1,3-difluoro-2,4,6-trinitrobenzene from *m*-difluorobenzene.

m-Difluorobenzene (I) was nitrated using the procedure described by Zahn and Würz.[1] Pure, 1,3-difluoro-4,6-dinitrobenzene (II) was obtained in 77% yield after recrystallization from boiling carbon tetrachloride.

Difluorotrinitrobenzene (III) was prepared in 28% yield by vigorously nitrating 1 mole of II with an acid mixture consisting of 4.5 moles of potassium nitrate and a quantity of 30% fuming sulfuric acid corresponding to 17.8 moles of free sulfur trioxide. The nitration was conducted for twelve hours at 180°. After pouring the cooled nitrating solution onto crushed ice, a white solid melting at 60° was obtained in 49% yield. A white needle-like solid melting at 147° was collected after carefully recrystallizing the low-melting material from carbon tetrachloride. Evaporation of the solvent gave II.

The molecular weight as determined by the Rast method using triphenylphosphate was found to be 236. Reaction of III with alcoholic ammonia and ethanol gave 1,3-diamino-2,4,6-trinitrobenzene and 1,3-diethoxy-2,4,6-trinitrobenzene, respectively. Nuclear magnetic proton resonance obtained at a frequency of 56.4 Mc. and a field strength of 13,247 gauss revealed that III contained 50% of the protons originally present in II. The elemental analysis was in agreement with the proposed structure.

Experimental[2]

1,3-Difluoro-4,6-dinitrobenzene.—*m*-Difluorobenzene (40 g., (0.195 mole) was added at 0°, with stirring, to an acid mixture containing 85 ml. of 98% nitric acid and 160 ml. of 96% sulfuric acid. The reaction mixture was held at 0° for 0.5 hr. The temperature was then raised slowly to 95° and maintained for 1 hr. The nitration mixture was cooled to −10° and quenched in 1000 g. of crushed ice. The temperature during quenching was not allowed to rise above −10°. The solid which separated was collected by filtration, washed with ice water, and air-dried. Yellow platelets were obtained by recrystallization from 550 ml. of carbon tetrachloride. The yield was 55 g. (77%), m.p. 75–76°, lit. 76°.

1,3-Difluoro-2,4,6-trinitrobenzene.—To a nitrating mixture consisting of 11 g. (0.11 mole) of potassium nitrate and 60 ml. of 30% fuming sulfuric acid was added, with stirring, 5 g. (0.025 mole) of difluorodinitrobenzene. The stirring was continued and the mixture was heated at 180° for 12 hr. The nitration solution was cooled to −10° and then poured slowly, with stirring, onto 120 g. of crushed ice. A cooling bath was used to keep the temperature below −10°. The solid which separated was collected by filtration, washed quickly with three 20-ml. portions of ice water and then dried over sodium hydroxide under approx. 5 mm. This product weighed 3.0 g. (49%) and melted at 60°. Purification was effected by recrystallization from 95 ml. of boiling carbon tetrachloride. The yield of III was 1.71 g. (28%), m.p. 147°. Upon cooling the mother liquor below room temperature, II was obtained.

(1) H. Zahn and A. Würz; *Biochem. Z.*, **325**, 182–194 (1954).

(2) All melting points are uncorrected. Microanalyses by Mr. Marcel Blais, Explosives Research Section, Picatinny Arsenal.

Anal. Calcd. for $C_6HN_3O_6F_2$: C, 28.93; H, 0.41; N, 16.87; F, 15.26. Found: C, 28.76; H, 0.44; N, 16.86; F, 14.58.

1,3-Diamino-2,4,6-trinitrobenzene.—Anhydrous ammonia was bubbled into a solution of 1 g. (0.005 mole) of III in 20 ml. of absolute methanol for 15 min. at 25°. The mixture was warmed on a steam bath for 10 min. and then cooled to room temperature. The yellow solid which separated was collected by filtration and washed with two 10-ml. portions of methanol and finally with 50 ml. of ether. The air-dried solid weighed 0.8 g. (82%), m.p. 288°, lit., 285°.

