of some derivatives of γ,δ-unsaturated acids substituted in the carboxyl group with iodine, in order to determine whether the participation of the carbonyl group is increased or decreased.

Experimental

2,2-Diphenyl-5-(2,4-dinitrobenzenemercapto)-4-pentanolactone (VI).—To 550 mg. of 2,2-diphenylpenten-4-oic acid dissolved in 15 ml. of chloroform was added 507 mg. of 2,4-dinitrobenzenesulfenyl chloride dissolved in 50 ml. of chloroform. The mixture was refluxed for four hours, washed with sodium carbonate solution (10%), twice with water, and dried with sodium sulfate. By evaporation of the chloroform, a solid yellow residue was obtained. By acidifying the carbonate solution, only starting material was recovered. After two recrystallizations from a mixture of benzene and ethanol, pale yellow needles were obtained, m.p. 222–225°, yield 410 mg. (41%). The compound does not contain chlorine.

Anal. Calcd. for $C_{23}H_{18}N_2O_6S$: N, 6.22. Found: N, 6.19.

9-[3-(2,4-Dinitrobenzenemercapto)-2-chloropropyl]-9-fluorenecarboxylic Acid (VII).—A solution of 400 mg. of 2,4-dinitrobenzenesulfenyl chloride and 495 mg. of 9-allyl-9-fluorenecarboxylic acid in 10 ml. of chloroform was refluxed for six hours. The solvent was evaporated at room temperature and a yellow residue was left. The residue was treated with benzene, and the yellow, insoluble crystals were collected and dried on a porous plate. The yield was 580 mg. (64.8%), m.p. 173–176°.

This compound contains chlorine and was recrystallized from a mixture of benzene and ethanol, giving yellow crystals, m.p. 176–178.5°.

Anal. Calcd. for $C_{23}H_{17}N_2O_6SCl$: C, 56.97; H, 3.53; N, 5.74. Found: C, 57.23; H, 3.73; N, 5.75.

Quantitative Measurements of the Reaction of Compounds IVa and Va with Iodine.—A solution of 0.5434 g. of 9-allyl-9-fluorenecarboxylic acid (Va) in 20 ml. of chloroform at 0° was mixed with 0.5511 g. of iodine dissolved in 23.43 ml. of chloroform at 0°. The initial concentration of the acid and iodine was 0.05 mole/l. The mixture was kept in a thermostat at 0 ± 0.02° and aliquots of 10 ml. were titrated with a $N/50$ $Na_2S_2O_3$ solution.

In the same manner, starting with 0.5467 g. of acid IVa and 0.5501 g. of iodine, a 0.05 mole/l. solution of these compounds was prepared.

Table I gives the values obtained in these experiments.

TABLE I

REACTION OF IODINE WITH ACIDS Va AND IVa IN CHLOROFORM SOI.N. AT 0°

Time, min.	Reaction, %	
	Cmpd. Va	Cmpd. IVa
15	6.6	
20		39.2
30	10.1	
60	14.9	43.2
130		46.6
160	22.2	
240		49.2
360	28.3	
480		50.2
1380	36.8	

Acknowledgment.—The author is greatly indebted to Professor Richard T. Arnold of the University of Minnesota and to Professor Heinrich Hauptmann of the University of São Paulo (Brazil) for reviewing the manuscript and for offering valuable suggestions, to Miss Maria Luiza Miranda Valle for the micro-analysis, and also to the Rockefeller Foundation for financial support.

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The Relative Reactivity of Functional Groups toward Diazomethane

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RECEIVED MAY 7, 1954

The relative reactivity of various functional groups toward diazomethane is of considerable interest when polyfunctional compounds are treated with this reagent. The data recorded in the literature are generally not adequate for the construction of a reactivity series,[2] as such a comparison was usually not the primary objective of previous investigators, and the yields (or presence) of side-reaction products are sometimes not given.

We have run a series of competition reactions between five substituted benzenes wherein equimolar quantities of each of two reactants and of diazomethane were allowed to react at −10° for two hours, and the amounts of each product and of unchanged reactant were determined. The results listed in Table I indicate that the relative reactivities of the groups studied are $-CO_2H > -COBr > -COCl > -OH > -COCH_3$. This order is in agreement with the following observations. The carbonyl chloride group of 9-oxo-4-fluorenoyl chloride reacts preferentially to the carbonyl group[3]; the carbonyl halide reacts faster than the hydroxy group in 2-hydroxy-3-naphthoyl chloride[4]; the carboxy function of 4-hydroxyphthalic acid is attacked in preference to the hydroxy substituent[5]; and the hydroxy group in *p*-hydroxyacetophenone is more reactive than the carbonyl toward diazomethane.[6]

Experimental

General Procedure.—Ethereal diazomethane solutions were prepared by the method of Arndt[7] and were standardized by adding aliquots to excess benzoic acid and titrating the unreacted acid with standard sodium hydroxide solution. The average of three such determinations was used to determine the volume of solution containing 8.41 g. (0.20 mole) of diazomethane.

