH-Ser); 61.63 ( $\beta$ - $\text{CH}_2$ -Ser); 78.22 ( $\text{C}(\text{CH}_3)_3$ -Boc); 129.0, 146.5, 162.08 (3 C-Thz); 155.67 (CO-Boc); 170.2, 170.64, 171.31 (3 CO).

**HCl·Boc-Ile-Thr-(Gly)Thz-OMe (13):** Boc-Ile-Thr-(Gly)Thz-OMe (350 mg; 0.72 mmol) was dissolved in 20 ml methanol and cooled to 0°C. Then approximately 30% volume (6 ml) of a saturated HCl in dioxane was added slowly, dropwise. The reaction was monitored with thin layer chromatography. After completion, the solvents were evaporated and the crude product was recrystallized from ethanol/diethylether. Yield: 84%.  $^1\text{H-NMR}$ :  $\delta_{\text{H}}$  : ( $\text{d}_6$ -DMSO, 200 MHz): 0.85 (m, 6H,  $\gamma$ - $\text{CH}_3$ -Ile und  $\delta$ - $\text{CH}_3$ -Ile); 1.05 (d, 3H,  $\text{CH}_3$ -Thr,  $^3J_{\text{HH}}$ : 7.3 Hz); 1.15 (m, 2H,  $\delta$ - $\text{CH}_2$ -Ile); 1.59 (m, 1H,  $\beta$ -CH-Ile); 3.80 (s, 3H,  $\text{OCH}_3$ ); 3.60-4.65 (mehrere m, 6H,  $\text{CH}_2$ -Gly,  $\alpha$ -CH-Thr,  $\alpha$ -CH-Ile,  $\beta$ -CH-Thr); 8.46 (s, 1H, CH-Thz); 8.25 (breites s,  $\text{NH}_3^+$ ); 8.35, 8.62, 9.01 (3m, 3H, NH-Ile, NH-Thr, NH-Gly);  $\delta_{\text{C}}$  : ( $\text{d}_6$ -DMSO, 50.32 MHz): 11.68 ( $\gamma$ - $\text{CH}_3$ -Ile); 15.18 ( $\delta$ - $\text{CH}_3$ -Ile); 20.09 ( $\text{CH}_3$ -Thr); 25.33 ( $\delta$ - $\text{CH}_2$ -Ile); 38.00 ( $\beta$ -CH-Ile); 41.65 ( $\text{CH}_2$ -Gly); 52.92 ( $\text{OCH}_3$ ); 58.87 ( $\alpha$ -CH-Ile); 60.36 ( $\alpha$ -CH-Thr); 68.44 ( $\beta$ -CH-Thr); 130.08, 146.33, 162.65 (3 C-Thz); 169.73, 172.25, 172.34 (3 CO).

