The Structure of Caperatic Acid

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The lichen compound caperatic acid (1) was first isolated from Parmelia caperata in 1897, and has subsequently been found in many other lichens.5 Zopf isolated an acid believed to be 1 from Cetraria glauca and Mycoblastus sanguinarius, and we have now confirmed that 1 can be isolated from the former species. Asano and Ohta found that the acid is a monomethyl ester of 2-hydroxy-1,2,3-heptadecanecarboxylic acid, but the position of the methyl ester group has hitherto been unknown. We now report that caperatic acid has the structure 1.

\[
\text{HO} - \text{COOH} \\
\text{COOH} \\
\text{HO}^+ \text{CD}_{3} \text{COOCD}_{3} \\
\text{COOCD}_{3} \\
\text{HO}^+ \text{CD}_{3} \text{COOCD}_{3}
\]

This result is based upon a comparison of the mass spectra of the trimethyl ester 2 and its corresponding \text{d}_4-ester 3 (Scheme 1), and also upon a chemical degradation of 1. In the upper parts of the mass spectra of 2 and 3 there are, respectively, three and four prominent peaks, and from the \text{m/e} values of these peaks, the structure of caperatic acid was deduced (Scheme 1). Support for the degradation shown in Scheme 1 was obtained from high resolution mass spectrometry of 2 and from the existence of analogous prominent peaks in the mass spectra of homologous trimethyl alkylketones.7

In a corroborative chemical degradation, 1 was oxidized with sodium bismuthate, a reagent which oxidizes α-hydroxy carboxylic acids to aldehydes or ketones.8 An NMR spectrum of the crude reaction product suggested that its major component was methyl 3-oxo-octadecanoate, the decarboxylation product of the initially formed β-keto carboxylic acid.

A CD investigation has shown that caperatic acid forms a complex with molybdate (VI) at pH 5.7.7 This demonstrates that 1 contains a free α-hydroxy carboxylic acid group.

Experimental. Melting points are corrected. The NMR spectrum was recorded on a Varian XL-100 spectrometer and the mass spectra on a Varian MAT 311 instrument using the direct inlet system.

Isolation of 1 from Cetraria glauca. From 300 g of fresh lichen, collected 30 km northeast of Stockholm, 1.6 g of 1 was isolated. After four recrystallisations from ethanol the product melted at 132.5–134 °C (lit.6 m.p. 132–133.5 °C [α]_D^{25} = -15.5 °C (c=0.9, dioxane). An authentic sample of 1, isolated from Parmelia caperata, was obtained from L. Tibell, University of Upsala, and this sample showed [α]_D^{25} = -15.7 °C (c=0.6, dioxane). The optical rotations of 1 have previously been measured in chloroform,9,10 but we found that all samples of 1 were only slightly soluble in ordinary ethanol-stabilized chloroform (c<0.1). Reaction with diazomethane in ether solution afforded the trimethyl ester 2, m.p. 56–58 °C (from ethanol), lit.6 m.p. 56.5–57.5 °C. MS: \text{m/e} (rel. intensity) 371 (35), 339 (100), 270 (44), 101 (48), 87 (49), 43 (37).

The \text{d}_4-ester 3 was prepared by reaction of 1-\text{d}_4 with diazomethane-\text{d}_4. The former reactant was obtained by dissolving 1 in a mixture of CH_3OD (99% isotopic purity) and dry ether, followed by evaporation of the solvent. Diazomethane-\text{d}_4 was prepared largely after Hecht and Kozarich,11 but the N-nitrosomethylurea was replaced with N-methyl-N-nitroso-p-toluene-sulfonamide and, instead of using the dimethoxyethane solution, dry ether was added and the diazomethane-\text{d}_4 was distilled together with ether into a flask containing a little D_2O (99.7% isotopic purity). The water in the receiving flask was frozen out and the etheral layer was then added to 1-\text{d}_4. The resulting ether solution was washed with water, dried (Na_2SO_4) and concentrated. The product 3 was crystallised from ethanol, m.p. 55.5–

\[
\text{m/e} = 273 (69) \\
\text{m/e} = 339 (100) \\
\text{m/e} = 342 (79) \\
\text{[2: 270(44)]} \\
\text{[2: 339(100)]} \\
\text{[2: 371(35)]}
\]

Scheme 1.

56.5°C. MS: 374(71), 342(79), 339(100), 273(69), 101(33), 90(42).

Bismuthate oxidation of 1. A mixture of 1 (55 mg), sodium bismuthate (56 mg), and glacial acetic acid (2 ml) was warmed (35°C, 80 min) with stirring in a stoppered flask. The resulting solution was poured into a mixture of cold water (100 ml) and ether (50 ml). The ether layer was repeatedly washed with sodium hydrogen carbonate solution and then twice with water. After drying (Na₂SO₄) and concentration of the ether layer, and finally drying in a vacuum desiccator over night, a residue (27 mg) was obtained. The NMR spectrum of this residue (CDCl₃) displayed singlets at δ = 3.66 and 3.38, and triplet at δ = 2.46 (integrals approximately 35, 18 and 21 mm, respectively), which indicate the partial structure —CH₃—CH₂—CO—CH₂—COOCH₃. No peaks from an isomeric β-keto ester could be detected.

Acknowledgements. We thank Professor Rolf Santesson, Naturhistoriska Riksmuseet, Stockholm for identifying the lichen material, Dr. Leif Tibell, University of Uppsala, for a gift of caperatic acid, and Dr. Lennart Kenne for the MS investigations. This work was supported by the Swedish Natural Science Research Council.


Received June 27, 1975.