Nomenclature, Synthesis and Applications of Spirocyclic Compounds

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PREFACE

Spirocycle compounds are twisted structures with two or more rings that share a single atom and plays a significant role in life. Spiro molecules are exciting classes of chemicals because of their rigid conformational features and three-dimensional geometry, which are used in organic optoelectronic devices, pharmaceutical chemistry, and materials science, and as an intermediate in organic chemistry. Developing spirocycle compounds is challenging in modern organic synthesis because it includes creating a quaternary center, one of the most challenging works among synthetic transformations.

This book comprehensively overviews the tremendous and advanced works reported about spiro compounds during the last 20 years. The primary purpose of this comprehensive book is introduction spiro compounds (chapter 1), naming (chapter 2), presentation of the most common, new, and diverse synthetic methodologies (chapters 3-5), and applications of spiro compounds (chapter 6) to academic staff and industry experts to become familiar with.

In particular, this book presents a considerable tool for chemists working in this research area. Moreover, the increasing necessity and interest in efficient, versatile, and potential synthetic procedures to achieve spiro compounds quickly and economically and the corresponding libraries makes this book a vital reference instrument in organic synthesis. This wide-ranging collection can inspire academics and industrialists and help in their future progress. We hope to comply with the expectations of a significant part of the scientific community, organic chemistry faculties, and students.

In the end, we would like to thank the colleagues who helped us in making this great work with their valuable and exciting reports.

LIST OF ABBREVIATIONS

AChE	Acetylcholine-esterase
AEMs	Anion-exchange membranes
AIBN	Azobisisobutyronitrile
AIDS	Acquired immunodeficiency syndrome
aza-MBH	Aza-Morita-Baylis–Hillman
BGTC	Bottom-gate and top-contact
BLHPC	Bent ladder-type hexaphenylene
Boc	*tert*-Butyloxy-carbonyl
BPI	Phenanthroimidazole
BuChE	Butyryl-cholinesterase
CAN	Ceric ammonium nitrate
CCR5	Chemokine receptor 5
CE	Current efficiency
CFA	Complete freund's adjuvant
CIP	Cahn-Ingold-Prelog
CM	Cross metathesis reaction
CNS	Central nervous system
CP	Cationic ring-opening polymerization
CPA	Chiral phosphoric acid
CTLs	Charge transport layers
CTMs	Charge transporting materials
DAB	1,4-Dideoxy-1,4-imino-*D*-arabinitol
DABCO	1,4-Diazabicyclo[2.2.2]octane
DAD	1,4-Diazabuta-1,3-diene
DAF	Diazafluorene
1,3-DC	1,3-Dipolar cycloaddition
1,3-DCRs	1,3-Dipolar cycloaddition reactions
DFT	Density functional theory
DIMCARB	*N*,*N*-Dimethyl ammonium *N*′,*N*′-dimethyl carbamate
DIPEA	*N*-Ethyldiisopropylamine
DLW	Direct laser writing
DMAD	Dimethyl acetylenedicarboxylate
DMAP	4-Di-methylaminopyridine

DMPA	Di-*p*-methoxy phenylamine
dr	Diastereoisomeric ratio
DSA-Ph	*p*-Bis(*p*-*N*,*N*-diphenyl-aminostyryl)benzene
DSCs	Dye-sensitized solar cells
D-Spiro-A	Donor-Spiro-Acceptor
DSX-LPP	Dispiroxanthene-ladderpenta phenylene
EBV	Epstein–Barr virus
ECD	Electrochromic devices
ee	Enantiomeric excess
EIS	Electrochemical impedance spectroscopy
EL	Electroluminescence
er	Enantiomeric ratio
ESE	Excess strain energy
ETL	Electron transporting layer
EQE	External quantum efficiency
FET	Field-effect transistor
FIB	The level of fibrinogen
FMO	Frontier molecular orbital
FOLEDs	Fluorescent OLEDs
FRAP	Ferric reducing anti-oxidant power
FRP	Free-radical polymerization
ΔG	Free binding energy
GER	Group equivalent reaction
GP	Glycogen phosphorylase
HAT	Hydrogen atom transfer
HAT	Human african trypanosomiasis
HDAc2	Histone deacetylase 2
HDF	Human dermal fibroblast
HGR	Human glutathione reductase
HOMO	Highest occupied molecular orbital
HTIB	[Hydroxy(tosyloxy)iodo]-benzene
HTL	Hole transport layer
HTM	Hole-transporting molecule
HWE	Horner–Wadsworth–Emmons
ICT	Intramolecular charge transfer
IE	Ionization energy
IEDDA	Inverse-electron-demand oxa-hetero-Diels–Alder
IEDDAR	Inverse-electron-demand Diels-Alder reaction
IL	Interlayers
IMDA	Intramolecular Diels-Alder
INH	Isoniazid

