The IUPAC Chemical Identifier

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IUPAC & Chemical Identity

- Mission
  - International, open standards for chemical communication
- Printed Media – Nomenclature
  - Human communication
  - Rules for structure to name conversion
- Digital Media – Identifier
  - Computer communication
  - Rules for structure to identifier conversion
    - Freed from restrictions of ‘pronouncibility’
    - Freed from ring index

Chemical Identifiers

- Structures
- Connection Tables
- ‘Trivial’ Names
- Systematic Names
- Index Numbers

Too Many Identifiers

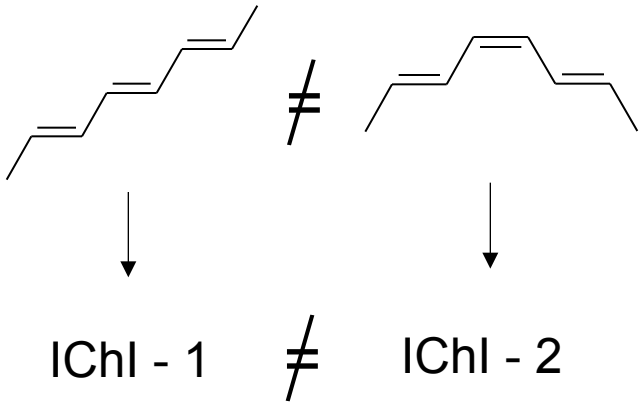
- Structure diagrams
  - various conventions
  - contain ‘too much’ information
- Connection Tables
  - MolFiles, Smiles, ROSDAL, ..
- Pronounceable names
  - IUPAC, CAS, trivial
- Index Numbers
  - EINECS, FEMA, DOT, RTECS, CAS, Beilstein, USP, RTECS, EEC, RCRA, NCI, UN, USAF

What kind of Identifier is needed?

- Exactly one Identifier per structure
- Defined by algorithms
- Comprehensive
- Openly available
- Implemented

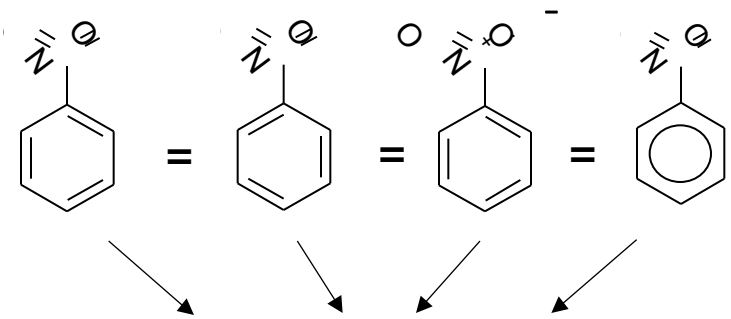
Requirements

- Different compounds have different identifiers
  - All distinguishing structural information is included



Requirements

- One compound has only one identifier
  - No unnecessary information is included



Same IChI

IChI Scope
First Version

- Discrete, covalently bonded compounds
  - foundation for other classes
- Isotopes
- Stereochemistry
  - sp3 - tetrahedral
  - Z/E - double bond
- Tautomers

3 Steps to IChI

- ‘Normalize’ Input Structure
  - Implement chemical rules
- ‘Canonicalize’ (label the atoms)
  - Equivalent atoms get the same label
- ‘Serialize’ the Labeled Structure
  - A unique series of bytes

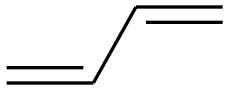
NORMALIZATION

Simplifications

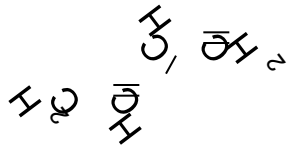
- Ignore ‘Electron Density’
  - Double/triple bonds, Odd-electrons, Charges
  - Still use for Z/E stereo perception
- Free Rotation Around Single Bonds
- Divide IChI into Layers

Ignore Electron Density

- Not required for compound identification
  - Distinguishes ‘excited states’
- Avoids problems
  - Delocalization, aromaticity, zwitterions, …

