the steam-bath was removed and 29.2 g. (0.20 mole) of ethyl oxalate (b. p. 184°) in ether was added at a rate to maintain gentle refluxing. The reaction mixture was refluxed and stirred rapidly for two hours with the formation of a yellow precipitate and then decomposed with cooling by addition of 120 ml. of 6 N acetic acid. Dilute (5 N) ammonium hydroxide (60 ml.) was added until the solution was neutral or faintly acid. The yellow solid was filtered from the cold solution and washed with ether yielding 11 g. (23%) of (II) melting at 161–163°. The aqueous filtrate was extracted with benzene, but very little more of the substance was obtained. After recrystallization from benzene, the yellow needles melted at 163–164°.

Anal. Calcd. for $C_{14}H_{12}N_2O_2$: C, 69.98; H, 5.04. Found: C, 70.00, 70.02; H, 4.80, 4.93.

This yellow water-soluble amino acid (II) decolorized dilute potassium permanganate solution and reacted with bromine in carbon tetrachloride to form an orange hygroscopic addition product. The amino acid (II) formed a dipicrate which, after recrystallization from ethanol, melted at 146–148°.

Anal. Calcd. for $C_{26}H_{18}O_2N_8$: C, 44.73; H, 2.60; N, 16.04. Found: C, 45.04; H, 2.68; N, 15.88.

2-α-Quinaldal-3-α′-quinolylpropionic Acid (III).—In a similar manner 43.5 g. (0.3 mole) of quinaldine (b. p. 245–246°) treated with 0.3 mole of potassium amide (or sodium amide) and then with 21.9 g. (0.15 mole) of ethyl oxalate in ether. After refluxing for one hour the reaction mixture was decomposed by pouring into 75 ml. of glacial acetic acid and 75 g. of ice. The resulting solution was neutralized by the addition of solid anhydrous sodium carbonate, the final neutralization being adjusted with a solution of sodium bicarbonate. The thick orange precipitate was filtered and washed twice with ether yielding 27 g. (53%) of (III), m. p. 219–223°. After recrystallization from large volumes of benzene, the orange-red crystals melted at 221–223°.

Anal. Calcd. for $C_{22}H_{16}O_2N_2$: C, 77.63; H, 4.74; N, 8.23. Found: C, 77.56; H, 4.90; N, 8.05.

This substance (III) in carbon tetrachloride solution reacted with bromine in this solvent to form an orange precipitate which was shown by sodium fusion to contain halogen. A red monopicrate of (III) was obtained by filtering a hot benzene solution of (III) into boiling ethanolic picric acid. After recrystallization of 0.4 g. of this picrate from one liter of acetone, the red crystals melted with decomposition at 220°.

Anal. Calcd. for $C_{28}H_{19}O_9N_5$: C, 59.05; H, 3.36. Found: C, 59.25; H, 3.42.

Ethyl (γ-Quinolyl)-pyruvate (I).—This ester was prepared by a modification of the method previously described.[3] To 0.60 mole of potassium amide in liquid ammonia was added 86 g. (0.60 mole) of lepidine (b. p. 262°) in ether. After the liquid ammonia was removed and replaced with ether, refluxing was continued thirty minutes. To this metal derivative was added dropwise 43.8 g. (0.30 mole) of ethyl oxalate in ether. After refluxing for one hour, the cooled reaction mixture was decomposed with 6 N acetic acid and neutralized with sodium carbonate. After filtering and washing with ether and water, there was obtained 62 g. (85%) of crude ethyl-(γ-quinolyl)-pyruvate, m. p. 185–189°. This product was insoluble in ether and only slightly soluble in boiling alcohol or benzene. Recrystallization from dioxane gave the pure compound, m. p. 188–189°, as previously reported.[3]

Ethyl (γ-Quinolyl)-pyruvate Oxime.—To a hot solution of 7.5 g. (0.31 mole) of compound (I) in 150 ml. of dioxane was added 7.5 g. of hydroxylamine hydrochloride, 7.5 g. of sodium acetate and sufficient water to effect solution. The solution was evaporated to a volume of 100 ml. and poured onto ice. There was obtained 7.1 g. (90%) of the oxime, m. p. 183–184°, after recrystallization from ethanol–water.

Anal. Calcd. for $C_{14}H_{14}O_3N_2$: C, 65.10; H, 5.46; N, .84. Found: C, 65.19; H, 5.74; N, 10.60.

The oxime (12.5 g., 0.048 mole) in 250 ml. of absolute ethanol was hydrogenated in the presence of Raney nickel at 800 pounds pressure and 75° for six hours yielding an amine, b. p. 193–198° at 3 mm. This amine formed a picrate and a picrolonate, but neither of these derivatives, after recrystallization from ethanol, gave satisfactory analytical values.