IRP	Intermolecular radical pair
$\boldsymbol{J}_{SC}$	Short-circuit current density
K–DA-E	Knoevenagel/Diels–Alder/epimerization
LEDs	Light-emitting diodes
LPDE	Lithium perchlorate in diethyl ether
LPPP	Ladder-type poly(*p*-phenylene)s
LRRK2	Leucine-rich repeat kinase 2
LUMO	Lowest unoccupied molecular orbital
MBH	Morita-Baylis-Hillman
MC	Merocyanine
MC2	*Mycobacterium smegmatis*
MDR	Multidrug resistance phenotype
MDR-TB	Multidrug-resistant *Mycobacterium tuberculosis*
MED	Minimal effective dose
MES	Maximum electroshock seizure
MIC	Minimum inhibitory concentration
MIT	Molecular integration technology
mitoKATP	Mitochondrial ATP-dependent potassium channels
MP2	Møller–Plesset perturbation theory
MPP^+	1-Methyl-4-phenylpyridinium
MTB	*Mycobacterium tuberculosis* $H_{37}Rv$
NBS	*N*-Boromosuccimide
NCS	*N*-Chlorosuccinimide
NDA	Nitroso Diels-Alder
NF-κB	B Cells
NHC	*N*-Heterocyclic carbene
NIS	*N*-Iodosuccinimide
NMP	*N*-Methyl-2-pyrrolidone
NPS007994	*Streptomyces nodosus*
NPSGs	Nanopolyspirogrids
OFBA	*o*-Fluorobenzoic acid
OFETs	Organic field-effect transistors
OLEDs	Organic light-emitting diodes
OPVs	Organic photovoltaic devices
***o*-QDMs**	*Ortho*-quinodimethanes
***o*-QMs**	*Ortho*-quinomethanes
OSCs	Organic semiconductors
PA	Phenylacridine
PCs	Photoredox catalysts
PCEs	Power conversion efficiency
PCMs	Piezochromic materials

PCR	Peptide coupling reagent
PE	Power efficiency
PET	Photoinduced electron transfer
PFF	Pore filling fraction
PhOLEDs	Phosphorescent organic light-emitting diodes
PI	Photoinitiator
PIA	Introduced photoinduced absorption
PIFA	[Bis(trifluoroacetoxy)iodo]benzene
PL	Photoluminescence
PPV	Poly(*p*-phenylene vinylene)
***p*-QMs**	*Para*-quinone methides
PSCs	Perovskite solar cells
PTAA	Poly(triarylamine)
PTC	Phase transfer catalysis
PTSA	*p*-Toluenesulfonic acid
PTZ	Pentylenetetrazol
RCEM	Ring-closing enyne metathesis
RCM	Ring-closing metathesis
RFID	Radio frequency identification
RH	Relative humidity
RON	Reductive oxy-Nazarov
rr	Regioselective ratio
RRM	Ring-rearrangement metathesis
RSE	Ring strain energy
RT	Room temperature
RT-PCR	Reverse transcription and polymerase chain reaction
rubrene	5,6,11,12-Tetraphenylnaphthacene
RVD	Regulatory volume decrease
SAF	Spiro-acridine-fluorene
SAMs	Self-assembled monolayers
sarcKATP	Sarcolemmal ATP-dependent potassium channels
SBF	9,9′-Spirobifluorene
SBTF	Spiro[benzotetraphenefluorene]
SC	Solar cell
SCD1	Stearoyl-CoA desaturase-1
SE	Strain energy
SEI	Semiconductor-electrolyte interface
SET	Single-electron transfer
SFX	Spiro[fluorene-9,9′-xanthene]
SGR	Seyferth−Gilbert reagent

