STRUCTURE OF L-TYROSYL-L-PHENYLALANINE MONOHYDRATE

E. SUBRAMANIAN, R. MURALI AND J. TROTTER†

Department of Crystallography and Biophysics, University of Madras, Guindy Campus, Madras 600 025, India.

† Department of Chemistry, University of British Columbia, Vancouver, British Columbia V6T 1Y6, Canada.

ABSTRACT

The crystal structure of a dipeptide, L-tyrosyl-L-phenylalanine, has been determined by direct methods, and refined isotropically using MoK α diffractometer data to a final R-value of 0.065 for 559 reflections with $I > 2\sigma$. The peptide unit is trans planar, and is nearly perpendicular to the plane of the carboxyl group (dihedral angle of 93°). The back bone torsion angles are $\psi_1 = 165°$,, $\omega_1 = 177°$, $\phi_2 = -69°$ and $\psi_2 = 148°$. The side-chain torsion-angles are: for tyrosine, $(\chi_1, \chi_2) = (46°, 79°)$, and for phenylalanine, $(\chi_1, \chi_2) = (-79°, 78°)$.

INTRODUCTION

IN the amino acid sequence of several peptides of biological importance, one frequently notes the presence of two contiguous aromatic residues. Examples are -phe-phe- in substance P and somatostatin; -tyr-phe- in vasopressin etc. The juxtaposition of two contiguous residues with bulky aromatic side-chains may introduce confirmational restrictions. Study of the structure and confirmation of such peptides should therefore provide valuable information in the analysis of structure-activity relationship among neuropeptides. This paper describes the results of the x-ray crystal structure analysis of L-tyrosyl-L-Phenylalanine.

EXPERIMENTAL

Very thin needle-shaped crystals of the dipeptide were obtained by cooling a hot aqueous solution of a commercial sample. The crystal data are summarized in table 1. A total of 1109 unique reflections with $\sin\theta/\lambda \leq 0.50\ A^{-1}$ were collected on a Nonius CAD-4 diffractometer using MoK α radiation; of these, 559 reflections had $I > 2\sigma$ and were considered to be "observed". The reflections were corrected for Lorentz and polarization effects.

The structure was solved by direct methods using the computer program MULTAN[1]. An E-map calculated for the set of phases showing the highest figure of merit revealed all of the non-hydrogen atoms and one water molecule. The positions of the hydrogen atoms were determined by geometrical considerations and stereochemistry. The trial structure obtained was refined isotropically by full-matrix least-squares procedures, with hydrogen atoms included only in the structure factor calculations. Convergence was reached at an R-value of 0.065 for the 559 observed reflections. Due to paucity of reflections, anisotropic refinement was not attempted. The atomic scattering factors for C, N and O were taken from the Internationals Tables (1962)[2], while those for the hydrogen atoms were taken from Stewart *et al*[3]. A list of the final parameters will be supplied on request.

DISCUSSION

Figure 1 shows a stereo view of the molecular confirmation. The peptide unit is trans and planar. The plane of the carboxyl group makes a dihedral angle of 93° to the peptide plane. The aromatic rings in the two side-chains are also planar within the accuracy of the observations. The torsion angles[4] observed in the molecule are: $\psi_1 = 165°$, $\omega_1 = 177°$, $\phi_2 = 69°$, $\psi_2 = 148°$. For tyrosine, $(\chi_1, \chi_2) = (46°\ 79°)$; for phenylalanine. $(\chi_1, \chi_2) = (-79°, 78°)$. In the related structure of L-tyrosyl-L-phenylalanine HCl[5], $\psi_1 = 154°$, $\omega_1 = 167°$, $\phi_2 = -58°$, $\psi_2 = 136°$; tyrosine $(\chi_1, \chi_2) = (-71°, 113°)$ and phenylalanine $(\chi_1, \chi_2) = (174°, 83°)$. The back-

TABLE I

Crystal Data for L-tyrosyl-L-phenylalanine monohydrate.

Molecular Formula	$C_{18}H_{20}N_2O_4 \cdot H_2O$
Molecular Weight	346
Crystal System	Orthorhombic, $P\ 2_12_12_1$
Unit Cell	a = 5.744 (2) A
	b = 8.284 (2)
	c = 35.518 (6)
Density (calculated)	1.360 g.cm^{-3}
Radiation used	MoK α (λ = 0.7107 Å)
Temperature	23° C (ambient)