1,3-Diethoxy-2,4,6-trinitrobenzene.—A solution of 1 g. (0.005 mole) of III in 10 ml. of absolute ethanol was warmed on the steam bath for 10 min. The solution was placed in a refrigerator for 3 hr. During this time a white solid separated. The solid was separated by filtration and recrystallized from ethanol. The yield of diethoxy product was 1.1 g. (91%), m.p. 121°.

Anal. Calcd. for $C_{10}H_{11}N_3O_8$: C, 39.87; H, 3.68; N, 13.95. Found: C, 39.84; H, 3.51; N, 14.23.

Synthesis of Quinolino Steroids

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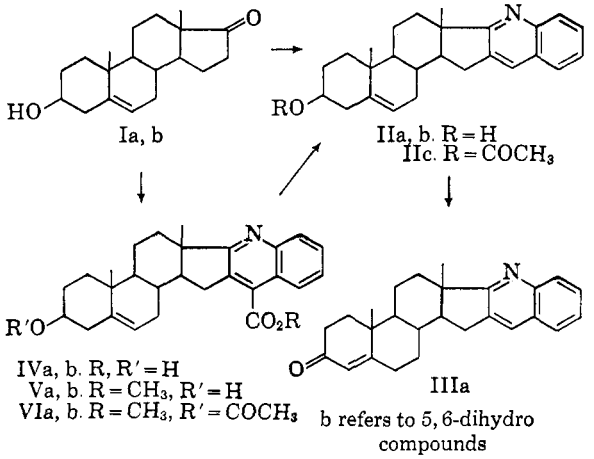
Quinolines fused to a steroid nucleus were first reported[1] in 1924 at a time when the structures of the starting ketocholanic acids were not well established. In 1944 Buu-Hoï and Cagniant[2] reported the preparation of a steroido-quinoline, VIII, and found that its sodium salt possessed hemolitic properties. As part of an effort towards the synthesis of potential carcinogens and antitumor agents, we were interested in studying methods of synthesis of steroido-heterocycles and in applying the Friedlander reaction[3] to the formation of quinolines fused to the D-ring of steroids.



(1) W. Borsche and R. Frank, *Ber.*, **57**, 1373 (1924).

(2) N. P. Buu-Hoï and P. Cagniant, *Ber.*, **77**, 118 (1944).

(3) J. Eliasberg and P. Friedlaender, *Ber.*, **25**, 1752 (1892).

(4) W. H. Perkin, Jr., and W. G. Sedgwick, *J. Chem. Soc.*, 2446 (1924).

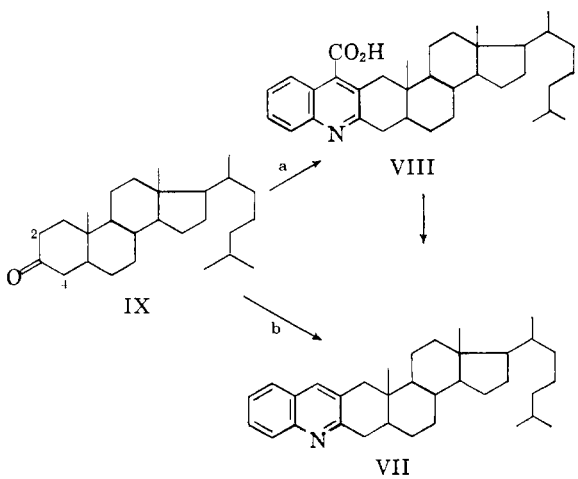
(5) N. H. Cromwell and V. L. Bell, *J. Org. Chem.*, **24**, 1077 (1959); **23**, 789 (1958).

Condensation of 5-androstene-3β-ol-17-one (Ia) with *o*-aminobenzaldehyde in basic solution gave in 90% yield quinolino steroid IIa, which could be converted by Oppenauer oxidation to the ketone IIIa. To verify the structure of IIa, we synthesized it by a route previously employed with other cyclic ketones.[4,5] Thus reaction of Ia with isatin gave the quinoline carboxylic acid IVa which was decarboxylated to quinoline IIa by heating with copper powder. Analogous reactions could be achieved in the 5,6-dihydro series.

