Where is the electron pair?

A QMC detective story

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The Towler Institute
Vallico Soto, Italy
July 26, 2007

Talk overview

What we will cover for sure and maybe cover...

Electrophilic amination: A QMC study

- The chemistry
- Electron-pair localization functions (original and modified)
- Sketch current and future work

Recently published: Amador *et al.*, J. Chem. Phys. **126**, 204308 (2007)

Electronic structure by quantum computation

- Polynomial algorithm for the *exact* solution of the Schrödinger equation on a quantum computer
- Recent results

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Making proteins: Synthesis of peptide bonds

Nucleophilic vs. electrophilic substitution

- Carbon-nitrogen bonds are usually formed by the nucleophilic attack of a nitrogen to an electrophilic carbon (S_N2)
- Reverse process: a nucleophilic carbon replaces a leaving group previously attached to an electrophilic nitrogen
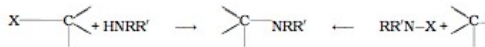
- Some reagents have been found and tested
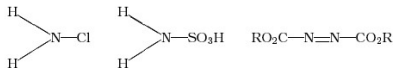
Exploration using QMC

The mission

- Is it possible to rationalize the electronic properties of the already known reagents so as to be able to direct the search for even more effective ones?
- Approach the answer by:
  - Use DMC to calculate energetics
  - Calculate the electron-pair localization function (EPLF)
    rationalize values, find trends, explain differences, make predictions

Representative molecules

- Typical nucleophilic behavior:
  NH_3, NH_2-CH_3 (MA), NH-$(CH_3)_2$ (DMA), N-$(CH_3)_3$ (TMA)
- Possible electrophilic behavior:
  NH_2F, NH_2CF_3

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DMC calculations

Calculation parameters

- geometries optimized with GAMESS at MP2//631G* level
- cc-pVTZ basis set
- fourth order SMBH correlation function, absolute deviation minimization
- collection of 10^6 walkers for EPLF
- $\approx 1\,week$ computational time on 8 cores.
- All calculations carried out with the Zori code (http://www.zori-code.com)

Atomization enthalpy differences

Single-determinant energies

Atomization enthalpy differences $\lvert \Delta E_a^{\mathrm{calc}} - \Delta E_a^{\mathrm{expt}} \rvert$ (kJ/mol)				
Method	Molecule			
	NH_3	MA	DMA	TMA
HF	394	693	984	1278
BLYP	24	1	170	34
B3LYP	21	8	4	2
B3PW91	6	1	2	3
MP2FC	29	58	70	75
MP2FC//HF/6-31G*	32	1121	76	86
MP2FC//B3LYP/6-31G*	32	1124	75	84
MP2FC//MP2FC/6-31G*	32	61	76	84
DMC-SMBH//MP2/6-31G*	3	9	14	91

Numbers are differences with the experimental value at 298.15 K.

Total energies are corrected by zero point energy (ZPE).

Electron Pair Localization Function

$$d_{\sigma\sigma}(\overrightarrow{r}) = \sum_{i=1}^{N} \langle\langle \delta(\overrightarrow{r} - \overrightarrow{r}_i) \min_{j;\sigma_j=\sigma_i} |\overrightarrow{r} - \overrightarrow{r}_j|\rangle\rangle,$$

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EPLF

In terms of these average distances, the EPLF is defined as

$$\mathrm{EPLF}(\overrightarrow{r}) = \frac{d_{\sigma\sigma}(\overrightarrow{r}) - d_{\sigma\bar{\sigma}}(\overrightarrow{r})}{d_{\sigma\sigma}(\overrightarrow{r}) + d_{\sigma\bar{\sigma}}(\overrightarrow{r})}.$$

EPLF range

(-1) unpaired (0) long-distance (1) Paired

A. Scemama, P. Chaquin, M. Caffarel. *J. Chem. Phys.*, 121:1725-1735, 2004.

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A nucleophilic amine
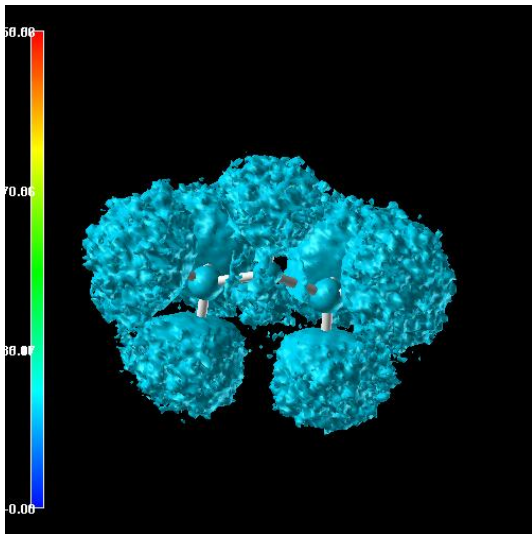
iso-EPLF surface for
dimethylamine

Fluoroamine

An electrophilic amine
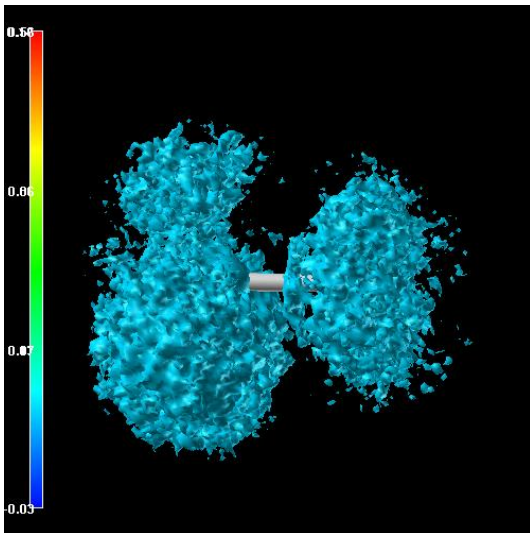
iso-EPLF surface for fluoroamine

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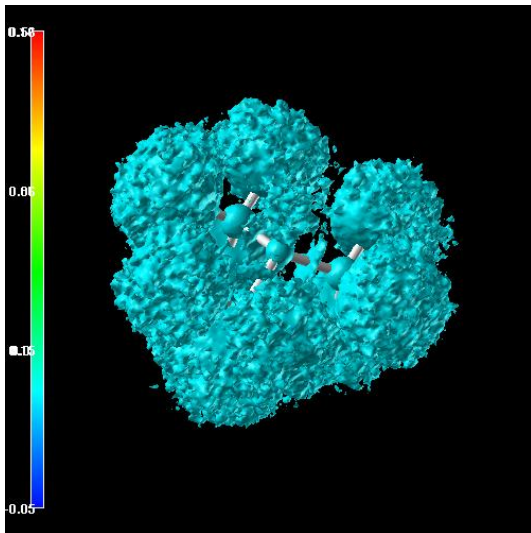
iso-EPLF surface for
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Ammonia
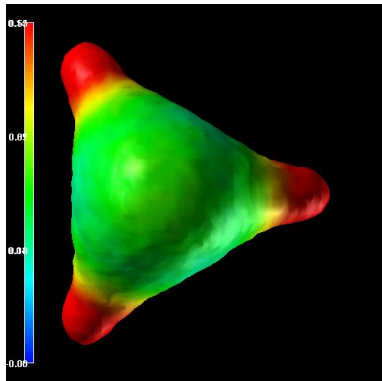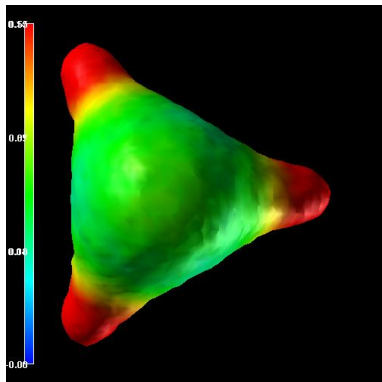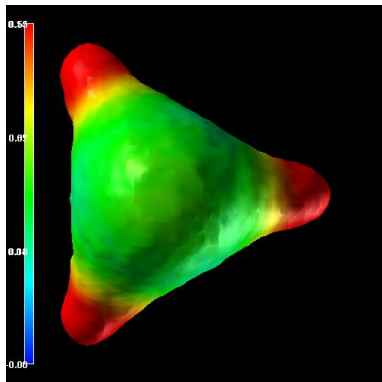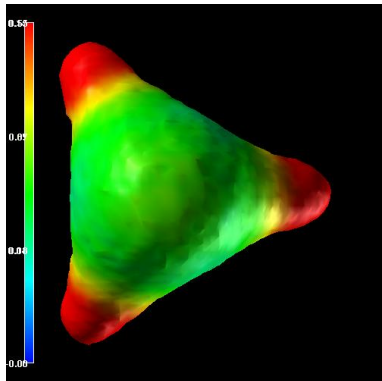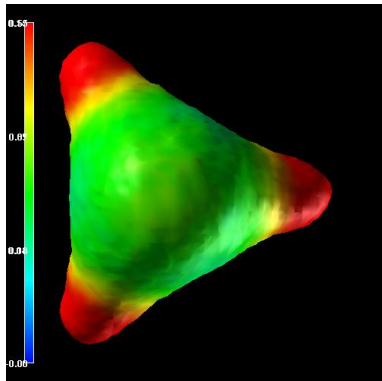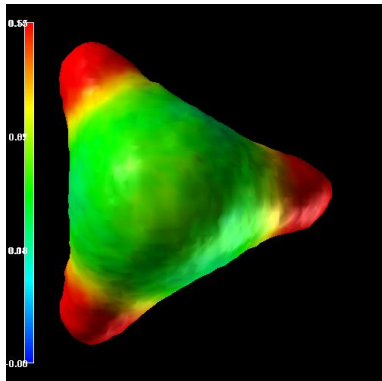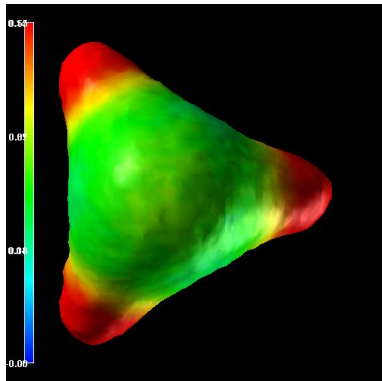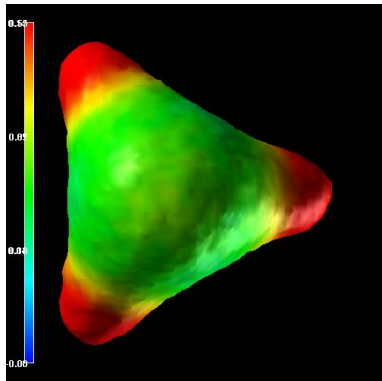EPLF projected on the electron density

iso-density surface with projected color coded EPLF for ammonia

Ammonia
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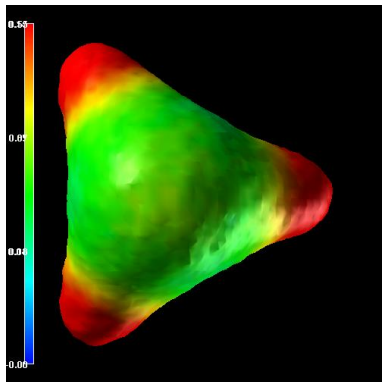iso-density surface with projected color coded EPLF for ammonia

