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On the Synthesis and Properties of 1-Thiacyclobutane-3-carboxylic Acid 1-Oxide

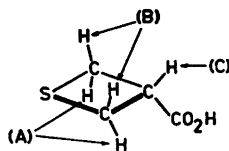
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Heretofore, compounds having a carboxyl group directly attached to a thiacyclobutane ring have not been reported. This paper will describe the synthesis of 1-thiacyclobutane-3-carboxylic acid 1-oxide and some of its chemical properties. The compound, however, was obtained as a mixture of its geometrical isomers which have not yet been separated.

For the synthesis of the thiacyclobutane-carboxylic acid, both ethyl β,β' -dibromoisobutyrate and β,β' -dibromoisobutyric acid were chosen as suitable starting materials. Treatment of the ester with sodium sulfide in absolute ethanol only led to the formation of polymers in spite of the fact that the reaction was carried out in very dilute solution by using the method of simultaneously adding the reaction components dropwise to the solvent over a period of several hours. However, when β,β' -dibromoisobutyric acid, neutralized with sodium carbonate, and sodium sulfide were allowed to react in water solution no polymers were formed but instead a small amount of the desired compound was obtained. The larger fraction of the reaction mixture

probably consisted of thiodimethacrylic acid, $(\text{CH}_2=\text{C}(\text{COOH})\text{CH}_2)_2\text{S}$. The synthesis was then modified in such a way that the neutralized β,β' -dibromoisobutyric acid was first treated with sodium hydrogen sulfide and a few drops of piperidine in water solution and later an equivalent amount of piperidine was added. In this way a 20 % yield of 1-thiacyclobutane-3-carboxylic acid could be obtained. The acid could be purified by distillation *in vacuo* yielding an oil which immediately solidified in the receiver to a white crystalline mass having a m.p. of 64.0–65.5°. The substance was very soluble in ether and acetone but only moderately soluble in carbon tetrachloride and water. The NMR-spectrum of the compound was complex and not easily interpreted, but it suggested an $\text{A}_2\text{B}_2\text{C}$ -type in accordance with the non-equivalent methylene hydrogens in the ring:



On titration of the compound with bromide-bromate in acid solution only slightly more than two equivalents of bromine were consumed, corresponding to an oxidation of the sulfide group to sulfoxide. This is somewhat unusual, because in most cases the oxidation by this method readily gives the sulfone, corresponding to a consumption of four equivalents of bromine. Therefore, such titrations have been used as an excellent method for determining equivalent weights of sulfide-acids.^{1,2} The oxidation of a thiacyclobutane ring, however, is likely to be accompanied by an increase of ring strain, so the result in this case is not quite unexpected.

The 1-thiacyclobutane-3-carboxylic acid 1-oxide was prepared by oxidation of the sulfide-acid with hydrogen peroxide in acetone. The compound obtained was a white solid which was almost insoluble in ether and acetone but extremely soluble in water. Its m.p. was not sharp but most of the substance melted in the region 95–100°. Its infra-red spectrum (in KBr) showed a strong double peak for the $\text{S}=\text{O}$ stretching vibration frequency: $\nu_{\text{SO}} = 1043$ and 1027 cm^{-1} , probably corresponding to the two geometrical isomers obtained.

Titration with bromide-bromate gave a bromine consumption of only 0.28 equivalents which is consistent with the results found for the titration of the sulfide-acid.

An attempt to study the reduction of the sulfoxide group by iodide in 2 M perchloric acid at 25° showed that no reaction could be observed with certainty after more than 15 h. In an earlier paper, however, the author reported that β -alkylsulfanylcarboxylic acids, R-SO-CR₂CH₂COOH (R' = Me or H), are reduced much faster by iodide than the corresponding α - or γ -compounds under the same conditions.³ The compound described in this paper also has its sulfoxide group in the β -position but is very different from the previously studied types because of its rigid ring system which does not allow any intramolecular interaction between the two groups. The resistance of this system towards reduction strongly indicates the existence of a cyclic intermediate, formed in an intramolecular reaction between the sulfoxide- and carboxyl groups, in the reaction between sulfoxide-acids and iodide ions in acid solution, previously studied by the author.^{3,4}

It is well known that certain sulfoxide-acids are not stable in acid solution.⁵ In order to check the stability of this compound its infra-red spectrum in about 2 M hydrochloric acid was studied. Under these conditions a strong peak at 1042 cm⁻¹ was obtained which did not change in intensity with time. The stability of the compound in acid media is therefore fully established.

Experimental. β, β' -Dibromoisobutyric acid (I) was prepared according to Ferris.⁶ M.p. 97.0–99.5°.

Ethyl β, β' -dibromoisobutyrate (II) was obtained by esterification of I, using the method of Brändström⁷ and using benzene as the solvent after Ferris.⁶ B.p. 85–87°/3 mm, $n_D^{24} = 1.4940$ (lit.⁶; $n_D^{20} = 1.4970$).

1-Thiacyclobutane-3-carboxylic acid (III). Sodium hydroxide 36 g (0.90 mole) was dissolved in about 500 ml of water and the solution was saturated with hydrogen sulfide. 221.5 g (0.90 mole) of I was first neutralized with sodium carbonate, a small amount of piperidine was dissolved and then the sodium hydrogen sulfide solution was added dropwise with stirring. After all had been added, the reaction mixture was allowed to stand for an hour at

room temperature and then 77 g (0.90 mole) of piperidine was poured into it with stirring. After gentle boiling under reflux for 2 h the solution was cooled, acidified and extracted with ether. The ether-solution was dried over anhydrous magnesium sulfate, filtered, the ether evaporated and the residue vacuum-distilled. The main fraction, b.p. 98–100°/0.25 mm, solidified immediately upon cooling. M.p. 64.0–65.5°. 21 g (19.7 %) was obtained. (Found: C 40.5; H 5.01; S 26.9; equiv. wt. 116.8 (NaOH). Calc. for C₄H₆O₂S: C 40.7; H 5.12; S 27.1; equiv. wt. 118.2). A molecular weight determination was carried out ebullioscopically in acetone: Found: 132. Calc.: 118.2.

1-Thiacyclobutane-3-carboxylic acid 1-oxide (IV). To 7.4 g of III dissolved in about 50 ml of acetone a hydrogen peroxide solution was added in a 10 % excess of the amount calculated for the oxidation to sulfoxide. The solution was kept at about 0° for 3 days and then filtered. The acetone was evaporated and the rest was finally dried over sulfuric acid *in vacuo*. The residue was a white crystal mass which was crushed and washed with dry ether. M.p. 95–100°. 8.3 g was obtained. (Found: C 35.5; H 4.33; S 23.5; equiv. wt. 135.4 (NaOH). Calc. for C₄H₆O₃S: C 35.8; H 4.51; S 23.9; equiv. wt. 134.2).

The infra-red spectra were recorded with a Perkin-Elmer model 237 spectrophotometer using slit program 25 and a speed of about 56 cm⁻¹/min. For the spectra of acid solutions, cells with windows of Irtran-2 and with 15 μ teflon spacers were used.

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