Liliana Mammino's short story

SURNAME Mammino

FIRST NAME Liliana

WHERE I AM FROM Italy

CURRENT POSITION

Professor emeritus
Department of Chemistry
University of Venda
(UNIVEN)
South Africa

AREA OF SPECIALISATION

theoretical/computational chemistry
other interest: chemistry education

EDUCATION

Ph.D. in chemistry

Moscow State University (Russia), 1982

Degree in chemistry

University of Pisa (Italy), 1973
A 5-year degree

Classical Lyceum Diploma

Liceo-Ginnasio A. Canova, Treviso (Italy)
(humanities-oriented secondary education)

WORK HISTORY SUMMARY

- National University of Somalia, 1974–1975
- University of Zambia, 1988–1992
- National University of Lesotho, 1993–1996
- At UNIVEN since 1997.

Another activity

- Research for the preparation of a chemistry textbook and textbook writing, 1983–1993.

BUILDING COMPUTATIONAL CHEMISTRY RESEARCH AT UNIVEN

- Built *de novo*, starting in 2004.
  - still ongoing process.

Overview of research themes (computational study of...)

- acylphloroglucinols
- antimalarial alkaloids of plant origin
- magnetically-induced currents through chemical bonds
- muchimangins
- sulphonylureas

Computational approaches

- **methods**: *in vacuo*: HF, MP2 (or MP2/HF),
  DFT/B3LYP
  bases 6-31G(d,p) 6-31+G(d,p)

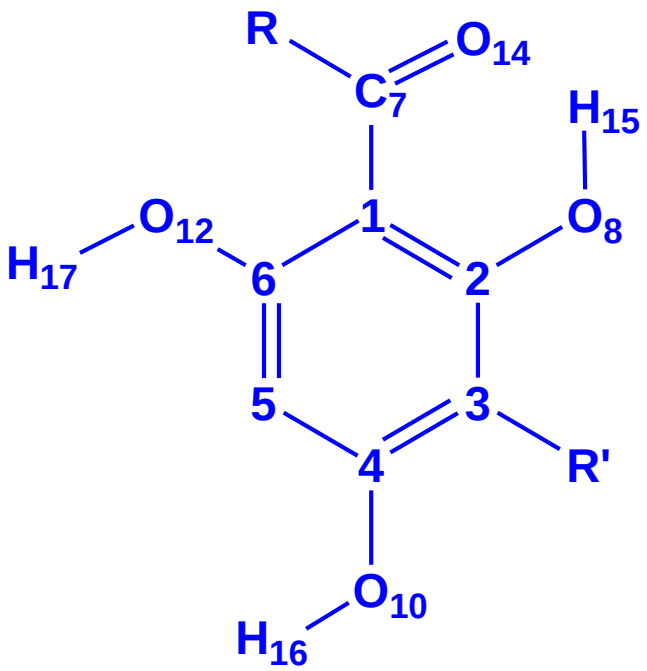
  in solution: PCM (polarizable continuum model)

- **calculation software**: GAUSSIAN 03
- **visualization**: GaussView, Chem3D

- **equipment**: desk-top PCs

ACYLPHLOROGLUCINOLS (ACPLs)

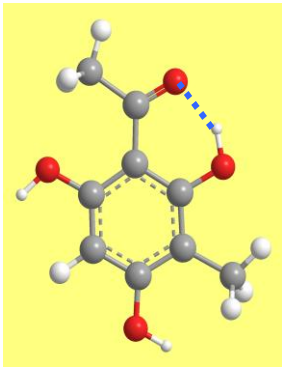
- A large class of compounds structurally derived from 1,3,5-trihydroxybenzene (phloroglucinol) and characterised by the presence of a **COR group**
- Many of them are of natural origin and exhibit a variety of **biological activities**: bactericide, antibiotic, fungicide, antioxidant, antimalarial, etc.
- Viewed as potential lead compounds for drug development

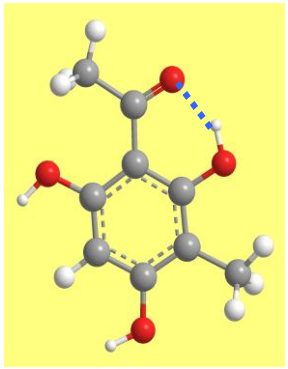


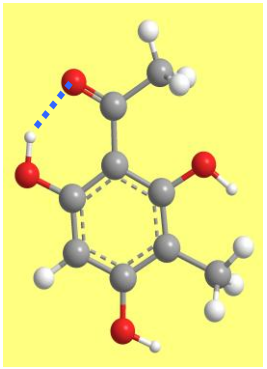
What has been done

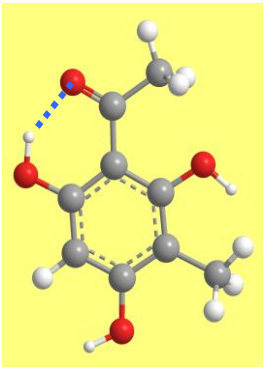
- **Conformational studies**
  - monomeric ACPLs as a class of compounds [1–5]
  - dimeric ACPLs as a class of compounds [6]
- **Study of solvent effects**
  - PCM studies in chloroform, acetonitrile and water [7]
  - study of adducts with explicit water molecules [8]
- **Study of individual ACPL molecules**
  - ACPLs with specific biological activities: antituberculosis [1, 9, 10], anticancer [11, 12], antioxidant [13–18]
  - other ACPL molecules [19, 20]
- **Study of supramolecular structures** [21]
- **Complementary studies:** the parent compound [22], its acid [23] and hydroxybenzenes in general [24, 25].

Patterns for the intramolecular hydrogen bond and the orientation of the OH groups in ACPLs


d-r


d-w


s-r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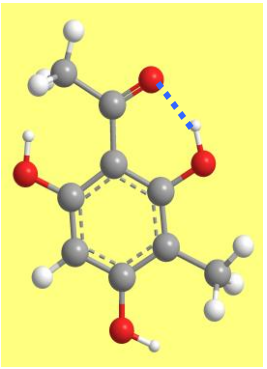
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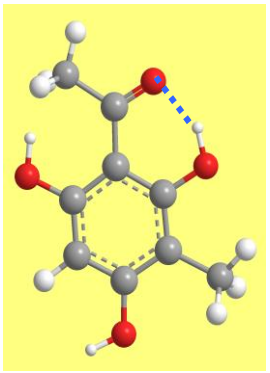
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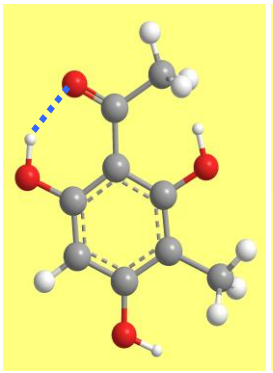
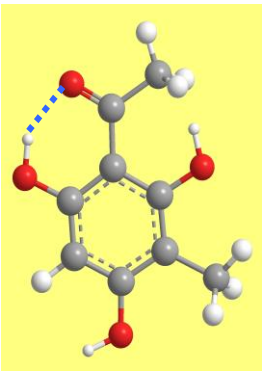

