disaccharide sugars, for use in the preparation of synthetic polymers. Such polymers with terminal carbohydrate determinant groups might then display antigenic properties.[2,3]

*p*-Ethylphenyl β-maltoside heptaacetate[4,5] and *p*-ethylphenyl β-cellobioside heptaacetate[6] were converted into the corresponding *p*-vinylphenyl disaccharide heptaacetates by the method that Helferich and Hofmann[7] used for the synthesis of the tetraacetate of *p*-vinylphenyl β-D-glucoside. The *p*-vinylphenyl cellobioside heptaacetate was also prepared directly from *p*-acetoxystyrene and acetobromocellobiose in aqueous acetone in the presence of alkali.[8] *O*-Deacetylations were effected with barium methoxide in methanol.

### Experimental

Melting points were determined on a Koffler hot stage. All solvent distillations were carried out at 40° (bath temperature) and 20 mm. Microanalyses are by the Analytical Services Unit of this Institute, Harold C. McCann, director.

***p*-Ethylphenyl β-Maltoside Heptaacetate.**—β-Maltose octaacetate (48 g.) and 2.5 ml. of acetic anhydride were added to a molten mixture of 0.7 g. of *p*-toluenesulfonic acid and 65 g. of *p*-ethylphenol. The mixture was heated at 100° (20 mm.) for 1 hr. and dissolved in 400 ml. of benzene. The solution was washed with water, 2 *N* sodium hydroxide, and water and dried ($CaCl_2$). The residue obtained after distillation of the benzene was crystallized and recrystallized from methanol to give white needles (21.7 g., 41%), m.p. 129–130°, $[\alpha]^{20}D$ +44.6° (*c* 1.15, $CHCl_3$).

*Anal.* Calcd. for $C_{34}H_{44}O_{18}$: C, 55.1, H, 6.0; acetyl, 40.7. Found: C, 55.2; H, 5.8; acetyl, 40.6.

***p*-(1-Bromoethyl) Phenyl β-Maltoside Heptaacetate.**—*p*-Ethylphenyl β-maltoside heptaacetate (7.4 g.), 50 ml. of chloroform, and 4.2 g. of anhydrous sodium bicarbonate in a quartz flask were irradiated with ultraviolet light and stirred at 25° while adding dropwise 1.6 g. of bromine in 16 ml. of chloroform. The colorless mixture was filtered from salts, concentrated to dryness, and crystallized and recrystallized from ether to give small white needles (6.2 g., 75%), m.p. 114–117°. Further recrystallization from ether gave 3.9 g. of white needles, m.p. 118–120°, $[\alpha]^{20}D$ +43.7° (*c* 1.0, $CHCl_3$).

*Anal.* Calcd. for $C_{34}H_{43}O_{18}Br$: C, 49.8; H, 5.3; Br, 9.75; acetyl, 36.8. Found: C, 50.8; H, 5.5; Br, 8.4; acetyl, 35.7.

The compound was unstable and no attempt was made to purify it further.

***p*-Vinylphenyl β-Maltoside Heptaacetate.**—To a refluxing mixture of 117 g. of anhydrous sodium acetate and 188 ml. of glacial acetic acid was added 18.1 g. of *p*-(1-bromoethyl) phenyl β-maltoside heptaacetate. Refluxing was continued for 6 hr. The hot mixture was poured with stirring into 2 l. of ice-water and the precipitate left to settle. The crude product (13.5 g.) was filtered, washed with water, and dried. The material (13.0 g.) in 300 ml. of dry methanol was deacetylated with 12.5 ml. 0.4 *N* barium methoxide in methanol and left at 5° for 24 hr. The solution was neutralized with dilute sulfuric acid, centrifuged, and the clear solution concentrated to dryness. The dry material was acetylated with 100 ml. of pyridine and 100 ml. of acetic anhydride over 2 days. The solution was poured into 1 l. of ice-water and the crystalline product was recrystallized from ethanol (charcoal) to give off-white needles (8.5 g., 52%), m.p. 150.5–151.5°, $[\alpha]^{20}D$ +49.3° (*c* 0.7, $CHCl_3$), $\lambda_{max}^{MeOH}$ 253.5 mμ (ε 19,300).