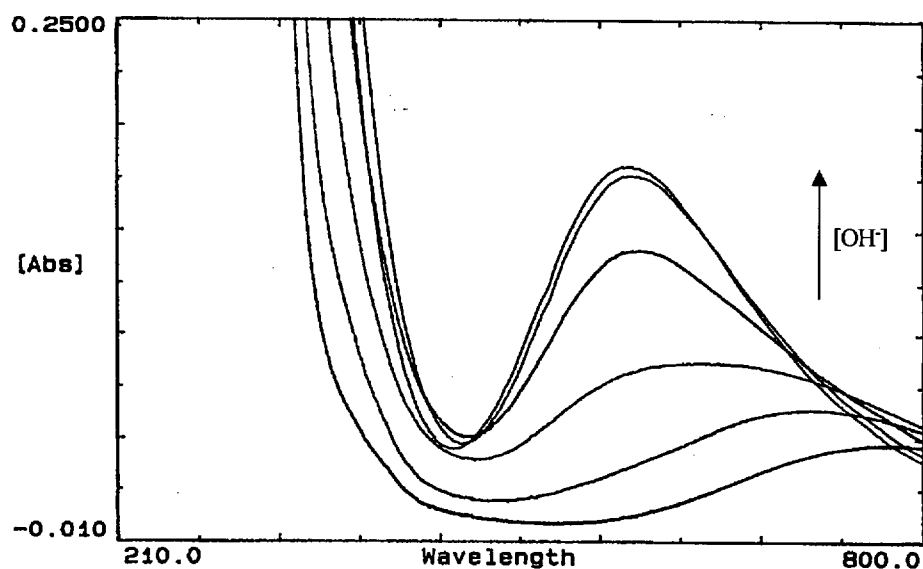
**Boc-Ile-Ser-(Gly)Thz-Ile-Thr-(Gly)Thz-OMe (14):** Boc-Ile-Ser-(Gly)Thz-OH (147 mg; 0.32 mmol) and N-methylmorpholine (98 mg; 0.96 mmol) were dissolved in methylenechloride and cooled to  $-20^{\circ}\text{C}$ . After addition of chloroformic acid ethylester (38 mg; 0.35 mmol) and stirring for 10 minutes, HCl·Boc-Ile-Thr-(Gly)Thz-OMe (136 mg; 0.32 mmol) was added. The reaction was stirred over night and allowed to reach room temperature. The mixture was diluted with methylenechloride and washed with 1 N aqueous  $\text{KHSO}_4$ , 1 N aqueous  $\text{KHCO}_3$ , and water, then dried over  $\text{Na}_2\text{SO}_4$ , filtered and the solvent evaporated. The crude product was recrystallized from  $\text{CH}_2\text{Cl}_2/\text{MeOH}/\text{diethylether}$ . Yield: 75%.  $^1\text{H-NMR}$ :  $\delta_{\text{H}}$ : ( $\text{d}_6$ -DMSO, 200 MHz): 0.8 (m, 6H, 2  $\gamma$ - $\text{CH}_3$ -Ile); 0.8 (m, 6H, 2  $\delta$ - $\text{CH}_3$ -Ile); 1.20 (m, 7H, 2  $\delta$ - $\text{CH}_2$ -Ile und  $\text{CH}_3$ -Thr); 1.41 (s, 9H,  $\text{CH}_3$ -Boc); 1.75 (m, 2H,  $\beta$ -CH-Ile); 3.85 (s, 3H,  $\text{OCH}_3$ ); 3.30-5.10 (mehrere m, 11H, 2  $\text{CH}_2$ -Gly,  $\alpha$ -CH-Ser, 2  $\alpha$ -CH-Ile,  $\beta$ - $\text{CH}_2$ -Ser,  $\beta$ -CH-Thr,  $\alpha$ -CH-Thr); 8.20, 8.45 (2s, 2H, 2 CH-Thz); 6.80-8.8 (6m, 6H, 2 NH-Ile, 2 NH-Ser, 2 NH-Gly);  $\delta_{\text{C}}$ : ( $\text{d}_6$ -DMSO, 50.32 MHz): 10.91, 11.13 (2  $\gamma$ - $\text{CH}_3$ -Ile); 15.40, 15.41 (2  $\delta$ - $\text{CH}_3$ -Ile); 20.00 ( $\text{CH}_3$ -Thr); 25.32, 25.44 (2  $\delta$ - $\text{CH}_2$ -Ile); 28.17 (3  $\text{CH}_3$ -Boc); 37.93, 38.30 (2  $\beta$ -CH-Ile); 41.73, 41.93 (2  $\text{CH}_2$ -Gly); 51.96 ( $\text{OCH}_3$ ); 54.94, 56.73 (2  $\alpha$ -CH-Ile); 58.52, 58.91 ( $\alpha$ -CH-Thr,  $\alpha$ -CH-Ser); 61.59 ( $\beta$ - $\text{CH}_2$ -Ser); 66.56 ( $\beta$ -CH-Thr); 78.22 ( $\text{C}(\text{CH}_3)_3$ -Boc); 124.67, 129.54, 145.15, 148.78, 159.87, 161.16 (6 C-Thz); 155.55 ( $\text{CO}$ -Boc); 170.27, 170.40, 170.55, 170.65, 170.84, 171.31 (6 CO).