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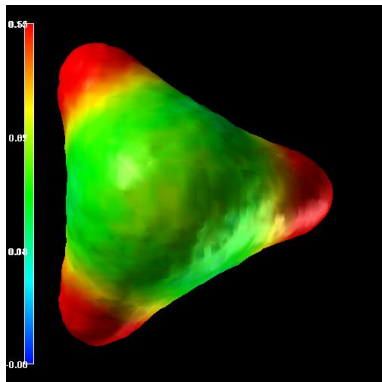EPLF projected on the electron density

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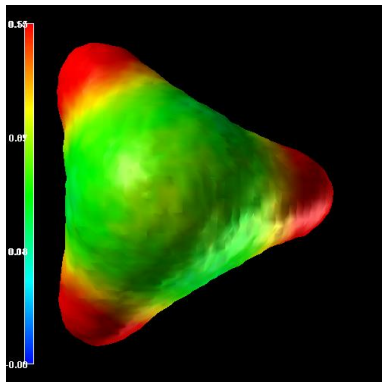projected color coded EPLF for
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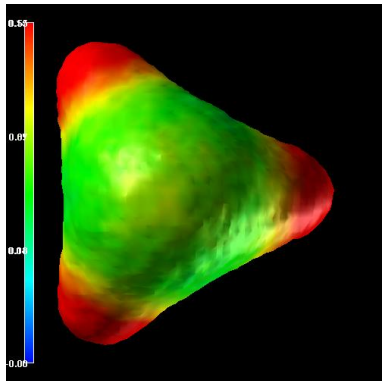iso-density surface with projected color coded EPLF for ammonia

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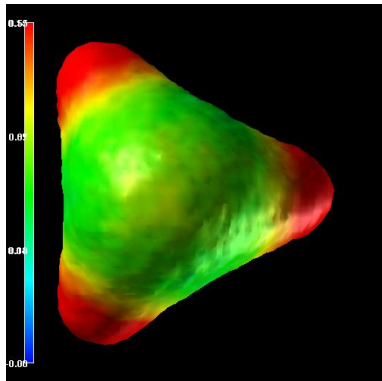projected color coded EPLF for
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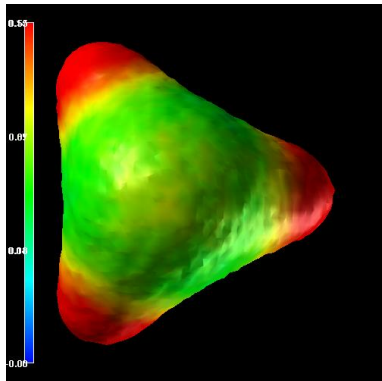projected color coded EPLF for
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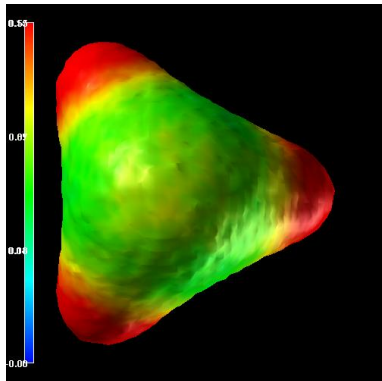projected color coded EPLF for
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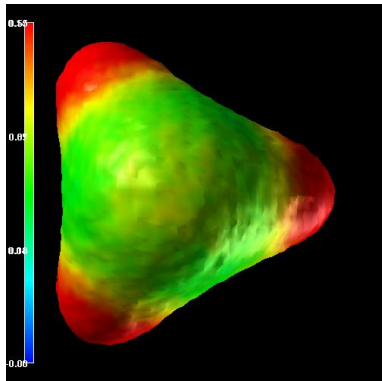EPLF projected on the electron density

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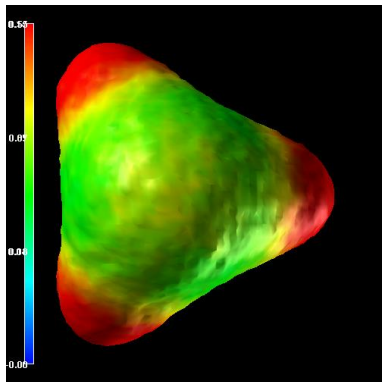projected color coded EPLF for
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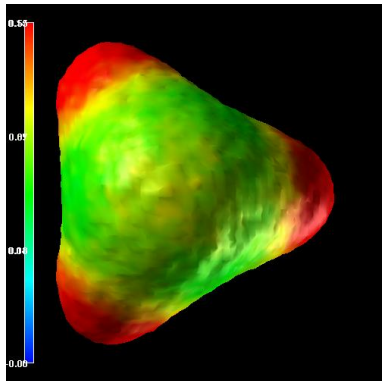EPLF projected on the electron density

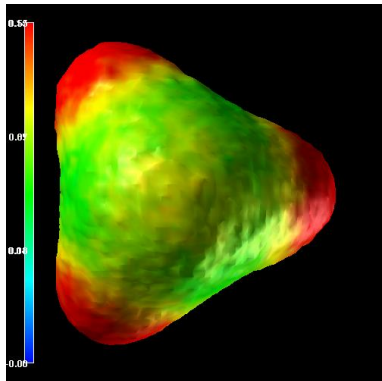iso-density surface with projected color coded EPLF for ammonia

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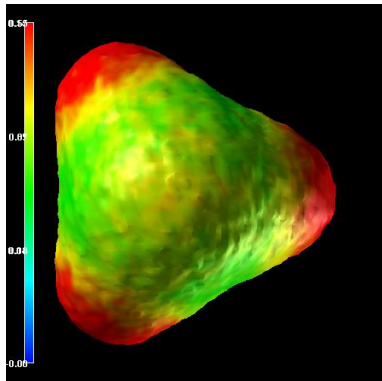projected color coded EPLF for
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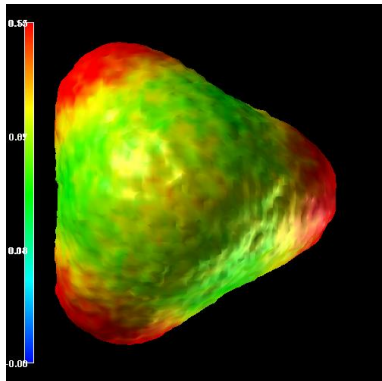projected color coded EPLF for
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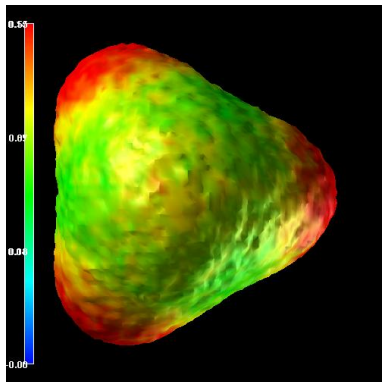projected color coded EPLF for
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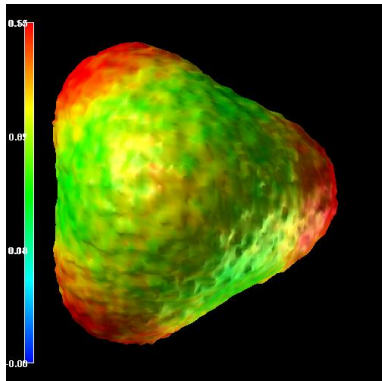iso-density surface with projected color coded EPLF for ammonia

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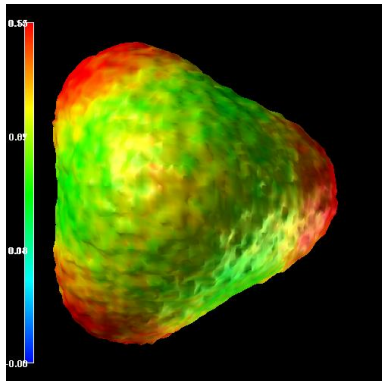projected color coded EPLF for
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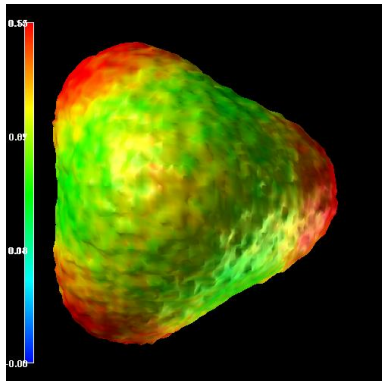EPLF projected on the electron density

