Theophil Eicher, Siegfried Hauptmann,
and Andreas Speicher

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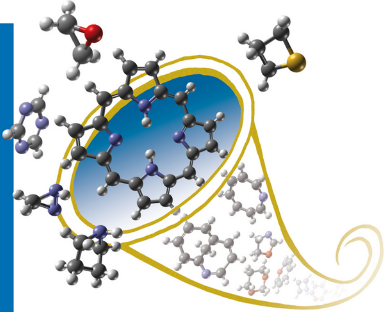
The Chemistry of Heterocycles

Structures, Reactions, Synthesis, and Applications

Third, Completely Revised and Enlarged Edition



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Structure, Reactions, Synthesis, and Applications

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Contents

Preface to the Third Edition

This enlarged and completely revised third edition of "*The Chemistry of Heterocycles*" is dedicated to the memory of Siegfried Hauptmann, who died after long illness on 18 April 2011. We gratefully acknowledge his achievements in the development of this book as well our fruitful collaboration with him during its first editions.

In the new edition, the structure decided on for the earlier editions of the book has been maintained. Thus, after the introductory Chapters 1 and 2 on the chemical structure and nomenclature of heterocyclic compounds, Chapters 3–8 (organized according to ring-size and number of hetero atoms) describe for a representative cross section of heterocyclic systems

- structural, physical, and spectroscopic features;
- chemical properties and characteristic transformations;
- aspects of synthesis, organized according to retroanalysis;
- selected derivatives, natural products, pharmaceuticals, and other biologically active compounds of related structure type;
- utility as vehicles in specific synthetic reactions.

The information given in Chapters 1–8 is supported by references from primary literature, reviews, and textbooks of Organic Chemistry, and aims to include the literature cited in ChemInform up to the year 2011.

Chapter 9 consists of a series of problems – presented in broad variety and selected almost exclusively from the most recent literature – and is intended to deepen the knowledge and understanding of the reader and to extend the topics of heterocyclic chemistry treated in this book. The concluding chapters contain the General Subject Index (10.1) and an Index of Named Reactions (10.2).

As in the earlier editions, this book is specifically addressed to (a) advanced students and research fellows as well as chemists in industry who are looking for a survey of well-tried fundamental concepts and for information on modern developments in heterocyclic chemistry and (b) lecturers in the field of Organic Chemistry, for whom the contents of this book may serve as building blocks for advanced courses on topics of heterocyclic chemistry.

Special thanks are due to Prof. Dr. Uli Kazmaier for his maintaining and encouraging collegial interest and support. We are indebted to Dres. Matthias Groh and Judith Holz for their valuable and reliable technical assistance; in addition, we especially and cordially thank Marcus Malter for his involvement in the production of the new formula diagrams (using the program ChemDraw Ultra 12.0 throughout) introduced in this new edition.

Finally, we are grateful to Bernadette Gmeiner and the staff of the editorial office of Wiley-VCH for their efficient collaboration.

Saarbrücken
Spring 2012

Theophil Eicher and
Andreas Speicher

Abbreviations and Symbols

General and spectroscopic abbreviations and symbols

bp	boiling point	de	diastereoisomeric excess
ca.	circa	ee	enantiomeric excess
cf.	certify	$h\nu$	photochemical
cf. p.	see page	%	percentage
concd	concentrated	IR	infrared spectrum
dil	dilute(d)	cm^{-1}	wave number
et al.	and other authors	UV	ultraviolet spectrum
mp	melting point	λ	wavelength
ref.	reference	ε	molar extinction coefficient
rfl.	heated under reflux	^{1}H NMR	proton resonance spectrum
r.t.	room temperature	^{13}C NMR	^{13}C resonance spectrum
AO	atom orbital	δ	chemical shift ($\delta_{TMS} = 0$)
INN	international nonproprietary name	ppm	parts per million (10^6)
MO	molecular orbital	$\Delta H^{\neq}$	activation enthalpy (kJ mol^{-1})
°C	degrees centigrade	nm	nanometer (10^{-9} m)
Δ	thermal	pm	picometer (10^{-12} m)
pK_A	refers to the acidity of a given acid (H-X)		
pK_a	refers to the acidity of the conjugate acid (HB$^+$) of a given base (B)		

Abbreviations for substituents . . .

