The chemistry of
phenols
Part 2

Edited by
ZVI RAPPOPORT
The Hebrew University, Jerusalem

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phenols

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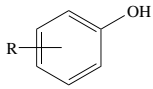

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Dedicated to

Gadi, Adina,

Sharon and **Michael**

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Foreword

This is the first volume in The 'Chemistry of Functional Groups' series which deals with an aromatic functional group. The combination of the hydroxyl group and the aromatic ring modifies the properties of both groups and creates a functional group which differs significantly in many of its properties and reactions from its two constituents. Phenols are important industrially, in agriculture, in medicine, in chemical synthesis, in polymer chemistry and in the study of physical organic aspects, e.g. hydrogen bonding. These and other topics are treated in the book.

The two parts of the present volume contain 20 chapters written by experts from 11 countries. They include an extensive treatment of the theoretical aspects, chapters on various spectroscopies of phenols such as NMR, IR and UV, on their mass spectra, on the structural chemistry and thermochemistry, on the photochemical and radiation chemistry of phenols and on their synthesis and synthetic uses and on reactions involving the aromatic ring such as electrophilic substitution or rearrangements. There are also chapters dealing with the properties of the hydroxyl group, such as hydrogen bonding or photoacidity, and with the derived phenoxy radicals which are related to the biologically important antioxidant behavior of phenols. There is a chapter dealing with polymers of phenol and a specific chapter on calixarenes — a unique family of monocyclic compounds including several phenol rings.

Three originally promised chapters on organometallic derivatives, on acidity and on the biochemistry of phenols were not delivered. Although the chapters on toxicity and on analytical chemistry deal with biochemistry related topics and the chapter on photoacidity is related to the ground state acidity of phenols, we hope that the missing chapters will appear in a future volume.

The literature coverage in the various chapters is mostly up to 2002.

I will be grateful to readers who draw my attention to any mistakes in the present volume.

Jerusalem
February 2003

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 labelled 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. A complete list of all above mentioned volumes published to date will be found on the page opposite the inner title page of this book. 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
June 2002

Contents

1	General and theoretical aspects of phenols **Minh Tho Nguyen, Eugene S. Kryachko and Luc G. Vanquickenborne**	1
2	The structural chemistry of phenols **Menahem Kaftory**	199
3	Thermochemistry of phenols and related arenols **Suzanne W. Slayden and Joel F. Liebman**	223
4	Mass spectrometry and gas-phase ion chemistry of phenols **Dietmar Kuck**	259
5	NMR and IR spectroscopy of phenols **Poul Erik Hansen and Jens Spanget-Larsen**	333
6	Synthesis of phenols **Concepción González and Luis Castedo**	395
7	UV-visible spectra and photoacidity of phenols, naphthols and pyrenols **Ehud Pines**	491
8	Hydrogen-bonded complexes of phenols **C. Laurence, M. Berthelot and J. Graton**	529
9	Electrophilic reactions of phenols **V. Prakash Reddy and G. K. Surya Prakash**	605
10	Synthetic uses of phenols **Masahiko Yamaguchi**	661
11	Tautomeric equilibria and rearrangements involving phenols **Sergei M. Lukyanov and Alla V. Koblik**	713
12	Phenols as antioxidants **L. Ross C. Barclay and Melinda R. Vinqvist**	839
13	Analytical aspects of phenolic compounds **Jacob Zabicky**	909
14	Photochemistry of phenols	1015

William M. Horspool

15 Radiation chemistry of phenols 1097
P. Neta

16 Transient phenoxyl radicals: Formation and properties in aqueous solutions 1107
S. Steenken and P. Neta

17 Oxidation of phenols 1153
Shosuke Yamamura

18 Environmental effects of substituted phenols 1347
Victor Glezer

19 Calixarenes 1369
Volker Böhmer

20 Polymers based on phenols 1455
D. H. Solomon, G. G. Qiao and M. J. Caulfield

Author index 1507

Subject index 1629

List of abbreviations used

Ac	acetyl (MeCO)
acac	acetylacetone
Ad	adamantyl
AIBN	azoisobutyronitrile
Alk	alkyl
All	allyl
An	anisyl
Ar	aryl
Bn	benzyl
Bz	benzoyl (C_6H_5CO)
Bu	butyl (C_4H_9)
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 sulphoxide
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

General and theoretical aspects of phenols

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I. INTRODUCTION 3
A. Summary of Key Physico-chemical Properties of Phenol 4
B. The History of the Discovery of Phenol 6
C. Usage and Production 7
II. MOLECULAR STRUCTURE AND BONDING OF PHENOL 20
A. The Equilibrium Structure of Phenol in the Ground Electronic State . . 20
B. Molecular Bonding Patterns in the Phenol S_0 21
C. Atom-in-Molecule Analysis 31
D. Vibrational Modes 34
E. Three Interesting Structures Related to Phenol 38
III. STRUCTURES AND PROPERTIES OF SUBSTITUTED PHENOLS . . . 47
A. Intramolecular Hydrogen Bond in *ortho*-Halogenophenols 47
B. *meta*- and *para*-Halogenophenols 57

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The Chemistry of Phenols. Edited by Z. Rappoport
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C. The Bonding Trends in Monohalogenated Phenols in Terms of the Electronic Localization Function (*ELF*) 68
1. Introduction to the *ELF* 68
2. Topology of the *ELF* 68
3. Vector gradient field $\nabla_r \eta(r)$ 70
4. The bonding in benzene, phenol and phenyl halides 71
5. Monohalogenated phenols: the bonding in terms of *ELF* 73
a. The *ortho*-substituted phenols 73
b. The *meta*-substituted phenols 76
c. The *para*-substituted phenols 76
D. Some Representatives of Substituted Phenols 78
IV. ENERGETICS OF SOME FUNDAMENTAL PROCESSES 83
A. Protonation 83
1. Protonation of phenol 83
2. Proton affinities of halophenols 86
3. Proton affinities of anisole and fluoroanisoles 88
4. Two views on the protonation regioselectivity 89
5. Interaction of phenol with Li^+, Na^+ and K^+ 92
B. Deprotonation 92
1. Phenolate anion 93
2. Gas-phase acidities 97
3. Acidity in solution 101
4. Correlation between intrinsic acidities and molecular properties . . . 101
5. Alkali metal phenolates 103
C. Electronic Excitation 105
D. Ionization 110
1. Molecular and electronic structure of phenol radical cation 111
2. Relative energies of the $(C_6H_6O)^{\bullet+}$ radical cations 114
3. The $(C_6H_6O)^{\bullet+}$ potential energy surface (PES) 116
4. Mass spectrometric experiments 121
5. Keto–enol interconversion 127
E. The O–H Bond Dissociation 129
1. Phenoxyl radicals 129
a. Electronic structure 129
b. Geometry and vibrational frequencies 132
c. Spin densities 135
d. Decomposition of phenoxy radical 137
2. Antioxidant activity of phenols 139
a. The O–H bond dissociation energies 139
b. Antioxidant activities 140
c. Features of hydrogen atom abstraction from phenols 141
V. HYDROGEN BONDING ABILITIES OF PHENOLS 143
A. Introductory Survey 143
B. Phenol–$(Water)_n$, $1 \leqslant n \leqslant 4$ Complexes 147
1. Introduction 147
2. Interaction of phenol with water 149
3. The most stable complexes of mono- and dihydrated phenol 149
4. Lower-energy structures of $PhOH(H_2O)_3$ 156
5. At the bottom of PES of $PhOH(H_2O)_4$ 160

C. Hydrogen Bonding between Phenol and Acetonitrile 170
1. Introductory foreground 170
2. Phenol–acetonitrile complex 171
3. Phenol bonding with two acetonitrile molecules 174
4. A rather concise discussion 177
D. Phenol–Benzonitrile Hydrogen-bonded Complex 177
E. A Very Short O–H ··· N Hydrogen Bond 178
VI. OPEN THEORETICAL PROBLEMS 178
VII. ACKNOWLEDGEMENTS 179
VIII. REFERENCES AND NOTES 179