The quinolines IIa, IIb, IVa, IVb, Va, Vb, VIa, VIb, VII and VIII exhibited characteristic ultraviolet absorption similar to that of 1,2,3,4-tetrahydroacridine and 2,3-cyclopentanoquinoline. However, the spectra of all cyclopentanoquinolines (including II, IV–VI) show a slight hypsochromic displacement of the multiplet absorption in the 305–320-mμ region with respect to the spectra of the cyclohexanoquinolines. This and the fact that the corresponding extinction coefficients are considerably lower (15–25%) in the cyclopentanoquinolines suggests that in the latter ring strain becomes more important than in the cyclohexanoquinolines.

Quinolino steroid IIb was obtained from Ib by reaction with *o*-aminobenzaldehyde. Pfizinger reaction of epiandrosterone (Ib) with isatin led to acid IVb (R = H) but decarboxylation of the latter to IIb under a variety of conditions was unsuccessful. Ketones Ia or Ib, unlike tetralones,[5] did not condense with *o*-nitrobenzaldehyde under acidic conditions. Under basic conditions, products that were not the expected *o*-nitrobenzalketones were formed.[6] It was however possible to prepare 3β-acetoxy-16-(*o*-nitrobenzal)-5-androstene-17-one *via* the magnesium enolate[6] of Ia and convert it into quinoline IIa by reduction with iron and acid.

In searching the literature, we found that 3-cholestanone (IX) had been used in analogous reaction sequences by different workers in the preparation of VII. Buu-Hoï[7] found a melting point of 193° for VII prepared *via* the isatin method (path a) while Antaki and Petrow[7] apparently unaware of Buu-Hoï's work reported a melting point of 184° for VII prepared *via* the Friedlander synthesis (path b).



(6) These reactions will be the subject of a subsequent publication.

(7) H. Antaki and V. Petrow, *J. Chem. Soc.*, 901 (1951).

This discrepancy was resolved by repeating their reactions. We were able to show that quinoline VII, m.p. 184°, obtained by route (a) was actually identical in melting point and infrared spectrum to the material obtained by route (b). There has been some question[7] whether *o*-aminobenzaldehyde condensed with 3-cholestanone (IX) to give a 2,3-quinolino compound (VII) or an alternate 3,4-quinolino steroid. We have tried to synthesize a 3,4-quinolino steroid for optical rotatory dispersion comparison, but attempted Friedlander synthesis starting with 2,2-dimethylcholestanone even under forcing conditions led to recovery of starting material.[8] This and the fact that enolization of 3-keto-5α-steroids is known to proceed almost exclusively towards the 2-position[9] establishes structure VII and thus also VIII for the quinolines derived from 3-cholestanone.

It is therefore possible to achieve the synthesis of steroid alkaloids of type II or VII by conventional methods used in the synthesis of quinolines. The quinolines prepared in this investigation have been submitted for phamacological screening, the results of which will be communicated separately.

Experimental[10]

Quinolino(3′:2′-16:17)-5-andostene-3β-ol (IIa).—5-Androstene-3β-ol-17-one (2.0 g., m.p. 147–149°) was dissolved in 95% ethanol (20 ml). Freshly prepared[11] *o*-aminobenzaldehyde (1.2 g.) was added, followed by 30% potassium hydroxide solution (4 ml.). After 18 hr. at room temperature, the solution was diluted with water (1 ml.) and allowed to stand in the cold for 2 days. The white solid that precipitated was collected by filtration and recrystallized from ethanol–water to give hard needles of IIa (2.0 g.) that melted at 259–261°. From the mother liquor, upon dilution with water and repeated recrystallization of the collected solid, a second crop (0.5 g.) of IIa was obtained. Similar yields were obtained if the crude reaction product was chromatographed.

The analytical sample melted at 259–261°, ν_{max} 3500 cm.$^{-1}$ (OH), 1640 cm.$^{-1}$ (C=N); λ_{max} 234, 238, 305, 310, 317 mμ

(8) This is analogous to findings by Barton, *et al.*, *J. Chem. Soc.*, 1927 (1960) that aldol condensations at C-4 cannot be achieved with 2-methyl-3-keto-5α-steroids.

(9) L. F. Fieser and M. Fieser, "Steroids," Reinhold, New York, 1959.

