COMMUNICATIONS TO THE EDITOR

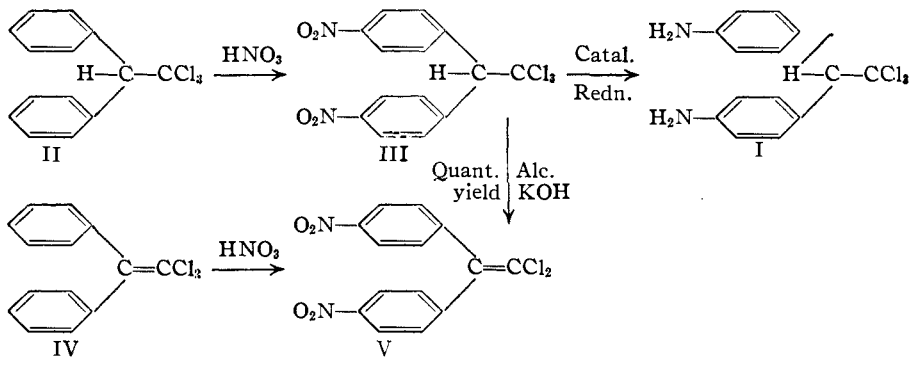
THE ANTITUBERCULAR ACTION OF 1,1,1-TRICHLORO-2,2-BIS-(*p*-AMINOPHENYL)-ETHANE

Sir:

In 1945 work was commenced at the Chemical Warfare Laboratories in Ottawa on the synthesis of the compound 1,1,1-trichloro-2,2-bis-(*p*-aminophenyl)-ethane (I).[1] It appeared from studies carried out on the Läuger hypothesis for the mechanism of action of DDT,[2] using fluorine analogs,[3,4] that this compound might possess marked antitubercular activity.

In view of similar work recently reported by Burger, Graef and Bailey,[5] we wish to report the progress of these researches at this time.

The synthesis of I seemed possible by the route



since the work of Lange and Zufall[6] showed that 1,1-dichloro-2,2-bis-(phenyl)-ethylene (IV) gave the compound 1,1-dichloro-2,2-bis-(*p*-nitrophenyl)-ethylene (V) as the main product of nitration.

The nitration of 1,1,1-trichloro-2,2-bis-(phenyl)-ethane (II) proceeded smoothly and a crystalline dinitro compound melting at 166–167° uncor. was isolated in good yield from the reaction mixture. This product was shown to be 1,1,1-trichloro-2,2-bis-(*p*-nitrophenyl)-ethane (III) by dehydrochlorination to V. The product from the dehydrochlorination proved to be identical with V prepared by the method of Lange and Zufall. Upon catalytic hydrogenation compound III took up six moles of hydrogen. The resulting amine was unstable in the crude form but was much more stable when purified by a procedure which will be described later. The substance crystallizes in the form of platelets melting with decomposition from 92–95° (uncor.) (calcd. for $C_{14}H_{13}N_2Cl_3$: N, 8.88. Found: N, 8.80). Repeated recrystallization of an analytically pure sample failed to raise the melting point or decrease the melting range. This is probably due to decomposition, with loss of hydrogen chloride, near the melting point.

In vitro tests on the activity of I showed that it gave complete inhibition of growth of *Mycobacterium tuberculosis* at dilutions of 1/100,000 and some inhibition at dilutions of 1/1,000,000. Transfer experiments showed that at dilutions of 1/100,000 the compound was bactericidal while at 1/1,000,000 it was bacteristatic. *In vivo* tests on the antitubercular activity of I, using the short assay of Feldman and Hinshaw,[7] showed remarkable control of experimentally induced tuberculosis in guinea pigs. The compound was fed at a level of 0.5% of the ration, this being the maximum well tolerated dose. The blood of guinea pigs fed this level of drug for a period of 56 days was found to contain an average of 1 mgm.% of I as determined by the method of Marshall.[8] This method has proven entirely satisfactory for the determination of I in biological material as well as in pure solution.

Full experimental details will be published later.

(1) Research Reports, Chemical Warfare Laboratories, Department of National Defense (army), Ottawa, Canada.

(2) P. Läuger, H. Martin and P. Müller, *Helv. Chim. Acta*, **27**, 892 (1944).

(3) S. Kirkwood and J. R. Dacey, *Can. J. Research*, **24B**, 69 (1946).