SI	Selectivity index
SIADH	Syndrome of inopportune anti-diuretic hormone
SMOLEDs	Small molecule organic light-emitting diodes
SOI	Secondary orbital interaction
SP	Spiropyran
SSDSCs	Solid-state dye-sensitized solar cells
SSYX	Shensong Yangxin capsule
STED	Stimulated-emission depletion
STP	Spirothiopyran
SZMC	Spirocyclic zwitterionic Meisenheimer
TADF	Thermally activated delayed fluorescence
TBAB	Tetra-*n*-butyl-ammonium bromide
TBAF	Tetra-*n*-butylammonium fluoride
TBAHS	Tetrabutylammonium hydrogen sulfate
TBHP	*tert*-Butyl hydroperoxide
TbTR	Trypanosoma brucei TR
TCO	Transparent conducting oxide
TDM	Transition density matrix
TFA	Trifluoroacetic acid
Th2	T Helper type 2
TMSCN	Trimethylsilyl cyanide
TMSOTf	Trimethylsilyl triflate
TNF-α	Tumor necrosis factor-alpha
TPD	*N*,*N*′-Diphenyl-*N*,*N*′-bis(3-methyl-phenyl)-1,1′-bi phenyl-4,4′-diamine
TPT	2,4,6-Triphenylpyrylium tetarfluoroborate
TR	Trypanothione reductase
TRPL	Time-resolved photoluminescence
TX	Thioxanthene
TXO_2	Dioxothioxanthene
U4CC	Ugi four-component condensation
UPS	Ultraviolet photoemission spectroscopy
V_{oc}	Open-circuit voltages
VECs	Vinylethylene carbonates
VOFET	Vertical organic field-effect transistor
V_2RA	V_2-receptor antagonists
YCK	Yuehchukene

1

SPIROCYCLIC COMPOUNDS

1.1. Introduction

Spirocyclic compounds, also known as spiro compounds, are twisted structures with two or more rings that share a single atom [1]. The connecting atom, also named the spiroatom, is most often a quaternary carbon (spiro carbon). Spirocyclic compounds can be broadly classified into two categories based on the nature of their rings: carbocyclic and heterocyclic. Carbocyclic spiro compounds contain only carbon atoms in their rings, while heterocyclic spiro compounds contain at least one heteroatom such as nitrogen, oxygen, or sulfur. These rings can be similar or different and the simplest spiro compounds are bicyclic. According to the number of spiro atoms, these compounds are classified as monospiro, dispiro, trispiro, etc.

In 1900, von Baeyer found the first spiro compound [2]. The spiro center in these compounds creates a naturally occurring three-dimensional structure which can reduce the conformational entropy penalty associated with target binding and produce diverse three-dimensional shapes [3]. Additionally, the perpendicular arrangement of spiro compounds results in the suppression of molecular interactions of π-systems, enhances solubility, and prevents the formation of excimers often observed in solid-state fluorescent dyes. Furthermore, the doubling of molecular weight, combined with the cross-shaped molecular structure and rigidity of spiro compounds, leads to entanglement in the amorphous solid state, inhibiting crystallization [4]. Spiro compounds can exhibit central or axial chirality, meaning spiroatoms can be chiral even without four different substituents (see Figure 1-1) [5].

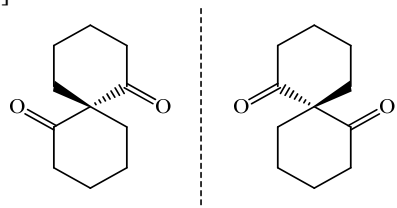


Fig. 1-1. Spirocycles with axial chirality.

Spiro molecules are an exciting class of chemicals due to their rigid conformational features and three-dimensional geometry which have numerous applications in organic optoelectronic devices, pharmaceutical chemistry, materials science, and as intermediates in organic synthesis [6-8]. Many natural products contain spiro motifs in their structure, such as Chitosenine **1**, Marcfortine B **2**, ACAT inhibitor **3**, Fredericamycin **4**, Elmenol G **5**, (-)-Horsfiline **6**, (+)-Elacomine **7**, Azaspiracid **8**, 6-Oxoleuconoxine **9**, among others (see Figure 1-2) [9-13].