(10) All melting points are corrected. Infrared spectra were determined in the solid phase (KBr) using a Beckman infrared spectrophotometer Model 1R5. Ultraviolet spectra were measured in methanol solution on a Cary Model XIV instrument. Optical rotations were measured in chloroform solution at concentrations of 1–2%. Alumina used for chomatography was neutral, Woelm Activity I. Elemental analyses were performed by Pascher Laboratories, Bonn, Germany. We are grateful to Dr. Mancera of Syntex, Mexico, for samples of 5-androstene-3β-ol-17-one. The presence of two hydroxy peaks in the infrared spectra of Va and IIb can be attributed to nonbonded (3590 cm.$^{-1}$) and bonded OH (3440 cm.$^{-1}$, broad). That intermolecular hydrogen bonding (probably to N) is involved here, was shown for IIb by the diminution of the 3440-cm.$^{-1}$ peak upon dilution in chloroform.

(11) I. Smith and J. W. Opie, *Org. Syntheses*, Coll. Vol. III, 56 (1955).

(ϵ 38,200, 39,300, 6250, 5190, 9550, respectively); $[\alpha]^{25}D$ -49.8 ± 1.

Anal. Calcd. for $C_{26}H_{31}ON$: C, 83.60; H, 8.37; N, 3.75. Found: C, 82.97; H, 8.33; N, 3.93.

Acetylation of IIa (200 mg.) with acetic anhydride in pyridine at room temperature yielded **quinoline(3′:2′–16:17)-5-androstene-3-β-ol acetate** (IIc) (200 mg.). An analytical sample from methanol melted at 216–217°; ν_{max} 3050 cm.$^{-1}$, 1725 cm.$^{-1}$ (C=O of acetate), 1625 cm.$^{-1}$ (C=N), 1600 cm.$^{-1}$, 1250 cm.$^{-1}$, 758 cm.$^{-1}$, 750 cm.$^{-1}$.

Anal. Calcd. for $C_{28}H_{33}O_2N$: C, 80.92; H, 8.00; N, 3.37. Found: C, 80.59; H, 8.12; N, 3.60.

4′-Carboxyquinolino(3′:2′–16:17)-5-androstene-3β-ol (IVa).—5-Androstene-3β-ol-17-one (2.0 g., m.p. 147–149°) was dissolved in alcoholic potassium hydroxide (10 ml. of 95% ethanol and 1 g. of potassium hydroxide). Isatin (1.0 g., m.p. 198–200°) was added to the solution. The dark violet solution was heated under reflux for 24 hr., then concentrated in vacuum to about 5 ml. The solid that precipitated upon cooling was collected, washed with cold water, and then digested with hot water. Filtration afforded a solid and an aqueous filtrate. The latter was acidified with dilute hydrochloric acid to give a gelatinous precipitate which was washed with water and dried (200 mg., m.p. >300). The hot water-insoluble solid was dissolved in ethanol with warming. Acidification with concd. hydrochloric acid yielded a gelatinous tan solid. The solid was washed with ethanol to furnish 350 mg. of nearly white product. Total yield of IVa was 550 mg., m.p. >300. ν_{max} 3590 cm.$^{-1}$, 3440 cm.$^{-1}$ (OH), 2600–2350 cm.$^{-1}$ (H-bonded CO_2H), 1710 cm.$^{-1}$ (C=O of CO_2H), 1640 cm.$^{-1}$ (C=N), 1230 cm.$^{-1}$ (broad).

Decarboxylation of 4′-Carboxyquinolino(3′:2′–16:17)-5-androstene-3β-ol (IVa).—4′-Carboxyquinolino(3′:2′–16:17)-5-androstene-3β-ol (IVa) (150 mg.) was mixed thoroughly with copper powder (500 mg.) and the mixture was placed in in a sublimer immersed in a Wood's metal bath. The sublimation was carried out at reduced pressure (0.5–1.0 mm.) and 250–255° bath temperature for 6 hr. The yellowish sublimed product (38 mg., m.p. 190–205°) was recrystallized twice from ethanol–water to furnish needles that melted at 259–261°. The identity with IIa was confirmed by infrared spectrum and mixed melting point with an authentic sample.