(4) S. Kirkwood and P. H. Phillips, *J. Pharmacol. and Exp. Therap.*, **87**, 375 (1946).

(5) A. Burger, E. Graef and M. S. Bailey, THIS JOURNAL, **68**, 1725 (1946).

(6) K. Lange and A. Zufall, *Ann.*, **271**, 1 (1893).

(7) W. H. Feldman and H. C. Hinshaw, *Am. Rev. Tuberc.*, **51**, 582 (1945).

(8) E. K. Marshall, *Proc. Soc. Exptl. Biol. Med.*, **36**, 422 (1937).

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SAMUEL KIRKWOOD
PAUL H. PHILLIPS
ELIZABETH MCCOY

RECEIVED SEPTEMBER 26, 1946

STREPTOMYCES ANTIBIOTICS. XI. THE STRUCTURE OF TETRAACETYLBISDESOXYSTREPTOBIOSAMINE

Sir:

Treatment of ethyl tetraacetylthiostreptobiosaminide diethyl mercaptal[1] with Raney nickel catalyst gave tetraacetylbisdesoxystreptobiosamine[1] and tetraacetyldesoxystreptobiosamine (m. p. 166–167°, $[\alpha]^{25}D$ −81° (*c*, 1.04 in chloroform). *Anal.* Calcd. for $C_{13}H_{21}NO_8(CH_3CO)_4$:

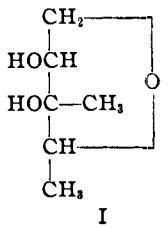
(1) (a) Kuehl, Flynn, Brink and Folkers, THIS JOURNAL, **68**, 2096 (1946); (b) Hooper, Klemm, Polglase and Wolfrom, *ibid.*, **68**, 2120 (1946).

C, 51.32; H, 6.77; N, 2.85; CH_3CO, 35.0. Found: C, 51.29; H, 6.94; N, 2.81; CH_3CO, 33.6). The additional oxygen atom of the latter product is present as a glycosidic hydroxyl group, as shown by the preparation of pentaacetyldesoxystreptobiosamine (m. p. 111–112°, $[\alpha]^{25}D$ −132° (*c*, 0.62 in chloroform)) and methyl tetraacetyldesoxystreptobiosaminide (m. p. 179–180.5°, $[\alpha]^{25}D$ −129° (*c*, 0.925 in chloroform)).

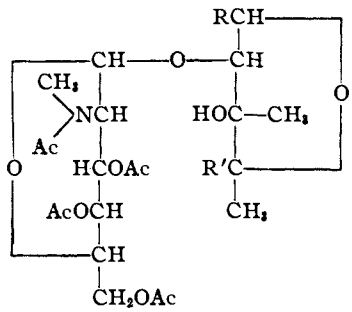
Acid hydrolysis of tetraacetylbisdesoxystreptobiosamine yielded N-methyl-L-glucosamine[2] and bisdesoxystreptose (m. p. 90–91°, $[\alpha]^{25}D$ +32° (*c*, 0.975 in chloroform). *Anal.* Calcd. for $C_6H_{12}O_3$: C, 54.52; H, 9.16; 2C—CH_3, 22.7; mol. wt., 132. Found: C, 54.63; H, 8.93; C—CH_3, 19.4; mol. wt., 141). Bisdesoxystreptose gave a bis-*p*-nitrobenzoate, m. p. 141–142°.

Bisdesoxystreptose was oxidized with one mole of periodic acid, and the product hydrolyzed with acid. Treatment of the solution with excess amounts of substituted hydrazines gave osazones of biacetyl. The derivatives prepared were the phenylosazone,[3] m. p. 247–249°; 5,6-dimethyl-2,3-diphenylosatetrazine,[4] m. p. 153–155°; the *p*-bromophenylosazone, m. p. 210–215°; and the *p*-nitrophenylosazone,[5] m. p. 312–316°.

These data show that bisdesoxystreptose is a 3,4 - dihydroxy - 2,3 - dimethyltetrahydrofuran (structure I). The compound formed an acidic complex with boric acid, indicating that the hydroxyl groups have the *cis* configuration. Structure II represents tetraacetylbisdesoxystreptobiosamine. The presence of a free tertiary hydroxyl group in streptobiosamine derivatives has been indicated.[1a,6] Periodate oxidations of N-acetylbisdesoxystreptobiosamine[1] indicate a pyranose ring structure for the methylamino hexose moiety. The primary rapid reaction appeared to be with one mole of periodate, and neither formic acid nor formaldehyde could be isolated.

