The chemistry of
Anilines
Part 1

Edited by
ZVI RAPPOPORT
The Hebrew University, Jerusalem

2007

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The chemistry of

Anilines

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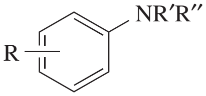

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BICENTENNIAL 1807 WILEY 2007

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John Wiley & Sons Ltd, The Atrium, Southern Gate, Chichester,
West Sussex PO19 8SQ, England

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Jossey-Bass, 989 Market Street, San Francisco, CA 94103-1741, USA

Wiley-VCH Verlag GmbH, Boschstr. 12, D-69469 Weinheim, Germany

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John Wiley & Sons Canada Ltd, 6045 Freemont Blvd, Mississauga, ONT, L5R 4J3, Canada

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in print may not be available in electronic books.

British Library Cataloguing in Publication Data

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

ISBN 978-0-470-87171-3

Typeset in 9/10pt Times by Laserwords Private Limited, Chennai, India
Printed and bound in Great Britain by Biddles Ltd, King's Lynn
This book is printed on acid-free paper responsibly manufactured from sustainable forestry
in which at least two trees are planted for each one used for paper production.

Dedicated to

Itzik and **Tzipi**

and to

Silvio

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Foreword

This is the second volume in ‘The Chemistry of Functional Groups’ series that deals with an aromatic functional group, following on from *The Chemistry of Phenols* published in 1993.

In the modern world there is no chemical functional group that has a longer and more varied history than the aromatic amino group. The organized scientific study of aromatic amines advanced greatly from the mid-1840s when August Wilhelm Hofmann began to develop his ammonia type theory. In this the simplest member, aniline, and its derivatives were expressed, by analogy, as compounds in which hydrogen atoms of ammonia were successively replaced by other atoms or groups of atoms. The study of these compounds, now conveniently labeled as anilines, received a tremendous stimulus after 1856, when the teenaged chemical inventor William Henry Perkin discovered the first aniline dye, later known as mauve. During the second half of the 19th century the anilines revolutionized the study of chemistry, led to the inauguration of industrial research laboratories and helped forge academic-industrial collaborations. As agents of modernity, anilines and their derivatives forced changes in patent law, fostered technology transfer and stimulated the emergence of the modern chemical industry. They contributed to the discovery of pharmaceutical products and new agrochemicals. Hence, there is reason enough for a historical review of the role of the anilines in the development of what was undoubtedly the first high-tech science-based industry, especially since 2006 marks the 150th anniversary of the beginning of the chemical industry based on anilines, following Perkin’s discovery.

The two parts of the present volume consist of 17 chapters written by experts from 10 countries. They start with historical background, followed by chapters on the theory, structure, thermochemistry, photophysics and photochemistry and electrochemistry of anilines, on their mass spectrometry, NMR spectra and analysis and on their modern syntheses by transition metal catalysed processes. Other chapters deal with their rearrangements, their reactivity as nucleophiles, their use as solvatochromic probes, their hydrogen bonded complexes, and their versatile uses in the chemical industry, and the relevant topic of toxicity and environmental aspects. A chapter on a special group of anilines—the proton sponges—ends the book.

A few promised chapters on the acidity of anilines, on polyanilines and on radical cations of triarylamine and phenylenediamine were not delivered. We hope to include these chapters in a future supplementary volume.

The literature coverage of most chapters is up to 2005.

I would be grateful to readers who draw my attention to mistakes or to missing topics in the present volume.

Jerusalem
October, 2006

Zvi Rappoport

The Chemistry of Functional Groups
Preface to the series

The series 'The Chemistry of Functional Groups' was originally planned to cover in each volume all aspects of the chemistry of one of the important functional groups in organic chemistry. The emphasis is laid on the preparation, properties and reactions of the functional group treated and on the effects which it exerts both in the immediate vicinity of the group in question and in the whole molecule.