s-r-u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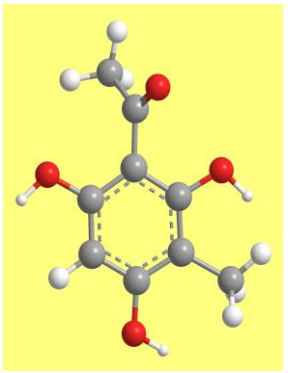
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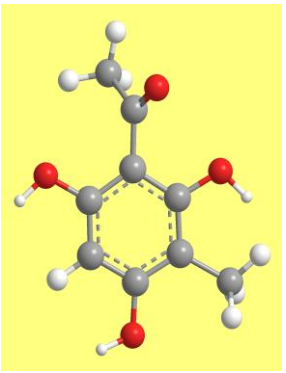
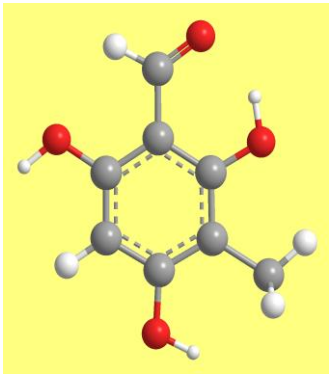
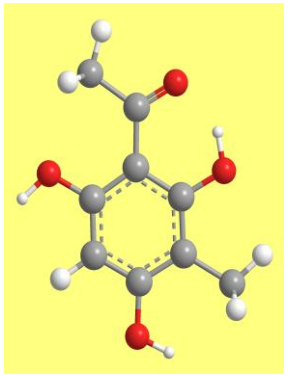

w

lowest energy conformers of selected structures


A-d-r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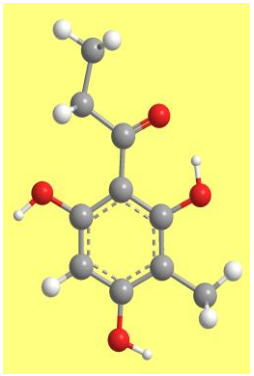
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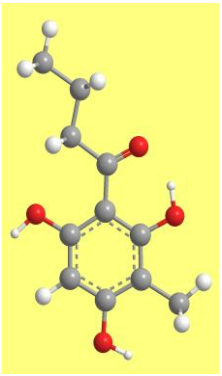
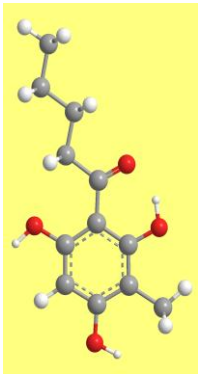

E1-d-r-1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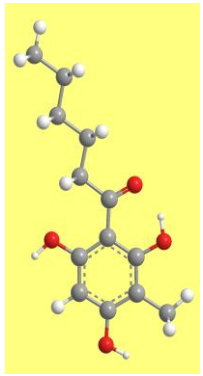
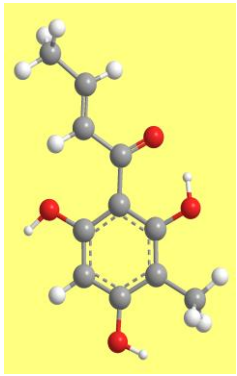
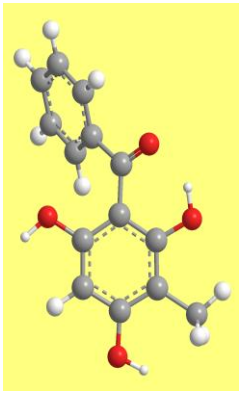
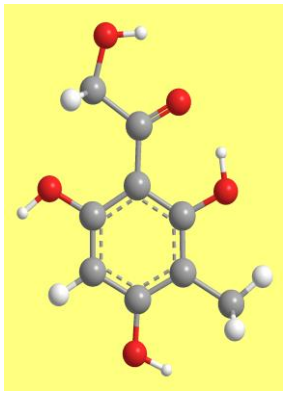
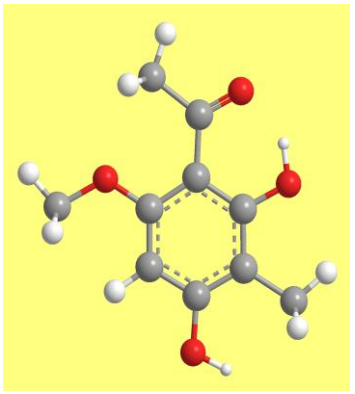
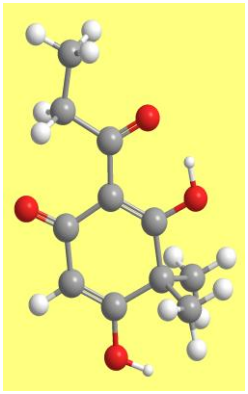