Glossary of Acronyms

BDE	bond dissociation enthalpy	LIF	laser-induced fluorescence
BIPA	*trans*-butenylidene-isopropylamine	LUMO	lowest unoccupied MO
		MO	molecular orbital
N-BMA	benzylidenemethylamine	MP2	second-order Møller-Plesset perturbation theory
CCSD(T)	coupled cluster singles doubles (triples)	MW	microwave spectroscopy
DF	dispersed fluorescence spectroscopy	NBO	natural bond orbital
		PA	proton affinity
DFT	density functional method	PCA	1-pyrrolidinecarboxaldehyde
N,*N*-DMBA	dimethylbenzylamine	PES	potential energy surface
		Ph	phenyl C_6H_5
DPE	deprotonation energy	PhOH	phenol
DRS	double-resonance spectroscopy	R2PI	resonant two-photon ionization spectroscopy
ED	electron diffraction		
HF	Hartree-Fock method	SOMO	singly occupied MO
HOMO	highest occupied MO	TMA	trimethylamine
IR-UV	infrared-ultraviolet spectroscopy	ZPE-ZPVE	zero-point vibrational energy

I. INTRODUCTION

The chemistry of phenols has attracted continuing interest in the last two centuries. Compounds bearing this functional group have several applications indispensable in our daily life, as discussed in the following chapters of this book. Let us mention one example: phenols constitute, among others, an important class of antioxidants that inhibit the oxidative degradation of organic materials including a large number of biological aerobic organisms and commercial products. In human blood plasma, α-tocopherol, well-known as a component of vitamin E, is proved to be the most efficient phenol derivative to date to trap the damaging peroxy radicals ($ROO^{\bullet}$). Phenols owe their activity to their ability to scavenge radicals by hydrogen or electron transfer in much faster processes than radical attacks on an organic substrate.

In this chapter, we attempt to give an overview on the general and theoretical aspects of phenols, including a brief history of their discovery. However, in view of the very large wealth of related literature, the coverage is by no means complete. It is also not intended to be a comprehensive review of all the theoretical work in the area, and there are certainly many important studies of which we were unaware, for which we apologize.

We refer to the compilation *Quantum Chemistry Library Data Base* (QCLDB)[1] for an extended list of available theoretical papers.

The focus of this chapter is a presentation of representative physico-chemical and spectroscopic properties of phenols revealed by quantum chemical calculations, many of them carried out by us specifically for this chapter. In the discussion, the description of methodological details will be kept to a minimum. Unless otherwise noted, all reported computations were performed using the GAUSSIAN 98[2] and MOPAC-7[3] sets of programs. The natural bond orbital analysis[4] was conducted using the NBO (natural bond orbital) module[5] of the GAUSSIAN 98 software package.[2] For the vibrational analyses, the force constant matrices were initially obtained in terms of the cartesian coordinates and the non-redundant sets of internal coordinates were subsequently defined[6]. The calculation of potential energy distribution (PED) matrices of the vibrational frequencies[7] was carried out using the GAR2PED program[8].

A. Summary of Key Physico-chemical Properties of Phenol

Phenol shown in Chart 1 is the parent substance of a homologous series of compounds containing a *hydroxyl group* bound directly to the aromatic ring. Phenol, or PhOH in shorthand notation, belongs to the family of *alcohols* due to the presence of the OH group and it is in fact the simplest aromatic member of this family. The hydroxyl group of phenol determines its acidity whereas the benzene ring characterizes its basicity. Thus, it is formally the *enol* form of the *carbonyl group* (for a review, see ref. 9).

In this subsection we briefly outline the key physico-chemical properties of phenol. For its other properties consult with the NIST data located at URL http://webbook.nist.gov.

Phenol has a low melting point, it crystallizes in colourless prisms and has a characteristic, slightly pungent odor. In the molten state, it is a clear, colourless, mobile liquid. In the temperature range $T < 68.4\,^{\circ}\mathrm{C}$, its miscibility with water is limited; above this temperature it is completely miscible. The melting and solidification points of phenol are quite substantially lowered by water. A mixture of phenol and *ca* 10% water is called phenolum liquefactum, because it is actually a liquid at room temperature. Phenol is readily soluble in most organic solvents (aromatic hydrocarbons, alcohols, ketones, ethers, acids, halogenated hydrocarbons etc.) and somewhat less soluble in aliphatic hydrocarbons. Phenol forms azeotropic mixtures with water and other substances.

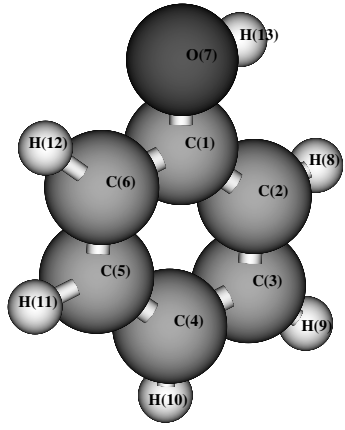


CHART 1. Chemical formulae of phenol: C_6H_5OH; early name: carbolic acid, hydroxybenzene; CAS registry number: 108-95-2

Other physical data of phenol follow below:

Molecular weight: 94.11 (molecular mass of C_6H_5OH is equal to 94.04186).
Weakly acidic: $pK_a(H_2O) = 9.94$ (although it varies in different sources from 9.89 to 9.95).
Freezing point: 40.91 °C.
Specific heats of combustion: $C_p = 3.06$ J mol^{-1} K^{-1}, $C_v = 3.07$ J mol^{-1} K^{-1}.
First ionization energy (IE_a): 8.47 eV (experimental), 8.49 ± 0.02 eV (evaluated).
Proton affinity (PA): 820 kJ mol^{-1} [10].
Gas phase basicity: 786.3 kJ mol^{-1} [10].
Gas-phase heat of formation $\Delta_f H_{298}$: -96.2 ± 8 kJ mol^{-1} (experimental); -93.3 kJ mol^{-1} (theoretical)[11].
Solvation free energy:
Experimental: -27.7 kJ mol^{-1} [12], -27.6 kJ mol^{-1} [13].
Theoretical: -17.3, -20.2, -16.4 kJ mol^{-1} (AMBER parameter[14]), -19.7, -23.8, -12.1 kJ mol^{-1} [1, 13–16].
Gas phase acidity: $\Delta_{acid} H_{298}$:
Experimental: 1465.7 ± 10 kJ mol^{-1} [17, 18]; 1461.1 ± 9 kJ mol^{-1} [18, 19]; 1471 ± 13 kJ mol^{-1} [20].
Theoretical: 1456.4 kJ mol^{-1} [20].
O–H bond dissociation energy $D_{298}(C_6H_5O{-}H)$:
Experimental: 362 ± 8 kJ mol^{-1} [21]; 363.2 ± 9.2 kJ mol^{-1} [22]; 353 ± 4 kJ mol^{-1} [23]; 376 ± 13 kJ mol^{-1} [24]; 369.5 kJ mol^{-1} [25]; 377 ± 13 kJ mol^{-1} [26].
Theoretical: 377.7 kJ mol^{-1} [20].

What else is worth noting, in view of the present review on the theoretical aspects of phenol, is that its electronic subsystem consists of 50 electrons and the ground state is a singlet closed-shell state designated as S_o.

Phenol can be considered as the enol of cyclohexadienone. While the tautomeric keto–enol equilibrium lies far to the ketone side in the case of aliphatic ketones, for phenol it is shifted almost completely to the enol side. The reason of such stabilization is the formation of the aromatic system. The resonance stabilization is very high due to the contribution of the *ortho*- and *para*-quinonoid resonance structures. In the formation of the phenolate anion, the contribution of quinonoid resonance structures can stabilize the negative charge.

In contrast to aliphatic alcohols, which are mostly less acidic than phenol, phenol forms salts with aqueous alkali hydroxide solutions. At room temperature, phenol can be liberated from the salts even with carbon dioxide. At temperatures near the boiling point of phenol, it can displace carboxylic acids, e.g. acetic acid, from their salts, and then phenolates are formed. The contribution of *ortho*- and *para*-quinonoid resonance structures allows electrophilic substitution reactions such as chlorination, sulphonation, nitration, nitrosation and mercuration. The introduction of two or three nitro groups into the benzene ring can only be achieved indirectly because of the sensitivity of phenol towards oxidation. Nitrosation in the *para* position can be carried out even at ice bath temperature. Phenol readily reacts with carbonyl compounds in the presence of acid or basic catalysts. Formaldehyde reacts with phenol to yield hydroxybenzyl alcohols, and synthetic resins on further reaction. Reaction of acetone with phenol yields bisphenol A [2,2-bis(4-hydroxyphenyl)propane].