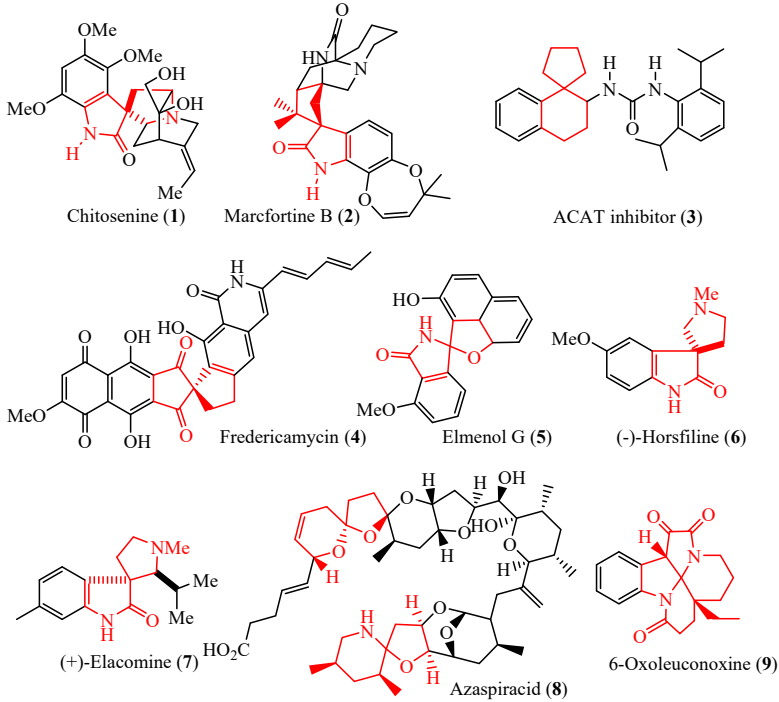


Fig. 1-2. Example of natural products containing spiro linkages.

Furthermore, spiro units form the core structures of essential commercial drugs like Spironolactone **10**, Drospirenone **11**, Ameinonide **12**, Buspirone **13**, Cevimeline **14**, Apalutamide **15**, Eplerenone **16**, Fenspiride **17**, and Fluspirilene **18**, as shown in Figure 1-3 [14].

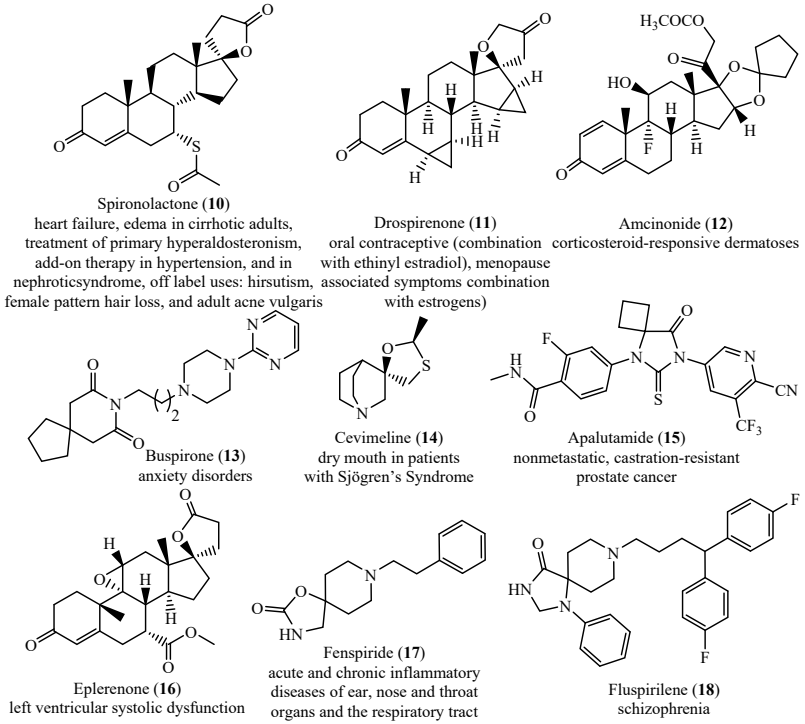


Fig. 1-3. Example of drugs containing spiro motifs.

1.2. Ring strain energy

One of the fundamental properties of spiro compounds is their ring strain energy (RSE), which refers to the increased energy of the molecule compared to its corresponding acyclic molecule. The concept of strain and strain energies (SEs) provides a basis for correlating molecular structures, stabilities, and reactivities. To quantitatively assess strain and SEs, one can take the difference between the enthalpy of formation, $\Delta H_f°(g)$, of the substance under consideration (either theoretically calculated or experimentally determined) and that of a hypothetical strain-free model. There are two approaches to this: (i) based on bond energies and (ii) based on group increments. Since spiro compounds contain multiple rings, it is important to determine whether the total RSE of a spiro compound is exclusively the sum of the RSE of the component rings. The excess strain energy (ESE) is the difference between the total RSE of a compound containing multiple rings and the sum of the RSE of the individual rings.