G1-d-r-1

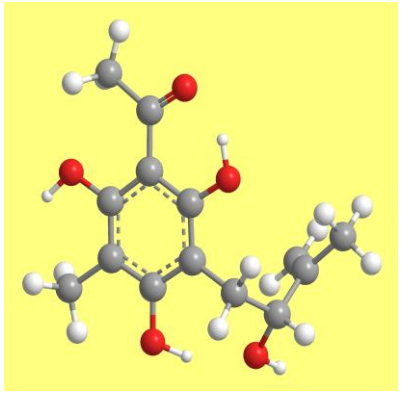

L-d-r

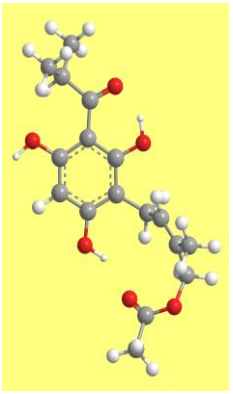

N-d-r


W-d-r-1


B-ET6-d-r

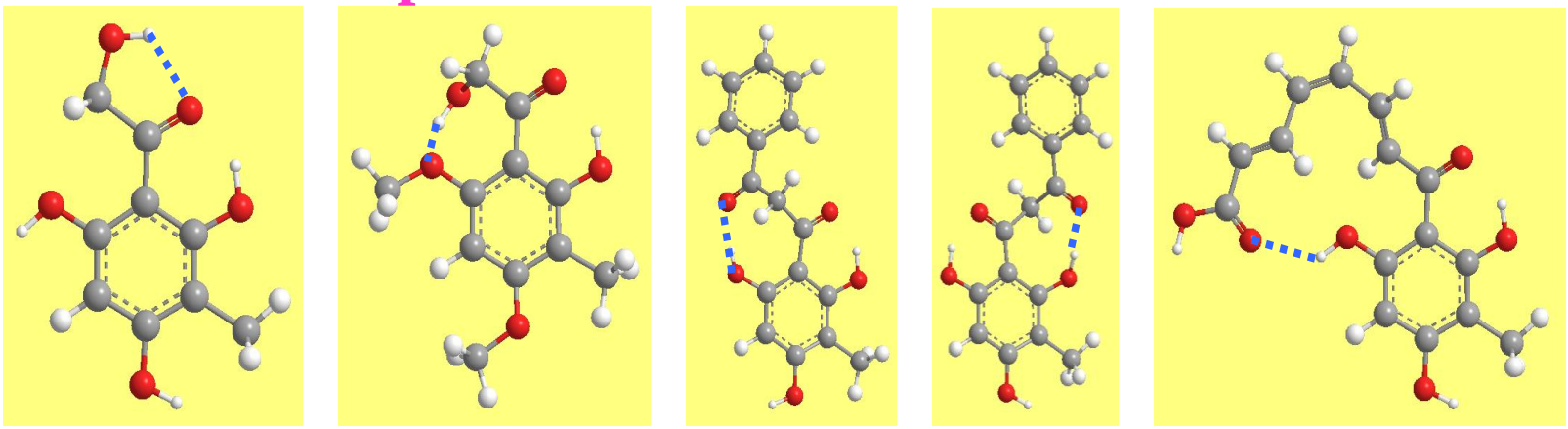

D-KT5-d-r


B-Y3B5-d-r-q2

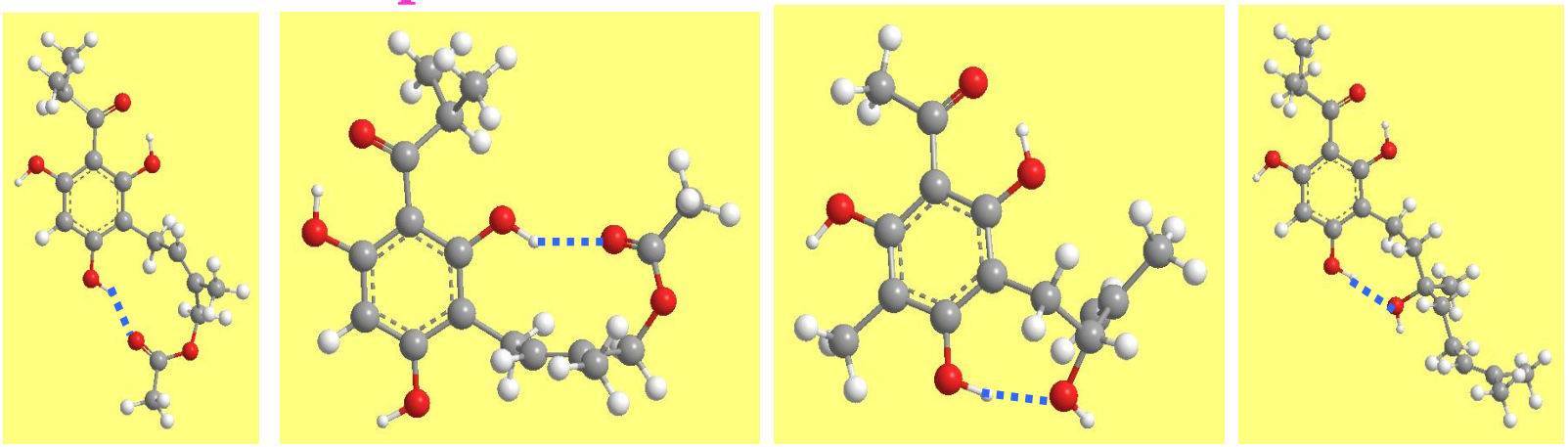

caespitate

structures with additional O–H···O IHBs

donor or acceptor in R

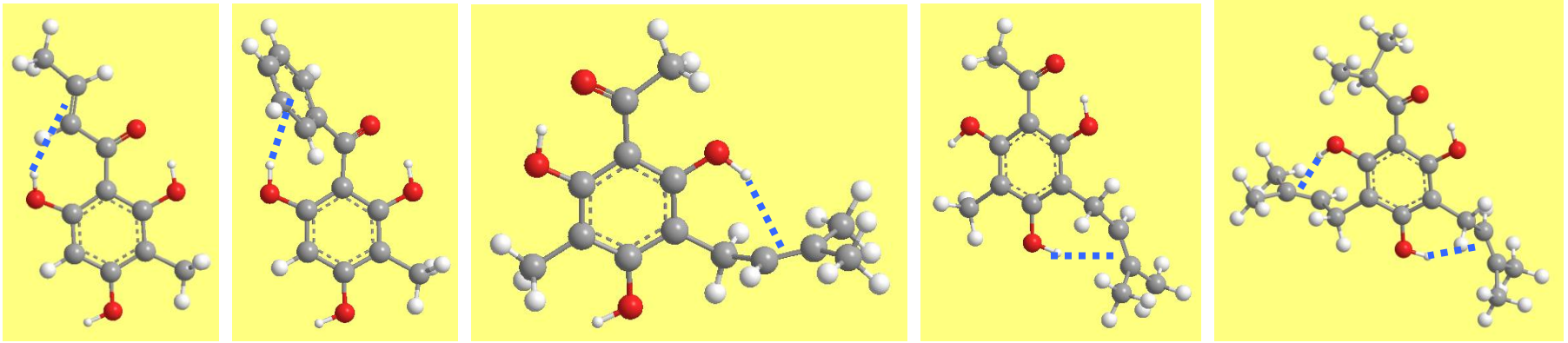


donor or acceptor in R′

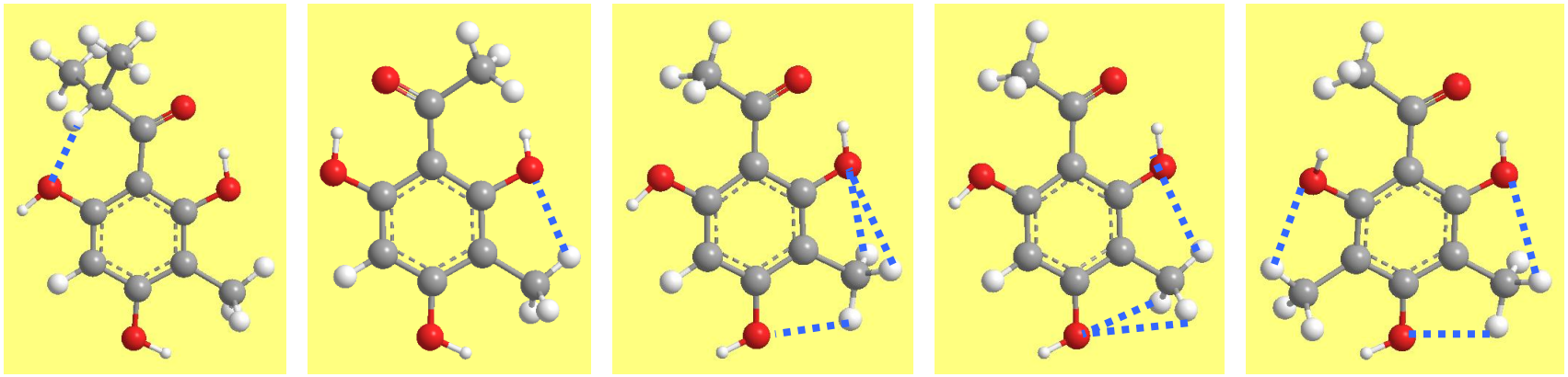


Other IHB types

Interaction of an OH with a π system



C–H···O interactions

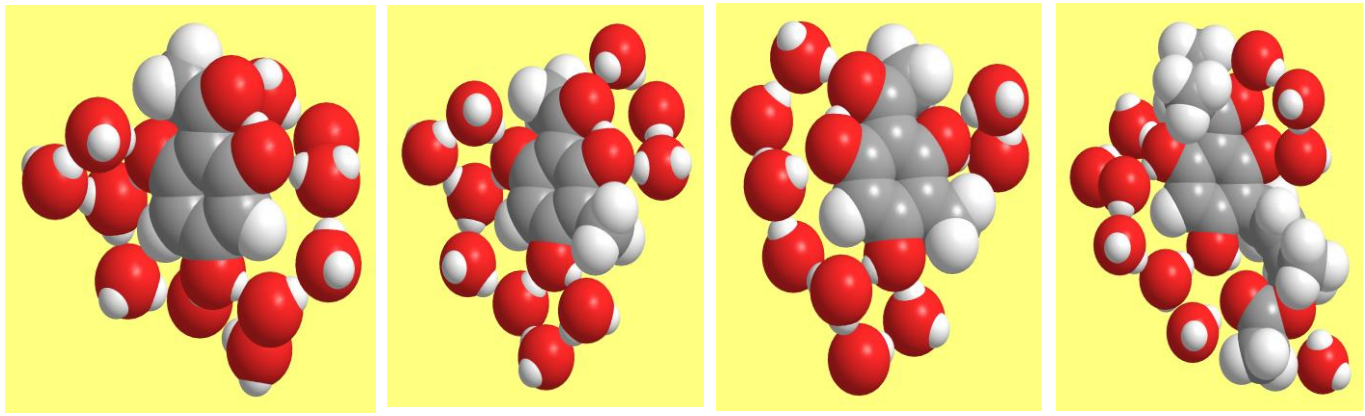


Adducts with explicit water molecules

- adducts with **one water molecule** attached in turn to different donor or acceptor sites via an intermolecular H-bond, whose energy is calculated:
  - 6–8 kcal/mol when H_2O is the acceptor
  - 3–5 kcal/mol when H_2O is the donor

- adducts with enough water molecules to approximate the **first solvation layer**
  - interaction energy between the central molecule and the water molecules:
    - 30–33 kcal/mol when **R′ = CH_3**
    - 38–40 kcal/mol when **R′ = H**

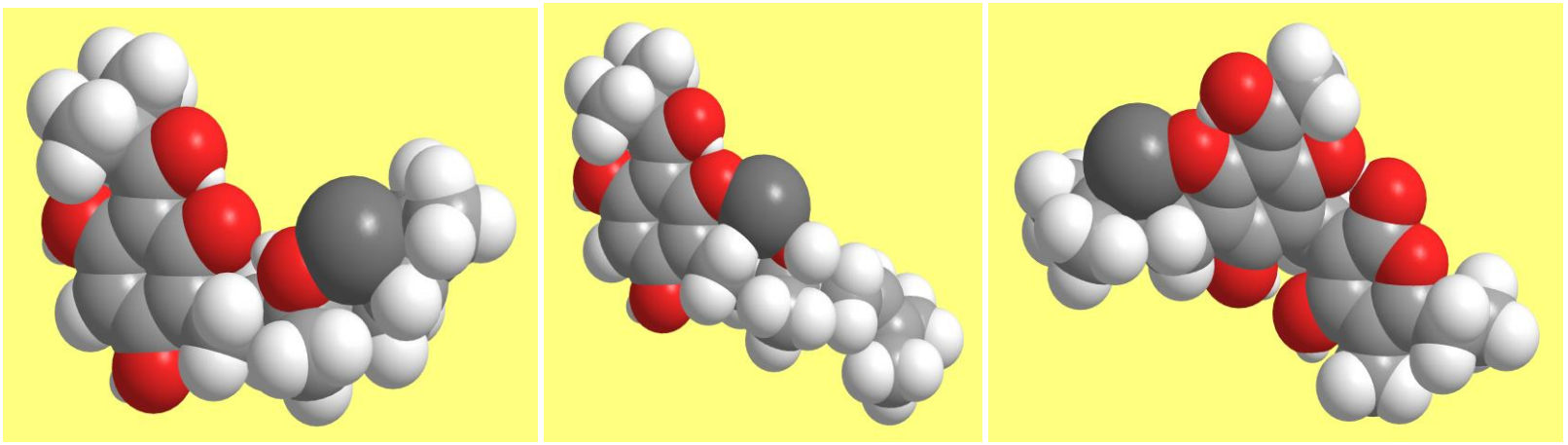
Adducts with explicit water molecules



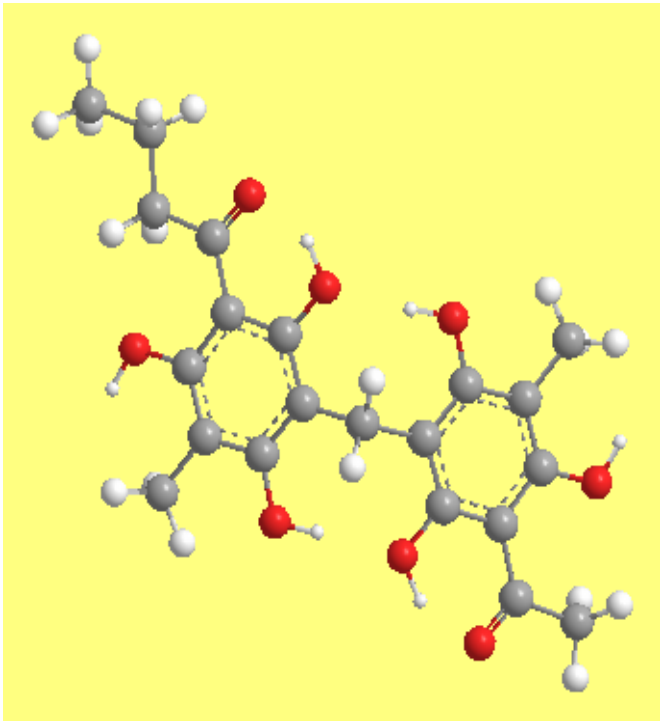
Study of antioxidant ACPLs

- Calculated complexes with a Cu^{2+} ion to test their reducing ability
  - Considering all the possible binding sites for the ion
  - The charge of the ion is always reduced

