Weak Intermolecular interactions: Insights from experimental and theoretical charge densities.

T. N. Guru Row
Solid State and Structural Chemistry Unit
Indian Institute of Science, Bangalore 560012,INDIA
Email: ssctng@sscu.iisc.ernet.in
website http://144.16.75.32

Atoms In Molecules(AIM)

Topological analysis: Bader's AIM approach*

At a critical point (CP) $\mathbf{r}_c$, Gradient of electron density, $\nabla\rho(\mathbf{r}_c) = 0$

⇩

(rank, signature)

Possible signatures for CP of rank 3:

(3, –3) ⇒ Atom

(3, –1) ⇒ Bond

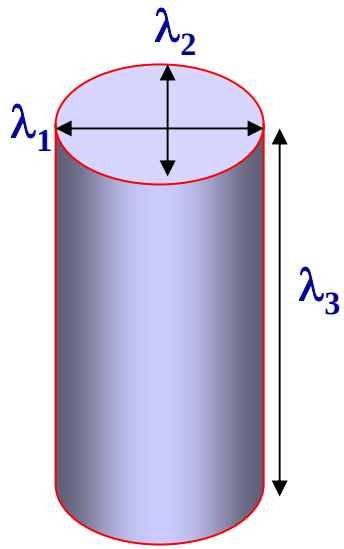
(3, +1) ⇒ Ring

(3, +3) ⇒ Cage

Laplacian $\nabla^2\rho(\mathbf{r}_c) = \lambda_1+\lambda_2+\lambda_3$

⇩

True representation of chemistry in the molecule



Shared Interactions
$\nabla^2\rho(\mathbf{r}_c) < 0$

Closed shell Interactions
$\nabla^2\rho(\mathbf{r}_c) > 0$

Bond ellipticity
$\varepsilon = \lambda_1/\lambda_2 - 1$

$\varepsilon = 0$; σ-bond
> 0 ; π-bond

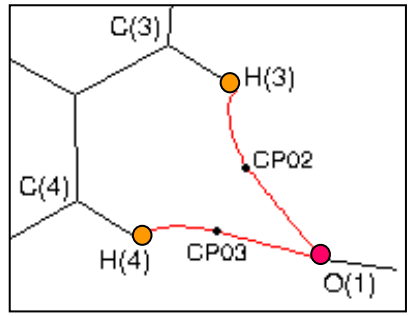
*R. F. W. Bader, *Atoms In Molecules*: A Quantum Theory, Oxford, 1990.

Characterization of Hydrogen Bonds

8 Criteria of Koch and Popelier

FIRST 4 CRITERIA

1. **Bond Critical Point (BCP) between a donor atom and an acceptor atom linked via a bond path.**



2. **Charge density evaluated at the BCP and its relationship with the bonding energy.**

$$G(r_{CP}) = \left(\frac{3}{10}\right)(3\pi^2)^{2/3}\rho^{5/3}(r_{CP}) + \left(\frac{1}{6}\right)\nabla^2\rho(r_{CP})$$

$$V(r_{CP}) = \left(\frac{1}{4}\right)\nabla^2\rho(r_{CP}) - 2G(r_{CP})$$

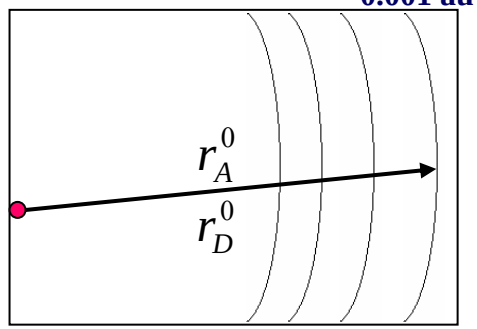
$$E(r_{CP}) = G(r_{CP}) + V(r_{CP})$$

3. **Positive value of the Laplacian at the BCP and correlation with the bonding energy.**

4. **Mutual penetration of the hydrogen and the acceptor atom**

Bonding radius

0.001 au



Non-bonding radius

$$\Delta r_D = (r^0_D - r_D) > \Delta r_A = (r^0_A - r_A) \text{ and } \Delta r_D + \Delta r_A > 0$$

Koch, U.; Popelier, P. L. A. ***J. Phys. Chem.*** **1995,** 99, 9747**; P. L. A. Popelier,** Atoms in Molecules. An Introduction**,** Prentice Hall, UK. **2000**, pp150-153.

REMAINING 4 CRITERIA

Evaluation of integrated properties over the basin of the H atoms

5. **Increased net charge on the H-atom due to loss of electrons; the difference in charge between the crystal and the bare molecule should be positive**

$$\Delta q \text{ (crystal – isolated)} > 0$$

6. **The energetic destabilization of the H atom**

$$\Delta E \text{ (crystal – isolated)} > 0$$

7. **Decrease of dipolar polarization of the H atom**

$$\Delta M \text{ (crystal – isolated)} < 0$$

8. **Depletion of atomic volume H atom**

$$\Delta V \text{ (crystal – isolated)} < 0$$

Experimental Requirements

Equipment:

➢ ***X-ray sources***

conventional

synchrotron,
rotating anode

Anode	$K\alpha_1$ (Å)	$K\alpha_2$ (Å)	$(\sin\theta/\lambda)_{max}$ (Å^{-1})
Cu	1.540	1.544	**0.65**
Mo	0.7093	0.7135	**1.41**
Ag	0.5594	0.5638	**1.78**

➢ ***detectors*** **CCD, Image Plate**

➢ ***low temperature*** **~ 100K**

Liquid N_2 & *He*

✓ **good quality crystals**

✓ **Electron Density Model (Multipole)**

Experimental data quality

- high resolution data for accurately fixing atomic position and thermal parameters

⇒ **$\sin\theta/\lambda > 1.0$ Å^{-1} ($d < 0.5$ Å)**

- small thermal motion, to better deconvolute the electron density

⇒ **low temperature**

- extensive and complete datasets, for allowing refinement of additional parameters and properly account for aspherical distribution of the density

⇒ **large redundancy**

- accurate corrections of the diffracted intensities measured

⇒ **extinction**, **absorption**, **TDS**, **background** etc.

Atom Models

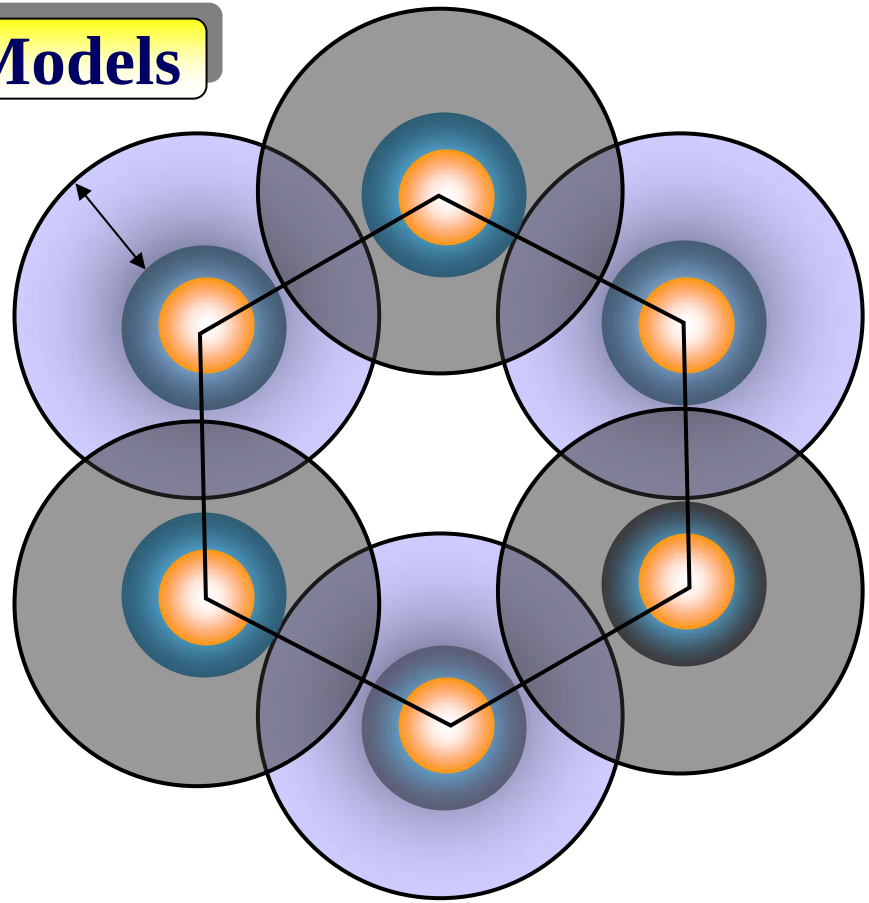
The atomic density

$$\rho_{atom}(\mathbf{r}) = \rho_{core} + \rho_{valence}(\mathbf{r})$$

Routine Refinement

κ = Contraction and expansion parameter, scales the radial coordinates r.

P_v = Population variable of the valence shell.



Modified Spherical Atom Model

Radial Refinement

$$\rho_{atom}(\mathbf{r}) = \rho_{core} + \rho'_{valence}(\kappa\mathbf{r}) = \rho_{core} + P_v\kappa^3\rho_{valence}(\kappa\mathbf{r})$$

P. Coppens, T. N. Guru Row, P. Leung, P. J. Becker, Y. W. Yang, E. D. Stevens, *Acta cryst.* 1979, *A35*, 63.

Multipole Model

Hansen & Coppens multipole formalism*

The atomic density

$$\rho_{at}(\mathbf{r}) = \rho_{core}(\mathbf{r}) + P_v \kappa^3 \rho_{valence}(\kappa \mathbf{r}) + \sum_{l=0}^{l_{max}} \kappa'^3 R_l(\kappa' \mathbf{r}) \sum_{m=0}^{l} P_{lm\pm} d_{lm\pm}(\vartheta, \varphi)$$

Spherical **Aspherical**

XD

Aspherical Refinement

P_v = Population variable

κ, κ' = Contraction and expansion parameter

R_l = Radial function

$P_{lm\pm}$, $d_{lm\pm}$ = Spherical Harmonic functions

*N. K. Hansen and P. Coppens, *Acta Cryst.* **1978,** *A34*, 909.

Refinement

Refinement strategy:

⇒ **spherical, aspherical (multipole) formalism**

⇒ **multipole expansion upto *hexadecapole/octapole* for non H atoms and *dipole* for H atoms**

⇒ **H atom treatment: refined isotropically with bond values from neutron data**

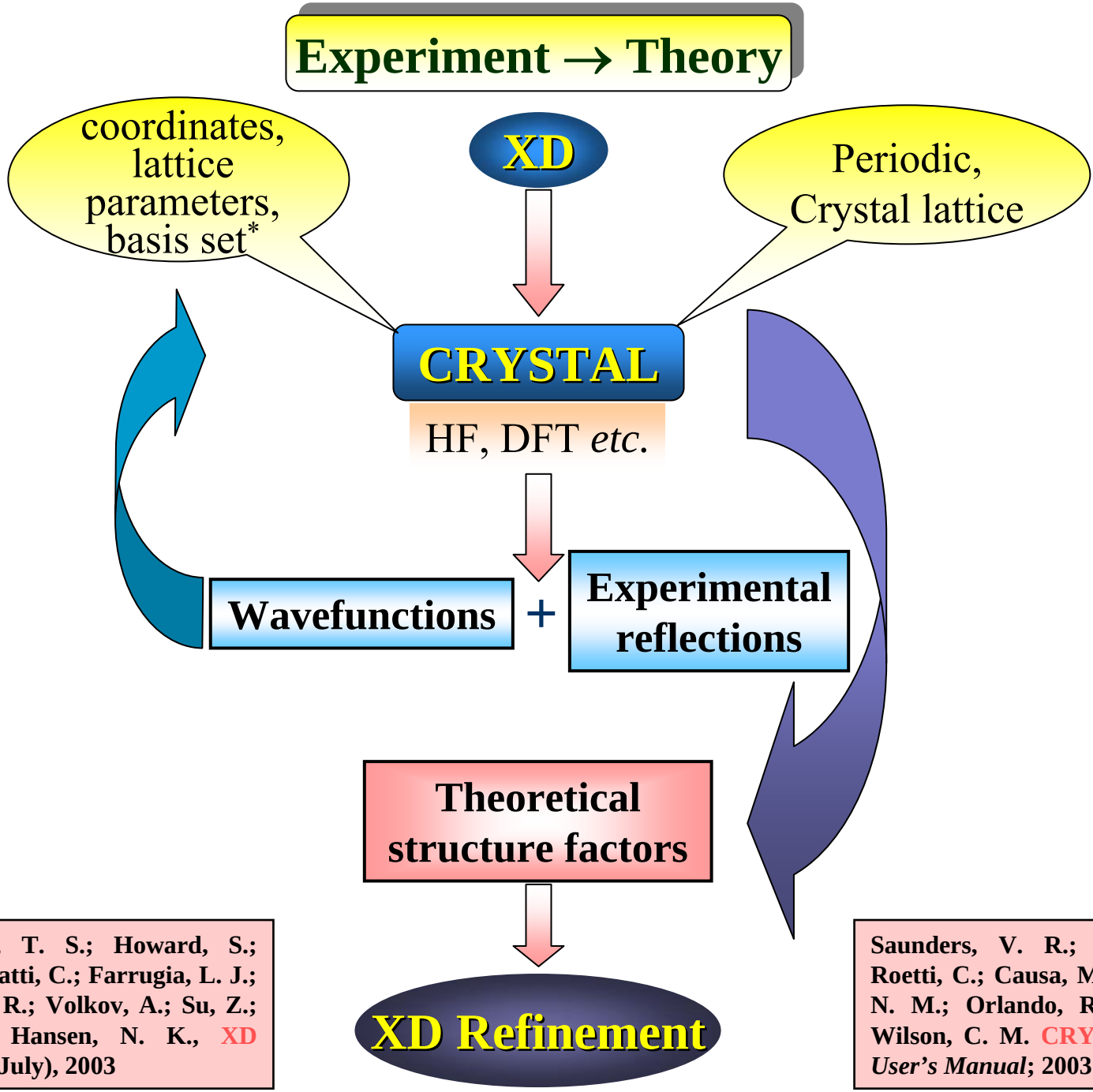
Residual density:

$$\Delta\rho(\mathbf{r}) = \rho_{obs}(\mathbf{r}) - \rho_{calc}(\mathbf{r}) = \frac{1}{V}\sum_{H} \Delta F \exp(-2\pi i H.\mathbf{r})$$

Deformation density:

⇒ **standard deformation density:** $\Delta\rho(\mathbf{r}) = \rho(\mathbf{r}) - \rho_{pro}(\mathbf{r})$

⇒ **static and dynamic deformation density**



Koritsanszky, T. S.; Howard, S.; Macchi, P.; Gatti, C.; Farrugia, L. J.; Mallinson, P. R.; Volkov, A.; Su, Z.; Richter, T.; Hansen, N. K., XD (version 4.10, July), 2003