The reaction in the presence of acid catalysts is used to remove impurities from synthetic phenol. Olefinic impurities or carbonyl compounds, e.g. mesityl oxide, can be polymerized into higher molecular weight compounds by catalytic quantities of sulphuric acid or acidic ion exchangers and can thus be separated easily from phenol, e.g. by its distillation.

Phenol readily couples with diazonium salts to yield coloured compounds. The latter can be used for the photometric detection of phenol as in the case of diazotized 4-nitroaniline. Salicylic acid (2-hydroxybenzoic acid) can be produced by the Kolbe–Schmitt reaction[26] (studied by the density functional method[27]) from sodium phenolate and carbon dioxide, whereas potassium phenolate gives the *para* compound. Alkylation and acylation of phenol can be carried out with aluminium chloride as catalyst; methyl groups can also be introduced by the Mannich reaction. Diaryl ethers can only be produced under extreme conditions.

With oxidizing agents, phenol readily forms a free radical which can dimerize to form diphenols or can be oxidized to form dihydroxybenzenes and quinones. Since phenol radicals are relatively stable, phenol is a suitable radical scavenger and can also be used as an oxidation inhibitor. Such a property can also be undesirable, e.g. the autoxidation of cumene can be inhibited by small quantities of phenol.

B. The History of the Discovery of Phenol

Phenol is a constituent of coal tar and was probably first (partly) isolated from coal tar in 1834 by Runge, who called it 'carbolic acid' (*Karbolsäure*) or 'coal oil acid' (Kohlenölsäure)[28–30].

Friedlieb Ferdinand Runge (born in Billwärder, near Hamburg, 8 February 1795—Oranienburg, died on 25 March 1867) began his career as a pharmacist and, after a long residence in Paris, became an associate professor in Breslau, Germany. Later, he served in the Prussian Marine in Berlin and Oranienburg. Runge published several scientific and technological papers and books (see References 31 and 32 and references therein). He rediscovered aniline in coal-tar oil and called it *kyanol*. He also discovered quinoline (*leukol*), pyrrole ($\pi\nu\rho\rho\sigma$), rosolic acid and three other bases.

Pure phenol was first prepared by Laurent in 1841. Auguste Laurent (La Folie, near Langres, Haute-Marne, 14 September 1808—Paris, 15 April 1853), the son of a wine-merchant, was assistant to Dumas at the Ecole Centrale (1831) and to Brongniart at the Sevres porcelain factory (1833–1835) in France. From 1835 until 1836, he lived in a garret in the Rue St. Andre, Paris, where he had a private laboratory. In December 1837 Laurent defended his Paris doctorate and in 1838 became professor at Bordeaux. Since 1845 he worked in a laboratory at the Ecole Normale in Paris. In his studies of the distillate from coal-tar and chlorine, Laurent isolated dichlorophenol (*acide chlorophénèsique*) $C^{24}H^{8}Cl^{4}O^{2}$ and trichlorophenol (*acide chlorophénisique*) $C^{24}H^{6}Cl^{6}O^{2}$, which both suggested the existence of phenol (phenhydrate)[33]. Laurent wrote: 'I give the name *phène* ($\varphi\alpha\tau\nu\omega$, I light) to the fundamental radical…'. He provided the table of 'general formulae of the derived radicals of phène' where phenol (*hydrate of phène*) was indicated by the incorrect formula $C^{24}H^{12} + H^{4}O^{2}$ ($=C_6H_8O$, in modern notation). In 1841, Laurent isolated and crystallized phenol for the first time. He called it 'hydrate de phényle' or 'acide phénique'[34]. His reported melting point (between 34 and 35 °C) and boiling point (between 187 and 188 °C) are rather close to the values known today. Apart from measuring these elementary physical properties, Laurent also gave some crystals to a number of persons with toothache to try it out as a possible pain killer. The effect on the pain was rather unclear, but the substance was 'very aggressive on the lips and the gums'. In the analysis of his experiments, Laurent applied the substitution hypothesis that was originally proposed by his former supervisor, Dumas. Apparently, however, Laurent went further than Dumas and assumed that the substitution reaction did not otherwise change the structural formula of the reactant and the product, whereas Dumas limited himself to the claim that the removal of one hydrogen atom was compensated by the addition of another group, leaving open the possibility of a complete rearrangement of the molecule[35].

The substitution hypothesis (especially in the form proposed by Laurent) was attacked rather strongly by Berzélius, who claimed that a simple replacement of the hydrogen atom by, for instance, the chlorine atom in an organic molecule should be utterly impossible 'due to the strong electronegative character' of chlorine[36, 37]. According to Berzélius, the very idea of Laurent contradicted the first principles of chemistry and 'seems to be a bad influence (une influence nuisible) in science' (see also Reference 32, p. 388). Instead, he reinterpreted all the results of Laurent by breaking up the reaction product into smaller (more familiar) molecules, satisfying the same global stoichiometry. It looks as if Berzélius was reluctant to accept the full richness of organic chemistry. He was unwilling to accept the existence of new molecules, if the atomic count (and a few other obvious properties) could be satisfied by known molecules. Dumas replied that Berzélius 'attributes to me an opinion precisely contrary to that which I have always maintained, viz., that chlorine in this case takes the place of the hydrogen. . . . The law of substitution is an empirical fact and nothing more; it expresses a relation between the hydrogen expelled and the chlorine retained. I am not responsible for the gross exaggeration with which Laurent has invested my theory; his analyses moreover do not merit any confidence'[38] (see also Reference 32, p. 388).

In 1843, Charles Frederic Gerhardt (Strasbourg, 21 August 1816—19 August 1856) also prepared phenol by heating salicylic acid with lime and gave it the name 'phénol'[39].

Since the 1840s, phenol became a subject of numerous studies. Victor Meyer studied desoxybenzoin, benzyl cyanide and phenyl-substituted methylene groups and showed that they have similar reactivities[31]. He subsequently published a paper on 'the negative nature of the phenyl group', where he noted how phenyl together with other 'negative groups' can make the hydrogen atoms in methylene groups more reactive. In 1867, Heinrich von Brunck defended his Ph.D. thesis in Tübingen under Adolph Friedrich Ludwig Strecker and Wilhelm Staedel on the theme 'About Derivatives of Phenol', where he particularly studied the isomers of nitrophenol[31].

The Raschig–Dow process of manufacturing phenol by cumene was discovered by Wurtz and Kekule in 1867, although the earlier synthesis was recorded by Hunt in 1849. Interestingly, Friedrich Raschig, working earlier as a chemist at BASF and known for his work on the synthesis of phenol and production of phenol formaldehyde adduct, later established his own company in Ludwigshafen.

It is also interesting to mention in this regard that in 1905, the BAAS subcommittee on 'dynamic isomerism' was established and included Armstrong (chairman), Lowry (secretary) and Lapworth. In the 1909 report, Lowry summarized that one of the types of isomerism involves the 'oscillatory transference' of the hydrogen atom from carbon to oxygen, as in ethyl acetoacetate (acetoacetic ester), or from oxygen to nitrogen, as in isatin, or from one oxygen atom to the other one, as in *para*-nitrosophenol[40, 41].

C. Usage and Production

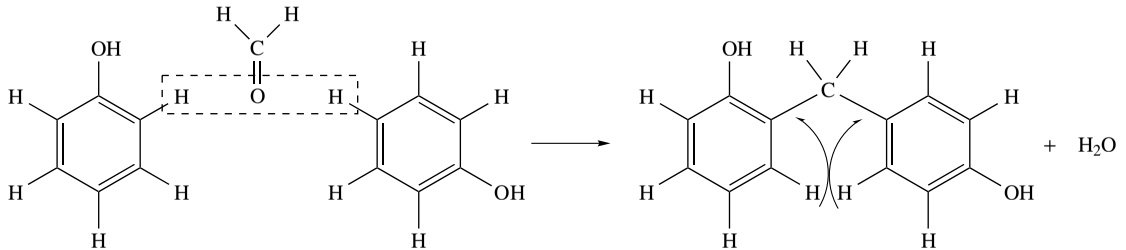
Phenol is one of the most versatile and important industrial organic chemicals. Until World War II, phenol was essentially a natural coal-tar product. Eventually, synthetic methods replaced extraction from natural sources because its consumption had risen significantly. For instance, as a metabolic product, phenol is normally excreted in quantities of up to 40 $mg\,L^{-1}$ in human urine. Currently, small amounts of phenol are obtained from coal tar. Higher quantities are formed in coking or low-temperature carbonization of wood, brown coal or hard coal and in oil cracking. The earlier methods of synthesis (via benzenesulphonic acid and chlorobenzene) have been replaced by modern processes, mainly by the Hock process starting from cumene, via the Raschig–Dow process and by sulphonation. Phenol is also formed during petroleum cracking. Phenol has achieved considerable importance as the starting material for numerous intermediates and final products.