Hence, Rüchard et al. evaluated the enthalpies of formation for triangulanes and spiro-cyclopropanated cyclobutanes by measuring their heat of combustion in a micro calorimeter (Figure 1-4). They found that in triangulanes **19-22** (in which every ring is a three-membered hydrocarbon), there is an excess ring strain energy of 8.6 kcal/mol per spiro atom. Such an additional strain increment is virtually nonexistent for **25** (0.8 ± 0.4 kcal/mol), **26** (0.6 ± 0.2 kcal/mol), and **27** (0.3 ± 0.3 kcal/mol) but significant for **28** (2.4 ± 0.5 kcal/mol) [15, 16].

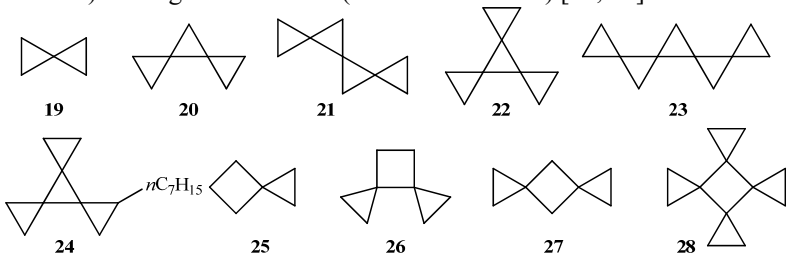
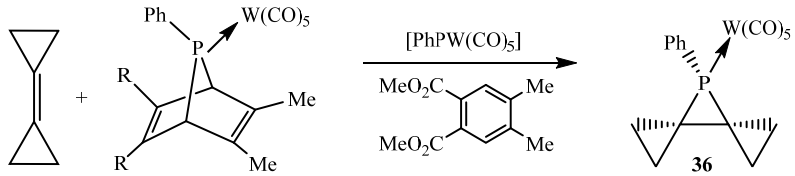


Fig. 1-4. Triangulanes and spirocyclopropanated cyclobutanes were studied by Rüchard et al.

Lammertsma et al. synthesized the first phospha[3]triangulane **36** as a $W(CO)_5$ complex which is a remarkably stable compound and possesses a Ph group (Scheme 1-1).



Scheme 1-1. Synthesis of phospha[3]triangulane **36**.

By comparing the X-ray structures of Ph-P substituted phospha-spiro-pentane **34** and phosphirane **35** complexes, researchers observed a denser structure. The heats of formation for the parent organophosphorus compounds and their hydrocarbon analogs were estimated using ring separation reactions and G2MP2 theory. The study found that the excess strain in phospha[*n*]triangulanes, which is the strain for spiro carbons over that of the three-membered rings, is approximately 5.3 kcal/mol per spiro carbon. This is around 40% less than the excess strain observed in linear [*n*]triangulane hydrocarbons (Figure 1-5) [17].

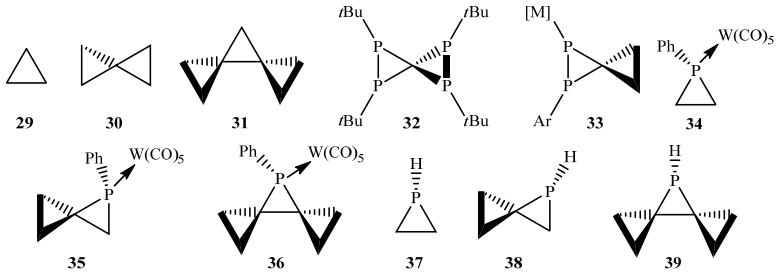


Fig. 1-5. Compounds **29-39** were studied by Rüchard et al.

The Lammertsma group investigated the ring strain in 2-aza-1-phospha-bicyclo[*n*.1.0]alkanes (n = 1-5) **40-44** using homodesmotic reactions at the G3(MP2) level. They compared the impact of cyclopropa(e)nation and heteroatom substitution with the corresponding bicyclic hydrocarbons and separate ring systems (Figure 1-6). The study revealed that the strain caused by fusion with cyclopropane is the sum of the individual rings. In contrast, the strain resulting from fusion with cyclopropene is much larger than the sum of rings due to the inverted nature of the bridgehead carbon. Substitution with nitrogen and phosphorus is favorable in all ring structures except in cyclohexane, and its effect is more pronounced in the more condensed structures. The evaluated SEs correlate very well with the experimental stability and reactivity of the bicyclic iron-amino phosphirane and phosphirene complexes [18].

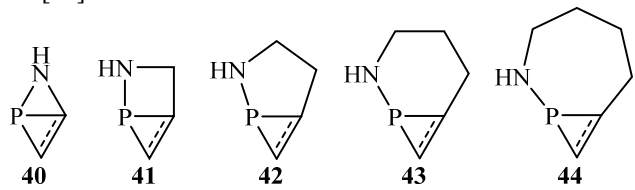


Fig. 1-6. Structure of 2-aza-1-phosphabicyclo[*n*.1.0]alka(e)nes **40-44**.