Ac	acetyl
Ar	aryl
Bn	benzyl
Boc	*tert*-butoxycarbonyl
*n*Bu	*n*-butyl
*sec*Bu	*sec*-butyl
*t*Bu	*tert*-butyl
Bz	benzoyl
Cy	cyclohexyl

Et	ethyl
EWG	electron-withdrawing group
Me	methyl
Mes	mesyl (methanesulfonyl)
Ms	mesityl
Ph	phenyl
*i*Pr	isopropyl
*n*Pr	*n*-propyl
Tf	trifluoromethanesulfonyl
Tos	tosyl (*p*-toluenesulfonyl)

. . . and commonly used compounds

ADE	diethyl acetylene dicarboxylate
AIBN	azoisobutyronitrile
BINAP	2,2’-bis(diphenylphosphino)-1,1’-binaphthyl
BINOL	1,1’-bis-2-naphthol
BMIM	1-(*n*-butyl)-3-methylimidazolium
COD	cyclooctadiene
DABCO	1,4-diazabicyclo[2.2.2]octane
DCE	1,2-dichloroethane
DCM	dichloromethane
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DEAD	diethyl azodicarboxylate
DET	diethyl tartrate
DIPEA	diisopropyl ethylamine (Hünig base)
DIPT	diisopropyl tartrate
DMAD	dimethyl acetylene dicarboxylate
DMAP	4-(dimethylamino)pyridine
DME	1,2-dimethoxyethane
DMF	dimethylformamide
DMPU	*N*,*N*′-dimethylpropylene urea
DMSO	dimethyl sulfoxide
EDCI	1-ethyl-3-(3-dimethylaminopropyl)carbodiimide
EDTA	ethylenediamine tetraacetic acid
EMIM	1-ethyl-3-methylimidazolium
HMDS	hexamethyldisilazane
HMPT	hexamethylphosphoric acid triamide
HOBt	1-hydroxybenzotriazole
LDA	lithiumdiisopropylamide
LiTMP	lithium-2,2,6,6-tetramethylpiperidide

MCPBA	*m*-chloroperbenzoic acid
NBS	*N*-bromosuccinimide
NCS	*N*-chlorosuccinimide
NIS	*N*-iodosuccinimide
NMP	*N*-methylpyrrolidone
PCC	pyridinium chlorochromate
PPA	polyphosphoric acid
Py	pyridine
TBAF	tetra-*n*-butylammonium fluoride
TBDMS	(*tert*-butyl)dimethylsilyl
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TMEDA	*N*, *N*, *N*′, *N*′-tetramethylethylenediamine
TMS	trimethylsilyl
TosMIC	(*p*-toluenesulfonyl)methylisocyanide

. . . and ligands for transition metal-catalyzed reactions

acac	acetylaceton(ate)
dba	dibenzylidene acetone
dppf	diphenylphosphanylferrocene
dppp	1,3-bis(diphenylphosphino)propane
S-Phos	2,6-dimethoxy-(2’-dicyclohexylphosphanyl)biphenyl
Xantphos	4,5-bis(diphenylphosphino)-9,9-dimethylxanthene

. . . and retrosynthesis

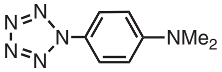
FGA	functional group addition
FGI	functional group interconversion
⇒	retrosynthetic operation, in general: bond disconnection, FGA, FGI

1
The Structure of Heterocyclic Compounds

Most chemical compounds consist of molecules. The classification of such chemical compounds is based on the structure of these molecules, which is defined by the type and number of atoms as well as by the covalent bonding within them. There are two main types of structure:

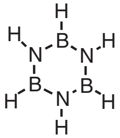
- The atoms form a chain – aliphatic (*acyclic*) compounds
- The atoms form a ring – *cyclic* compounds.

Cyclic compounds in which the ring is made up of atoms of one element only are called *isocyclic compounds*, for example, **1**. If the ring consists of C-atoms only, then we speak of a *carbocyclic compound*, for example, **2**. Cyclic compounds with at least two different atoms in the ring (as ring atoms or members of the ring) are known as *heterocyclic compounds*. The ring itself is called a *heterocycle*. If the ring contains no C-atom, then we speak of an *inorganic heterocycle*, for example, **3**. If at least one ring atom is a C-atom, then the molecule is an *organic heterocyclic compound*, for example, **4**. In this case, all the ring atoms which are not carbon are called *heteroatoms*.