A voluntary restriction on the treatment of the various functional groups in these volumes is that material included in easily and generally available secondary or tertiary sources, such as Chemical Reviews, Quarterly Reviews, Organic Reactions, various 'Advances' and 'Progress' series and in textbooks (i.e. in books which are usually found in the chemical libraries of most universities and research institutes), should not, as a rule, be repeated in detail, unless it is necessary for the balanced treatment of the topic. Therefore each of the authors is asked not to give an encyclopaedic coverage of his subject, but to concentrate on the most important recent developments and mainly on material that has not been adequately covered by reviews or other secondary sources by the time of writing of the chapter, and to address himself to a reader who is assumed to be at a fairly advanced postgraduate level.

It is realized that no plan can be devised for a volume that would give a complete coverage of the field with no overlap between chapters, while at the same time preserving the readability of the text. The Editors set themselves the goal of attaining reasonable coverage with moderate overlap, with a minimum of cross-references between the chapters. In this manner, sufficient freedom is given to the authors to produce readable quasi-monographic chapters.

The general plan of each volume includes the following main sections:

(a) An introductory chapter deals with the general and theoretical aspects of the group.

(b) Chapters discuss the characterization and characteristics of the functional groups, i.e. qualitative and quantitative methods of determination including chemical and physical methods, MS, UV, IR, NMR, ESR and PES—as well as activating and directive effects exerted by the group, and its basicity, acidity and complex-forming ability.

(c) One or more chapters deal with the formation of the functional group in question, either from other groups already present in the molecule or by introducing the new group directly or indirectly. This is usually followed by a description of the synthetic uses of the group, including its reactions, transformations and rearrangements.

(d) Additional chapters deal with special topics such as electrochemistry, photochemistry, radiation chemistry, thermochemistry, syntheses and uses of isotopically labeled compounds, as well as with biochemistry, pharmacology and toxicology. Whenever applicable, unique chapters relevant only to single functional groups are also included (e.g. 'Polyethers', 'Tetraaminoethylenes' or 'Siloxanes').

This plan entails that the breadth, depth and thought-provoking nature of each chapter will differ with the views and inclinations of the authors and the presentation will necessarily be somewhat uneven. Moreover, a serious problem is caused by authors who deliver their manuscript late or not at all. In order to overcome this problem at least to some extent, some volumes may be published without giving consideration to the originally planned logical order of the chapters.

Since the beginning of the Series in 1964, two main developments have occurred. The first of these is the publication of supplementary volumes which contain material relating to several kindred functional groups (Supplements A, B, C, D, E, F and S). The second ramification is the publication of a series of 'Updates', which contain in each volume selected and related chapters, reprinted in the original form in which they were published, together with an extensive updating of the subjects, if possible, by the authors of the original chapters. Unfortunately, the publication of the 'Updates' has been discontinued for economic reasons.

Advice or criticism regarding the plan and execution of this series will be welcomed by the Editors.

The publication of this series would never have been started, let alone continued, without the support of many persons in Israel and overseas, including colleagues, friends and family. The efficient and patient co-operation of staff-members of the Publisher also rendered us invaluable aid. Our sincere thanks are due to all of them.

The Hebrew University SAUL PATAI
Jerusalem, Israel ZVI RAPPOPORT

Sadly, Saul Patai who founded 'The Chemistry of Functional Groups' series died in 1998, just after we started to work on the 100th volume of the series. As a long-term collaborator and co-editor of many volumes of the series, I undertook the editorship and I plan to continue editing the series along the same lines that served for the preceeding volumes. I hope that the continuing series will be a living memorial to its founder.

The Hebrew University ZVI RAPPOPORT
Jerusalem, Israel
May 2000

Contents

List of abbreviations used

Ac	acetyl (MeCO)
acac	acetylacetone
Ad	adamantyl
AIBN	azoisobutyronitrile
Alk	alkyl
All	allyl
An	anisyl
Ar	aryl
Bn	benzyl
Bu	butyl (C_4H_9)
Bz	benzoyl (C_6H_5CO)
CD	circular dichroism
CI	chemical ionization
CIDNP	chemically induced dynamic nuclear polarization
CNDO	complete neglect of differential overlap
Cp	η^5-cyclopentadienyl
Cp*	η^5-pentamethylcyclopentadienyl
DABCO	1,4-diazabicyclo[2.2.2]octane
DBN	1,5-diazabicyclo[4.3.0]non-5-ene
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DIBAH	diisobutylaluminium hydride
DME	1,2-dimethoxyethane
DMF	*N*,*N*-dimethylformamide
DMSO	dimethyl sulfoxide
ee	enantiomeric excess
EI	electron impact
ESCA	electron spectroscopy for chemical analysis
ESR	electron spin resonance
Et	ethyl
eV	electron volt
Fc	ferrocenyl
FD	field desorption