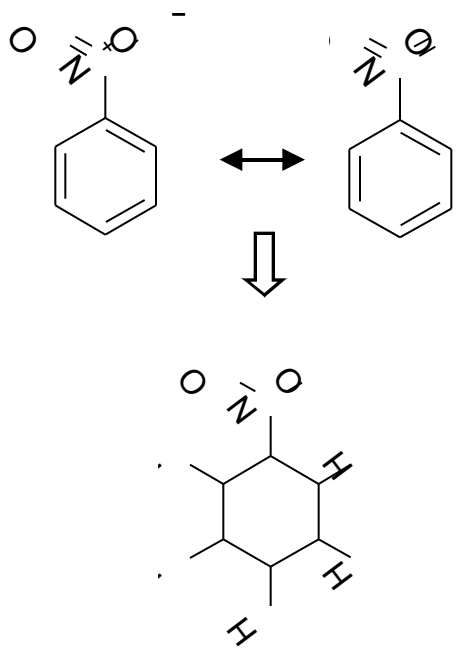


conventional

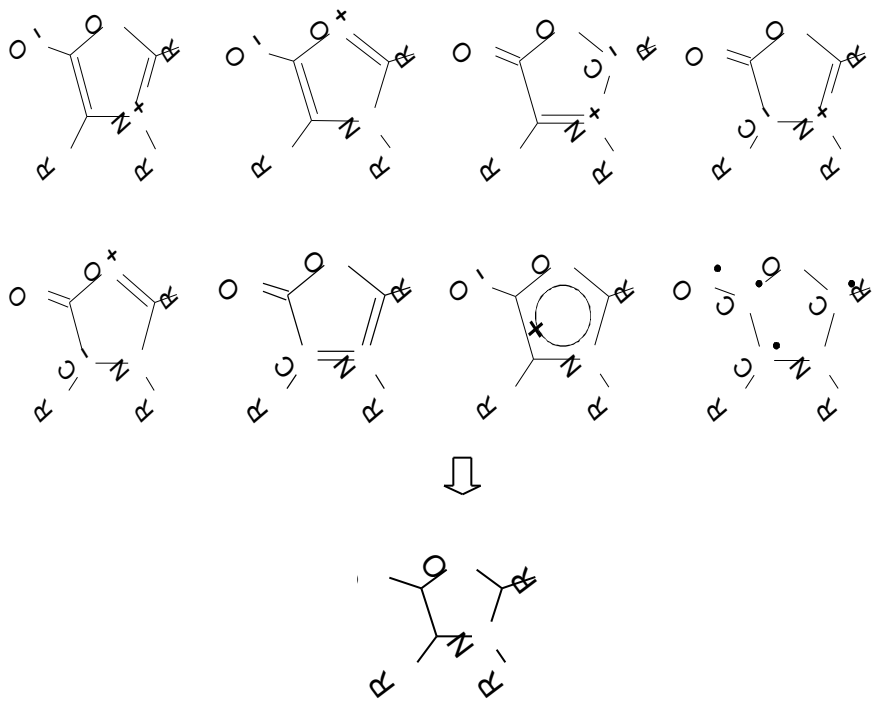


redundant

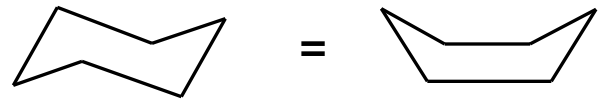
lChl

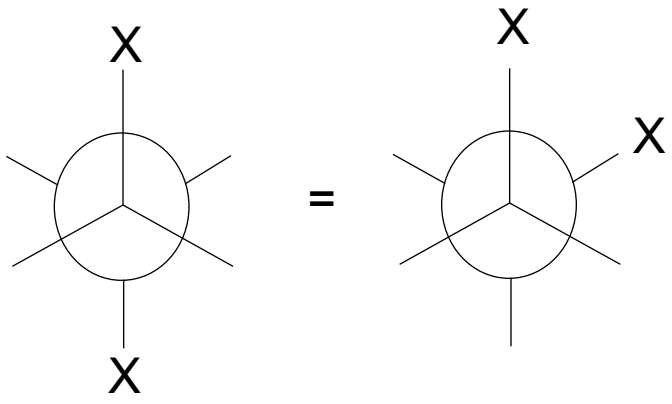


Münchnones



Assume Free Rotation Around Single Bonds





Ignore Conformation

LAYERS

Divide into ‘Layers’

