Alchemical Enantiomers

Guido Falk von Rudorff, O. Anatole von Lilienfeld

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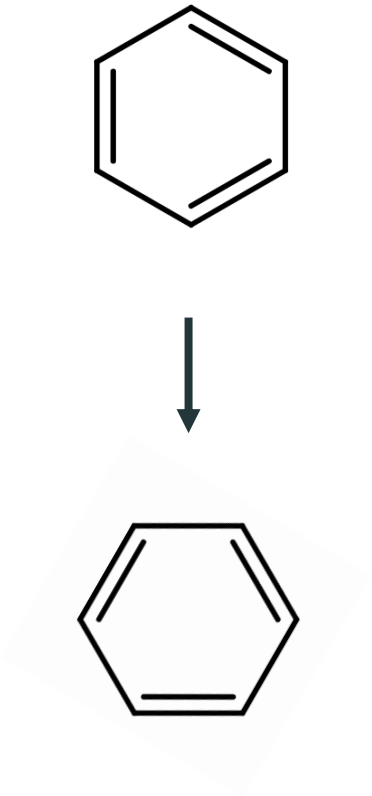
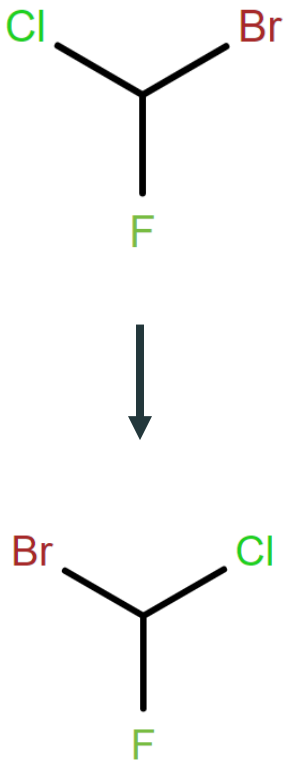
Alchemical Enantiomers