4′-Carbomethoxyquinolino(3′:2′–16:17)-5-androstene-3β-ol (Va).—Acid IVa (340 mg.) was esterified with diazomethane in ether–methanol. The product (340 mg.) was unsatisfactorily recrystallized from petroleum ether (b.p. 80–90°) to afford rosettes of Va that melted at 186–191°. No other adequate solvent was found for recrystallization. ν_{max} 3590 cm.$^{-1}$, 3440 cm.$^{-1}$ (OH), 1715 cm.$^{-1}$, (C=O of ester), 1600 cm.$^{-1}$, (C=N), 1230 cm.$^{-1}$, 775 cm.$^{-1}$, 760 cm.$^{-1}$.

4′-Carbomethoxyquinolino(3′:2′–16:17)-5-androstene-3β-ol Acetate (VIa).—Alcohol Va (330 mg.) was acetylated with acetic anhydride in pyridine at room temperature overnight. The crude product (340 mg.) was recrystallized from 95% ethanol to furnish 200 mg. of white needles, m.p. 197–199°. More product was obtained from a second crop (55 mg., m.p. 195–197°). The analytical sample of VIa melted at 197–199°; λ_{max} 240, 306–314, 321 mμ, (ϵ 24,700, 6500, 7700, respectively); ν_{max} 1725 cm.$^{-1}$ (C=O of acetate), 1710 cm.$^{-1}$ (C=O of ester), 1600 cm.$^{-1}$ (C=N), 1250 cm.$^{-1}$ (acetate), 1220 cm.$^{-1}$ (methyl ester); $[\alpha]^{25}D$ $-104°$.

Anal. Calcd. for $C_{30}H_{35}O_4N$: C, 76.08; H, 7.47; N, 2.96. Found: C, 76.14; H, 7.27; N, 3.05.

Quinolino(3′:2′–16:17)-4-androstene-3-one (IIIa).—A solution of 100 mg. of quinoline IIa, 1.0 ml. of cyclohexanone, and 120 mg. of aluminum isopropoxide in 100 ml. of dry benzene was heated overnight under reflux. The benzene solution was washed with water and with dilute sodium hydroxide solution, dried, and chromatographed over alumina. From the benzene–ether (4:1) eluents there was obtained 90 mg. of IIIa, m.p. 243–246°. Recrystallization from methanol raised the m.p. to 250–251°. ν_{max} 1680 cm.$^{-1}$ (conjug. C=O), 1620 cm.$^{-1}$ (conjug. C=C).

Anal. Calcd. for $C_{26}H_{29}ON$: C, 84.05; H, 7.87; N, 3.77. Found: C, 83.64, 83.62; H, 7.82, 7.82; N, 3.93.

Quinolino(3′:2′–16:17)androstane-3β-ol (IIb).—From reaction of 2.0 g. of androstane-3β-ol-17-one (m.p. 174–177°) with 1.2 g. of freshly prepared[11] *o*-aminobenzaldehyde, as described for the preparation of IIa, there was obtained 0.9 g. of IIb, white needles from ethanol–water, m.p. 228–230°. The mother liquors afforded 0.56 g. more of the product. ν_{max} 3610 cm.$^{-1}$, 3340 cm.$^{-1}$ (OH), 1635 cm.$^{-1}$ (C=N); λ_{max} 234, 238, 305, 310, 317 mμ (ϵ 37,500, 39,300, 6200, 5120, 9550, respectively); $[\alpha]^{25}D$ $+46°$.

Anal. Calcd. for $C_{26}H_{33}ON$: C, 83.15; H, 8.86; N, 3.73. Found: C, 82.93; H, 8.84; N, 3.69.

4′-Carboxyquinolino(3′:2′–16:17) androstane-3β-ol (IVb).—Acid IVb was prepared from androstane-3β-ol-17-one (2.0 g.) and isatin (1.0 g.) by heating in alcoholic potassium hydroxide as described for the preparation of IVa. The potassium salt (2.1 g.) obtained by concentrating the solution in vacuum, was dissolved in ethanol and acidified with concd. hydrochloric acid (4 drops). There was thus obtained 550 mg. of IVb which melted above 300°. No adequate solvent was found for recrystallization.

ν_{max} 3590 cm.$^{-1}$, 3440 cm.$^{-1}$ (OH), 2520–2250 cm.$^{-1}$ (broad), 2000–1800 (broad), 1700 cm.$^{-1}$ (C=O of CO_2H), 1600 cm.$^{-1}$ (C=N). Decarboxylation attempts on IVb in the presence of copper, copper chromite, or quinoline were unsuccessful.

