be relatively insensitive to variation of substrate structure.

Values of K_m , but not of V_{max} , showed relationships with substrate structure, increasing in the order *para*, *ortho*, *meta*. This suggests that electronic rather than steric factors are the dominant influence on K_m values. The energy of the highest occupied molecular orbital has been calculated for nine of the substrates studied (Pettersson, 1970b). These values correlate with $\log K_m$, higher orbital energies being associated with lower K_m values. K_m values are also affected by negatively charged groups attached to the benzene ring; the more highly charged the group, the higher the K_m value.

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Immunochemical Studies on Human Calcitonin M Leading to Information on the Shape of the Molecule

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Antigen-antibody interactions are sensitive to conformational changes in the antigen (Brown, 1962, 1963; Sela, Schechter, Schechter & Borek, 1967; Goodman, 1969). We have used changes in such interactions (assessed qualitatively) to derive information on the conformation of human calcitonin M.

Two highly specific antisera to the hormone were obtained from a single rabbit. The first was taken 8 months after immunization and boosting with crude extracts of human thyroid-medullary carcinoma: the second was obtained after a further 9 months of boosting with the pure synthetic hormone. By using the radioimmunoassay system described by Clark, Boyd, Byfield & Foster (1969), the reactions of the hormone and its derivatives and fragments with these antisera were studied. It was shown that antiserum I reacts with two major sites, one within the sequence 11-18 of the 32-residue peptide amide and the second located around residue 28. Antiserum II reacts mainly with

a site around residue 28, which may be different from the site in this region recognized by the first antiserum. Neither antiserum reacts appreciably with the *N*-terminal end of the peptide. This may be correlated with the fact that only residues 1, 3, 4, 5, 6, 7, 9, 28 and 32 are conserved in the five species known and that immunogenicity often resides in non-conserved regions (Schwyzer, 1968).

An analysis of the data suggests that the conformation of the *C*-terminal antigenic sites is influenced by the *N*-terminal region. Studies on oxidized derivatives locate the site of influence near the methionine⁸ residue, but the 1-7 disulphide bond, the residues of the ring and the terminal amino group do not appear to be involved.

All the data suggest that human calcitonin M is not a random coil but has some degree of preferred conformation. It is suggested that the peptide is folded to bring the *N*- and *C*-termini into close proximity with non-covalent interaction between separate parts of the linear sequence, perhaps near residues 8 and 28.

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Patterns of Serum γ G-Globulin Heterogeneity in Health, Rheumatoid Arthritis and Cancer

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Several workers have suggested that the serum immunoglobulin concentrations of the individual in normal health may be genetically determined, a view supported by recent studies on monozygotic and dizygotic twins (Kalf & Hijmans, 1969). Differences in the relative proportions of the immunoglobulins may indicate differences in the type and extent of the immune response of each individual and correlate with certain disease patterns. The increased incidence of lymphoma in patients with