*Anal.* Calcd. for $C_{34}H_{42}O_{18}$: C, 55.3; H, 5.7; acetyl, 40.8. Found: C, 55.4; H, 6.0; acetyl, 41.3.

***p*-Ethylphenyl β-Cellobioside Heptaacetate.**—*p*-Ethylphenol (40.3 g., 0.3 mole) and potassium hydroxide (3.2 g., 0.06 mole) in 40 ml. of water were added to a solution of acetobromocellobiose[9] (21 g., 0.03 mole) in 60 ml. of acetone and the mixture was left in a shaking machine at 25° for 25 hr. Acetone was distilled, and the remaining solution was extracted with 100 ml. of benzene. The benzene layer was washed with 2 *N* sodium hydroxide and with water, dried ($CaCl_2$), and concentrated to a sirupy residue (22.6 g.). Addition of ether induced crystallization. Recrystallization was effected with ethanol to give white needles (14.2 g., 33%), m.p. 214–216°, $[\alpha]^{20}D$ −27.8° (*c* 0.5, $CHCl_3$).

*Anal.* Calcd. for $C_{34}H_{44}O_{18}$: C, 55.1; H, 6.0; acetyl, 40.7. Found: C, 55.3; H, 5.9; acetyl, 40.45.

***p*-Vinylphenyl β-Cellobioside.**—*p*-Ethylphenyl β-cellobioside heptaacetate (3.7 g.), 30 ml. of chloroform and 2.1 g. of sodium bicarbonate in a quartz flask were stirred and irradiated (25°) with ultraviolet light during the dropwise addition of 0.8 g. of bromine in 10 ml. of chloroform. The colorless solution was filtered and concentrated, and the residue was crystallized from chloroform–petroleum ether. The product, *p*-(1-bromoethyl)-phenyl β-cellobioside heptaacetate (2.4 g., m.p. 190–191.5°), was unstable and no attempt was made further to purify it before carrying out the next step. The heptaacetate (16 g.) was added to a refluxing mixture of 117 g. of anhydrous sodium acetate and 188 ml. of glacial acetic acid. The mixture was then refluxed for 6 hr. and poured hot into 2 l. of ice-water (stirring), when a brown solid was precipitated. The material (9.6 g.) was washed with water and dried before being dissolved in 300 ml. of methanol. To the solution was added 9.0 ml. of 0.4 *N* barium methoxide in methanol. After 24 hr. at 5° the solution was neutralized with dilute sulfuric acid, centrifuged, and the clear supernatant solution concentrated to dryness. The residue (4.3 g., 49.5%) was crystallized and recrystallized from water (charcoal) to give soft, chunky crystals, m.p. 175–176°, $[\alpha]^{20}D$ −65.5° (*c* 0.4, $H_2O$).

*Anal.* Calcd. for $C_{20}H_{28}O_{11}$: C, 54.0; H, 6.35. Found: C, 53.6; H, 6.6.

***p*-Vinylphenyl β-Cellobioside Heptaacetate.** (a) **From *p*-Vinylphenyl β-Cellobioside.**—This glycoside (2.5 g.), 20 ml. of acetic anhydride, and 20 ml. of pyridine were kept for 3 days at 25° and poured into 500 ml. of ice-water. The crystalline precipitate was filtered, washed with water, and recrystallized from methanol (charcoal); fine white needles (2.5 g., 59%), m.p. 197–198°, $[\alpha]^{20}D$ −31.1° (*c* 0.8, $CHCl_3$), $\lambda_{max}^{MeOH}$ 253.5 mμ (ε 19,300).

*Anal.* Calcd. for $C_{34}H_{42}O_{18}$: C, 55.3; H, 5.7; acetyl, 40.8. Found: C, 55.1; H, 5.9; acetyl, 40.4.

