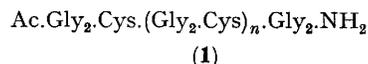


## Direct Formation of Peptide Analogues of Rubredoxins and Four-iron Ferredoxins from their Components

By GEORGE CHRISTOU, BRIAN RIDGE, and H. N. RYDON\*  
(Department of Chemistry, The University, Exeter EX4 4QD)

**Summary** Cysteine peptides react with iron(III) chloride in dimethyl sulphoxide in the presence of base to form rubredoxin analogues (**2**), which are converted by addition of aqueous sodium sulphide into four-iron ferredoxin analogues (**4**).

The reactions between a number of cysteine peptides, iron(III) chloride, and sodium sulphide, in the presence of base, in dimethyl sulphoxide under strictly anaerobic conditions was studied spectroscopically. The results for the tetracysteine peptide (**1**;  $n = 3$ )<sup>2</sup> are shown in the Figure. Addition of triethylamine to a solution of the



ALTHOUGH peptide analogues of four-iron ferredoxins have been prepared by ligand exchange of cysteine peptides with the cluster compound  $[\text{Fe}_4\text{S}_4(\text{SBU}^t)_4]^{2-}$ , their direct synthesis from their components has not previously been achieved.<sup>1</sup> We now report their formation, in solution, from their components; the corresponding rubredoxin analogues are intermediates in the process, thus establishing a direct experimental link between these two major types of iron-sulphur protein.

peptide and iron(III) chloride results in the immediate appearance of a red-violet colour; at this stage the spectrum (curve B) is very similar to those of the oxidised rubredoxins<sup>3</sup> and of (**2**;  $4\text{SR} = 2\text{SCH}_2\text{C}_6\text{H}_4\text{CH}_2\text{S}$ )<sup>4</sup> and it seems clear that the solution contains the oxidised rubredoxin analogue [**2**;  $4\text{SR} = (\mathbf{1}; n = 3)$ ].<sup>5</sup> The colour fades

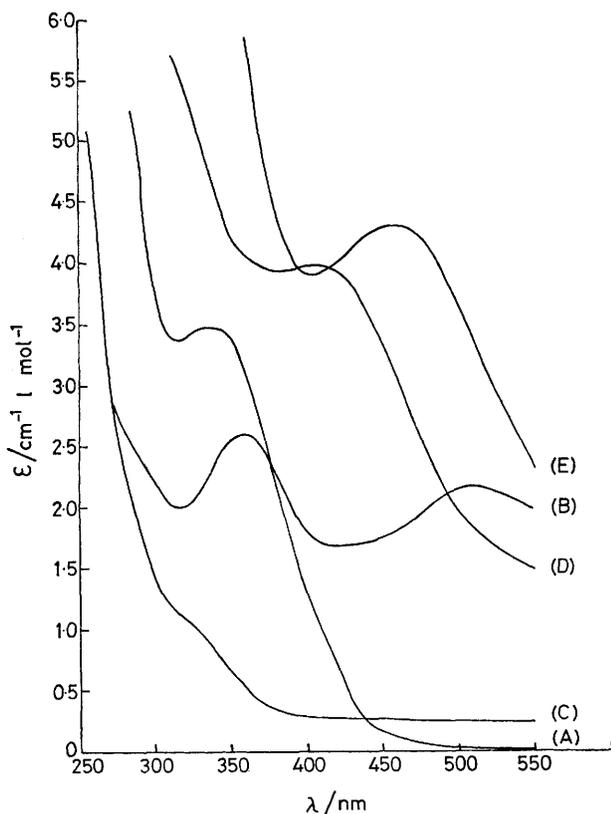
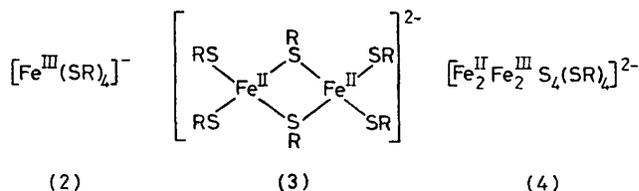