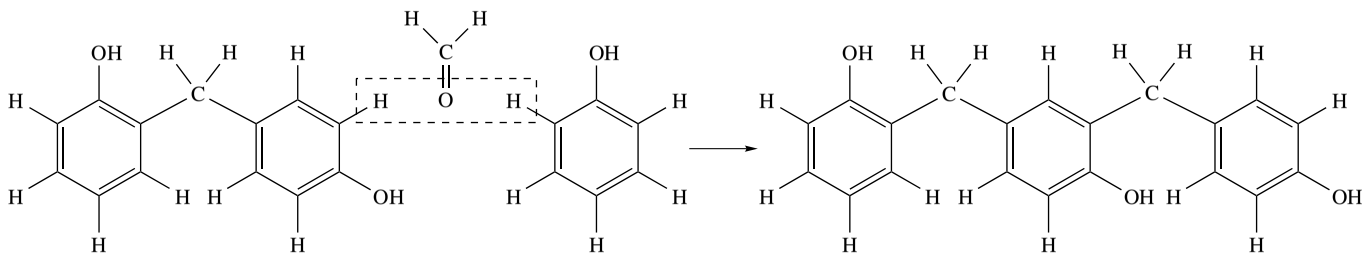
Phenol occurs as a component or as an addition product in natural products and organisms. For example, it is a component of lignin, from which it can be liberated by hydrolysis. Lignin is a complex biopolymer that accounts for 20–30% of the dry weight of wood. It is formed by a free-radical polymerization of substituted phenylpropane units to give an amorphous polymer with a number of different functional groups including aryl ether linkages, phenols and benzyl alcohols[42]. Most pulp-processing methods involve oxidative degradation of lignin, since its presence is a limitation to the utilization of wood pulps for high end uses such as print and magazine grade paper. Such limitation is due to the photoinduced yellowing of lignin-rich, high-yield mechanical pulps and, as a result, the photooxidative yellowing has been extensively studied in the hope of understanding its mechanism and ultimately preventing its occurrence[42, 43]. Phenoxyl radicals are produced during the photooxidation of lignin and their subsequent oxidation ultimately leads to quinones, which are actually responsible for the yellow colour.

Phenol was first used as a disinfectant in 1865 by the British surgeon Joseph Lister at Glasgow University, Scotland, for sterilizing wounds, surgical dressings and instruments. He showed that if phenol was used in operating theatres to sterilize equipment and dressings, there was less infection of wounds and, moreover, the patients stood a much better chance of survival. By the time of his death, 47 years later, Lister's method of antiseptic surgery (Lister spray) was accepted worldwide. Its dilute solutions are useful antiseptics and, as a result of Lister's success, phenol became a popular household antiseptic. Phenol was put as an additive in a so-called carbolic soap. Despite its benefits at that time, this soap is now banned. In Sax's book *Dangerous Properties of Industrial Materials* (quoted in Reference 44), one finds frightening phrases like 'kidney damage', 'toxic fumes' and 'co-carcinogen'. Clearly, phenol is totally unsuitable for general use, but the benefits 130 years ago plainly outweighed the disadvantages. However, because of its protein-degenerating effect, it often had a severely corrosive effect on the skin and mucous membranes.

Phenol only has limited use in pharmaceuticals today because of its toxicity. Phenol occurs in normal metabolism and is harmless in small quantities according to present knowledge, but it is definitely toxic in high concentrations. It can be absorbed through the skin, by inhalation and by swallowing. The typical main absorption route is the skin, through which phenol is resorbed relatively quickly, simultaneously causing caustic burns on the area of skin affected. Besides the corrosive effect, phenol can also cause sensitization of the skin in some cases. Resorptive poisoning by larger quantities of phenol (which is possible even over small affected areas of skin) rapidly leads to paralysis of the central nervous system with collapse and a severe drop in body temperature. If the skin is wetted with phenol or phenolic solutions, decontamination of the skin must therefore be carried out immediately. After removal of contaminated clothing, polyglycols (e.g. lutrol) are particularly suitable for washing the skin. On skin contamination, local anesthesia sets in after an initial painful irritation of the area of skin affected. Hereby the danger exists that possible resorptive poisoning is underestimated. If phenol penetrates deep into the tissue, this can lead to phenol gangrene through damage to blood vessels. The effect of phenol on the central nervous system—sudden collapse and loss of consciousness—is the same for humans and animals. In animals, a state of cramp precedes these symptoms because of the effect phenol has on the motor activity controlled by the central nervous system. Caustic burns on the cornea heal with scarred defects. Possible results of inhalation of phenol vapour or mist are dyspnea, coughing, cyanosis and lung edema. Swallowing phenol can lead to caustic burns on the mouth and esophagus and stomach pains. Severe, though not fatal, phenol poisoning can damage inner organs, namely kidneys, liver, spleen, lungs and heart. In addition, neuropsychiatric disturbances have been described after survival of acute phenol poisoning. Most of the phenol absorbed by the body is excreted in urine as phenol and/or its metabolites. Only smaller quantities are excreted with faeces or exhaled.

The reactions are:





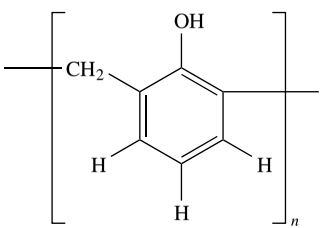


CHART 2. Production of a phenolic resin

Phenol is a violent systemic poison. Less irritating and more efficient germicides (component of some plastics) replace phenol; nevertheless, it is widely used in the manufacture of phenolic resins (e.g. with formaldehyde—see Chart 2, with furfural etc.), epoxy resins, plastics, plasticizers, polycarbonates, antioxidants, lube oil additives, nylon, caprolactam, aniline insecticides, explosives, surface active agents, dyes and synthetic detergents, polyurethanes, wood preservatives, herbicides, fungicides (for wood preparation), gasoline additives, inhibitors, pesticides and as raw material for producing medical drugs like aspirin.

Acetylsalicylic acid was first synthesized by Bayer in 1897 and named Aspirin in 1899[45–47]. Nevertheless, its analgesic and antipyretic effects had been known long before. For example, in the 18th century, Stone discovered the medical effects of the salicin of willow bark and, since that time, salicylic acid was recognized as the active ingredient. Salicin is enzymatically hydrolysed to saligenin and glucose by β-glucosidase. Saligenin is then slowly oxidized to salicylic acid in the blood and in the liver. As is well known, the sodium salt of salicylic acid was used in the 19th century as a painkiller despite the fact that it causes stomach irritations. In his search for less-irritating derivatives of salicylic acid, the Bayer chemist Felix Hoffmann synthesized acetylsalicylic acid (Figure 1).