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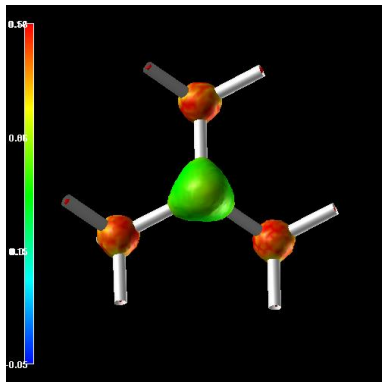
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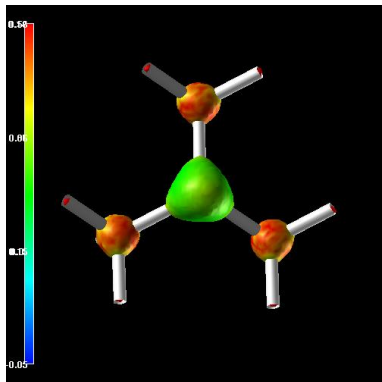ammonia

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Trimethylamine: A nucleophile

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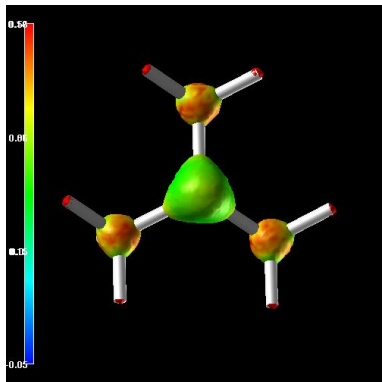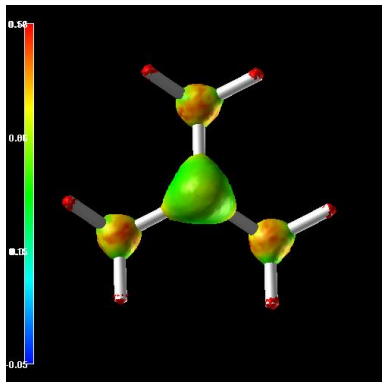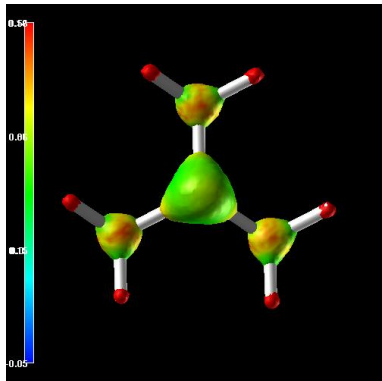# Trimethylamine: A nucleophile

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iso-density surface with projected color coded EPLF for trimethyl amine

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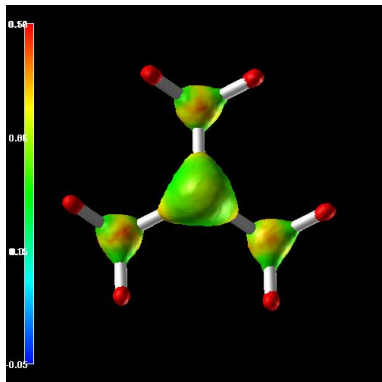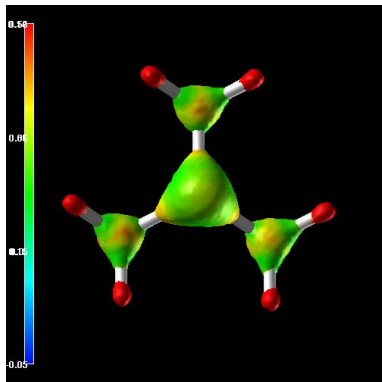
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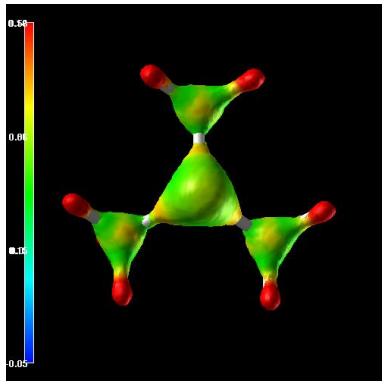
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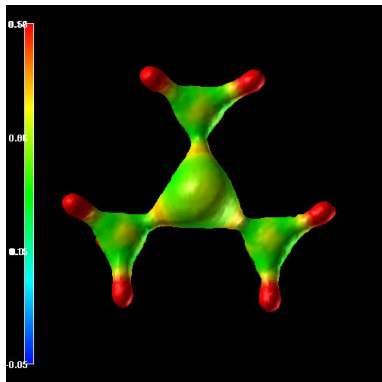
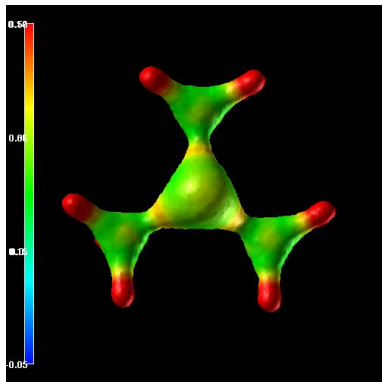EPLF projected on the electron density

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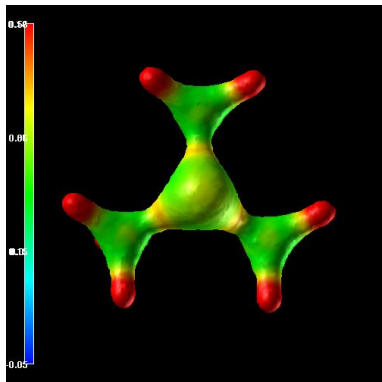
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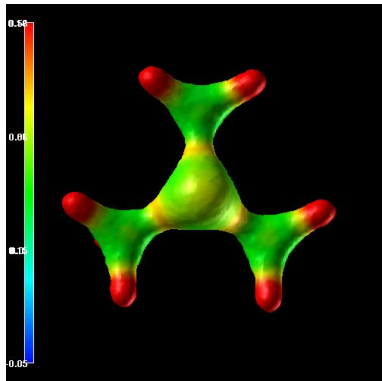
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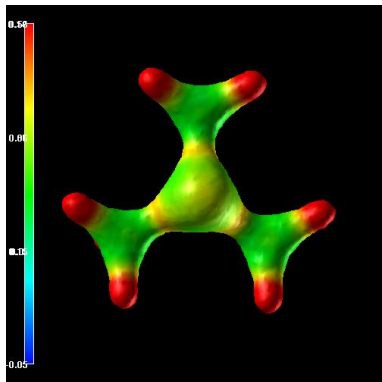
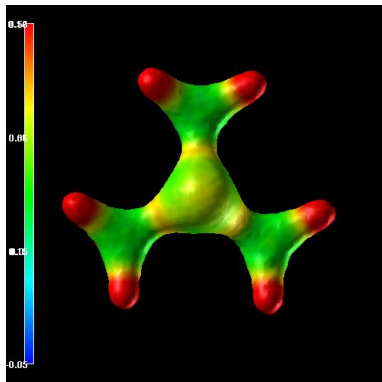EPLF projected on the electron density

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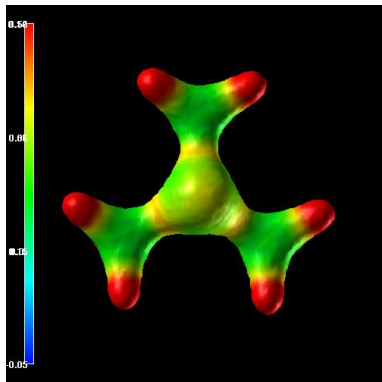
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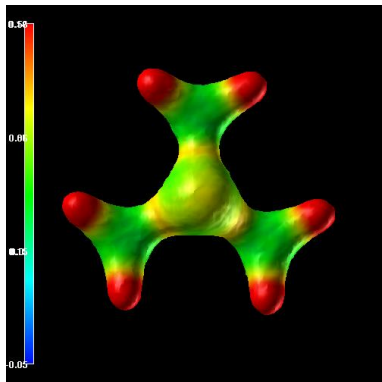
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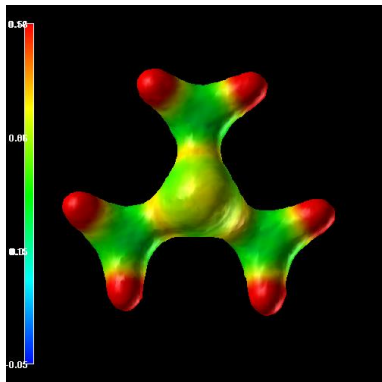
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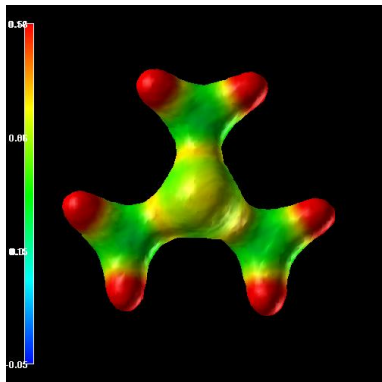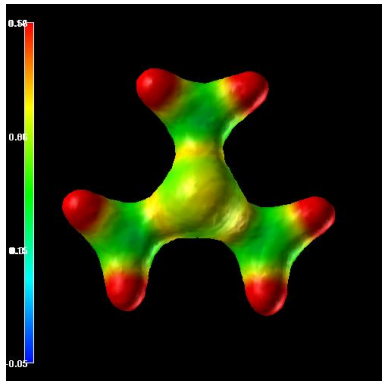projected color coded EPLF for
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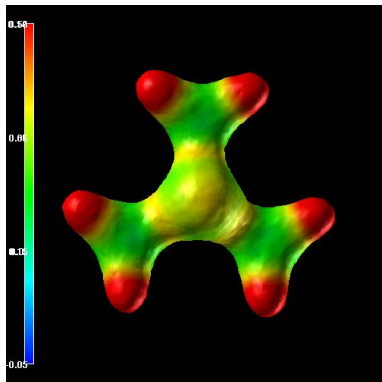
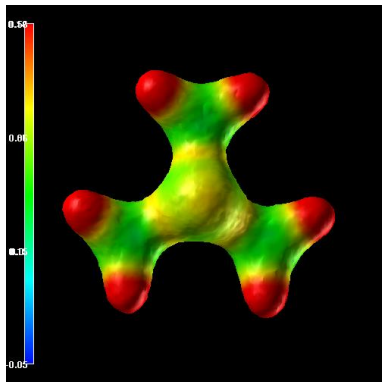EPLF projected on the electron density

