left 20.4 g. of crystals. These were extracted with hot benzene to remove the product from 3.9 g. of solid melting above 250°. Concentration of the benzene extracts and addition of Skellysolve B precipitated the product; m.p. 111–114°. It was very soluble in water and neutral to litmus. There was no absorption in the ultraviolet. The infrared spectrum showed the presence of an amide linkage and possibly an OH group. A sample, recrystallized from ethyl acetate, melted at 114–115.5°.

Anal. Calcd. for $C_{12}H_{21}NO_2$: C, 68.21; H, 10.02; N, 6.63; ethoxyl, none. Found: C, 67.86; H, 10.03; N(D), 6.85; ethoxyl, none.

2-Methyl-2-azaspiro[5.5]hendecan-9-ol.—When an equivalent amount of methanol was substituted for ethanol in the above experiment there was obtained 2.4 g. of by-product melting above 290° and 17.9 g. of sirup which could not be induced to crystallize even on seeding with the product melting at 115°. The crude sirup was reduced with lithium aluminum hydride to give 3 g. of very viscous pale yellow sirup distilling at 110–120° (0.7 mm.).

Anal. Calcd. for $C_{11}H_{21}NO$: N, 7.64. Found: N(AP), 7.54.

Decahydro-7-quinolinol.—Reduction of 45.1 g. of IV with 39.0 g. of sodium and 87.6 g. of 2-methylpentanol-4 in toluene gave 39.8 g. of oil most of which crystallized while still hot. Trituration with ether gave about 12 g. melting at 162–165°. This was a strong base in water and reacted with acetic anhydride to give a viscous oil. A mixed m.p. with the starting material was depressed (m.p. 137–157°). A sample, recrystallized from ethyl acetate, melted at 170.3–171.4° cor.

Anal. Calcd. for $C_9H_{17}NO$: C, 69.65; H, 11.04; N, 9.03. Found: C, 69.60; H, 10.98; N(AP), 8.94.

Ethyl 2-(2-Cyanoethyl)-cyclohexanone-2-carboxylate Ethylene Glycol Ketal.—A mixture of 22.3 g. of ethyl 2-(2-cyanoethyl)-cyclohexanone-2-carboxylate, 38 g. of ethylene glycol, 1.5 g. of toluenesulfonic acid monohydrate and 100 ml. of benzene was refluxed overnight using a water separator. The benzene phase was washed with water, aqueous potassium carbonate and water. The product (22.5 g.) was collected at 110–139° at 0.07 mm., but most boiled at the higher temperature; n^{25}D 1.4818.

Anal. Calcd. for $C_{14}H_{21}NO_4$: N, 5.24. Found: N(K), 5.21.

2-Aza-spiro[5.5]hendecan-1,7-dione.—Reduction of 21 g. of the above ketal in 70 ml. of ethanol with a Raney nickel catalyst at 60° required two hours. It was necessary to distil out some 4a-carbethoxydecahydroquinoline, b.p. 82–84° at 0.09 mm. before the product (11.3 g.) crystallized. After trituration with a small amount of benzene and three recrystallizations from isopropyl alcohol–ether, the product melted at 226.5–228.5°.

Anal. Calcd. for $C_{10}H_{15}NO_2$: N, 7.73. Found: N(K), 7.67.

The picrate of 4a-carbethoxydecahydroquinoline was prepared. It melted at 181.7–183.2° cor., from ethanol.

Anal. Calcd. for $C_{12}H_{21}NO_2 \cdot C_6H_3N_3O_7$: N, 12.72. Found: N(D), 12.82.

Methyl Ethyl 2-(2-Cyanoethyl)-adipate.—To 0.1 g. of sodium in 35 ml. of ethanol was added 38 g. of methyl cyclopentanone-2-carboxylate. Then 20 ml. of acrylonitrile was added slowly at an initial temperature of 30°. The reaction mixture was allowed to heat up to 75° and was then kept from heating up further by cooling as required. After two hours several milliliters of acetic acid was added, the solvent removed and the residue washed with water. Fractionation gave 7.9 g. of starting material and 45.4 g. of product boiling at 137–156° (0.6 mm.). It gave no color with ferric chloride.

