



<http://researchspace.auckland.ac.nz>

ResearchSpace@Auckland

Copyright Statement

The digital copy of this thesis is protected by the Copyright Act 1994 (New Zealand).

This thesis may be consulted by you, provided you comply with the provisions of the Act and the following conditions of use:

- Any use you make of these documents or images must be for research or private study purposes only, and you may not make them available to any other person.
- Authors control the copyright of their thesis. You will recognise the author's right to be identified as the author of this thesis, and due acknowledgement will be made to the author where appropriate.
- You will obtain the author's permission before publishing any material from their thesis.

To request permissions please use the Feedback form on our webpage.

<http://researchspace.auckland.ac.nz/feedback>

General copyright and disclaimer

In addition to the above conditions, authors give their consent for the digital copy of their work to be used subject to the conditions specified on the Library Thesis Consent Form.

THE HYDROLYSIS OF AMIDES AND

UREAS IN ACID SOLUTIONS

A Thesis presented to the

University of Auckland

for the degree of

Doctor of Philosophy

by

Carolyn Janet Giffney

(nee Hyland)

Chemistry Department
University of Auckland

August, 1974

To Colin,
whose help and encouragement
have been invaluable.

Also to My Parents,
whose belief in a good education
made this possible.

ABSTRACT

Despite the vast amount of research reported on the acid-catalysed hydrolysis of amides, the mechanism of reaction has remained a source of controversy. The various literature results have been summarised in the introduction.

Two series of amides have been studied in this investigation, one a series of N-substituted, 4-chlorobenzamides, the other a series of substituted acetanilides. Their basicity (or acid-dissociation) constants have been evaluated in sulphuric acid, and the rates of hydrolysis measured over a wide range of acid concentrations. Within each series, variation of the substituent causes the rate constant to vary in a way which is typical of a bimolecular reaction involving rate-determining nucleophilic attack of water on the protonated intermediate. By drawing a comparison between the two series of amides, (i.e. the difference in basicities and rates of hydrolysis) it becomes apparent that the O-protonated amide, which is thermodynamically favoured, is not the kinetically active species. A new rate equation is proposed, the equation being based on a mechanism in which water attacks the carbonyl carbon in the rate-determining step. The equation confidently predicts the experimental rate-profiles for the acid-hydrolysis of simple amides. It has been applied, in two forms, to the experimental rate data; the first form allows for the involvement of three water molecules in the slow step of hydrolysis, and the second form allows for the involvement of only two water molecules. The rate equation, in these two forms, has also been applied to much of the hydrolysis data reported in the literature and again it has proved to be very successful.

In contrast to the amides, ureas have not been subjected to extensive research. In this investigation, the basicity constants of a series of

substituted phenylureas have been measured, (if not already available) and the hydrolysis reactions carried out over a wide range of sulphuric acid concentrations, as well as in water. The 4-methyl and 4-chloro-phenylureas have also been hydrolysed in a range of hydrochloric and perchloric acid solutions; the effects of added salt were studied and the solvent isotope effects on the rate were evaluated. All these results, together with information obtained from application of the Hammett equation to the rate data, were in agreement with a mechanism involving a pre-equilibrium protonation to form the minor, N-protonated conjugate acid. This is followed by a slow transfer of the proton attached to the alternate nitrogen atom to form the appropriately substituted phenylisocyanate, and rapid reaction of this intermediate to form products.

The substituent effects on the n.m.r. spectra of the substituted acetanilides and phenylureas have also been reported.

TABLE OF CONTENTS

PAGE

PART ONE

Introduction

1	Acidity Functions	1
1.1	The H_0 Acidity Function	1
1.2	Other Acidity Functions	6
1.3	Amide Acidity Function	8
2	Criteria of Reaction Mechanism	10
2.1	Zucker-Hammett Criterion of Mechanism	10
2.2	Bunnett w Criterion of Mechanism	14
2.3	Bunnett w^* Criterion of Mechanism	15
2.4	Hydration Treatment of Bunnett w and w^* Values	16
2.5	Yates' Treatment of the Bunnett Equation	19
2.6	Bunnett and Olsen Linear Free Energy Relationship, (l.f.e.r.)	20
2.7	Kresge's α Coefficient	24
3	Linear Free Energy Relationships	25
3.1	The Hammett Equation	25
3.1.1	σ_I and σ_R	28
3.1.2	σ^n or σ^o Scale	28
3.1.3	σ^+ and σ^- Scales	29
3.2	The Taft Equation	32
4	Methods of Determining Basicity Constants	35
4.1	Determination of pK_{BH^+} Using the Acidity Function H_x	35
4.2	Bunnett and Olsen's Linear Free Energy Relationship	43

TABLE OF CONTENTS CONTD.		PAGE
5	Position of Protonation	45
5.1	Amides	45
5.1.1	Infrared Spectra	46
5.1.2	N.M.R. Spectra	50
5.1.3	Ultraviolet Spectra	52
5.1.4	Basicities	54
5.1.5	Conclusion	59
5.2	Urea	59
6	The Mechanism of Acid-Catalysed Hydrolysis	63
6.1	Hydrolysis of Amides	63
6.1.2	A Change of Mechanism in Concentrated Acids	79
6.2	Hydrolysis of Ureas	82
PART TWO		
Interpretation and Discussion of Results		
7	Basicity Constants	87
7.1	Acetanilides	88
7.2	Benzamides and Phenylureas	95
7.3	Discussion	101
7.4	Literature Values of pK_{BH^+}	106
8	Hydrolysis of Amides in Acid Solutions	114
8.1	Hydrolysis of N-Substituted, 4-ChloroBenzamides	114
8.1.1	Use of the Taft Equation	123
8.2	Hydrolysis of Substituted Acetanilides	137
8.2.1	Hydrolysis in Concentrated Sulphuric Acid	137
8.2.2	Hydrolysis in Dilute and Moderately Concentrated Sulphuric Acid	144
8.3	A New Rate Equation	158

TABLE OF CONTENTS CONTD.	PAGE
9 Hydrolysis of Phenylureas	177
9.1 Hydrolysis in Concentrated Acid	177
9.2 Hydrolysis in Different Acids	181
9.3 Moodie's Urea Equation	183
9.4 The Rate Maxima and Effects of Added Salt	184
9.5 Evidence for a Unimolecular Mechanism	189
9.6 Aqueous Hydrolysis of Phenylureas; A Mechanism of Reaction	192
9.7 The Hammett Equation	197
9.8 Solvent Isotope Effects	207
9.9 Criteria of Mechanism	211
9.10 Conclusion	213
10 Substituent Effects on the N.M.R. Spectra of Substituted Acetanilides and Phenylureas	216

PART THREE

Experimental

11 Experimental	223
11.1 Materials	223
11.1.1 Acids	223
11.1.2 Lithium Chloride	223
11.1.3 4-Chlorobenzamides	223
11.1.4 Acetanilides	224
11.1.5 Ureas	224
11.2 Apparatus	226
11.3 Methods of Hydrolysis	227
11.3.1 Hydrolysis of Phenylureas in Acid Solutions	227
11.3.2 Hydrolysis of Phenylureas in Water	228
11.3.3 Hydrolysis of Acetanilides	230
11.3.4 Hydrolysis of Benzamides	230

TABLE OF CONTENTS CONTD.

PAGE

11.4 Sulphonation

233

11.5 Product Analysis

234

11.6 Hydrolysis Data

236

11.7 Measurement of Basicity Constants

236

11.8 Basicity Data

237

ACKNOWLEDGEMENTS

256