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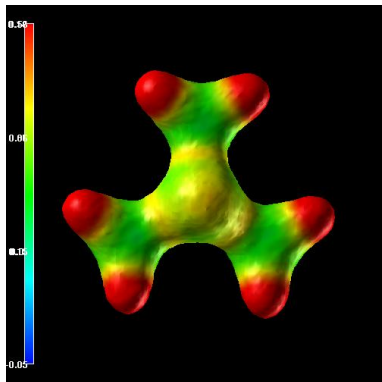
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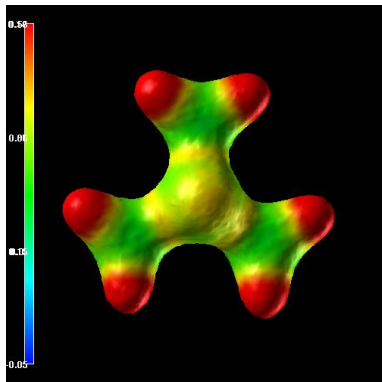
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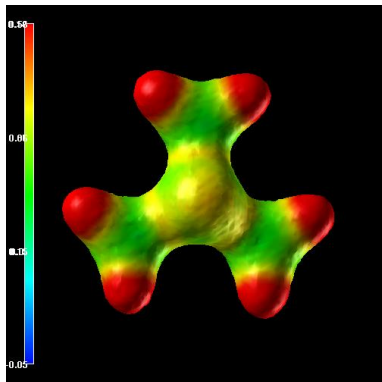
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projected color coded EPLF for
trimethyl amine

Trimethylamine: A nucleophile
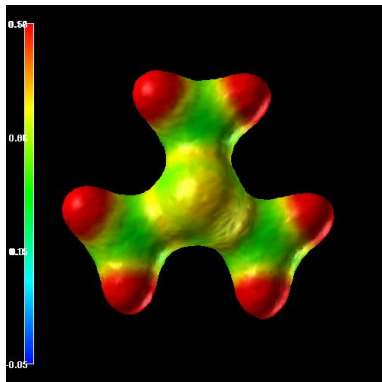
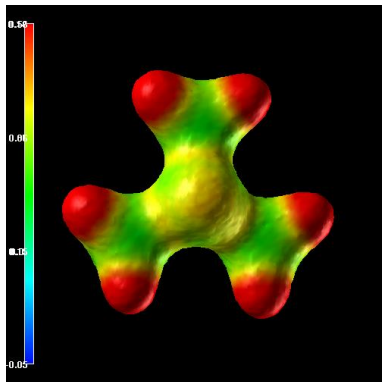EPLF projected on the electron density

iso-density surface with projected color coded EPLF for trimethyl amine

Trimethylamine: A nucleophile

EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
trimethyl amine

Trimethylamine: A nucleophile

EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
trimethyl amine

Trimethylamine: A nucleophile
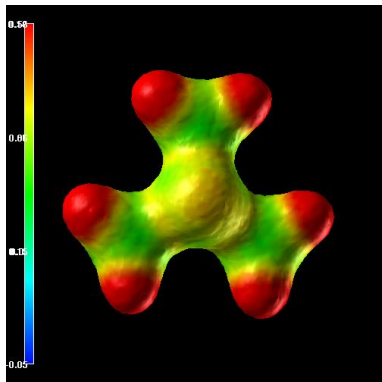
EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
trimethyl amine

Trimethylamine: A nucleophile
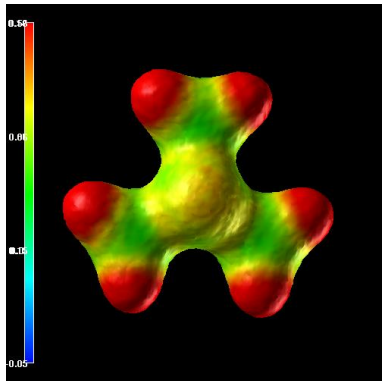
EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
trimethyl amine

Trimethylamine: A nucleophile
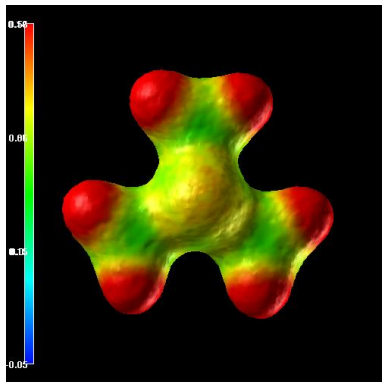
EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
trimethyl amine

Trimethylamine: A nucleophile

EPLF projected on the electron density

iso-density surface with
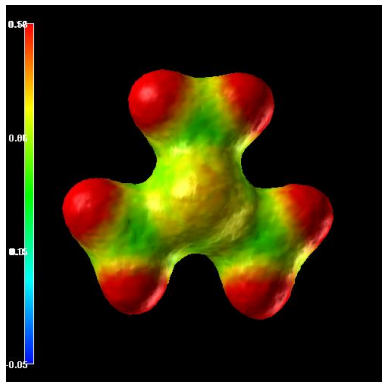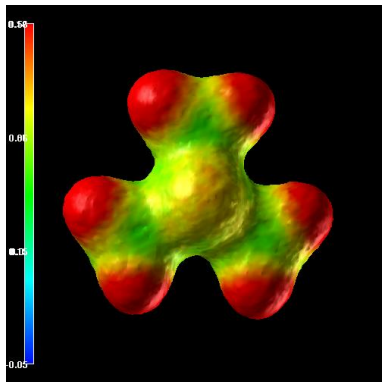projected color coded EPLF for
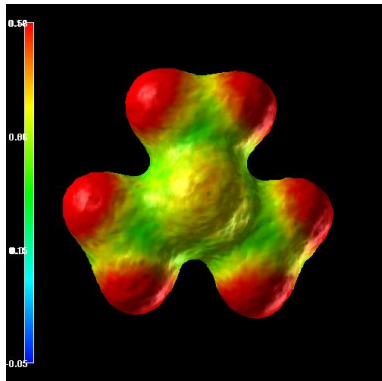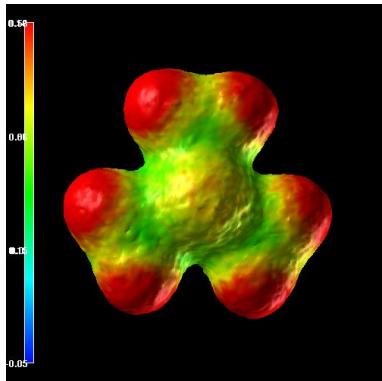trimethyl amine

iso-density surface with
projected color coded EPLF for
trimethyl amine

Trimethylamine: A nucleophile

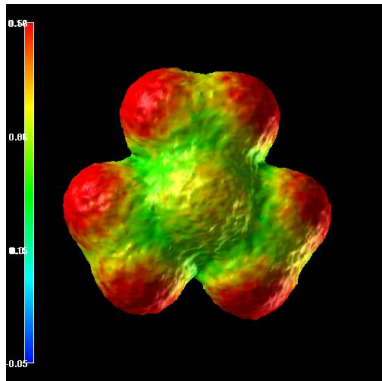EPLF projected on the electron density

iso-density surface with projected color coded EPLF for trimethyl amine

Trimethylamine: A nucleophile

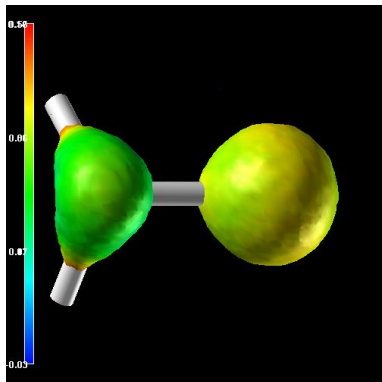EPLF projected on the electron density

iso-density surface with projected color coded EPLF for trimethyl amine

Fluoroamine: An electrophile

EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
fluoroamine

Fluoroamine: An electrophile

EPLF projected on the electron density

iso-density surface with projected color coded EPLF for fluoroamine

Fluoroamine: An electrophile

EPLF projected on the electron density

iso-density surface with projected color coded EPLF for fluoroamine

Fluoroamine: An electrophile

EPLF projected on the electron density

iso-density surface with projected color coded EPLF for fluoroamine
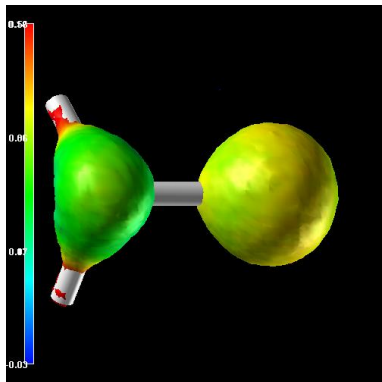
Fluoroamine: An electrophile

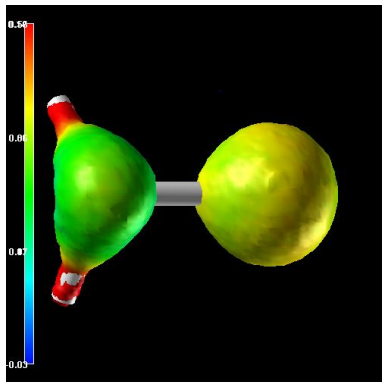EPLF projected on the electron density

iso-density surface with projected color coded EPLF for fluoroamine

Fluoroamine: An electrophile

EPLF projected on the electron density

iso-density surface with projected color coded EPLF for fluoroamine

Fluoroamine: An electrophile

EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
fluoroamine
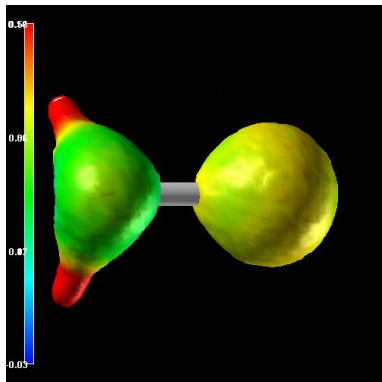
Fluoroamine: An electrophile

EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
fluoroamine
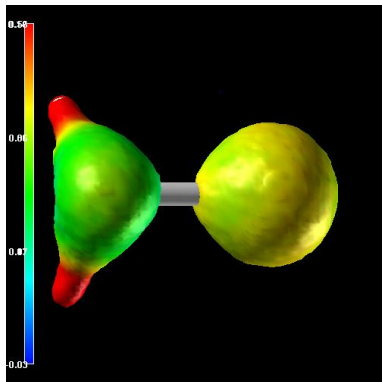
Fluoroamine: An electrophile

EPLF projected on the electron density

iso-density surface with projected color coded EPLF for fluoroamine

Fluoroamine: An electrophile
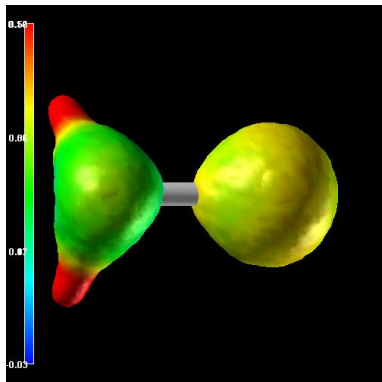
EPLF projected on the electron density

iso-density surface with projected color coded EPLF for fluoroamine

Fluoroamine: An electrophile

EPLF projected on the electron density

iso-density surface with projected color coded EPLF for fluoroamine
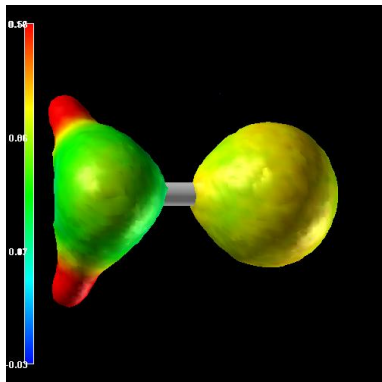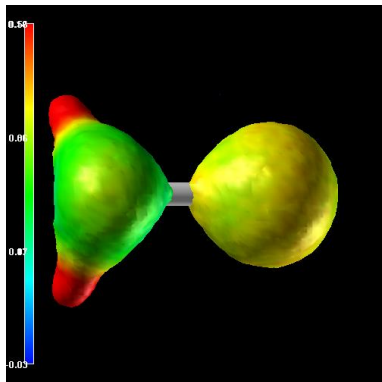
Fluoroamine: An electrophile

EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
fluoroamine

Fluoroamine: An electrophile

EPLF projected on the electron density

iso-density surface with projected color coded EPLF for fluoroamine

Fluoroamine: An electrophile

iso-density surface with projected color coded EPLF for fluoroamine
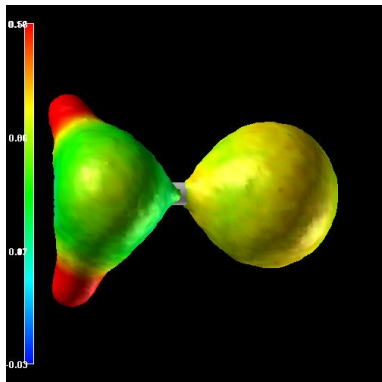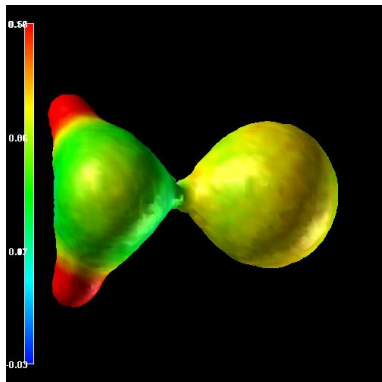
Fluoroamine: An electrophile

EPLF projected on the electron density

iso-density surface with projected color coded EPLF for fluoroamine

Fluoroamine: An electrophile

EPLF projected on the electron density

iso-density surface with projected color coded EPLF for fluoroamine
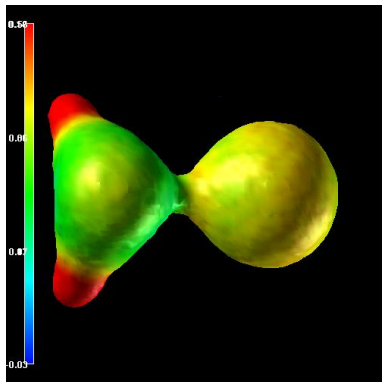
Fluoroamine: An electrophile

EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
fluoroamine

Fluoroamine: An electrophile
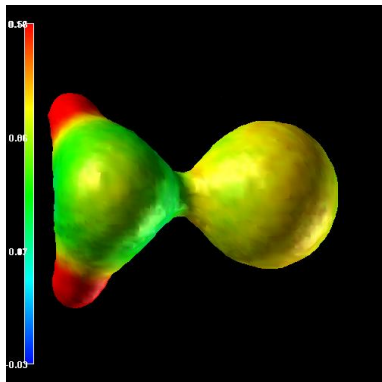
EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
fluoroamine

Fluoroamine: An electrophile
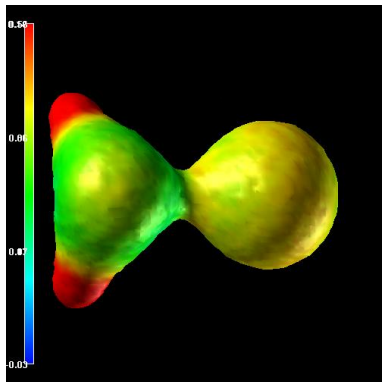
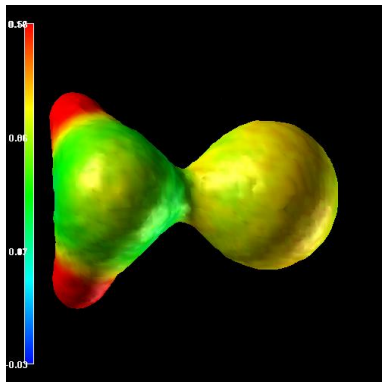EPLF projected on the electron density

iso-density surface with projected color coded EPLF for fluoroamine

Fluoroamine: An electrophile

EPLF projected on the electron density

iso-density surface with projected color coded EPLF for fluoroamine

Fluoroamine: An electrophile

EPLF projected on the electron density

iso-density surface with projected color coded EPLF for fluoroamine
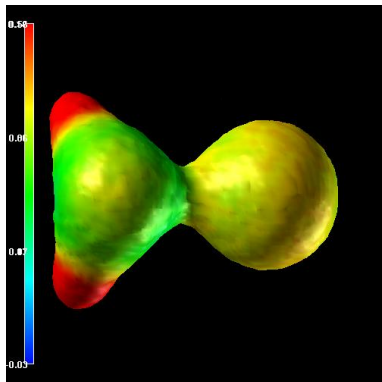
Fluoroamine: An electrophile

EPLF projected on the electron density

iso-density surface with projected color coded EPLF for fluoroamine

Fluoroamine: An electrophile
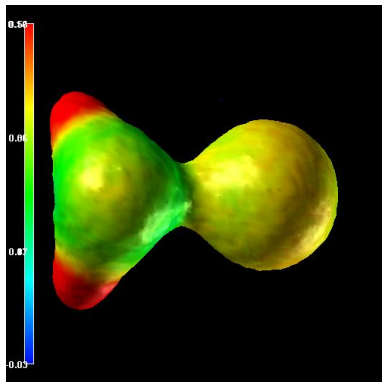
EPLF projected on the electron density

iso-density surface with projected color coded EPLF for fluoroamine
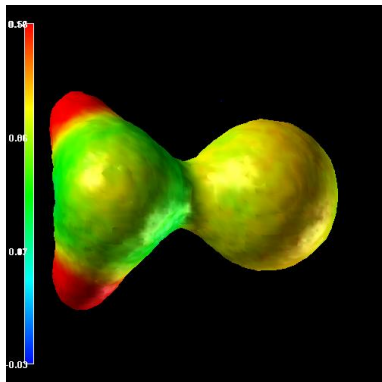
Fluoroamine: An electrophile

EPLF projected on the electron density

iso-density surface with projected color coded EPLF for fluoroamine
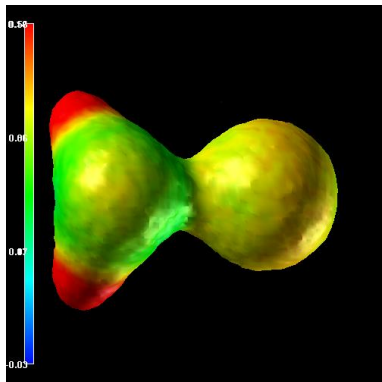
Fluoroamine: An electrophile

EPLF projected on the electron density

iso-density surface with projected color coded EPLF for fluoroamine

Fluoroamine: An electrophile

EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
fluoroamine
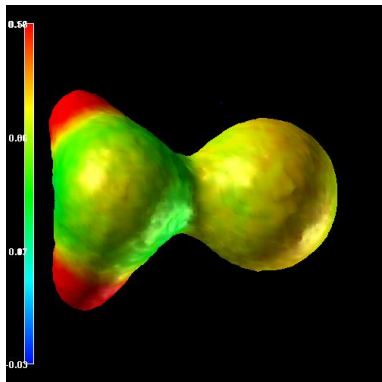
Fluoroamine: An electrophile

EPLF projected on the electron density

iso-density surface with projected color coded EPLF for fluoroamine
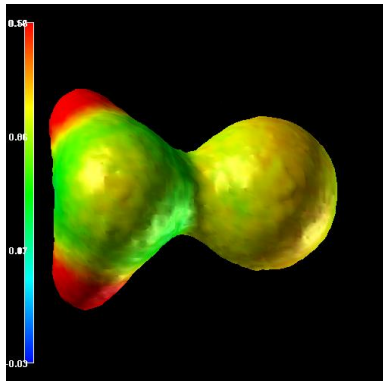
Fluoroamine: An electrophile