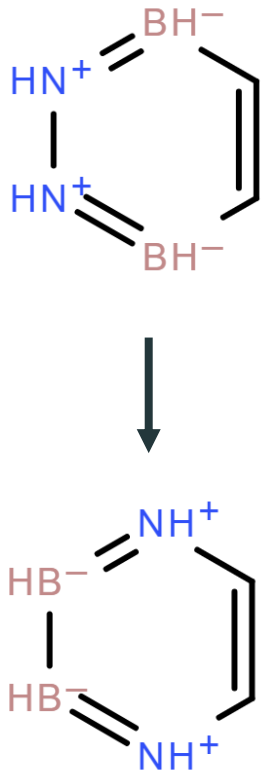
Translation
Exact



Rotation
Exact



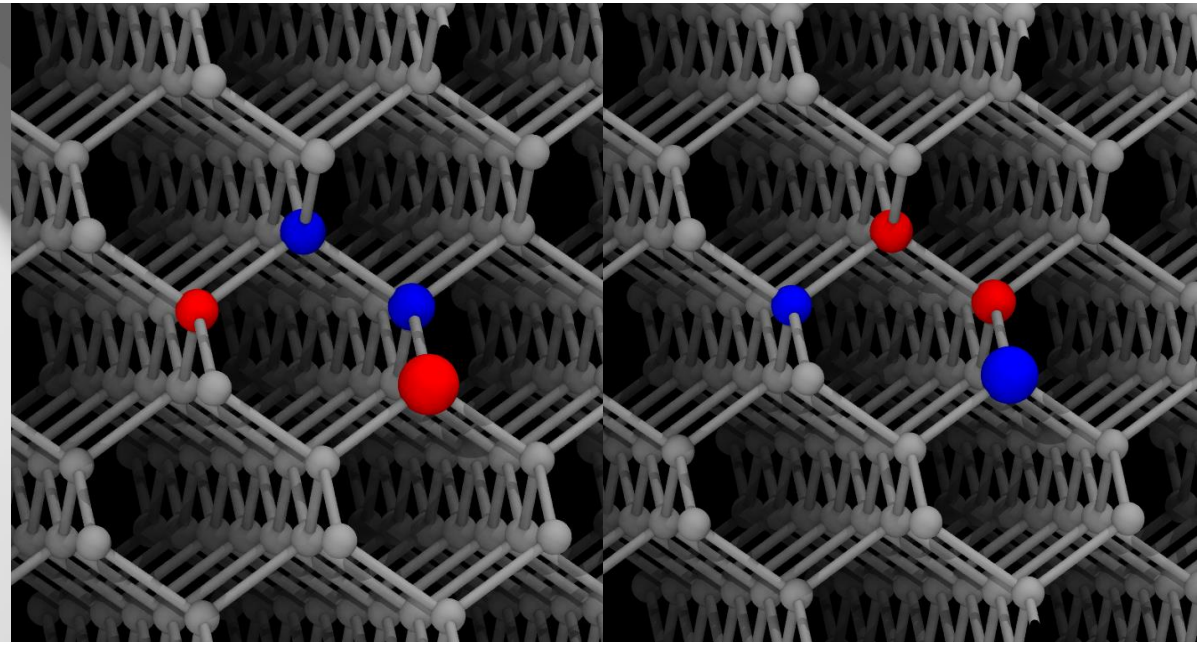
Spatial reflection
Approximate



Alchemical reflection
More approximate

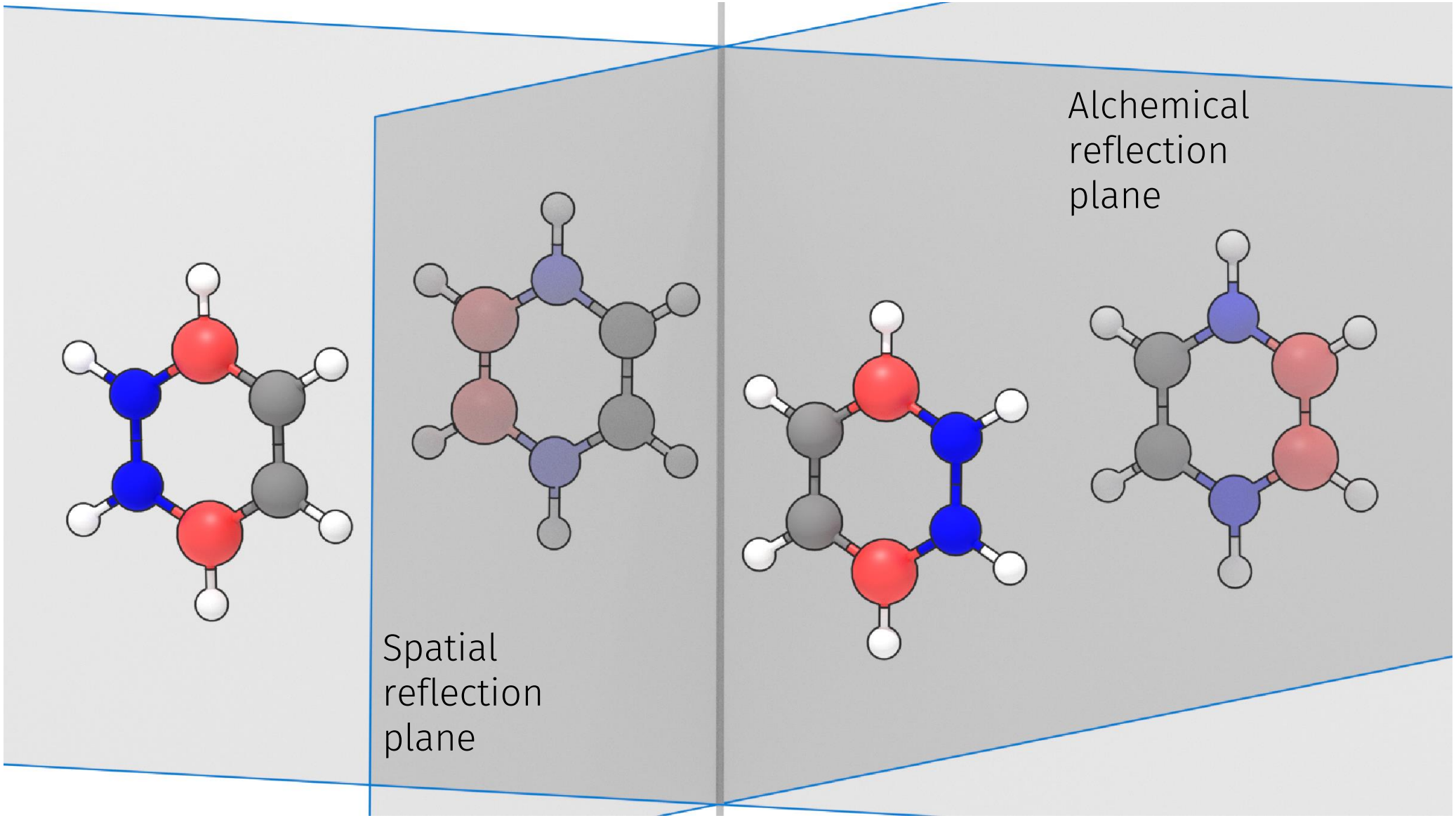
Alchemical Enantiomers

Spatial reflection
Enantiomers



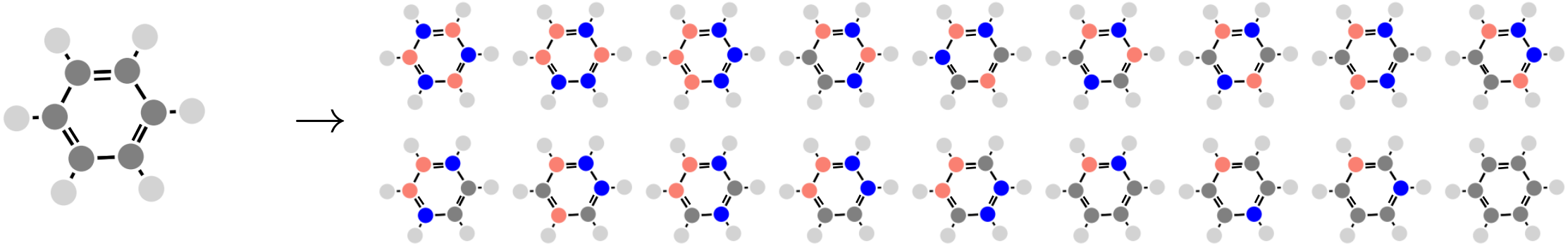
Alchemical reflection
Alchemical enantiomers

Alchemical Enantiomers



Quantum Alchemy

Alchemical Perturbation Density Functional Theory (APDFT)
Uses calculations of *one* molecule to estimate *many* molecules



$$E, \rho, \{\partial^i_\lambda \rho\} \quad \rightarrow \quad \{E_i\}, \{\rho_i\}, \{F_i\}, \{\mu_i\}, \{Q_i\}, \ldots$$

1 system $\rightarrow$ Potentially millions of systems

$$\hat{H}(\lambda) \equiv \lambda \hat{H}_\mathrm{t} + (1-\lambda)\hat{H}_\mathrm{r} \qquad \lambda \in [0,1]$$

GFvR, O. A. von Lilienfeld, *Phys. Rev. Res.* **2020** (*arXiv* 1809.01647).

Theory

Alchemical Perturbation Density Functional Theory (APDFT)

$$E_\mathrm{t} = E_\mathrm{r} + \Delta E^\mathrm{NN} + \int_\Omega d\mathbf{r} \sum_{n=0}^{\infty} \frac{1}{(n+1)!} \Delta v \frac{\partial^n \rho_\lambda(\mathbf{r})}{\partial \lambda^n}\bigg|_{\lambda=0}$$

$$\rho_t = \sum_{n=0}^{\infty} \frac{1}{n!} \frac{\partial^n \rho}{\partial \lambda^n}\bigg|_{\lambda=0}$$

- Gives consistent energies, densities, forces, ...
- Uses the same derivatives for all predictions
- Improves with higher order *n*
- In practice: truncate after some order *n*

GFvR, O. A. von Lilienfeld, *Phys. Rev. Res.* 2020.