FIGURE. (A),  $\text{FeCl}_3$  ( $1.2 \mu\text{mol}$ ) and (**1**;  $n = 3$ ) ( $1.5 \mu\text{mol}$ ) in  $\text{Me}_2\text{SO}$ ; (B), as (A) plus  $\text{NEt}_3$  ( $6.0 \mu\text{mol}$ ) immediately after mixing; (C), as (B) after 5 min; (D), as (C) plus  $\text{Na}_2\text{S}$  ( $1.96 \mu\text{mol}$ ) and  $\text{H}_2\text{O}$  ( $2.4\%$ ); (E), as (D) plus  $\text{PhSH}$  ( $20 \mu\text{mol}$ ). The values of  $\epsilon$  are based on the molar concentration of Fe, however combined.



rapidly and the final spectrum (curve C), observed after 5 min, is consistent with the major component at this stage being the dimeric bridged compound [**3**;  $4\text{SR} = (\mathbf{1}; n = 3)$ ], the *o*-xylylene analogue of which was prepared by Holm *et al.*;<sup>4</sup> the shoulder at *ca.* 315 nm is ascribed to the presence of some reduced ( $\text{Fe}^{\text{II}}$ ) rubredoxin analogue, resulting from the reduction of (**2**) by excess of peptide present in the reaction mixture. Addition of sodium sulphide results in the rapid development of a stable golden-brown colour and a spectrum (curve D) identical with that of the four-iron ferredoxin analogue [**4**;  $4\text{SR} = (\mathbf{1}; n = 3)$ ], prepared by ligand exchange between the peptide (**1**;  $n = 3$ ) and the cluster compound (**4**;  $\text{R} = \text{Bu}^t$ ). The presence of the ferredoxin analogue is supported by the e.s.r. spectrum and confirmed by the addition of an excess of benzenethiol, which causes the rapid development of a spectrum (curve E), identical with that of the independently synthesised phenyl cluster compound (**4**;  $\text{R} = \text{Ph}$ );<sup>1</sup> the intensity of absorption at 458 nm shows that 98% of the original iron(III) chloride has been converted into (**4**;  $\text{R} = \text{Ph}$ ). Similar results have been obtained with several other cysteine peptides, *e.g.* (**1**;  $n = 0, 1, \text{ and } 2$ ).

This is the first time that peptide analogues of four-iron ferredoxins have been prepared directly from their components. The method is rapid and especially useful for the

preparation of such analogues in solution for studies of physical properties (*e.g.*, e.s.r. spectra) for which the isolated compounds are not needed.

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<sup>1</sup> Cf. L. Que, J. R. Anglin, M. A. Bobrik, A. Davison, and R. H. Holm, *J. Amer. Chem. Soc.*, 1974, **96**, 6042; B. V. De Pamphilis, B. A. Averill, T. Herskovitz, L. Que, and R. H. Holm, *ibid.*, p. 4159.

<sup>2</sup> R. J. Burt, B. Ridge, and H. N. Rydon, unpublished work; R. J. Burt, Ph.D. Thesis, University of Exeter, 1975.

<sup>3</sup> W. Lovenberg and B. E. Sobel, *Proc. Nat. Acad. Sci. U.S.A.*, 1965, **54**, 193.

<sup>4</sup> R. W. Lane, J. A. Ibers, R. B. Frankel, and R. H. Holm, *Proc. Nat. Acad. Sci. U.S.A.*, 1975, **72**, 2868.

<sup>5</sup> The formation of a reduced rubredoxin analogue from Boc.(Gly.Cys.Gly)<sub>4</sub>.NH<sub>2</sub> and iron(II) chloride in Me<sub>2</sub>SO solution has been reported by J. R. Anglin and A. Davison, *Inorg. Chem.*, 1975, **14**, 234.