Anal. Calcd. for $C_{12}H_{19}NO_4$: C, 59.73; H, 7.94; N, 5.81. Found: C, 60.18; H, 7.73; N, 5.65.

By using 105 g. of ethyl cyclopentanone-2-carboxylate, there was obtained 148 g. of diethyl 2-(2-cyanoethyl)-adipate; b.p. 158–162° at 0.2 mm.; n^{25}D 1.4442.

Anal. Calcd. for $C_{13}H_{21}NO_4$: N, 5.49. Found: N(K), 5.45.

3-(3-Carbethoxypropyl)-2-piperidone.—Reduction of 90.5 g. of methyl ethyl-2-(2-cyanoethyladipate) in 500 ml. of methanol with Raney nickel catalyst at 80° and 700 lb. initial hydrogen pressure required five hours. Removal of the catalyst and solvent left 76 g. of oil which crystallized in several hours. Recrystallization from ether gave a solid melting at 54–56°. The same compound was obtained by reduction of 132 g. of diethyl 2-(2-cyanoethyladipate) in ethanol, and was shown by means of mixed melting point to be identical with the by-product previously reported.[1]

Anal. Calcd. for $C_{11}H_{19}NO_3$: N, 6.57. Found: N(K), 6.56.

3-(3-Carboxypropyl)-glutarimide.—A mixture of 4 g. of methyl ethyl-2-(2-cyanoethyl)-adipate, 4 g. of sodium carbonate and 36 ml. of water was refluxed for six hours, acidified to congo paper with hydrochloric acid and extracted with ethyl acetate. Concentration gave 2.9 g. of sirup which was dried over phosphorus pentoxide–potassium hydroxide. Some of the sirup was warmed in a test-tube for several minutes over a free flame to effect cyclization. Upon cooling and addition of water white crystals readily formed in good yield; m.p. 149–151.5° after recrystallization from water. The m.p. was not depressed on admixture with the $C_9H_{13}NO_4$ compound previously reported[1] to result from hydrolysis of ethyl 2-(2-cyanoethyl)-cyclopentanone-2-carboxylate, followed by distillation of the intermediate.

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The Separation of Mixtures of *cis*- and *trans*-Estradiols

BY NORMAN BARSEL

Estrone on reduction with Raney nickel in aqueous potassium hydroxide, forms a mixture of estradiol-17-β, m.p. 178° (85–90%) and estradiol-17-α, m.p. 223° (10–15%). Recrystallization from aqueous ethanol usually removes the 17-β and leaves a residue in solution that is enriched in estradiol-17-α. Originally, a separation of the 17-beta compound as its slightly soluble digitonide[1] was suggested. Later, an insoluble urea complex was used to separate this same epimer.[2]

We have found that sharp separations may be more easily accomplished through the dipropionates of this mixture.[3] The 17-β dipropionate crystallizes from hot methanol before the 17-α dipropionate which melts at 76–77°, $[\alpha]^{25}$D + 36, 1% in dioxane. *Anal.* Calcd. for $C_{24}H_{32}O_4$: C, 74.95; H, 8.40. Found: C, 75.04; 8.50. The latter separates as an oil only after the solution had been concentrated.

We further noted that propionation of such a mixture of diols in pyridine below 95° forms the 17-monopropionates whereas above 105° the dipropionates are produced.

Saponification of the dipropionates in methanolic potassium hydroxide yields the pure diols.

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(1) O. Wintersteiner, THIS JOURNAL, **59**, 765 (1937).

(2) H. Priewe, U. S. Patent 2,300,134 (1942).

(3) K. Miescher and C. R. Scholz, *Helv. Chim. Acta*, **20**, 268 (1937).