Theory

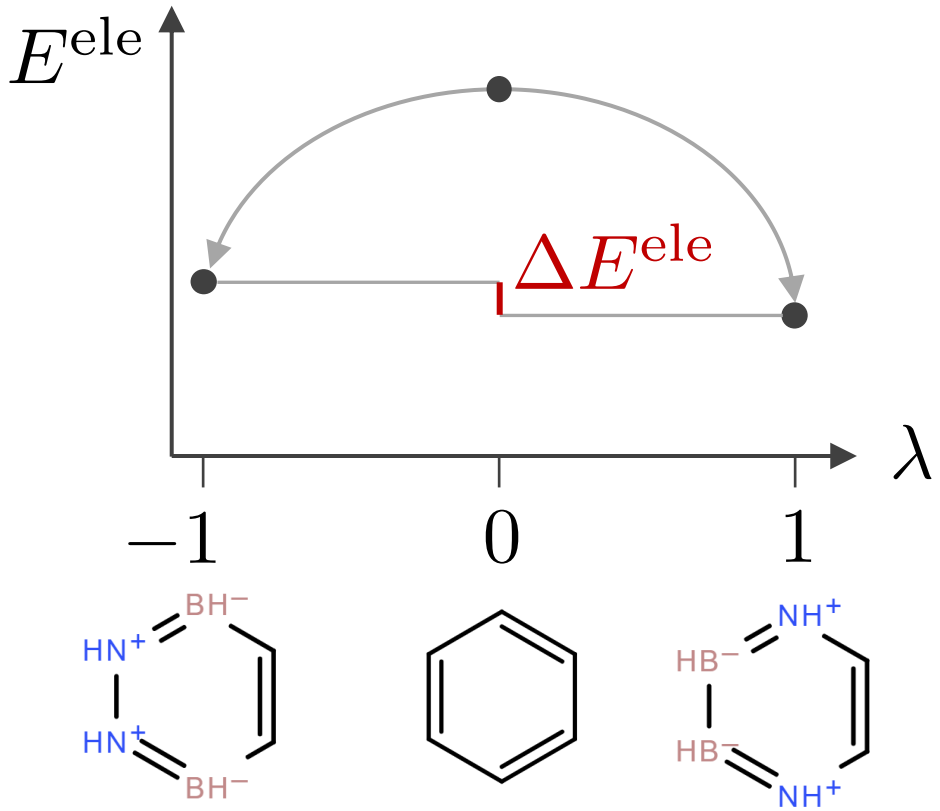
$$\Delta E_{ij}^{\mathrm{ele}} = E_0 - E_0 + \int_\Omega d\mathbf{r} \sum_{n=0}^{\infty} \frac{\Delta v_i}{(n+1)!} \left[\frac{\partial^n \rho}{\partial \lambda_i^n} + \frac{\partial^n \rho}{\partial \lambda_j^n} \right]$$

$$\Delta E_{(0)}^{\mathrm{ele}} = E_0 - E_0 = 0$$

$$\Delta E_{(1)}^{\mathrm{ele}} = 2 \int_\Omega \Delta v \rho = \int_\Omega e \cdot o = 0$$

$$\Delta E_{(2)}^{\mathrm{ele}} = \int_\Omega \Delta v \left[\frac{\partial \rho}{\partial \lambda_i} + \frac{\partial \rho}{\partial \lambda_j} \right]$$

$$= \int_\Omega \Delta v \left[\sum_I \frac{\partial \rho}{\partial Z_I} \frac{\partial Z_I}{\partial \lambda_i} + \frac{\partial \rho}{\partial Z_I} \frac{\partial Z_I}{\partial \lambda_j} \right] = 0$$

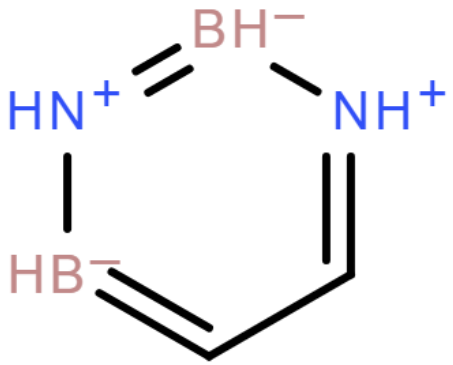


GFvR, O. A. von Lilienfeld, *Science Adv.* **2021** (arXiv 2008.02784)

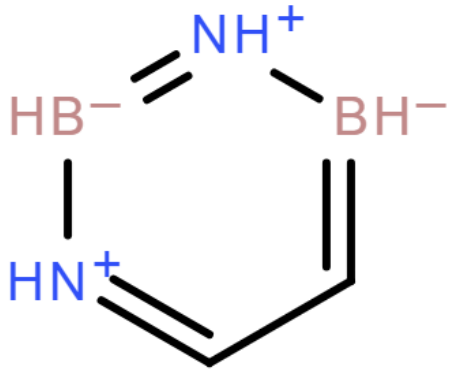
Definition

Alchemical enantiomers are

- two spatially non-superimposable,
- alchemically coupled,
- and iso-electronic compounds with the same formal charge,
- where each transmutating atom is assigned to exactly one subset within each of which averaging of nuclear charges results in identical chemical environments.



These are no alchemical enantiomers!



GFvR, O. A. von Lilienfeld, *Science Adv.* **2021** (arXiv 2008.02784)

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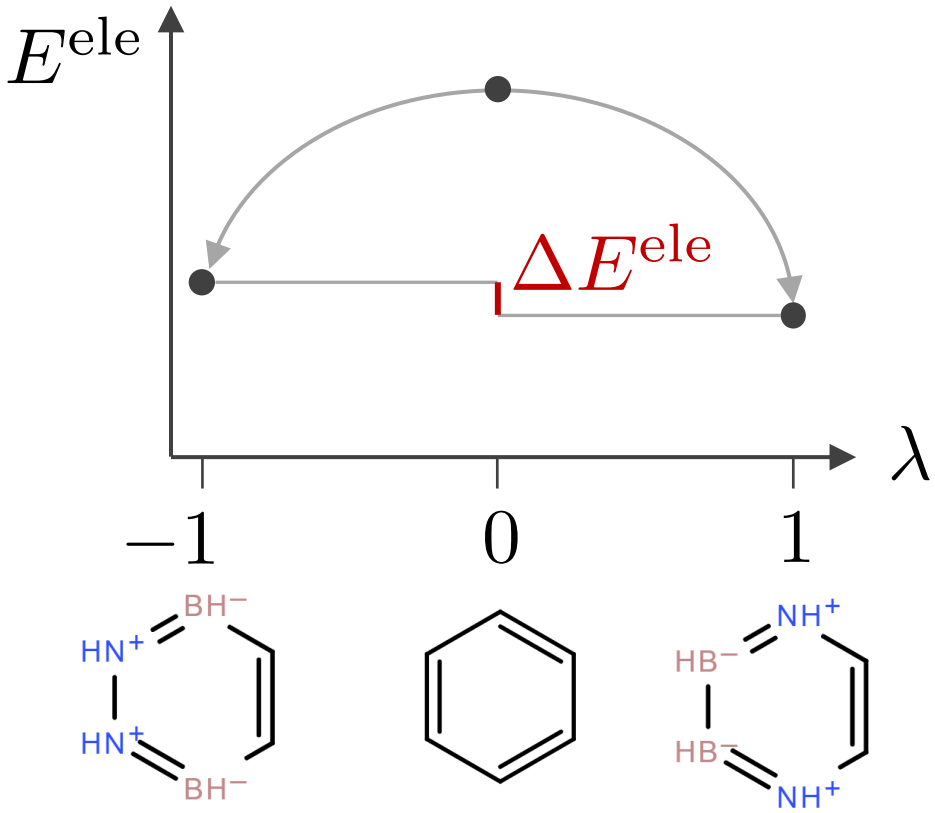

