

The Preparation of 1,2-Dithiolane-4-carboxylic Acid

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In order to complete an investigation of the substituent influence on the spectral behaviour of the disulphide group in 1,2-dithiolane derivatives^{1,2}, it seemed important to include 1,2-dithiolane-4-carboxylic acid.

The related dimercaptan, β,β' -dimercapto-*isobutyric* acid, was first obtained in 1948 by Jansen³ upon reduction of a sulphur-containing polymeric material isolated from asparagus juice. The mercapto acid appeared to be the first dithiol substance reported from a natural source. The structural proof involved identification of the methylated compound with authentic β,β' -di-methylmercapto-*isobutyric* acid (obtained from the related di-iodo acid and methyl mercaptan). Recently the preparation of β,β' -dimercapto-*isobutyric* acid was described by Corse and Jansen⁴. Reduction of β,β' -dibenzylmercapto-*isobutyric* acid with sodium in liquid ammonia yielded the expected substance, whereas hydrolysis of the related di-*isothiuronium* salt was unsuccessful.

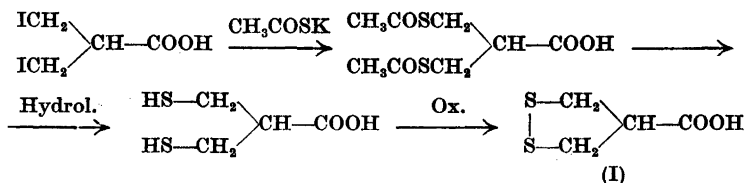
1,2-Dithiolane-4-carboxylic acid (I) has now been prepared from the mercaptan (without intermediate isolation) by oxidation with oxygen⁵. The β,β' -dimercapto-*isobutyric* acid was obtained from the corresponding di-iodo compound^{3,6} and potassium thiolacetate with subsequent hydrolysis of the bis-acetyl substance formed.

The spectrochemical (UV and IR) and polarographic properties of (I) have been discussed in a previous communication³ where also comparison was made with the 3-isomer, prepared by Claesson⁷.

The presence of disulphide in asparagus juice has been qualitatively shown by Jansen. His results might suggest that the disulphide material present in asparagus is of polymeric nature but the experience of the present authors indicates that the conditions used by Jansen³ were not mild enough to ensure the isolation of a possible monomer. As the 1,2-dithiolane system is reactive (*cf.* 6-thioctic acid) and cleavage of the S—S bond with formation of polymers readily occurs, it seems reasonable to assume the presence of (I) in the plant. In view of the properties of 6-thioctic acid it will therefore be very interesting to find out if the occurrence of the reactive ring system is in some way important for the biochemical processes in the rapidly growing asparagus.

Both the monomeric disulphide and the polymer give β,β' -dimercapto-*isobutyric* acid when reduced according to Fredga⁸ with zinc in ammoniacal solution. The data of the mercapto acid coincide with those previously reported.

Experimental. 1,2-Dithiolane-4-carboxylic acid. 11 g (0.032 mole) of β,β' -diiodo-*isobutyric* acid was suspended in 40 ml of water and neutralized with an aqueous solution (40 ml) of 2.1 g (0.032 mole) of 86% KOH. A solution of 5.2 g (0.0685 mole) of thiolacetic acid and 4.45 g (0.0685 mole) of 86% KOH in 40 ml of water was added dropwise, and the mixture heated in an oil bath at 80° for 8 hours. Acidification with dilute H₂SO₄ caused precipitation of the bis-acetylmercapto acid as a heavy oil. After its separation the product



The disulphide acid obtained was contaminated with polymeric material, which, however, could be removed by treatment with benzene in which the polymers are insoluble. Recrystallized from benzene-cyclohexane (I) was obtained as transparent yellow prisms.

