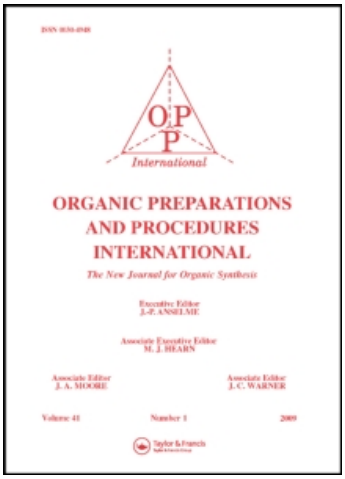

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5-ETHYL-5-(1-METHYL-3-CARBOXYPROPYL)-BARBITURIC ACID

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5-ETHYL-5-(1-METHYL-3-CARBOXYPROPYL)-BARBITURIC ACID[1]

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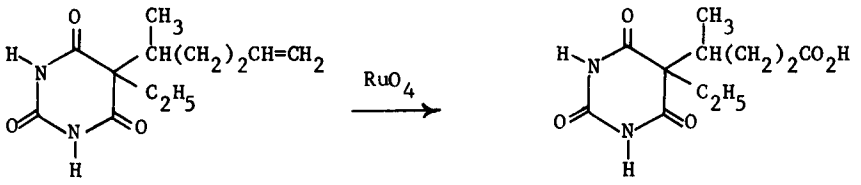

I II

5-Ethyl-5-(1-methyl-3-carboxypropyl)-barbituric acid (II), an important metabolite of 5-ethyl-5-(2'-pentyl)-barbituric acid, (pentobarbital) has been prepared in 3% yield by the ozonization of 5-ethyl-5-(1-methyl-4-pentenyl)-barbituric acid (I).[2] The use of ruthenium tetroxide in place of ozone increases the yield to 81% and greatly facilitates the work-up procedure. This procedure is another example where ruthenium tetroxide is superior to ozone for the cleavage of a carbon-carbon double bond to the corresponding carboxylic acid derivative.[3]

EXPERIMENTAL

A solution of ruthenium tetroxide was prepared by adding 1.0 g (4.68 mmoles) of sodium metaperiodate in 20 ml of water to a suspension of 0.30 g (1.26 mmoles) of ruthenium dioxide[4] in 50 ml of acetone (distilled from potassium permanganate) and 50 ml of water. The ruthenium dioxide reacted to give a yellow solution and a white precipitate formed. To this mixture

was added dropwise a solution of 2.5 g (10.6 mmole) of 5-ethyl-5-(1-methyl-4-pentenyl)-barbituric acid[2] in 50 ml of acetone. The reaction mixture turned dark as the olefin was added. A sodium periodate solution prepared by dissolving 10 g (46.8 mmoles) of sodium metaperiodate in 100 ml of water and adding an equal volume of acetone is used to regenerate the ruthenium tetroxide. As the mixture turns from yellow (RuO_4) to black (RuO_2) during the addition of the olefin and during the reaction time, portions of the periodate solution are introduced. After 2 hr the reaction was terminated by the addition of 60 ml of isopropanol. The mixture was filtered through a short Celite column and the precipitate washed well with acetone. The filtrate was concentrated to approximately 100 ml and extracted with 4 x 100 ml portions of ether. The ethereal extract was dried (sodium sulfate) and concentrated on a rotary evaporator. The resulting solid was dried under high vacuum and recrystallized from a mixture of ethyl acetate and hexane to give 2.2 g (81%) of II, mp 194-196°. The analytical sample prepared by recrystallization from the same solvent had mp 194-196°, lit.[2] mp 192-194°. The ir, nmr and uv spectra were in agreement with the expected structure.

Anal. Calcd. for $C_{11}H_{16}O_5N_2$: C, 51.55; H, 6.29; N, 10.90. Found: C, 51.45; H, 6.21; N, 10.82.

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1. This work was carried out under Contract PH43-65-1057 of the National Institutes of General Medical Sciences, National Institutes of Health, Bethesda, Maryland.
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4. Obtained from Engelhard Minerals and Chemicals Corporation.

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