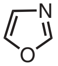
1
(4-dimethylaminophenyl)-
pentazole
isocyclic

2
cyclopenta-1,3-diene
isocyclic,
carbocyclic

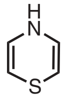


3
borazine
inorganic
heterocycle

heteroatoms:



4
oxazole
O and N



5
4*H*-1,4-thiazine
S and N

organic heterocycles

Along with the type of ring atoms, their total number is important, since this determines the ring size. The smallest possible ring is three-membered. The most important rings are the five- and six-membered heterocycles. There is no upper limit; there exist seven-, eight-, nine-, and larger-membered heterocycles.

In principle, all elements except the alkali metals can act as ring atoms. Although inorganic heterocycles have been synthesized, this book limits itself to organic ones. In these, the N-atom is the most common heteroatom. Next in importance are O- and

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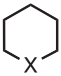
S-atoms. Heterocycles with Se-, Te-, P-, As-, Sb-, Bi-, Si-, Ge-, Sn-, Pb-, or B-atoms are less common.

To determine the stability and reactivity of heterocyclic compounds, it is useful to compare them with their carbocyclic analogs. In principle, it is possible to derive every heterocycle from a carbocyclic compound by replacing appropriate CH_2 or CH groups by heteroatoms. If one limits oneself to monocyclic systems, one can distinguish four types of heterocycles as follows:

(1) Saturated heterocycles (heterocycloalkanes), e.g.



X = O: oxane
X = S: thiane
X = NH: piperidine

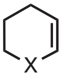
X = O: 1,4-dioxane
X = S: 1,4-dithiane
X = NH: piperazine

compare:

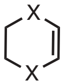
cyclohexane

In this category, there are no multiple bonds between the ring atoms. The compounds react largely like their aliphatic analogs, for example, oxane (tetrahydropyran) and dioxane behave like dialkyl ethers, thiane and 1,4-dithiane like dialkyl sulfides, and piperidine and piperazine like secondary aliphatic amines.

(2) Partially unsaturated systems (heterocycloalkenes), e.g.



X = O: **6**
X = S
X = NH



X = O
X = S
X = NH

X = O$^+$
X = S$^+$
X = NH

compare:

cyclohexene

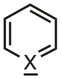
If the multiple bonds are between two C-atoms of the ring, as, for instance, in 3,4-dihydro-2*H*-pyran (**6**), the compounds react essentially like alkenes or alkynes, enolethers, enamines, and so on. The heteroatom can also be part of a double bond. In the case of $X = O^+$, the compounds behave like oxenium salts, in the case of $X = S^+$ like sulfenium salts, and in the case of $X = N$ like imines (azomethines).

(3) Systems with the greatest possible number of noncumulated double bonds (heteroannulenes), e.g.

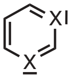
From the annulenes, one can formally derive two types of heterocycles:

- systems of the same ring size, if CH is replaced by X
- systems of the next lower ring size, if HC=CH is replaced by X.

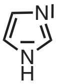
X = O: furan
X = S: thiophene
X = NH: pyrrole



X = O⁺: pyrylium ion
X = S⁺: thiinium ion
X = N: pyridine



X = N: pyrimidine

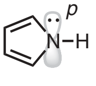


imidazol

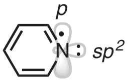
compare:

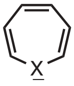
[6]annulene
benzene

"pyrrole-like" N-atom



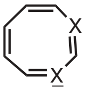
"pyridine-like" N-atom





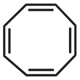
X = O: oxepine
X = S: thiepine
X = NH: azepine

X = O
X = S
X = N: azocine



X = N: 1,3-diazocine

compare:



[8]annulene
cyclooctatetraene

In both cases, the resulting heterocycles are iso-π-electronic with the corresponding annulenes, that is, the number of π-electrons in the ring is the same. This is because in the pyrylium and thiinium salts, as well as in pyridine, pyrimidine, azocine, and 1,3-diazocine, each heteroatom donates *one electron* to the conjugated system and its nonbonding electron pair does not contribute. However, with furan, thiophene, pyrrole, oxepin, thiepin, and azepine, *one electron pair* of the heteroatom is incorporated into the conjugated system (delocalization of the electrons). Where nitrogen is the heteroatom, this difference can be expressed by the designation *pyridine-like N-atom* or *pyrrole-like N-atom*. In imidazole both types can be found.

(4) Heteroaromatic systems

This includes heteroannulenes, which comply with the Hückel rule, that is, which possess $(4n + 2)$ π-electrons delocalized over the ring. The most important group of these compounds derives from [6]annulene (benzene). They are known as *heteroarenes*, for example, furan, thiophene, pyrrole, pyridine, and the pyrylium and thiinium ions. As regards stability and reactivity, they can be compared to the corresponding benzenoid compounds [1a–d].

