acidification; acidification and ether extraction of the sodium hydroxide solution gave 18.09 g. of phenol, b.p. 179–180°.

Benzoic Acid–Acetophenone.—Bicarbonate extraction of the reaction mixture removed no benzoic acid. Distillation of the residue yielded 49.74 g. of material boiling at 84–87° (18 mm.), $n^{18.5}$D 1.5256. Reference to a refractive index–composition curve for methyl benzoate–acetophenone mixtures showed the composition of the distillate to be 49.8 mole % ester–50.2 mole % ketone.

Acetophenone–Phenol.—Phenol (16.22 g.) was isolated by extraction with sodium hydroxide solution. Fractionation of the residue gave 1.82 g. of anisole, b.p. 49–50° (19 mm.), n^{20}D 1.5170; and 23.14 g. of acetophenone, b.p. 89–90° (19 mm.), n^{18}D 1.5345.

Benzoic Acid–Benzoyl Bromide.—Hydrogen bromide, in place of hydrogen chloride was passed into the reaction mixture. After the solution had remained overnight in contact with saturated sodium bicarbonate solution (hydrolysis of benzoyl bromide), 23.21 g. of benzoic acid, m.p. 122–124°, was obtained. Distillation of the ethereal solution gave 23.97 g. of methyl benzoate, b.p. 86–87° (18 mm.), $n^{18.7}$D 1.5164; the distillation residue was recrystallized from aqueous methanol, and 2.40 g. of phenacyl bromide, m.p. 49–50°, was collected.

Benzoic Acid–Benzoyl Chloride.—The reaction mixture was treated with saturated sodium bicarbonate solution as in the preceding experiment, and 4.07 g. of benzoic acid was isolated. Methyl benzoate and unhydrolyzed benzoyl chloride were removed from the ethereal solution by vacuum distillation, and recrystallization of the residue from petroleum ether (30–60°) yielded 0.45 g. of phenacyl chloride, m.p. 52–53°. The ester–acyl halide mixture was shaken with aqueous silver nitrate until the precipitation of silver chloride was complete, and the precipitate (21.43 g. ≡ 18.26 g. benzoic acid) was collected and washed repeatedly with ether and with water. The filtrate and washings yielded 25.89 g. of methyl benzoate, b.p. 86–87° (18 mm.), $n^{18.7}$D 1.5170.

TABLE I

Reactants A	Reactants B	Reaction ratio A/B[a]	Mole % recovery[a]
Phenol	Benzoic acid	0	97
Acetophenone	Benzoic acid	0	97
Acetophenone	Phenol	0	95
Benzoyl bromide	Benzoic acid	0.19[b]	94
Benzoyl chloride	Benzoic acid	0.16[b]	93

[a] All figures represent the average of two runs. [b] Based on ester and benzoic acid recovered; if the calculations are based on the recovered phenacyl halide and ester, the values for bromide and chloride are 0.067 and 0.011, respectively.

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Reduction Studies on Unsaturated Steroids

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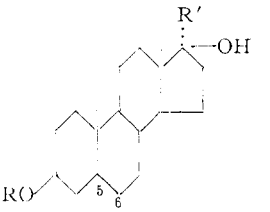
A previous paper[1] described our work on selective reductions of C-21 steroids containing unsaturation at C-5, C-16, C-17 and C-20. It was demonstrated that the choice of solvent determined the extent to which the double and triple bonds in the D-ring and side-chain were reduced: a palladium catalyst in pyridine solution reduced a triple bond only to a double bond, while in neutral solution either a triple or double bond could be completely reduced. In neither instance was a C-5 double bond affected.

These same considerations also apply when no C-5 unsaturation is present, *e.g.*, by using palladium-on-calcium carbonate in pyridine, 17-ethinylandrostan-3β,17β-diol (II) is reduced only to the corresponding 17-vinyl compound (III).

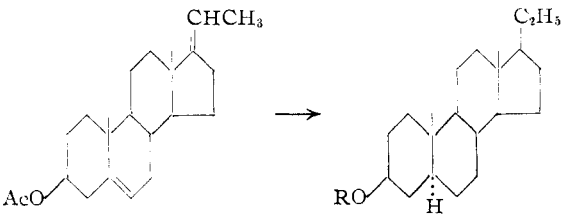
To complete the study, the use of palladium catalyst in acidic medium (acetic acid) was applied to Δ⁵-compounds, some of which contained additional unsaturation at C-20 or C-17. Such a combination smoothly reduced both side-chain unsaturation (when present) and the B-ring double



II, R = H, R′ = —C≡CH
III, R = H, R′ = —CH=CH₂
IV, R = H, R′ = —C₂H₅[a]
V, R = H, R′ = —C₂H₅
Va, R = Ac, R′ = —C₂H₅
VI, R = H, R′ = —C≡CH[a]
VII, R = H, R′ = —CH=CH₂[a]

All compounds satd. at C₅–C₆ belong to the allo series

[a] Double bond at C₅–C₆.