In 2014, Stedjan et al. calculated the RSEs for oxygen-containing spiro compounds **45-50** using the group equivalent reaction formalism (Figure 1-7). They found that the compounds containing two three-membered rings possess the highest RSEs and showed the most significant ESE of about 12 kcal/mol. The RSEs of cyclic lactones differ with ring size from those of cyclic ethers. Cyclic ethers' RSEs decrease by a small amount from the three- to four-membered rings, then decrease drastically

as the ring increases to 5 atoms, and approach zero for the six-membered ring, representing the same unexpected behavior as seen in cycloalkanes. Cyclic lactones' RSEs reduce linearly to almost zero from the three- to the five-membered ring, then increase by 1-2 kcal/mol in the six-membered ring. Lactone-containing spiro compounds reveal regularly diminishing ESE as the size of the lactone ring increases, down to about 3 kcal/mol in the δ-lactone-containing spiro compound. Substitution of methyl group decreases RSE in these oxygen-containing spiro compounds, but fluorine substitution remarkably increases RSE, as has been reported in other compounds. But it has been shown that RSE alone is not fully related to the chemical reactivity of these spiro compounds [15].

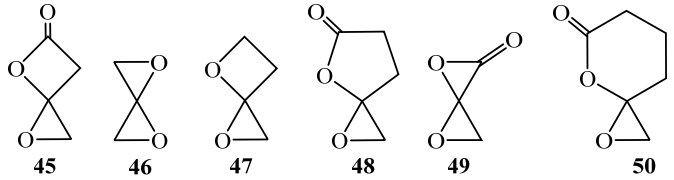


Fig. 1-7. Structure of oxygen-containing spiro compounds **45-50**.

1.3. Chirality

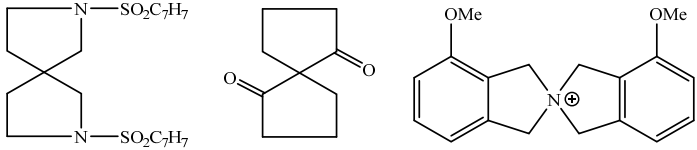
Chiral spiro compounds have attracted the attention of researchers and scientists owing to their potential applications in the pharmaceutical industry as either active pharmaceutical ingredients, catalysts in synthesizing active enantiomers, or surface modifiers on silica particles to resolve enantiomers [19].

The spatial orientation of molecules, i.e., their stereochemistry, has been one of the most important features of organic compounds since the tetrahedral structure of carbon atoms in organic molecules was introduced by van't Hoff and Lebel in the 19th century. In the pharmaceutical sciences, stereochemistry is of prime significance in the interaction of drugs and organisms since all receptors in human body are chiral and probably show different pharmacologic effects and pharmacokinetics between enantiomers. Hence, the US FDA required in 1992 that the properties of each enantiomer in a racemate should be explored individually before the drug is taken to the market as a pure enantiomer or as a racemate [20].

Absolute configuration is the spatial arrangement of the atoms of a chiral molecular entity (or group) and its stereochemical description, e.g., *R* or *S*. Neither the sign nor the magnitude for the rotation per se offers any information concerning the absolute configuration of a substance [21].

Historically, Cahn-Ingold-Prelog (CIP) sequence rules were first introduced to identify a molecule's spatial arrangement of atoms using simple, mostly atom- or bond-based stereo descriptors in 1956 [22].

Molecules with carbon and metal atoms can exhibit chirality in three ways: axial, central, and planar chirality [23]. Determining the absolute configuration of molecules with axial symmetry, which are dissymmetric but not asymmetric, presents intriguing challenges due to the absence of a formal asymmetric carbon that can serve as a basis for configurational correlations. Compounds with C_2 symmetry, such as allenes, spiranes, hindered biphenyls, hexahelicene, and *trans*-cyclooctene, are of particular interest. Both chemical and crystallographical methods have been used to address these cases, leading to ingenious solutions. Spiranes, due to their relatively rigid geometry, offer a unique opportunity to study interactions between functional groups held in fixed relative orientations. As a result, they are valuable substrates for chiroptical studies, including rotation of the sodium D line, ORD, and CD. However, assignments of absolute configuration to chiral C_2 spiranes were not made until 1968-1969, when configurations were assigned for spiranes **5l**, **52**, and **53** (Figure 1-8) [24].