4′-Carbomethoxyquinolino(3′:2′–16:17)androstane-3β-ol Acetate (VIb).—A suspension of IVb (300 mg.) in ether–methanol was treated with excess diazomethane. Usual work up gave 290 mg. of oil which solidified. Chromatography of the latter on neutral alumina gave a solid (eluted with benzene), m.p. 85–105°. No satisfactory solvent could be found for recrystallization of 4′-carbomethoxyquinolino (3′:2′–16:17) androstane-3β-ol (Vb); ν_{max} 3400 cm.$^{-1}$ (OH), 1715 cm.$^{-1}$ (C=O of ester), 1600 cm.$^{-1}$ (C=N), 1200 cm.$^{-1}$ (CH_3OC), 775 cm.$^{-1}$, 760 cm.$^{-1}$.

$$\overset{\overset{\|}{O}}{}$$

The above crude alcohol (275 mg.) was acetylated in acetic anhydride–pyridine at room temperature. Usual work up with ice water, gave 250 mg. of VIb (m.p. 190–195°). Recrystallization from ethanol–water furnished shiny plates (150 mg.) that melted at 197–199°. A second crop afforded 50 mg., m.p. 190–196°. An analytical sample melted at 200–201°, λ_{max} 240, 306–314, 321 mμ (ϵ 24,600, 6500, 7700, respectively); $[\alpha]^{25}D$ $-22°$; ν_{max} 1720 cm.$^{-1}$ (C=O of acetate), 1690 cm.$^{-1}$ (shoulder, C=O of ester), 1610 cm.$^{-1}$ (C=N), 1250 cm.$^{-1}$ (broad), 1200 cm.$^{-1}$.

Anal. Calcd. for $C_{30}H_{37}O_4N$: C, 75.76; H, 7.84; N, 2.95. Found: C, 75.42; H, 8.02; N, 3.06.

Quinolino(3′:2′–2:3)cholestane (VII).—Condensation of 3-cholestanone (IX) with *o*-aminobenzaldehyde as described by Antaki and Petrow[4] gave white needles of VII recrystallized from 95% ethanol, m.p. 184°. Reaction of IX with isatin according to Buu-Hoï and Cagniant[2] gave acid VIII in poor yield. Decarboxylation of the latter as described for the decarboxylation of IVa afforded VII, m.p. 184°. There was no melting point depression on admixture with VII prepared *via* the Friedlander reaction and the infrared spectra of the two samples were identical. ν_{max} 1620 cm.$^{-1}$ (C=N), 1600 cm.$^{-1}$, 780 cm.$^{-1}$, 750 cm.$^{-1}$; λ_{max} 234, 238, 307, 314, 321 mμ (ϵ 44,000, 48,700, 7040, 5630, 10,440, respectively).

1,2,3,4-Tetrahydroacridine.—This compound was prepared as described by Perkin[4] m.p. 55–56° (lit.,[12] m.p. 55–56°); λ_{max} 234, 238, 307, 314, 321, mμ (ϵ 46,500, 49,700, 8000, 3370, 11,100, respectively); ν_{max} 1620 cm.$^{-1}$ (C=N), 1590 cm.$^{-1}$, 1550 cm.$^{-1}$, 780 cm.$^{-1}$, 750 cm.$^{-1}$.

2,3-Cyclopentanoquinoline was prepared according to Borsche,[12] m.p. 58.5–59.5° (lit.,[12] 59–60°); λ_{max} 234, 238,

(12) W. Borsche, *Ann.*, **377**, 120 (1910).

305, 313, 318 mμ (ε 34,200, 35,000, 5800, 5640, 9340, respectively); ν_{max} 1620 (C=N), 1560 cm.$^{-1}$, 785 cm.$^{-1}$, 752 cm.$^{-1}$.

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The Acid-Catalyzed Conversion of Diethyl Ketone to Methyl Propyl Ketone—A Reinvestigation[1]

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In a previous note,[2] Fry, Eberhardt, and Ookuni reported that diethyl ketone (3-pentanone) rearranged to the extent of 63% to methyl propyl ketone (2-pentanone) upon treatment with 70% perchloric acid for three hours at steam bath temperature. We have been unable to demonstrate such extensive rearrangement in more recent experiments at Michigan State University and at the University of Arkansas. 3-Pentanone is converted to 2-pentanone upon treatment with acid but not to as great an extent as previously reported.