**Boc-Ile-Ser-(Gly)Thz-Ile-Thr-(Gly)Thz-OH (15):** Boc-Ile-Ser-(Gly)Thz-Ile-Thr-(Gly)Thz-OMe (197 mg; 0.24 mmol) was dissolved in freshly distilled DMF and 0.24 ml of a 1 N aqueous NaOH solution were added. The mixture was stirred overnight and the reaction was monitored with thin layer chromatography. After completion, DMF was evaporated (the temperature should not rise above  $30^{\circ}\text{C}$ ) and the solution was diluted with water and subsequently treated as in (3) after evaporation

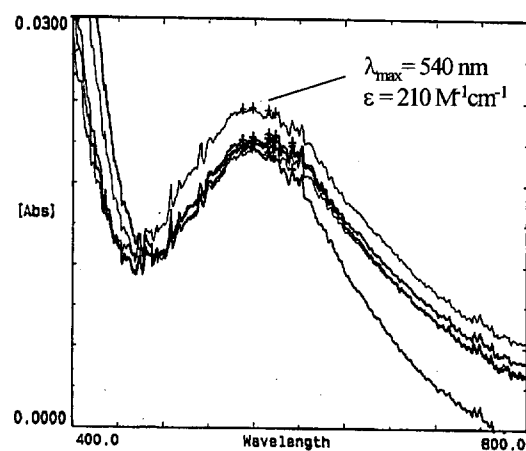
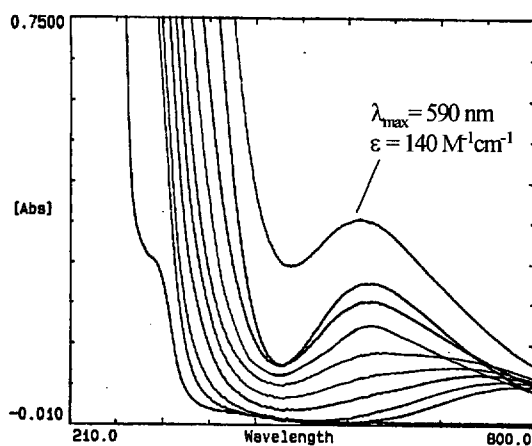


of methanol (using diluted HCl as an acid). If the mixture becomes a gel during extraction, a few drops of methanol can be added. Yield: 78%.  $^1\text{H-NMR}$ :  $\delta_{\text{H}}$ : ( $\text{d}_6$ -DMSO, 200 MHz): 0.80 (m, 6H, 2  $\gamma\text{-CH}_3\text{-Ile}$ ); 0.85 (m, 6H, 2  $\delta\text{-CH}_3\text{-Ile}$ ); 1.10 (m, 7H, 2  $\delta\text{-CH}_2\text{-Ile}$  und  $\text{CH}_3\text{-Thr}$ ); 1.42 (s, 9H,  $\text{CH}_3\text{-Boc}$ ); 1.65 (m, 2H,  $\beta\text{-CH-Ile}$ ); 3.20-5.00 (mehrere m, 11H, 2  $\text{CH}_2\text{-Gly}$ ,  $\alpha\text{-CH-Ser}$ , 2  $\alpha\text{-CH-Ile}$ ,  $\beta\text{-CH}_2\text{-Ser}$ ,  $\beta\text{-CH-Thr}$ ,  $\alpha\text{-CH-Thr}$ ); 8.17, 8.30 (2s, 2H, 2  $\text{CH-Thz}$ ); 6.70-8.2 (6m, 6H, 2  $\text{NH-Ile}$ , 2  $\text{NH-Ser}$ , 2  $\text{NH-Gly}$ );  $\delta_{\text{C}}$ : ( $\text{d}_6$ -DMSO, 50.32 MHz): 10.90, 11.16 (2  $\gamma\text{-CH}_3\text{-Ile}$ ); 15.40, 15.43 (2  $\delta\text{-CH}_3\text{-Ile}$ ); 19.98 ( $\text{CH}_3\text{-Thr}$ ); 23.07, 24.36 (2  $\delta\text{-CH}_2\text{-Ile}$ ); 28.43 (3  $\text{CH}_3\text{-Boc}$ ); 36.38, 36.56 (2  $\beta\text{-CH-Ile}$ ); 39.02, 39.29 (2  $\text{CH}_2\text{-Gly}$ ); 55.00, 56.86 (2  $\alpha\text{-CH-Ile}$ ); 58.65, 59.77 ( $\alpha\text{-CH-Thr}$ ,  $\alpha\text{-CH-Ser}$ ); 61.66 ( $\beta\text{-CH}_2\text{-Ser}$ ); 66.47 ( $\beta\text{-CH-Thr}$ ); 78.27 ( $\text{C}(\text{CH}_3)_3\text{-Boc}$ ); 124.67 - 161.16 (6  $\text{C-Thz}$ ); 155.55 ( $\text{CO-Boc}$ ); 169.62 – 174.62 (6  $\text{CO}$ ).