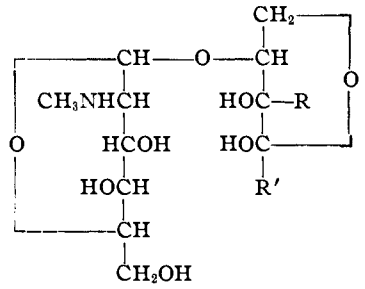


I

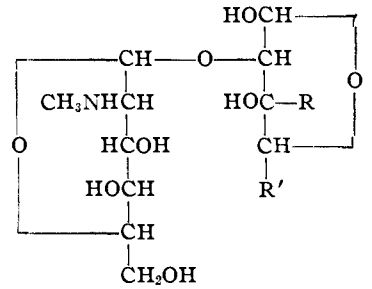


II, R, R′ = H
III, R = OH, R′ = H
IV, R = H, R′ = OH

Tetraacetyldesoxystreptobiosamine would have either structure III or IV. On the basis of structure II for tetraacetylbisdesoxystreptobiosamine, structures V, VI, VII and VIII may now be written for streptobiosamine.



V, R = —CHO, R′ = —CH_3
VI, R = —CH_3, R′ = —CHO



VII, R = —CH_3, R′ = —CHO
VIII, R = —CHO, R′ = —CH_3

Other degradations, to be published shortly,[7] will demonstrate which of these formulas is correct.

(7) Kuehl, Flynn, Brink and Folkers, *ibid.*, in press.

NORMAN G. BRINK
RESEARCH LABORATORIES FREDERICK A. KUEHL, JR.
MERCK & CO., INC. EDWIN H. FLYNN
RAHWAY, N. J. KARL FOLKERS

RECEIVED OCTOBER 15, 1946

2,3-DICHLORO-1,4-DIOXANE

Sir:

We have made two interesting and previously unrecorded observations in our study of the chlorination of dioxane.[1-7]

Repeated contact of 2,3-dichloro-1,4-dioxane (made from technical or purified[8] dioxane) with the skin, or inhalation of its vapor, quickly produces vertigo, nausea, headache, and inflamed eyes. These symptoms persist for several days: the inhalation of ammonia gives partial relief.

The uncatalyzed[1-6] chlorination of dioxane proceeded without mishap. When the chlorination was catalyzed by stannic chloride,[7] the reaction proceeded satisfactorily for about sixteen hours

(1) Böeseken, Tellegen and Henriquez, *Rec. trav. chim.*, **50**, 909 (1931).
(2) Summerbell and Christ, THIS JOURNAL, **54**, 3777 (1932).
(3) Baker, *J. Chem. Soc.*, 2666 (1932).
(4) Butler and Cretcher, THIS JOURNAL, **54**, 2987 (1932).
(5) Wilson, Baker and Shannon, *J. Chem. Soc.*, 1598 (1933).
(6) Böeseken, Tellegen and Henriquez, THIS JOURNAL, **55**, 1284 (1933).
(7) Kucera and Carpenter, *ibid.*, **57**, 2346 (1935).
(8) Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., New York, N. Y., 1941, pp. 368–369.

(2) Kuehl, Flynn, Holly, Mozingo and Folkers, THIS JOURNAL, **68**, 536 (1946).
(3) Neuberg and Reinfurth, *Biochem. Z.*, **148**, 563 (1923).
(4) H. v. Pechmann, *Ber.*, **21**, 2751 (1888).
(5) Hirsch, *Biochem. Z.*, **131**, 184 (1922); Neuberg and Kobel, *ibid.*, **160**, 255 (1925).
(6) Brink, Kuehl, Flynn and Folkers, THIS JOURNAL, in press.