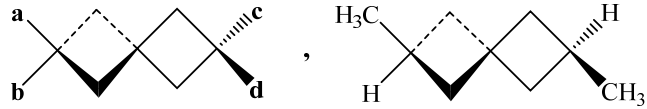


51 **52** **53**

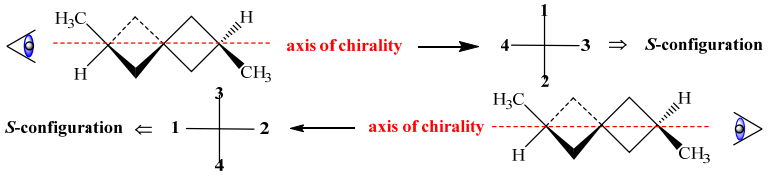
Fig. 1-8. Chemical structure of spiro compounds **51-53**.

The spiro compound is chiral when:

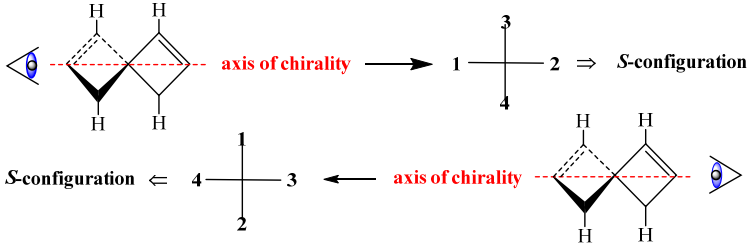
The representations a, b, c, and d are different in such a way that the molecule does not have the chiral center, chiral axis, and chiral plane.



So, the eye can be put in the left or right of the molecule as below and the priority of representations a, b, c, and d is determined according to the CIP rule:



In the spiro-alkadiene compound, the eye can be put in left or right of the molecule as below and the priority of groups (double and single bonds) is determined according to the CIP rule:



1.4. Spiro-aromaticity

Aromaticity is a fundamental concept in chemistry, but a precise definition has remained elusive [25]. Typically, aromatic compounds exhibit the following characteristics, although there are exceptions: (i) planarity with cyclic delocalized 4n+2 π electrons (Hückel's rule); (ii) equalization of bond lengths; (iii) deshielded chemical shifts of exocyclic protons in the ^{1}H NMR spectrum; (iv) the ability to undergo electrophilic substitution reactions; and (v) greater stability than their non-aromatic isomers [26]. According to van't Hoff's "tetrahedral carbon theory," organic compounds with a spiro carbon atom cannot be aromatic due to the sp^3 hybridization of the carbon atom. However, in 2002, Rzepa et al. suggested that the spiro atom itself could participate in conjugation to form a class of spiro-aromatic systems in which each ring could maintain aromaticity independently or join together to exhibit global aromaticity. When the spiro atom is carbon, spiro-aromaticity cannot be achieved because it has only four valence electrons. However, by using transition metals as the spiro atom, Huang et al. discovered two types of bis-spiro metallic-aromatics with square planar (Type I, Figure 1-9a) and tetrahedral (Type II, Figure 1-9b) geometries. The d electron configurations of the metal centers largely dictate their geometric and electronic structures. Huang et al. suggested that the metal center should have more empty d-orbitals to form more metal-aromatic tris-spiro structures. Rzepa et al.

evaluated some tris-spiro-aromatic candidates theoretically, using P, As, or V as the spiro atom, which demonstrated a certain degree of aromaticity, but none of them have been synthesized yet. Although Craig-Möbius type molecular orbitals were found in $Ta(DAD)^{3+}$ (DAD = 1,4-diazabuta-1,3-diene), there is not enough evidence to support its aromaticity. Additionally, the presence of Möbius-type orbitals in metallacycles is only a necessary condition, rather than sufficient, for Möbius aromaticity because Hückel aromatic systems with transition metals may also involve such orbitals, as revealed by Mauksch et al. The Huang group disclosed a hexalithio spiro vanada-cycle as a tris-spiro metalla-aromatic compound (Type III, Figure 1-9c). The V atom interacts with the π* orbital of the three biphenyl ligands via its two 3d-orbitals, resulting in three metallaaromatic rings that form a 40π Craig-Möbius aromatic system [27].

