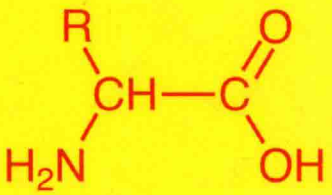

SPECIALIST PERIODICAL REPORTS

AMINO ACIDS, PEPTIDES AND PROTEINS

VOLUME 28

SENIOR REPORTER J.S. DAVIES

THE ROYAL SOCIETY OF CHEMISTRY

A Specialist Periodical Report

Amino Acids, Peptides and Proteins

Volume 28

A Review of the Literature Published during 1995

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Amino Acids, Peptides and Proteins

Volume 28

Preface

We have reached an age when genetic engineering can generate orphan receptors awaiting suitable ligands to be discovered, bringing us to the era of inverse pharmacology. Prion proteins and their conformational changes are on their way to being acclaimed as the source of BSE and CJD and other diseases of the ageing process. Yet researchers in these fields complain that the lack of physical techniques to identify the modified prions is hampering developments. So as all our Reporters in this series once more report expansion and consolidation within their areas, we can only hope that amongst the hard work put into the original research, reported in 1995, there are developments which will assist in catching up with the increased demands at the frontiers. The strides taken in applying physical techniques to protein folding seem to be well advanced in this direction.

To bring together another compilation of published papers has again depended on long hours of dedication from my fellow reporters, listed on the title page of this book. The core of stalwart reporters from previous volumes remain a core source of Chapter reviews for this volume as well, and we welcome back Dr. Chris Schofield and his Oxford colleagues for their biennial look at the β-lactam scene, which is under continuous evolution in trying to win the battles against the microbes' wish to survive. Topics in Chapter 3 recently have been ably reviewed for us by Michael North and colleagues at Bangor. Due to other calls on his 'reviewing' time, Michael is withdrawing from the team for the next volume, but does so with much appreciation for his support for the series.

Two Peptide Symposia on the American (Columbus, Ohio) and European (Edinburgh) sides of the Atlantic have taken place since the appearance of Volume 27 in this series, and the books of Proceedings from them will serve as hors-d'oeuvres to await the appearance of full papers from which our Reports are compiled.

Once again, my sincere thanks go to my co-authors, and book editors at the RSC at Cambridge under the watchful eye of Janet Freshwater. It is their effort that has been instrumental in ensuring the continuation of this series into yet another volume – Diolch yn fawr.

John S. Davies
University of Wales, Swansea

Abbreviations

The abbreviations for amino acids and their use in the formulation of derivatives follow in general the 1983 Recommendations of the IUB-IUPAC Joint Commission, which were reprinted as an Appendix in Volume 16 of this series. These are also published in :-

Eur J. Biochem. 1984, **138**, 9-37; *Int. J. Pept. Protein Res.*, 1984, **24,** after p.84; and *J. Biol. Chem.*, 1985, **260**, 14-42.

Recently the Joint Commission have issued the following corrections to the above Recommendations:-

Section 3AA-13.4 For Ala-Thr-Gly-Asp-Gly, read Ala-Thr-Gly-Asp-Gly

Section 3AA-13.5 The correct name is (7*E*,9*E*,11*Z*,14*Z*)-(5*S*,6*R*)-6-[(cysteinyl-glycin)-*S*-yl]-5- hydroxyicosa-7,9,11,14-tetraenoic acid.

A complete listing of the single-letter code for amino acids appeared in the Abbreviations section of Volume 24 of these Reports, together with structures for the closely related BOP family of coupling reagents.

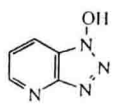
Chapter authors have been encouraged annually to include new abbreviations in their texts. With the ever increasing diversification in structures, lists of unusual abbreviations are periodically compiled. Some examples are listed below.

Abo	2-azabicyclo[2.2.2]octane-3-carboxylic acid
Abu	α-aminobutyric acid
A_2bu	2,4-diaminobutyric acid
ACCA	4-aminocyclohexanecarboxylic acid
εAhx	6-aminohexanoic acid
Aib	α-aminoisobutyric acid
Aic	2-aminoindan-2-carboxylic acid
A_2pr	2,3-diaminopropionic acid
Atc	2-aminotetralin-2-carboxylic acid
Ava	5-aminopentanoic acid
Aze	azetidine-2-carboxylic acid
Cha	3-cyclohexylalanine
Cpg	α-cyclopentylglycine
Cpp	1-mercaptocyclohexaneacetic acid, *or* β-mercapto-β,β-cyclopentamethylene propionic acid, *or* Pmp (*below*)
*c*PzACAla	*cis*-3-(4-pyrazinylcarbonylaminocyclohexyl)alanine
Dab	2,4-diaminobutyric acid