EPLF projected on the electron density

iso-density surface with projected color coded EPLF for fluoroamine
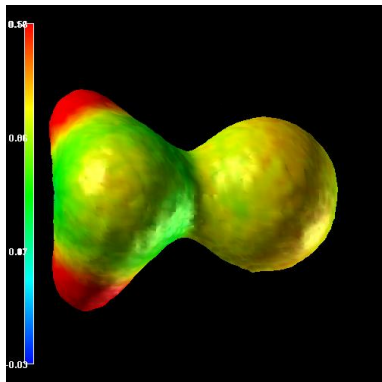
Fluoroamine: An electrophile

EPLF projected on the electron density

iso-density surface with projected color coded EPLF for fluoroamine

Fluoroamine: An electrophile

EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
fluoroamine

Fluoroamine: An electrophile

iso-density surface with projected color coded EPLF for fluoroamine
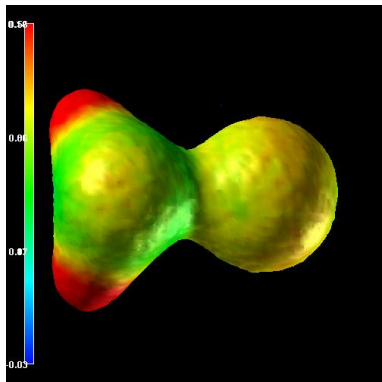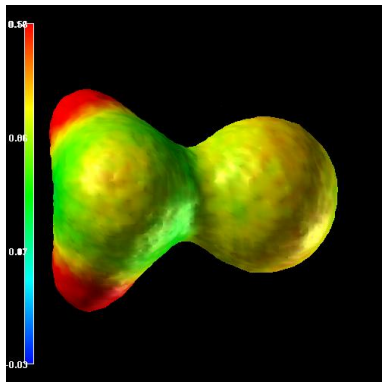
Fluoroamine: An electrophile

EPLF projected on the electron density

iso-density surface with projected color coded EPLF for fluoroamine

Fluoroamine: An electrophile
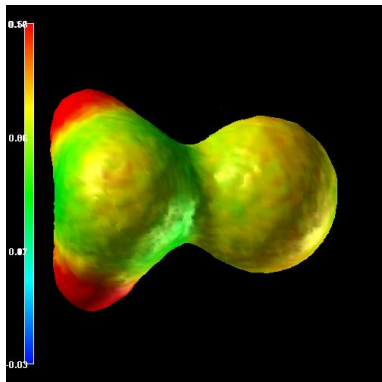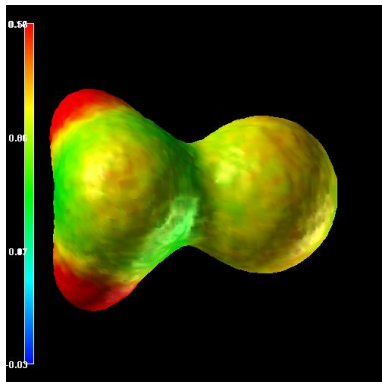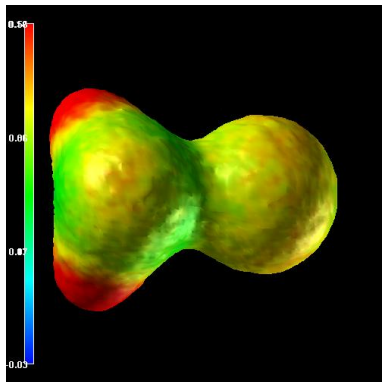
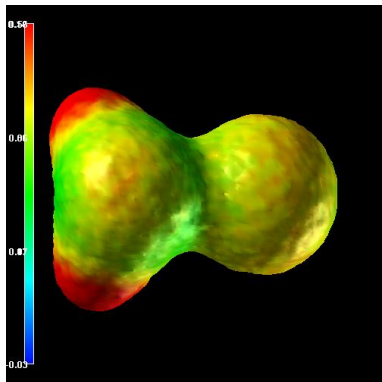EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
fluoroamine

Fluoroamine: An electrophile

EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
fluoroamine

Trifluoromethyl amine: An electrophile

EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
trifluoromethyl amine

Trifluoromethyl amine: An electrophile

EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
trifluoromethyl amine

Trifluoromethyl amine: An electrophile

EPLF projected on the electron density

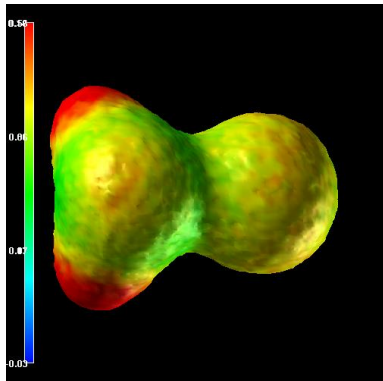iso-density surface with projected color coded EPLF for trifluoromethyl amine

Trifluoromethyl amine: An electrophile

EPLF projected on the electron density
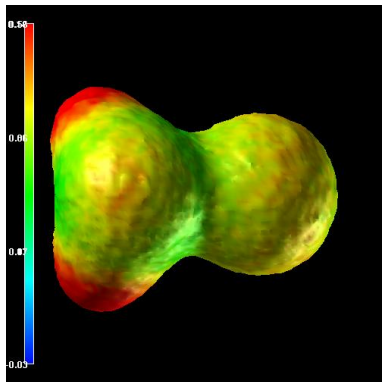

iso-density surface with
projected color coded EPLF for
trifluoromethyl amine

Trifluoromethyl amine: An electrophile

EPLF projected on the electron density
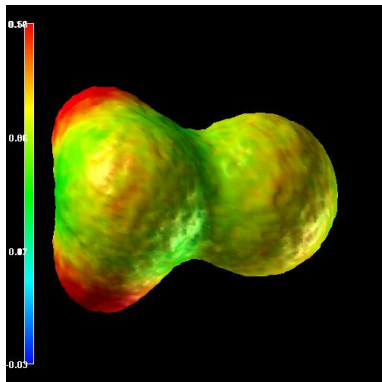

iso-density surface with
projected color coded EPLF for
trifluoromethyl amine

Trifluoromethyl amine: An electrophile

EPLF projected on the electron density
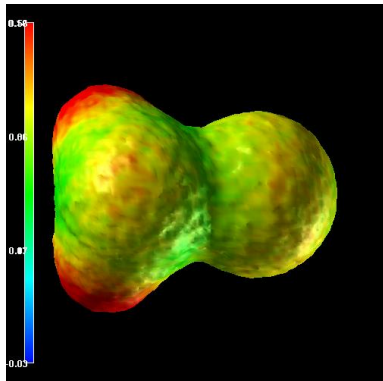

iso-density surface with
projected color coded EPLF for
trifluoromethyl amine

Trifluoromethyl amine: An electrophile

EPLF projected on the electron density

iso-density surface with
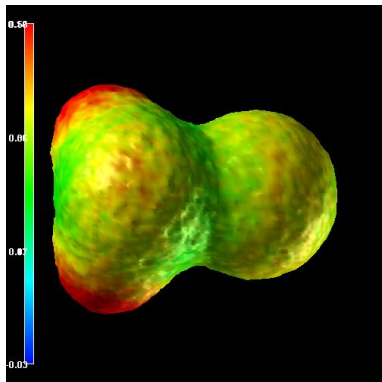projected color coded EPLF for
trifluoromethyl amine

Trifluoromethyl amine: An electrophile

EPLF projected on the electron density
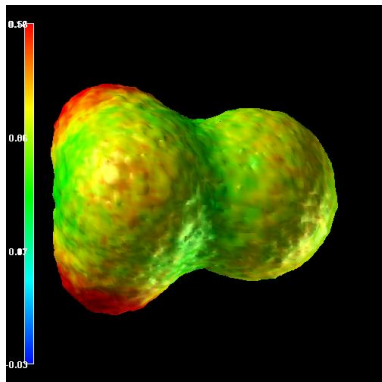

iso-density surface with
projected color coded EPLF for
trifluoromethyl amine

Trifluoromethyl amine: An electrophile

EPLF projected on the electron density
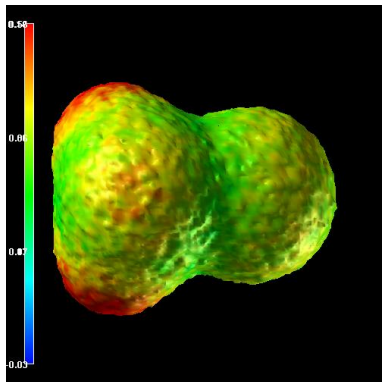

iso-density surface with
projected color coded EPLF for
trifluoromethyl amine

Trifluoromethyl amine: An electrophile

EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
trifluoromethyl amine

Trifluoromethyl amine: An electrophile

EPLF projected on the electron density
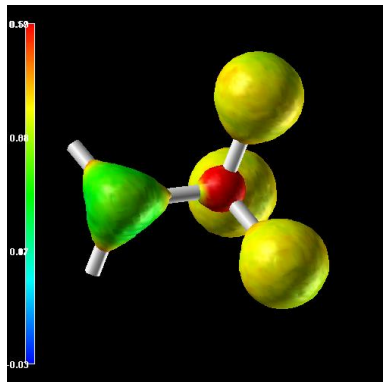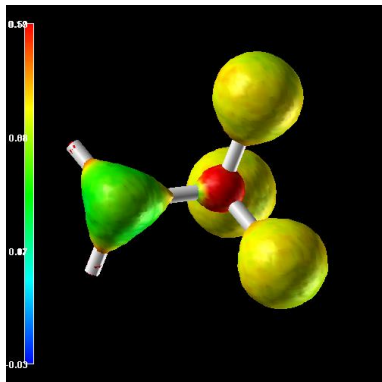

iso-density surface with
projected color coded EPLF for
trifluoromethyl amine

Trifluoromethyl amine: An electrophile

EPLF projected on the electron density

iso-density surface with projected color coded EPLF for trifluoromethyl amine

Trifluoromethyl amine: An electrophile

EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
trifluoromethyl amine

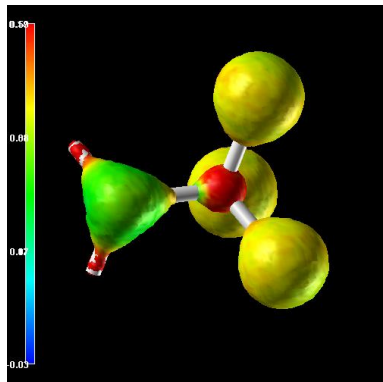# Trifluoromethyl amine: An electrophile

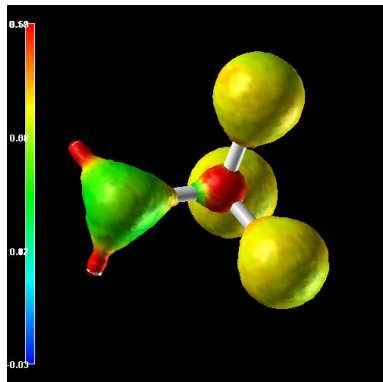EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
trifluoromethyl amine

