were placed 5.8 g. of N-(2-nitro-4-bromophenyl)-*dl*-α-alanine, 50 ml. of 95% ethanol, and 5 g. of Raney nickel catalyst.[7] Hydrogen uptake ceased when about 75% of the theoretical quantity of hydrogen had been absorbed by the reaction mixture in 25 minutes at 25° and 60 p.s.i.

The reaction mixture was filtered, and the filtrate was evaporated to dryness on a steam-bath. To the residue were added 50 ml. of 10% sodium hydroxide solution and 15 ml. of 30% hydrogen peroxide. After being heated on the steam-bath for 1 hour, the mixture was filtered; the filtrate was brought to *p*H 4 with 20% hydrochloric acid to give 3.3 g. of tan powder m.p. 252–265°. Sublimation of the crude product at 195°/1 mm. gave 2.9 g. of yellow powder m.p. 273–280°. The sublimate was purified for analysis by 6 recrystallizations, using charcoal and filter aid, from 95% ethanol (100 ml./g.) to give 1.0 g. (21%) of white platelets m.p. 291–293° dec.

Absorption maxima, mμ, and molar absorptivity ($\epsilon \times 10^{+3}$), 95% ethanol: 232 (20.3); 282.5 (7.0); 327.5 (9.2); 338 (9.6); 0.1 *N* NaOH: 240 (29.8); 343.5 (11.1).

Dawson, *et al.*,[2] reported molar absorptivity in 0.1 *N* NaOH for 3-methyl-7-chloro-2-quinoxalinol to be 240 (27); 345 (9.1).

Anal. Calc'd for $C_9H_7BrN_2O$ (239.1): C, 45.21; H, 2.95; Br, 33.43; N, 11.72. Found: C, 45.32; H, 2.88; Br, 33.11; N, 11.60.

2,4-Dibromoacetanilide. This substance was prepared by a modification of Chattaway, Orton, and Hurtley's[8] procedure. In a 10 l. square battery jar equipped with a broad bladed stirrer were placed 84 g. of sodium bicarbonate, 1 l. of water, and 54 g. of acetanilide. While the mixture was violently stirred, 41 ml. of bromine was added dropwise over a 1 hour period at 25°. The light yellow precipitate of N,4-dibromoacetanilide was filtered, rinsed with water, then stirred with 300 ml. of boiling water for 1 hour. The crude 2,4-dibromoacetanilide was filtered from the cool mixture, rinsed, and again boiled in 300 ml. of water for 5 minutes. The product was filtered, rinsed, and dried to give 102.5 g. of tan powder m.p. 130–135°.

Two recrystallizations from 95% ethanol (3 ml./g.), using charcoal and filter aid, gave 78.2 g. (67%) of 2,4-dibromoacetanilide m.p. 145–147°. Reported[8,9] for this compound m.p. 146°.

The amide was hydrolyzed and steam-distilled, according to the direction of Chattaway and Clemo,[9] to give 2,4-dibromoaniline in 71% yield.

2,4-Dibromonitrobenzene. This material was prepared from *m*-dibromobenzene[10] using the same directions given by Hammond and Modic[6] for the nitration of *p*-dibromobenzene. The crude product, m.p. 55–59°, was recrystallized from 95% ethanol-ligroin (60–90°) (1:4; 2 ml./g.) in 74% yield, m.p. 61–62°. Reported[11] for 2,4-dibromonitrobenzene, m.p. 62°.

N-(2-nitro-5-bromophenyl)-dl-α-alanine. This material was prepared in 36% yield from 2,4-dibromonitrobenzene and *dl*-α-alanine using the same procedure given above for the preparation of N-(2-nitro-4-bromophenyl)-*dl*-α-alanine. The crude product, m.p. 165–170°, was recrystallized twice from benzene (20 ml./g.), using charcoal and filter aid, to give yellow needles m.p. 175–177°.

Anal. Calc'd for $C_9H_9BrN_2O_4$ (289.1): Br, 27.65; N, 9.69. Found: Br, 27.42; N, 9.66.

3-Methyl-6-bromo-2-quinoxalinol. This material was prepared in 11.4% yield from N-(2-nitro-5-bromophenyl)-*dl*-α-alanine, using the same procedure given above for the preparation of 3-methyl-7-bromo-2-quinoxalinol. The crude product, m.p. 200–220°, was sublimed (m.p. 205–230°), then recrystallized four times from 95% ethanol (10 ml./g.), using charcoal and filter aid, to give a felt-like mat of white needles, which melted at 252.5–254°, then solidified to a mass of interlacing prisms which melted again at 260–262° dec.