The antiaromatic systems, that is, systems possessing 4n delocalized electrons, for example, oxepine, azepine, thiepine, azocine, and 1,3-diazocine, as well as the corresponding annulenes, are, by contrast, much less stable and very reactive.

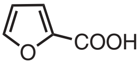
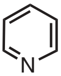
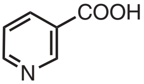
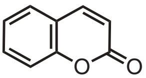
The classification of heterocycles as heterocycloalkanes, heterocycloalkenes, heteroannulenes, and heteroaromatics allows an estimation of their stability and reactivity. In some cases, this can also be applied to inorganic heterocycles. For instance, borazine (**3**), a colorless liquid, bp 55 °C, is classified as a heteroaromatic system.

Reference

1. (a) von Rague Schleyer, P. and Jiao, H. (1996) *Pure Appl. Chem.*, **68**, 209; (b) von Rague Schleyer, P. and Jiao, H. (2001) *Chem. Rev.*, **101**, 1115; (c) Bird, C.W. (1998) *Tetrahedron*, **54**, 10179; (d) Krygowski, T.M., Cyranski, M.K., Czarnocki, Z., Häfelinger, G., and Katritzky, A.R. (2000) *Tetrahedron*, **56**, 1783.

2
Systematic Nomenclature of Heterocyclic Compounds

Many organic compounds, including heterocyclic compounds, have a *trivial name*. This usually originates from the compounds occurrence, its first preparation, or its special properties.

Structure	**Trivial name**	**Systematic name (IUPAC)**
	ethylene oxide	oxirane
	pyromucic acid	furan-2-carboxylic acid
	pyridine	pyridine (instead of azine)
	nicotinic acid	pyridine-3-carboxylic acid
	coumarin	2*H*-chromen-2-one

The derivation of the *systematic name* of a heterocyclic compound is based on its structure. Nomenclature rules have been drawn up by the IUPAC Commission and these should be applied when writing theses, dissertations, publications, and patents. These rules are listed in Section R-2 of the IUPAC ‘‘Blue Book’’ together with worked examples (H. R. Panico, W. H. Powell, J.-C. Richer, *A Guide to IUPAC Nomenclature of Organic Compounds, Recommendations 1993;* Blackwell Scientific: Oxford, 1993; the previous IUPAC Blue Book: J. Rigandy, S. P. Klesney *Nomenclature of Organic Chemistry;* Pergamon: Oxford, 1979).

The IUPAC rules are not given in detail here, rather instructions are given for formulating systematic names with appropriate reference to the Blue Book.

Every heterocyclic compound can be referred back to a *parent ring system*. These systems have only H-atoms attached to the ring atoms. The IUPAC rules allow two nomenclatures.

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The *Hantzsch-Widman nomenclature* is recommended for 3- to 10-membered heterocycles. For larger ring heterocycles, *replacement nomenclature* should be used.

It should be noted that in some cases, for example, for pyridine, the trivial name has become a ''permitted trivial name'' and should be used as the systematic name instead of the *Hantzsch-Widman* indication (see below).

2.1
Hantzsch-Widman Nomenclature

(1) Type of heteroatom

The type of heteroatom is indicated by a prefix according to Table 2.1. The sequence in this table also indicates the preferred order of prefixes (*principle of decreasing priority*).

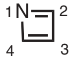
(2) Ring size

The ring size is indicated by a suffix according to Table 2.2. Some of the syllables are derived from Latin numerals, namely *ir* from tri, *et* from tetra, *ep* from hepta, *oc* from octa, *on* from nona, and *ec* from deca.

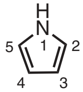
(3) Monocyclic systems

The compound with the maximum number of noncumulative double bonds is regarded as the parent compound of the monocyclic systems of a given ring size. The naming is carried out by combining one or more prefixes from Table 2.1 with a suffix from Table 2.2. If two vowels succeed one another, the letter a is omitted from the prefix, for example, azirine (not azairine).

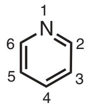
azirine



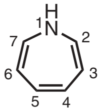
azete



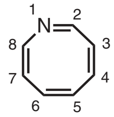
pyrrole
(azole)



pyridine
(azine)



azepine



azocine

Table 2.1 Prefixes to indicate heteroatoms.