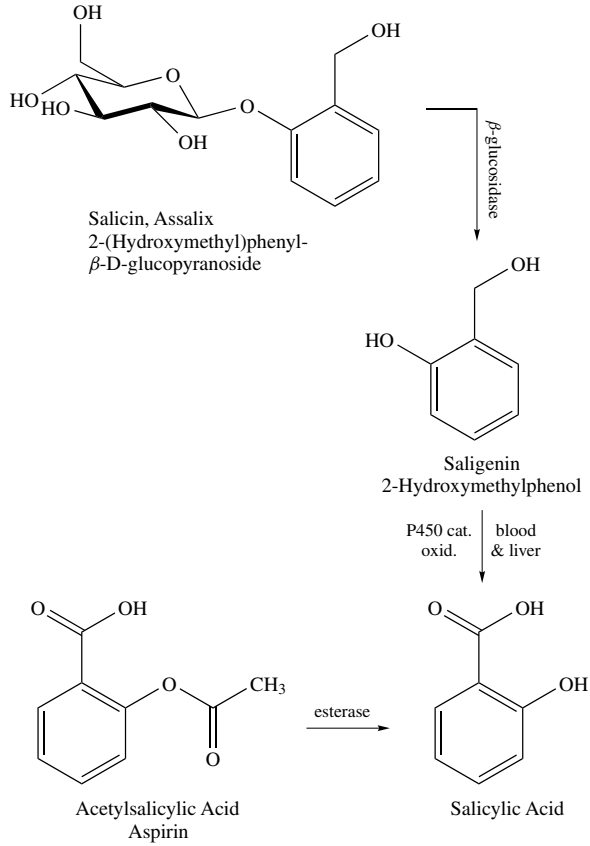


FIGURE 1. Salicin, saligenin, salicylic acid, and aspirin

The success of aspirin was terrific. In a 1994 article[48] in the *Medical Sciences Bulletin*, it was written that 'Americans consume about 80 billion aspirin tablets a year, and more than 50 nonprescription drugs contain aspirin as the principal active ingredient'. The Aspirin Foundation of America provides systematically scientific, regulatory, legislative and general educational information about aspirin to the medical community and the public[49]. In 1971, Vane[50] discovered that aspirin interferes with the biosynthesis of prostaglandins. In 1982 he was awarded the Nobel Prize in medicine in recognition of his work on the mechanism of the action of aspirin. In 1994, Garavito and coworkers[51, 52] elucidated the mechanism of aspirin interference with prostaglandin synthesis.

The crystal structure of aspirin was first determined by Wheatley[53] in 1964 and was refined later, in 1985, by Kim and coworkers[54]. Its crystal structure data can be obtained from the Cambridge Crystallographic Database[55]. The key features of the crystal structure of aspirin are shown in Figure 2. Quite recently, the potential energy surface of aspirin was studied using the B3LYP/6-31G(d) method and all its nine conformational isomers were located[56].

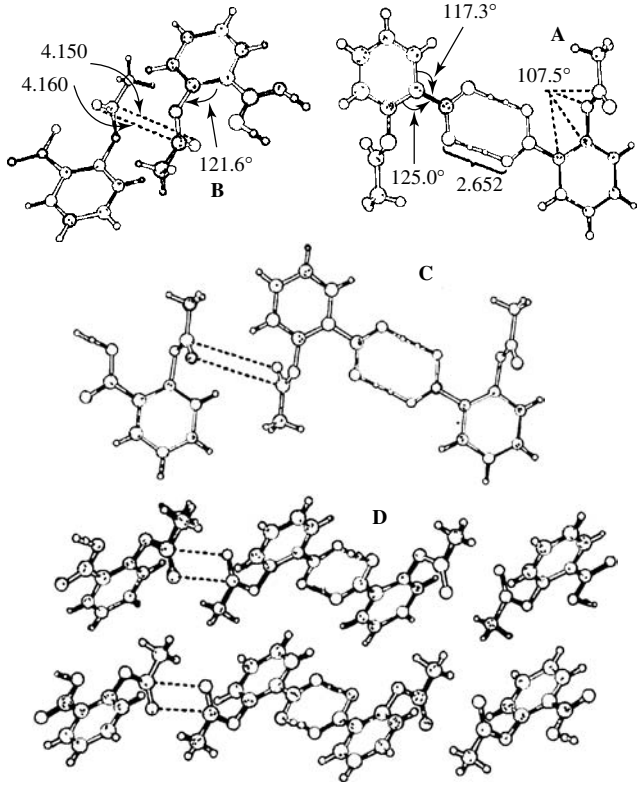


FIGURE 2. Hydrogen bonding patterns and dipole alignment in the crystal structure of aspirin. Two positions are shown for each of the hydrogen-bonded hydrogen atoms (**A**). Aspirin may also form another conformation of the dimer structure, a sort of inversion-symmetric dimer, with a perfect dipole–dipole alignment of the carbonyl groups of two ester functions (**B**). Actually, each aspirin is partly involved in a dimer of **A** and **B**. This is shown in **C**. **D** demonstrates the arrangement of the chains in the crystal. Adapted from Reference 56 with permission

Phenol is mainly used in the production of phenolic resins (plastics). These resins are important components of such items as appliance knobs, handles and housings, washing machine agitators and electrical devices. One example of its commercial usage is the phenol–formaldehyde polymer or phenol–formaldehyde resin called Bakelite (Formica, Micarta), first made in the USA in 1909. It took its name from its discoverer Leo Baekeland who developed it commercially between 1905 and 1910, and it was actually the first truly synthetic polymer. It is characterized by low cost, dimensional stability, high strength, stiffness and resistance to ageing; it is much safer than celluloid. It has insulating properties and could be moulded easily. Bakelite was the ideal plastic for electrical appliances, and in fact it was Bakelite which made possible the generation and distribution of electricity; it made electrical appliances safer for home utilization. It is also widely used in handles, table tops, cabinets and wall panels. The reaction between phenol and formaldehyde is a typical reaction of condensation polymerization, shown in Chart 2[57].

A phenol derivative, phenolphthalein is prepared by the reaction of phenol with phthalic anhydride in the presence of sulphuric acid and used as an indicator for acidity or alkalinity. Chlorinated phenol is much safer than phenol. Chlorine gas reacts with phenol to add one, two or three chlorine atoms and to form, respectively, chlorophenol, 2,4-dichlorophenol and 2,4,6-trichlorophenol[58]. The chlorination of phenol proceeds by electrophilic aromatic substitution. The latter two molecules are less soluble in water than phenol and appear to be a stronger antiseptic than phenol. Interestingly, in the first half of the past century, a bottle of antiseptic chlorophenols was a common attribute as a medicine in many homes. Its solution was used for bathing cuts, cleaning grazes, rinsing the mouth and gargling to cure sore throats. Nevertheless, it was revealed that its solution likely contains dioxins.

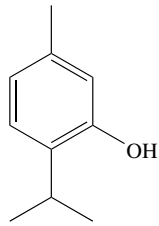
There are actually 31 different chloro- and polychlorophenols[57]. One of them, 2,4-dichlorophenoxyacetic acid (2,4-D), acts as a growth hormone. This makes it particularly effective as a weedkiller against broad-leaf weeds, even in a tiny drop. Surprisingly, it is actually a superb selective weedkiller for lawns and grain crops because it does not affect grass and cereals. Sometimes, 2,4-D is used to trick plants into flowering. This is widely used in Hawaii, where visitors are greeted with pineapple flowers during the whole year! It is safe for animals in low quantity, but 35 g of it is likely a fatal dose for an average person weighing about 70 kg. 2,4-D is quite inexpensive, effective, more selective than other weedkillers and much safer than the sodium arsenate and sodium chlorate which were popular weedkillers in the 1950s. In 1948, 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) came into the market[44] and contained larger quantities of dioxin than 2,4-D[59]. It was used as a killer for tough weeds and was so successful in killing woody plants that it was deployed in the Vietnam War. From 1962 to 1969, at least 50,000 tonnes of a 50:50 mixture of 2,4-D and 2,4,5-T (called defoliant and widely known as Agent Orange) was sprayed from the air to destroy the dense foliage of trees covering the troops of the Vietnam National Front of Liberation. Agent Orange was contaminated with *ca* 2–4% of dioxins and for this reason it caused birth defects in new-born babies in Vietnam. It may also be linked to a form of acute myelogenous leukaemia, which represents 8% of childhood cancers among the children of Vietnam veterans, as the US Institute of Medicine (IOM) committee has recently reported[60].

Interestingly, phenols from peat smoke are included in the flavours of Scotch whisky to dry the malt[44].

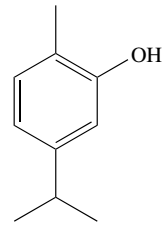
Complex phenols are widespread in nature, although the simple ones are relatively uncommon. Phenol is particularly found in mammalian urine, pine needles and oil tobacco leaves. Abundant natural substances such as thymol (**1**) and carvacrol (**2**) are derivatives of phenols.