Absorption maxima, mμ, and molar absorptivity ($\epsilon \times 10^{+3}$), 95% ethanol: 240 (24.4); 275 (1.76); 347 (6.48); 0.1 *N* NaOH: 244 (25.8); 350 (8.25).

Anal. Calc'd for $C_9H_7BrN_2O$ (239.1): C, 45.21; H, 2.95; Br, 33.43; N, 11.72. Found: C, 45.28; H, 2.67; Br, 33.54; N, 11.81.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF MIAMI
CORAL GABLES 46, FLORIDA

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3β-Hydroxypregn-4-en-20-one

MARCEL GUT

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This compound was required for a series of biological studies. Its progestational activity is of the same order as progesterone.

3β-Hydroxypregn-5-en-20-one acetate was converted to its 20-ethylene ketal by treating with ethylene glycol in benzene solution with a catalytic amount of *p*-toluenesulfonic acid. This acetate was saponified with methanolic sodium hydroxide and the resulting free alcohol was oxidized with aluminum isopropoxide to progesterone-20-ethylene ketal.[1] The latter compound was reduced with sodium borohydride presumably to a mixture of 3α- and 3β-hydroxypregn-4-en-20-one-20-ethylene ketal. The pure 3β-isomer, obtained by digitonide separation, furnished the desired 3β-hydroxypregn-4-en-20-one on treatment with ethanolic oxalic acid[2] at room temperature.

EXPERIMENTAL[3]

3β-Hydroxypregn-5-en-20-one-20-ethylene ketal acetate. A solution of 15 g. of 3β-hydroxypregn-5-en-20-one acetate in 530 cc. of dry benzene and 16 cc. of ethylene glycol was refluxed with 1.0 g. of *p*-toluenesulfonic acid employing a water separator. After 18 hours, the separation of water was complete and the mixture was washed with a saturated aqueous bicarbonate solution, dried over sodium sulfate,

(1) K. Junkmann, *Arch. exptl. Pathol. Pharmakol.*, **223**, 244 (1954).

(2) In view of the facile elimination of the allylic hydroxyl only very mild acidic conditions can be used. Compare H.-W. Wanzlick, G. Gollmer, and H. Milz, *Ber.*, **88**, 69 (1955).

(3) All melting points are uncorrected. Microanalyses are by the Schwarzkopf Microanalytical Laboratory, Woodside 77, N. Y., IR absorption spectra by Mr. Paul Skogstrom. The rotations are for chloroform solutions and were determined in a 1-dm. tube at wave length 5893 A. (D). "Woelm," non-alkaline aluminum oxide, activity grade 1 was used for chromatography.

and evaporated. There remained a semicrystalline residue weighing 14.6 g.

A small sample was chromatographed on aluminum oxide and gave after recrystallization from methanol colorless plates melting at 157–161°. $[\alpha]_D^{26}$ −40° ± 2°.

Anal. Calc'd for $C_{25}H_{38}O_4$: C, 74.59; H, 9.52. Found: C, 74.59; H, 9.47.

Infrared analysis indicated the absence of a ketone (no band from 1818–1538 cm.$^{-1}$).

3β-Hydroxypregn-5-en-20-one-20-ethylene ketal. Crude 3β-hydroxypregn-5-en-20-one-20-ethylene ketal acetate (10 g.) was saponified with 500 cc. of 5% methanolic sodium hydroxide at 26° during 4 hours which gave 8.1 g. of crude 3β-hydroxypregn-5-en-20-one-20-ethylene ketal. A sample was chromatographed on aluminum oxide and gave after recrystallization colorless prisms with the following constants: melting point, 163–166°; $[\alpha]_D^{26}$ −39° ± 2°. Infrared analysis indicated the absence of a ketone (no band from 1818–1538 cm.$^{-1}$) and the presence of a hydroxyl (band at 3650 cm.$^{-1}$).

Anal. Calc'd for $C_{23}H_{36}O_3$: C, 76.62; H, 10.07. Found: C, 76.97; H, 9.57.

Progesterone-20-ethylene ketal. A solution of 3.0 g. of aluminum isopropoxide in 30 cc. of toluene was added to a solution of 7.0 g. of crude 3β-hydroxypregn-5-en-20-one-20-ethylene ketal in 250 cc. of toluene and 55 cc. of cyclohexanone. The mixture was refluxed for 1 hour, steam-distilled, and taken up in benzene. The benzene layer was washed successively with water, ammonium chloride solution, and water again, and finally the benzene layer was dried and evaporated. The crude residue was purified by chromatography on aluminum oxide and gave after recrystallization from methanol 5.9 g. of pure progesterone-20-ethylene ketal (colorless prisms), melting at 189–191°; $[\alpha]_D^{26}$ +119° ± 2°.