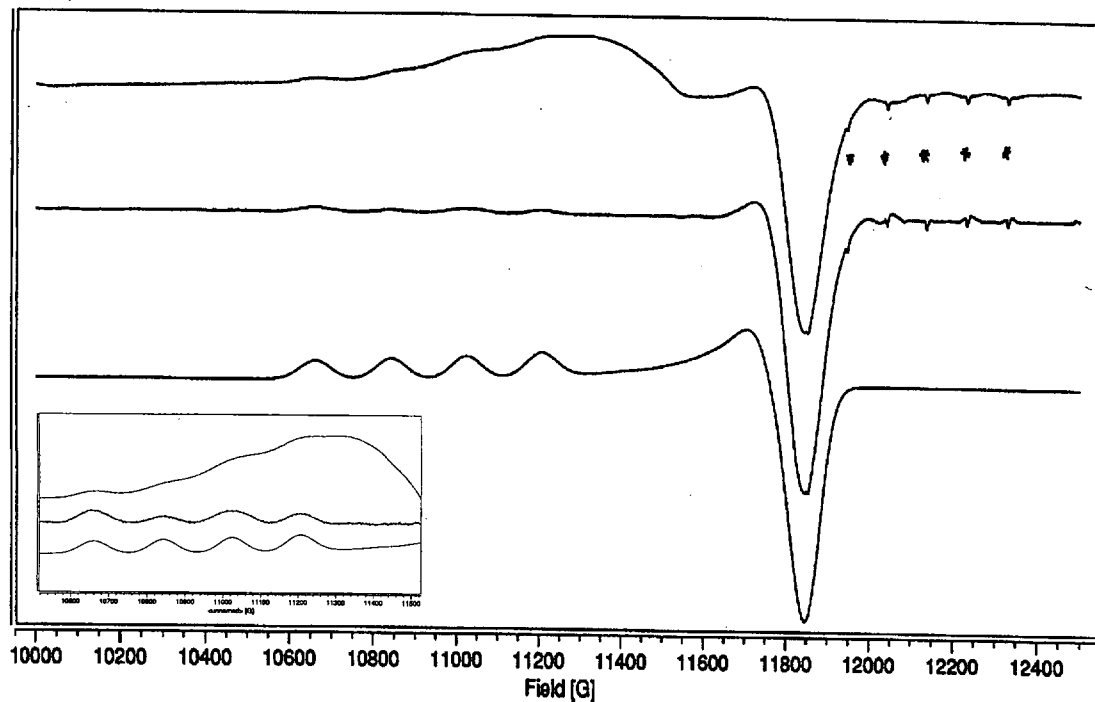
**HCl-Boc-Ile-Ser-(Gly)Thz-Ile-Thr-(Gly)Thz-OH (16):** analogous (13). Yield: 85%.  $^1\text{H-NMR}$ :  $\delta_{\text{H}}$ : ( $\text{d}_6$ -DMSO, 200 MHz): 0.9 (m, 6H, 2  $\gamma\text{-CH}_3\text{-Ile}$ ); 1.0 (m, 6H, 2  $\delta\text{-CH}_3\text{-Ile}$ ); 1.20 (m, 7H, 2  $\delta\text{-CH}_2\text{-Ile}$  und  $\text{CH}_3\text{-Thr}$ ); 1.65 (m, 2H,  $\beta\text{-CH-Ile}$ ); 3.70-4.90 (mehrere m, 11H, 2  $\text{CH}_2\text{-Gly}$ ,  $\alpha\text{-CH-Ser}$ , 2  $\alpha\text{-CH-Ile}$ ,  $\beta\text{-CH}_2\text{-Ser}$ ,  $\beta\text{-CH-Thr}$ ,  $\alpha\text{-CH-Thr}$ ); 8.15, 8.29 (2s, 2H, 2  $\text{CH-Thz}$ );  $\delta_{\text{C}}$ : ( $\text{d}_6$ -DMSO, 50.32 MHz): 11.39, 11.61 (2  $\gamma\text{-CH}_3\text{-Ile}$ ); 15.12, 16.00 (2  $\delta\text{-CH}_3\text{-Ile}$ ); 20.21 ( $\text{CH}_3\text{-Thr}$ ); 25.41, 26.08 (2  $\delta\text{-CH}_2\text{-Ile}$ ); 37.82, 38.41 (2  $\beta\text{-CH-Ile}$ ); 41.73, 41.93 (2  $\text{CH}_2\text{-Gly}$ ); 56.90, 59.00 (2  $\alpha\text{-CH-Ile}$ ); 59.52, 60.32 ( $\alpha\text{-CH-Thr}$ ,  $\alpha\text{-CH-Ser}$ ); 62.95 ( $\beta\text{-CH}_2\text{-Ser}$ ); 68.30 ( $\beta\text{-CH-Thr}$ ); 125.91, 129.76, 147.81, 149.83, 136.21, 163.99 (6  $\text{C-Thz}$ ); 169.60, 170.84, 171.51, 172.22, 172.83, 173.72 (6  $\text{CO}$ ).