GFvR, O. A. von Lilienfeld, *Science Adv.* **2021** (arXiv 2008.02784)

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GFvR, O. A. von Lilienfeld, *Science Adv.* **2021** (arXiv 2008.02784)

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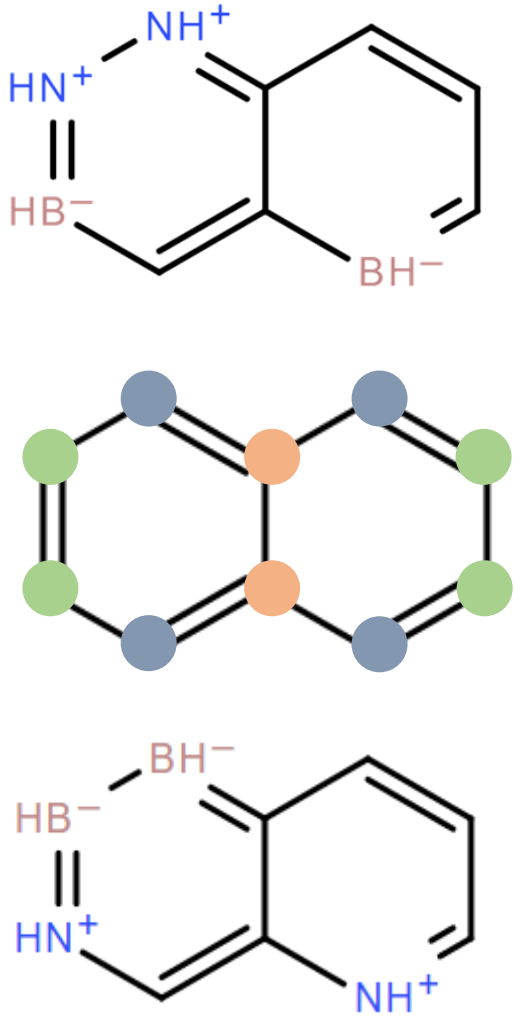
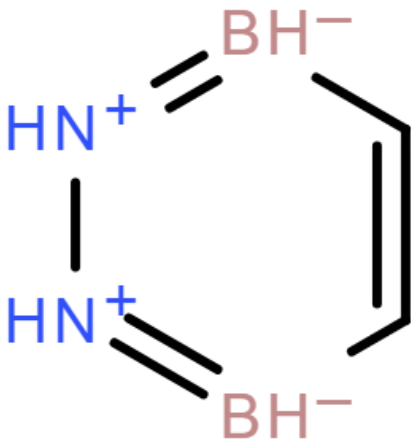
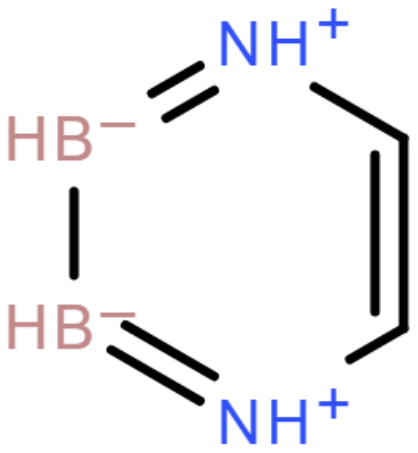


GFvR, O. A. von Lilienfeld, *Science Adv.* **2021** (arXiv 2008.02784)

Consequences



CC
2BC
2BN
NN



CC
2NC
2BN
BB

Consecutive Elements

Q R S

B C N

$$E_{\mathrm{QR}} \simeq E_{\mathrm{SR}} + 0.5(E_{\mathrm{QQ}} - E_{\mathrm{SS}})$$

