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Short Communications

1,2-Dithiolane and Thietane Derivatives Related to Levulinic Acid

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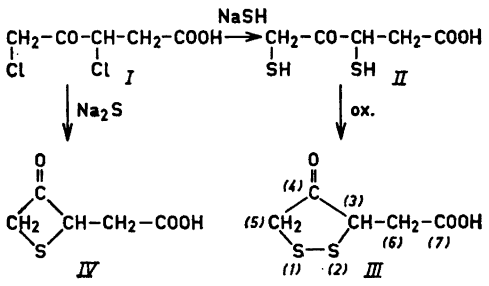
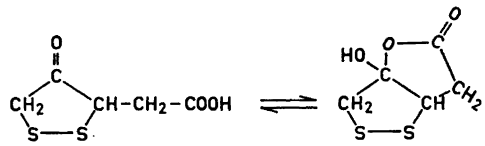
In previous communications [1,2] we have described syntheses of 3,3,5,5-tetramethyl-1,2-dithiolane-4-one and 2,2,4,4-tetramethyl-thietane-3-one. In the present paper we wish to report syntheses of new derivatives of the same ring systems.

Motoki [3] has prepared 3,5-dichlorolevulinic acid (I), the structure of which has been verified from its NMR spectrum.[4] We treated the dichloro-acid with sodium hydrosulphide, thus obtaining a dimercapto acid the NMR spectrum of which was compatible with structure II. Iodine oxidation of the mercapto acid gave the cyclic



disulphide III in the form of pale yellow crystals with m.p. 61–63°; the observed signals of the NMR spectrum (chloroform solution) are in accordance with those expected for this compound. The carboxylic proton gives a signal at $\tau = -1.20$. Due to the asymmetric carbon atom 3, the two $6-CH_2$ protons are slightly non-equivalent (even if the rotation around C_3-C_6 might be rapid). They are also split by the 3–CH proton and give the quartet at $\tau = 7.05$. The 3–CH proton produces the quartet at $\tau = 6.03$. The remaining $5-CH_2$ protons seem to be so nearly equivalent that they give rise to a single peak at $\tau = 6.61$.

The infra-red spectra in chloroform solution and in KBr are quite different and indicating the existence of keto-lactol tautomerism:



An infra-red absorption band in the OH stretching region was observed at 3420 cm^{-1}, and a C=O absorption band at 1773 cm^{-1}. These bands were present in the KBr phase spectrum but not in that of the chloroform solution. They are attributed to the lactol-form of the acid.

The UV spectrum of the disulphide is similar to that of 3,3,5,5-tetramethyl-1,2-dithiolane-4-one [1] and thus in good agreement with the structure of the cyclic ketodisulphide III.

The thietane derivative IV was prepared from the dichlorolevulinic acid and sodium sulphide. The NMR spectrum of IV resembles that of the corresponding disulphide III, verifying structure IV.

Experimental. 3,5-Dichlorolevulinic acid. Motoki's procedure [3] was used with some modification. Chlorine was bubbled through a solution of 232 g (2 mole) of levulinic acid in 200 ml of chloroform at such a rate that moderate

reflux was maintained. When heat evolution ceased and the mixture became yellow (after about 8 h) the chlorine-inflow was stopped and the solution left at −15° overnight for crystallization. 159 g (43 %) of crude acid were obtained and dried on a porous plate; m.p. 72−76°. Recrystallization from chloroform gave colourless needles of pure 3,5-dichlorolevulinic acid, which was identified by its NMR spectrum [4] (*cf.* 3,5-dibromolevulinic acid [5]). The yield was 101 g (27 %), m.p. 85−86° (Seissl [6] 77°; Overend *et al.*[7] 77°). (Found: C 32.51; H 3.27; Cl 38.15. Calc. for $C_5H_6O_3Cl_2$ (185.01): C 32.46; H 3.27; Cl 38.33). IR spectrum (KBr phase) showed carbonyl absorption bands at 1705 and 1733 cm^{-1}.