Element	Prefix	Element	Prefix
O	oxa	**Bi**	bisma
S	thia	**Si**	sila
Se	selena	**Ge**	germa
Te	tellura	**Sn**	stanna
N	aza	**Pb**	plumba
P	phospha	**B**	bora
As	arsa	**Hg**	mercura
Sb	stiba		

Table 2.2 Stems to indicate the ring size of heterocycles.

Ring size	Unsaturated	Saturated
3	irene[a]	irane[b]
4	ete	etane[b]
5	ole	olane[b]
6A[c]	ine	ane
6B[c]	ine	inane
6C[c]	inine	inane
7	epine	epane
8	ocine	ocane
9	onine	onane
10	ecine	ecane

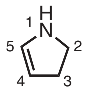
[a] The stem "irine" may be used for rings containing only N.

[b] The traditional stems "iridine", "etidine", and "olidine" are preferred for N-containing rings and are used for saturated heteromonocycles having three, four, or five ring members, respectively.

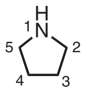
[c] The stem for six-membered rings depends on the least preferred heteroatom in the ring: that immediately preceding the stem. To determine the correct stem for a structure, the set below containing this least-preferred heteroatom is selected.
6A: O, S, Se, Te, Bi, Hg, 6B: N, Si, Ge, N, Pb, and 6C: B, P, As, Sb.

Note that trivial names are permitted for some systems, for example, pyrrole and pyridine. Permitted trivial names can be found in the latest IUPAC Blue Book pp. 166–172; if a trivial name is permitted then it should be used.

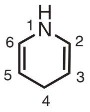
Partly or completely saturated rings are denoted by the suffixes according to Table 2.2. If no ending is specified the prefixes dihydro-, tetrahydro-, and so on should be used.



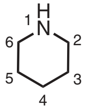
2,3-dihydropyrrole



pyrrolidine



1,4-dihydropyridine



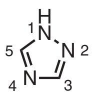
piperidine (hexahydropyridine)

- Monocyclic systems, one heteroatom

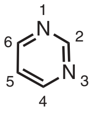
  The numbering of such systems starts at the heteroatom.

- Monocyclic systems, two or more identical heteroatoms

The prefixes di-, tri-, tetra-, and so on, are used for two or more heteroatoms of the same kind. When indicating the relative positions of the heteroatoms, the principle of the lowest possible numbering is used, that is, the numbering of the system has to be carried out in such a way that the heteroatoms are given the lowest possible set of locants:



1,2,4-triazole
(not 1,3,5-triazole)

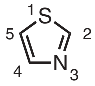


pyrimidine
(1,3-diazine, not
1,5-diazine)

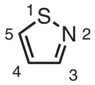
In such a numerical sequence, the earlier numbers take precedence, for example, 1,2,5 is lower than 1,3,4.

- Monocyclic systems, two or more different heteroatoms

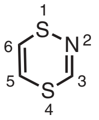
For heteroatoms of different kinds, prefixes are used in the order in which they appear in Table 2.1, for example, thiazole, not azathiole; dithiazine, not azadithiine. The heteroatom highest in Table 2.1 is allocated the 1-position in the ring. The remaining heteroatoms are assigned the smallest possible set of number locants:



thiazole
(1,3-thiazole)



isothiazole
(1,2-thiazole)

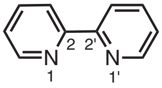


1,4,2-dithiazine

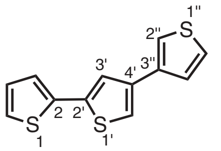
Although in the first example the systematic name is 1,3-thiazole, the locants are generally omitted because, except for isothiazole (1,2-thiazole), no other structural isomers exist. Similar rules apply to oxazole (1,3-oxazole) and isoxazole (1,2-oxazole).

- Identical systems connected by a single bond

Such compounds are defined by the prefixes bi-, ter-, quater-, and so on, according to the number of systems, and the bonding is indicated as follows:



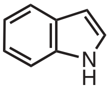
2,2'-bipyridine



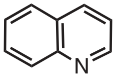
2,2':4',3'-terthiophene

(4) Bicyclic systems with one benzene ring

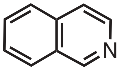
Systems in which at least two neighboring atoms are common to two or more rings are known as *fused systems*. For several bicyclic benzo-fused heterocycles, trivial names are permitted, for example:



indole

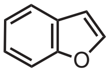


quinoline

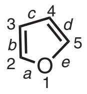


isoquinoline

If this is not the case, and only the heterocycle has a trivial name, then the systematic name is formulated from the prefix benzo- and the trivial name of the heterocyclic component as follows:



benzo[*b*]furan



furan

The system is dissected into its components. The heterocyclic component is regarded as the *base component*. The bonds between the ring atoms are denoted according to the successive numbers of the ring atoms by the letters *a*, *b*, *c*, and so on. The letter *b* in brackets between benzo and the name of the base component denotes the atoms of the base component which are common to both rings. The letter must be as early as possible alphabetically, and hence benzo[d]furan is incorrect.

