transfer bands, the values given in Table 1 for the peaks of these latter may be considered to be only fairly accurate; but there is practically no doubt as to the order of these values.

Using the Benesi–Hildebrand equation, it was then found that both adenine and cytosine, and guanine hydrochloride, produced 1 : 1 complexes and that the equilibrium constants amounted to approximately $10^{-2}$ in each case.

Furthermore, as the same acceptor is involved throughout the whole series of compounds, it was to be expected that the lower the ionization potential of the nucleic bases, the longer would be the wave-length of the charge transfer bands. It is gratifying to see, on comparing columns 3 and 4 of Table 1, that the values predicted by Pullman[5]

Table 1

| Complexes | Red limits (Å) | Positions of peaks (Å) | $\pi$-Ionization potentials of bases[5] (eV) |
|---|---|---|---|
| Guanine. Chloranil | ~7,510 | 5,230 | 7·8 |
| Adenine. Chloranil | ~6,500 | 4,920 | 8·3 |
| Cytosine. Chloranil | ~6,500 | 4,780 | 8·6 |

for the $\pi$-ionization potentials under consideration are in excellent agreement with this rule.

It is now of special interest to emphasize the importance of the diversity in the time-lags, which must express a scale of activation energies for the formation of the complexes. In this respect, it is to be noted that the building-up of the guanine complex is in fact governed by the greatest activation energy, and this in spite of the fact that the complex is the most stable, as is shown by the longer wave-length charge transfer band. Moreover, tetracyanoethylene does produce quite similar results to chloranil. It is therefore now quite clear that a complete analysis of such fundamental phenomena must take the factor of activation energy fully into account. In relation with this, it is perhaps worth while noting that guanine and thymine produce charge transfers much less easily than their associates in DNA's, respectively cytosine and adenine.

As a consequence, the characteristic distribution of activation energies might perhaps throw some light on the origin of the complementarity of the bases, as found by Watson and Crick[6]. One could indeed suggest that, in each pair, this would have emerged through natural selection from the need for protection of one base by the other, against external chemical agents.

As it seems now established that nucleic acids constitute the essential target for the action of mutagenic substances[7], the mechanisms of this, and also of carcinogens, are now being investigated in our laboratory, using the method here developed.

We thank Prof. L. D'Or for the loan of a Cary spectrophotometer. One of us (P. M.) acknowledges with thanks a EURATOM grant.

PAUL MACHMER
JULES DUCHESNE

Department of Atomic and Molecular Physics,
University of Liège,
Institut d'Astrophysique,
Cointe-Sclessin, Belgium.

[1] Mulliken, R. S., *J. Amer. Chem. Soc.*, **72**, 600 (1950); *J. Chim. Phys.*, France, **61**, 20 (1964). Ferguson, E. E., *J. Chim. Phys.*, France, **61**, 257 (1964). Hassel, O., and Rømming, Chr., *Quart. Revs.*, **16**, 1 (1962). Cornil, P., Duchesne, J., Read, M., and Cahay, R., *Bull. Acad. Roy. Sci.*, Belgium, **50**, 235 (1964). See also Briegleb, G., *Elektronen-Donator-Acceptor-Komplexe* (Springer Verlag, Berlin, 1961).

[2] Szent-Györgyi, A., *Introduction to a Submolecular Biology* (Academic Press, London, 1960).

[3] Szent-Györgyi, A., Isenberg, I., and Baird, S. L., *Proc. U.S. Nat. Acad. Sci.*, **46**, 1444 (1960).

[4] See Pullman, B., *J. Cell. and Comp. Physiol.*, supp. 1, **64**, 91 (1964).

[5] Pullman, B., *C.R. Acad. Sci., Paris*, **259**, 3101 (1964).

[6] Watson, J. D., and Crick, F. H. C., *Nature*, **171**, 737, 964 (1953).

[7] See Pullman, B., *Biopolymers, Symp.* No. 1, 141 (1964).