BC NC BB

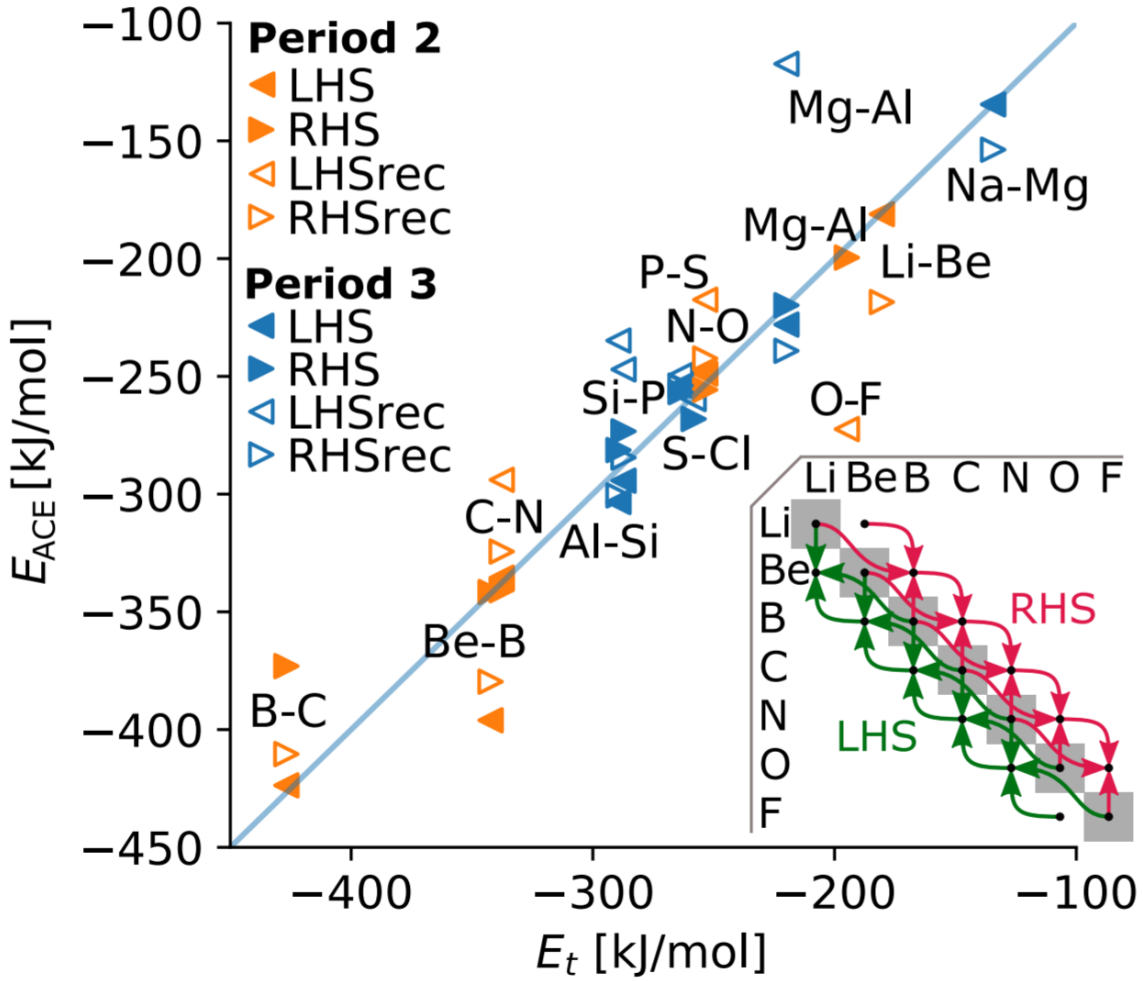
NN

Other skeletons and all substitution patterns

- More such rules
- No violations

GFvR, O. A. von Lilienfeld, *Science Adv.* **2021** (arXiv 2008.02784)

Consequences



Mean absolute error

Direct:	~10 kJ/mol
Chained:	~22 kJ/mol

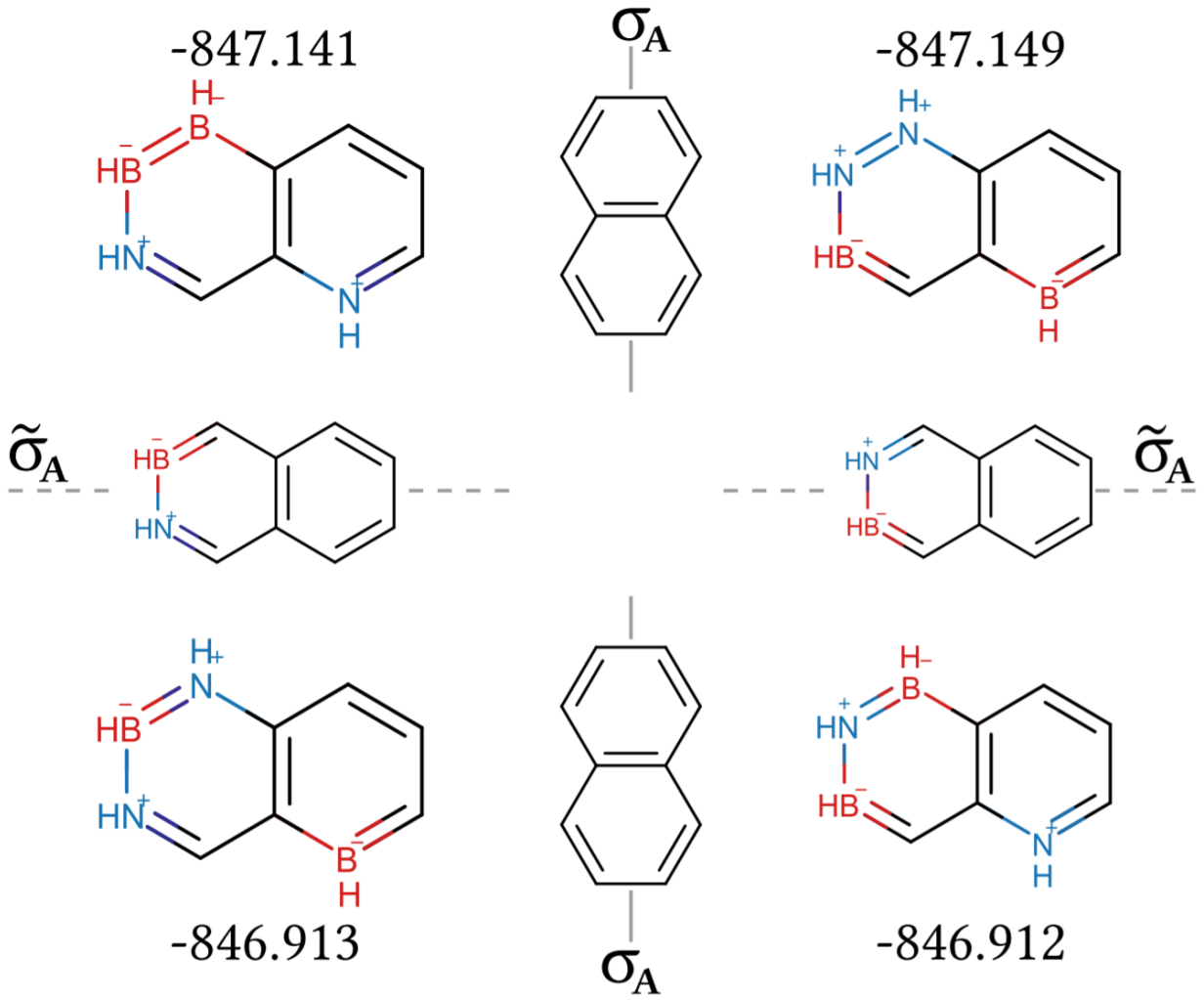
< **Bond dissociation**
G3//B3LYP
Literature

GFvR, O. A. von Lilienfeld, *Science Adv.* **2021** (arXiv 2008.02784)