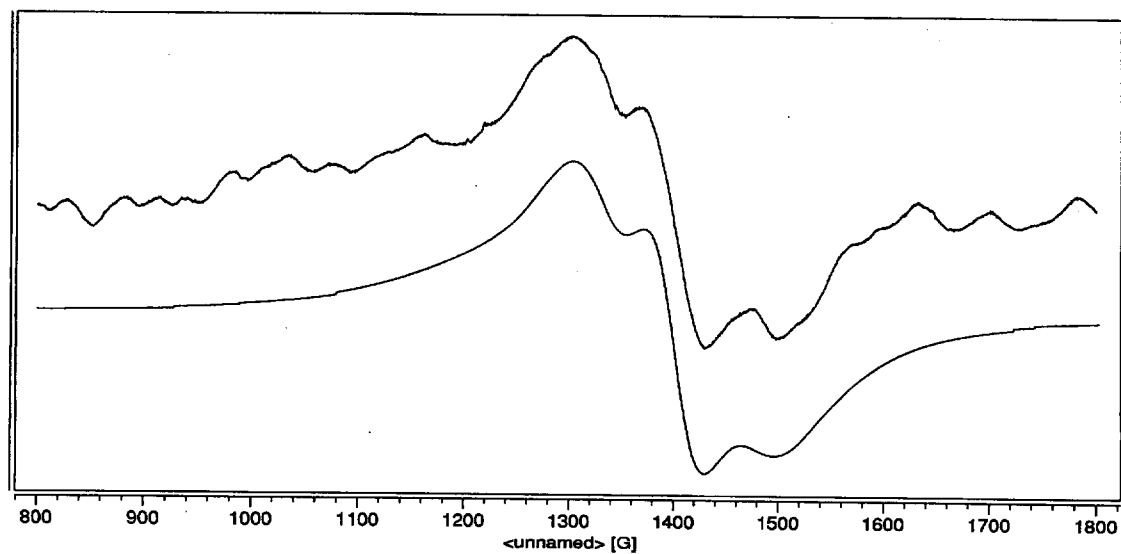
UV-vis titration of PatN and 1 equivalent of Cu(II) with triethylamine



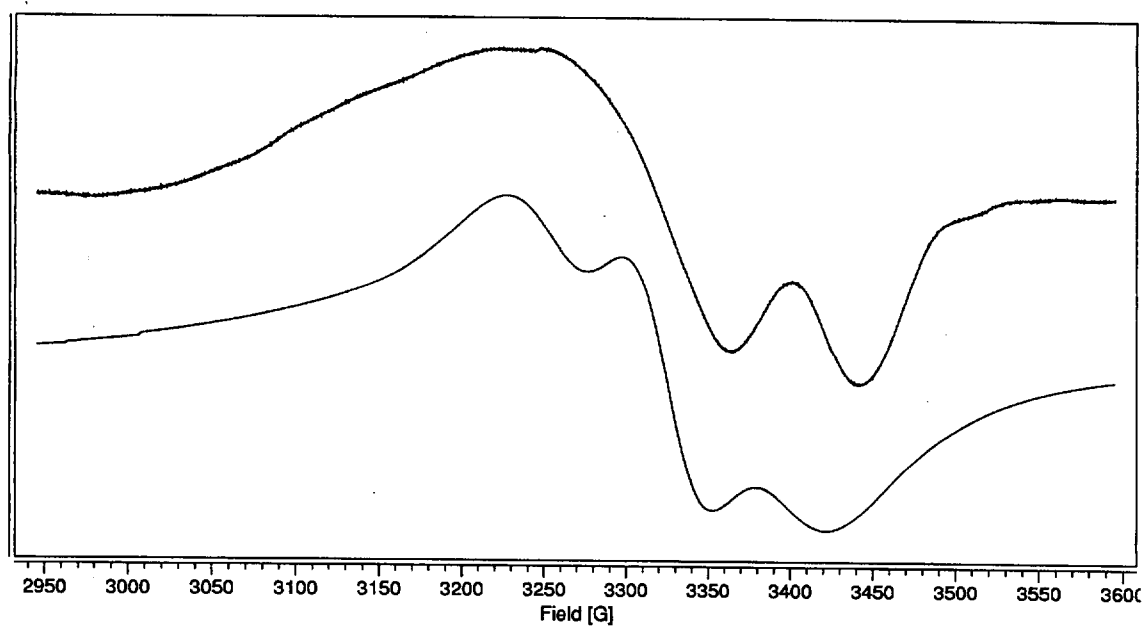
titration in presence of two equivalents of Cu(II); left: up to 8 equivalents of base (blue dicopper(II) complex); right: addition of 5-8 equivalents of base (purple complex)



