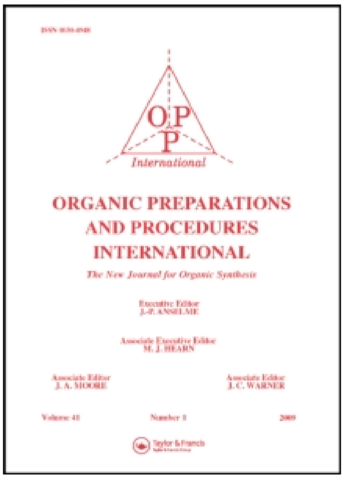

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ON THE PREPARATION OF α-KETOADIPIC ACID

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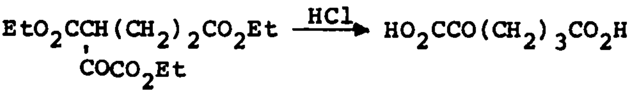
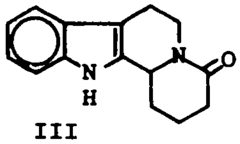
In contrast to a recent literature inference,[3] we have been able to obtain α-ketoadipic acid (I) according to the procedure of Gault.[4] The Claisen condensation of diethylglutarate with diethyl oxalate gave a 67% yield of ethyl α-oxalylglutarate (II), which on treatment with conc. hydrochloric acid afforded I in 71% yield.[5] The identity of crude I was confirmed by its reaction with tryptamine to give III in 89% yield.[6] The ready availability of the starting materials makes this a more convenient procedure than the other reported methods.[7-9]



$$\underset{\text{II}}{EtO_2C\underset{\substack{|\\ COCO_2Et}}{C}H(CH_2)_2CO_2Et} \xrightarrow{HCl} \underset{\text{I}}{HO_2CCO(CH_2)_3CO_2H}$$

II

I



III

EXPERIMENTAL

Ethyl α-oxalylglutarate (2). - A 250 ml 3 neck round bottom flask equipped with reflux condenser, heating mantle, and mechanical stirrer was charged with 150 ml of absolute ethanol (distilled from Mg/I_2). To the stirred ethanol was added over a period of 10 min., 4.6 g (0.20 g-atom) of Na spheres. The last portions of Na required external heating to achieve solution. The mixture was then distilled to near dryness and allowed to cool to room temperature under a nitrogen atmosphere. To the NaOEt was added 120 ml anhydrous ether, followed by 29.2 g (0.20 mol) of distilled diethyl oxalate and 36.7 g (0.20 mol) diethyl glutarate. The resulting mixture rapidly turned yellow and was allowed to stand at room temperature under nitrogen for 16 hr; 110 ml of water was then added and the mixture was suction-filtered. The filtrate was extracted twice with ether and the aqueous layer acidified with 35 ml of 12 M HCl. The oily material which formed was extracted with 100 ml ether and the aqueous layer extracted twice with ether. The combined ethereal extracts are combined and dried over anhydrous Na_2SO_4. Filtration and evaporation under reduced pressure gives 37.9 g (67%) of II as an amber oil. nmr ($CDCl_3$) 1.18 ppm (q, 9H), 2.27 ppm (m, 4H), 4.10 ppm (m, 7H). The material is not stable to distillation.[4]

<u>α-Ketoadipic acid (I)</u>. - A mixture of 32.8 g (0.11 mol) of II and 150 ml of 4 M HCl was refluxed with stirring for 4 hrs. Vigorous gas evolution was observed. After 4 hrs, the amber solution was distilled to near dryness (20 ml) and allowed to cool to room temperature. The resulting tan precipitate was filtered to give 12.4 g (71%) of I, mp. 92-96°, lit.[4] mp. 90-95° (hydrate) and mp. 124-128°, lit.[4] mp. 126-127° (anhydrous). The anhydrous form can be obtained by allowing the crude product to stand in an oven at 40° for 2 hr.

4-Keto-1,2,3,4,6,7,12,12b-octahydroindolo[2,3-a]quinolizine (III). - A mixture of 11.5 g (0.0587 mol) of tryptamine-HCl, 9.4 g (0.0587 mol) of I, 2.35 g (0.0587 mol) of NaOH, and 375 ml of glacial HOAc was refluxed under N_2 for 4 hr. The cooled mixture was poured into 1 ℓ. of water. The white solid was collected, washed with 1N NaOH, 1N HCl, and water until neutral. After drying, 12.6 g (89%) of III was obtained as a white powder, homogenous by tlc. Recrystallization from MeOH gave tiny prisms, mp. 248-252°, lit.[6] mp. 245-247.5°.

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