Definition

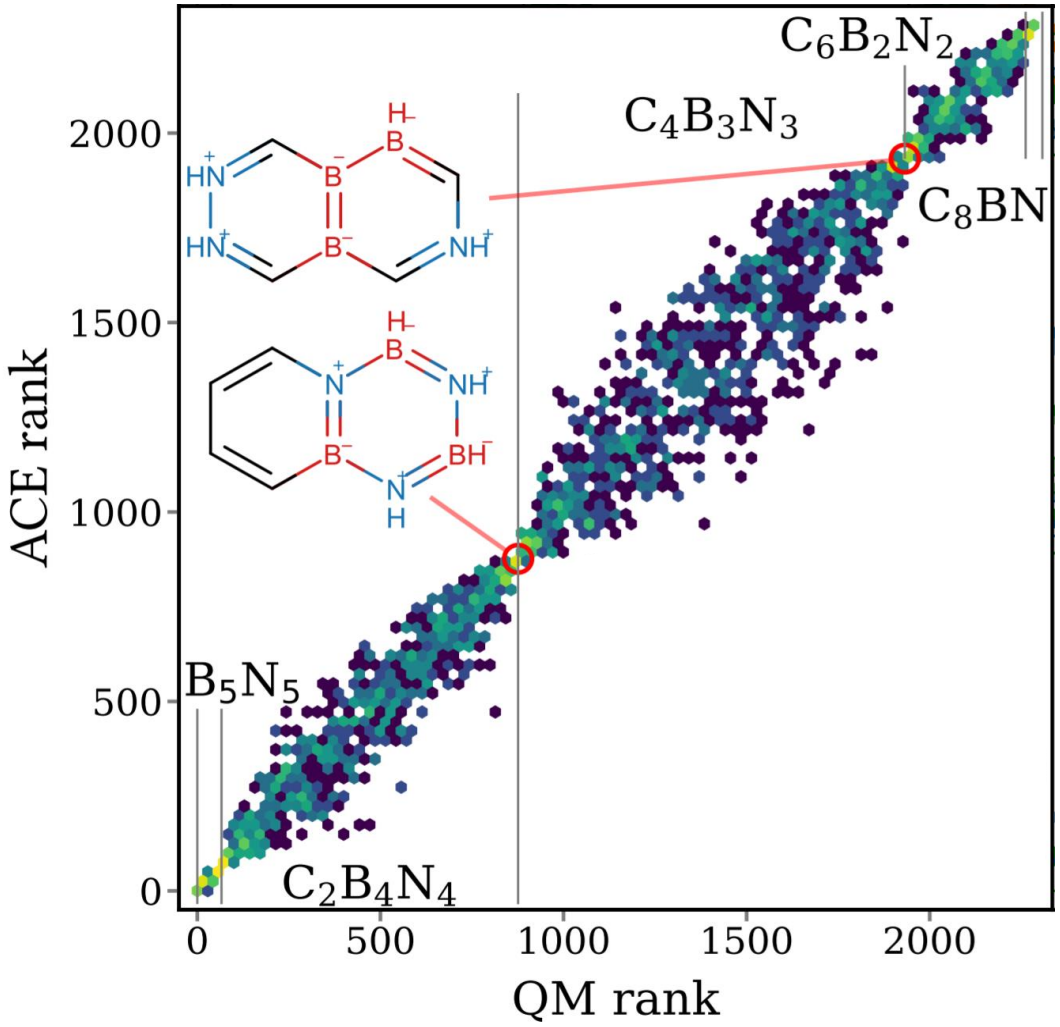
Approximate **alchemical enantiomers** are
- two spatially non-superimposable,
- alchemically coupled,
- and iso-electronic compounds with the same formal charge,
- where each transmutating atom is assigned to exactly one subset within each of which averaging of nuclear charges results in *nearly identical* chemical environments.

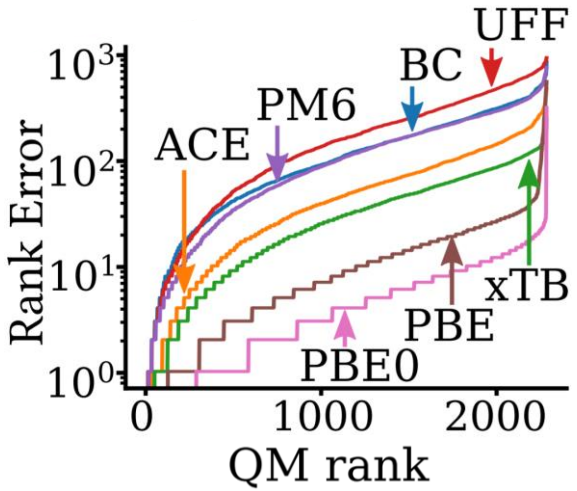
BN-doped naphthalene >
CCSD/cc-pVDZ
Molpro



GFvR, O. A. von Lilienfeld, *Science Adv.* **2021** (arXiv 2008.02784)

Ranking



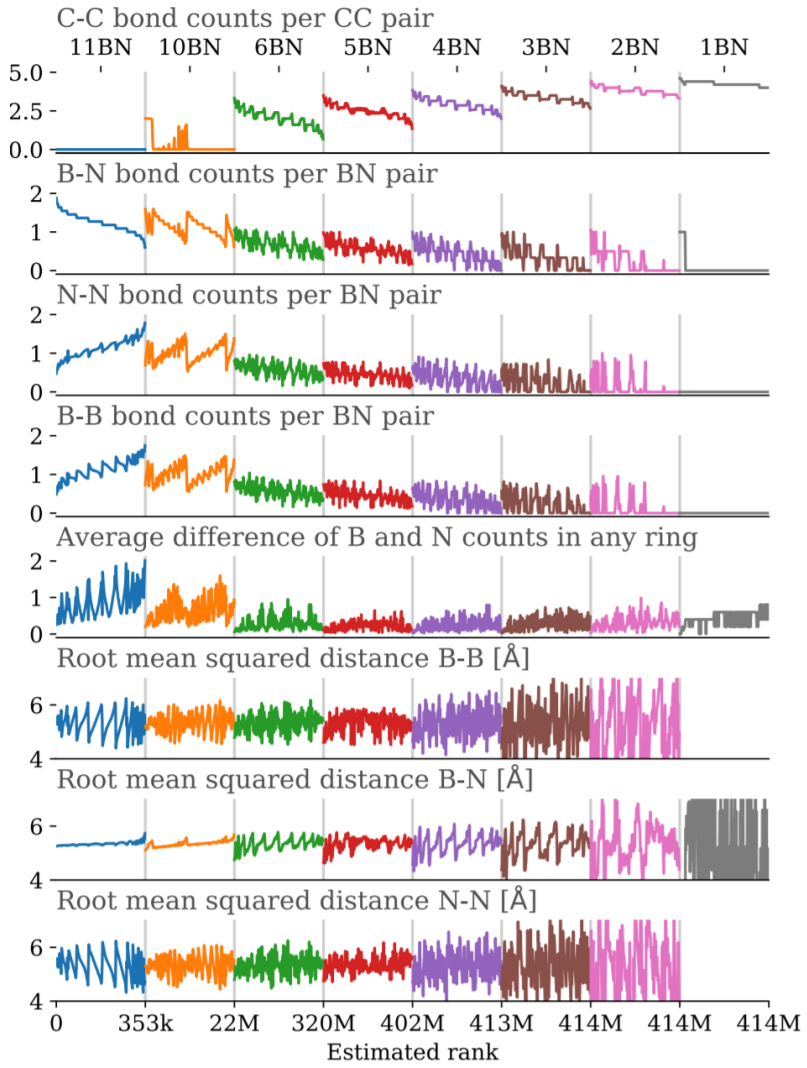


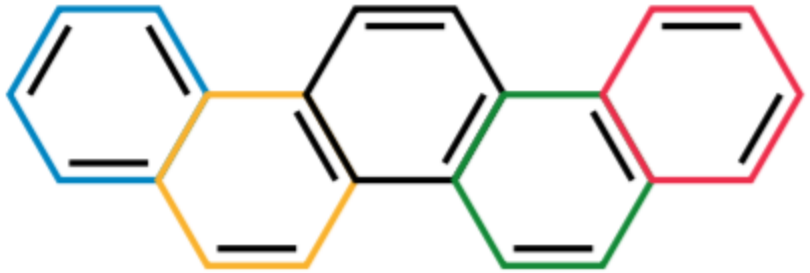
^ BN-doped naphthalene
CCSD/cc-pVDZ
Molpro/MRCC/xTB-GFN2/mopac/OpenBabel