Saunders, V. R.; Dovesi, R.; Roetti, C.; Causa, M.; Harrison, N. M.; Orlando, R.; Zicovich-Wilson, C. M. CRYSTAL03 *1.0 User's Manual*; 2003

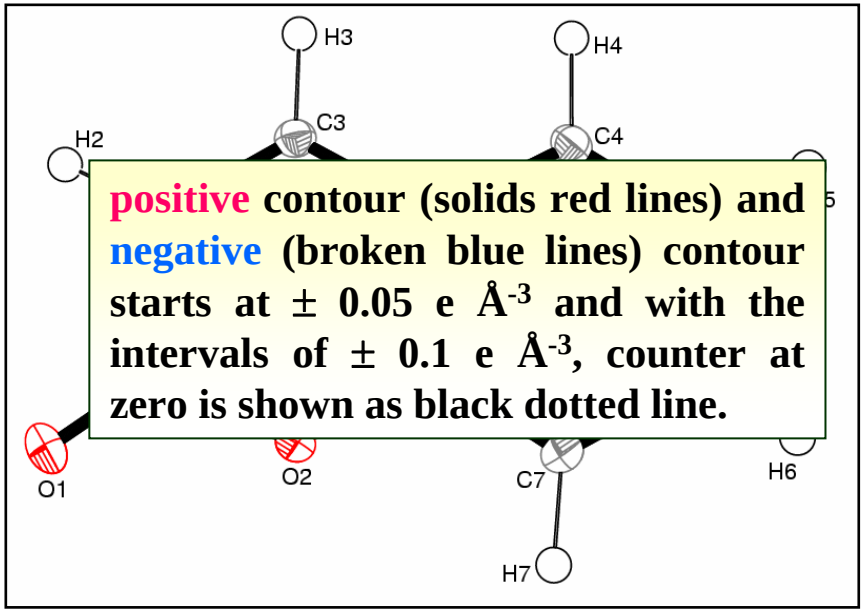
Single Crystal X-ray Diffraction Data at 90K

Compounds	Coumarin	1-thiocoumarin	2-thiocoumarin	dithiocoumarin
Formula	$C_9H_6O_2$	C_9H_6OS	C_9H_6OS	$C_9H_6S_2$
Crystal size/mm	0.60×0.17×0.09	0.40×0.21×0.18	0.60×0.37×0.10	0.40×0.26×0.06
Formula weight	146.14	162.2	162.2	178.28
Crystal system	Orthorhombic	Monoclinic	Orthorhombic	Triclinic
Unit cell dimensions/Å				
a	5.6091(13)	3.8056(3)	4.0515(2)	7.4510(5)
b	7.7343(19)	8.4552(7)	10.1749(6)	7.5751(4)
c	15.478(4)	11.3651(10)	17.6519(9)	8.2553(5)
α/°	90	90	90	83.268(3)
β/°	90	95.629(4)	90	112.569(3)
γ/°	90	90	90	114.414(3)
Z; V/Å^3	4; 671.5(3)	2; 363.93(5)	4; 727.67(7)	2; 391.31(4)
Space group	$Pc2_1b$	Pc	$P2_12_12_1$	$P\bar{1}$
D_c/g cm^{-1}	1.446	1.48	1.481	1.513
μ/mm^{-1}	0.103	0.369	0.369	0.599
$(\sin\theta/\lambda)_{max}$/Å^{-1}	**1.08**	**1.08**	**1.08**	**1.08**
Reflection nos. (unique)	6288	6373	6878	5689
$R(F)$; $R_w(F)$	**0.0278**; 0.0251	**0.0158**; 0.0145	**0.0202**; 0.0204	**0.0208**; 0.0208
S	2.1	1.41	1.64	1.45
N_{obs}/N_{par}	**14.68**	**20.14**	**21.7**	**19.03**
Range of residuals/eÅ^{-3}	-0.241; 0.174	-0.203; 0.324	-0.206; 0.346	-0.282; 0.472

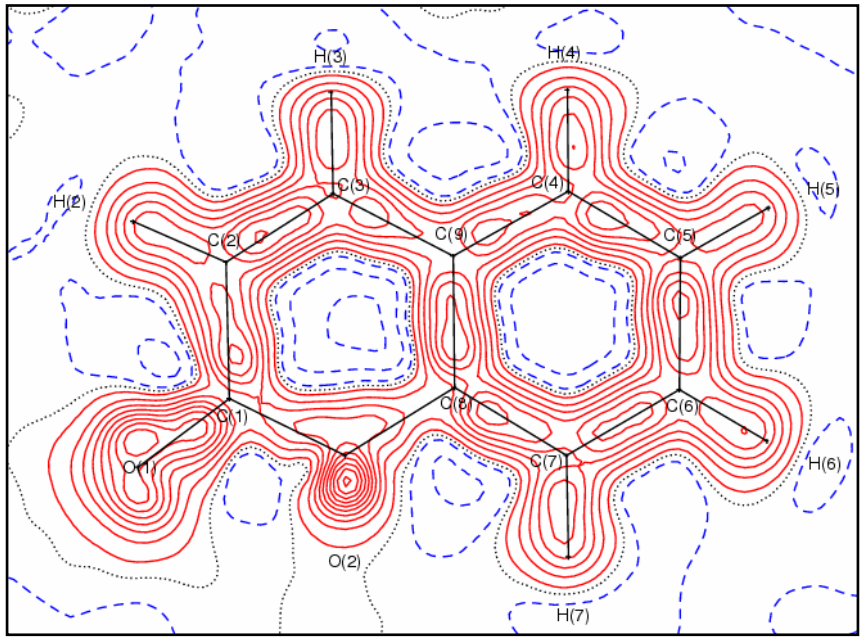
Electron Density Maps

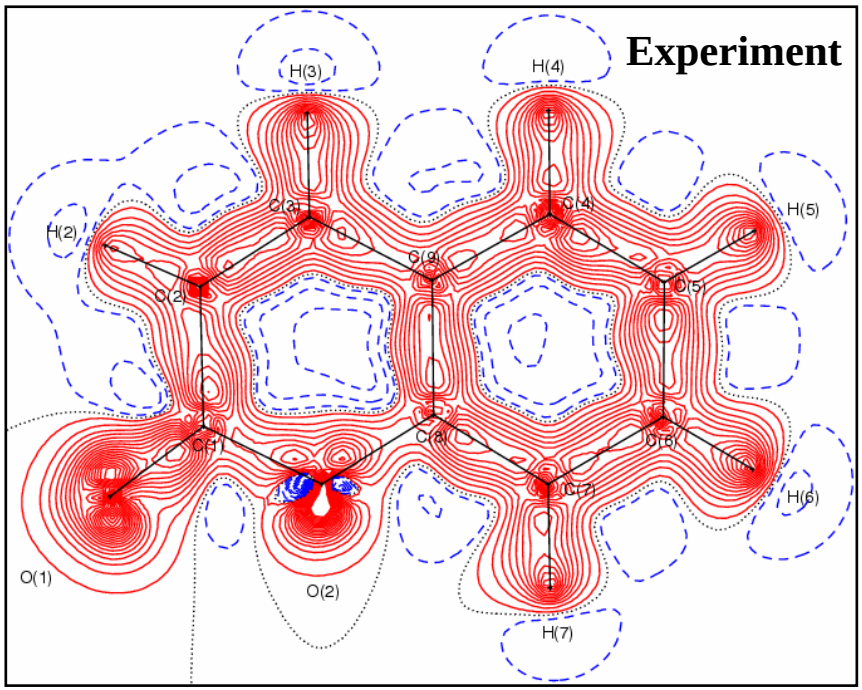
Coumarin

Dynamic Deformation

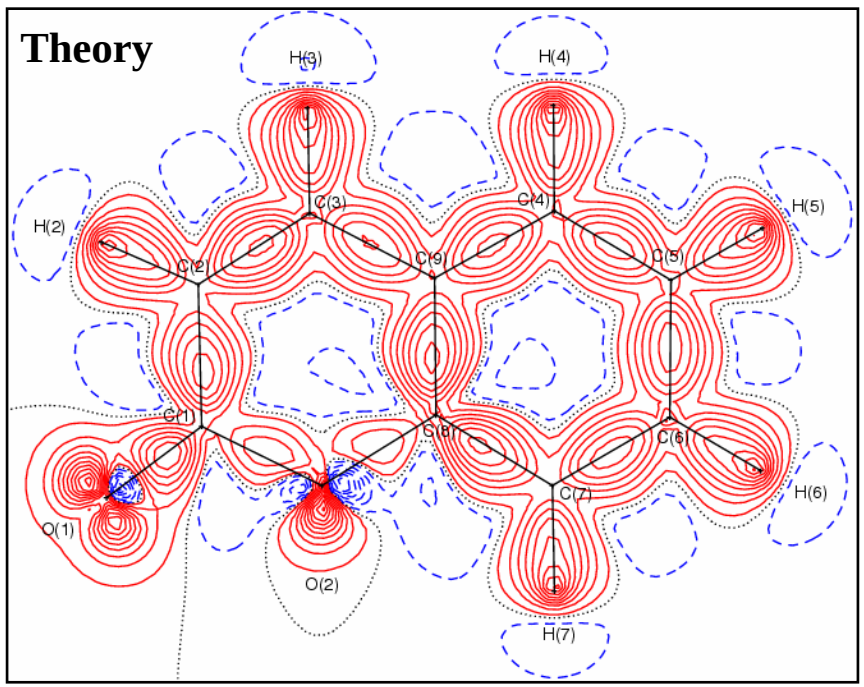


positive contour (solids red lines) and **negative** (broken blue lines) contour starts at ± 0.05 e Å^{-3} and with the intervals of ± 0.1 e Å^{-3}, counter at zero is shown as black dotted line.





