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INFORMAL IN-PERSON *INCHI* INTERACTION IN DENVER

TUESDAY AUGUST 20TH 2024

DENVER

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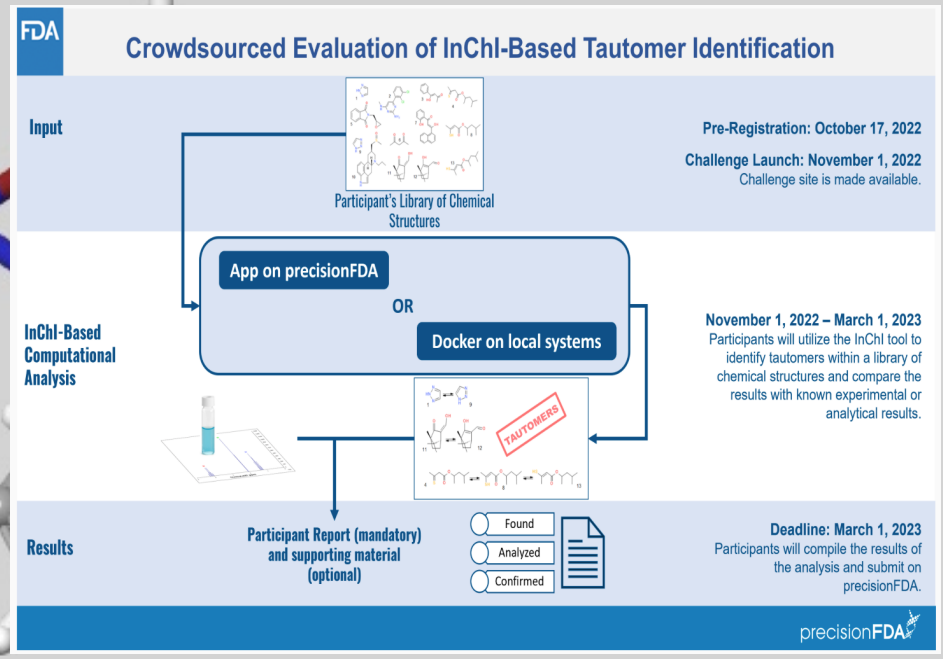
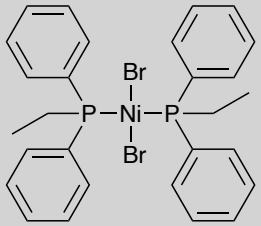
- topics covered included:
  - Organometallics
  - Tautomers
    https://precision.fda.gov/challenges/29
  - Markush
  - Programming framework (RMN+)InChI
  - Documentation and papers

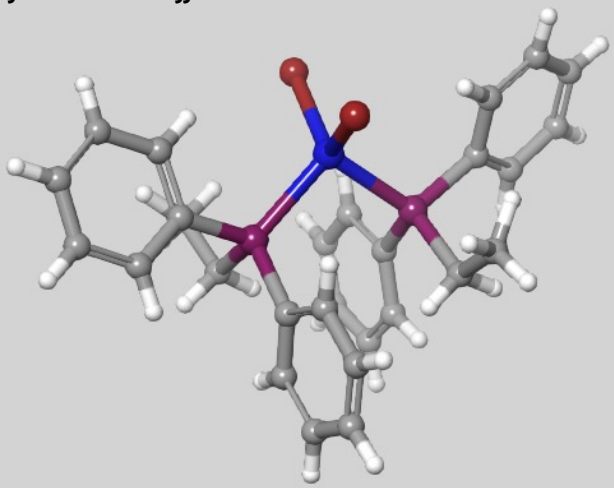


InChI v1.07

InChI=1S/2C14H15P.2BrH.Ni
/c2*1-2-15(13-9-5-3-6-10-13)14-11-7-4-8-12-14;;;
/h2*3-12H,2H2,1H3;2*1H;/q;;;;+2/p-2
InChIKey=LRGOJBHMPWNRJJ-UHFFFAOYSA-L