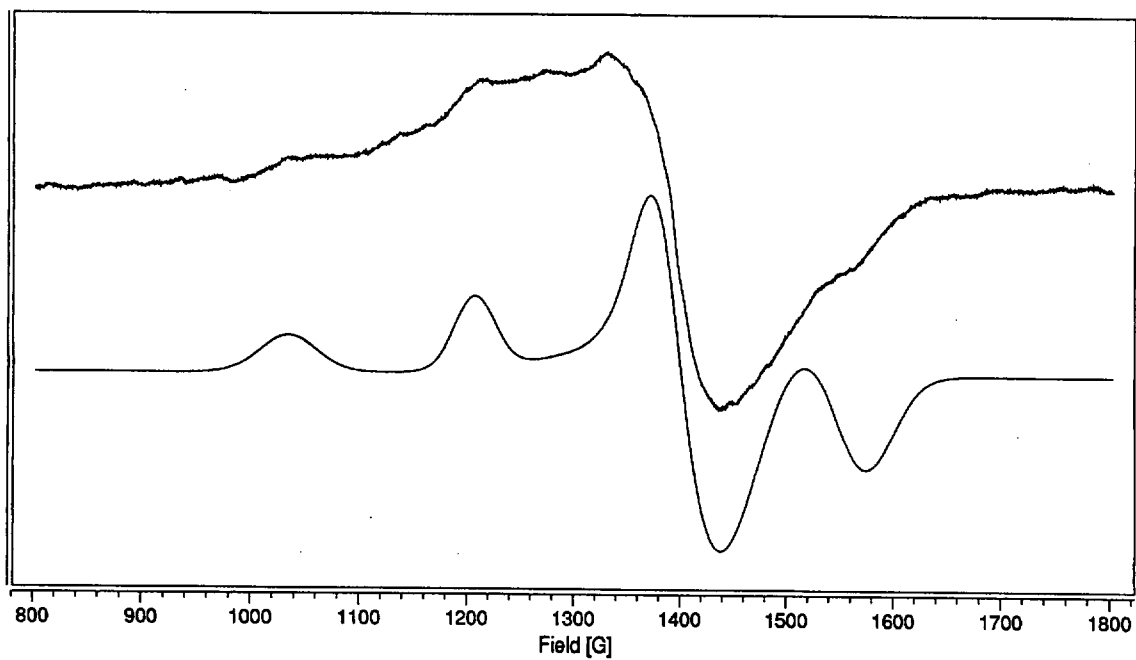
Q-band EPR spectra of the mononuclear PatN complex; top: experimental; middle: spectrum of dinuclear copper complex deducted from experimental spectrum; bottom: simulation