When 3-pentanone is treated with perchloric acid, concentrated sulfuric acid, or benzenesulfonic acid under conditions which allow a reasonably large recovery (~20% or more) of nonpolymeric ketonic material, only a trace of 2-pentanone could be detected by NMR or gas chromatographic analysis of the pentanone fraction.

Under more drastic conditions in which the recovered ketonic fraction amounts to only a few per cent, up to 15% of the recovered pentanone fraction is 2-pentanone. The results of a series of experiments of this type are summarized in Table I.

It is clear that 2-pentanone is formed from 3-pentanone and that its concentration relative to that of 3-pentanone increases with time.[3] The extensive condensation to polymeric material prevents longer time studies. The possibility that the 2-pentanone did not come from the 3-pentanone at all, but that it might have been present as a trace impurity in the starting material and have been concentrated by undergoing a much slower condensation to polymeric material than the 3-pentanone was considered. This possibility was eliminated by showing that the pentanone fraction recovered from treatment of a 50:50 mixture of 2- and 3-pentanones with 70% perchloric acid at 100° for nine hours contained ~25% 2-pentanone and ~75% 3-pentanone. That the conversion is reversible was shown by treatment of 2-pentanone with ~70% perchloric acid at 75° for twenty-four hours. 3-Pentanone was shown to be present by NMR analysis, and the amount was estimated to be ~1% by gas chromatography.

It is interesting to note that the iodoform reaction used in the identification of 2-pentanone in the previous report[2] is not completely reliable in characterizing the methyl ketone. Both 2- and 3-pentanones give iodoform under our usual conditions, although at greatly different rates. This type of behavior has been noted before by Cullis and Hashmi.[4]

TABLE I

PERCHLORIC ACID-CATALYZED CONVERSION OF 3-PENTANONE TO 2-PENTANONE[a]

Temp.	Time, Hr.	Recovered Material, B.P. 50–110°, %	Recovered Pentanone Fraction, %	2-Pentanone in Recovered Pentanone Fraction,[b] %
75	24	[c]	[c]	2
75	48	[c]	1.8	5[d]
100	3	12.0	[c]	3
100	6	10.4	2.4	5
100	9	7.0	1.5	7
100	12	9.1	1.9	12[e]
100	15	5.2	0.6	11
100	24	3.4	0.2	14

[a] Three milliliters of ~70% perchloric acid per gram of 3-pentanone. [b] Determined by gas chromatography (see Experimental). [c] Not determined. [d] Infrared analysis shows 6% 2-pentanone; NMR analysis shows 3–5% 2-pentanone. [e] Infrared analysis shows 14% 2-pentanone; NMR analysis shows 15.0% 2-pentanone. We are indebted to Dr. Harold F. Smith of Continental Oil Co. for this NMR analysis.

Experimental

Conversion of 3-Pentanone to 2-Pentanone.—A typical experiment is described here. Other experiments differed in the relative concentrations of acid and ketone used, the temperature, the time, and the acid used. These variables were changed over a wide range. Much less decomposition takes place in perchloric acid than in sulfuric acid, so perchloric acid was used in most cases. A mixture of 100 g. of 3-pentanone and 300 ml. of 71.7% perchloric acid was heated with stirring for 48 hr. in an oil bath at 75.0 ± 0.2°. The reaction mixture, initially light yellow, gradually turned almost black. The solution was poured into ice and neutralized with sodium hydroxide. The aqueous phase was saturated with sodium chloride and extracted with ether. The ether layer was distilled and several fractions were collected. Most of the organic material remained as a brown, viscous residue. Gas chromatography

(1) Supported in part by the U. S. Atomic Energy Commission.

(2) A. Fry, M. Eberhardt, and I. Ookuni, *J. Org. Chem.*, **25**, 1252 (1960).

(3) That this type of behavior is not restricted to this case is clear from the observation that treatment of 2-butanone-1-C^{14} with perchloric acid results in the distribution of the label between the methyl and ethyl groups (I. Ookuni and A. Fry, unpublished data).

(4) C. F. Cullis and M. H. Hashmi, *J. Chem. Soc.*, 1548 (1957).