TABLE I

ACETAMIDE

Compound	Basic hydrolysis[a] CH_3——COOH		Basic hydrolysis[a] CH_3——CH_2——COOH			Acidic Hydrolysis[b] CH_3——COOH		Acidic Hydrolysis[b] CH_3——CH_2——COOH		
1 Specific activity, mμc./mg. C	0.539	0.840	3.30	1.44	1.49	0.886	1.520	1.496	0.759	0.573
2 Per cent. of summed activity by position	39.1	60.9	52.9	23.1	23.9	36.9	63.1	52.9	26.8	21.0
3 Specific activity, assay on compd.	0.715[c]		2.18[d]			1.24[c]		1.01[d]		
4 Activity accounted for by degradation, %	95.8		95.4			96.8		93.5		
5 Activity relative to total activity in irradiated sample, %	6.44		6.69			8.12		5.00		

[a] 4965 megawatt hr. irradiation of acetamide. [b] 6254 megawatt hr. irradiation of acetamide. [c] Neat. [d] Carrier material.

TABLE II

BENZENE + 2-METHYLPYRAZINE[a]

Compound	C_6H_5——CH_3		C_6H_6[b]
1 Specific activity, mμc./mg. C	0.024	1.01	0.068[c]
2 Per cent. of activity summed by position	13.9	86.1	
3 Specific activity, assay on compd.	0.173[d]		
4 Activity relative to total activity in irradiated sample, %	1.05		1.92

[a] 2404 megawatt hr. irradiation of mixture. [b] *Cf.* A. P. Wolf, C. S. Redvanly and R. C. Anderson, *Nature*, 176, 831 (1955). [c] This is an upper limit. [d] Carrier material.

though most of the activity in the methyl group may arise by this path. A possible mechanism for formation of *synthesis* products would involve the inelastic collision of fragments such as CH_3· or CH_2:, having energies in excess of 0.5 e.v. but not above 10 e.v., with the molecules in question. In this way, propionamide with the methylene carbon active might be formed by the insinuation of CH_2: between the methyl and carbonyl carbon. Unstable three carbon intermediates leading to partial equilibration of the three positions in propionamide may also be possible precursors. Malonic and succinic acids produced by hot atom and radiation chemical processes could ultimately lead to acetic acid and propionic acid. Note the higher activity yield in acetic acid for the acid hydrolysis.

Since the material is produced in a strong radiation field,[9] one must also consider the possibility of radical recombinations in and around any radiation damage or recoil track leading to these products. We hope that experiments underway at present may distinguish between these pathways.

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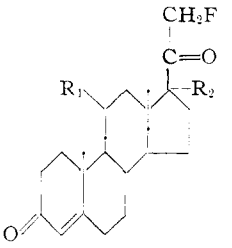
(9) Thermal neutron flux ≅ 4 × 10^{12} neutrons/cm.² sec.; fast neutron flux ≅ 10^{12} neutrons/cm.² sec.; gamma exposure ≅ 5 × 10^6 *r*/hr.

(10) Guest Associate Chemist, Brookhaven National Laboratory, Fall, 1955, from Martinez Research Laboratory, Shell Oil Co., Martinez, California.

THE PREPARATION OF 21-FLUOROSTEROIDS

Sir:

In connection with the search for compounds useful in the regulation of endocrine balance,[1] we have prepared the 21-fluorinated analogs of a number of steroid hormones by a convenient procedure of general applicability. Such products show promise of interesting physiological properties.



	R_1	R_2
III	H_2	H
IV	OH, H	H
V	=O	OH
VI	OH, H	OH

When a 21-iodosteroid dissolved in moist acetonitrile is treated with a slight excess of a 50% aqueous solution of silver fluoride[2] at 30 to 40°, a precipitate of silver iodide soon separates leaving the fluorosteroid in solution. In this way 21-iodo-5-pregnen-3β-ol-20-one acetate, prepared by the action of N-iodosuccinimide on 5,20-pregnadiene-3β,20-diol diacetate,[3] was converted in 45% yield to 21-fluoro-5-pregnen-3β-ol-20-one acetate (I), m.p. 155–156°, $[\alpha]^{25}D$ +32° ($CHCl_3$); *Anal.* Calcd. for $C_{23}H_{33}O_3F$: C, 73.37; H, 8.83; F, 5.04. Found: C, 72.78; H, 8.73; F, 5.17. Treatment of I with 1% methanolic hydrogen chloride at room temperature gave 85% of 21-fluoro-5-pregnen-3β-ol-20-one (II), m.p. 178.5–179.5°, $[\alpha]^{25}D$ +25° ($CHCl_3$); *Anal.* Calcd. for $C_{21}H_{31}O_2F$: C, 75.41; H, 9.34; F, 5.68. Found: C, 75.56; H, 9.34; F, 5.59.