(b) **Direct Method.**—*p*-Acetoxystyrene (6.4 g.) and 5.25 g. of sodium hydroxide in 20 ml. of water were added to a solution of 5 g. of acetobromocellobiose[9] in 30 ml. of acetone and left at 25° for 24 hr. Acetone was distilled and the residual aqueous solution was diluted with an equal volume of water and extracted with four 25-ml. portions of chloroform. The combined chloroform extracts were washed with 2 *N* sodium hydroxide, then water and dried ($CaCl_2$). Concentration of the solution left a sirup which crystallized after addition of ether. Recrystallization from methanol gave fine white needles (0.73 g., 14%), m.p. 197–198°, $[\alpha]^{20}D$ −28.5° (*c* 0.7, $CHCl_3$), identical with the material previously prepared.

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(3) O. Westphal, *Naturwissenschaften*, **46**, 50 (1959).
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(8) J. Conchine, G. A. Levvy, and C. A. Marsh, *Advan. Carbohydrate Chem.*, **12**, 157 (1957).
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# *Book Reviews*

**Advances in Pharmacology.** Vol. 2. Edited by SILVIO GARATTINI and PARKHURST A. SHORE. viii + 392 pp. 16 × 24 cm. Academic Press, Inc., New York 3, N. Y. $12.00.

The second volume of this series features six chapters, five of which take the reader from the theoretical background and laboratory pharmacology, to the clinical and therapeutic applications of the topic under discussion. In this way, they represent fine examples of today's medical science. The sixth chapter (by Hans Meier), no less excellent, is excused from clinical consequences: it deals with pharmacological research in genetically controlled mice. Gerhard Zbinden writes on experimental and clinical aspects of drug toxicity, a survey badly needed at this time when drug manufacturers, pharmacologists, clinicians, and government agencies are groping for criteria of toxic and teratogenic phenomena, and for the extrapolation of laboratory data to clinical situations including transplacental toxicities. The classes of toxic interferences with metabolic, immunological, and

other reactions are detailed beautifully. This chapter should be read even by nonscientists who are charged with policy decisions in the introduction or removal of drugs with special and occasional toxic manifestations. It strikes an acceptable balance between a frank admission of such toxic reactions and the need for taking these toxicities into one's stride if the successful therapy of a vast majority of patients is at stake.

Myasthenia gravis is reviewed by Gilbert H. Glaser. Its history, pathology, diagnosis, pharmacology, and drug therapy is presented comprehensively in this chapter. Manuel R. Malinow offers a highly timely discussion of hormonal factors in atherosclerosis. In this disputed field, opinions and facts have shifted and reversed themselves during the last decade, and a searching compilation of these data is indeed welcome.

It has been said that more investigators have been kept alive by grants in the field of cancer chemotherapy, than have been killed by cancer. The two most overworked topics in this area have been alkylating agents and analogs of natural purine and pyrimidine constituents of nucleotides. This is an opportune time to review these two research fields which have proliferated at a rate approximating that of the malignant neoplasms that they are to inhibit. Stanley S. Brown surveys nitrogen mustards and related alkylating agents, and J. Henderson and H. G. Mandel present purine and pyrimidine antimetabolites in cancer chemotherapy. Trends in synthesis, leads obtained from metabolic, biochemical, and toxicological studies, and the mechanisms of action of such drugs are discussed lucidly. The ever-present dilemma of resistance to these agents, their use in the clinic, and a forecast of future trends of research and therapeutic usefulness are considered. Every medicinal chemist, medical scientist, and chemotherapist who wants to get into, or out of this area, should read these two chapters attentively. All chapters are documented with extensive reference lists, and a good author and subject index uphold the now established high tradition of this series of volumes.

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**High Molecular Weight Substances in Human Urine.** By J. STANTON KING and WILLIAM H. BOYCE, Bowman Gray School of Medicine. xvi + 165 pp. 24 × 16 cm. Charles C Thomas, Publisher, Springfield, Ill., 1963. $7.50.

