an active-site-directed alkylation of the activating enzymes, owing to their structural resemblance to the substrate. The synthesis was achieved by reaction of *N*-t-butyloxycarbonyl-amino acids with dicyclohexylcarbodi-imide to form the corresponding anhydrides, which on treatment with diazomethane gave the diazoketones. The latter compounds reacted with HCl in ether to furnish the chloromethyl

ketone hydrochlorides $\text{Cl}^+ \text{H}_3\text{N}(\text{CHR})\text{--CO--CH}_2\text{Cl}$ (R =amino acid side chain). The chloromethyl ketone analogue of leucine was found to inhibit the action of leucine-activating enzyme in a time-dependent fashion at a concentration of 10mM, and the activity was not recovered on dialysis, showing the irreversible nature of the inhibition. It was found that the chloromethyl ketone analogues of both DL- and D-alanine were also effective irreversible inhibitors, as were the chloromethyl ketone analogues of *N*-trifluoroacetylalanine and bromopyruvate, which lack the specificity requirement of a free amino group.

The alkylation observed with these compounds and with classical thiol-group inhibitors (Boyko & Fraser, 1964; De Luca & McElroy, 1965, 1966; Baldwin & Berg, 1966; Harvey & Meister, 1967; Iaccarino & Berg, 1969), which occurs at or near the active site, suggests the presence of a nucleophile at the active centre. This appears to be sufficiently exposed for alkylation to occur without the prior formation of a Michaelis complex. This highlights the need for the synthesis of new types of inhibitors that can react to a significant extent only after the formation of a Michaelis complex.

The chloromethyl ketone analogues of DL-leucine and alanine proved to be powerful reversible inhibitors of the activity of leucine aminopeptidase, both producing 70% inhibition at a concentration of 17 μM . The chloromethyl ketone analogue of D-alanine showed no inhibition at concentrations up to 300 μM . This and other evidence will be presented to suggest that chloromethyl ketone analogues of L-alanine and leucine may inhibit the action of leucine aminopeptidase through a specific active-site-directed property.

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Computer Handling of Radioactive-Isotope Counting Data for Competitive Binding and Enzyme Kinetic Studies

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Three programs have been developed for processing radioactive-isotope counting data in connexion with competitive binding and enzyme kinetic studies. They are written in the BASIC programming language for use with the Honeywell G265 computer time-sharing system.

Radioactivities of the radioactive samples are counted in a Packard Tri-Carb liquid-scintillation spectrometer with punched-tape output. This tape is read into the computer from a remote terminal located in the laboratory, telephone lines being used for data transmission. Each program incorporates loops to locate any errors in the data arising either from tape-punch malfunction or transmission faults, and to ensure that the correct sequence of data is maintained.

Program 1 is used to determine the concentration of oestradiol receptors in uterine and breast-biopsy samples (Feherty *et al.*, 1970; Feherty & Kellie, 1971). The equation of the best-fitting line for the Scatchard-plot analysis is calculated for each set of data (Scatchard, 1949), and the receptor concentration and dissociation constant are evaluated from the gradient and intercept of this line, together with their confidence limits.

Program 2 is used to assay plasma oestradiol concentrations by competitive binding with uterine oestradiol receptor (Mester *et al.*, 1971; Robertson *et al.*, 1971). The experimental values are interpolated into the Scatchard plot of the interaction of the uterine receptor preparation with known amounts of oestradiol. An assessment of errors and determination of the dissociation constant and receptor concentration are thus possible; this is of value in assessing interassay variation.

Program 3 is used for enzyme kinetic studies, both of dopa decarboxylase (3,4-dihydroxy-L-phenylalanine carboxy-lyase, EC 4.1.1.26) (D. A. Bender & W. F. Coulson, unpublished work) and phenylalanine 4-hydroxylase (Coulson & Hughes, 1971). Data are corrected for counting efficiency by means of the channels-ratio method (Bush, 1963), and the enzymic activity is calculated from the radioactivity present in the substrate and the product. The double-reciprocal plot ($1/s$ versus $1/v$) is computed and extrapolated to determine the K_m and V_{max} of the enzyme preparation.

These programs have allowed objective assessment of results and achieved a very considerable saving of

time compared with either manual calculation or use of a small electronic calculator.

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Computer-Operated Systems for the Retrieval of Information from Current Biochemical Literature

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Several machine-readable information systems encompassing the biological sciences are now operating in Britain, with the Biochemical Society officially involved in their development and evaluation through its links with the Consortium on Chemical Information and the Biological Council's Committee on Biological Information. The 'selective dissemination of information' is particularly difficult in biochemistry, which refuses to be confined within conventional disciplinary boundaries. The modes of operation of, and typical outputs from, two current systems, namely SCISEARCH and BA-PREVIEWS, will be demonstrated and compared.

SCISEARCH, now commercially available (via Cybernet Time Sharing Ltd.), can search the total data base of all the *Current Contents* publications of the Institute for Scientific Information (Philadelphia) for the current month, i.e. about 30000 references per month. This is a direct interrogation procedure, the enquirer using a teletype terminal to receive instant references to articles that include specified words or phrases in their titles. A terminal connected to the SCISEARCH programme and data will be displayed.

We thank Mr. A. E. Cawkell, Director of ISI European Branch, Uxbridge, and CYBERNET Time Sharing Ltd., London W.1, for their participation and the provision of additional facilities.

The BA-PREVIEWS system uses the data base of *Biological Abstracts*, covering a quarter of a million references per year. The user's interest is expressed as a 'profile', built from freely chosen items, e.g. keywords, word stems, group concepts, methods, authors' names and so on, each with a weighting factor to achieve various types of logical connexion between the items specified. An article's title and reference are only part of the data: each title is enriched with terms expressing concepts, biological and chemical names, techniques. The computer searches the data tapes as they are issued at fortnightly intervals, and prints out the current references that satisfy the profile. The BA-PREVIEWS system is under experimental study by the Office for Scientific and Technical Information, through the Experimental Information Unit at Oxford and Nottingham; several members of the Biochemical Society are involved in this evaluation.

An Interactive Computer Program for Teaching the Use of Computers to Medical Students

By D. A. BENDER (*Courtauld Institute of Biochemistry, The Middlesex Hospital Medical School, London W1P 5PR, U.K.*)

As part of an experiment in teaching some aspects of the use of computers to all preclinical medical students in this School, an interactive program has been written, to demonstrate the way in which the computer and operator can interact and how the computer can extract information from the user. The program has been written in the BASIC programming language for use on the Leasco-Response computer time-sharing system.

The computer calls for simple anthropometric data (age, height and weight) that the student should have readily available. This input has to be in standardized format, so the computer issues appropriate instructions and reports errors. From the data are calculated and printed, with explanation, the approximate value of the basal metabolic rate and total daily energy requirement. The student is quizzed on his appreciation of the underlying physiology: lack of understanding produces a short remedial lesson. As well as introducing the student to an aspect of computers other than solely as rapid calculating devices this program reinforces teaching from other departments.

The generosity of Leasco-Response in making available a video display terminal for this demonstration is gratefully acknowledged.