Trifluoromethyl amine: An electrophile

EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
trifluoromethyl amine

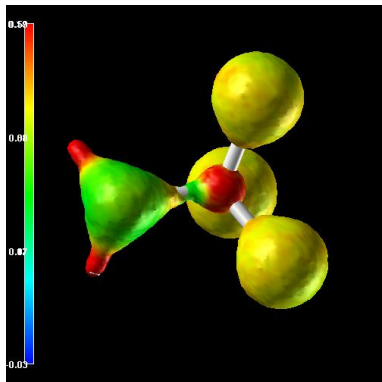# Trifluoromethyl amine: An electrophile

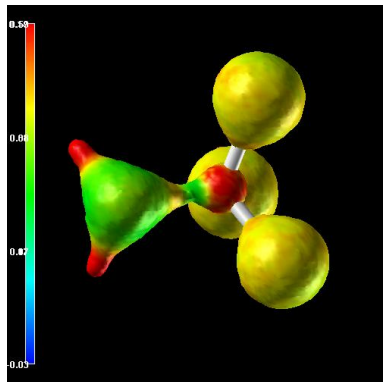EPLF projected on the electron density

iso-density surface with projected color coded EPLF for trifluoromethyl amine

Trifluoromethyl amine: An electrophile

EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
trifluoromethyl amine

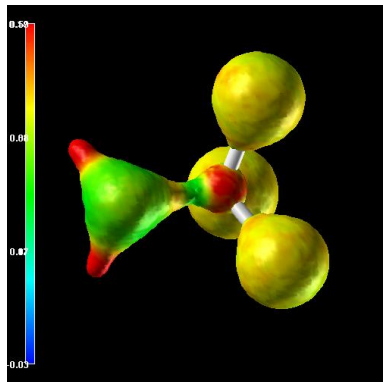# Trifluoromethyl amine: An electrophile

EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
trifluoromethyl amine

Trifluoromethyl amine: An electrophile

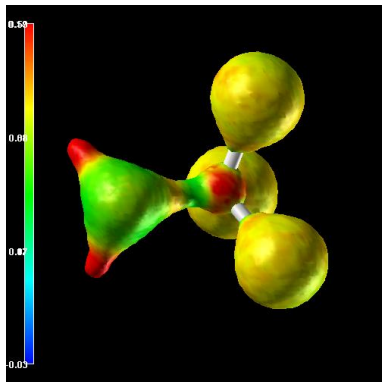EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
trifluoromethyl amine

Trifluoromethyl amine: An electrophile

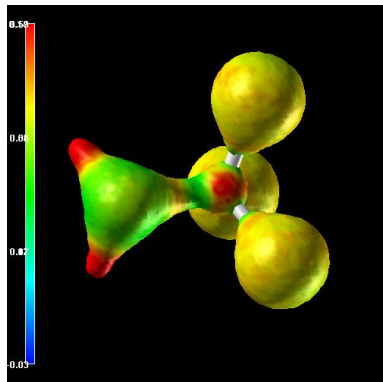EPLF projected on the electron density

iso-density surface with projected color coded EPLF for trifluoromethyl amine

Trifluoromethyl amine: An electrophile

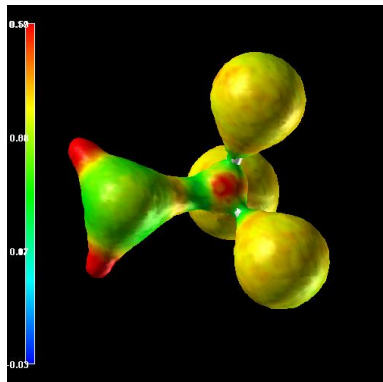EPLF projected on the electron density

iso-density surface with projected color coded EPLF for trifluoromethyl amine

Trifluoromethyl amine: An electrophile

EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
trifluoromethyl amine

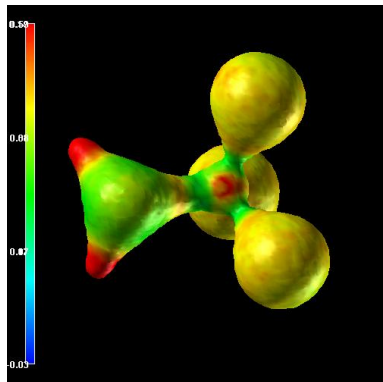# Trifluoromethyl amine: An electrophile

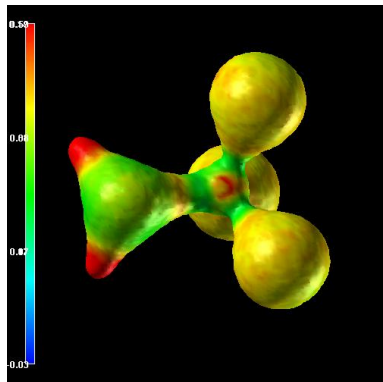EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
trifluoromethyl amine

Trifluoromethyl amine: An electrophile

EPLF projected on the electron density

iso-density surface with projected color coded EPLF for trifluoromethyl amine

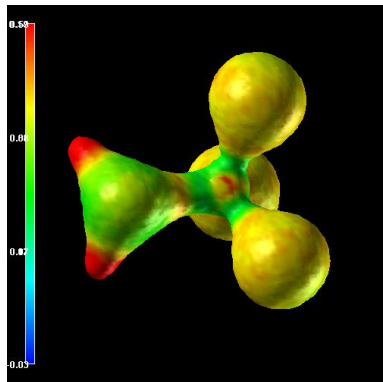# Trifluoromethyl amine: An electrophile

EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
trifluoromethyl amine

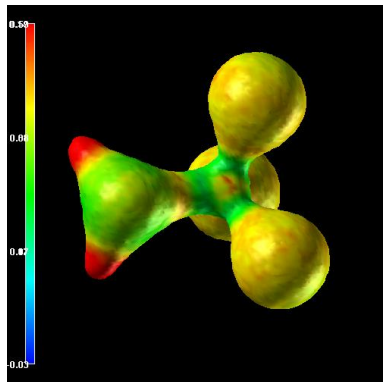# Trifluoromethyl amine: An electrophile

EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
trifluoromethyl amine

Trifluoromethyl amine: An electrophile

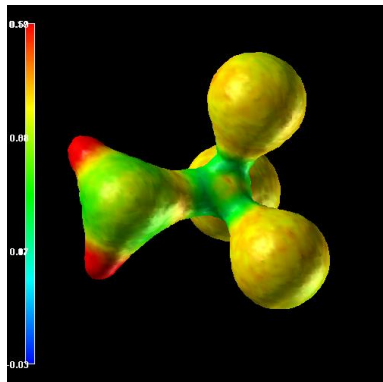EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
trifluoromethyl amine