FI	field ionization
FT	Fourier transform
Fu	furyl(OC_4H_3)
GLC	gas liquid chromatography
Hex	hexyl(C_6H_{13})
c-Hex	cyclohexyl(c-C_6H_{11})
HMPA	hexamethylphosphortriamide
HOMO	highest occupied molecular orbital
HPLC	high performance liquid chromatography
i-	iso
ICR	ion cyclotron resonance
Ip	ionization potential
IR	infrared
LAH	lithium aluminium hydride
LCAO	linear combination of atomic orbitals
LDA	lithium diisopropylamide
LUMO	lowest unoccupied molecular orbital
M	metal
M	parent molecule
MCPBA	*m*-chloroperbenzoic acid
Me	methyl
MNDO	modified neglect of diatomic overlap
MS	mass spectrum
n	normal
Naph	naphthyl
NBS	*N*-bromosuccinimide
NCS	*N*-chlorosuccinimide
NMR	nuclear magnetic resonance
Pen	pentyl(C_5H_{11})
Ph	phenyl
Pip	piperidyl($C_5H_{10}N$)
ppm	parts per million
Pr	propyl (C_3H_7)
PTC	phase transfer catalysis or phase transfer conditions
Py, Pyr	pyridyl (C_5H_4N)
R	any radical
RT	room temperature
s-	secondary
SET	single electron transfer
SOMO	singly occupied molecular orbital

t-	tertiary
TCNE	tetracyanoethylene
TFA	trifluoroacetic acid
THF	tetrahydrofuran
Thi	thienyl(SC_4H_3)
TLC	thin layer chromatography
TMEDA	tetramethylethylene diamine
TMS	trimethylsilyl or tetramethylsilane
Tol	tolyl(MeC_6H_4)
Tos or Ts	tosyl(*p*-toluenesulphonyl)
Trityl	triphenylmethyl(Ph_3C)
Xyl	xylyl($Me_2C_6H_3$)

In addition, entries in the 'List of Radical Names' in *IUPAC Nomenclature of Organic Chemistry*, 1979 Edition, Pergamon Press, Oxford, 1979, p. 305–322, will also be used in their unabbreviated forms, both in the text and in formulae instead of explicitly drawn structures.

CHAPTER 1

Anilines: Historical background

ANTHONY S. TRAVIS

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The chemistry of anilines
Edited by Z. Rappoport