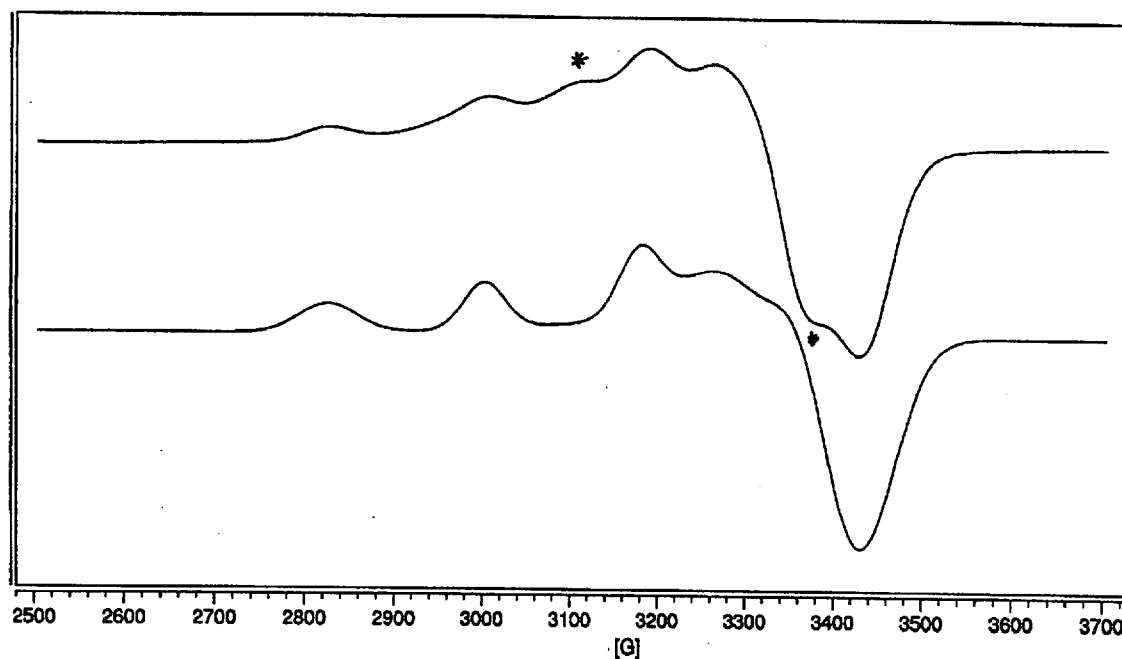
S-band spectrum of the mononuclear compound at ambient temperature; top: experimental; bottom: simulation



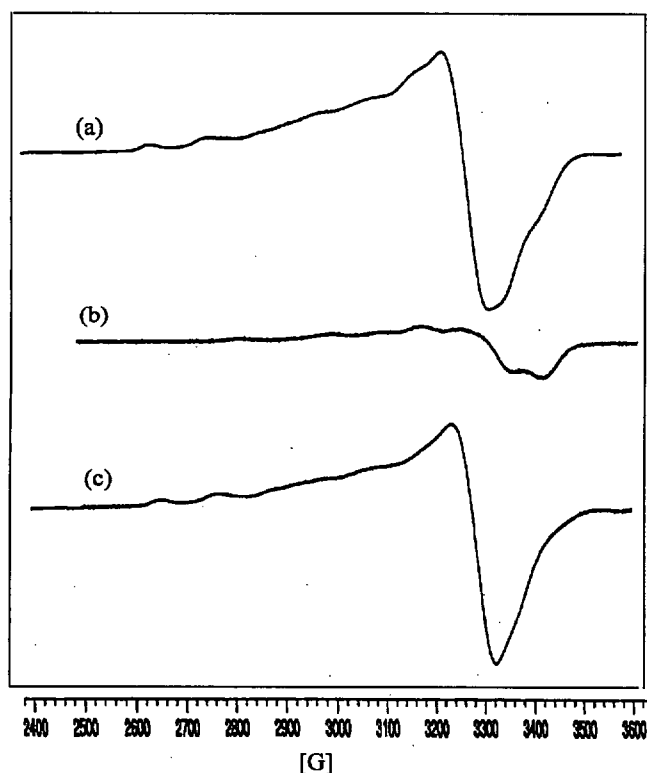
X-band spectrum of the mononuclear compound at ambient temperature; top: experimental, bottom: simulation