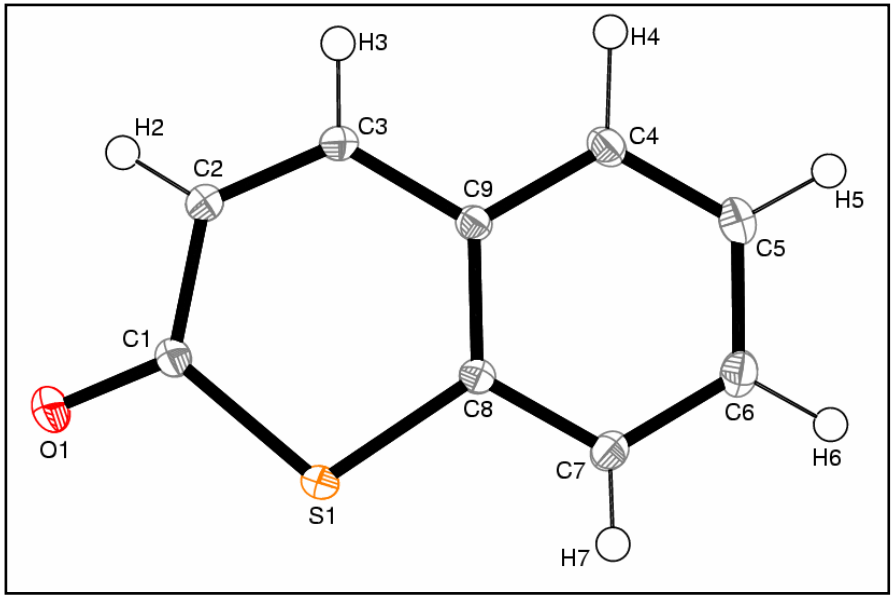
STATIC



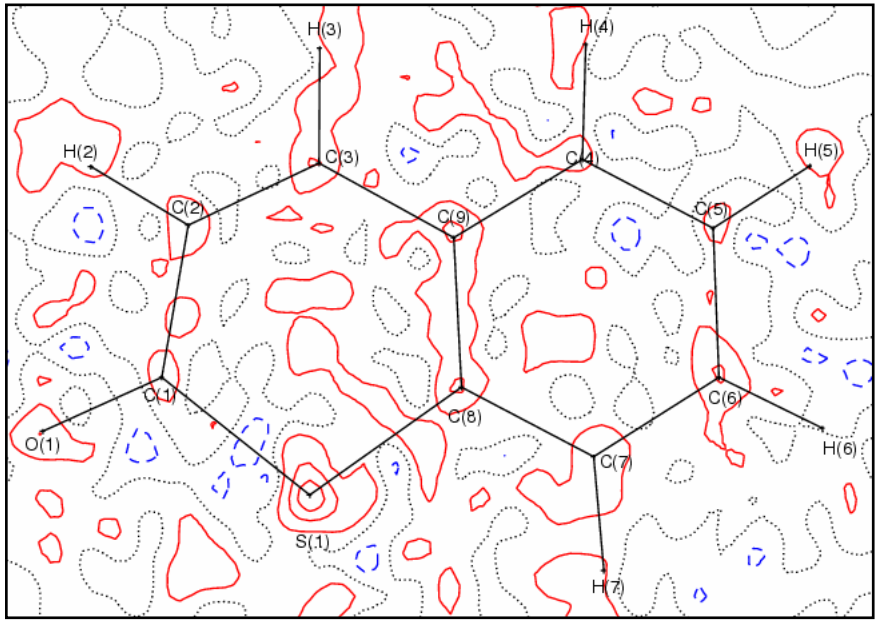
ORTEP @ 90K

1-thiocoumarin

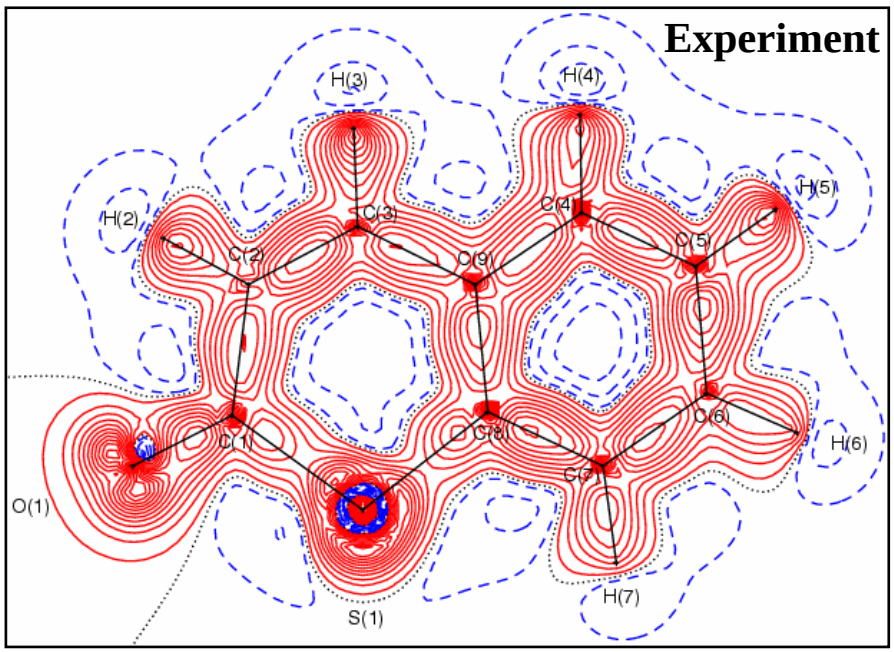
Electron Density Maps

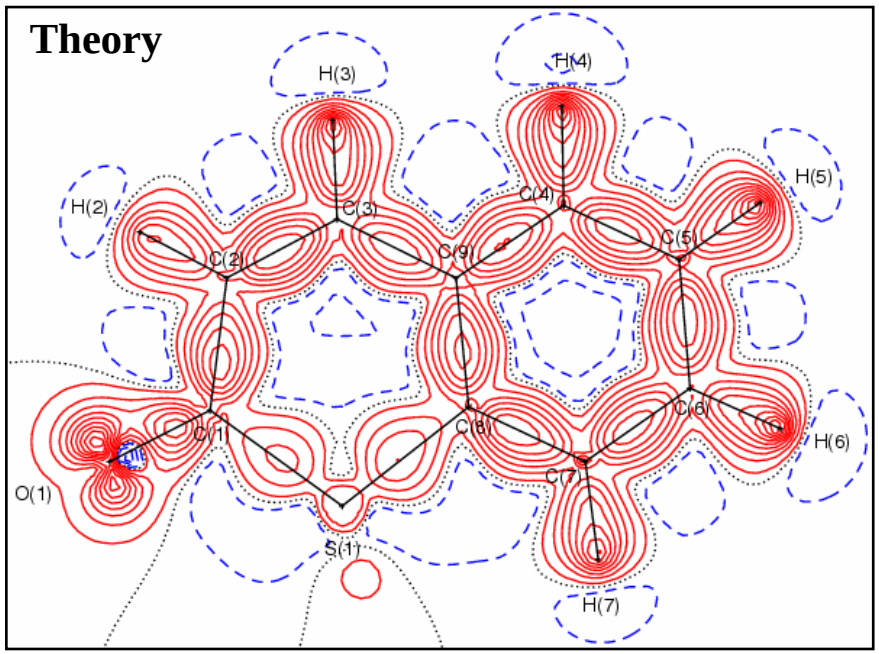


RESIDUAL



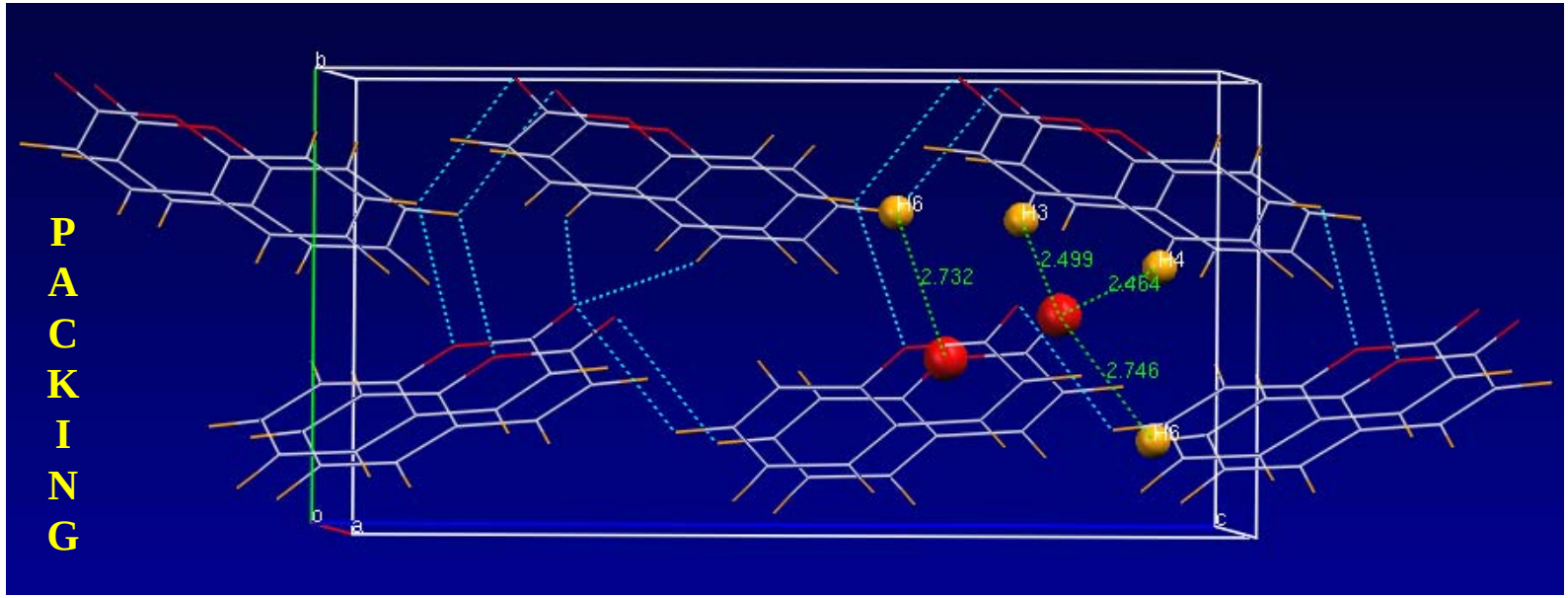
STATIC



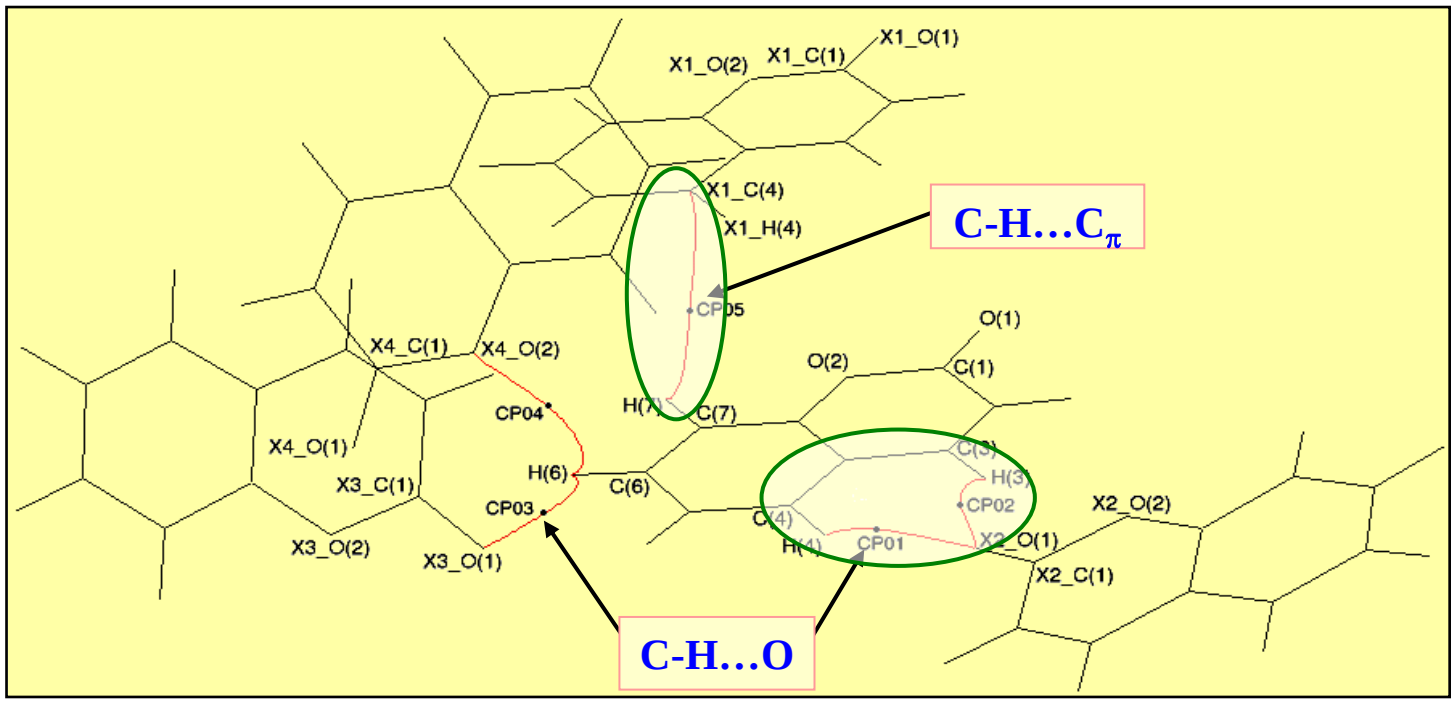


COUMARIN

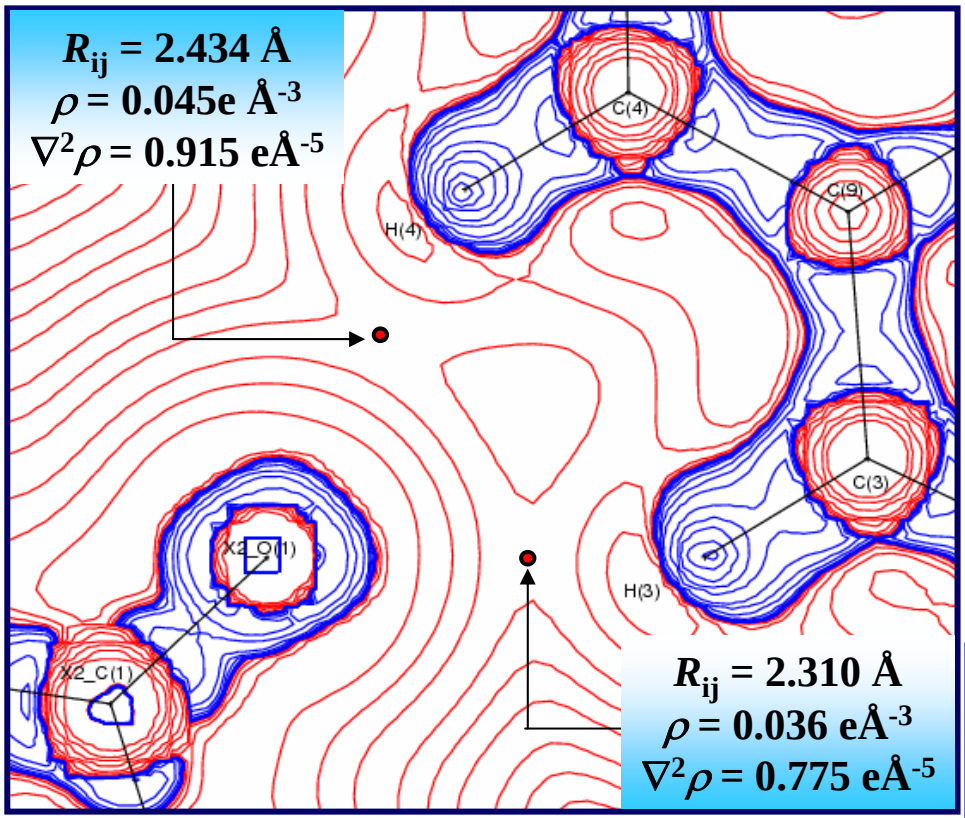
PACKING



BOND PATHS & CRITICAL POINTS

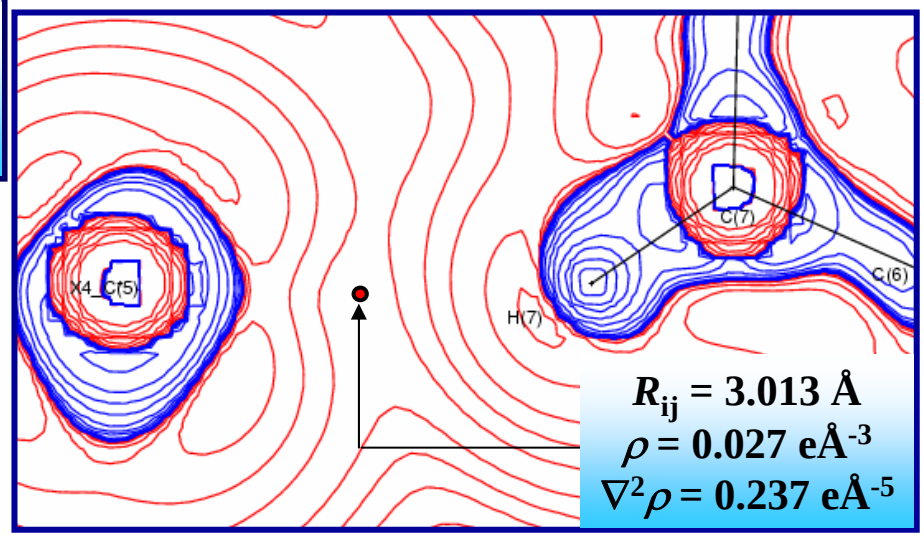


LAPLACIAN MAP



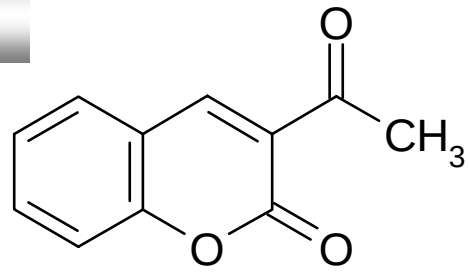
The contours are drawn at logarithmic intervals in $-\nabla^2\rho_b$ eÅ^{-5}