It is generally accepted that the numbering of the whole system in the case of bi- and polycyclic systems should be done independently of the numbering of the components, and as follows:

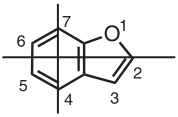
The ring system is projected onto rectangular coordinates in such a way that

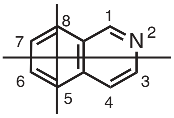
- as many rings as possible lie in a horizontal row
- a maximum number of rings are in the upper right quadrant.

The system thus oriented is then numbered in a clockwise direction commencing with that atom which is not engaged in the ring fusion and is furthest to the left

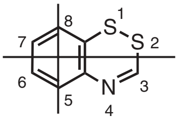
- in the uppermost ring or
- in the ring furthest to the right in the upper row.

C-Atoms which belong to more than one ring are omitted. Heteroatoms in such positions are, however, included. If there are several possible orientations in the coordinate system, the one in which the heteroatoms bear the lowest locants is valid:

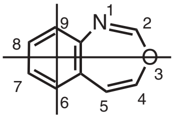




If the base component does not have a trivial name, the entire system is numbered as explained above and the resulting positions of the heteroatoms are placed before the prefix benzo:



1,2,4-benzodithiazine



3,1-benzoxazepine

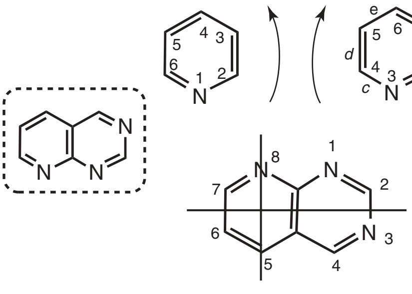
(5) Bi- and polycyclic systems with two or more heterocycles

First the base component is established. To this end the criteria in the order set out below are applied, one by one, to arrive at a decision. The base component is

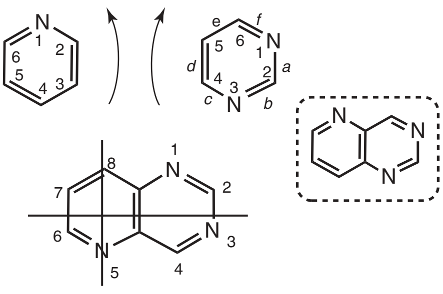
- a nitrogen-containing component
- a component with a heteroatom, other than nitrogen, which is as high as possible in Table 2.1
- a component with as many rings as possible (e.g., bicyclic condensed systems or polycyclic systems which have trivial names)

- the component with the largest ring
- the component with most heteroatoms
- the component with the largest number of heteroatoms of different kinds
- the component with the greatest number of heteroatoms which are highest in Table 2.1
- the component with heteroatoms which have the lowest locant numbers.

Two isomers are given as an example:



pyrido[2,3-*d*]pyrimidine

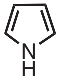


pyrido[3,2-*d*]pyrimidine

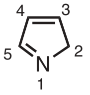
First, the system is dissected into its components. The base component cannot be established until the fifth criterion has been reached: pyrimidine. The bonds between the ring atoms are marked by consecutive lettering according to the serial numbering of the base component. In contrast to the example on p. 8, the fused component must also be numbered, always observing the principle of assignment to the lowest possible locants. The name of the fused component, by the replacement of the terminal "e" with "o," is put before the name of the base component. The atoms common to both rings are described by numbers and letters in square brackets, where the sequence of the numbers must correspond to the direction of the lettering of the base component. Finally the whole system is numbered.

(6) Indicated hydrogen

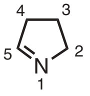
In some cases, heterocyclic systems occur as one or more structural isomers which differ only in the position of an H-atom. These isomers are designated by indicating the number corresponding to the position of the hydrogen atom in front of the name, followed by an italic capital H. Such a prominent H-atom is called an *indicated hydrogen* and must be assigned the lowest possible locant.



pyrrole



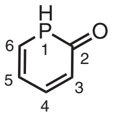
2*H*-pyrrole
(not 5*H*-pyrrole)



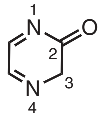
3,4-dihydro-2*H*-pyrrole
(not 4,5-dihydro-3*H*-pyrrole
or Δ^1-pyrroline)

The name pyrrole implies the 1-position for the H-atom.