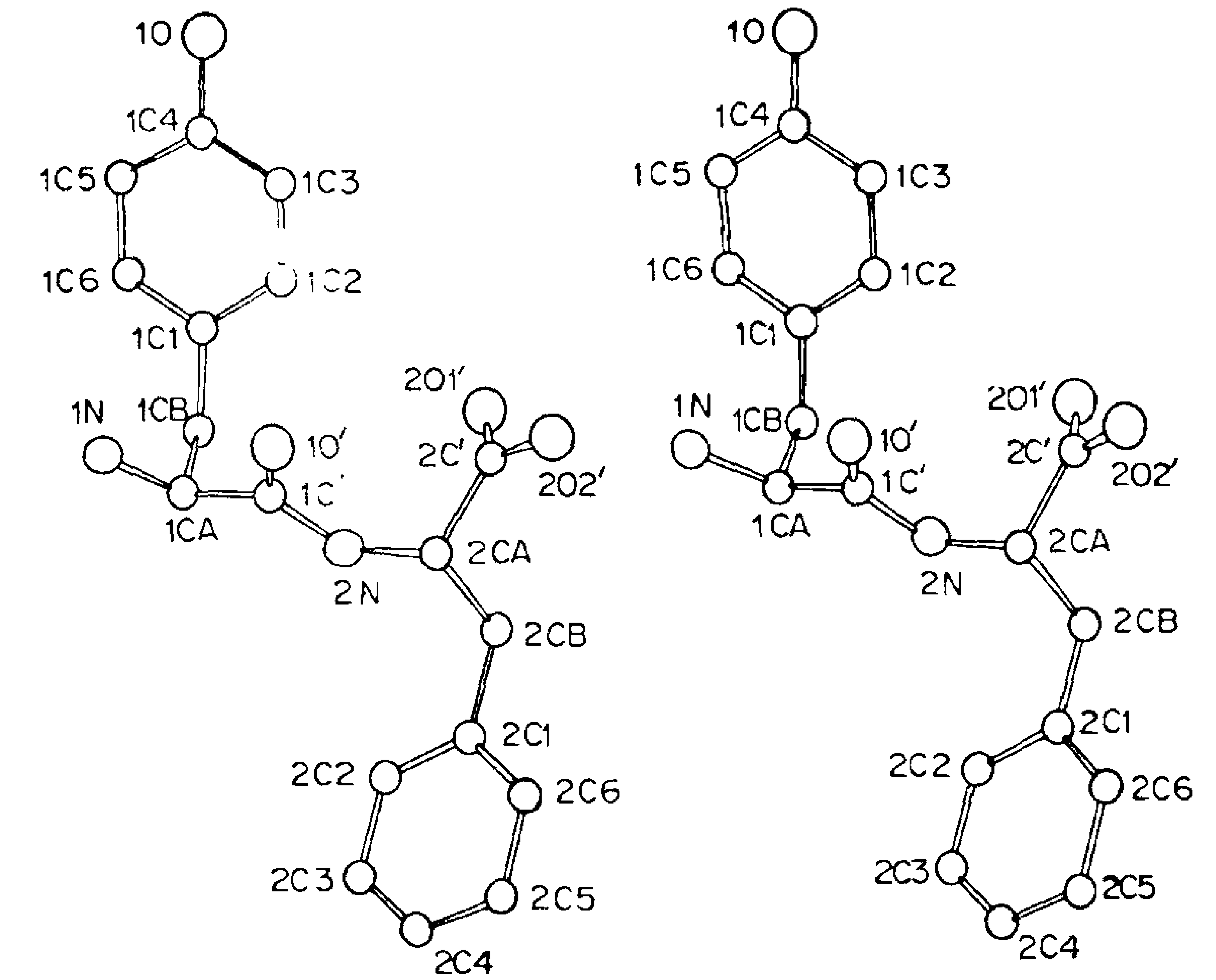

Figure 1. Stereoscopic view of the molecule of L-tyrosyl-L-phenylalanine.

bone conformation is essentially similar in the two molecules, but the side-chain conformations are different.

Figure 2 shows a projection of the structure down the b-axis. Six out of seven available protons are used in the formation of hydrogen bonds as listed below: IN..... 10 (= 2.92A), IN..... Water (=2.63), 2N.....202' (=2.87), 10..... 201' (=2.59). Water ..... 201' (=2.71) and Water..... 202' (=2.62). The packing arrangement of the molecules consists of segregated regions of polar and non-polar groups alternating along the *c*-axis.

ACKNOWLEDGEMENT

RM thanks the CSIR, India for the award of a Junior Research Fellowship.