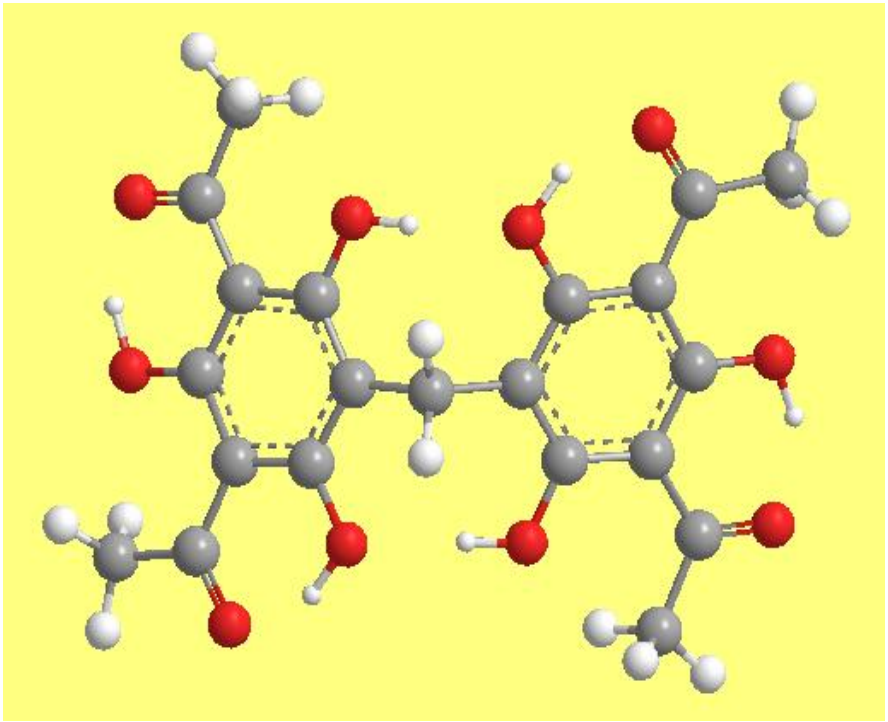
Complexes of antioxidant ACPLs with a Cu^{2+} ion



Dimeric acylphloroglucinols



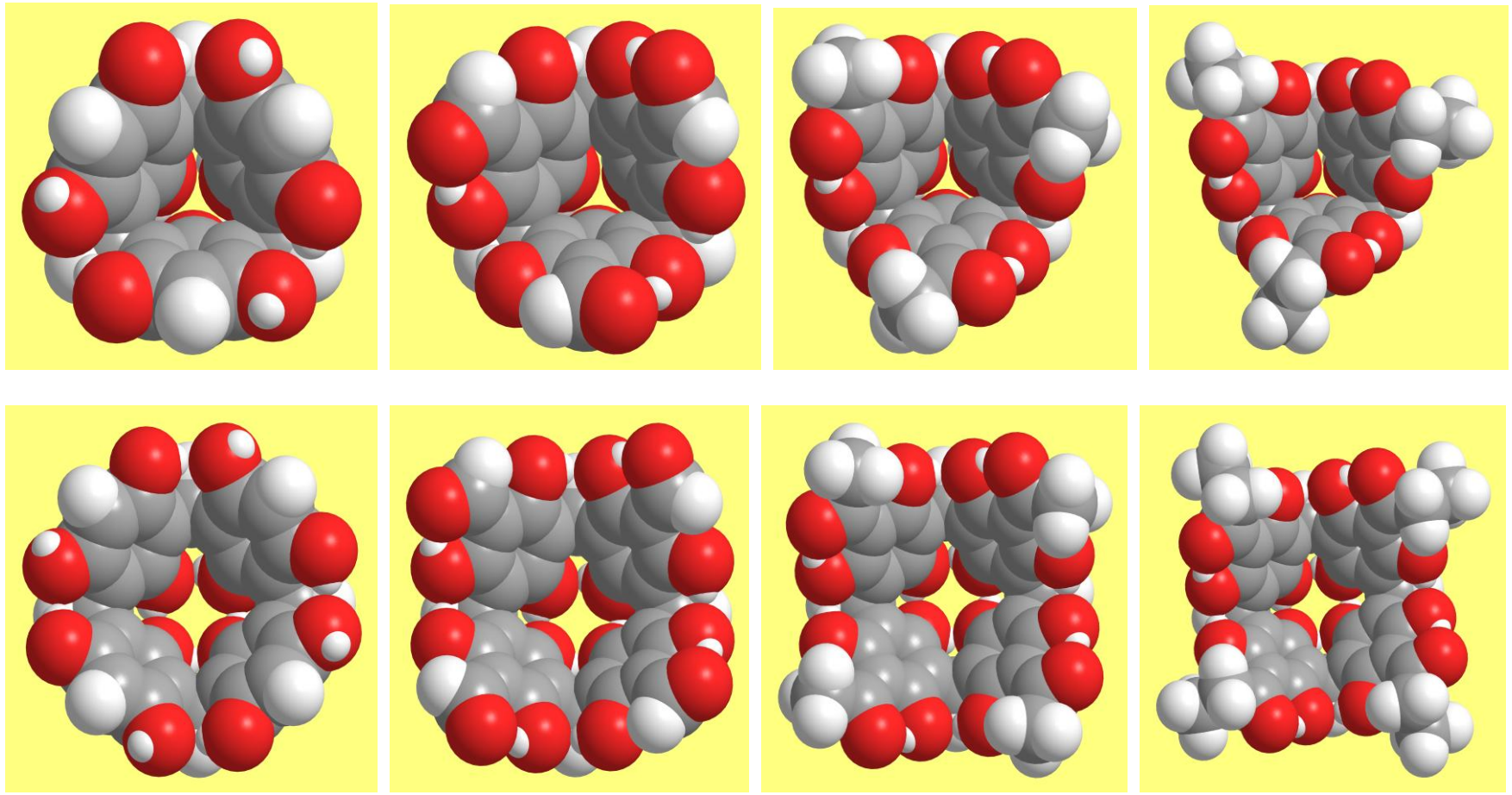
abbreviatin AB



bis(2,4-diacetylphloroglucyl) methane

antibiotic, antimalarial

Bowl-shaped structures (potential)