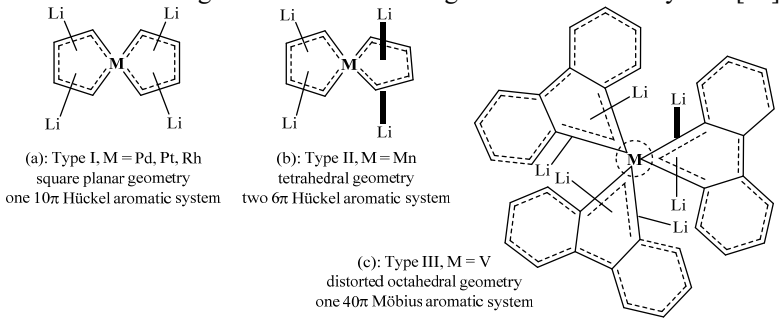


Fig. 1-9. Three types of spiro metallaaromatics.

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2

NOMENCLATURE OF SPIRO COMPOUNDS

2.1. IUPAC Nomenclature of Spiro Compounds

The nomenclature and name "spirane" were first proposed by von Baeyer for bicyclic compounds with one common atom to both rings which intersect at a single point. Later, Radulescu extended this nomenclature to include spiro-fused ring systems and recognized that each ring must be named individually, along with specifying the spiro-fusion details. Patterson also utilized these two systems in his analysis of ring systems. The Chemical Society introduced a third method for naming spiro compounds which was later incorporated into the IUPAC rules along with the other two methods [1, 2].

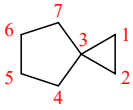
2.2. Compounds with only monocyclic ring components

Monospiro hydrocarbons are composed of two saturated cycloalkane rings and are named using a specific nomenclature convention. The prefix "spiro" is added to a von Baeyer descriptor that indicates the number of carbon atoms connected to the spiro atom in each ring, arranged in ascending order and separated by a period and enclosed in square brackets. The name of the original hydrocarbon indicates the total number of skeletal atoms.

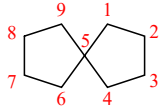
In non-substituted monospiro compounds, the carbon atoms are numbered continuously, beginning from a ring atom that is adjacent to the spiro atom, proceeding through the smaller ring (if present), then through the spiro atom, and finally, around the second ring. Therefore, the general format for writing IUPAC nomenclature for non-substituted spiro compounds is spiro[a.b]alkane.

For substituted spiro compounds, the nomenclature convention is slightly different. The name starts with the prefix indicating the position of the substituents followed by the spiro descriptor which includes the number of atoms in the smaller and larger rings, respectively, in the spiro ring system, enclosed in square brackets. The numbering of carbon atoms is done from the smaller ring to the larger ring, giving the substituents the lowest possible numbers. When there are two or more substitutions, the

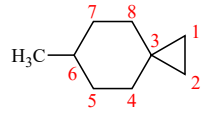
numbering is done in such a way that it gives the substitutions the lowest numbers [1, 2].



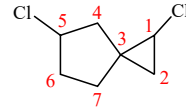
Spiro[2.4]heptane



Spiro[4.4]nonane

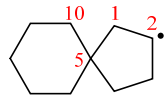


6-Methylspiro[2.5]octane



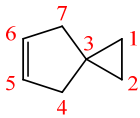
1.5-Dichlorospiro[2.4]heptane

The method mentioned for monocyclic spiro compounds is also used for radical monocyclic spiro rings, with the difference that they are named by replacing the "-ane" ending of the systematic name of the parent hydride with "-yl" [1].

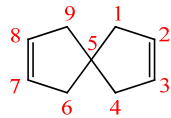


Spiro[4.5]decan-2-yl

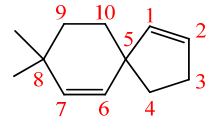
When monospiro compounds possess a double bond, the same numbering pattern is retained, but in such a direction around the rings that the double bonds receive numbers as low as possible. The format of writing the IUPAC nomenclature for spiro compounds in the presence of a double bond is spiro[a.b]alkyene (y = position number of double bonds) [2].



Spiro[2.4]hept-5-ene

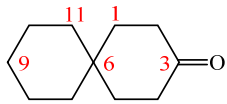


Spiro[4.4]nona-2,7-diene

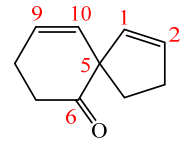


8,8-Dimethylspiro[4.5]deca-1.6-diene

The same numbering pattern is retained when monospiro compounds possess a functional group, but low locants are allocated for the principal functional group. Low locants are allocated for the double bond if there is a double bond [1].



Spiro[5.5]undecan-3-one



Spiro[4.5]deca-1,9-diene-6-one