While many reviews on urinalysis and the identification of small ions and low-molecular weight compounds are available, such information and a thorough scientific interpretation of the observed facts had not been assembled for macromolecules. After two introductory chapters on the over-all aspects of the fractionation and methodology of urinary high-molecular weight materials, the following are discussed in detail: macromolecules found both in plasma and urine; fourteen classes of urinary enzymes and enzyme inhibitors; peptide hormones in urine; uromucoid, acid polysaccharides, and blood group substances in urine. The text is well written, easily readable, and yet heavily documented and critically surveyed. The clinical chemist, the urologist concerned with calculous disease and its biochemical causation, and the renal physiologist will all appreciate the compilation of the thousands of observations in this book. Interesting facets are the origin, role, and functions of uromucoid in different human races, the chemistry of the blood group substances, and the description of normal and pathological events associated with urinary macromolecules. The book fills a real need in interdisciplinary writing in a complicated and important biochemical and clinical area.

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**Outline of Pharmacology and Therapeutics.** By SISTER M. MARIEL, C. S. A. xvi + 297 pp. 23.5 × 16 cm. Charles C Thomas, Publisher, Springfield, Ill. $12.50.

Nurses, pharmacy and medical students, and practising physicians will welcome this summary of drugs. It lists abbreviations used in prescription writing, conversion tables of weights and measures, dosage forms for adults and children, drug standards and combinations, drug names, side-effects, safety and legal measures in dispensing drugs, and many other facets of a practical *materia medica*. Written in telegraphic style, the book nevertheless presents a few basic facts about the history and mode of action of drugs. Notably absent are chemical names. For a quick survey and orientation in a given therapeutic situation, the small volume will serve as a satisfactory guide especially for those who do not ask too many questions about the "why" of drug action but want to know the "how" of practical drug applications. For nurses and pharmacists, the book can be recommended as a terse but useful text.

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**Medizin und Chemie.** Vol. VII. Articles from the medicinal chemical research departments of Farbenfabriken Bayer Aktiengesellschaft. 822 pp. 24 × 16 cm. Verlag Chemie, Weinheim, West Germany, 1963.

The 7th volume of this well known series of periodic publications from one of Europe's oldest (75 years) pharmaceutical chemical companies follows the footsteps of its six predecessors: it represents a peculiar mixture of exact scientific reports on subjects at the frontiers of medicinal science, of rose-colored accounts of relatively inefficient drugs and biological methods, and of overt though dignified indulgence in company history and advertising. This last facet appears prominently in the bibliographies which contain mostly references to articles from investigators within, or supported by the company, with considerable disregard of earlier or simultaneous achievements elsewhere. In some cases, this becomes too obvious: the discovery of the sulfonamide drugs occurred at the Pasteur Institute in Paris, to be sure, based on the work of G. Domagk at Bayer, but was neither achieved nor understood by the discoverers of the sulfonamide dyestuffs.

Nevertheless, the present book gives the history of a great tradition of fundamental medicinal studies and applications up to about 20 years ago until the interruption by World War II and the subsequent disorganization from which a complete recovery has not yet been achieved. Among the authors of new articles are many names which one associates with progressive thinking in medicinal science. The fields covered comprise pharmacodynamic agents, analgetics, antispasmodics, anticonvulsants, chemotherapeutic agents for tropical and bacterial infections, anthelmintics, antiviral agents, anticancer drugs, vitamins, polypeptides, sterilizing agents, and insecticides. Much of this wide spectrum of activity at Bayer is a direct duplication of effort in many other pharmaceutical companies, but a few chapters, *e.g.*, that on an inactivator of kallikrein, present novel ideas.

Medicinal scientists in all fields will find much of interest in the extensive synthetic and molecular modifications, descriptions of exact biological laboratory methods, and the instances of speculative ingenuity which may spark future advances in the great past tradition of the company publishing these researches.

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