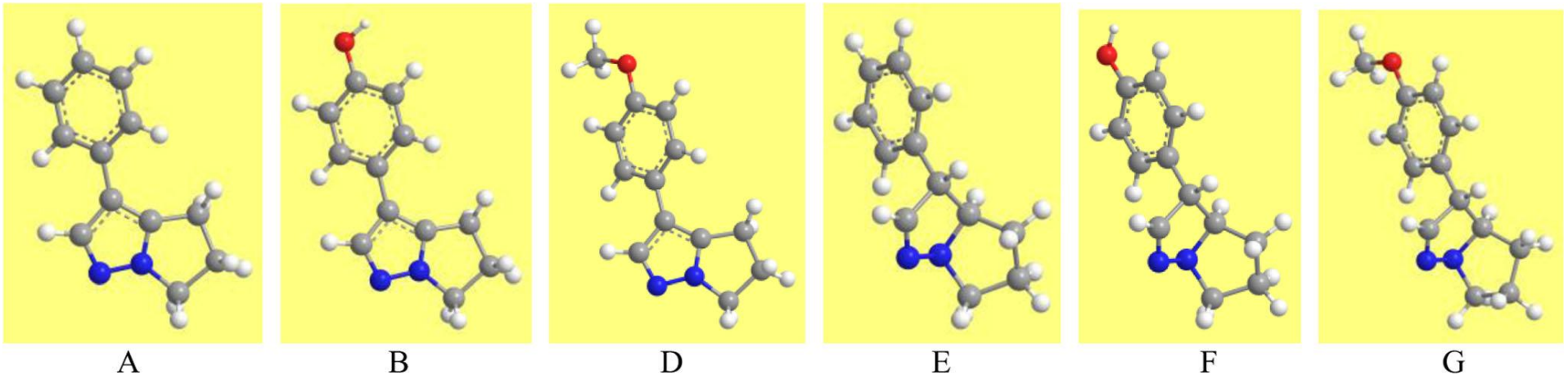


- **interesting feature**: particularly deep bowls

ANTIMALARIAL ALKALOIDS OF PLANT ORIGIN

postgraduate student Kabuyi Mireille Bilonda (DRC)

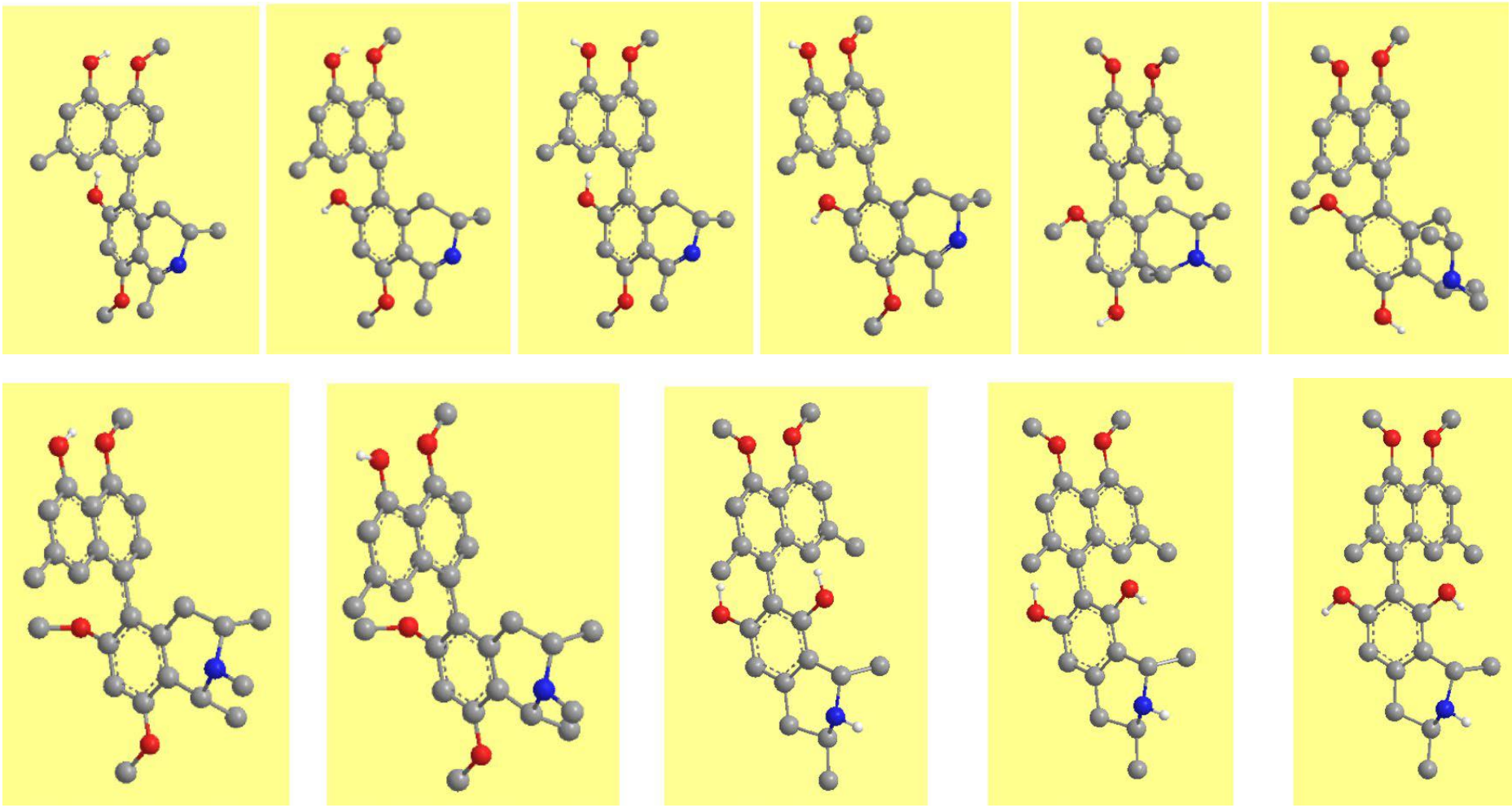
pyrazole alkaloids [26]



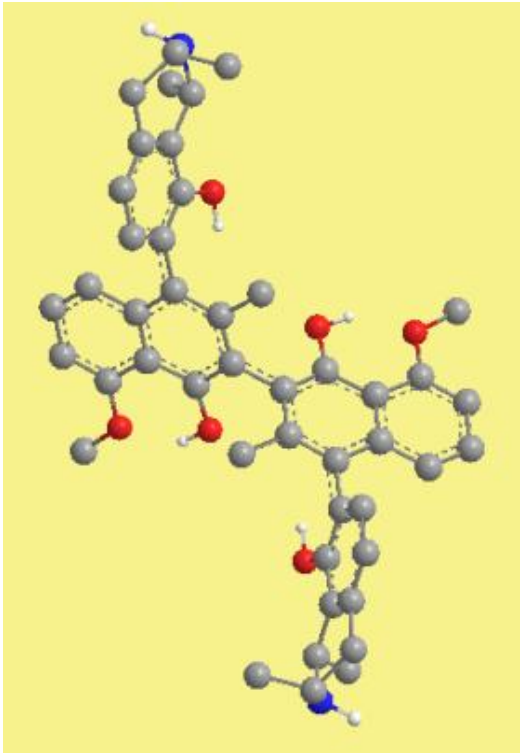
A: withasomnine, B: p-hydroxy derivative of withasomnine, D: p-methoxy derivative of withasomnine, E: newbouldine, F: p-hydroxy derivative of newbouldine, G: p-methoxy derivative of newbouldine

