Two further series of compounds were noted as present in the alcohol fraction, and from the close similarity of their retention times to those of the normal straight-chain series, it is concluded that these are related compounds.

This work is published by permission of the Director of the Warren Spring Laboratory, Department of Scientific and Industrial Research.

> V. A. EDWARDS P. J. KIPPING P. G. JEFFERY

Warren Spring Laboratory, Stevenage, Herts.

<sup>1</sup> Hewett, D. R., Kipping, P. J., and Jeffery, P. G., Nature, **192**, 65 (1961).
<sup>2</sup> Wollrab, V., Streibl, M., and Sorm, F., Chem. and Indust., 1762 (1962).
<sup>3</sup> Metcalfe, L. D., Nature, **188**, 142 (1960).
<sup>4</sup> Tanner, D. W., Poll, A., Potter, J., Pope, D., and West, D., J. App. Chem., **12**, 547 (1962).

## **Temperature Dependence of Irradiation** Damage to Polythene

In the course of work on radiation damage to polythene using the Woolwich 4.3 MeV linear accelerator, it was observed that a dose of 1,000 megarep raised the elastic modulus of 'Alkathene 7' by a factor of three without apparently affecting crystal content. This was confirmed both by an X-ray diffraction analysis of the material<sup>1</sup> and by a spherulite analysis. The density of the material was also found to have increased by 0.95 per cent.

These results are to be compared with those obtained by Charlesby and Hancock<sup>2</sup> using the B.E.P.O. reactor, where an equivalent dose<sup>8</sup> of 22 pile units was found to destroy all crystallinity and to create a product with elastic modulus lower than original. This was shown to be the net result of an initial sharp fall in modulus up to a dose of 7 units due to rapid destruction of crystallinity followed by partial recovery due to radiation cross-linking of the now fully amorphous material. Full recovery occurred at 30 units dose and continued irradiation then increased the modulus above original.

The difference between accelerator and reactor results is almost certainly not due to differences in the quality of the respective radiations. Charlesby<sup>4</sup> has considered the effect of ionizing radiation in some detail and concludes that the ionizing effect of direct collision of neutrons with atoms is relatively very small. He further shows that there is little difference in the effects produced by different radiations of equivalent absorbed energy.

This being so, the most likely factor to influence the nature of the radiation damage from accelerator and reactor appears to be the temperature at which irradiation is carried out. In the case of the accelerator, specimen temperature does not exceed 30° C whereas, with a nuclear reactor, heat from the unit can raise the specimen temperature to near its melting point. At these elevated temperatures, polythene is intrinsically more amorphous due to partial melting of the crystalline component, and it seems reasonable that radiation cross-linking of the amorphous increment at an elevated temperature will prevent it recrystallizing on return to normal temperature. This would result in an apparent destruction of the crystalline component although the mechanism would still be the simple one of cross-linking, common to both types of radiation.

Work is proceeding to examine the effect of X-rays on polythene at elevated temperatures. If the suggested temperature dependence is established, we have clearly a method of directly raising or lowering the elastic modulus of polythene by irradiation with the same dose but at the appropriate temperature.

> G. TODD G. A. WILD

War Office, **Royal Armament Research** and Development Establishment, Fort Halstead,

Sevenoaks.

<sup>1</sup> Krimm, S., and Tobolsky, A. V., J. Polymer Soi., 7, 57 (1951).

<sup>3</sup> Charlesby, A., and Hancock, N. H., Proc. Roy. Soc., A, 218, 245 (1953).
<sup>3</sup> Bovey, F. A., The Effects of Ionizing Radiation on Natural and Synthetic High Polymers, 33 (Interscience, London, 1958).

<sup>4</sup> Charlesby, A., Proc. Roy. Soc., A, 215, 187 (1952).

## BIOCHEMISTRY

## **Total Synthesis of Adrenocorticotrophic** Hormone

THE total synthesis of  $\beta$ -corticotropin (ACTH), with the amino-acid sequence characteristic of the porcine species<sup>1</sup> (Fig. 1), has been achieved<sup>2</sup> using methods especially designed and developed for preparing large and complicated peptides<sup>3</sup>. They are: (a) formation of peptide bonds mainly by means of active esters<sup>4</sup> (for example, *p*-nitrophenyl esters<sup>5,4</sup>); (b) protection of amino and carboxyl functions with such blocking groups derived from *t*-butanol that easily can be removed in the last stage of the synthesis without destruction of sensitive peptides<sup>3</sup>.

The latter method has proved to be essential for success, because ACTH is prone to severe alteration under conditions necessary for removing other, more common protecting groups such as carbobenzoxy<sup>7</sup>, formyl<sup>8</sup>, acetyl<sup>8</sup>, and tosyl<sup>9</sup>. We also have successfully applied it to the syntheses of  $\alpha$ -melanotropin ( $\alpha$ -MSH) (ref. 10),  $\beta$ -melanotropin ( $\beta$ -MSH) (refs. 2, 11), and of  $\beta^{1-24}$ -cortico-tropin (the peptide comprising the *N*-terminal 24 amino-acids of ACTH) (ref. 12) as well as of other, similar peptides ( $\beta^{1-16}$ -corticotropin (ref. 13),  $\beta^{1-19}$ -corticotropin (ref. 14), Ac-Ser<sup>1</sup>  $\beta^{1-19}$ -corticotropin (ref. 15), etc.).

The synthetic route to ACTH starts from L-phenylalanine t-butyl ester (pos. No. 39) and proceeds in a stepwise manner by addition of one appropriately substituted amino-acid p-nitrophenyl ester after the other (removal of carbobenzoxy groups by hydrogenation, usually in 80 per cent acetic acid with palladium on charcoal; the resulting acetate salts may be reacted with the active ester to follow without addition of base) to the protected penta-decapeptide (pos. No. 15-39, Fig. 2). This compound, obtained in a pure state by counter-current distribution, was then reacted with the protected octapeptide (pos. No. 17-24) by the method of mixed anhydrides (mixed anhydride with trimethyl-acetic acid). The resulting derivative (pos. No. 17-39) was purified by countercurrent distribution (CHCl<sub>3</sub>, CCl<sub>4</sub>, MeOH, 0.05 M NH<sub>4</sub>OAc, pH=6.5; 5:5:8:2 vol.; K=2.3), hydrogenated and condensed with the azide of the protected hexapeptide (pos. No. 11-16) (ref. 16). The resulting protected nonacosapeptide (pos. No. 11-39) was extensively purified by counter-current distribution in the same solvent system (K=0.8) and hydrogenated. Condensation with the decapeptide derivative (pos. No. 1–10) (ref. 17) by means of dicyclohexyl carbodiimide gave a crude, protected nonatriacontapeptide which was purified by countercurrent distribution (CHCl<sub>3</sub>, CCl<sub>4</sub>, MeOH, 0·1 M NH<sub>4</sub>OAc, pH=6.5; 8:8:17:7 vol.; K=1.1). The purification by counter-current distribution was followed by chromatography on thin layers of alumina in the solvent system 100 (ref. 10) (Fig. 3). Material from the pure fractions was then treated with trifluoroacetic acid to remove all protecting groups and converted to the acetate salt. The