AMINES

Synthesis, Properties and Applications

The understanding of amine chemistry is of paramount importance to numerous chemical industries, as well as to academic research. This book provides an authoritative account of the properties and applications of amines with respect to the characteristics of bonded substituents and the nature of their chemical and physical environments. The synthesis of alkyl, aryl and heterocyclic amines and inorganic amines with a review of their typical reactions is comprehensively treated, whilst practical synthetic and analytical methods for laboratory preparation and detection are provided. The importance of amine chemistry from the nineteenth century to the modern day, with a brief history of the development of ammonia synthesis, is included. This book is an invaluable reference source for undergraduates, postgraduates and chemical researchers working in industry.

STEPHEN A. LAWRENCE is a professionally qualified chemist with over 20 years' experience in the pharmaceutical and fine-chemicals industries. He is currently Director of the chemical consultancy firm Mimas Ltd.

AMINES

Synthesis, Properties and Applications

STEPHEN A. LAWRENCE



> PUBLISHED BY THE PRESS SYNDICATE OF THE UNIVERSITY OF CAMBRIDGE The Pitt Building, Trumpington Street, Cambridge, United Kingdom

> > CAMBRIDGE UNIVERSITY PRESS The Edinburgh Building, Cambridge, CB2 2RU, UK 40 West 20th Street, New York, NY 10011–4211, USA 477 Williamstown Road, Port Melbourne, VIC 3207, Australia Ruiz de Alarcón 13, 28014 Madrid, Spain Dock House, The Waterfront, Cape Town 8001, South Africa

> > > http://www.cambridge.org

© S. A. Lawrence 2004

This book is in copyright. Subject to statutory exception and to the provisions of relevant collective licensing agreements, no reproduction of any part may take place without the written permission of Cambridge University Press.

First published 2004

Printed in the United Kingdom at the University Press, Cambridge

Typeface Times 11/14 pt. System $IAT_EX 2_{\mathcal{E}}$ [TB]

A catalogue record for this book is available from the British Library

Library of Congress Cataloguing in Publication data Lawrence, Stephen A., 1960– Amines: synthesis, properties, and applications / Stephen A. Lawrence. p. cm. Includes bibliographical references and index. ISBN 0 521 78284 8 1. Amines. I. Title. QD305.A8.L38 2004 547'.042 – dc22 2003065415

ISBN 0 521 78284 8 hardback

The publisher has used its best endeavours to ensure that the URLs for external websites referred to in this book are correct and active at the time of going to press. However, the publisher has no responsibility for the websites and can make no guarantee that a site will remain live or that the content is or will remain appropriate.

Contents

	Preface		page ix
1	An i	1	
	1.1	Introducton	1
	1.2	Nitrogen	2
	1.3	The history of ammonia and its importance to mankind	5
	1.4	The chemistry of ammonia	18
		References	23
2 Aliphatic, fatty		hatic, fatty and cyclic amines	25
	2.1	The physical properties and geometries of amines	25
	2.2	Aliphatic amines	33
	2.3	Cyclic amines	55
	2.4	Diamines and polyamines	62
		References	68
3	Ary	amines	71
	3.1	An introduction to aryl amines	71
	3.2	Synthesis of (mono) aryl amines	74
	3.3	Reactions of aryl amines	85
	3.4	Aminophenols	100
	3.5	Aryl diamines	104
	3.6	Diaryl amines	109
	3.7	Triaryl amines	116
		References	117
4	Heterocyclic amines		119
	4.1	An introduction to heterocyclic amines	119
	4.2	Azirine	122
	4.3	Aziridine (ethyleneimine)	123
	4.4	Diazirene	129
	4.5	Azetidine	130

