

## The Preparation of $\alpha$ -Hydroxymethylserine

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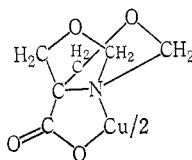
### Abstract

Convenient methods for the preparation of  $\alpha$ -hydroxymethylserine in high yield by the treatment of the copper(II) complex of dihydro-1*H*,3*H*,5*H*-oxazolo[3,4-*c*]oxazole-7*a*-carboxylic acid with hydrogen sulphide or by catalytic hydrogenation of the complex are described.

Several methods<sup>1,2</sup> have been described for the preparation of the amino acid  $\alpha$ -hydroxymethylserine. The first, due to Christensen<sup>1</sup> involves the treatment of an acidic aqueous solution of tris(hydroxymethyl)aminomethane with barium permanganate solution. In our hands the method was unreliable and the yield was usually less than 30%.

A more successful preparation<sup>2</sup> involves a metal ion assisted condensation of formaldehyde and glycine in the presence of cupric sulphate. The aqueous reactants are heated at 100° for 2 h in the presence of 1 M sodium carbonate. Although ion exchange treatment of the acidified filtrate gives yields of approximately 80% of the amino acid in some preparations, the result is not reproducible and much lower yields are normally obtained. Significant decomposition often occurs during heating.

The synthesis, characterization and some reactions of the copper(II) complex (1) of dihydro-1*H*,3*H*,5*H*-oxazolo[3,4-*c*]oxazole-7*a*-carboxylic acid have been recently reported.<sup>3,4</sup> The complex is readily prepared by the reaction of aqueous formaldehyde and basic bis((*S*)-serinato)copper(II).



(1)

<sup>1</sup> Christensen, H. N., *Biochem. Prep.*, 1958, **6**, 49.

<sup>2</sup> Otani, T. T., and Winitz, M., *Arch. Biochem. Biophys.*, 1960, **90**, 254.

<sup>3</sup> Brush, J. R., Magee, R. J., Teo, S. B., O'Connor, M. J., Geue, R. J., and Snow, M. R., *J. Am. Chem. Soc.*, 1973, **95**, 2034.

<sup>4</sup> O'Connor, M. J., Smith, J. F., and Teo, S. B., *Aust. J. Chem.*, 1976, **29**, 375.

It has been shown that treatment of (1) under the basic conditions of sodium borohydride reduction causes removal of the copper without ring cleavage<sup>4</sup> whereas catalytic hydrogenation or treatment with hydrogen sulphide gives high yields of  $\alpha$ -hydroxymethylserine.

The copper(II) complex is simple to prepare in quantity and the two treatments to remove the copper(II) ion and cleave the oxazolidine rings which are described in the present paper are less involved than previous methods which have been used to prepare  $\alpha$ -hydroxymethylserine.

## Experimental

### Reagents

Adams platinum catalyst<sup>5</sup> was prepared from chloroplatinic acid.

Bis(dihydro-1*H*,3*H*,5*H*-oxazolo[3,4-*c*]oxazole-7*a*-carboxylato)copper(II) (1) was prepared by the reaction of formaldehyde with basic bis(*S*-serinato)copper(II).<sup>3,4</sup>

### Hydrogenation Apparatus

An instrument manufactured by the Parr Instrument Company (U.S.A.) was used for the hydrogenation under pressure.

### Hydrogenation of Copper(II) Complex (1)

The finely ground copper(II) complex (3.0 g) and freshly prepared Adams catalyst (0.2 g) were slurried with distilled water (50 cm<sup>3</sup>) and hydrogenation of the slurry was carried out at 60 p.s.i. at room temperature until no further uptake of hydrogen was observed (16 h). At this stage the colourless solution was filtered and the filtrate was poured with vigorous stirring into absolute ethanol (600 cm<sup>3</sup>). The resultant white solid was collected, dried and then recrystallized from water/ethanol (50% volume/volume). The white crystals obtained were collected and dried in a vacuum for 5 h at 50°C. Yield 1.7 g (80%), m.p. 242–243° (Found: C, 35.9; H, 6.6; N, 10.5. Calc. for C<sub>4</sub>H<sub>9</sub>NO<sub>4</sub>: C, 35.6; H, 6.7; N, 10.4%).

### Reaction of Hydrogen Sulphide with Copper(II) Complex (1)

A stirred and warmed (approximately 45°C) slurry containing the copper(II) complex (1.5 g) in distilled water (30 cm<sup>3</sup>) was saturated with hydrogen sulphide. After all the copper had been precipitated as the black sulphide, the mixture was filtered and excess hydrogen sulphide was removed by heating the stirred solution at approximately 80°C for 1–2 h.

The slightly yellow coloured solution was poured into absolute ethanol (600 cm<sup>3</sup>) and the white precipitate was treated as above to give white crystals, yield 0.9 g (85%), m.p. 242–243°.

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<sup>5</sup> Adams, R., Vorhees, V., and Shriner, R. L., *Org. Synth.*, 1941, Coll. Vol. I, 463.