and then started to flash (brilliant yellow green flame) at five-minute intervals. After six of these flashes the chlorination was stopped. There was a heavy deposit of carbon on the inside of the flask and condenser. Distillation of the mahogany-red reaction product gave a 32% yield of dichlorodioxane (b. p., 58–60° (5 mm.)) instead of the expected 96.6% yield.[7] The forerun (25% of the reaction product) was dioxane and the distillation residue was a black tar, non-volatile at 250° (5 mm.). The 58–60° boiling fraction contained about 24% of a colorless solid which melted at 20–28°. Triple crystallization from ethanol raised the melting point to 30°. Wilson, *et al.*,[5] isolated a solid isomer of 2,3-dichlorodioxane (m. p., 30°) from a liquid product which had stood several weeks. Both our liquid and solid products were 2,3-dichlorodioxane, as proved by hydrolysis to glyoxal which was identified by means of its *p*-nitrophenylhydrazone and dioxime, and by conversion to the known naphthodioxanes.[1]

UNIVERSITY OF CALIFORNIA
CITRUS EXPERIMENT STATION — FRANCIS A. GUNTHER
RIVERSIDE, CALIFORNIA — ROBERT L. METCALF

RECEIVED OCTOBER 4, 1946

A CHEMICAL ASSAY METHOD FOR PENICILLIN G

Sir:

It is now recognized that commercial penicillin is a mixture of at least four different penicillins, G, X, F and K, apparently differing markedly in efficacy, and that the less satisfactory results since May, 1944, of penicillin treatment of early syphilis may be due to the variation in the relative proportion of these penicillins, particularly to an increase in the content of less effective K in commercial penicillin.

We have developed a rapid, convenient and accurate chemical method for determining the minimum penicillin G content of clinical and "crystalline" penicillin which depends on the sparing solubility of the N-ethylpiperidine salt of penicillin G in amyl acetate–acetone mixtures.

K, F, and the degradation products of G apparently do not here interfere (penicillin X has not been tested). Although the method is most useful in definitely establishing a minimum penicillin G content, the recovery appears to be essentially quantitative when the G content is over 50% and the potency is over 800 U./mg. With highly purified crystalline sodium penicillin G, the recovery as N-ethylpiperidine salt is 98.6% (average of 11 assays).

Procedure.—By means of a 2-ml. syringe inserted through the rubber cap, the contents of a weighed penicillin vial (100,000 or 200,000 units) is transferred quantitatively to a chilled centrifuge tube, using a total of 3 ml. of ice-cold distilled water. The vial may then be opened, dried and tared. To the aqueous solution is added exactly 2 ml. of ice-cold amyl acetate saturated with the N-ethylpiperidine salt of penicillin G (the solubility is approximately 0.6 mg./ml.). With shaking and cooling in an ice-bath, 0.5 ml. of a 20% phosphoric acid solution is added and the mixture is centrifuged. About 1.8 ml. of the amyl acetate layer containing the penicillins is removed and dried over sodium sulfate (0.1 g.) using a sintered glass micro filter crucible for the filtration of the drying agent. The *p*H of the spent aqueous layer should be about 2.

Exactly 1 ml. of the dried amyl acetate solution is transferred to a 10-ml. micro beaker in an ice-bath. After dilution with 1 ml. of acetone saturated with the N-ethylpiperidine salt of penicillin G (the solubility is about 2 mg./ml.) 0.5 ml. of a 10% solution of N-ethylpiperidine in amyl acetate saturated with the amine salt (about 2 mg./ml.) is added. After two hours at 0–5°, the mixture is filtered through a tared micro filter stick, washed with 1 ml. of cold acetone (saturated with amine salt), and dried *in vacuo* at room temperature for one hour.

The practically colorless N-ethylpiperidine salt of penicillin G melts (capillary) with decomposition at 152–154° when placed in a bath at 140° and heated 3° per minute. *Anal.* Calcd. for $C_{23}H_{33}O_4N_3S$: C, 61.71; H, 7.43; N, 9.39. Found: C, 61.55; H, 7.50; N, 9.51.

The physical and biological constants of the N-ethylpiperidine salt of penicillin G correspond very well with values for sodium penicillin G on a molar basis. Against *S. aureus*, the activity is 1328 U./mg. The ultraviolet absorption in water is $E_M = 271$ at 2575 Å. (the benzyl maximum),[1] and the optical rotation is $[\alpha]^{23}D$ +240° (1% in water).

RESEARCH AND CONTROL LABS. — JOHN C. SHEEHAN[2]
MERCK AND CO., INC. — W. J. MADER
RAHWAY, NEW JERSEY — DONALD J. CRAM[3]

RECEIVED OCTOBER 29, 1946

(1) Determined by Dr. N. R. Trenner.