Naphthylisoquinoline alkaloids

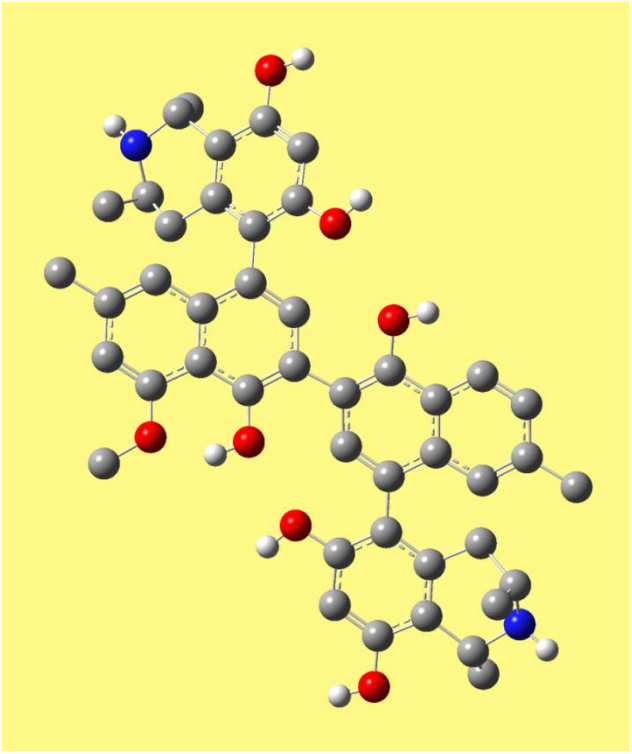
monomeric structures [27]



dimeric structures [28–30]

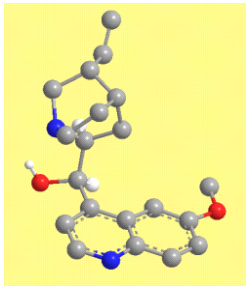


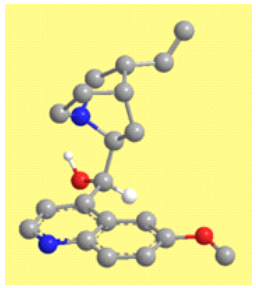
Josemine A_2
anti-HIV

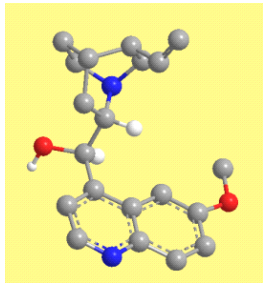


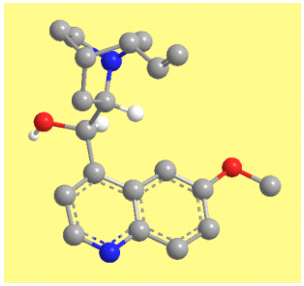
Michellamine A
antimalarial

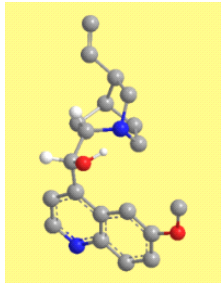
intramolecular hydrogen bond in quinine

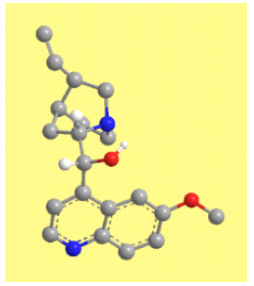

quin-1-*cis*


quin-1-*trans*


quin-2-*cis*


quin-1-*trans*

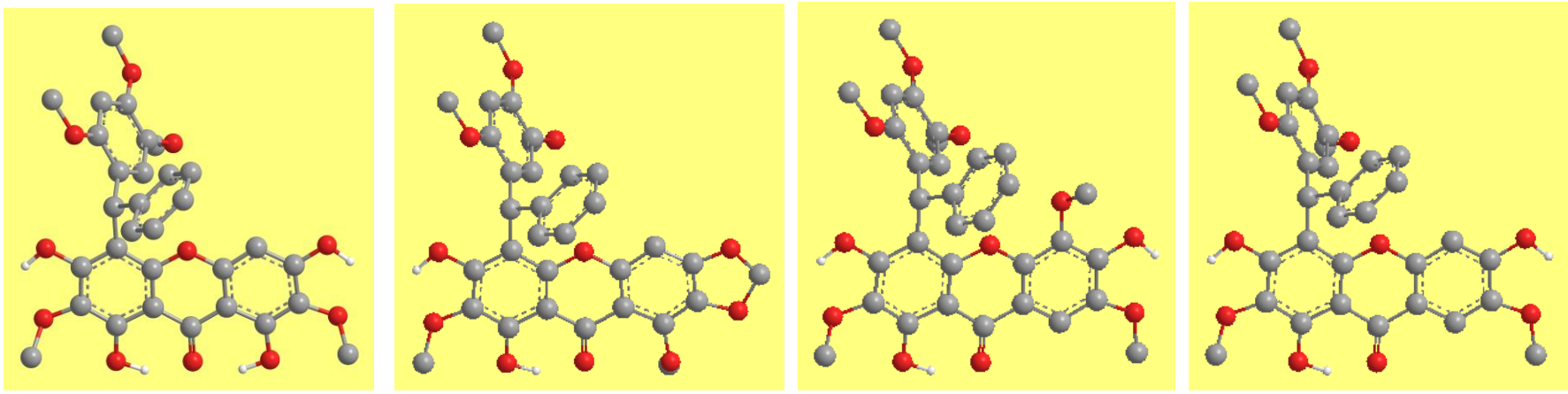

quin-3-*cis*


quin-3-*trans*

- first realization of the possibility of an IHB in the quinine molecule [31]