Ethyl (α-Quinolyl)-pyruvate Oxime.—Ethyl (α-quinolyl)-pyruvate (m. p. 130–131°), prepared by means of potassium ethoxide as previously described,[5] was readily soluble in alcohol or ether. This ester (10 g., 0.41 mole) yielded 9.1 g. (85%) of the corresponding oxime, which after recrystallization from ethanol melted at 162–163°.

Anal. Calcd. for $C_{14}H_{14}O_3N_2$: C, 65.10; H, 5.45; N, 10.84. Found: C, 65.32; H, 5.29; N, 11.03.

Hydrogenation of the oxime yielded an amine b. p. 178–183° at 2 mm. The picrate salt failed to analyze satisfactorily.

DEPARTMENT OF CHEMISTRY
DUKE UNIVERSITY   RECEIVED FEBRUARY 23, 1950
DURHAM, NORTH CAROLINA

The Degradation of Silver Trifluoroacetate to Trifluoroiodomethane

BY ALBERT L. HENNE[1] AND WILLIAM G. FINNEGAN

Trifluoroiodomethane, CF_3I, has been shown to break homolytically and is presently the only source of trifluoromethyl free-radicals. Its value has been proved by efficient addition across a carbon to carbon double or triple bond. Its preparation has called for carbon tetraiodide and iodine pentafluoride, neither of which is current or convenient to handle.[2,3,4]

The degradation of silver trifluoroacetate by means of an excess of iodine appealed to us as a more promising synthesis. It can be written: $CF_3COOAg + I_2 \rightarrow CF_3I + AgI + CO_2$. The first step is the formation of an iodinated complex such as $CF_3CO_2AgI_2$, in which iodine has a definitely positive character. The electropositive nature of the CF_3 group should enhance its ability to migrate as a negative fragment toward the positive, iodinated end of the molecule and form CF_3I in preference to CF_3COOCF_3; this is the opposite of the reaction with unfluorinated silver salts, which favors ester formation.

Experimentally, the careful heat-decomposition of an equimolecular mixture of dry silver salt and iodine gave an 80% yield of CF_3I and no other compound was traced. The mechanical losses, estimated at 10% were relatively high because no solvent or dispersing medium could be used, as all were affected by the silver or the positive iodine. A one-step synthesis of CF_3I from commercially available reagents is thus at hand.[5]

(1) Visiting Professor from Ohio State University.

(2) Haszeldine and Emeleus, *Research,* 1, 715 (1948).

(3) Banks, Emeleus, Haszeldine and Kerrigan, *J. Chem. Soc.,* 2188 (1948).

(4) Haszeldine, *ibid.,* 2856 (1949); *Nature,* 165, 152 (1950).

(5) A letter from R. N. Hazseldine, Cambridge University, informs us that he has obtained parallel results, which he is now submitting to *Nature.*

Experimental

Silver trifluoroacetate can be prepared by adding trifluoroacetic acid to a slight excess of suspended silver hydroxide, filtering, evaporating to dryness, grinding to a powder, and completing the desiccation *in vacuo*, on a steam-bath. The pure, dry salt is not sensitive to light.

From commercial sodium trifluoroacetate, an alternate method consists in dissolving silver nitrate in an equal amount of water, adding an equimolecular quantity of sodium trifluoroacetate, and extracting with portions of ether of about equal volume. Vigorous agitation for thirty minutes on a mechanical shaker is recommended, as the difference in density tends to keep the layers apart. After three extractions, it is well to distil off as much water as can be taken from the aqueous layer without causing crystallizing out, because the crystals are a mixture of sodium nitrate and silver trifluoroacetate. The extraction is then repeated with three portions of ether. On distillation, the ether solution leaves a mushy residue of silver salt and ether, which must be desiccated *in vacuo* on the steam-bath, as above.

Dry salt (0.3 mole) was finely ground and mixed with powdered iodine (0.32 mole). The mixture was placed in a horizontally held tube, 25 mm. in diameter and 25 cm. long; this tube was sealed at the far end, while its near end was connected to a wide trap cooled in ice water, backed by two traps cooled in Dry-Ice and a small water bubbler showing the rate of evolution of the carbon dioxide. The ice trap collected a fine sublimate of iodine and prevented clogging of the Dry-Ice traps, the first of which collected practically all of the trifluoroiodomethane.

The mixture of silver salt and iodine was heated cautiously with a gas burner, starting at the far end of the tube. The heat-decomposition is smooth at about 100°, but tends to propagate spontaneously and escape control when the heating is not done patiently. The bubbling of carbon dioxide is used as an indicator for the speed at which the burner can be moved toward the near end. With the small equipment used, it took 90 minutes to complete the reaction. The crude CF$_3$I amounted to 47 g., or 0.24 mole, an 80% yield. A series of larger runs averaged 87% yields. Purification was done by fractional distillation, which removed less than one gram of heads and tails and gave a material boiling at −21.8°, close to the reported[2] boiling point of −22.5°.