3,5-Dimercaptolevulinic acid. 3.70 g (0.02 mole) of 3,5-dichlorolevulinic acid were dissolved in 20 ml of water and neutralized under cooling with 1.68 g (0.02 mole) of sodium bicarbonate. An aqueous solution of sodium hydrosulphide (prepared by saturating a solution of 1.60 g (0.04 mole) of sodium hydroxide in 30 ml of water with hydrogen sulphide) was added dropwise. The mixture was left at room temperature for 5 h, then acidified with dilute sulphuric acid and extracted with benzene (ten times). After drying over anhydrous magnesium sulphate, the solvent was removed *in vacuo* leaving a colourless oil, which on cooling over ice, crystallized within a few minutes. The yield of crude product was 2.20 g (61 %); m.p. 50−54°. Recrystallization from methylene chloride - petroleum ether gave 0.83 g (23 %) of 3,5-dimercaptolevulinic acid as colourless needles; m.p. 62−63°. (Found: Equiv. wt. 180.5; C 33.56; H 4.51; S 35.26. Calc. for $C_5H_8O_3S_2$ (180.25): Equiv.wt. 180.2; C 33.32; H 4.47; S 35.58). The infrared spectrum (KBr phase) showed a mercapto group absorption at 2555 cm^{-1} and very weak splitting of the carbonyl absorption band (1712 and 1723 cm^{-1}).

1,2-Dithiolane-4-one-3-acetic acid. 1.85 g (0.01 mole) of 3,5-dichlorolevulinic acid were dissolved in 20 ml of water and neutralized under cooling with 0.84 g (0.01 mole) of sodium bicarbonate. An aqueous solution of sodium hydrosulphide (prepared by saturating a solution of 0.80 g (0.02 mole) of sodium hydroxide in 30 ml of water with hydrogen sulphide) was added dropwise. The mixture was left at room temperature for 5 h, then acidified with dilute sulphuric acid and extracted with ether (three times). After drying over anhydrous magnesium sulphate, the solvent was removed *in vacuo* leaving 1.80 g of a colourless oil, which did not solidify on cooling. The oil was taken up in 500 ml of benzene (only 1.45 g was soluble), 200 ml of water were added and the mixture was oxidized with iodine in benzene solution. When the colour of the reaction mixture (pale violet) indicated an excess of the oxidizing agent, a few drops of aqueous sodium bisulphite solution were added and the mixture was stirred vigorously for a few minutes. The benzene layer was separated and dried over anhydrous magnesium sulphate. The solvent was removed *in vacuo* leaving a pale yellow oil, which soon solidified on cooling. The yield of crude product was 0.47 g (26 %); m.p. 53−56°. Recrystallization from methylene chloride - petroleum ether gave 0.40 g (22 %) of pure 1,2-dithiolane-4-one-3-acetic acid as pale yellow needles; m.p. 61−63°. (Found: Equiv. wt. 178.6; C 33.84; H 3.41; S 35.94. Calc. for $C_5H_6O_3S_2$ (178.23): Equiv.wt. 178.2; C 33.70; H 3.39; S 35.98). Spectrochemical data: UV, $\lambda_{max}^{ethanol}$ 280, 292, 308 and 338 mμ. The infra-red spectrum (KBr phase) showed an evident splitting of the carbonyl absorption band (1724, 1741 and 1773 cm^{-1}) and a hydroxyl absorption band at 3420 cm^{-1}.

Thietane-3-one-2-acetic acid. 2.40 g (0.01 mole) of sodium sulphide nonahydrate were dissolved in 25 ml of water. 1.85 g (0.01 mole) of 3,5-dichlorolevulinic acid, dissolved in 20 ml of water and neutralized under cooling with 0.84 g (0.01 mole) of sodium bicarbonate, were added dropwise. The mixture was left at room temperature for 1.5 h, then acidified with dilute sulphuric acid and extracted with methylene chloride (six times). After drying the combined extracts over anhydrous magnesium sulphate, the solvent was removed *in vacuo* leaving 0.35 g (24 %) of a pale yellow solid, m.p. 68−75°. Recrystallization from methylene chloride - petroleum ether gave 0.22 g (15 %) of thietane-3-one-2-acetic acid as a white microcrystalline solid; m.p. 85−89°. Three further recrystallizations from benzene-cyclohexane raised the m.p. to 93.5−95°. (Found: Equiv. wt. 146.5; C 41.08; H 4.12; S 21.88. Calc. for $C_5H_6O_3S$ (146.17): Equiv. wt. 146.2; C 44.09; H 4.14; S 21.94). Spectrochemical data: UV, $\lambda_{max}^{ethanol}$ 248 mμ. The infra-red spectrum (KBr phase) showed an evident splitting of the carbonyl band (1698 and 1768 cm^{-1}). NMR (chloroform solution) showed the following signals: A singlet at $\tau = -0.78$, a triplet at $\tau = 6.97$, a doublet at $\tau = 5.73$ and a quartet at $\tau = 4.92$.