Anal. Calc'd for $C_{23}H_{34}O_3$: C, 77.05; H, 9.56. Found: C, 77.32; H, 9.71.

The structure of this product was further established by its infrared analysis, indicating the presence of the conjugated ketone (band at 1681 cm.$^{-1}$) and the absence of a saturated ketone. An ultraviolet absorption spectrum showed a λ_{max}^{EtOH} 242 mμ (ε 16,800).

3β-Hydroxypregn-4-en-20-one-20-ethylene ketal. Progesterone-20-ethylene ketal (2 g.) was dissolved in 40 cc. of methanol and 1.0 g. of sodium borohydride was added in small portions with magnetic stirring over a period of four hours. The solution was stored overnight, water was added, the methanol was evaporated off *in vacuo*, and the mixture was filtered and recrystallized from methanol resulting in 1.8 g. of colorless prisms, melting from 157–175°. The infrared analysis indicated the presence of hydroxyl (band at 3700 cm.$^{-1}$) and the absence of a ketone (no band from 1818–1538 cm.$^{-1}$). The ultraviolet analysis showed no absorption from 225–270 mμ. An 800-mg. sample of the above mixture was carried through a digitonin separation and gave 609 mg. of the *beta*-fraction, which, after chromatography on aluminum oxide, crystallized in prisms from methanol, melting from 170–173°; $[\alpha]_D^{26}$ +71° ± 2°.

Anal. Calc'd for $C_{23}H_{36}O_3$: C, 76.62; H, 10.07. Found: C, 76.65; H, 9.98.

3β-Hydroxypregn-4-en-20-one. Crude 3β-hydroxypregn-4-en-20-one-20-ethylene ketal (300 mg.) was dissolved in 20 cc. of 0.08% ethanolic oxalic acid solution and allowed to stand for 16 hours at 25°. Then the mixture was neutralized with concentrated ammonia solution, the ethanol evaporated off *in vacuo*, and the resulting crystallizate was filtered off. After chromatography on aluminum oxide and recrystallization from methanol 230 mg. of colorless prisms, melting at 155–161° were obtained, $[\alpha]_D^{26}$ +135° ± 2°.

Anal. Calc'd for $C_{21}H_{32}O_2$: C, 79.70; H, 10.14. Found: C, 79.96; H, 9.98.

The structure of this product was further established by infrared analysis, indicating the presence of a hydroxyl (band at 3750 cm.$^{-1}$) and a ketone (band at 1705 cm.$^{-1}$). The ultraviolet analysis showed no absorption from 225–250 mμ (in ethanol).

THE WORCESTER FOUNDATION
FOR EXPERIMENTAL BIOLOGY
SHREWSBURY, MASSACHUSETTS

The Preparation and Properties of Some Fluorine-Containing Epoxides

DOUGLAS A. RAUSCH, ALAN M. LOVELACE, AND LESTER E COLEMAN, JR.

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In an investigation directed toward the polymerization of fluorine-containing epoxides, six hitherto unreported fluorine-containing epoxides of the general formula $R_fCHCXYO$ (when X = H; Y = CH_3, C_2H_5; when X = CH_3; Y = CH_3; R_f = CF_3, *n*-C_3F_7) have been prepared. The procedure described by McBee, *et al.*[1,2] for the conversion of 1,1,1-trifluoroacetone to 3,3,3-trifluoro-1,2-epoxypropane was found to be satisfactory for the preparation of these new epoxides.

The alkyl perfluoroalkyl ketones were most conveniently prepared using the method described by Dishart and Levine[3] in which one mole of perfluorocarboxylic acid was treated with three moles of alkyl Grignard reagent. By this procedure, the ketones were prepared in 40–60% yields accompanied by considerable amounts of the corresponding secondary alcohols. It was found, however, that the alkyl perfluoroalkyl ketones could also be prepared in similar yields by the reaction of 1.1 moles of the alkyl Grignard reagent with one mole of the lithium salt of the perfluorocarboxylic acid using the reverse addition technique. Using this procedure no secondary alcohols were isolated; however, perfluorocarboxylic acid-diethyl ether complexes[4] were obtained accounting for 20 to 35% of the perfluorocarboxylic acid. Other workers[5] have also shown that *n*-butyl trifluoromethyl ketone can be prepared in a 61% yield by treating lithium trifluoroacetate with *n*-butyllithium.

Bromination of the alkyl perfluoroalkyl ketones in concentrated sulfuric acid resulted in each case in a single monobromo derivative. These monobromoketones were shown to be the α-bromo derivatives by their subsequent conversion to substituted 1,2-epoxides.

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