was dissolved in 100 ml of KOH water solution (containing 10 g (0.154 mole) of 86% KOH). The mixture was kept at room temperature for 16 hours and then acidified (dil. H₂SO₄). The mercapto acid was extracted five times with ether. The substance remaining after spontaneous evaporation of the dried solvent was

dissolved (without previous purification) in 400 ml of aqueous NaHCO_3 solution (containing 8.5 g (0.10 mole) of NaHCO_3). A small amount of FeCl_3 was added as a combined catalyst and indicator and oxygen bubbled through the mixture until the violet colour disappeared (about two hours). After acidification (dil. H_2SO_4) and removal of small amounts of polymeric material by filtration the product was extracted with ether (6×75 ml). The ether solution was dried with anhydrous Na_2SO_4 and the solvent evaporated (*in vacuo*). 1.3 g (27 %) of crude acid (mixture of monomer and polymer) with m. p. $60-70^\circ$ was obtained; after treatment with benzene for some minutes at room temperature it left an insoluble viscous substance. Evaporation of the solvent yielded 0.8 g (16.5 %) of dry acid (monomer) with m. p. $75-77^\circ$. This product was now recrystallized from benzene-cyclohexane and obtained as transparent yellow prisms with m. p. $76.5-77.5^\circ$. (Found: Equiv. wt. 151.1; C 31.96; H 3.92; S 42.72; Mol. wt. 146. Calc. for $\text{C}_7\text{H}_6\text{O}_2\text{S}_2$ (150.22): Equiv. wt. 150.2; C 31.98; H 4.03; S 42.68; Mol. wt. 150).

β, β' -Dimercapto-isobutyric acid. 0.5 g of (I) or the related polymer (insoluble in benzene) was dissolved in 20 ml of 4 M ammonia, and the solution sucked through a layer of zinc powder four times. The reaction mixture was neutralized with dil. H_2SO_4 and the precipitated zinc mercaptide filtered. The acid was liberated and extracted with ether. Evaporation of the solvent gave the dimercapto acid, which crystallized after being kept for some days at -15° . M. p. $57-60^\circ$. (Found: Equiv. wt. 75.7. Calc. for $\text{C}_4\text{H}_4\text{O}_2\text{S}_2$ (152.22): 76.1).

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Ein Beispiel für die Variationsmöglichkeiten in der Zusammensetzung der freien Aminosäuren in einer Pflanzenart

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Im Sommer 1954 isolierten Virtanen, Uksila und Matikkala¹ α -Amino- γ -hydroxy-pimelinsäure aus *Asplenium septentrionale*. Das Pflanzenmaterial war in den Monaten Mai, Juni, Juli und August gesammelt und gesondert auf seinen Aminosäuregehalt geprüft worden. Alle Alkoholextrakte zeigten im zwei-dimensionalen Papierchromatogramm (Butanol-Essigsäure- H_2O und Phenol-Ammoniak) die in Fig. 1 A dargestellte Zusammensetzung. Vom gleichen Standort wurde im August 1955—Juni und Juli waren aussergewöhnlich trocken — *Asplenium septentrionale* geerntet und der Alkoholextrakt dieses Materials ergab das Chromatogramm in Fig. 1 B, auf dem zwischen Asparaginsäure und Glutaminsäure ein Ninhydrinpositiver Fleck sichtbar ist.

Die Trennung dieser Aminosäure von Asparaginsäure und Glutaminsäure gelang zum Teil an Dowex 50 (200—400 mesh) mit 0.2 M Natriumcitratpuffer pH 3,48². Die Lage der Aminosäure im Chromatogramm deutete auf die von Steward *et al.*³ aus *Adiantum pedatum* und von Virtanen und Berg⁴ aus *Phyllitis scolopendrium* isolierte γ -Hydroxy- γ -methylglutaminsäure hin.

Die Reduktion mit 66 % HJ ($d = 1.9$) und rotem Phosphor bei 130°C für 4 Stdn. ergab Methylglutaminsäure. Nach Oxydation mit KMnO_4 in saurer Lösung erhielten wir im Chromatogramm einen gelben Flecken im Bereich der neutralen Aminosäuren, den wir bisher nicht identifiziert haben. Die reine Substanz enthält Kristallwasser, welches durch Erhitzen auf 105°C für 16 Stdn. mit $\frac{1}{2}$ H_2O pro Mol. bestimmt wurde. Dies stimmt mit dem von Steward nach Elementaranalyse gefundenen Wert überein.

Der Perjodat-test auf nachbarständige Hydroxy- und Aminogruppe war negativ. N-Bestimmung: gef. 8.03 %; theor. 7.53 %. Die Substanz verkohlt ab 165° . Papier-