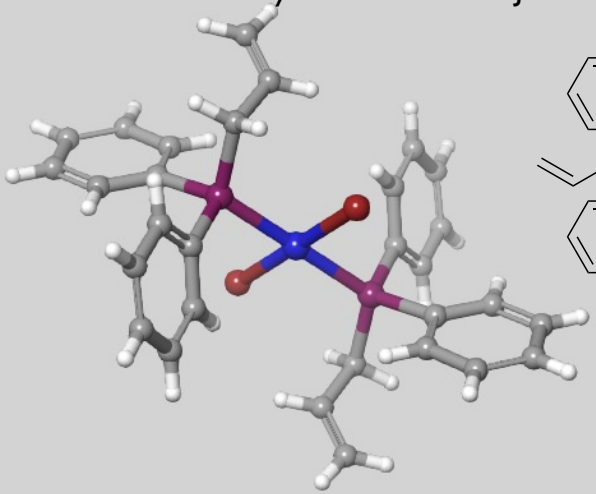
No
stereoisomers

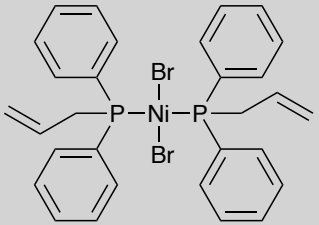




CSD refcode: KOMHEZ
J.-O.Malm, V.Alfredsson, G.Svensson, J.Albertsson
(1992) *Acta Crystallogr., Sect.C:Cryst.Struct.Commun.*, **48**, 406

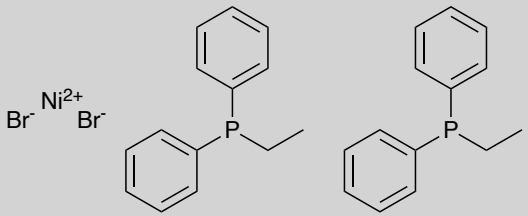
InChI=1S/2C15H15P.2BrH.Ni
/c2*1-2-13-16(14-9-5-3-6-10-14)15-11-7-4-8-12-15;;;
/h2*2-12H,1,13H2;2*1H;/q;;;;+2/p-2
InChIKey=PUFLLCFASVLTJA-UHFFFAOYSA-L