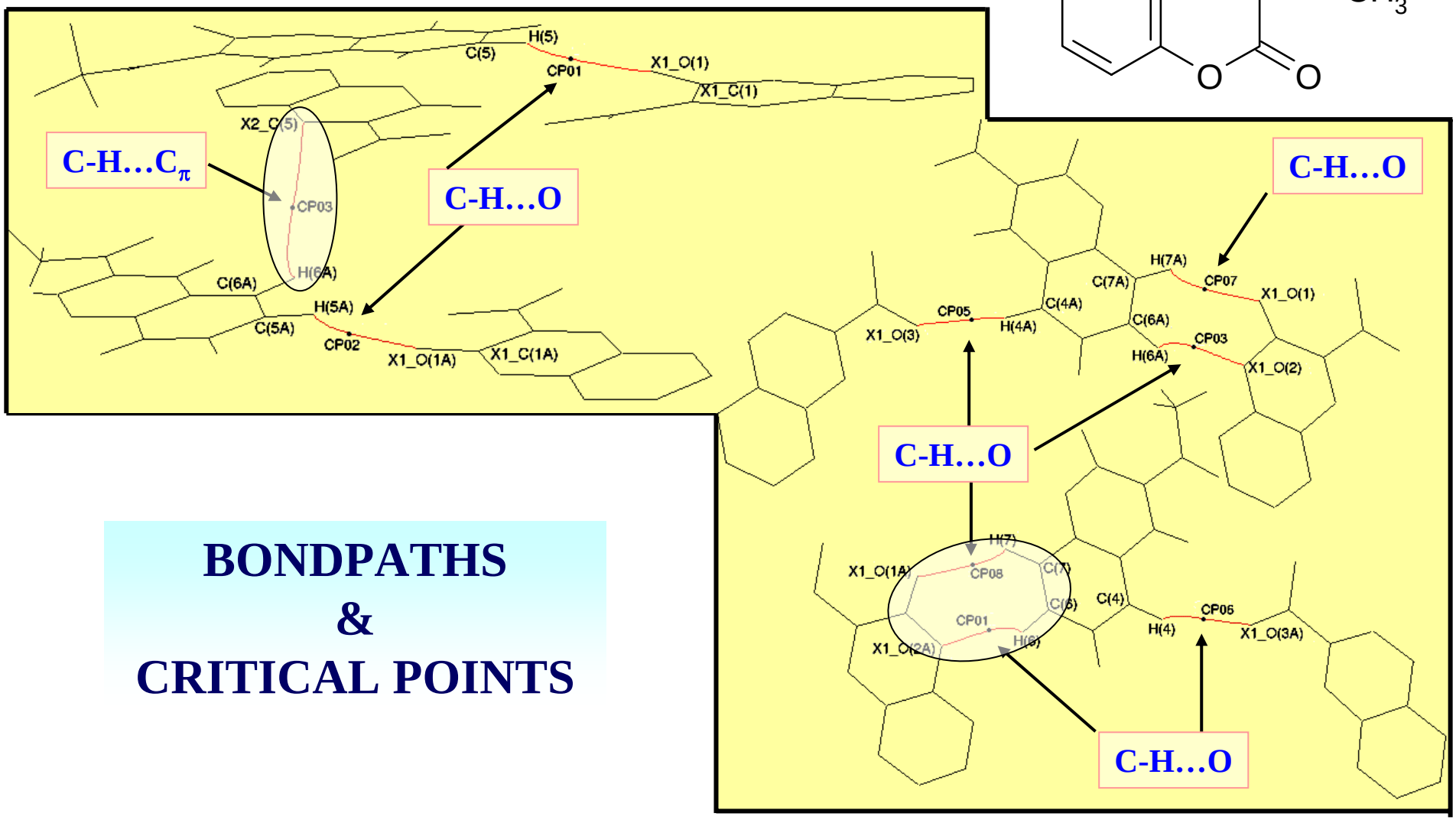
C-H…C$_\pi$ Interactions



C-H…O Interactions

BCP along bond path [K &P 1]





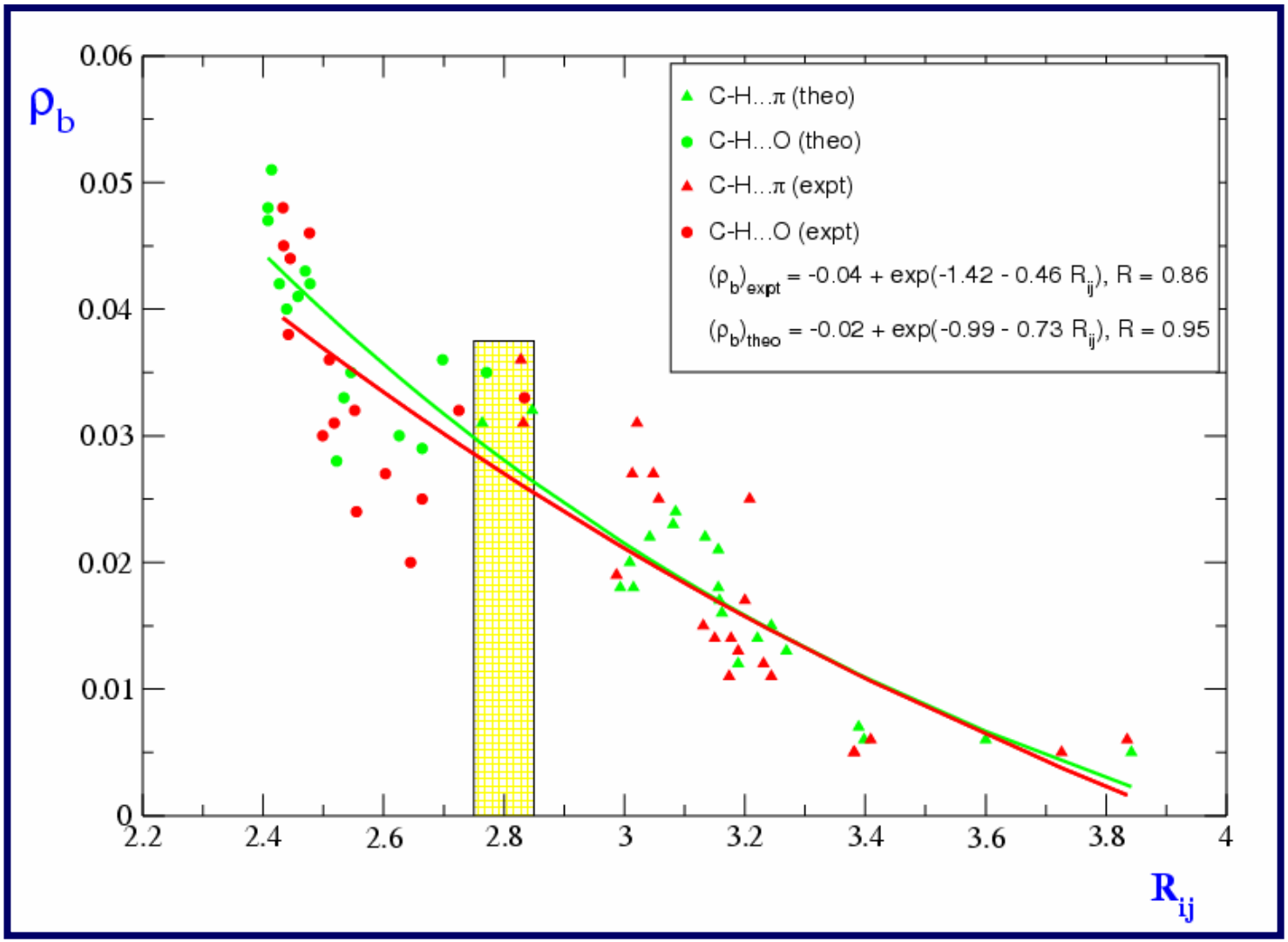
BONDPATHS
&
CRITICAL POINTS

15 (C-H…O)

21 (C-H…C_π)

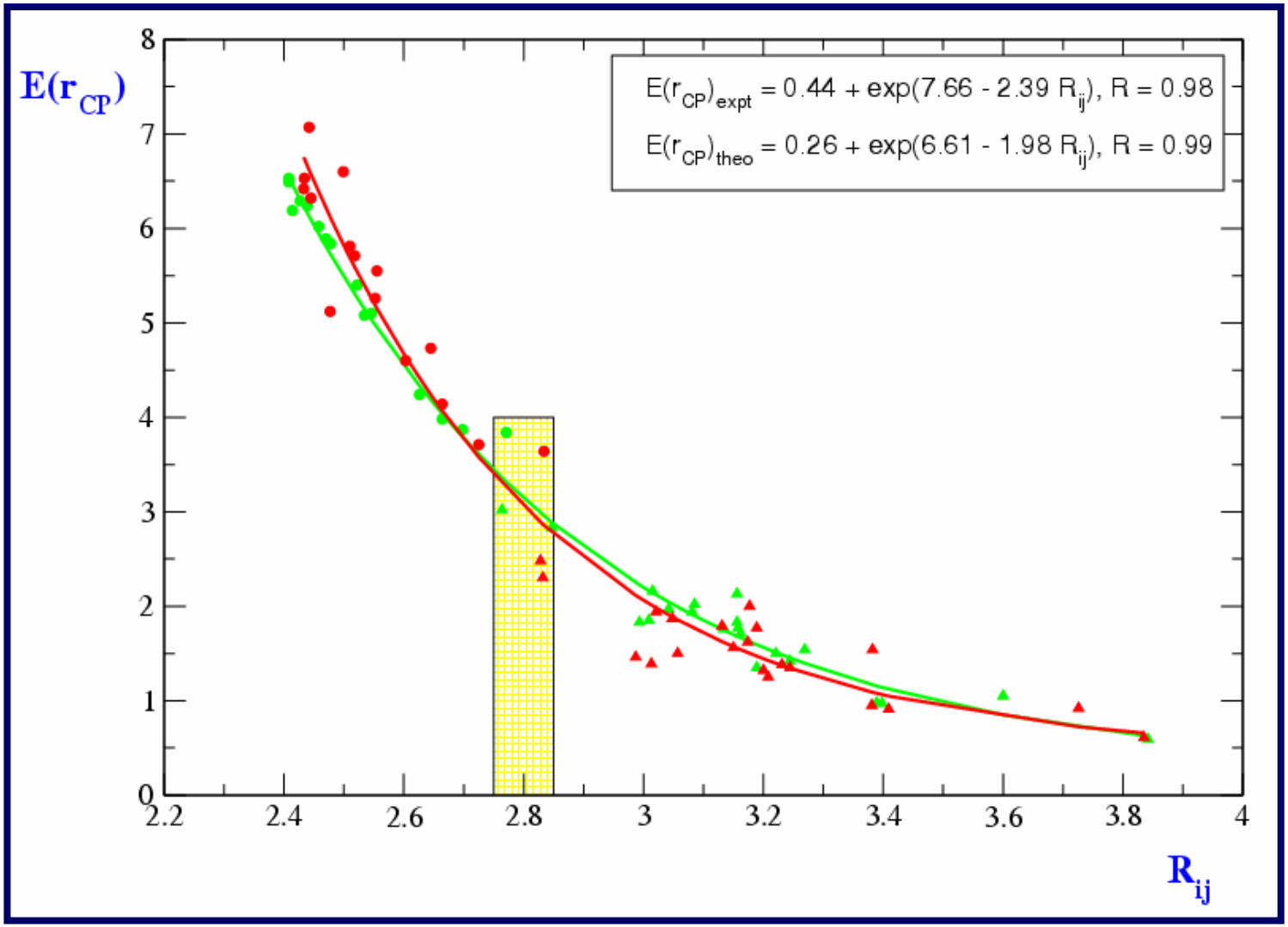
Data points N = 36

Charge density KP 2



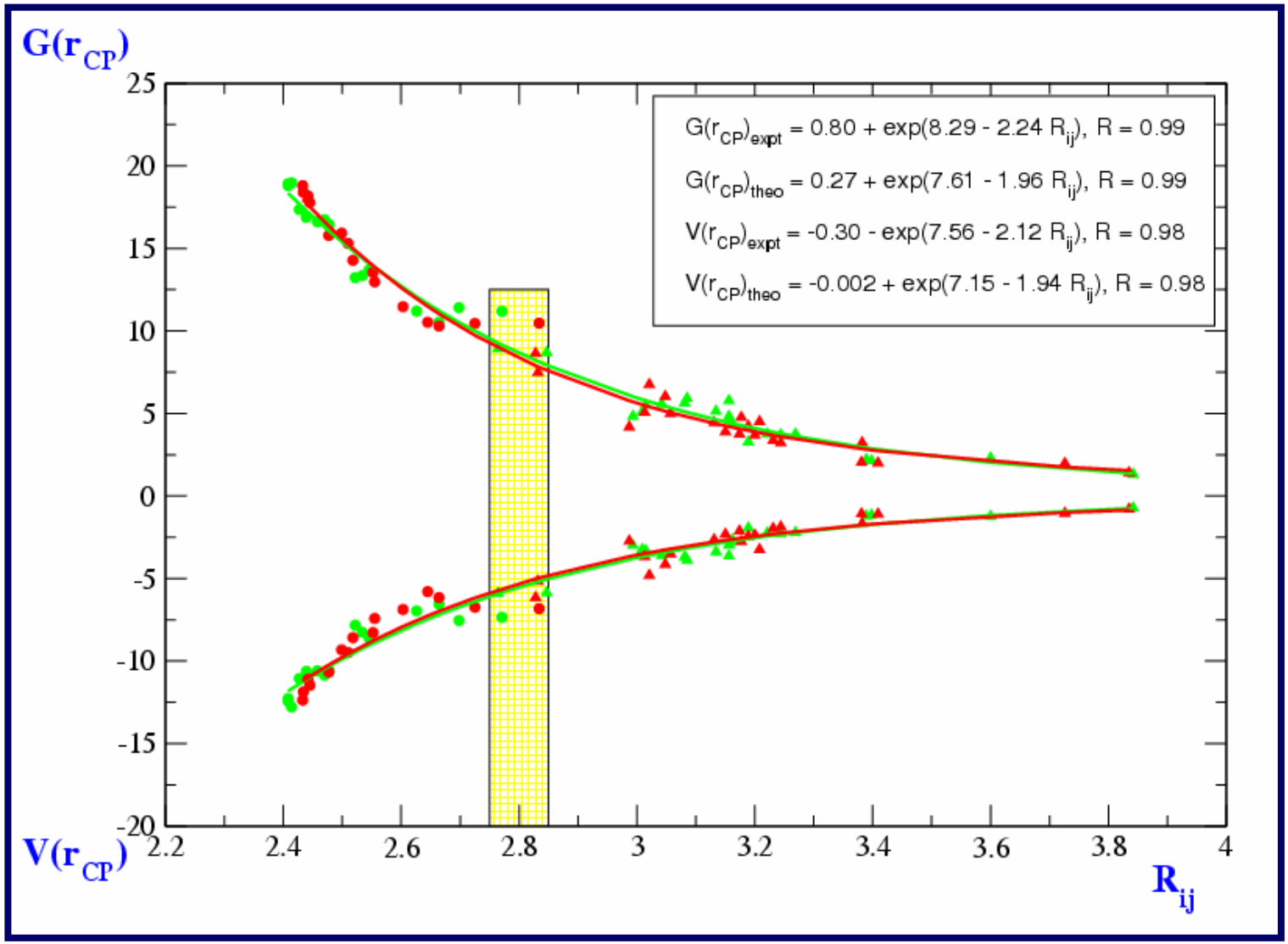
Exponential dependence of ρ_b [eÅ^{-3}] on the interaction length R_{ij} [Å]