Heterocyclic compounds in which a C-atom of the ring is part of a carbonyl group are named with the aid of indicated hydrogen as follows:



phosphinin-2-(1*H*)-one



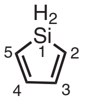
pyrazin-2-(3*H*)-one

2.2

Replacement Nomenclature

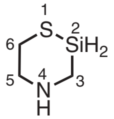
(1) Monocyclic systems

The type of heteroatom is indicated by a prefix according to Table 2.1. As all prefixes end with the letter a, replacement nomenclature is also known as *"a" nomenclature*. Position and prefix for each heteroatom are written in front of the name of the corresponding hydrocarbon. This is derived from the heterocyclic system by replacing every heteroatom by CH_2, CH, or C:



silacyclopenta-2,4-diene
(H.-W.: silole)

cyclopentadiene



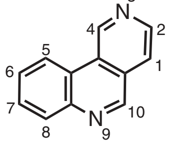
1-thia-4-aza-2-silacyclohexane
(H.-W.: 1,4,2-thiazasilane)

cyclohexane

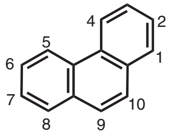
Sequence and numbering of the heteroatoms follow the rules given in Section 2.1. The two compounds chosen as examples could also be named according to the Hantzsch-Widman system.

(2) Bi- and polycyclic systems

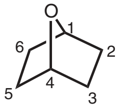
Again, position and prefix are put in front of the name of the corresponding hydrocarbon, but *the numbering of the hydrocarbon is retained*:



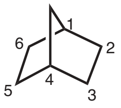
3,9-diazaphenanthrene



phenanthrene

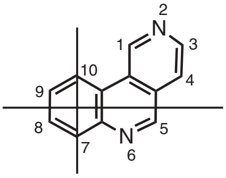


7-oxabicyclo[2.2.1]heptane



bicyclo[2.2.1]heptane

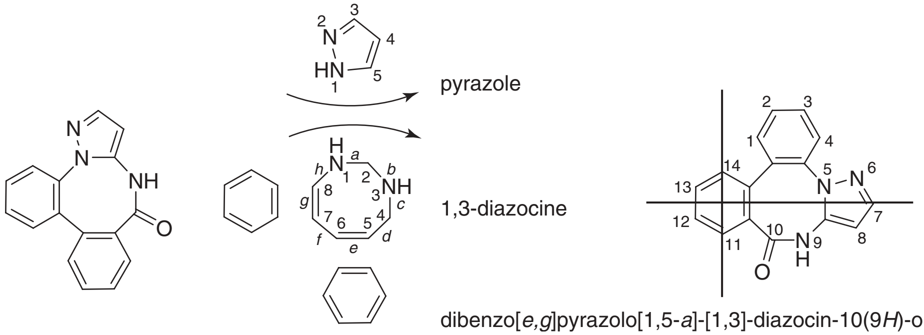
The *Hantzsch-Widman* nomenclature can only be applied to the first example, and this then results in different numbering.



pyrido[4,3-*c*]quinoline

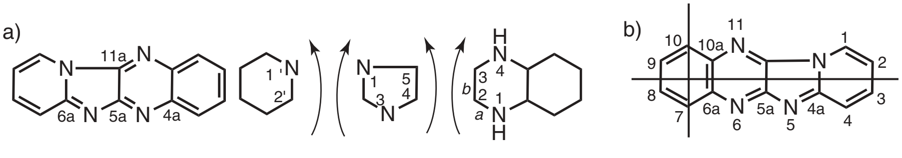
2.3
Examples of Systematic Nomenclature

Finally, the systematic nomenclature of heterocyclic compounds will be illustrated by a few complex examples:



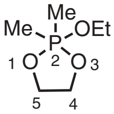
dibenzo[*e,g*]pyrazolo[1,5-*a*]-[1,3]-diazocin-10(9*H*)-one

An analysis of the system reveals two benzene rings, one pyrazole ring and one 1,3-diazocine ring, the latter ring being the base component according to the fourth criterion. The square brackets [1,3] indicate that the position of the two heteroatoms is not the basis for numbering the whole system.