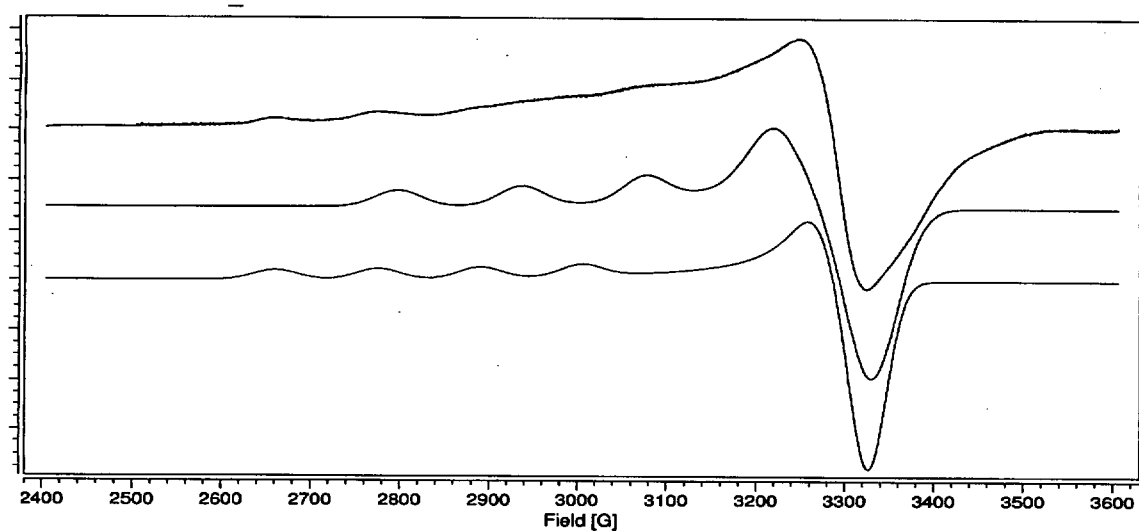
S-band spectrum of the mononuclear compound at 130K; top: experimental, bottom: simulation



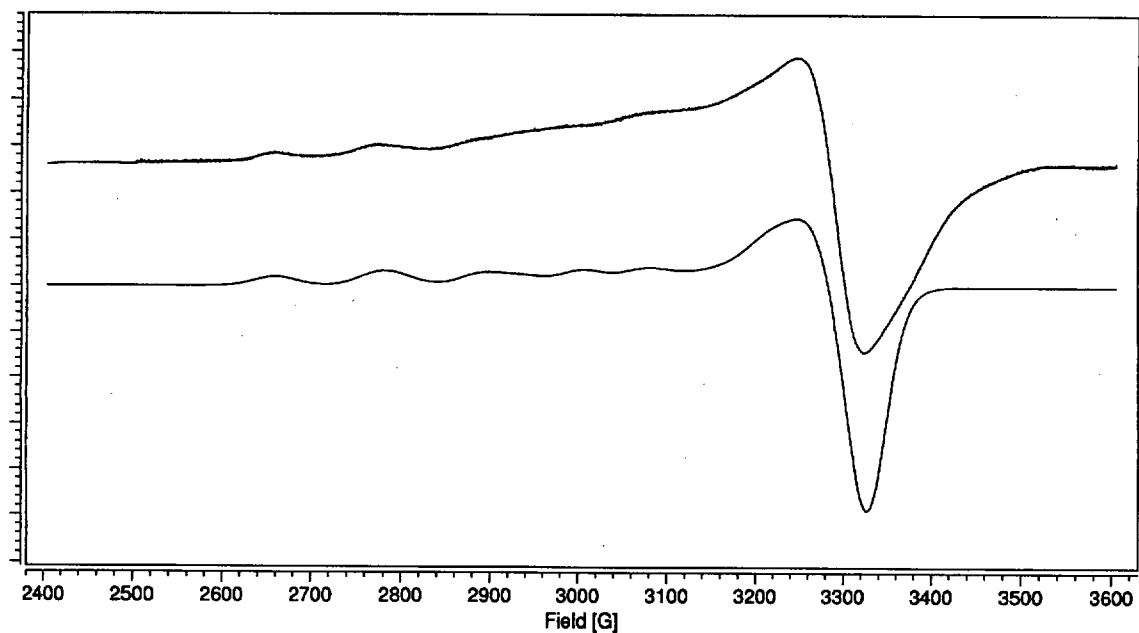
X-band spectrum of the mononuclear compound at 130K; asterisked signals are from the dinuclear compound; top: experimental; bottom: simulation



X-band spectra; top: PatN, 1 equivalent of Cu(II) and 1 equivalent of base; middle: as top but two equivalents of base (monoI); bottom: {a-0.1b}, that is monoII and monoIII



X-band spectra (as Figure above); top {a-0.1b}; middle: simulation of monoIII; bottom: simulation of monoII



X-band spectra (as above); top {a-0.1b}; bottom: simulation (2.327 monoII) + monoIII