Energy KP 2



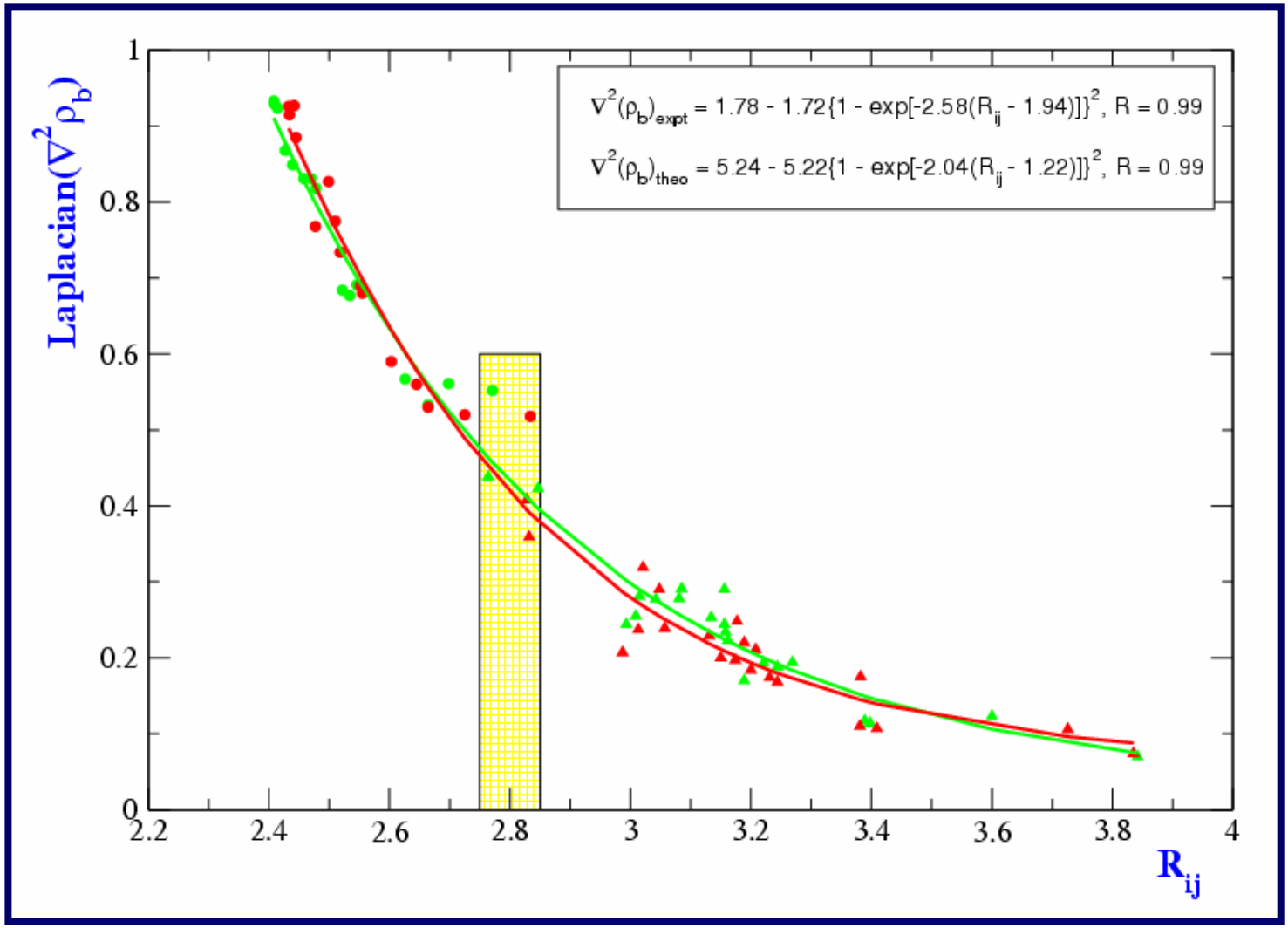
Exponential dependence of total local electron density $E(r_{CP})$ [kJ mol^{-1}bohr^{-3}] on R_{ij} [Å]

Potential And Kinetic Energy Density KP 2



Exponential fitting of $V(r_{CP})$ [kJ mol^{-1}bohr^{-3}] and local kinetic energy density $G(r_{CP})$ [kJ mol^{-1}bohr^{-3}] values on R_{ij} [Å]

Laplacian KP 3



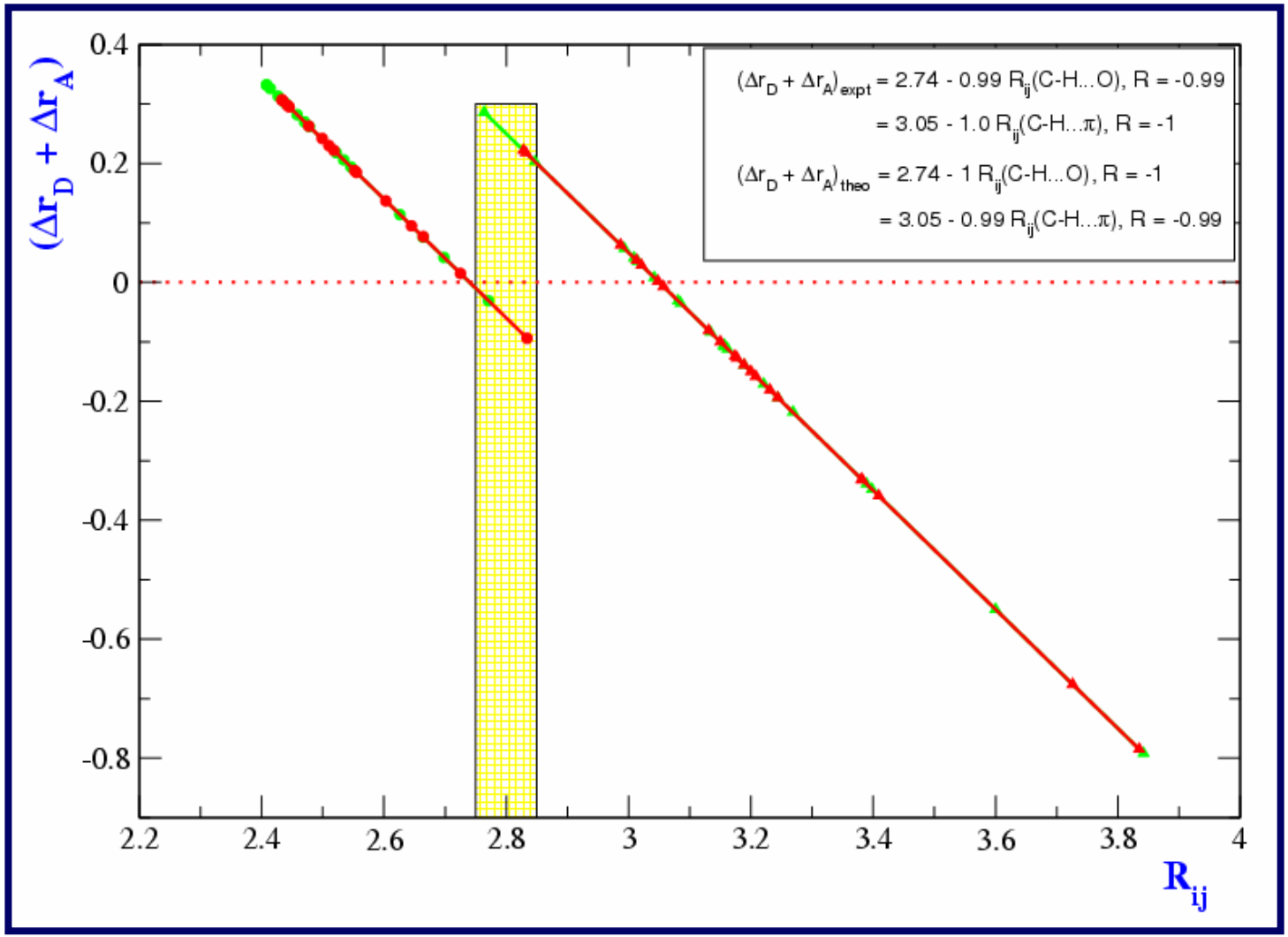
Morse-like dependence of Laplacian [$\nabla^2\rho_b$] (eÅ^{-5}) on R_{ij} [Å]

15 (C-H…O)

21 (C-H…C_π)

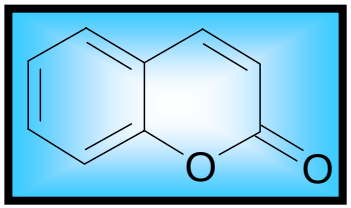
Munshi, P.; Guru Row, T. N. *J. Phys. Chem. A* 2005, *109*, 659-672

Mutual Penetration KP 4

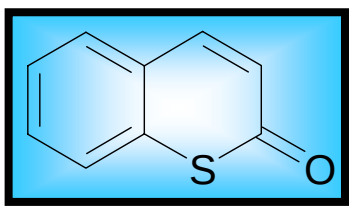


Linear dependence of $(\Delta r_D + \Delta r_A)$ [Å] on R_{ij} [Å]

Coumarin



CRITERION 5

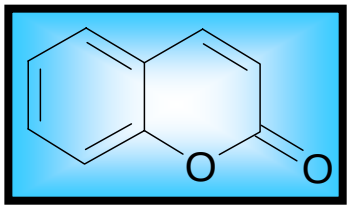


1-thiocoumarin

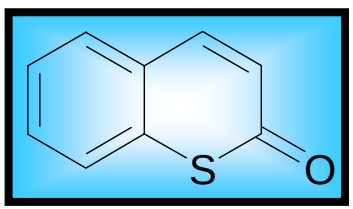
interactions	atom	q (crystal)		q (isolated)		Δq (crystal – isolated)			
		expt.(E)	theo.(T)	HF	DFT	E–HF	E–DFT	T–HF	T–DFT
C(4)…H(2)[a]	H(2)	0.2569	0.1080	0.0144	0.0441	0.2425	0.2128	0.0936	*0.0639* 4
C(9)…H(2)[a]									
O(1)…H(3)[b]	H(3)	0.0991	0.1280	-0.0083	0.0222	0.1074	0.0769	0.1291	*0.0986* 1
O(1)…H(4)[b]	H(4)	0.0957	0.0792	-0.0305	0.0074	0.1262	0.0883	0.1097	*0.0718* 3
C(7)…H(4)[c]									
C(7)…H(4)[d]									
C(7)…H(5)[e]	H(5)	0.0331	0.0655	-0.0317	0.0080	0.0648	0.0251	0.0972	*0.0575* 5
C(8)…H(5)[e]									
O(1)…H(6)[f]	H(6)	-0.0292	0.0859	-0.0241	0.0128	-0.0051	-0.0420	0.1100	*0.0731* 2
O(2)…H(6)[g]									
C(4)…H(7)[h]	H(7)	0.0662	0.0902	0.0026	0.0353	0.0636	0.0309	0.0876	*0.0549* 6
C(5)…H(7)[h]									
O(1)…H(3)[i]	H(3)	0.0991	0.0980	-0.0164	0.0155	0.1155	0.0836	0.1144	*0.0825* 2
O(1)…H(4)[i]	H(4)	0.2872	0.1092	-0.0334	0.0058	0.3206	0.2814	0.1426	*0.1034* 1
O(1)…H(6)[j]	H(6)	0.3029	0.0809	-0.0250	0.0126	0.3279	0.29.3	0.1059	*0.0683* 3
C(2)…H(6)[j]									
C(4)…H(7)[k]	H(7)	0.2810	0.0561	-0.0193	0.0185	0.3003	0.2625	0.0754	*0.0376* 4
C(5)…H(7)[k]									

Symmetry codes: [a](x,y+1/2,-z+3/2), [b](x+1,y-1/2,-z+3/2), [c](x+1,y,z), [d](-x+1,y-1/2,-z+1), [e](-x+1,y-1/2,-z+1), [f](-x,y,z-1/2), [g](-x,y-1/2,-z+1), [h](x-1,y,z), [i](x,-y+2,z+1/2), [j](x,y-1,z), [k](x,-y+1,z-1/2).

Coumarin



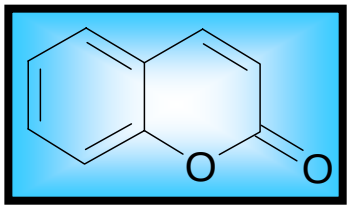
CRITERION 6



1-thiocoumarin

interactions	atom	P.E. (crystal)		P.E. (isolated)		ΔP.E. (crystal – isolated)			
		expt.(E)	theo.(T)	HF	DFT	E–HF	E–DFT	T–HF	T–DFT
C(4)…H(2)	H(2)	-1.0446	-1.1936	-1.2514	-1.2189	0.2068	0.1743	0.0578	0.0255
C(9)…H(2)									
O(1)…H(3)	H(3)	-1.2564	-1.1901	-1.2733	-1.2368	0.0169	-0.0196	0.0832	0.0467
O(1)…H(4)	H(4)	-1.2461	-1.2245	-1.2916	-1.2486	0.0455	0.0025	0.0671	0.0241
C(7)…H(4)									
C(7)…H(4)¶									
C(7)…H(5)	H(5)	-1.3213	-1.2410	-1.2932	-1.2502	-0.0281	-0.0711	0.0522	0.0092
C(8)…H(5)									
O(1)…H(6)	H(6)	-1.4029	-1.2230	-1.2886	-1.2474	-0.1143	-0.1555	0.0656	0.0244
O(2)…H(6)									
C(4)…H(7)	H(7)	-1.2700	-1.2091	-1.2608	-1.2247	-0.0092	-0.0453	0.0517	0.0156
C(5)…H(7)									
O(1)…H(3)	H(3)	-1.2408	-1.2098	-1.2865	-1.2461	0.0457	0.0053	0.0767	0.0363
O(1)…H(4)	H(4)	-1.0306	-1.2061	-1.2960	-1.2498	0.2654	0.2192	0.0899	0.0437
O(1)…H(6)	H(6)	-0.9684	-1.2293	-1.2887	-1.2454	0.3203	0.2770	0.0594	0.1610
C(2)…H(6)									
C(4)…H(7)	H(7)	-0.9787	-1.2526	-1.2837	-1.2400	0.3050	0.2613	0.0311	-0.0126
C(5)…H(7)									

Coumarin



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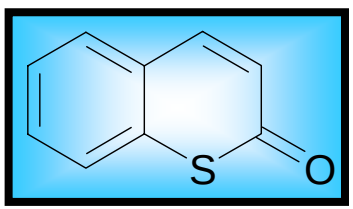
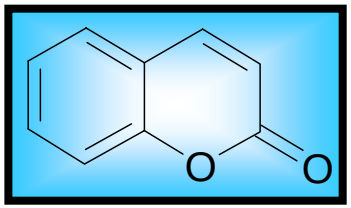