(2) Present address: Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts.

(3) Present address: Converse Memorial Laboratory, Harvard University, Cambridge, Massachusetts.

ORIENTED FILAMENTS OF AMYLOSE AND ALKALI AMYLOSE

Sir:

By deësterifying oriented potato amylose acetate we have obtained excellent fiber diagrams corresponding to A, B, V and branched chain alcohol-precipitated amylose powder patterns, and previously unreported alkali amylose. Heretofore only a B fiber pattern has been obtained.[1]

Alkali amylose is produced directly on deacetylation of clamped filaments at 25° in 2% potassium hydroxide solution in 75% methanol or ethanol or in saturated butanol. Contained alcohol is not an integral part of the fiber structure, since identical patterns are given by amylose

(1) Rundle, Daasch and French, THIS JOURNAL, 66, 130 (1944).

prepared in the three alcohols, and also (with greater difficulty) in aqueous alkali. On extracting alkali from the filaments with absolute methanol, the fiber pattern disappears, and is not restored by humidification. Soaking in 75% alcohol containing 2% alkali restores the original pattern, whereas 75% alcohol alone produces the V structure. The fiber pattern (Fig. 1) can be indexed on the basis of an orthorhombic unit cell having $a_0 = 9.0$ Å., $b_0 = 22.7$ Å. and $c_0 = 12.7$ Å. and containing twelve $C_6H_{10}O_5 \cdot (KOH)_x$ groups. x has not been established and may be variable, since the alkali uptake of the fibers giving this pattern depends on the alkali concentration in the deacetylating medium. Lithium, sodium and cesium hydroxide amylose have similar structure and composition.

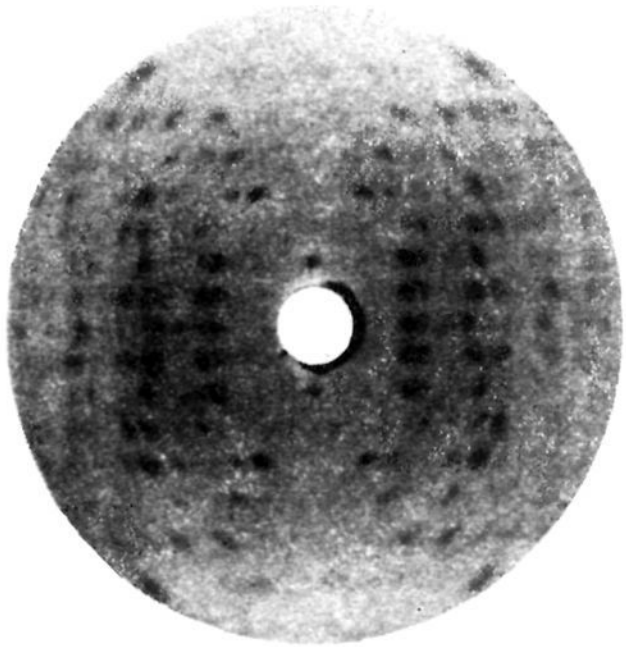


Fig. 1.—Fiber diagram of potassium hydroxide amylose. Fiber axis vertical, filtered Cu radiation, 5 cm. distance.

Transformation of the alkali amylose structure to the V structure is effected most easily in 75% methanol, allowing the clamped filaments to contract 10 to 15%. The diffraction pattern is independent of the primary alcohol and shows a fiber repeat period of 8 Å. Lateral spacings vary with moisture content. Extraction of alkali with 75% *t*-butanol results in a fiber pattern with similar fiber period, 7.9 Å., but lateral reflections are considerably shifted and indicate a monoclinic unit cell.

Filaments giving fiber patterns that correspond to the A (cereal starch) structure are obtained by exposing alkali amylose to high humidity (80%) for several days. The fiber identity period is 10.5 Å., at variance with the unit cell proposed[2] from powder patterns.

In saturated water vapor the A structure changes to the B (tuber starch) structure. Complete conversion and sharpest fiber patterns result from boiling vapor-treated filaments in water.

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U. S. DEPARTMENT OF AGRICULTURE F. R. SENTI
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RECEIVED OCTOBER 21, 1946

(2) Bear and French, THIS JOURNAL, **63**, 2298 (1941).