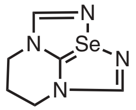
pyridine imidazole quinoxaline pyrido[1',2':1,2]imidazo[4,5-*b*]quinoxaline

According to the third criterion, quinoxaline is the base component. The heterocycle imidazole, which is fused to the base component, is numbered in the usual way; the pyridine ring, however, is denoted by 1′, 2′, and so on, and it is not necessary to mark the double bonds. Pyrido[1′,2′ : 1,2]imidazo denotes one ring fusion, imidazo[4,5-b]quinoxaline the other. For numbering polycyclic systems, five-membered rings must be drawn as shown above and not as regular pentagons. For the orientation in a system of coordinates, an additional rule has to be observed, namely that C-atoms common to two or more rings must be given the lowest possible locant. The numbering in (b) is therefore correct, while that in (a) is wrong, because 10a < 11a.

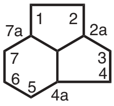


2-ethoxy-2,2-dimethyl-1,2,3λ^5-dioxaphospholane
(the standard bonding number of P is 3)

With ring atoms such as phosphorus, which can be tri- or pentavalent, a non-standard bonding number is indicated as an exponent of the Greek letter λ after the locant. In the example, this is shown by λ^5 (the 1993 Blue Book, p. 21).

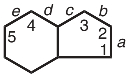


5*H*-2aλ^4-selena-2,3,4a,7a-
tetraazacyclopenta[*c,d*]indene



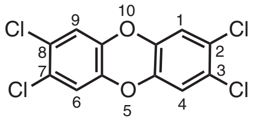
cyclopenta[*c,d*]indene

cyclopentadiene



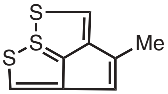
indene

The name is constructed according to replacement nomenclature. The basic hydrocarbon with the greatest number of noncumulative double bonds is cyclopenta[c,d]indene. Note the retention of the numbering.

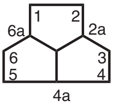


2,3,7,8-tetrachlordibenzo[1,4]dioxin

In this case, [b,e] is omitted after dibenzo since there is no other possibility for ring fusion. This compound is also known as *TCDD* or *Seveso dioxin*.



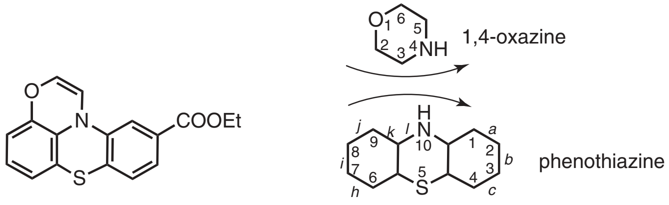
3-methyl-1,6,6aλ^4-trithia-
cyclopenta[c,d]pentalene



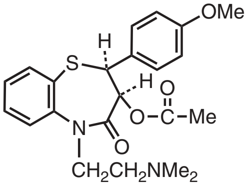
cyclopenta[c,d]pentalene

cyclopentadiene

pentalene

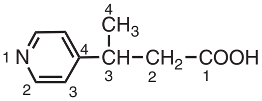


ethyl[1,4]oxazino[2,3,4-*kl*]phenothiazine-6-carboxylate



(2*S*,3*S*)-3-acetoxy-5-(2-dimethylaminoethyl)-2-(4-methoxyphenyl)-2,3,4,5-tetrahydro-1,5-benzothiazepin-4-one

So far, in all the examples, the base compound has been the heterocyclic system. If this is not the case, the univalent radical of the heterocyclic system is regarded as a substituent, for example:



3-(4-pyridyl)butyric acid

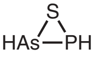
The names of some univalent heterocyclic substituent groups are to be found in the list of trivial names in the 1993 Blue Book, p. 172.

The most important source of information on heterocyclic and isocyclic systems is the *Ring Systems Handbook* of the Chemical Abstracts Service (CAS) published by the American Chemical Society. The 1988 edition is arranged as follows:

Band 1:	Ring Systems File I:	RF 1–RF 27595,
Band 2:	Ring Systems File II:	RF 27596–RF 52845,
Band 3:	Ring Systems File III:	RF 52846–RF 72861,
Band 4:	Ring Formula Index, Ring Name Index.	

Since 1991, cumulative supplements have been published annually.

The *Ring Systems File* is a catalog of structural formulas and data. It lists the systems consecutively with numbering RF 1 to RF 72861 on the basis of a ring analysis. The Ring Systems File starts with the following system:



The ring analysis shows:

1 RING: 3
AsPS