I. INTRODUCTION

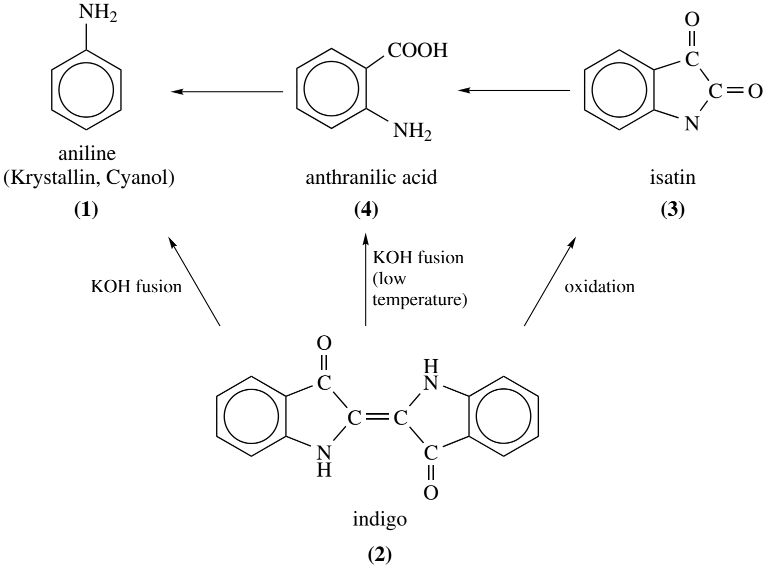
One-hundred-and-fifty years ago, in March 1856, a teenaged chemical inventor in London, England, discovered in his makeshift home laboratory a process that converted aniline, made in two steps from coal-tar benzene, into a purple dyestuff, or colorant. The young man was William Henry Perkin, assistant to the German chemist August Wilhelm Hofmann, then head of the Royal College of Chemistry. From Perkin's single serendipitous discovery the anilines went on to become a generic class of organic chemicals that would make tremendous contributions to material well-being. Quite apart from providing routes to synthetic dyestuffs—that were also called 'anilines'—pharmaceuticals, products for the processing of rubber, and new polymers, the anilines revolutionized the study of chemistry, led to the inauguration of industrial research laboratories, and helped forge academic–industrial collaborations. It is difficult to convey now the day-to-day excitement that infused the academic and industrial laboratories that pursued the anilines during the half century following Perkin's discovery. The endeavor made reputations and attracted the greatest stars of organic chemistry, including August Wilhem Hofmann, Adolf Baeyer and Emil Fischer. No less profound were the economic and political consequences. The anilines and their derived colorants, as agents of modernity, forced changes in patent law, fostered technology transfer, stimulated the emergence of the modern chemical industry and decimated cultivation of dye-yielding plants. Aniline products contributed to the growth of Germany as a major economic power, to the extent that successors to the early coal-tar dye companies enabled Germany to wage world war twice in the 20th century. After the aniline dye industry was adopted by the US, from 1915, its mode of applied research led to the discovery of synthetic polymers and new agrochemicals. Apart from the intrinsic chemical interest in the early story of aniline and its products, these few facts make a compelling reason for the inclusion of a historical introduction to the anilines.

In this chapter, with its emphasis on historical events and chemists engaged in both academic and industrial investigations, first names of participants are given wherever possible. Also, many trivial and common names of products are retained, in order to aid understanding of the historical literature and earlier textbooks. Several are still in common usage, particularly for the aminonaphthalenesulfonic acids that are known by special names rather than by their structural designations. In accord with common usage, lower case letters are used for what have become both generic and trademark names, such as Bismarck brown, chrysoidine, mauve, mauveine and rosaniline. However, capitals are used for arcane names, to avoid confusion, for example, between Benzidin and benzidine, as well as for more recent trade names, mainly for products introduced from around 1940.

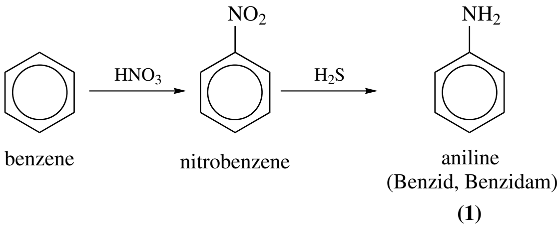
This chapter also revisits some of the major chemical firms of former times that were completely transformed at the end of the 20th century. Reflecting the former importance of, and prestige associated with, aromatic amines, a number included the word Aniline in their corporate titles, notably, in Germany, Badische Anilin- & Soda Fabrik (BASF) and Aktiengesellschaft für Anilinfabrikation (AGFA), in the US, General Aniline and Film (GAF) and National Aniline & Chemical Co. (NACCO), and in the UK, CIBA's Clayton Aniline Company Limited. Extensive and ongoing historical studies into the aniline dye industry are today stimulated by the fact that it was the first high-technology industry, and became the exemplar of all science-based industries. Moreover, and despite the decline in its use for colorants, the manufacture of aniline is still carried out on a vast scale for the production of polyurethanes.

II. IDENTIFYING ANILINE

The feebly basic oil that we now call aniline **(1)** was perhaps first handled, though not identified, during the 18th century by the French chemists and dye experts Jean Hellot (in 1740) and Lepileur d'Apligny. The raw material for their experiments was the leaf of the indigo plant that afforded a blue dye. What is certain is that in 1826, by destructive distillation of indigo **(2)**, the German chemist Otto Unverdorben isolated a substance that he called Krystallin. During the next 15 years the same base would be independently obtained by several investigators. Friedrich Ferdinand Runge in 1834 extracted what he called Cyanol, or Kyanol, from coal tar. The indigo connection remained important. In 1841, Jean Baptiste André Dumas established a formula for the indigo colorant (C_8H_5NO), and Auguste Laurent and Otto Linné Erdmann independently isolated the oxidation products isatin **(3)** and isatic acid[1] (Scheme 1).