THE STRUCTURE OF KETENE

Sir:

In a recent paper Hannay and Smyth[1] have found ketene to possess a dipole moment considerably less than those of aldehydes and ketones and have concluded that "the oxygen has much less negative charge than the ordinary carbonyl oxygen." This fact they explain in terms of four resonance structures.

In two papers[2,3] the printing of one of which has been greatly delayed owing to post-war difficulties in this country, we have been able—mainly from a study of the ionization potentials of the non-bonding electrons on the oxygen atoms—to arrange a long series of carbonyl molecules in the order of increasing C=O bond polarity. As a result it has become clear that as the polarity increases so the bond weakens, that is, the stretching force constant and bond energy decrease and the bond length increases. It is therefore not satisfactory to describe the polarity of a carbonyl bond in terms of covalent–ionic resonance, for such a description would imply an *increase* of bond strength with increasing bond polarity (up to 50% ionic character) and a greater strength in the polar than in the non-polar bond.

Our work showed that ketene had a C=O bond polarity considerably less than that of the aldehydes, with which fact the work of Hannay and Smyth is in accord. A simple and satisfactory explanation is possible without recourse to the postulation of resonance forms. It is essential to realize that the central carbon atom in ketene is really an "acetylenic" or "digonal" one, that is, it is forming two hybrid s–p bonds at 180° and two π bonds. The two π bonds have their central planes at right angles, so that conjugation does not occur between them. Now a carbon atom exerting a hybrid valency has a stronger electronegativity the greater the proportion of s character in that valency. In other words a carbon atom of a CH bond exerts a greater "pull" on those CH electrons if the carbon is part of a triple than of a single C–C bond. This statement may either be regarded as a strongly founded theoretical conclusion[4] or as a simple deduction from such experimental facts as the acidity of acetylene. It is therefore clear that the C=O bond in ketene will have considerably reduced C^+O^- polarity relative to formaldehyde. The other properties of ketene (for example, low carbonyl bond length, high carbonyl bond stretching force constant, high carbonyl bond energy, all relative to aldehydes and ketones) then follow from this reduced carbonyl polarity.[3]

Carbon dioxide is another example of a molecule containing a "digonal" carbon atom. In this case the competition of the two C=O bonds is a further factor reducing the bond polarity. Ac-

(1) Hannay and Smyth, THIS JOURNAL, **68**, 1357 (1946).
(2) Walsh, *Trans. Faraday Soc.*, **42**, 56 (1946).
(3) Walsh, *ibid.*, in press.
(4) Coulson, private communication.

cordingly, carbon dioxide has a carbonyl bond polarity much smaller than that of ketene. Again the cumbrous resonance description is neither necessary nor desirable. The organic isocyanates of course occupy an intermediate position. Carbon suboxide, with all its carbon atoms in the "digonal" state must have a carbonyl bond polarity close to that of ketene. Accordingly its chemical properties resemble those of ketene.

LABORATORY OF PHYSICAL CHEMISTRY
CAMBRIDGE, ENGLAND A. D. WALSH

RECEIVED OCTOBER 7, 1946

NEW BOOKS

Physical Methods of Organic Chemistry. Vol. II.[1] ARNOLD WEISSBERGER, Editor. Interscience Publishers, Inc., 215 Fourth Avenue, New York 3, N. Y., 1946. vii + 631 pp. $23^1/_2 \times 15$ cm. Price, $8.50.

With this second volume, the editor has completed a work which will be of considerable value to organic chemists. The subjects covered in it are as follows: XVII, Spectroscopy and Spectrophotometry; XVIII, Colorimetry, Photometric Analysis and Fluorimetry; XIX, Polarimetry; XX, Determination of Dipole Moments; XXI, Conductometry; XXII, Potentiometry; XXIII, Polarography; XXIV, Determination of Magnetic Susceptibility; XXV, Determination of Radioactivity; XXVI, Mass Spectrometry.

The quality and value of the several chapters varies greatly. The chapter on polarimetry is quite complete and appears to the reviewer to be the best modern monograph on the subject. The chapter on dipole moments is the shortest in the book (22 pages) and is hardly more than a qualitative description of a method of determining the dipole moment.

The chapter on the measurement of radioactivity is good as far as it goes. The discussion of the measurement of soft beta rays, however, is definitely inadequate in view of the fact that the most important activities for organic chemists, namely, C^{14} and H^3 are both very soft beta emitters. It is almost certain that special treatises on this subject will appear soon.