7 March 1983; Revised 23 May 1983

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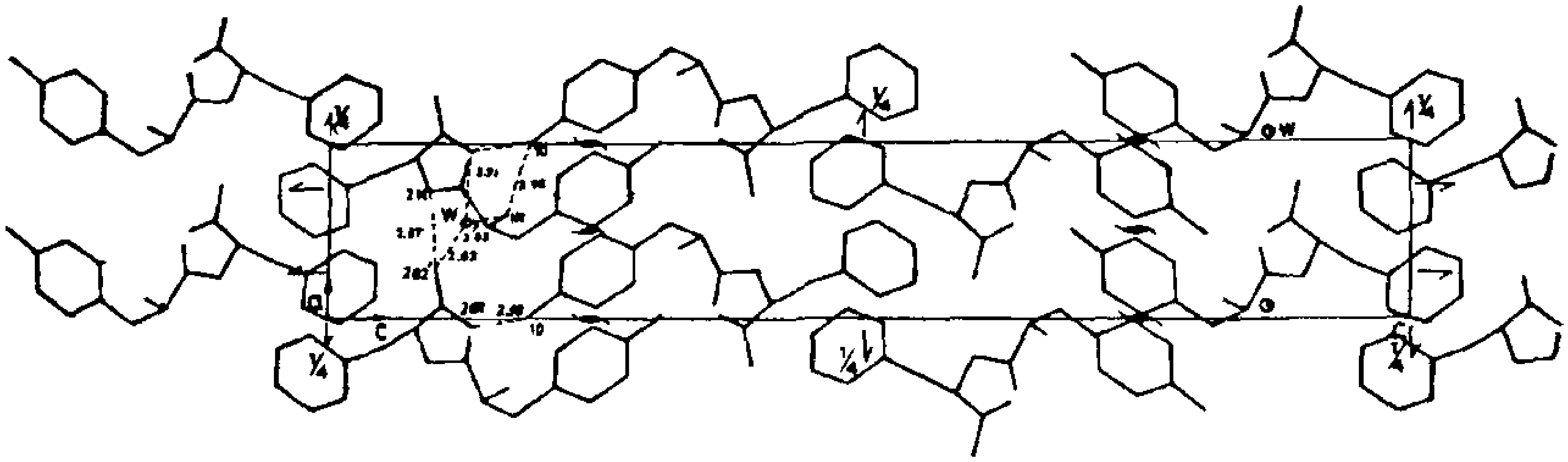

Figure 2. Projection of the unit cell contents down the crystallographic b-axis.

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SYSTEMATIC ENTOMOLOGY IN INDIA—PAST, PRESENT AND FUTURE

B. R. SUBBA RAO
Commonwealth Institute of Entomology, C/o, British Museum (Natural History), Cromwell Road, London SW7 5BD, UK.

WHILE man originated about a million years ago, insects are known to have been in existence for the past 200 to 400 million years. Also insects have one to several generations every year or so, man one every 20 years or so. Consequently the insects have an immense degree of evolutionary maturity *vis-a-vis* that of man.

The number of species of insects known todate is still empirical and no one can give an exact answer. It is even hard to guess what the insect fauna is the world over. According to one estimate in 1948 approximately 686,000 species of insects had been named and described for the entire world and it is probable that this number is nearer a million today. Whatever the number of species, one must realise that we are surrounded by millions of insects.

There is no doubt that insects were known to Indians from Vedic times. Lac, silk and honey, products of insects have been mentioned in classical literature. In Mahabharata we read the story of sage Mandavya who as a child innocently pinned a fly (Diptera) and had to pay for his sins in torturing the fly. The termitarium has also been mentioned in connection with the story of sage Chyavana and Sati Sukanya.

However, the earliest record of Indian insects in the modern era dates from Linnaeus[1] who included 12 species of insects from India in his treatise 'Systema Naturae'. It is a well known fact that several Christian missionaries and employees of the East India Company were amateur entomologists who collected insects and sent them to taxonomists in Europe. Fabricius studied and described over 1000 species of insects from India. When East India Company firmly established themselves on Indian soil and entered into politics and the warfare of the princely states of India, their army included several high ranking officers who were keen amateur entomologists. Insects were collected from various parts of India and were sent to several specialist entomologists in Europe for their diagnosis. The most noteworthy example is that of Dr Koenig who was a student of Linnaeus. Koenig came to India as a medical officer to the Tranquebar mission. He collected a good deal of insects and these were studied and named by Linnaeus and Fabricius. Koenig[2] himself published what was then a real scientific contribution on termites of Tanjore district. The other important early publications were Donovans[3] 'Natural History of insects of India' this was revised by Westwood[4]. Westwood[5] also published 'Cabinet of Oriental Entomology'. Hope[6] published a fine paper on the 'Entomology of the Himalayas and of India' in which he recorded and described several taxa belonging to the orders of Coleoptera, Dermaptera, Lepidoptera, Orthoptera, Heteroptera and Deptera.

The establishment of the Asiatic Society of Bengal in 1785 was the origin of entomology in India in its true sense. The Indian Museum was established in Calcutta in 1875 and all the insect collections of the Asiatic Society were transferred to the Indian Museum. Many early workers of the Indian Museum added further collections of insects between 1884 and 1894. The Bombay Natural History Society was founded in 1883 and the society naturally established its own insect collection and published very useful papers on the taxonomy and biology of several groups of insects.

The real impetus to taxonomy of insects was provided by the publication of a series entitled 'Fauna of British India', the first volume coming out in 1892 and the series is still being continued and published by the Zoological Survey of India as 'Fauna of India'. Mention must be made of the contributions of Bingham, Hampson, Bell and Scott on moths and butterflies (Lepidoptera); Brunetti and van Emden on Diptera; Bingham and Morley on Hymenoptera; Moulik on Coleoptera. Lefroy[7] published Indian insect life and Fletcher[8] made his monumental contribution by publishing a treatise on South Indian insects. The establishment of the Imperial Agricultural Institute at Pusa, Bihar in 1905; the Forest Research Institute with