

Oxidative Esterification of Retinal and 3-Dehydroretinal to Methyl Esters of Retinoic Acid and 3-Dehydroretinoic Acid

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A method for the preparation of retinoic acid and 3-dehydroretinoic acid was reported from this laboratory (Barua & Barua, 1964; Barua & Nayar, 1968). Although the method is simple and yields are good, the method has two disadvantages: the high cost of AgNO_3 and the occasionally explosive nature of Tollens reagent. Recently a new method for oxidation of aldehydes to carboxylic acids and esters has been reported (Corey, Gilman & Ganem, 1968), but has not hitherto been utilized for the conversion of retinal, with a long chain of conjugated double bonds, into retinoic acid. This communication describes the conversion of retinal and dehydroretinal by this new procedure, into the methyl esters of retinoic acid (yield > 90%) and dehydroretinoic acid (yield > 90%) respectively.

A 110mg. sample of retinal (prepared from retinol by the method of Ball, Goodwin & Morton, 1948) was stirred in the dark with a mixture of 198mg. of NaCN, 0.06ml. of acetic acid and 1.5g. of MnO_2 (British Drug Houses Ltd., Poole, Dorset) in 50ml. of methanol for 19hr. at 20–25°. The solution was filtered, water was added and the product was extracted with ether. The extract was dried over anhydrous Na_2SO_4 and the solvent was removed *in vacuo*. The residue was dissolved in light petroleum and chromatographed on a column of water-deactivated (7%, v/w) alumina. The main zone containing retinoic acid methyl ester was eluted with light petroleum. The methyl ester (98mg.) was crystallized from methanol–water (6:1, v/v), m.p. 54–55°, λ_{max} . 350nm. (light petroleum), SbCl_3 product λ_{max} . 570nm. The methyl ester was saponified with ethanolic KOH, the solution was acidified with HCl and the product was extracted with ether. The extract was dried over anhydrous Na_2SO_4 and the solvent was removed *in vacuo*. The residue was dissolved in light petroleum and chromatographed on a column of water-deactivated (8%, v/w) alumina. The main zone containing retinoic acid was very strongly

adsorbed and was eluted, after extrusion, with ethanol containing NH_3 . The eluate was acidified with HCl and the product was extracted with ether. Ether was removed *in vacuo* and retinoic acid was crystallized from light petroleum. The crystals had m.p. 179–180°, λ_{max} . 350nm. (ethanol) shifted to 335nm. when a trace of alkali was present and then to 350nm. on addition of acid, SbCl_3 product λ_{max} . 570nm. The methyl ester was reduced with LiAlH_4 when retinol was obtained, λ_{max} . 325nm. (ethanol), SbCl_3 product λ_{max} . 618nm.

Similarly oxidation of 28mg. of 3-dehydroretinal (prepared from natural 3-dehydroretinol) with a mixture of 125mg. of NaCN, 0.10ml. of acetic acid and 756mg. of MnO_2 in 25ml. of methanol for 40hr. gave, after chromatographic purification, 25.5mg. of 3-dehydroretinoic acid methyl ester, m.p. 44–45°, λ_{max} . 370 and ~303nm. (light petroleum), SbCl_3 product λ_{max} . 643nm. Saponification of the methyl ester yielded 3-dehydroretinoic acid, which was crystallized from light petroleum. The crystals had m.p. 178–180°, λ_{max} . 370 and ~303nm. (ethanol) shifted to 355nm. with trace of alkali and then to 370nm. with trace of acid, SbCl_3 product λ_{max} . 643nm. The ester gave 3-dehydroretinol, λ_{max} . 350, 287 and ~276nm. (light petroleum), on reduction with LiAlH_4 .

The physical, spectroscopic and chemical properties of the retinoic acid and dehydroretinoic acid and their methyl esters obtained by this new procedure are in good agreement with those of authentic samples.

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Ball, S., Goodwin, T. W. & Morton, R. A. (1948). *Biochem. J.* **42**, 516.

Barua, R. K. & Barua, A. B. (1964). *Biochem. J.* **92**, 21c.

Barua, R. K. & Nayar, P. G. (1968). *Curr. Sci.* **37**, 364.

Corey, E. J., Gilman, N. W. & Ganem, B. E. (1968). *J. Amer. chem. Soc.* **90**, 5616.