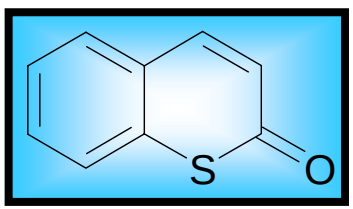
1-thiocoumarin

interactions	atom	M (crystal)		M (isolated)		ΔM (crystal – isolated)			
		expt.(E)	theo.(T)	HF	DFT	E–HF	E–DFT	T–HF	T–DFT
C(4)…H(2)	H(2)	0.0540	0.1006	0.0978	0.1209	-0.0447	-0.0669	0.0019	-0.0203
C(9)…H(2)									
O(1)…H(3)	H(3)	0.0251	0.0652	0.0972	0.1236	-0.0736	-0.0985	-0.0320	-0.0584
O(1)…H(4)	H(4)	0.0588	0.1013	0.0978	0.1258	-0.039	-0.0670	0.0035	-0.0244
C(7)…H(4)									
C(7)…H(4)									
C(7)…H(5)	H(5)	0.0386	0.0768	0.0975	0.1237	-0.0589	-0.0851	-0.0207	-0.0469
C(8)…H(5)									
O(1)…H(6)	H(6)	0.0725	0.0969	0.0970	0.1230	-0.0245	-0.0505	-0.0001	-0.0261
O(2)…H(6)									
C(4)…H(7)	H(7)	0.1076	0.1126	0.0975	0.1218	0.0101	-0.0142	0.0151	-0.0092
C(5)…H(7)									
O(1)…H(3)	H(3)	0.1033	0.0953	0.0986	0.1253	0.0047	-0.0220	-0.0300	-0.0300
O(1)…H(4)	H(4)	0.0478	0.0505	0.0978	0.1260	-0.0500	-0.0782	-0.0755	-0.0755
O(1)…H(6)	H(6)	0.1021	0.0743	0.0969	0.1230	0.0052	-0.0209	-0.0487	-0.0487
C(2)…H(6)									
C(4)…H(7)	H(7)	0.1561	0.0943	0.0971	0.1233	0.0590	0.0328	-0.0290	-0.0290
C(5)…H(7)									

Coumarin



CRITERION 8

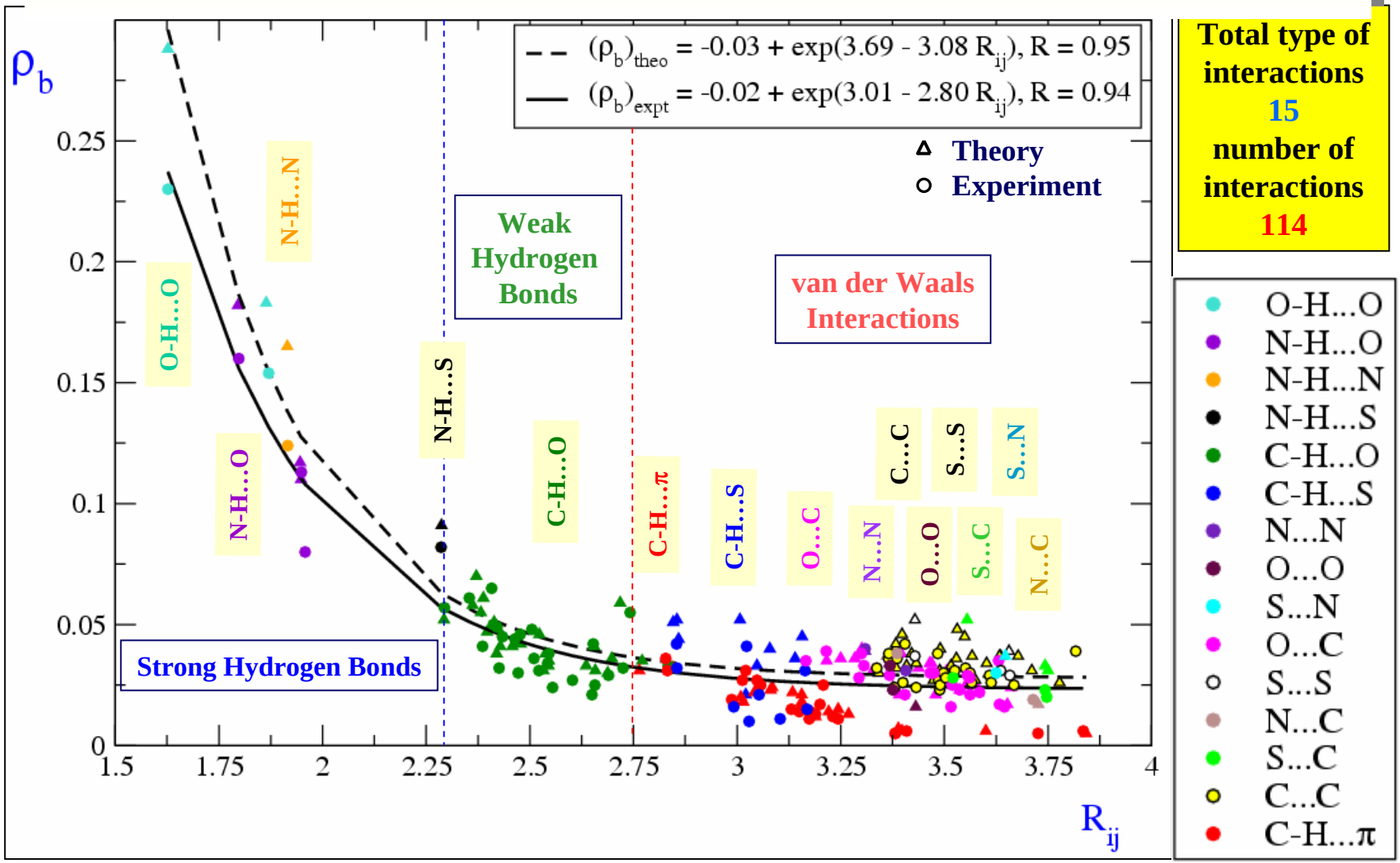


1-thiocoumarin

interactions	atom	V (crystal)		V (isolated)		ΔV (crystal – isolated)			
		expt.(E)	theo.(T)	HF	DFT	E–HF	E–DFT	T–HF	T–DFT
C(4)…H(2)	H(2)	35.10	46.02	46.36	46.66	-11.26	-11.56	-0.34	-0.64
C(9)…H(2)									
O(1)…H(3)	H(3)	35.64	40.43	47.95	48.35	-12.31	-12.71	-7.52	-7.92
O(1)…H(4)	H(4)	38.64	41.84	48.89	49.12	-10.25	-10.48	-7.05	-7.28
C(7)…H(4)									
C(7)…H(4)									
C(7)…H(5)	H(5)	39.47	44.82	48.80	48.84	-9.33	-9.37	-3.98	-4.02
C(8)…H(5)									
O(1)…H(6)	H(6)	38.82	43.47	48.54	48.51	-9.72	-9.69	-5.07	-5.04
O(2)…H(6)									
C(4)…H(7)	H(7)	42.18	47.22	46.87	47.18	-4.69	-5.00	0.35	0.04
C(5)…H(7)									
O(1)…H(3)	H(3)	34.45	41.27	47.44	47.96	-12.99	-13.51	-6.17	-6.69
O(1)…H(4)	H(4)	27.97	40.90	48.53	48.68	-20.56	-20.71	-7.63	-7.78
O(1)…H(6)	H(6)	34.80	43.28	48.54	48.52	-13.74	-13.72	-5.26	-5.24
C(2)…H(6)									
C(4)…H(7)	H(7)	38.90	45.16	47.94	48.06	-9.04	-9.16	-2.78	-2.90
C(5)…H(7)									

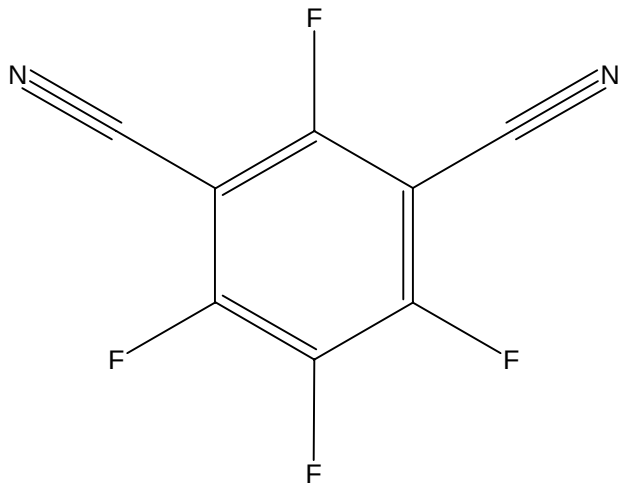
Continuum of a Strong Hydrogen Bonds to Weak Interactions

Munshi, P.; Guru Row, T. N. *CrystEngComm* **2005**, *7*, 608-611.

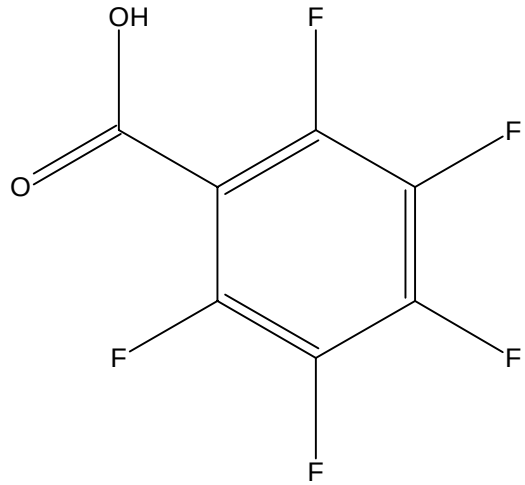


Exponential dependence of ρ_b [eÅ^{-3}] on the interaction length R_{ij} [Å]

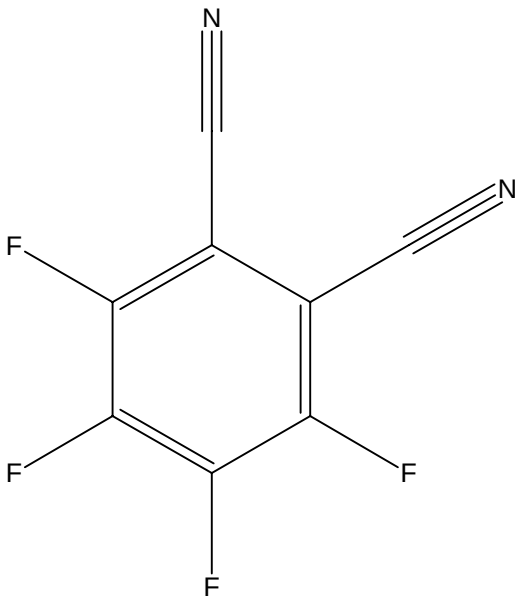
Some Recent Literature reports on charge density analysis performed on molecules containing organic fluorine



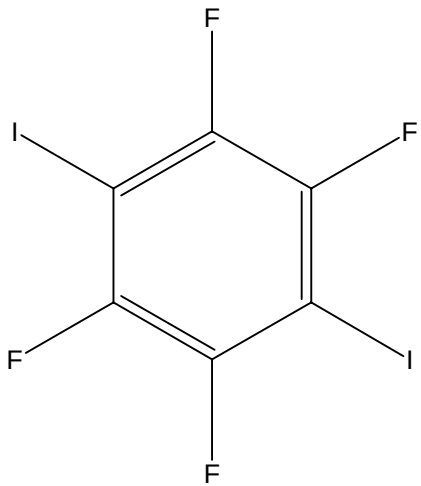
Luger group, *J. Phys. Chem., A* 2001, *105*, 7405

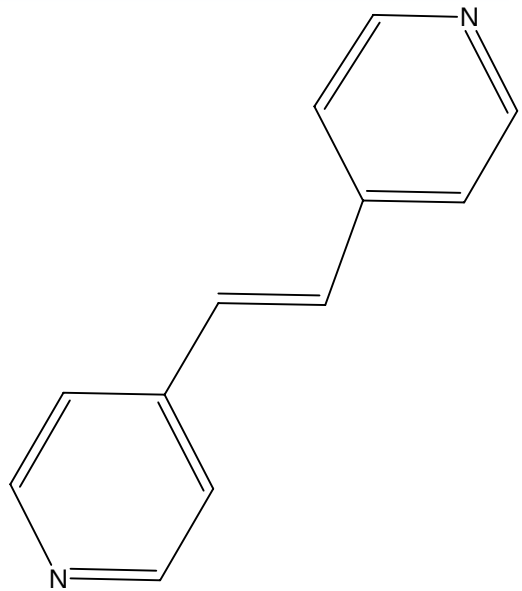


Hursthouse group, *J. Phy. Chem. B.*, 2004, *108*, 3663

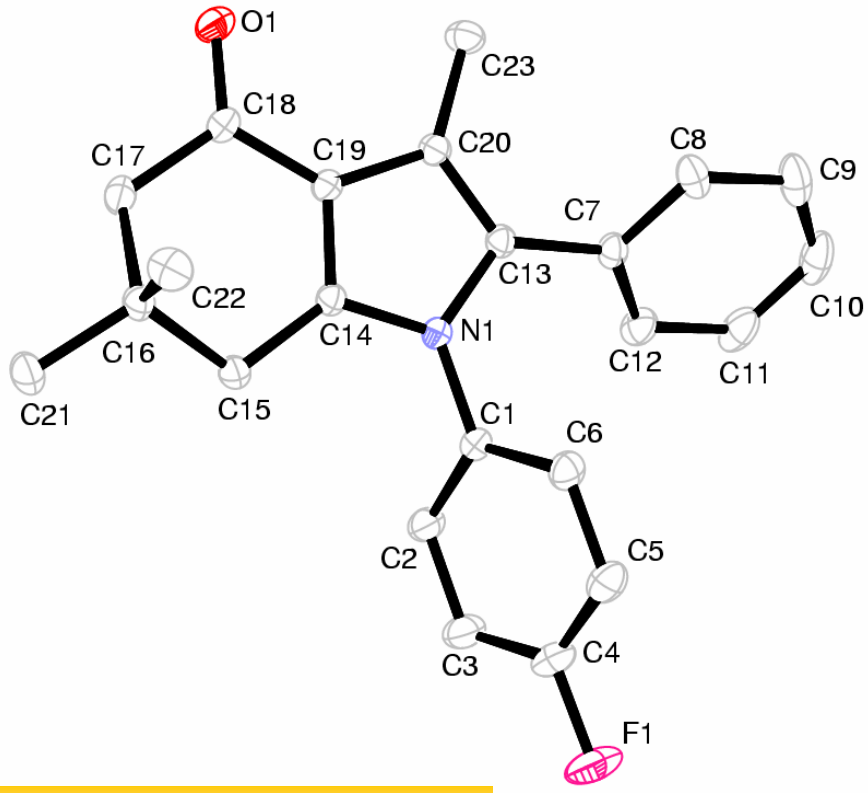


Pilati group, *Chem. Eur. J.*, 2003, *9*, 1631





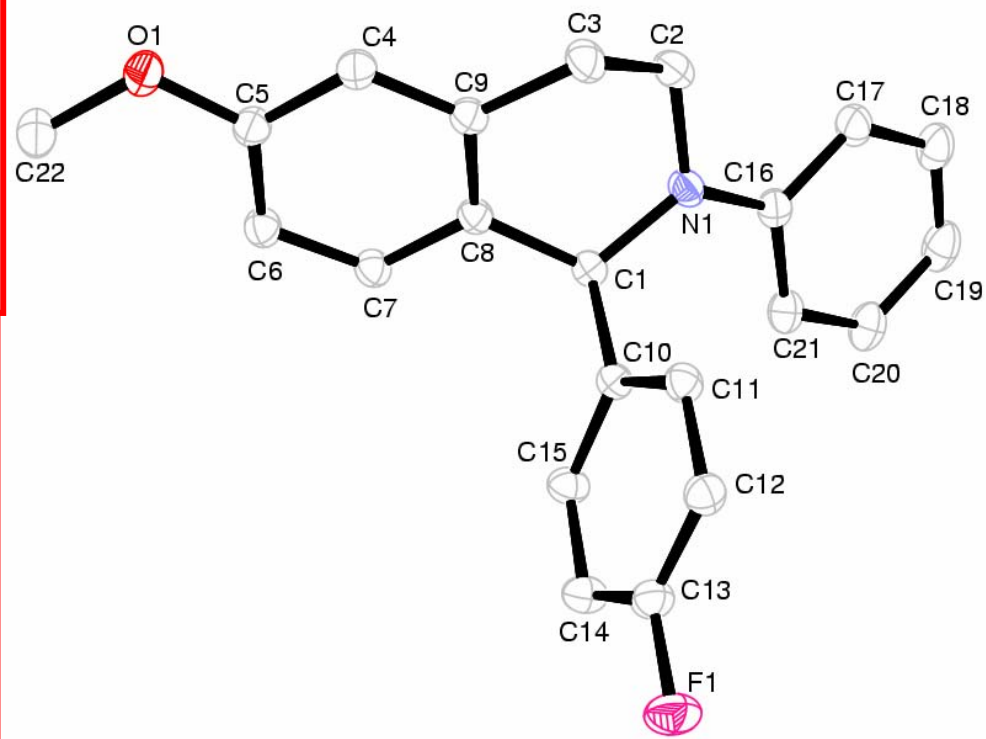
Molecules Designed for Charge Density analysis