CF$_3$I is conveniently stored in glass ampules. Exposed to light it slowly becomes pink, then purple, which is in agreement with its reported easy dissociation into free radicals.

Sodium Estradiol-3-benzoate-17-sulfate and Sodium Estradiol-17-monosulfate

BY GEORGE W. HOLDEN AND ROBERT BROMLEY

In a previous note the preparation of sodium testosterone sulfate was described.[1] Tests indicate that this compound is inactive androgenically in rats in ten times the effective dose of testosterone propionate, by subcutaneous injection in propylene glycol.

It therefore seemed of interest to prepare sodium estradiol-3-benzoate-17-sulfate and sodium estradiol-17-monosulfate, neither of which has been described previously, in order to compare their estrogenic activity with that of the corresponding free 17-hydroxyl compound. The re-

(1) Holden and Bromley, THIS JOURNAL, **71**, 3844 (1949).

sults of the biological tests will be reported later.

Estradiol-3-mono-benzoate (I) was used as starting material for the preparation of sodium estradiol-17-monosulfate (III) which was readily obtained by saponification of the intermediate sodium estradiol-3-benzoate-17-sulfate (II).

(II) is insoluble in water but readily soluble in alcohol and propylene glycol. The ultraviolet absorption curve in alcohol is similar to that of (I). Neither (II) nor (I) exhibits a region of maximum absorption.

Sodium estradiol-17-monosulfate is soluble to the extent of approximately 0.5% in water at room temperature. At a concentration of 2% in water a thick gel is formed. It is readily soluble in alcohol and propylene glycol. In alcohol the characteristic absorption maximum for estradiol at 280 mμ was obtained; in water it was slightly displaced at 276–278 mμ.

Experimental

Sodium Estradiol-3-benzoate-17-sulfate.—A solution of chlorosulfonic acid, prepared by dissolving chlorosulfonic acid (2.4 ml.) in dry chloroform (72 ml.), cooling to 0° and adding dry pyridine (36 ml.), was added to a solution of estradiol-3-monobenzoate (5 g.) in dry pyridine (48 ml.) and dry chloroform (120 ml.). After sixty-eight hours at room temperature the solvent was removed *in vacuo* at a bath temperature of 40–50°. The residue was dissolved in methanol (125 ml.), the solution filtered from a small amount of insoluble matter and a 10% aqueous solution of sodium carbonate (55 ml.) was added to the clear filtrate. During this addition the product separated as a lustrous crystalline solid. The mixture was now poured into one liter of water and, after standing several hours, the solid was collected and washed with water (500 ml.). The product was dried *in vacuo* over sulfuric acid.

As thus obtained sodium estradiol-3-benzoate-17-sulfate starts to soften[2] at 155°, partially liquefies around 165° and yields a slightly opaque almost colorless fluid at 195° with effervescence; [α]^{25}D + 34.8° (1% in alc.). On heating to 110° in an oven it decomposes to yield estradiol benzoate.

Anal. Calcd. for C$_{25}$H$_{28}$O$_6$SNa·0.5H$_2$O: C, 61.5; H, 5.98; Na, 4.71. Found: C, 61.6; H, 5.8; Na, 4.6; yield, 6.49 g.; 100%.

Sodium Estradiol-17-monosulfate.—(II) (3 g.) was saponified by refluxing 1 hour in a solution of methanol (200 ml.) and sodium hydroxide (300 mg.). Water (100 ml.) was added to the cooled solution which was then treated with an excess of carbon dioxide. On removal of the bulk of methanol *in vacuo* at a bath temperature of 40–50°, the product separated. After short refrigeration it was collected, sucked as dry as possible and dried *in vacuo* over sulfuric acid. As thus obtained sodium estradiol-17-monosulfate shows no definite melting point but starts to decompose with formation of a brilliant red color at 160° and finally becomes liquid at 180° with effervescence and with color changing to orange yellow; [α]^{25}D + 42.5 (1% in alc.); + 15.8° (0.5% in water); ϵ (280) = 2000[3] (in alc.); ϵ (276–278) = 1770 (in H$_2$O). *Anal.* Calcd. for C$_{18}$H$_{24}$O$_5$SNa·H$_2$O: C, 54.95; H, 6.66; Na, 5.85. Found: C, 54.79; H, 6.53; Na, 5.85; yield, 1.97 g.; 83.3%.

Hydrolysis of Sodium Estradiol-17-Monosulfate.—(a) Fifty milligrams was refluxed four hours with the barium chloride–sodium acetate mixture described by Talbot.[4] The solids which separated on cooling were filtered off and dried *in vacuo* over sulfuric acid. Forty-five milligrams (90%) was recovered, m. p. 135–150° with the red

(2) All melting points on Fisher-Johns apparatus.
(3) Estradiol in alc. gave an ϵ value at 280 mμ of 1985.
(4) Talbot, Ryan and Wolfe, *J. Biol. Chem.*, **148**, 593 (1943).