Trifluoromethyl amine: An electrophile

EPLF projected on the electron density

iso-density surface with projected color coded EPLF for trifluoromethyl amine

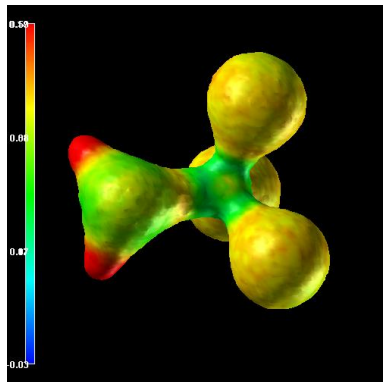# Trifluoromethyl amine: An electrophile

EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
trifluoromethyl amine

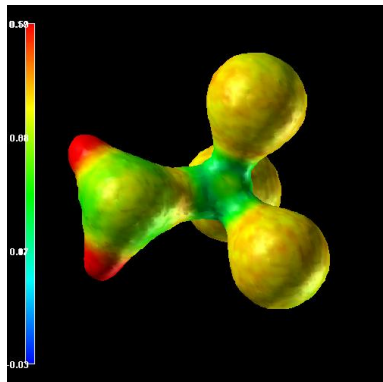# Trifluoromethyl amine: An electrophile

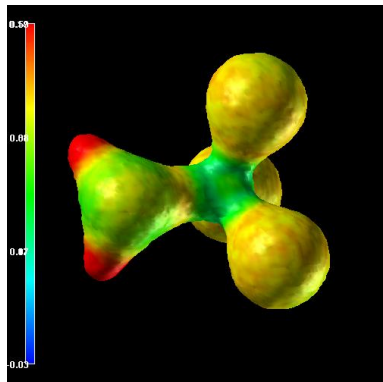EPLF projected on the electron density

iso-density surface with projected color coded EPLF for trifluoromethyl amine

Trifluoromethyl amine: An electrophile

EPLF projected on the electron density

iso-density surface with projected color coded EPLF for trifluoromethyl amine

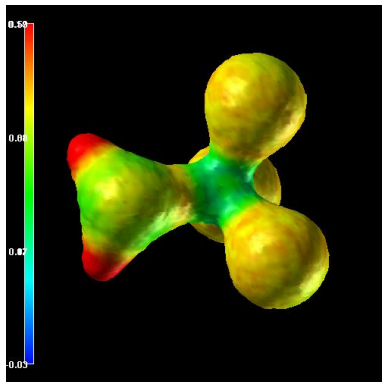# Trifluoromethyl amine: An electrophile

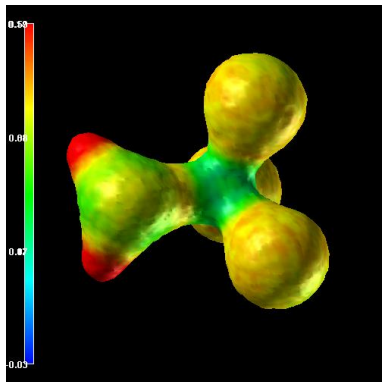EPLF projected on the electron density

iso-density surface with projected color coded EPLF for trifluoromethyl amine

Trifluoromethyl amine: An electrophile

EPLF projected on the electron density

iso-density surface with
projected color coded EPLF for
trifluoromethyl amine

Trifluoromethyl amine: An electrophile

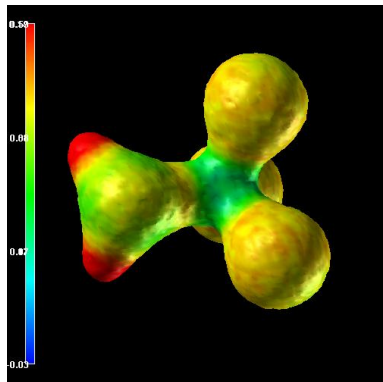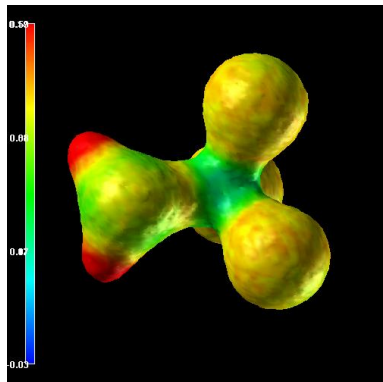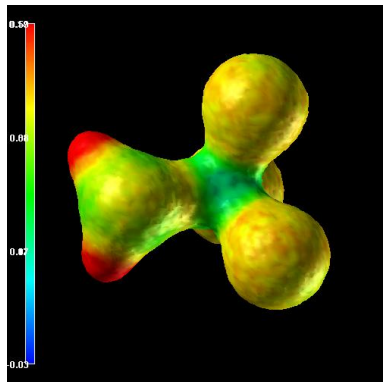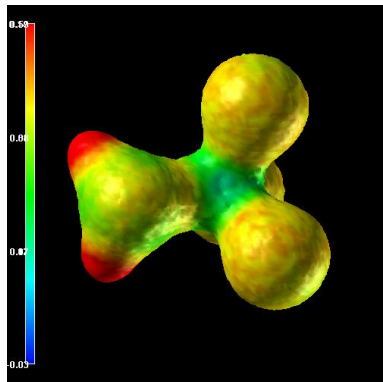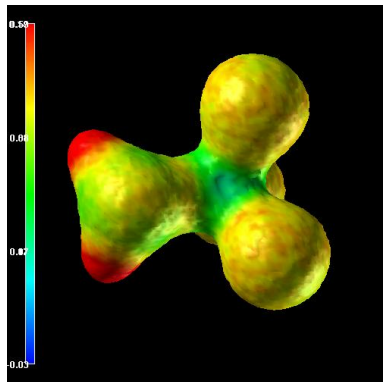EPLF projected on the electron density

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A conclusion

EPLF seems to be a very good hydrogen locator!

Let's go back to definition...

$$\mathrm{EPLF}(\overrightarrow{r}) = \frac{d_{\sigma\sigma}(\overrightarrow{r}) - d_{\sigma\bar{\sigma}}(\overrightarrow{r})}{d_{\sigma\sigma}(\overrightarrow{r}) + d_{\sigma\bar{\sigma}}(\overrightarrow{r})}.$$

If the $\sigma\sigma$ and $\sigma\bar{\sigma}$ distances are proportional to each other, EPLF is insensitive to the inter-electronic distance

Assume $d_{\sigma\bar{\sigma}}(\overrightarrow{r}) = x d_{\sigma\sigma}(\overrightarrow{r})$
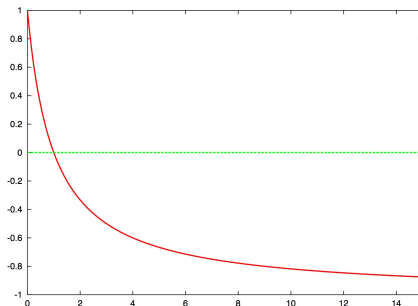
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EPLFN
A distance-dependent variant of EPLF

For characterizing an **electro-nucleophilicity** scale , we are interested in measuring how *paired* and *localized* are electrons.
We introduce the EPLFN family of functions. In particular EPLF3, the EPLF density

$$\text{EPLF}N(\overrightarrow{r}) = \frac{d_{\sigma\sigma}(\overrightarrow{r}) - d_{\sigma\bar{\sigma}}(\overrightarrow{r})}{\left(d_{\sigma\sigma}(\overrightarrow{r}) + d_{\sigma\bar{\sigma}}(\overrightarrow{r})\right)^{N+1}}$$
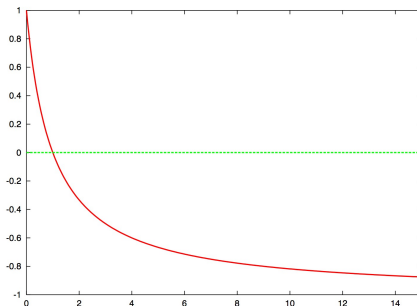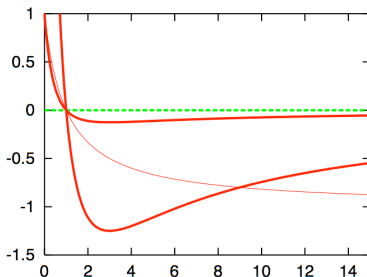
But... where is the electron pair region?

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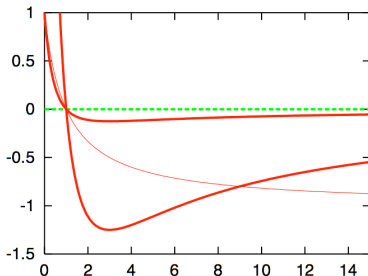
But... where is the electron pair region?

Electron Localization Function (ELF)
The DFT original formula and inspiration for EPLF and EPLFN

Electron Localization Function (ELF)
Conditional pair probability for same spin —spherical average—,

$$P_{\text{cond}}^{\sigma\sigma}(\mathbf{r}, s) = \frac{1}{3}\left[\sum_j |\nabla \phi_j|^2 - \frac{1}{4}\frac{|\nabla \rho_\sigma|^2}{\rho_\sigma}\right] s^2 + \dots$$

(smaller probability, more localization)
Defíne

$$D_\sigma(r) = \sum_j |\nabla \phi_j|^2 - \frac{1}{4}\frac{|\nabla \rho_\sigma|^2}{\rho_\sigma};$$

and the corresponding quantity for the uniform electron gas

$$D_\sigma^0(r) = \frac{3}{5}(6\pi^2)^{2/3}\rho_\sigma^{5/3}.$$

Electron Localization Function

Definition

Thus, ELF is defined as

$$\mathrm{ELF}(r) = \frac{1}{1 + \left(D_\sigma/D_\sigma^0\right)^2}.$$

Interpretation

- ELF equals one when D_σ is zero —highest localization.
- ELF equals one half when the localization corresponds to that of the uniform electron gas.
- ELF is smaller for even smaller localization.

A. D. Becke and K. E. Edgecombe. *J. Chem. Phys.* 92:5397-5403, 1990.
B. Silvi and A. Savin. *Nature* 371:683-686, 1994.

EPLF in the ELF basin
Effect of electron correlation on the electron pair region density

For our purposes, the most important property of ELF is that defines a well-defined basin around the lone pair, *i. e.* defines the *pair's volume*.

Descriptors of the electron pair basin				
Molecule	Integral		Distance	Volume
	LDA	QMC		
TMA	2.295	2.382	0.94	354
DMA	2.251	2.324	0.95	775
MA	2.215	2.232	0.95	1488
NH_3	2.167	2.211	0.95	2294
NH_2CF_3	2.060	2.144	0.97	1656
NH_2F	2.386	2.386	0.86	1852

Alternative localization ideas
Can break down when orbitals are delocalized

But it is also possible to study the electron pair without information from ELF, by projecting the EPLFN onto the orbital corresponding to the lone pair

$$\epsilon_N = \frac{\langle \phi_{\text{lp}} | \text{EPLF}N | \phi_{\text{lp}} \rangle}{\langle \phi_{\text{lp}} | \phi_{\text{lp}} \rangle}$$

EPLF projected on the lone pair orbital			
Molecule	$\epsilon_0 \times 10^2$	$\epsilon_3 \times 10^6$	N
TMA	8.28	1.21	557
DMA	8.34	1.21	514
MA	8.48	1.96	659
NH_3	8.36	7.11	1299
NH_2CF_3	8.32	7.19	1000
NH_2F	8.95	5.41	1452

EPLF3 in the ELF basin
A descriptor sensitive to the availability of the electron pair

Finally, the proposed descriptors from EPLFN, integrated over the basin defined by ELF, are presented.

EPLF integrated on the ELF basin				
Molecule	ϵ_0	d_0^c	$\epsilon_3 \times 10^3$	d_3^c
TMA	5.16	2.35	2.89	3.52
DMA	5.59	2.38	3.10	3.45
MA	6.20	2.28	4.78	3.01
NH_3	5.80	2.05	7.76	2.48
NH_2CF_3	4.28	2.07	6.15	2.70
NH_2F	5.10	1.93	7.02	2.43

Summary

- ϵ_3 and d_3^c are proposed as descriptors of the lone pair availability
- EPLF may not be the ultimate tool for analyzing electron pair localization
- EPLF*N* together with ELF provides a reliable, unambiguous description of the lone pair

Outlook

- Study the effect of more sophisticated trial wave functions ψ_T
- Use forward-walking or reptation MC to obtain pure EPLFN estimator
- Currently applying to a set of 15 experimentally relevant molecules of $100 - 200$ electrons.
- Explore EPLFN for the description of chemical bonds, radicals, and other kinds of lone pairs.

Thanks!

- José Alfredo Vázquez-Martínez (UNAM, México)