Dap	2,3-diaminopropionic acid
Dbf	3-(2-dibenzofuranyl)alanine
Dip	3,3-diphenylalanine
Dph	α,α-diphenylglycine
Dpr	2,3-diaminopropionic acid
Gly(Ph)	phenylglycine
Har	homoarginine
Hib	α-hydroxyisobutyric acid
Hyp	*trans*-4-hydroxyproline
Iva	isovaline
Mpt	*trans*-4-mercaptoproline
1-Nal	3-(1-naphthyl)alanine
2-Nal	3-(2-naphthyl)alanine
Nap	β-(1′-naphthyl)alanine
Oic	octahydroindolecarboxylic acid
Opt	*O*-phenyltyrosine
3-Pal	3-(pyridyl)alanine
Pen	penicillamine
Phg	phenylglycine
Pip	pipecolic acid
Pmp	β,β-pentamethylene-β-mercaptopropionic acid, *or* Cpp (*above*)
Qal	3-(3-quinolyl)alanine
Qua	quinoline-2-carboxamide
Sar	sarcosine
Thi	β-thienylalanine
Tic	1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

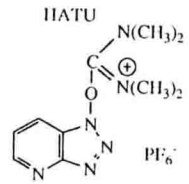
In the Abbreviations section of Volume 24 (1993) of this series, it was deemed timely to give structures to clarify the acronyms for the plethora of coupling agents currently in use. Since then the popularity of HATU and HOAt justifies structural clarification of these acronyms as follows:

HOAt



1-hydroxy-7-azabenzotriazole

HATU



O-(7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate

Contents

1
Amino Acids

BY GRAHAM C. BARRETT

1 Introduction

The literature of the amino acids for 1995 is reviewed in this Chapter, aiming particularly at thorough coverage of developments in chemical and analytical areas. Although the literature covering routine biological studies of common amino acids is excluded, the more innovative biological and pharmaceutical work is covered. Scrutiny of the hard copy literature (the major journals, and *Chemical Abstracts* from issue 11 of Vol 122 to issue 9 of Vol 124 inclusive) has provided the citations that make up the Chapter.

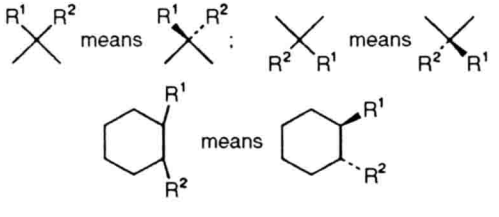
Continuity with preceding Volumes of this Specialist Periodical Report has been a prime consideration, so the Chapter has been sub-divided in the style used in all previous Volumes in this series. The device '(see p. XX, Vol YY)' that is used in this Chapter provides reference back to preceding Volumes, and helps the reader to keep track of important amino acid topics that have been developing over the years.

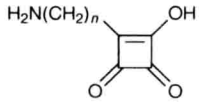
This Report has acknowledged in recent Volumes, that the term 'amino acids' has numerous meanings, but that the almost exclusive emphasis of this Chapter is on the α-aminoalkanoic acids. The reason for acknowledging this is the rising interest in the study of amino acids incorporating other oxyacid functions, particularly phosphorus analogues of the common aminoalkanoic acids. Short sections are included in this Chapter, on this topic, even though coverage must be

---

Three-dimensional features at chiral centres of structures depicted in this chapter follow the convention:–

(a) horizontally-ranged atoms, and their bonds, and atoms in rings, are understood to be in the plane of the paper;
(b) atoms and groups attached to these atoms in (a) are ABOVE the page if ranged LEFTWARDS and BELOW the page if ranged RIGHTWARDS:





(1)

selective in order that the literature of aminoalkanoic acids may receive thorough treatment. The unusually acidic 3-hydroxy-3-cyclobuten-1,2-dione grouping, established to be a bio-isostere of the carboxy group, has stimulated the synthesis of the corresponding amino acid analogues (1).[1]

2 Textbooks and Reviews

Several recent textbooks give either partial[2,3] or exclusive[4] coverage of amino acid topics. A symposium report[5] covers a wide range of recent studies on amino acids in higher plants.

Reviews have appeared covering derivatives of natural amino acids as radioprotectants,[6] and industrial aspects of the uses of amino acids.[7] The unusual amino acids hypusine [N^{ϵ}-(4-amino-2-hydroxybutyl)-L-lysine],[8] ovothiols (mercaptohistidines),[9] and the pyridinolines[10] have been reviewed from the point of view of their occurrence; members of the last-mentioned family, particularly pyridinoline itself and deoxypyridinoline, that derive from collagen breakdown, are present in urine at levels related to bone resorption activity, and these levels may be used as an osteoporosis index for individual patients (see also Ref. 849). The occurrence in proteins of the fluorescent crosslinking amino acid, pentosidine, has been reviewed;[11] its formation accompanies glycoxidation *in vivo*, and it accumulates at a greatly accelerated rate in uraemic patients; thus it is linked with the ageing process, and this suggests that its accumulation can be used as a diagnostic indicator. A review[12] covers the extensive literature on the non-natural amino acid threo-dihydroxyphenylserine, whose importance lies with the fact that it undergoes L-aromatic amino acid decarboxylase-catalyzed decarboxylation to give neurally-active norepinephrine.

Other recent reviews are more appropriately located in later Sections of this Chapter.

3 Naturally Occurring Amino Acids

The work described in this Section concentrates mainly on new amino acids, and on the more unusual of the known amino acids discovered in previously-unknown natural compounds.

3.1 Isolation of Amino Acids from Natural Sources – If reliable results are to emerge from such endeavours, then reliable methods of isolation of individual amino acids from complex mixtures are needed. This section has been introduced