A solution of 0.20 mole of each reactant in 150 ml. of anhydrous ether contained in a 1-l. erlenmeyer flask was maintained at approximately −10° by means of an ice-salt mixture. The diazomethane solution (0.20 mole) was added, the flask was protected against moisture by means of a calcium chloride drying tube, and the reaction was allowed to proceed for 2 hr. If the yellow color of unreacted diazomethane were still noticeable, the excess reagent was destroyed by shaking the solution with a small volume of hydrochloric acid or by passing in hydrogen chloride.

All reactants were reagent grade or were center cuts of freshly distilled samples. All figures cited below represent the average of two runs.

Benzoic Acid–Phenol.—The solution was extracted with dilute sodium bicarbonate solution, then with several portions of 10% sodium hydroxide solution, and was finally distilled to give 18.1 g. (0.13 mole) of methyl benzoate, b.p. 84–85° (17 mm.); $n^{18.5}D$ 1.5167.

The bicarbonate extract yielded no benzoic acid upon

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[2] For a review see B. Eistert in "Newer Methods of Preparative Organic Chemistry," Interscience Publishers, Inc., New York, N. Y., 1948, pp. 513 ff.

[3] W. E. Bachmann and J. C. Sheehan, THIS JOURNAL, **62**, 2687 (1940).

[4] H. Krzikalla and B. Eistert, *J. prakt. Chem.*, **143**, 55 (1935).

[5] R. Wegscheider and H. Gehringer, *Monatsh.*, **29**, 528 (1917).

[6] A. Schönberg and A. Mustafa, *J. Chem. Soc.*, 746 (1946).

[7] F. Arndt, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 165.

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.), $n^{18.5}\mathrm{D}$ 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.), $n^{20}\mathrm{D}$ 1.5170; and 23.14 g. of acetophenone, b.p. 89–90° (19 mm.), $n^{18}\mathrm{D}$ 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.), $n^{18.7}\mathrm{D}$ 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.), $n^{18.7}\mathrm{D}$ 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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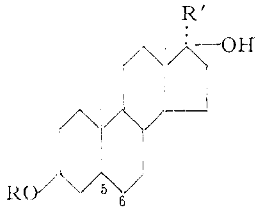
RECEIVED APRIL 16, 1954

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).

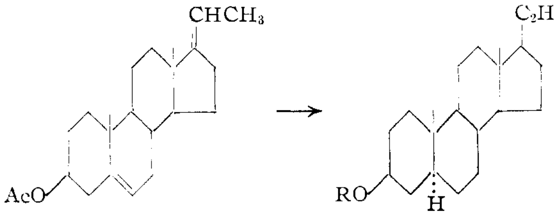
To complete the study, the use of palladium catalyst in acidic medium (acetic acid) was applied to Δ^5-compounds, some of which contained additional unsaturation at C-20 or C-17. Such a combination smoothly reduced both side-chain unsaturation (when present) and the B-ring double bond to give in high yield the completely saturated 17-isoallopregnanes. Thus Δ^5-pregnen-3β,17β-diol (IV), 17-ethinyl-Δ^5-androsten-3β,17β-diol (VI), 17-ethinylandrostan-3β,17β-diol (II) and 17-vinyl-Δ^5-androsten-3β,17β-diol (VII), all gave, upon reduction with palladium-in-acetic acid, 17-isopregnan-3β,17β-diol (V). Similarly, $\Delta^{5,17(20)}$-pregnadien-3β-ol acetate gave allopregnan-3β-ol acetate.



II, R = H, R′ = $-\mathrm{C{\equiv}CH}$
III, R = H, R′ = $-\mathrm{CH{=}CH_2}$
IV, R = H, R′ = $-\mathrm{C_2H_5}$[a]
V, R = H, R′ = $-\mathrm{C_2H_5}$
Va, R = Ac, R′ = $-\mathrm{C_2H_5}$
VI, R = H, R′ = $-\mathrm{C{\equiv}CH}$[a]
VII, R = H, R′ = $-\mathrm{CH{=}CH_2}$[a]

All compounds satd. at C_5–C_6 belong to the allo series

[a] Double bond at C_5–C_6.



VIII

IX, R = H
IXa, R = Ac

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

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(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.