Natural phenols[57, 61, 62] arise in the three following manners[57]:

(i) Poly-β-ketones, for example (**3**), derived from the acid RCO_2H and three malonate units, are intermediates (enzyme-bound) in phenol biosynthesis. Cyclization can be envisaged as being similar to the aldol reaction (cf. **4**) or the Claisen condensation (cf. **5**) yielding phenolic acids like orsellinic acid (**6**), R = Me, or phenolic ketones, e.g. phloracetophenone (**7**), R = Me, respectively, after enolization of the carbonyl functions. Modification processes may ensue or intervene. The reduction of a carbonyl to secondary alcohol, away from the cyclization site, may thus afford a phenol with one less hydroxyl. However, such a mode of biogenesis[63–65] leads to phenols with *meta*-disposed hydroxyls. This character may be diagnostic of the origin.



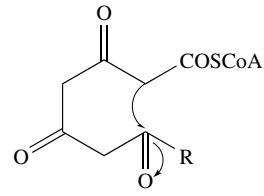
(1)



(2)

$RCOCH_2COCH_2COCH_2CO_2H$

(3)



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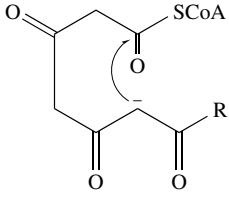

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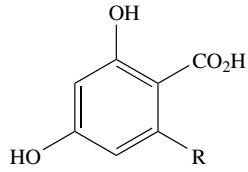

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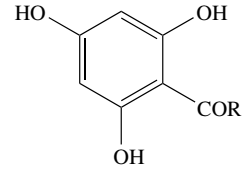
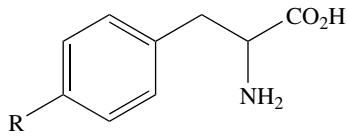
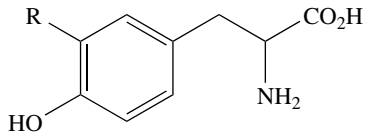


(7)

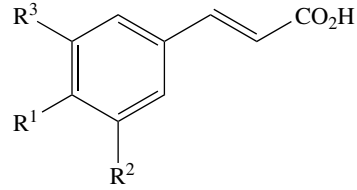
(ii) Aromatic rings may be hydroxylated in vivo by mono-oxygenases. Such reactions are often encountered in aromatics derived from the shikimate–prephenate pathway[66]. Phenylalanine (**8**) is thus *p*-hydroxylated to tyrosine (**9**) by phenylalanine mono-oxygenase using molecular oxygen. Cinnamic acid (**10a**) can be hydroxylated to *p*-hydroxycinnamic acid (**10b**), and on to di- and tri-hydroxy acids like, for instance, caffeic (**10c**) and gallic (**10d**) acids, with adjacent hydroxy functions. A useful list of micro-organisms and higher plant mono-oxygenases and phenolases is given elsewhere[67]. Hydroxylations such as



(8)



(9)



(10) **(a)** $R^1 = R^2 = R^3 = H$
(b) $R^1 = OH$, $R^2 = R^3 = H$
(c) $R^1 = R^2 = OH$, $R^3 = H$
(d) $R^1 = R^2 = R^3 = OH$

(**8** → **9**) may be accompanied by proton rearrangements as (**8**, R = D) → (**9**, R = D), the so-called 'National Institute of Health' ('NIH') shift, whose mechanism[68,69] is displayed in Chart 3. Related 'NIH' shifts have been observed in vitro for various synthetic arene oxides and in oxidation of aromatics by permanganate and by chromyl compounds[70] such as CrO_2Cl_2 and $CrO_2(OAc)_2$.

(iii) Alicyclic rings with oxygen functions may be dehydrogenated to phenols. Compounds **1** and **2** are likely derived from monocyclic monoterpenes carrying a 3- or 2-oxygen function. Phenolic steroids like, for instance, estrone and equilenin can be derived in a similar way. This route to phenolic products is not yet well understood.

Phenol moieties are present in salvarsan (**11**) and neosalvarsan (**12**) synthesized by the German scientist Paul Ehrlich (1854–1915), considered as the father of chemotherapy for

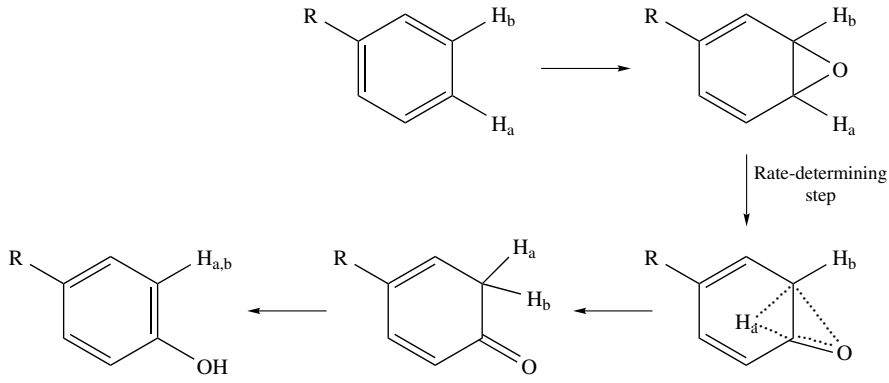
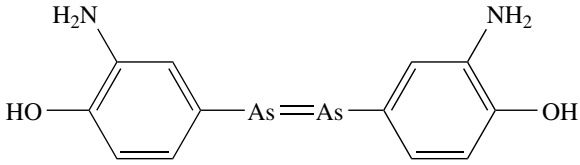


CHART 3. Mechanism of the so-called 'NIH'-shift

use in syphilis treatments prior to the discovery of penicillin. He received a Nobel Prize in 1908 for his work.



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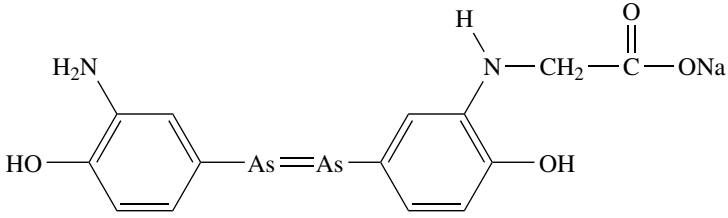


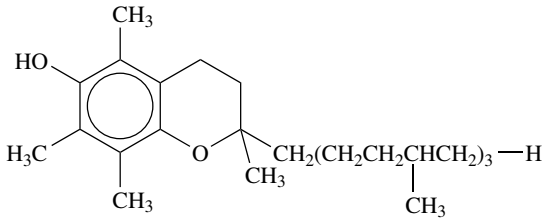
(12)

Phenol serves as a basic unit of larger molecules, e.g. tyrosine residues in proteins. The phenoxyl radical is treated as a model system for the tyrosyl radical whose formation via abstraction of the hydrogen atom from the hydroxyl group of tyrosine is a typical feature of oxidative stress in the physiological pH range[71, 72].

Phenols are an extremely important class of antioxidants whose utilization in living organisms and synthetic organic materials reduces the rate of the oxidative degradation which all organic materials undergo by being exposed to air[73–77]. The antioxidant property can be related to the readily abstractable phenolic hydrogen as a consequence of the relatively low bond dissociation enthalpy of the phenolic O–H group [BDE(O–H)]. A large variety of *ortho*- and/or *para*-alkoxy-substituted phenols have been identified as natural antioxidants, such as α-tocopherol (**13**), which is known as the most effective lipid-soluble chain-breaking antioxidant in human blood plasma, and ubiquino-10 (**14**), both present in low-density lipid proteins. The mechanism of action of many phenolic antioxidants relies on their ability to transfer the phenolic H atom to a chain-carrying peroxyl radical at a rate much faster than that at which the chain-propagating step of lipid peroxidation proceeds[73–77]. Natural phenolic antioxidants can be also isolated from plants[78] such as sesamolinol (**15**), from sesame seeds and coniferyl alcohol (**16**), one of the three precursors for the biosynthesis of lignin. For example, Vitamin E (**17**) is a chain-breaking antioxidant that interferes with one or more of the propagation steps in autooxidation by atmospheric oxygen[79].

Phenolic compounds are also known to suppress the lipid peroxidation in living organisms. Furthermore, they are widely used as additives in food technology.