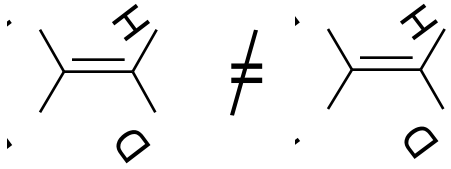
- Separate ‘Name’ into Fragments by
  - Connectivity
  - Isotopes
  - Stereochemistry
  - Tautomerism

Basic Layer
Simple Connectivity

- Just atoms and their neighbors
  - Ignore everything else
- Robust basic identifier

Isotopes

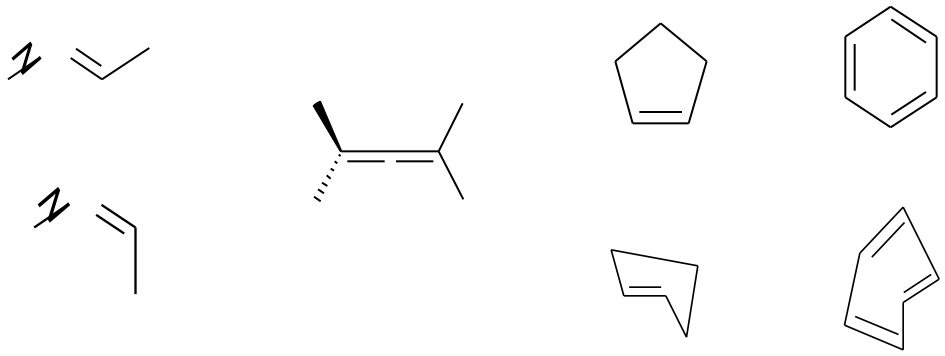
Treat isotopes as distinct atom types



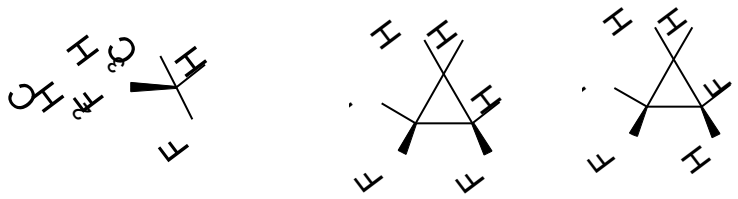
Stereochemistry

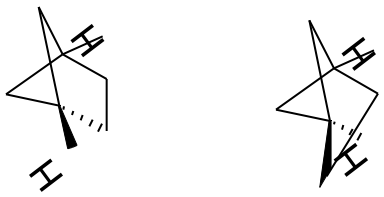
- Double Bond (Z/E)
  - from coordinates or bonding
- Tetrahedral (sp^3)
  - ‘in/out’ bonds or x,y,z coordinates