By an analogous reaction with aqueous silver fluoride in acetonitrile, 21-iodoprogesterone, prepared by the action of sodium iodide on desoxycorticosterone methanesulfonate,[4,5] was converted in 63% yield to 21-fluoroprogesterone (III), m.p. 141.5–142.2°, $[\alpha]^{25}D$ +208 ($CHCl_3$); *Anal.* Calcd. for $C_{21}H_{29}O_2F$: C, 75.87; H, 8.79; F, 5.72. Found: C, 75.83; H, 8.92; F, 5.77. Similarly, corticosterone 21-methanesulfonate was transformed, *via* the 21-iodosteroid, to 21-fluoro-11β-hydroxyproges-

(1) T. C. Myers, R. J. Pratt, R. L. Morgan, J. O'Donnell and E. V. Jensen, THIS JOURNAL, **77**, 5655 (1955).

(2) The use of anhydrous silver fluoride in dry acetonitrile has been employed for the fluorination of α-acetobromoglucose: B. Helferich and R. Gootz, *Ber.*, **62**, 2505 (1929).

(3) C. Djerassi and C. T. Lenk, THIS JOURNAL, **75**, 3493 (1953).

(4) The 21-methanesulfonate esters of desoxycorticosterone, corticosterone, cortisone and hydrocortisone were prepared by treatment of the 21-hydroxysteroids with methanesulfonyl chloride and pyridine according to the procedure of J. Fried (private communication).

(5) The preparation of 21-iodosteroids by the action of sodium iodide on the corresponding 21-*p*-toluenesulfonate esters has been described recently: P. Borrevang, *Acta Chem. Scand.*, **9**, 587 (1955).

terone (IV), m.p. 207–208°, $[\alpha]^{25}D$ +236 ($CHCl_3$); *Anal.* Calcd. for $C_{21}H_{29}O_3F$: C, 72.38; H, 8.39; F, 5.45. Found: C, 72.19; H, 8.56; F, 5.44; cortisone 21-methanesulfonate was converted to 21-fluoro-4-pregnen-17α-ol-3,11,20-trione (V), m.p. 249–252°, $[\alpha]^{25}D$ +245 ($CHCl_3$); *Anal.* Calcd. for $C_{21}H_{27}O_4F$: C, 69.59; H, 7.51; F, 5.24. Found: C, 69.35; H, 7.29; F, 5.47; and hydrocortisone 21-methanesulfonate gave 21-fluoro-4-pregnene-11β,17α-diol-3,20-dione (VI), m.p. 240–242°, $[\alpha]^{25}D$ +145° ($CHCl_3$); *Anal.* Calcd. for $C_{21}H_{29}O_4F$: C, 69.20; H, 8.02; F, 5.21. Found: C, 69.30; H, 8.04; F, 5.29.

Preliminary physiological testing, kindly provided by Dr. W. W. Byrnes of the Upjohn Company, indicates that 21-fluoroprogesterone is a strong progestational hormone, being 2 to 4 times as active as progesterone in the Corner–Allen test when administered either subcutaneously or orally. In experiments carried out in the Ben May Laboratory by Dr. Charles Huggins, 21-fluoroprogesterone produced an inhibition of the uterotrophic and vaginal keratinizing action of estrone, equal to or greater than that observed[6] with 9α-fluoro-11β-hydroxyprogesterone.[7] The results of more complete physiological testing of the foregoing 21-fluorosteroids will be reported separately.

(6) C. Huggins and E. V. Jensen, *J. Exp. Med.*, **102**, 347 (1955).
(7) J. Fried, J. E. Herz, E. F. Sabo, A. Borman, F. M. Singer and P. Numerof, THIS JOURNAL, **77**, 1068 (1955).