VIII

IX, R = H
IXa, R = Ac

bond to give in high yield the completely saturated 17-isoallopregnanes. Thus Δ⁵-pregnen-3β,17β-diol (IV), 17-ethinyl-Δ⁵-androsten-3β,17β-diol (VI), 17-ethinylandrostan-3β,17β-diol (II) and 17-vinyl-Δ⁵-androsten-3β,17β-diol (VII), all gave, upon reduction with palladium-in-acetic acid, 17-isopregnan-3β,17β-diol (V). Similarly, Δ⁵,¹⁷⁽²⁰⁾-pregnadien-3β-ol acetate gave allopregnan-3β-ol acetate.

The solvent is therefore a dominant factor when palladium catalysts are used to hydrogenate unsaturated steroids.

Experimental[2]

17-Ethinylandrostan-3β,17β-diol (II).—Potassium acetylide was prepared by dissolving 2.0 g. of potassium metal in 100 ml. of liquid ammonia and bubbling in acetylene gas. After 10 minutes the original blue color had disappeared; the acetylene addition was continued for another ten minutes. To this was added first 25 ml. of anhydrous pyridine, and then, over a period of 0.5 hour, a solution of 5 g. of epiandrosterone in 35 ml. of anhydrous pyridine. The mixture was stirred for four hours more, keeping the temperature below −15°. The insulation around the flask was removed and it was allowed to warm to room temperature overnight. To decompose the mixture, it was blanketed with a layer of carbon dioxide, then ice and water were cautiously added until a volume of one liter was reached. The solids were collected by filtration; yield 4.85 g. (88.8%), m.p. 254–257°. Recrystallization from methanol yielded

(1) E. B. Hershberg, E. P. Oliveto, C. Gerold and L. Johnson, THIS JOURNAL, **73**, 5073 (1951).

(2) All melting points are corrected. All rotations were taken in chloroform in a 1-dm. tube at a concentration of *ca.* 1%. Analyses and optical data were obtained by the Microanalytical and Physical Chemistry Departments of these laboratories.

TABLE I

SUMMARY OF HYDROGENATION EXPERIMENTS

Starting compound	Catalyst and solvent	Product	Yield, %	M.p., °C.	$[\alpha]_D$	Empirical formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Recrystn. solvent
II	Pd/$CaCO_3$;	III	96.5	207.4–208.8[a]	0.0°	$C_{21}H_{34}O_2$	79.19	79.09	10.76	11.06	Methanol
	pyridine	III acetate		154.8–155.6	− 9.4	$C_{23}H_{36}O_3$	76.62	76.83	10.07	10.25	
IV	PtO_2; HAc	V	97.5	219.0–220.4[b]	−30.5	$C_{21}H_{36}O_2 \cdot H_2O$	74.51	74.76	11.32	11.26	MeOH–H_2O
		Va		166.2–167.4	−14.2	$C_{23}H_{38}O_3$	76.19	76.22	10.56	10.61	
IV	Pd/C; HAc	Va	65.0	165.8–166.8							MeOH–H_2O
V	Pd/C; HAc	Va	80.0	167.6–168.0	−15.7						MeOH–H_2O
VI	Pd/C; HAc	Va	68.5	166.4–167.4							MeOH–H_2O
II	Pd/C; HAc	Va	97.0	167.2–168.2	−14.2						MeOH–H_2O
VIII	Pd/C; HAc	IXa	70.0	115.0–115.4[c]	+ 7.4	$C_{23}H_{38}O_2$	79.71	79.78	11.05	11.06	Methanol
		IX		138.0–138.4[d]	+21.9	$C_{21}H_{36}O$	82.83	82.61	11.92	11.98	Methanol

[a] Lit. m.p. 207° [ref. 4; A. Serini and W. Logemann, *Ber.*, **71**, 1362 (1938)]. [b] Lit. m.p. 204–205° [L. Ruzicka, M. W. Goldberg and H. R. Rosenberg, *Helv. Chim. Acta*, **18**, 1487 (1935)], m.p. 221–222°; [T. Reichstein and K. Gätzi, *ibid.*, **21**, 1185 (1938)]. [c] Lit. m.p. 115–116° [L. Ruzicka, M. Goldberg and E. Hardegger, *ibid.*, **22**, 1294 (1939)]. [d] Lit. m.p. 137–138° [note *c*].

3.92 g. of II (71.8%), m.p. 262.2–263.6°, $[\alpha]_D$ −42.6°; lit. m.p. 255–257°,[3] 257°.[4]

Anal. Calcd. for $C_{21}H_{32}O_2$: C, 79.69; H, 10.19. Found: C, 80.00; H, 10.27.