Varieties of Double Bond Isomers



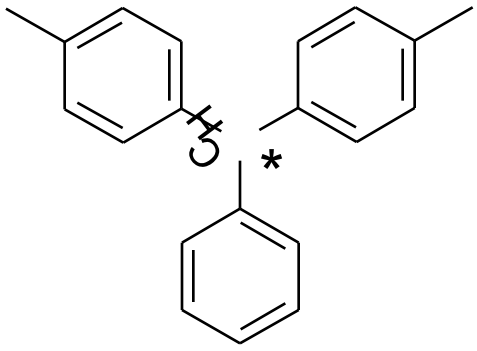
sp^3 (tetrahedral) stereoisomers





Stereodescriptor needed

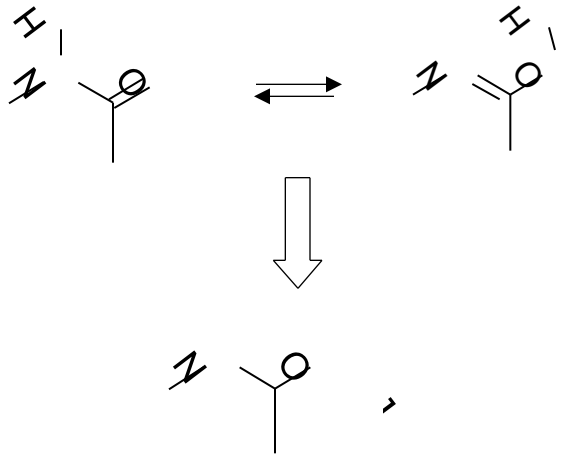
Identify Stereogenic Centers



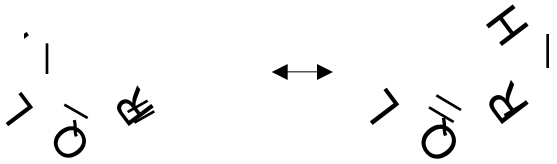
- Speed up processing
- Helpful for chemists

Basic Tautomer Layer

H-migration between 1,3 heteroatoms



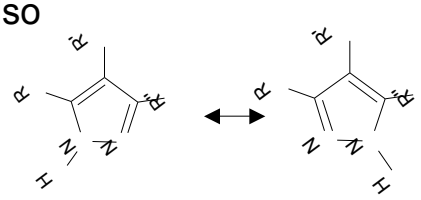
Tautomers



L,R = N, O, S, Se, Te

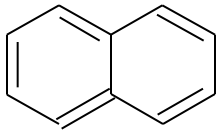
Q = C, N, S, P, …

also



Electronic Layer

Simply Store Net Charge



Possiblities:
Neutral
-1 (anion)
+1 (radical cation)
+2 (doubly charged)

Electronic State?

OUTPUT

lChI Output

9 possible fields

- Basic ##
  - Isotopic ##
    - Stereo ##
  - Stereo ##

- Tautomeric ##
  - Isotopic ##
    - Stereo ##
  - Stereo ##

- Electronic ##

Possible Output Format

Example: Benzene

Represent atoms as sequence number in formula

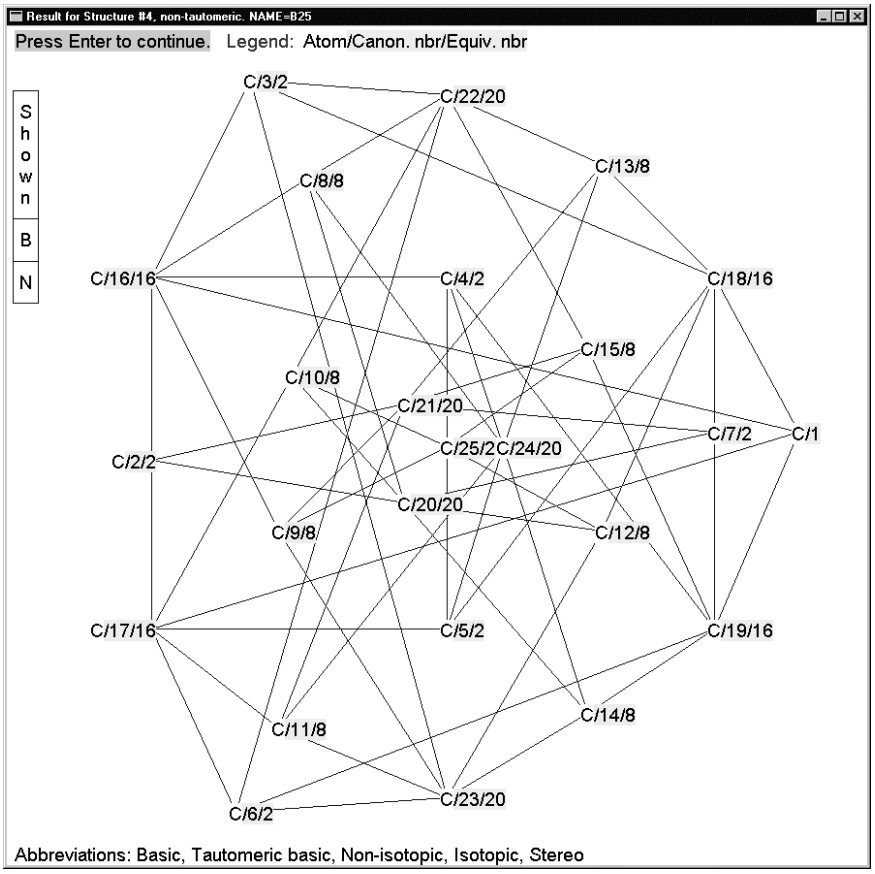
C6H6 = C C C C C C H H H H H H
tags 1 2 3 4 5 6 7 8 9 10 11 12