Regarding the production of phenol, small quantities of phenol are isolated from tars and coking plant water produced in the coking of hard coal and the low temperature carbonization of brown coal as well as from the wastewater from cracking plants. Most of the past and currently employed phenol syntheses are based on using benzene as a precursor which, however, is known as a volatile organic carcinogen. About 20% of the global benzene production is used for the manufacture of phenol[80]. By far the greatest proportion is obtained by oxidation of benzene or toluene. Although direct oxidation of



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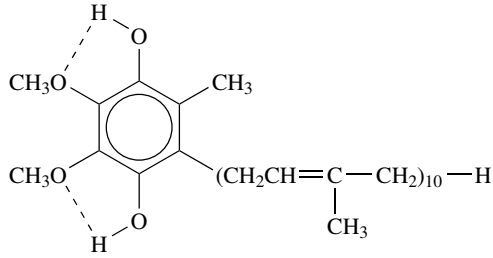

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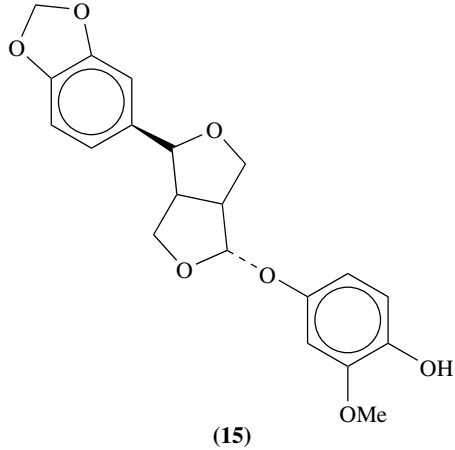

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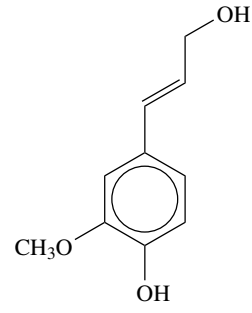

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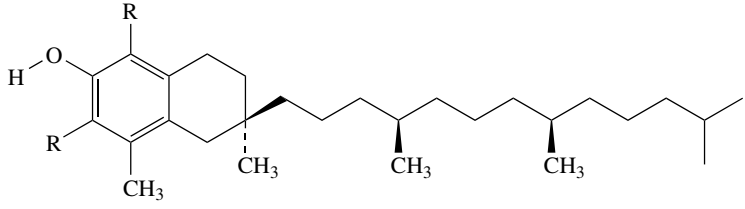

(17)

benzene is possible in principle, the phenol formed is immediately further oxidized. It is worth mentioning that a recent study[81] performed a thorough computational study of the potential energy surface for the oxidation reaction of benzene in the lowest-lying triplet state (equation 1)

$$C_6H_6 + O(^3P) \longrightarrow \text{Products} \qquad (1)$$

followed by a kinetic analysis using the Rice–Ramsperger–Kassel–Marcus (RRKM) reaction theory[82] based on the electronic structure calculations employing the MP4/6-31G(d)//HF/6-31G(d) and B3LYP/cc-pVDZ computational levels. Below we outline the key results of this work.

Reaction 1 has a large number of energetically feasible product channels. In Figure 3, we display the theoretical triplet potential energy surface (PES) for reaction 1. The reaction initially proceeds via the addition of $O(^3P)$ to benzene, and this first step is exothermic by -37 kJ mol^{-1} and characterized by a barrier of approximately 21 kJ mol^{-1}. The chemically activated adduct reacts on the triplet PES in forming a number of products. The two lowest barriers lead to the formation of phenoxyl radical (-14 kJ mol^{-1}) and formylcyclopentadiene (-8 kJ mol^{-1}, both barriers taken relative to the reactant)[81]. The reaction route resulting in phenol is exothermic (-33 kJ mol^{-1} [81]). However, it has a rather high barrier of 100 kJ mol^{-1}. The calculated enthalpy of the reaction of the formation of

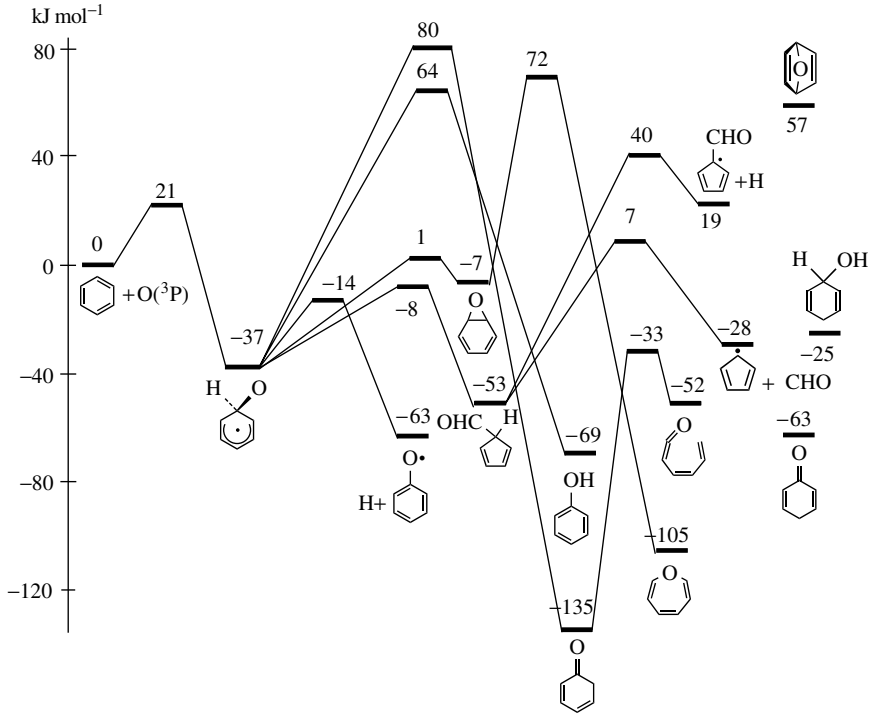

FIGURE 3. The potential energy profile of triplet products and transition structures in reaction 1. Adapted from Reference 81 with permission

phenol amounts to $-433\ \mathrm{kJ\,mol^{-1}}$, which agrees fairly well with the experimental value of $-428\ \mathrm{kJ\,mol^{-1}}$[81]. The theoretical singlet–triplet splitting of phenol ($352\ \mathrm{kJ\,mol^{-1}}$) is also very close to its experimental value of $341\ \mathrm{kJ\,mol^{-1}}$. One may conclude that such high activation is likely sufficient to overcome the barrier in order to form phenoxy radical ($372\ \mathrm{kJ\,mol^{-1}}$), and therefore one might expect that the formation of the latter dominates on the singlet PES. This concurs with the flame data of Bittner and Howard[83] indicating that a direct reaction route to phenol is not possible.

It has been recently revealed that ZSM-5 zeolite exhibits an extremely high catalytic selectivity for the oxidation of benzene to phenol. The high reactivity of the zeolite should be ascribed to iron impurity arising in the intermediary steps in the zeolite synthesis[84, 85]. A surface oxygen (O) or α-oxygen, generated on Fe-ZSM-5 zeolite during N_2O decomposition[84, 85] (equation 2)

$$N_2O \xrightarrow{\text{zeolites}} (O) + N_2 \tag{2}$$

takes part in the formation of phenol via equation 3

$$(O) + C_6H_6 \longrightarrow C_6H_5OH \tag{3}$$

Reactions 2 and 3 have been thoroughly studied theoretically at the B3LYP computational level. In particular, a sound model of α-oxygen has been proposed[85, 86]. According to Reference 87, Solutia has recently developed a one-step technology producing phenol directly from benzene and N_2O. Due to the fact that such a process provides a very high yield and can use waste N_2O from the production of adipic acid, it is now considered to be a rather promising technology in the new millennium.