MUCHIMANGINS

- muchimangin B is active against pancreatic cancer, the others are not



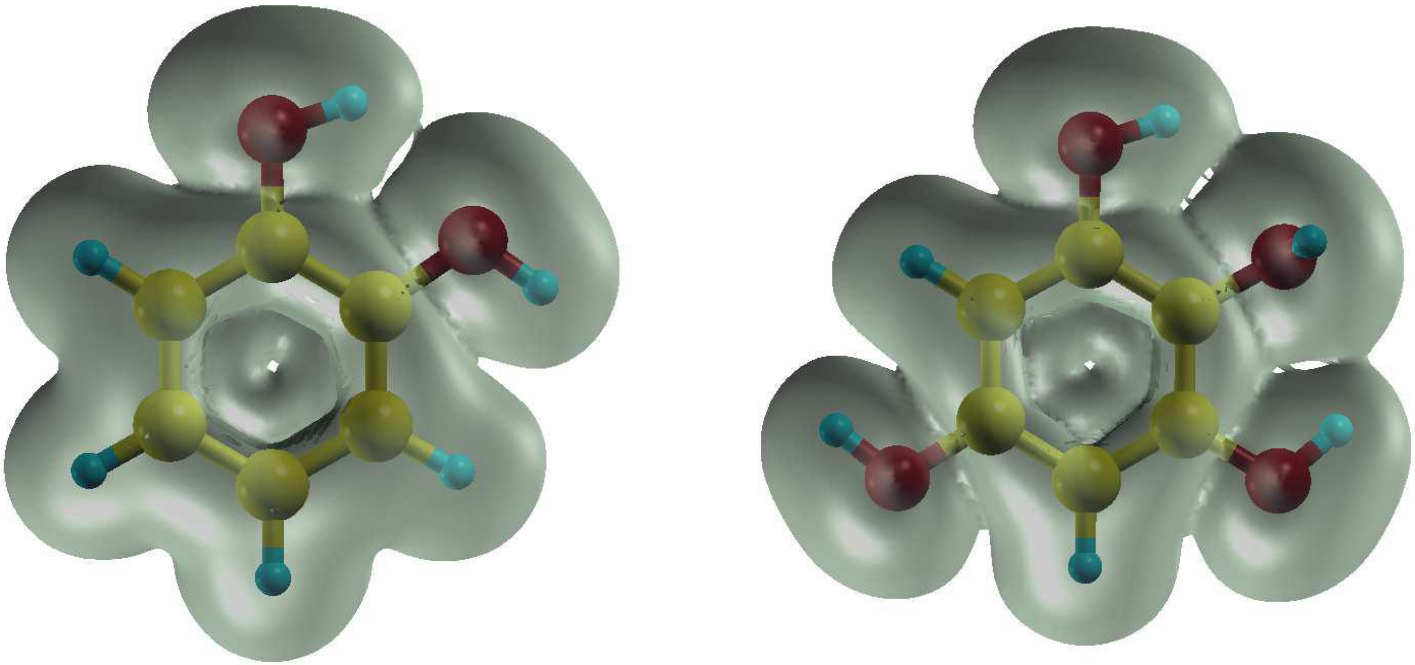
B A C D

- calculated both actual and model structures [32, 33]
- dominant importance of IHB patterns
- importance of moieties' orientations

MAGNETICALLY INDUCED CURRENTS THROUGH CHEMICAL BONDS

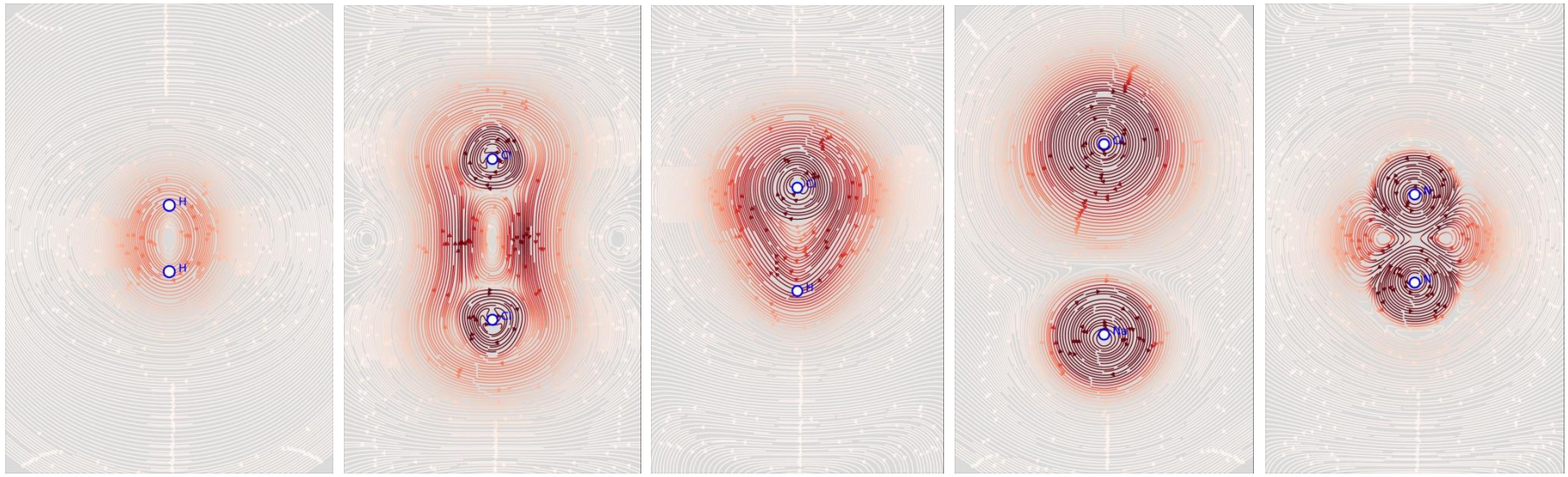
collaboration with Prof Luis Alvarez Thon

Aromaticity and IHBs in hydroxybenzenes



Isosurface of the magnitude of the current density (isovalue = 0.005) [34]

Current through the bond in diatomic molecules [35]



H_2 Cl_2 HCl NaCl N_2

MY GROUP

Size of the group

- two M.Sc. students
- one Ph.D. student
- myself

Possibilities of further expansion

- attracting more postgraduate students
  - challenge: many students consider this research area as too difficult

An interesting feature

- the way research was developed can be viewed as a possible **model for capacity building** in computational chemistry research in institutions in which it is not yet present [36, 37]
  - the area is still scarce-skills in many contexts
  - importance to **share existing expertise**:
    - for research capacity building, including under challenging conditions
    - for education and training
      - training trainers

WHAT I WOULD LIKE SEEING HAPPENING

General features

- **developing** this research where it is not yet present
- **fostering** other specialists' **familiarisation** with its core activities and consequent collaboration possibilities
  - exploration of new options, including sustainability
- **increasing** general **familiarisation** with the theoretical background of chemistry
- **networking**
- "**sharing**" of available specialists where useful and feasible
- **conduction of parallel projects** in different institution/countries, above all in the initialisation stage

A suggestion

- developing the **computational study of antimalarial molecules of natural origin** in several countries **simultaneously** and **co-ordinately**
- envisaged **advantages**:
  - **generation of information** useful to drug development
    - retaining relevant stages of it in the continent
  - connection with an issue (**malaria**) that is an actual and urgent problem in many African countries
    - contributing to highlight the relevant **roles of computational chemistry research** for other types of research and for the search aimed at addressing health problems
  - connection with **indigenous knowledge system**

THANK YOU

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