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BOOK REVIEWS

The Alkaloids. Chemistry and Physiology. Volume V. Pharmacology. Edited by R. H. F. MANSKE, Dominion Rubber Research Laboratory, Guelph, Ontario. Academic Press, Inc., Publishers, 125 East 23rd Street, New York 10, N. Y. ix + 388 pp. 16 × 23.5 cm. Price, $9.50.

This book is the final volume in a survey of our knowledge of the alkaloids. It contains the following sections on the pharmacology of the alkaloids: "Narcotics and Analgesics" by H. Krueger (concerned principally with the analgetic effects of morphine and related compounds, as well as with drug addiction and the metabolism of morphine), "Cardioactive Alkaloids" by E. L. McCawley, "Respiratory Stimulants" by M. J. Dallemagne, "Antimalarials" by L. H. Schmidt, "Uterine Stimulants" by A. K. Reynolds, "Alkaloids as Local Anesthetics" by T. P. Carney, "Pressor Alkaloids" by K. K. Chen, "Mydriatic Alkaloids" by H. R. Ing and "Curare-like Effects" by L. E. Craig. In addition there are a five page section on "The Lycopodium Alkaloids" and a brief survey of "Minor Alkaloids of Unknown Structure," both written by R. H. F. Manske. This final section devotes a paragraph or two to what is known, both chemically and pharmacologically, of seventy-one minor alkaloids.

The present volume on pharmacology does not seem as useful a book as the four preceding volumes on the chemistry of the alkaloids. It suffers principally from two faults. First, the number of organ systems and types of action covered is fairly limited, only nine in number. Important topics such as central nervous system stimulants are not included. Second, the various pharmacological actions of an alkaloid are frequently presented in separate sections, since many alkaloids have actions on more than one organ system. For instance, quinine, cocaine and ephedrine are each discussed in four different parts of the book and still some of their important pharmacological actions are not included. Atropine is included in the discussions on "Respiratory Stimulants" and on "Mydriatic Alkaloids," but many of its more important properties are not discussed in any detail. Muscarine, pilocarpine and physostigmine, alkaloids which affect many organ systems, are discussed only as uterine stimulants.

However, the topics included are covered with satisfactory thoroughness, and the book should serve as a good reference for anyone interested in these particular phases of pharmacology. For the most part the sections are well written although one of the authors is rather dogmatic concerning several controversial topics. The volume contains a total of 1361 references as well as a subject index for volumes I-IV.

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Nuclear and Radiochemistry. Revised Version of Introduction to Radiochemistry. By GERHART FRIEDLANDER, Senior Chemist, Brookhaven National Laboratory, and JOSEPH W. KENNEDY, Professor of Chemistry, Washington University, St. Louis. John Wiley and Sons, Inc., 440 Fourth Avenue, New York 16, N. Y. 1955. ix + 468 pp. 15.5 × 23.5 cm. Price, $7.50.

This is the revised and up to date edition of Introduction to Radiochemistry first published in 1949 and written by the same authors. While the title has been changed to conform to a somewhat narrower meaning for "radiochemistry," the revised text will continue to fill the same needs as the original edition.

Like the earlier version, it is written as a textbook for the teaching of nuclear science to chemists and those in borderline fields. It is suitable for a graduate or advanced undergraduate course. Being also an excellent reference volume, it should be on the desk of anyone concerned with tracer techniques.

The revision contains more factual information than the earlier edition, largely in the form of additional graphs and tables.

The topics covered include: fundamentals of radioactivity, nuclear reactions (fission is treated more thoroughly than before), production of nuclear reactions and target chemistry, equations of radioactive decay and growth, nuclear states and a study of the several types of radioactive decay processes, interaction of various radiations with matter including biologically permissible doses and a new section on radiation chemistry, measurement of radiation and the statistical aspects of such measurements, techniques for the study of radionuclides, and applications of tracers to chemistry.

Chapters 12 and 13 are new. Chapter 12 deals with the fission chain reaction, types of nuclear reactors, nuclear power and the chemical processing and hazards connected with nuclear reactors. A section on military applications is included.

Chapter 13 is concerned with cosmic rays, the production of energy in stars, age determinations of the earth, of