Degradation products of indigo (modern formulae)



Zinin's method for preparing aniline

SCHEME 1

Laurent and Erdmann oxidized isatin, from which they obtained anthranilic acid **(4)**. Carl Julius Fritzsche (also known as Iulii Federovich Fritsshe) in 1840 subjected anthranilic acid to alkaline distillation and obtained 'a powerful base, devoid of oxygen', that he called Anilin, from anil, the Portuguese word for indigo, which in turn had been derived from Arabic and Sanskrit. In 1842, the Russian chemist Nikolai N. Zinin reduced, with hydrogen sulfide, Nitrobenzid (nitrobenzene) to what was called Benzid (also Benzidam, and later Benzidin) (Scheme 1). Fritsche drew attention to the identities of Anilin and Benzid. From nitronaphthalene, Zinin obtained Naphthalid (an aminonaphthalene). During 1844–1846 he reported reduction of dinitrobenzene to diaminobenzene with ammonium sulfide, reduction of dinitronaphthalene and the synthesis of the diaminobiphenyl (benzidine) from nitrobenzene. Zinin also reported azoxybenzene[2].

Zinin was a former student at Giessen of Justus Liebig, who investigated the chemical constitution of indigo, as well as other natural products. Liebig also undertook studies into novel raw materials from which useful products might be derived. Of particular interest around 1840 was the vast amount of coal-tar waste available from coal-gas works and distilleries. Ernst Sell, a former student of Liebig, owned a coal distillery and sent samples of the tar to Giessen for further study. It was Liebig's practice to assign research projects to his students, including, around 1837, August Wilhelm Hofmann (Figure 1). Hofmann extracted several nitrogen-containing oils from coal tar by trituration with acid. He showed that of these bases the one present in greatest abundance was identical with the product earlier obtained from isatin and Zinin's Benzidin. Hofmann preferred the name Krystallin, but the chemical community chose aniline (though aminobenzene, phenylamine, as well as the more modern benzeneamine have been used). Hofmann's results were published in 1843 and became the foundation for his life's work and international reputation[3].

Among many other experiments that Hofmann undertook with aniline was treatment of the indigo-derived base with chlorine. He identified the products. They were used to demonstrate that the two main rival theories of chemical combination were entirely compatible. These were the electrochemical theory of attraction of Jöns Jacob Berzelius and the substitution theory of Jean Baptiste André Dumas. This work was published in 1845 when Hofmann was at Bonn[4]. Hofmann then moved on to synthesis of aniline in

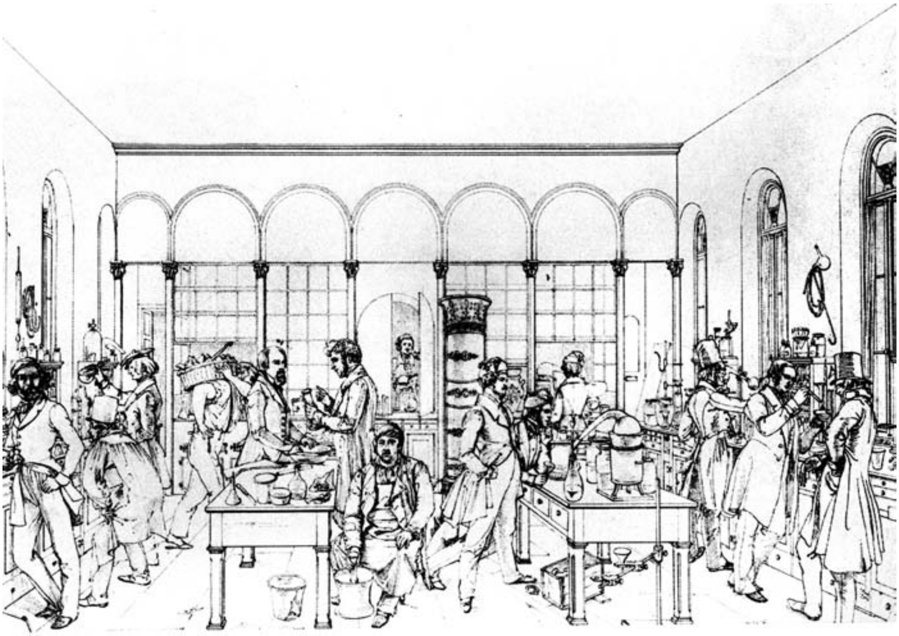


FIGURE 1. The Giessen laboratory of Justus Liebig, *ca* 1840. August Wilhelm Hofmann at extreme right (with top hat). Edelstein Collection