Compound (A)

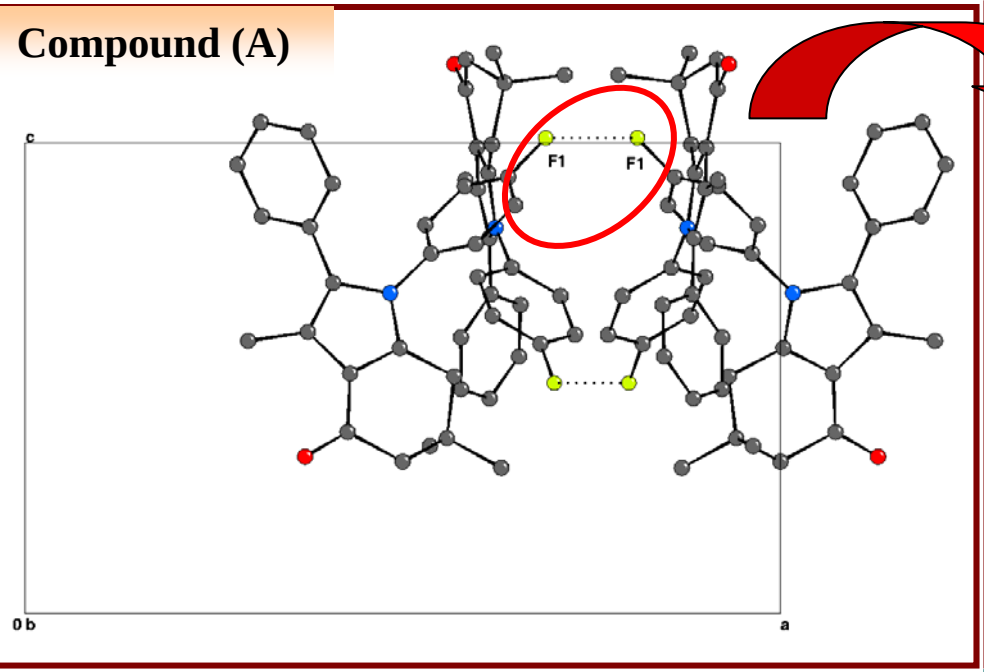
Deepak Chopra, T. S. Cameron, J. D. Ferrara, and T N. Guru Row
J. Phys. Chem. A 2006, *110*, *10465-10477*

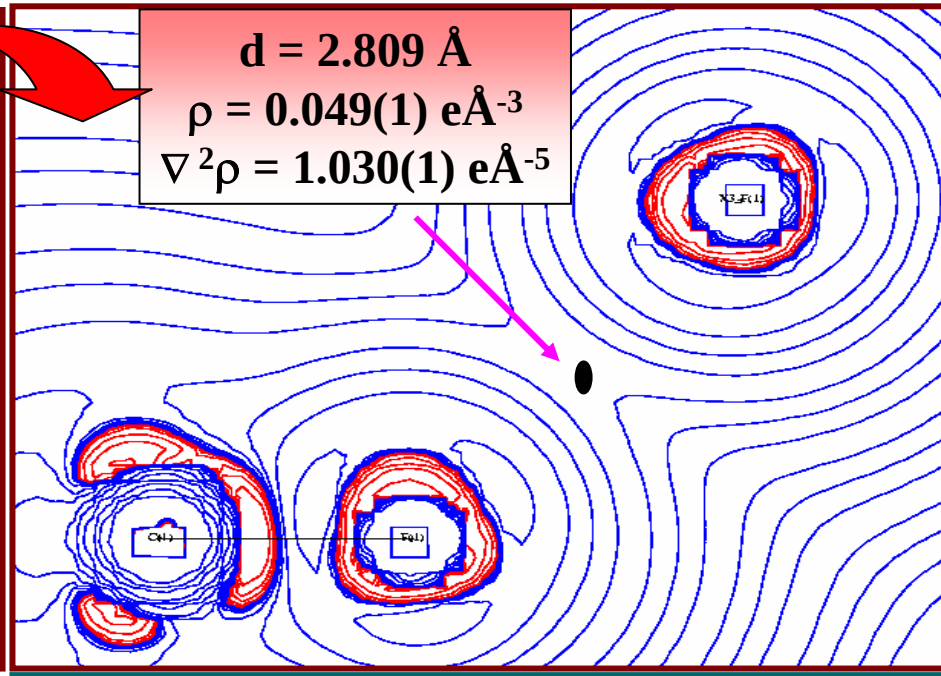
Compound (B)



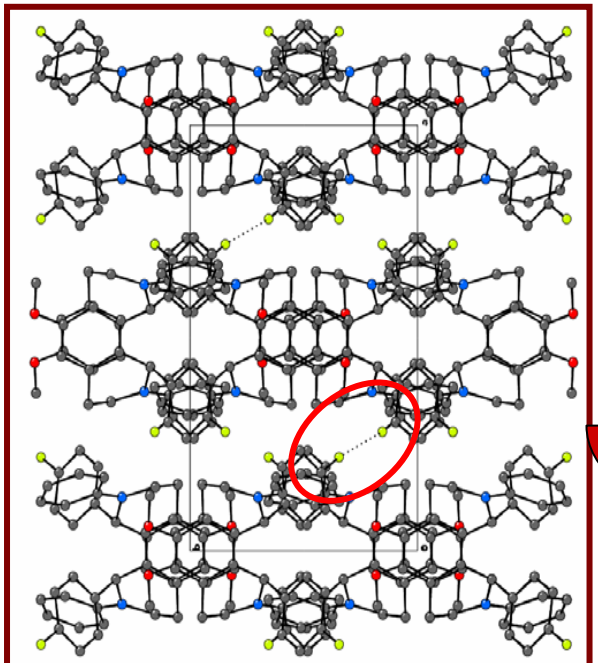
Laplacian Distribution in the F…F interaction regime

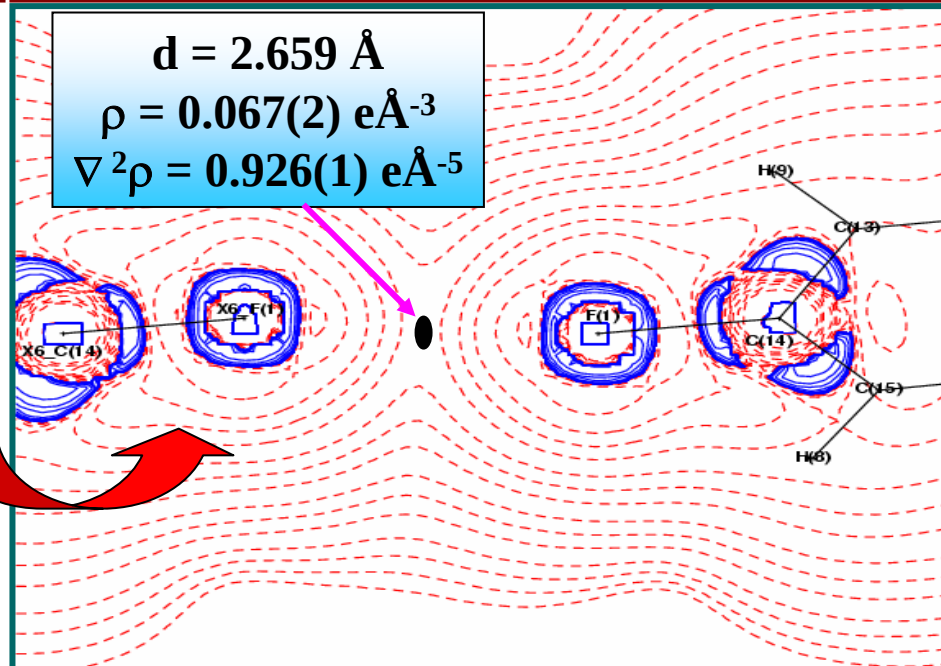
Compound (A)



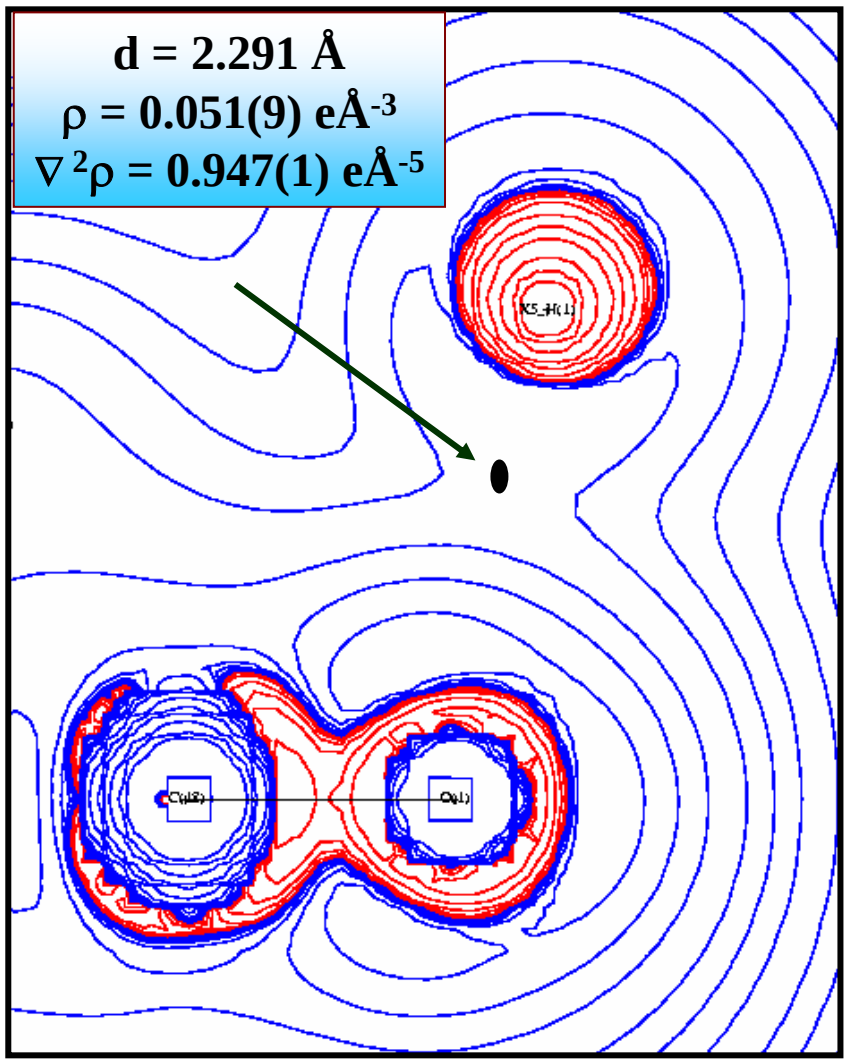


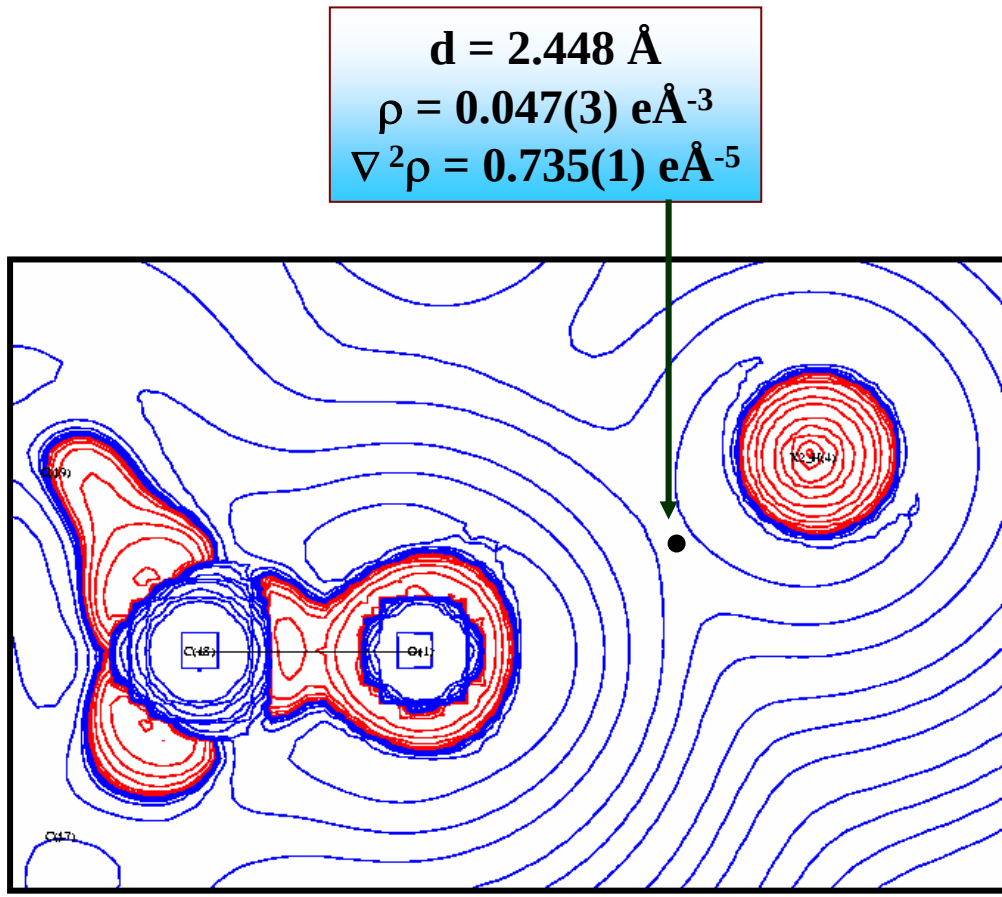
Compound (B)