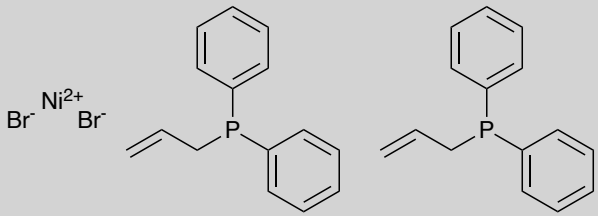


Possibility of *cis* / *trans*
stereoisomers

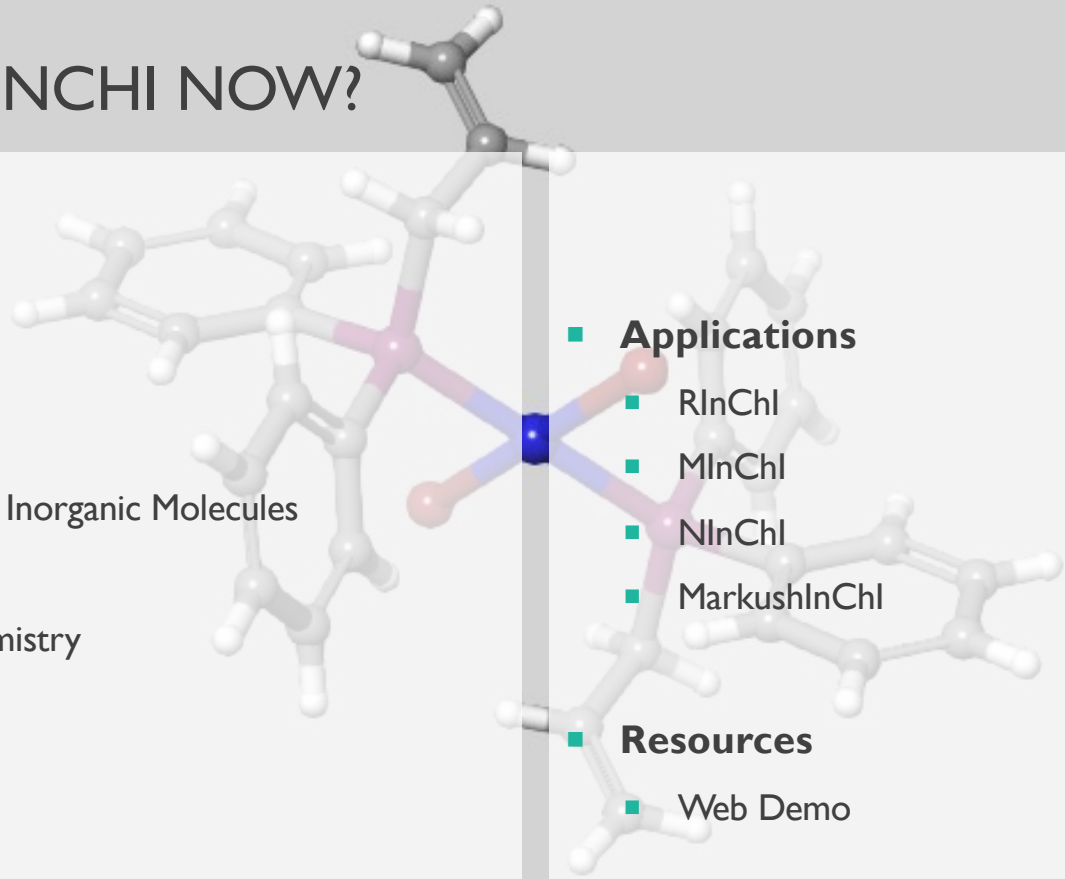
CSD refcode: XIKWEX
M.L.Clapson, D.J.Nelson, M.W.Drover (2023) *ACS Org. Inorg. Au*, **3**, 217



The change in nickel geometry probably reflects a change in the electronic state of the nickel, which is very sensitive to the ligands



WHERE IS THE INCHI NOW?



- **Developments**
  - Organometallics and Inorganic Molecules
  - Atropisomers
  - Extended stereochemistry
  - Tautomers

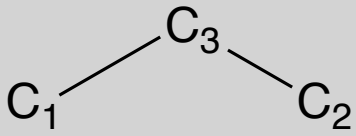
- **Applications**
  - RInChI
  - MInChI
  - NInChI
  - MarkushInChI

- **Resources**
  - Web Demo

https://iupac-inchi.github.io/InChI-Web-Demo/

INCHI

Propane:
InChI=1S/C3H8/c1-3-2/h3H2,1-2H3



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A few notes…

- What is the scope of the InChI?
  Moving beyond molecules?
- FDA would like more on tautomers:
  v1.07 has new options
- The code has been tidied and moved to GitHub with v1.07
- Still in C, and should now be easier to extend and modify
- There is only one bond type
- Extension of the InChI to include (subjective) properties would be a fundamental change

- InChI users may need to move to new version with significant changes every twenty-five years or so
- Such a change might happen within the next five years
- Markush/Variable InChI is being explored
- From a regulatory perspective, polymer endgroups can be ignored if <2% of the material
- Preprocessing steps may be needed
- In an ideal world, there would be a definitive specification of the InChI, distinct from the C code

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A few more notes…

- It was pointed out that proteins, nucleic acids, polymers, mixtures and nanomaterials are qualitatively different to molecules which are precisely defined at an atomic level. Molecules can have exact identifiers, whereas more complex substances require descriptions. There are other standards specifically created to convey information necessary for identification of complex materials. A discussion should continue about whether InChI should compete with those standards or be incorporated into them.

- Systems incoprrporating metals are hard to describe
- If bonds are broken, difficult to decide where charges go
- If bonds are retained, have to know where they are
- Organic molecules described well by molfiles; organometallics more complicated
- Stereochemistry more than tetrahedral centres
- More documentation is needed
- There is a lot to do!

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In attendance

- Gerd Blanke
- Yulia Borodina
- Steve Boyer
- Alex Clarke
- Sharon George
- Jonathan Goodman
- Wendy Patterson
- Michelle Rogers