Therefore, alternative routes must be chosen for the production of phenol, e.g. via halogen compounds which are subsequently hydrolysed or via cumene hydroperoxide which is then cleaved catalytically. The following processes were developed as industrial syntheses for the production of phenol[88]:

1. Sulphonation of benzene and production of phenol by heating the benzenesulphonate in molten alkali hydroxide[89].
2. Chlorination of benzene and alkaline hydrolysis of the chlorobenzene.
3. Chlorination of benzene and catalytic saponification by Cu in the steam hydrolysis of the chlorobenzene[90, 91] (Raschig process, Raschig–Hooker, Gulf oxychlorination).
4. Alkylation of benzene with propene to isopropylbenzene (cumene), oxidation of cumene to the corresponding *tert*-hydroperoxide and cleavage to phenol and acetone (Hock process).
5. Toluene oxidation to benzoic acid and subsequent oxidizing decarboxylation to phenol (Dow process).
6. Dehydrogenation of cyclohexanol–cyclohexanone mixtures.

Among these processes, only the Hock process and the toluene oxidation are important industrially. The other processes were discarded for economic reasons. In the Hock process acetone is formed as a by-product. This has not, however, hindered the expansion of this process, because there is a market for acetone. New plants predominantly use the cumene process. More than 95% of the 4,691,000 $\mathrm{m\,y^{-1}}$ (m = metric tonnes) consumed is produced by the cumene peroxidation process. Phenol's consumption growth rate of 3% is primarily based on its use in engineering plastics such as polycarbonates, polyetherimide and poly(phenylene oxide), and epoxy resins for the electronic industry. The Mitsui Company is, for instance, the world's second largest producer of phenol. Japan's production

output (in thousands of metric tonnes) is shown below[92].

Chemicals/Year	1996	1997	1998	1999	2000	Change 1999–2000
Phenol	768	833	851	888	916	3.2%
Phenolic resins	294	303	259	250	262	4.8%

The cumene process is based on the discovery of the oxidation of cumene with oxygen to cumene hydroperoxide and its acidic cleavage to phenol and acetone published in 1944[93]. This reaction was developed into an industrial process shortly after World War II by the Distillers Co. in the United Kingdom and the Hercules Powder Co. in the United States. The first plant was put into operation in 1952 by Shawinigan in Canada and had an initial capacity of 8000 $t\,y^{-1}$ of phenol. Today, phenol is predominantly produced by this process in plants in the USA, Canada, France, Italy, Japan, Spain, Finland, Korea, India, Mexico, Brazil, Eastern Europe and Germany with an overall annual capacity of 5×10^6 tons[94, 95]. In addition to the economically favourable feedstock position (due to the progress in petrochemistry since the 1960s), the fact that virtually no corrosion problems occur and that all reaction stages work under moderate conditions with good yields was also decisive for the rapid development of the process. To produce cumene, benzene is alkylated with propene using phosphoric acid (UOP process) or aluminium chloride as catalyst.

The phenol-forming process via toluene oxidation developed originally by Dow (USA)[96–98] has been carried out in the USA, Canada and the Netherlands. Snia Viscosa (Italy) uses the toluene oxidation only for the production of benzoic acid as an intermediate in the production of caprolactam[99, 100]. The process proceeds in two stages. At the first stage, toluene is oxidized with atmospheric oxygen in the presence of a catalyst to benzoic acid in the liquid phase. At the second stage the benzoic acid is decarboxylated catalytically in the presence of atmospheric oxygen to produce phenol. This is a radical-chain reaction involving peroxy radicals. The activation energy of the exothermic oxidation of toluene to benzoic acid is 136 $kJ\,mol^{-1}$[99].

Most of the phenol produced is processed further to give phenol–formaldehyde resins. The quantities of phenol used in the production of caprolactam via cyclohexanol–cyclohexanone have decreased because phenol has been replaced by cyclohexane as the starting material for caprolactam. The production route starting from phenol is less hampered by safety problems than that starting from benzene, which proceeds via cyclohexane oxidation. Bisphenol A, which is obtained from phenol and acetone, has become increasingly important as the starting material for polycarbonates and epoxy resins. Aniline can be obtained from phenol by ammonolysis in the Halcon process. Adipic acid is obtained from phenol by oxidative cleavage of the aromatic ring. Alkylphenols, such as cresols, xylenols, 4-*tert*-butylphenol, octylphenols and nonylphenols, are produced by alkylation of phenol with methanol or the corresponding olefins. Salicylic acid is synthesized by addition of CO_2 to phenol (Kolbe synthesis). Chlorophenols are also obtained directly from phenol. All these products have considerable economic importance because they are used for the production of a wide range of consumer goods and process materials. Examples are preforms, thermosets, insulating foams, binders (e.g. for mineral wool and molding sand), adhesives, laminates, impregnating resins, raw materials for varnishes, emulsifiers and detergents, plasticizers, herbicides, insecticides, dyes, flavours and rubber chemicals.

It is worth noting the recent work on the benzene-free synthesis of phenol[101], which is actually a part of longstanding efforts[102] to elaborate the alternatives to benzene. This new

alternative synthesis is based on the aromatization of shikimic acid which is now readily available by the elaboration of a microbe-catalysed synthesis from glucose in near-critical water, where phenol is the primary reaction product. An aqueous solution of shikimic acid is heated to and maintained at 350 °C for 30 min yielding 53% of phenol.

II. MOLECULAR STRUCTURE AND BONDING OF PHENOL

A. The Equilibrium Structure of Phenol in the Ground Electronic State

Until the mid-thirties of the 20th century electron diffraction or microwave studies of phenol had not yet been conducted and so, rather peculiarly, the equilibrium configuration of phenol remained uncertain although some indirect evidence suggested its ground electronic state S_o to be certainly planar. The first X-ray structural data became available by 1938 for several phenolic compounds[103]. At that time, it was suggested that the C−O bond is about 1.36 Å, that is by *ca* 0.07 Å shorter than the C−O bond in aliphatic alcohols. This was accounted for by the decrease in the effective radius of the carbon atom due to the change of hybridization from sp^3 to sp^2, even though some degree of electron delocalization across the C−O bond could be assumed. Such increase in double-bond character favours a completely planar equilibrium configuration of phenol in its ground electronic state.

This character results from quinonoid resonance structures in addition to the more important Kekulé-type structures[104] and tends to cause the hydrogen atom to be placed in the molecular plane. This leads to two equivalent configurations with the hydrogen of the OH group being on one side of the other of the C−O bond[104]. It implies the existence of the activation barrier V_τ of the OH torsion motion around the C−O bond estimated in the mid-thirties as equal to 14 kJ mol^{-1}.

The molecular geometry of phenol was later determined experimentally by microwave spectroscopy[105–108] and electron diffraction[109] (ED). In 1960, MW experiments[105] of some phenol derivatives showed that their equilibrium configurations are planar (C_s symmetry). In 1966, two possible r_o-structures were determined by examining four new isotopic modifications of phenol[106], and three years later a partial r_s-structure was presented on the basis of the six monodeuteriated species[107]. The full r_s-structure of phenol was reported[108] in 1979 and is presented in Table 1[109]. Generally speaking, the structure of the phenyl ring in phenol deviates only slightly from the regular isolated phenyl ring. This is shown in Figure 4. All C−H distances are nearly equal, within the experimental uncertainties, although the *para*-distance seems to be shorter than the other ones. The CCC bond angles are slightly perturbed, viz. the bond angle $C_1C_3C_5$ is larger than 120° whereas the $C_2C_6C_4$ angle is smaller than 120°. The angle between the C_6O_7 bond and the C_1−C_4 axis was reported equal to 2.52°[108]. Our calculation performed at the B3LYP/6-31+G(d,p) computational method predicts it to be equal to 2.58°.

Since the first quantum mechanical calculation of phenol performed in 1967 using the CNDO/2 method[110], the phenol geometry was considered at a variety of computational levels[111–125] ranging from the HF to the MP2 method of molecular orbital theory and density functional theory (DFT) employed with several basis sets, mainly of the split valence type as, e.g. 6-31G(d,p) and 6-31+G(d,p). These computational results are summarized in Tables 1–3 and Figure 4. It seems noteworthy that the semi-empirical geometries listed in Table 1 are rather close to the experimental observations. Also, to complete the theoretical picture of the phenol molecule, its theoretical inertia moments calculated at the B3LYP/6-31+G(d,p) level are equal to 320.14639, 692.63671 and 1012.78307 a.u.

Table 3 summarizes the key properties of phenol[107–130]. Inspecting its rotational constants collected in Table 2, we may conclude that fair agreement between experiment and