vi		Contents	
	4.6	Pvrrole	133
	4.7	Pyrazole and imidazole	139
	4.8	Fused five-membered nitrogen heterocycles	144
	4.9	Pyridine	150
	4.10	Pyrimidine, pyrazine and pyridazine	157
	4.11	Quinoline, isoquinoline and quinolizine	162
	4.12	Nitrogen-containing heterocycles with large rings	164
		References	167
5	Inorg	anic amines, hydrazine, hydroxylamine and amine ligands	169
	5.1	Introduction to the inorganic chemistry of the amines	169
	5.2	Chloramine	171
	5.3	Nitrogen trichloride	174
	5.4	Hydrazine	176
	5.5	Hydroxylamine	185
	5.6	Nitrogen-containing donor ligands	188
	5.7	Nitrogen-containing macrocyclic ligands	194
	5.8	Sulphur-nitrogen compounds	202
		References	204
6	Small-scale syntheses and analytical methods for amines		205
	6.1	Introduction	205
	6.2	Synthetic methods for alkyl and aryl amines	205
	6.3	Amino-acid protection	215
	6.4	The synthesis of heterocyclic amines	216
	6.5	Analytical methods for amines	220
References		References	234
7	Amine protection, amine oxides and amino acids		235
	7.1	Amine protection	235
	7.2	Amine oxides	245
	7.3	Amines and amino acids	252
		References	262
8	Selected commercial applications of amines		265
	8.1	Amines as corrosion inhibitors	265
	8.2	Amines in pharmaceuticals	269
	8.3	Amines as anti-cancer agents and DNA alkylators	274
	8.4	Amines in the cosmetics and toiletries industries	278
	8.5	The applications of amines in colour reprography	284
	8.6	The applications of hydrazines	288
	8.7	The applications of amines in agrochemicals	290
	8.8	Azine and azo dyes	300
	8.9	Indigo dyes	305

References

306

	Contents	vii
Appendix 1	Molecular structures and isosurface electronic charges of	
	selected amines	309
Appendix 2	Physical properties of selected amines	315
Appendix 3	Named reactions involving amines	317
Index		361

Preface

Much of the chemistry of the amines was discovered in the nineteenth century by pioneering chemists such as Hofmann, Leuckart, Gabriel and Knoll. The introduction of the Cyanamide Process and Electric Arc Process at the begining of the twentieth century made amines commercially available for the first time at low cost and no longer an academic curiosity or restricted for use only in high-value products. However, the implementation of the Haber–Bosch Process at Leuna in Eastern Germany in 1917 marks the beginning of the modern age of amine chemistry.

Having worked with amines for many years, both on a small scale in the laboratory producing gram quantities of novel amines and also on a larger scale on full-sized manufacturing plants producing several hundred tonnes per year of aminebased pharmaceutical intermediates, it has always been a problem for me that I could never find a single, up-to-date, resource book specifically dedicated to the synthesis, properties and reactions of amines. The most recent examples that I was able to find that cover the whole area of amine chemistry were David Ginsburg's Concerning Amines, which dates from 1968, and the third edition of Neville Sidgwick's The Organic Chemistry of Nitrogen (first published in 1910 but revised in 1966 by I. T. Miller and H. D. Springham), although most general organic chemistry books contain a chapter or two on amines. Eventually I decided that the best way to rectify this situation would be for me to write such a book, and so this was my reason for approaching Cambridge University Press, who agreed to my proposal. It is my hope that the readers of this book will find that it contains the answers to many of their unanswered questions about amines and also provides suitable references for further study.

This book contains eight chapters and three appendices. Chapter 1 reviews the history and properties of ammonia and nitrogen. Chapters 2 and 3 are concerned with the properties, syntheses and reactions of alkyl and aryl amines respectively. Heterocyclic amines are found in Chapter 4; inorganic amines including macrocyclic ligands are the subject of Chapter 5, and Chapter 6 contains some laboratory

х

Preface

synthetic routes to amines and also details of analytical procedures. Amine oxides, protected amines and amino acids are reviewed in Chapter 7, and Chapter 8 covers the applications and commercial uses of amines. At the end of the text there are three appendices, which shown the structures and isosurface electronic charges of some amines (Appendix 1), a table of the physical properties of selected amines (Appendix 2) and the named reactions and named syntheses of amines (Appendix 3).

The reader's attention is drawn to the safety advice given in, for example, Section 6.1. Some of the chemicals mentioned in this book are dangerous, and although the author can vouch that the experiments described do work, if properly conducted, neither he nor the publisher will be liable for accidents that may take place in the course of experimentation!

I would like to thank Frau Urte Thiele and Dr Klaus Baehr of Chemtec Leuna for the photographs of the plant at Leuna, and also Inegard Rafn and Kai Evensen of Norsk Hydro for the photographs of the plant and laboratories at Notodden in Norway.

I would like also to thank Tim Fishlock, Simon Capelin, Michelle Carey, Robert Whitelock, Jayne Aldhouse and Emily Yossarian at Cambridge University Press for their encouragement and patience while I produced the typescript.

Finally I would like to thank my wife Beverley for her support during the writing process whilst this book came to fruition.