< BN-doped naphthalene
CCSD/cc-pVDZ
Molpro/MRCC

GFvR, O. A. von Lilienfeld, *Science Adv.* **2021** (arXiv 2008.02784)

Ranking





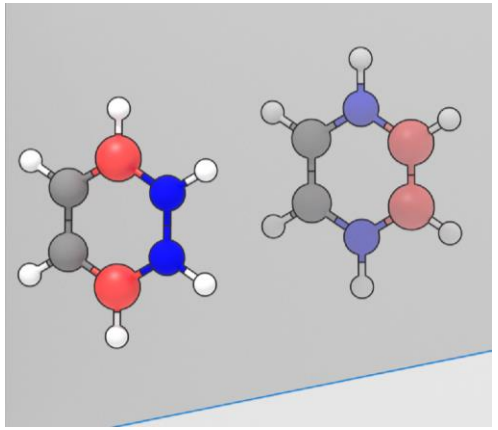
Design rules in order of **decreasing strength**

- Add BN pairs
- Maximize CC bonds
- Substitute sites shared between rings
- Maximize BN bonds
- Avoid N substitutions on rings sharing a larger amount of bonds with other rings
- Balance BN substitutions in each ring

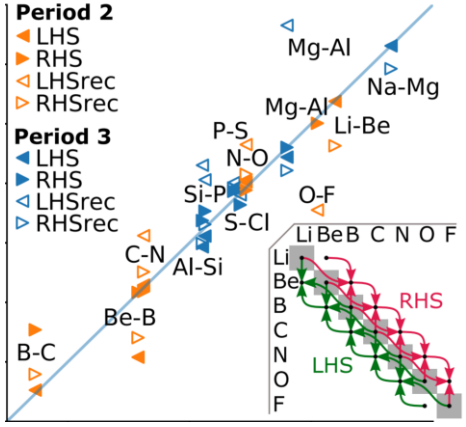
Not a single QM calculation required!

GFvR, O. A. von Lilienfeld, *Science Adv.* **2021** (arXiv 2008.02784)

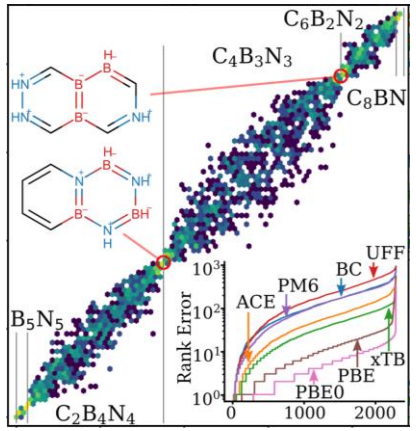
Summary



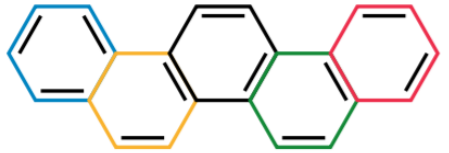
Alchemical enantiomers constitute a new symmetry.



Approximate symmetry remarkably accurate.



Bonding rules and ranking without QM calculations.



x 414 M

Combinatorial scaling with size of system.

APDFT | Guido Falk von Rudorff, O. A. von Lilienfeld, *Phys. Rev. Res.* **2020** (*arXiv* 1809.016

Alchemical enantiomers | Guido Falk von Rudorff, O. A. von Lilienfeld, *Science Adv.* **2021** (arXiv 2008.02784)

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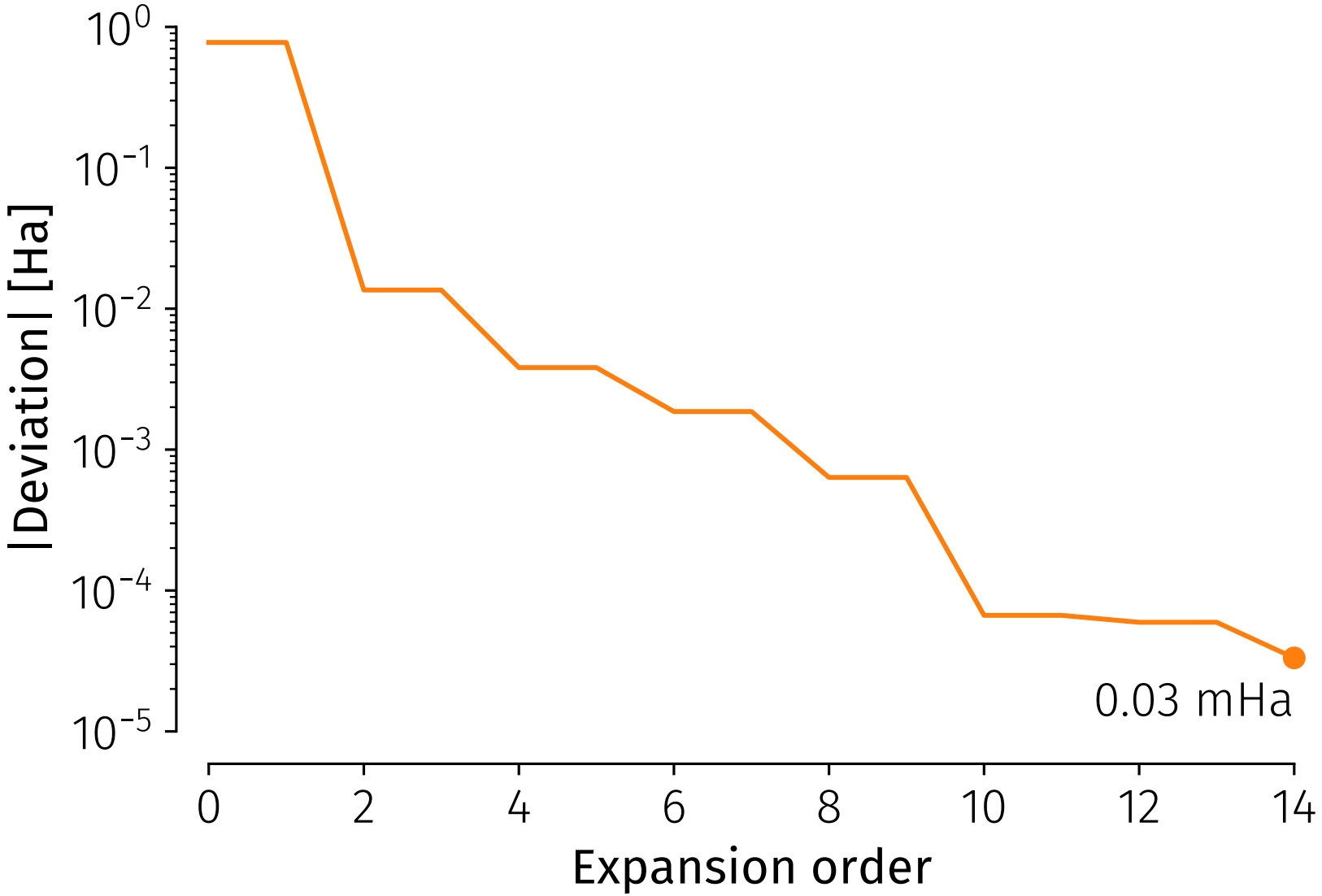
Convergence