For most of the subjects discussed in this volume there already exist quite complete monographs.

The general impression one gets on reading this volume is one of pleasure and interest in the unfamiliar subjects and disappointment in the familiar ones. This would seem to indicate that the book will only partially fulfill its purpose of "... relieving him (the chemist) of much of this burden ... to search through periodicals and specialized books."

It is undoubtedly a valuable book to have on ones desk primarily for the purpose of becoming generally familiar with a heretofore unfamiliar physical method, but for actual laboratory use it will still be necessary, in most cases, to go to the specialized literature which is quite amply documented in this book.

(1) Vol. I is reviewed in THIS JOURNAL, **67**, 2278 (1945).

MELVIN CALVIN

Semi-Micro Quantitative Organic Analysis. By R. BELCHER, F.R.I.C., Scientific Officer, British Coke Research Association, and A. L. GODBERT, M.Sc., Ph.D., Scientific Officer, Safety in Mines Research Board. Longmans, Green and Co., Inc., 55 Fifth Avenue, New York, N. Y., 1946. viii + 168 pp. 42 figs. 14.5 × 23 cm. Price, $3.00.

The book presents in orderly fashion quantitative semi-micro methods for the determination of the more common elements and groups, as well as molecular weights of organic compounds. The chapters on the various analyses are preceded by a rather thorough treatment of the ordinary analytical balance. Thus detailed directions for assembling, dismantling, cleaning and testing are given as well as procedures for the determination of its sensitivity and precision and the calibration of weights. The "swing method" of weighing is utilized and for the average sample size of 20 milligrams employed throughout, a balance with a precision "not worse than 0.04 mg." is recommended.

The analytical methods are followed by description of a few physical tests (determination of density, melting and boiling points (Mulliken, Emich and Siwoloboff methods)). This is followed by appendices containing procedures for the purification of small amounts of organic solids and liquids and directions for the preparation and standardization of the various standard solutions used (0.025 *N* hydrochloric acid, sodium hydroxide, barium chloride, potassium dichromate, ferrous ammonium sulfate, sodium thiosulfate and 0.05 and 0.02 *N* silver nitrate solutions). In addition to this, the book contains a list of 46 references and a short index.

The determination of carbon and hydrogen, for which an accuracy of $\pm 0.2\%$ is claimed and which is one of the few gravimetric methods (the others being the determination of residues and of phosphorus) presented, employs the principle of removable combustion tube fillings. The apparatus dispenses with the usual bubble counter, but employs a suitable flow-meter instead. With the exception of the larger combustion tube (57 cm. length instead of 52 cm. and 1–1.2 cm. diameter, instead of 0.8 cm.) the rest of the apparatus, as well as the procedure, is exactly the same as in the corresponding micro-method. The removable combustion tube filling consists of a platinum wire gauze, a mixture of copper oxide, lead chromate and ceric oxide wrapped in copper gauze and lead super oxide contained in a porcelain boat. The latter is good for about 15 combustions. The combustion boat is placed between the two metal gauzes. Combustion is carried out in an atmosphere of oxygen only. The absorption tubes, the construction and the filling of which are again exactly the same as in the conventional micro method, are weighed without replacement of the oxygen by air.

The determination of nitrogen, gasometric (Dumas) as well as volumetric (Kjeldahl) procedures are available, patterned after the corresponding micro methods. The nitrometer is graduated up to 8 ml. with subdivisions into 0.02 ml. instead of the usual 1.5 ml. with 0.01 ml. subdivisions. For the volumetric determination of sulfur and the halogens (chlorine, bromine and iodine) the dry combustion method is employed. The accuracy claimed for all these determinations is again $\pm 0.2\%$.

In the structure analytical methods, for which accuracies varying from $\pm 0.3\%$ (methoxyl) to $\pm 0.5\%$ (carboxyl and acetyl) are claimed, no new principles are employed, while in the chapter dealing with the determination of molecular weights, the methods of Sucharda-Bobranski (ebullioscopic), Rast (cryoscopic) and Bratton and Loclite (vaporimetric), with accuracies of $\pm 5\%$, are given.

The book, the individual chapters of which follow the by now well acclaimed arrangement of subdivision into principle, apparatus, reagents, method and calculation, is primarily intended for teaching purposes. It appears, however, that the volumetric methods might well lend