Basic Layer:
<basic>C6H6 1-2-7 2-3-8 3-4-9 4-5-10 5-6-11 7-12</basic>

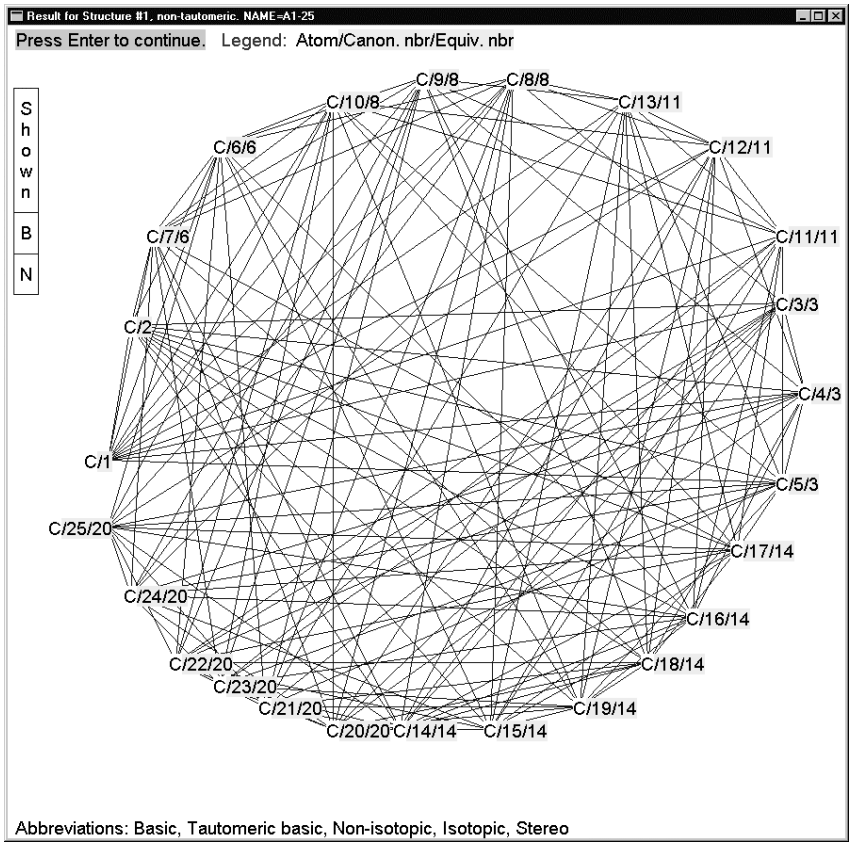
Other Output

- Information Only
  - For user verification
    - Label true stereogenic atoms
    - Identify equivalent atoms
- Warnings
    - Unusual valences
    - Unrecognized input
- ‘Reversibility’ Information
  - Coordinates
  - Electron density
    - Positions of double/triple bonds, charges, odd electrons

TESTING



Mathon, R. “Sample Graphs for Isomorphism Testing”
Congressus Numerantium V21, pp. 499-517, 1978