two steps from coal-tar benzene, first nitration, second reduction. He also collaborated with Liebig and others in an attempt to produce a quinine substitute.

In 1845 also, at Liebig's instigation, Hofmann moved to London to head the new Royal College of Chemistry. There he continued his studies into aniline and its reactions. Through this work he made major contributions to constitutional formulae. At that time, thirteen years before quadrivalent carbon was drawn, there were no modern structural formulae, only so-called type formulae. These indicated chemical constitutions and were used as a system of classification. Type formulae were based on simple compounds, such as water and methane. Significantly, Adolphe Wurtz had indicated that methyl and ethyl amines might be considered derivatives of ammonia. Hofmann extended this to organic bases in general, by comparing aniline with ammonia, and also with a compound discovered in 1834 by Liebig and called melamine. Hofmann demonstrated that the three hydrogens of ammonia, and those of the ammonium radical, could be replaced to give primary, secondary and tertiary amines, and quarternary ammonium derivatives. From these results he developed what in 1850 he would call the ammonia type theory. With this, it was now possible to classify organic bases using a formula that, as with the other type formulas, separated one atom, in this case nitrogen, with a bracket from other atoms and groups of atoms. Thus aniline was an ammonia derivative in which one hydrogen was replaced by what we now call an aryl group. This is in keeping with the modern definition of aromatic amines, in which the remaining two hydrogens are replaceable by aryl or alkyl groups[5].

III. THE ANILINE DYES

Despite the availability of methods for extracting aniline from coal tar, this source hardly provided an abundant supply of the aromatic amine. Some chemists worked on the development of the two-step synthesis from coal-tar benzene. They included Hofmann's assistant Charles Blachford Mansfield, who pioneered the separation by distillation of coal-tar hydrocarbons, undertook nitration of benzene, and reduction of the nitrobenzene, probably by the method of Zinin. Mansfield's experiments came to an abrupt end early in 1855 when, while preparing samples for the Paris International Exhibition, a still in his laboratory caught fire. He was badly burned and died in hospital a few days later.

Hofmann introduced to the college a new method for reducing nitrobenzene, based on the use of iron and glacial acetic acid as the source of reducing hydrogen, as first described by André Béchamp in 1854. It was put to good use by several of Hofmann's students, including William Henry Perkin, who had entered the college in 1853, at the age of fifteen (Figure 2). Perkin showed a remarkable industriousness. In 1856, he created the first synthetic dye made from aniline. It is worth considering how he got there.

In the mid-1850s, there was great interest in quinine, much needed to control malaria among the British colonists. Hofmann reasoned that it might be synthesized from coal-tar naphthalene. Perkin decided, instead, to start with allyltoluidine, through oxidative condensation. The reaction, undertaken at home in his primitive laboratory during the 1856 Easter vacation, failed. However, he wisely decided to repeat the experiment using the simplest aromatic amine, aniline, that was known to be sensitive to the action of oxidants. The result of treating it with dichromate was a mixture from which an alcoholic extract colored a piece of silk a brilliant, and persistent, purple. It spread like an uncontrollable stain, coloring everything that it touched. This triggered an immediate response. Perkin recognized the potential as a dyestuff, particularly since the color was not fugitive, as was the case for other important purple dyes, namely the semi-synthetic murexide (Roman purple) and lichen-derived products. The teenaged inventor filed a patent for his process, resigned from the college and, with the backing of his brother and father, set up a

FIGURE 2. August Wilhelm Hofmann and students at the Royal College of Chemistry, London, *ca* 1855. William Henry Perkin is in the back row, fifth from right. Edelstein Collection