## BIOCHEMISTRY

### Gliotoxin from *Aspergillus chevalieri* (Mangin) Thom et Church

THE antibiotic, gliotoxin, first described by Weindling and Emerson[1], has been isolated from cultures of various organisms, *Trichoderma viride*[1,2], *Gliocladium fimbriatum*[3], *Aspergillus fumigatus*[4], *Penicillium obscurum*[5], *P. cinerascens*[6] and *P. terlikowski*[7].

We have now also obtained it from *Aspergillus chevalieri*, which, when grown on the medium, malt extract 6 per cent, lactose 4 per cent, sodium nitrate 0·5 per cent and added trace metals, was found to produce an antibiotic, reaching peak concentration after 7 days at 23° C in surface culture. The active material was readily extracted from the culture filtrate with chloroform. Purification of the chloroform extractive by chromatography on acetic acid-inactivated alumina, followed by crystallization from methanol or ethanol, gave colourless crystals (25 mg/l. of filtrate), m.p. 194°–195° (decomp.), $[\alpha]_D^{22} = -289{\cdot}1°$ ($c = 0{\cdot}3$ in methanol). (Found: C, 47·8; H, 4·1; N, 8·6; S, 19·9. $C_{13}H_{14}N_2O_4S_2$ requires C, 47·8; H, 4·3; N, 8·6; S, 19·7 per cent.) On a silica-gel thin-layer chromatogram the substance had $R_F$ 0·61 in the solvent system, chloroform containing 5 per cent methanol.

The identity of the crystals was established by direct comparison with an authentic sample of gliotoxin.

S. WILKINSON
J. F. SPILSBURY

Wellcome Research Laboratories,
Beckenham, Kent.

[1] Weindling, R., and Emerson, O., *Phytopath.*, **26**, 1068 (1936).

[2] Brian, P. W., *Nature*, **154**, 667 (1944). Brian, P. W., and Hemming, H. G., *Ann. App. Biol.*, **32**, 214 (1945). Wright, J. M., *Ann. App. Biol.*, **41**, 280 (1954).

[3] Johnson, J. R., Bruce, W. F., and Dutcher, J. D., *J. Amer. Chem. Soc.*, **65**, 2005 (1943).

[4] Glister, G. A., and Williams, T. I., *Nature*, **153**, 651 (1944). Menzel, A. E. O., Wintersteiner, O., and Hoogerhide, L. J. C., *J. Biol. Chem.*, **152**, 419 (1944). Kidd, J. G., *Science*, **105**, 511 (1947).

[5] Mull, R. P., Townley, R. W., and Scholtz, C. R., *J. Amer. Chem. Soc.*, **67**, 1626 (1945).

[6] Bracken, A., and Raistrick, H., *Biochem. J.*, **41**, 569 (1947).

[7] Johnson, J. R., Kidwai, A. R., and Warner, J. S., *J. Amer. Chem. Soc.*, **75**, 2110 (1953).

### All-D-Bradykinin and the Problem of Peptide Antimetabolites

IN the past there has been much speculation about the effect of the incorporation of D-amino-acids into biologically active peptides. Several of the antibiotic peptides, as well as penicillin, contain D-amino-acids. The antibacterial activity may be associated with the presence of these D-amino-acids. In the case of the peptide hormones, where all the amino-acids are of the L series, the replacement of one amino-acid by the D isomer has usually failed to destroy the biological activity. Thus hormonal activity of bradykinin was retained when either serine[1] or one of the phenylalanines[2] was changed to the D-configuration. In angiotensin, inversion of arginine[3], aspartic acid[4], or phenylalanine[5] did not destroy the biological activity, although the D-tyrosine analogue was inactive[5]. Examination of melanophore stimulating hormone (MSH)[6,7] and eledoisin[8] has shown that the biological activity was retained when one amino-acid was changed to the D-configuration. In contrast to these data on the change of a single residue, the inversion of all the amino-acid residues in a pentapeptide which has the hormonal activity of MSH was found not only to cause loss of hormonal activity, but to produce an antimetabolite of MSH[9]. This peptide, D - histidyl - D - phenylalanyl - D - arginyl - D - tryptophylglycine, was found to antagonize the action of the corresponding all-L pentapeptide as well as that of MSH. Because we have been attempting to make specific