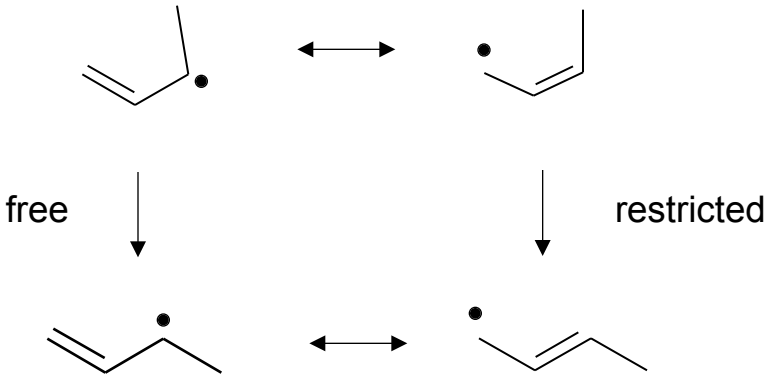

Result for Structure #1, non-tautomeric. NAME=A1-25
Press Enter to continue.
Legend: Atom/Canon. nbr/Equiv. nbr
Shown
B
N
C/9/8
C/8/8
C/10/8
C/13/11
C/6/6
C/12/11
C/7/6
C/11/11
C/3/3
C/2
C/4/3
C/1
C/5/3
C/25/20
C/17/14
C/24/20
C/16/14
C/22/20
C/18/14
C/23/20
C/21/20
C/19/14
C/20/20
C/14/14
C/15/14
Abbreviations: Basic, Tautomeric basic, Non-isotopic, Isotopic, Stereo

PROBLEMS

Two Fundamental Problems

- Chemists
  - Different ways to represent the same thing
  - Different definitions of tautomerism
  - Different guesses
- Chemicals
  - Structures can depend on conditions
  - Tautomers can depend on conditions

When to allow double bond stereoisomerism?

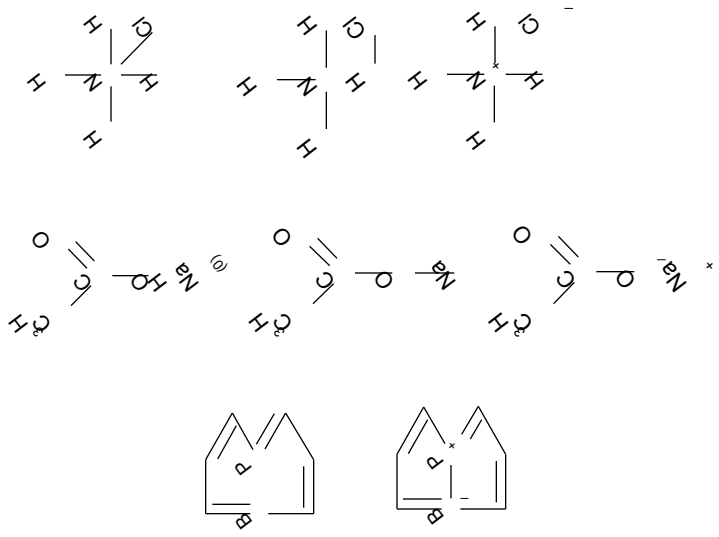


Proposed: If a bond can be single, no Z/E stereo allowed

Considered: Allow users to override default behavior

Drawing Standard Needed?

Bond/No bond



Allow Full ‘Reversibility’?

- Coordinates
  - Structure display
- Original bonds and charges
  - For display and future use
- Original numbering
  - Map to input data

IChI – What can't it do?

- Discover that two structures with different connectivity represent the same compound
  - Unless they are tautomers
- Predict potential for *Z*/*E* isomerism in open shell conjugated networks
  - Cannot predict rotational barriers
- Fix improperly entered data
  - Guarantees wrong IChI for bad data
- Properly treat non-covalent bonding
  - Coordinate bonds
- Represent 'exotic' stereochemistry

Version I

- Implement All Normalization Rules – 12/02
- Test against available data sets – 3/03
- Final External Testing and Refinement – 7/03
- Documentation, source, executable – 12/03?
- Open discussions
  - ichi-l@list.rsc.org

Future Extensions

- Organometallics
  - Coordinate bonds
- Other Stereo Forms
  - Non-atom centered
  - Conformations
  - Hydrogen Bonding
- Polymers/Macromolecules
- Compound Classes
  - Markush structures