The 3-acetate, prepared by the action of acetic anhydride and pyridine, had m.p. 202–204°, $[\alpha]_D$ −40.4°.

Anal. Calcd. for $C_{23}H_{34}O_3$: C, 77.07; H, 9.55. Found: C, 77.43; H, 9.49.

Hydrogenation Reactions.—These were all run at room temperature and atmospheric pressure using 15–25% by weight of catalyst. The hydrogenations were stopped when uptake had essentially ceased, the catalyst removed by filtration and the filtrate taken to a residue under vacuum. This residue was then either saponified to remove traces of esters that formed during the hydrogenation from the action of the acetic acid solvent, or was completely acetylated by means of acetic anhydride in pyridine. These products were then crystallized from appropriate solvents. The results are summarized in Table I.

(3) L. Ruzicka and K. Hofmann, *Helv. Chim. Acta*, **20**, 1280 (1937).

(4) J. Kathol, W. Logemann and A. Serini, *Naturwissenschaften*, **25**, 682 (1937).

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Characterization of α-Keto Acids as Quinoxalinols[1]

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The reaction of pyruvic acid and its homologs with *o*-phenylenediamine is known to give 3-alkyl-2-hydroxy quinoxalines (3-alkyl-2-quinoxalinols), but these have not been used to characterize the α-keto acids. Since a number of α-keto acids, corresponding to the natural amino acids, were desired for work in progress in this Laboratory, it was decided to prepare the quinoxalinols for analytical derivatives. These compounds have an advantage over 2,4-dinitrophenylhydrazones, etc., in that most other carbonyl compounds do not readily form precipitates with the diamine, and the products are stable and easily purified substances.

The α-keto acids were obtained by a modification of the method of Wieland,[2] involving reaction of a Grignard reagent with diethyl oxalate. This author gives experimental details for the synthesis of only two of the keto acids, but his method was found to be easily extendable to others. Reaction of the aqueous α-keto acid with a solution of *o*-phenylenediamine in dilute acetic acid caused rapid crystallization of the desired quinoxalinol, which was obtained in about 80% yield.

Of the 3-alkyl-2-hydroxyquinoxalines with simple and unsubstituted alkyl groups, only three are mentioned in the literature. These are: 3-methyl,[3,4] 3-ethyl[4] and 3-*t*-butyl.[5] Five additional representatives of the class were prepared in the present work, and these are listed in Table I along with melting points and analyses. The previously known compounds and the unsubstituted 2-quinoxalinol[6] are also listed for comparison.

TABLE I

3-ALKYL-2-QUINOXALINOLS

3-Alkyl[a] group	M.p., °C.	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
None	271[6]	...	...	..	..
Methyl	245[3] 250[4]	...	...	..	..
Ethyl	198[4]	...	...	..	..
n-Propyl	182–183	70.21	70.57	6.38	6.51
Isopropyl	228.5	70.21	70.35	6.38	6.42
n-Butyl	153.5–154	71.29	71.43	6.93	6.55
Isobutyl	186–187	71.29	71.41	6.93	6.85
s-Butyl	180–181	71.29	71.28	6.93	6.85
t-Butyl	Dec. above 300[5]	...	...	..	..

[a] With the exception of the *t*-butyl compound, all were prepared from the corresponding α-keto acid.

Experimental

The reaction with α-ketovaleric acid is used as a representative example. A solution of 1.143 g. (9.85 mmoles) of the keto acid in 25 ml. of water was added slowly, with stirring, to a solution of 4 g. (37.0 mmoles, an excess) of *o*-phenylenediamine in 50 ml. of 10% acetic acid. The solution darkened temporarily, and then formed a crystalline, voluminous precipitate of 3-*n*-propyl-2-quinoxalinol. After standing five hours, the suspension was filtered and the product washed with water and dried in air. There was a slight loss on washing but the filtrates, when concentrated, gave a little more product. The yield of dried, white quinoxalinol, obtained in two crops, was 1.523 g. (8.1 mmoles) or 82%.

Other quinoxalinols were prepared similarly and were recrystallized from benzene or aqueous acetone for analysis.

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(2) T. Wieland, *Ber.*, **81**, 314 (1948); *C. A.*, **43**, 4227 (1949).

(3) O. Hinsberg, *Ann.*, **292**, 249 (1896).

(4) Y. L'Italien and C. K. Banks, THIS JOURNAL, **73**, 3246 (1951).

(5) F. Krohnke, *Ber.*, **80**, 298 (1947); *C. A.*, **42**, 3747 (1948).

(6) A. H. Gowenlock, G. T. Newbold and F. S. Spring, *J. Chem. Soc.*, 622 (1945).