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1. Claeson, G. and Thalén, A. *Acta Chem. Scand.* **17** (1963) 1172.
2. Claeson, G., Thalén, A. and Schotte, L. *Arkiv Kemi* **21** (1963) 295.
3. Motoki, S. *Nippon Kagaku Zasshi* **82** (1961) 256; (*cf. Chem. Abstr.* **56** (1962) 9948).
4. Varian associates, A—60 at work series, No. 4 (advertisment).
5. Rappe, C. *Arkiv Kemi* **13** (1959) 425.
6. Seissl, J. *Ann.* **249** (1888) 272.
7. Overend, W. G., Turton, L. M. and Wiggins, L. F. *J. Chem. Soc.* **1950** 3500.

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Comments on the Preparation of α-Halogeno-*sec.*-alkyl Esters

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The preparation of α,β-dichloro-*sec.*-propyl acetate and butyrate, and α, β, β′-trichloro-*sec.*-propyl acetate from the acid chlorides and chloroacetones in the presence of anhydrous zinc chloride was reported recently by Euranto and Kujanpää.[1] Attempts to prepare α-chloro-*sec.*-propyl acetate by the above method or by treating *sec.*-propenyl acetate with hydrogen chloride or *sec.*-propyl acetate with chlorine failed. At the same time, however, a patent description was published [2] where the preparation of α-halogeno-*sec.*-alkyl esters from acid halides and ketones in the presence of stronger condensing agents such as aluminium chloride and boron trifluoride was described. As examples, α-bromo-*sec.*-propyl acetate and α-chlorocyclohexyl acetate were mentioned, but only the preparation and properties of the first-mentioned compound were described.

Attempts were made to prepare α-bromo-*sec.*-propyl acetate by closely following the procedure described in the patent. Fractions were collected with a somewhat higher boiling point (*e.g.*, 48°C/11 torr) than that given in the patent (43—44°C/13 torr). The fractions could be analysed by conductometric measurement and argentometric titration by making use of the different hydrolysis rates of acetyl bromide (estimated half-life 0.5 s at 25°C in acetone-water containing 50 g of water per litre), α-bromo-*sec.*-propyl acetate (90 s), and 2-methyl-2-bromopentanone-4 (more than 100 days), which were found among the reaction products. Even the fractions richest in α-bromo-*sec.*-propyl acetate contained only about 1 % of that compound. The main product was found to be 2-methyl-2-bromopentanone-4 by measuring conductometrically the rate of hydrolysis at 25°C in acetone-water containing 300 g of water per litre. The first-order rate coefficient was found to be 1.6×10^{-5} s^{-1}, whereas the ketone (b.p. 49°C/10 torr, lit.[3] 52—53°C/11 torr) prepared from mesityl oxide and hydrogen bromide [3] gave a value of 1.8×10^{-5} s^{-1} (the corresponding value for *tert.*-butyl bromide was found to be 6.1×10^{-4} s^{-1}; both values are in accord with those expected on the basis of the structures of these tertiary bromides). The same ketone (b.p. 46—47°C/11 torr) was prepared also from acetyl bromide and mesityl oxide. The formation of 2-methyl-2-bromopentanone-4 in the attempted synthesis of α-bromo-*sec.*-propyl acetate may thus be explained by assuming that mesityl oxide is formed from acetone and acid halide [1] and that hydrogen bromide derived from acetyl bromide then adds to the double bond of mesityl oxide.

Aluminium chloride proved to be a good catalyst in the preparation of α-chloro-*sec.*-alkyl esters from ketones and acid chlorides even in cases where zinc chloride was ineffective or led to other products. Boron trifluoride was found to be a much weaker catalyst than aluminium chloride. Several esters were prepared by the following method. Equimolar amounts of freshly distilled acid chloride and ketone, which had been dried with anhydrous potassium carbonate and distilled, were mixed and a small amount of anhydrous aluminium chloride was added. The reaction mixture became slightly warm (in the case of α-chlorocyclohexyl acetate initial cooling of the reaction mixture was needed) and turned yellow or reddish. After it had stood overnight at room temperature, excess of ketone and acid chloride was evaporated at a temperature below 20°C, the crude ester was distilled rapidly at