Carotenoid Sulfates. 1. Partial Syntheses of Lycoxanthin Sulfate and Zeaxanthin Disulfate

THOMAS RAMDAHL and
SYNNØVE LIAAEN-JENSEN

Organic Chemistry Laboratories, Norwegian Institute of Technology, University of Trondheim, N-7034 Trondheim-NTH, Norway

Sulfates are encountered within many classes of natural products,[1-6] particularly in the carbohydrate field.[7,8] No carotenoid sulfates have hitherto been reported. In the present work two carotenoid sulfates have been prepared for spectroscopic model studies in order to facilitate the structural elucidation of naturally occurring carotenoid sulfates of more complex structure.[9] Since carotenoid sulfates proved to have considerable water solubility, they may have practical application.

Lycoxanthin (*1*, Scheme 1) was converted to lycoxanthin sulfate (*2*) by treatment with a pyridine-SO_3 complex prepared from pyridine and chlorosulfonic acid.[10,11] Zeaxanthin (*3*) yielded the corresponding disulfate *4* by the same procedure.

The sulfates *2* and *4*, isolated as sodium salts, were strongly polar. The disulfate *4* had considerable water solubility, a unique property in the carotenoid field. Monoesters of sulfuric acid are approximately as acidic as sulfuric acid itself,[12] consistent with the properties of *2* and *4*.

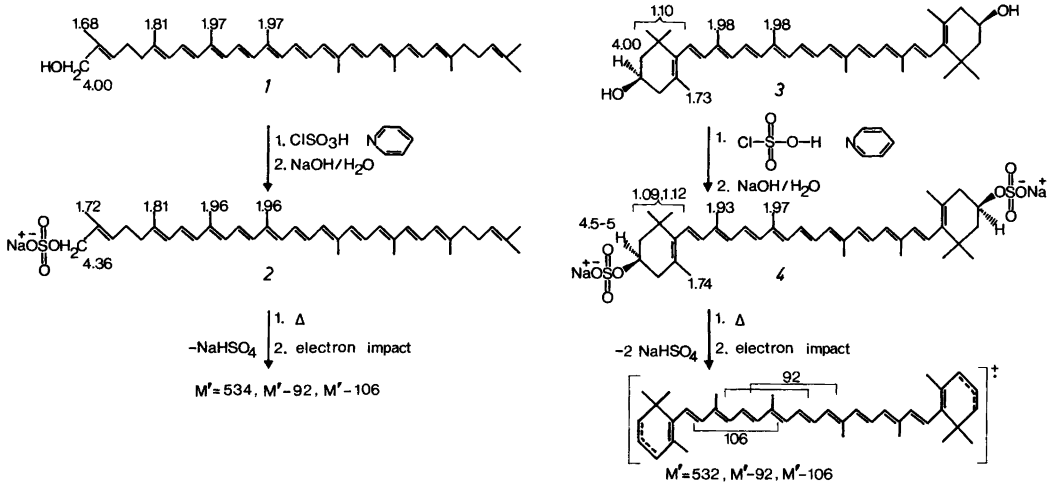
The sulfate groups had no distinct influence on the electronic spectra of the synthetic carotenoid sulfates. A small hypsochromic shift is ascribed to the formation of minor quantities of mono-*cis* isomers, inseparable from the all-*trans* isomers by preparative TLC. In the IR spectra, recorded in KBr, strong absorption at *ca.* 1240 cm^{-1} is associated with the sulfate substituents.[13,14] The ^1H NMR spectra of the sulfates *2* and *4* differed little from those of the parent carotenols *1* and *3*, respectively, *cf.* signal assignments in Scheme 1. For lycoxanthin (*1*) the ^1H NMR (CD_3OD) singlet caused by the protons at C-16 shifted from δ 4.00 to 4.34 upon sulfatation to *2*.

For zeaxanthin (*3*) sulfatation had a similar effect to acetylation on the chemical shift of the geminal dimethyl groups in the ^1H NMR spectrum. The mass spectra of the two synthetic sulfates, obtained with some difficulty, suggested that $NaHSO_4$ is eliminated thermally in the ion source prior to ionization, see Scheme 1. The resulting carotenoid products, in which the site of the eliminated hydrogen(s) is unknown, exhibited common carotenoid cleavages upon electron impact.

Other carotenoid sulfates are currently being prepared with the aim of optimizing yields, testing water solubilities, checking further the spectroscopic characteristics and studying the chemical reactions of carotenoid sulfates.

Experimental. Pyridine-SO_3 complex (*5*) was prepared by addition of chlorosulfonic acid (1 g) to pyridine (5 ml) with stirring at −20 °C.[10,11]

Lycoxanthin sulfate (*2*). A solution of *1* (5 mg) in pyridine (9 ml) was added to a solution of 5, prepared as above at −20 °C. The reaction mixture was stirred overnight at room temp., diluted with 10% aqueous NaOH to pH 9 and extracted with ethyl



Scheme 1.

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acetate. The residue of the ethyl acetate extract was chromatographed by preparative HPLC (Merck Lobar Si60 column, 15 % methanol in ethyl acetate) providing *2* (0.75 mg, 15 %); λ_{max} (methanol) 359, 443, *468* and 498 nm; ν_{max} (KBr) 1230 (s), 1065 (m), 960 (s) cm^{-1}; $\delta(CD_3OD)$ 1.62s(3H, CH_3-1'), 1.68s(3H, CH_3-1'), 1.72s(3H, CH_3-1), 1.81s(6H, CH_3-5,5'), 1.96s(12H, CH_3-9,13,9',13'), 4.36s (2H, $-CH_2O-$); *m/e* (200 °C) 534 (M − $NaHSO_4$(M'), 89 %), 442 (M' − 92, 3 %), 428 (M' − 106, 11 %) and 91 (100 %).

Zeaxanthin disulfate (*4*) was prepared from *3* (5 mg) by the same procedure as above, yield 1.18 mg (24 %); λ_{max} (methanol) 424, *448* and 474 nm; ν_{max} (KBr) 1230 (s), 1065 (s), 965 (s) cm^{-1}; $\delta(CD_3OD)$ 1.09s and 1.12s (6 + 6H, CH_3-1,1'), 1.74s (6H, CH_3-5,5'), 1.93s and 1.97s (6 + 6H, CH_3-9,13,9',13'), 6.13s (4H, H-7,8,7',8'); *m/e* (230 °C) 532 (M − $2NaHSO_4$ (M'), 70 %) 440 (M' − 92, 4 %), 426 (M' − 106, 1 %) and 43 (100 %).

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