< H_2 to He
HF / def2-TZVP
DiffiQult, algopy

Theory

Interpolate between molecular isoelectronic Hamiltonians

$$\hat{H}(\lambda) \equiv \lambda \hat{H}_\mathrm{t} + (1-\lambda)\hat{H}_\mathrm{r} \qquad \lambda \in [0,1]$$

Taylor expansion around reference molecule

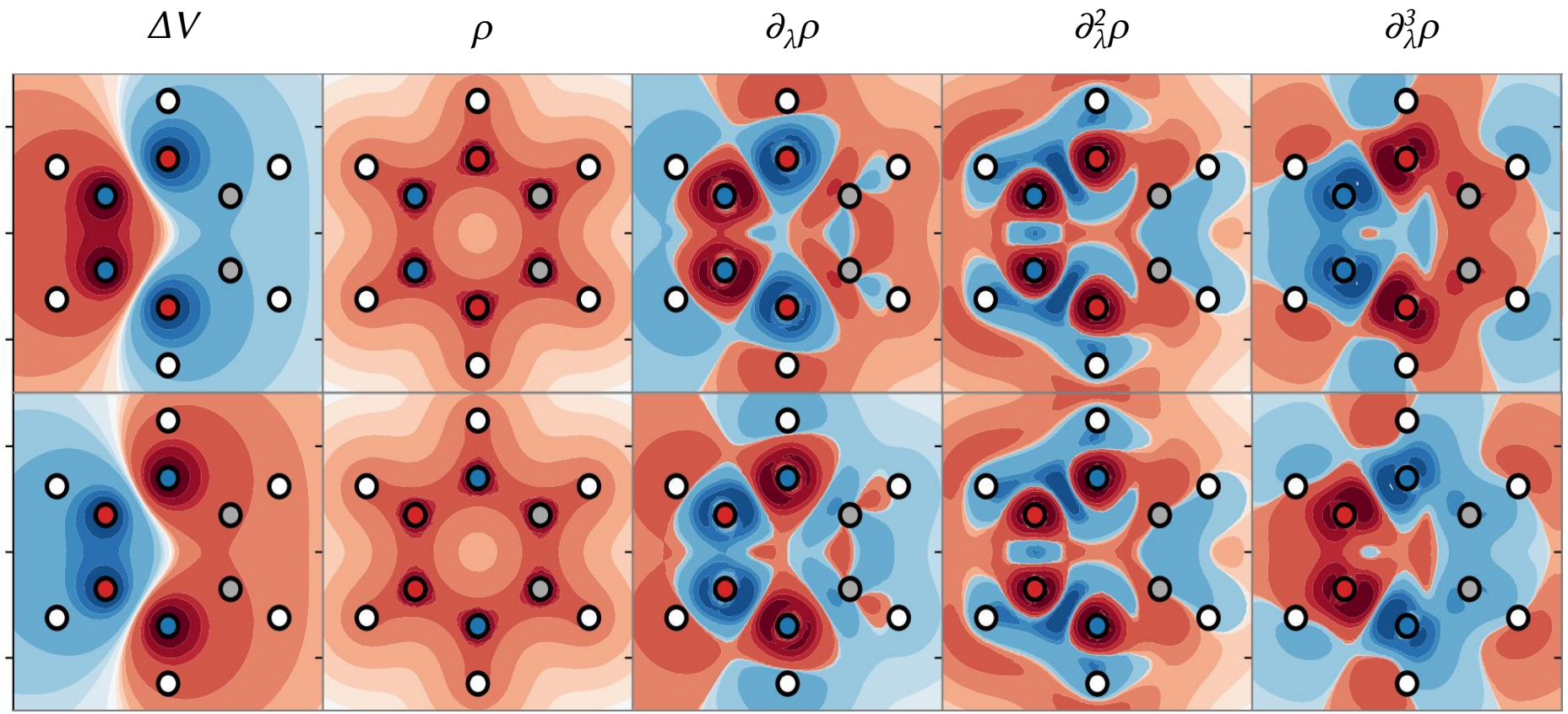
$$E_\mathrm{t} = \sum_{n=0}^{\infty} \frac{1}{n!} \frac{\partial^n}{\partial \lambda^n} \left\langle \psi_\lambda \middle| \hat{H}(\lambda) \middle| \psi_\lambda \right\rangle \Big|_{\lambda=0} = E_\mathrm{r} + \sum_{n=1}^{\infty} \frac{1}{n!} \left. \frac{\partial^n E(\lambda)}{\partial \lambda^n} \right|_{\lambda=0}$$

Hellmann-Feynman theorem

$$\partial_\lambda E = \left\langle \psi_\lambda \middle| \hat{H}_\mathrm{t} - \hat{H}_\mathrm{r} \middle| \psi_\lambda \right\rangle = \Delta E^\mathrm{NN} + \int_\Omega d\mathbf{r} \underbrace{\left(v_\mathrm{t}(\mathbf{r}) - v_\mathrm{r}(\mathbf{r})\right)}_{\equiv \Delta v} \rho_\lambda(\mathbf{r})$$

O. A. von Lilienfeld, *J. Chem. Phys.* 2009.

Theory



< BN-doped benzene
CCSD/def2-TZVP
Gaussian09

GFvR, O. A. von Lilienfeld, *Science Adv.* **2021** (arXiv 2008.02784)