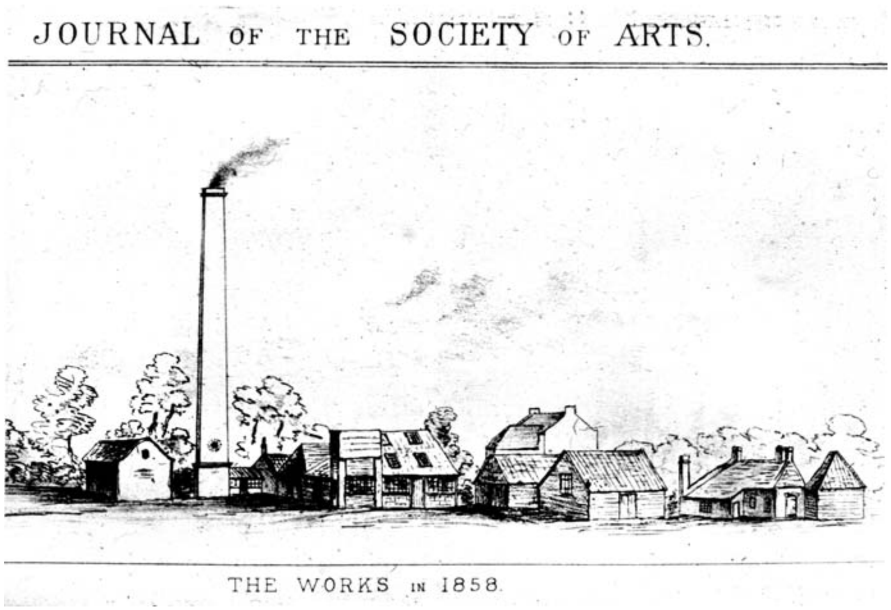
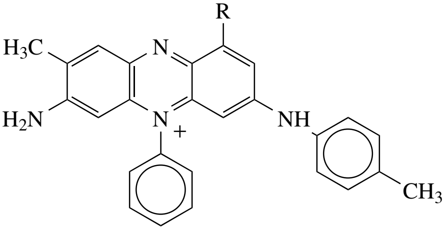


FIGURE 3. The works of Perkin & Sons, Greenford Green, northwest London, 1858. From a sketch by William Henry Perkin. Edelstein Collection

small factory at Greenford Green, northwest of London, to manufacture his novel product (Figure 3). There from 1858, coal tar was distilled to provide a mixture of aromatic hydrocarbons, mainly, if not exclusively, it was believed, benzene. By successive nitration of benzene to nitrobenzene, with mixed sulfuric and nitric acids, reduction of the nitro compound to aniline, with iron and acid, and oxidation, the colorant was obtained. The working conditions in the small buildings were far from salubrious. Originally the nitration and reduction apparatus was made of glass, but soon hand-cranked horizontal iron reactors were introduced. The aniline purple was a success with silk dyers, and once a number of fixing agents, or mordants, for cotton, were developed, the highly fashionable synthetic colorant, originally marketed as Tyrian purple, was quickly adopted by calico printers. By 1859, the aniline-derived colorant was the main color of fashion among the ladies of Britain and France. The English gave the aniline purple a new name, mauve, from the French word for the mallow flower. Perkin prepared crystalline salts of the principal component of his colorant, which in 1863 he called mauveine[6]. The correct structure, **5**, was established only in 1994[7], showing how mauveine arose from the presence of toluidines in the impure aniline.

Commercial success made a fortune for Perkin (Figure 4). It also stimulated further investigations into reactions of aniline that might yield other colorants. At the end of 1859, an aniline red **(6)**, made by treating what was believed to be aniline alone with stannic chloride, was discovered in Lyon by François Emmanuel Verguin. A more successful process was discovered by two of Hofmann's former students in London, Henry Medlock and Edward Chambers Nicholson (Figure 5), who independently treated aniline with arsenic acid. The red colorant was known as fuchsine in France and magenta in England. Nicholson, a partner in the London chemical manufacturing firm of Simpson, Maule



mauveine
(Tyrian purple, aniline purple)
R = H
R = CH_3 (minor component)
(5)

FIGURE 4. William Henry Perkin (1838–1907), in 1860. Edelstein Collection