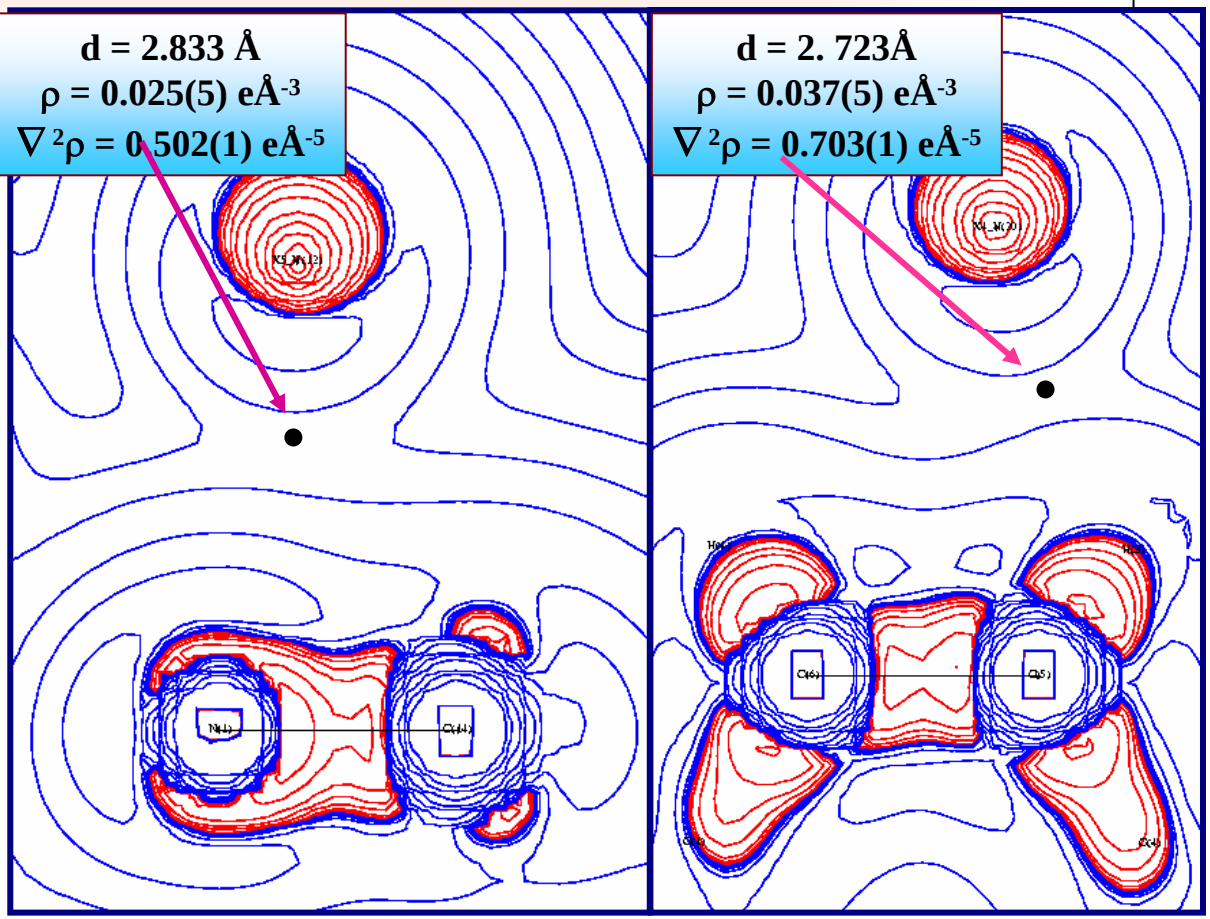


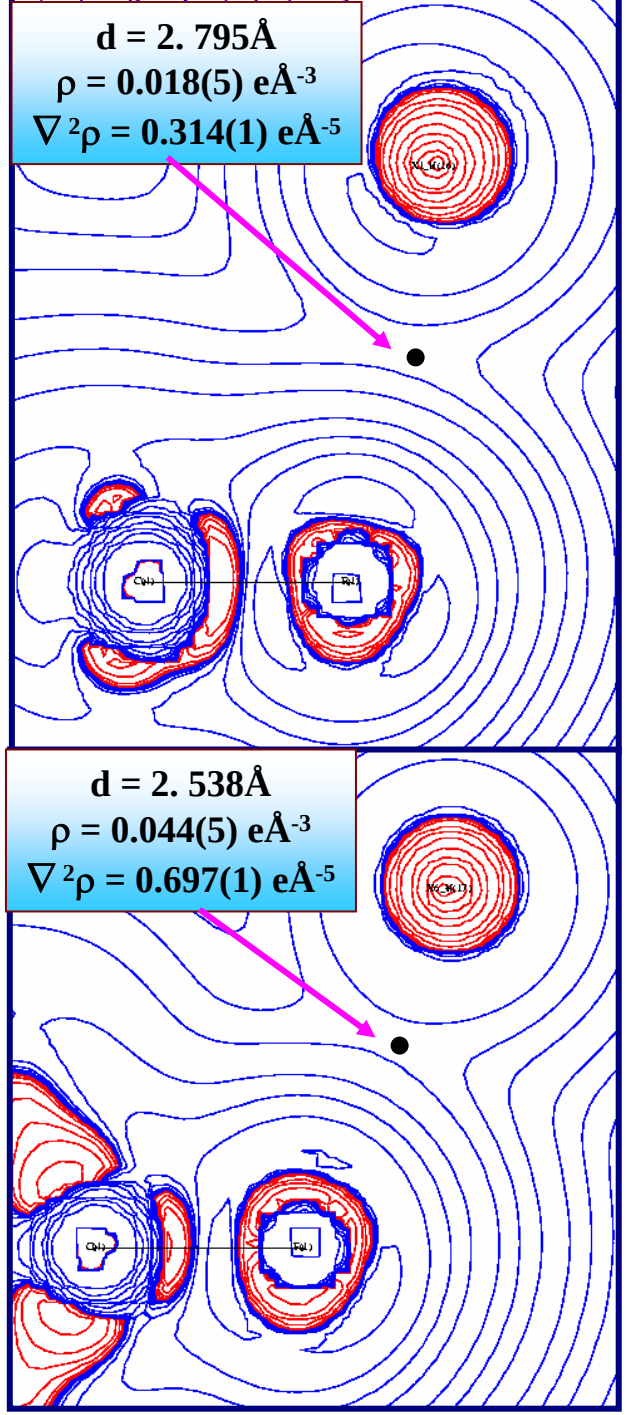
Charge Density Features associated with C-H…O Hydrogen Bonding in Compound (A)





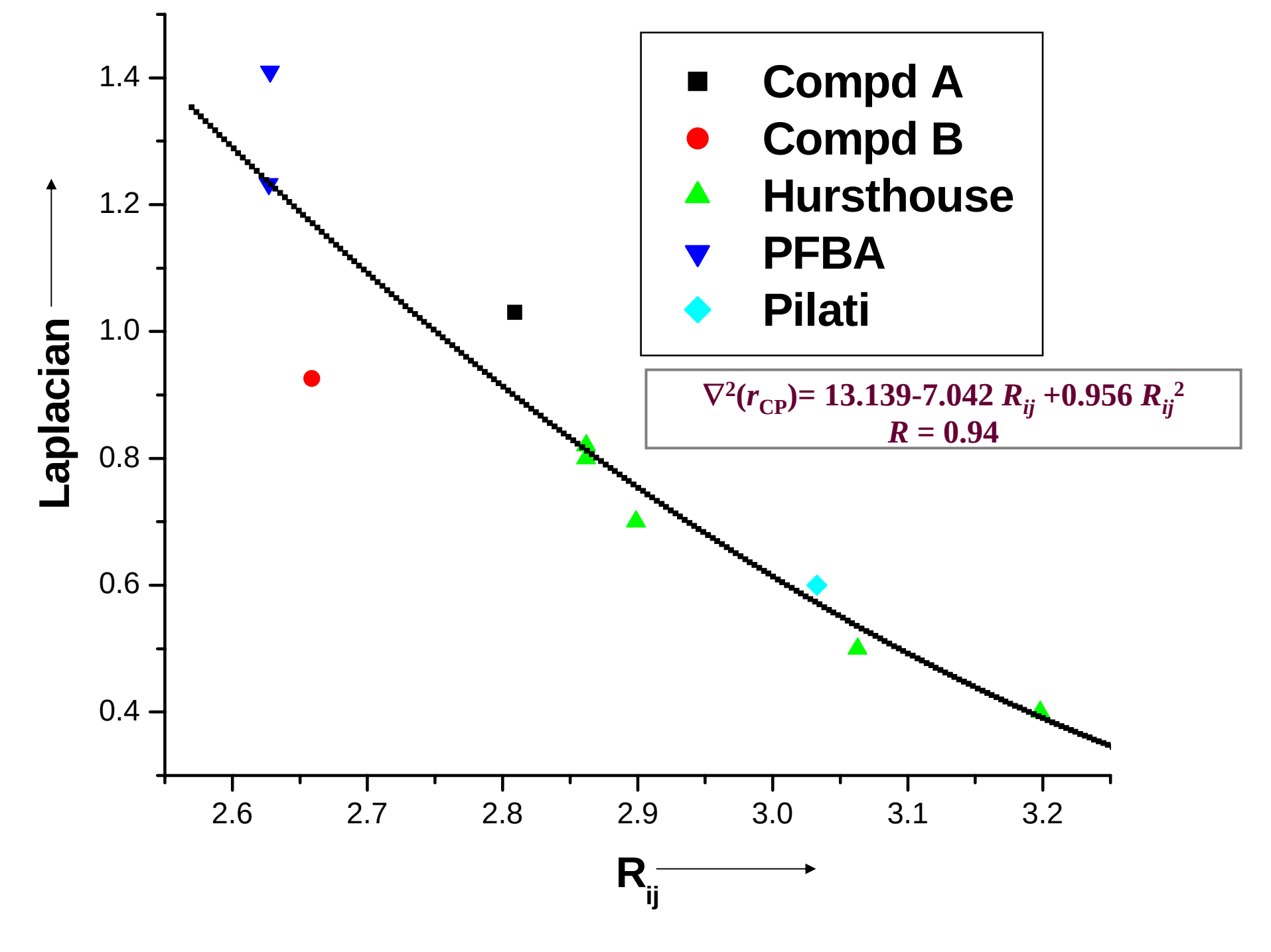
Aromatic C-H…π and C-H…F Hydrogen Bond in Compound (A)

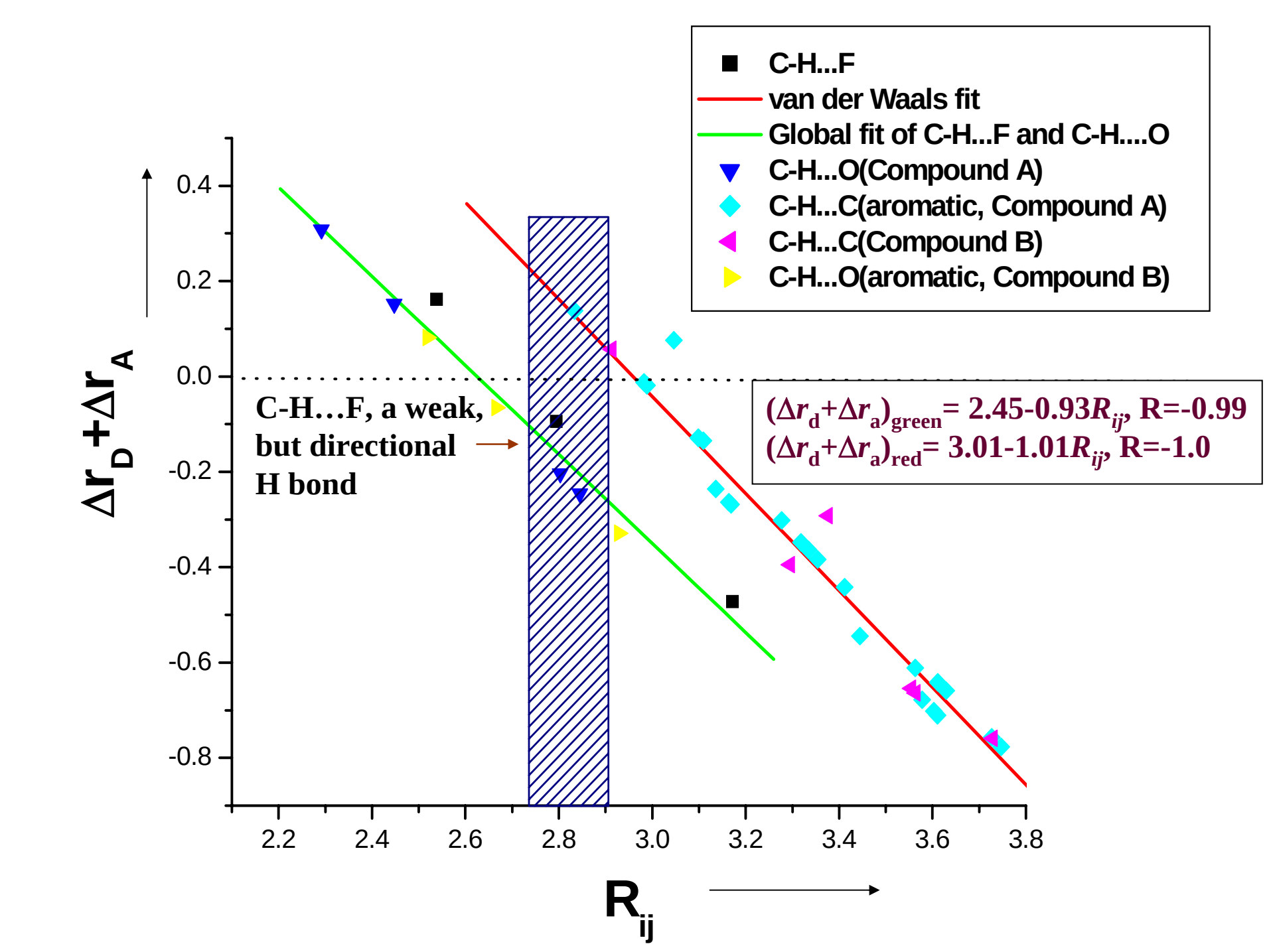




Topological parameters in C-F…F-C interactions [K & P 1-4]

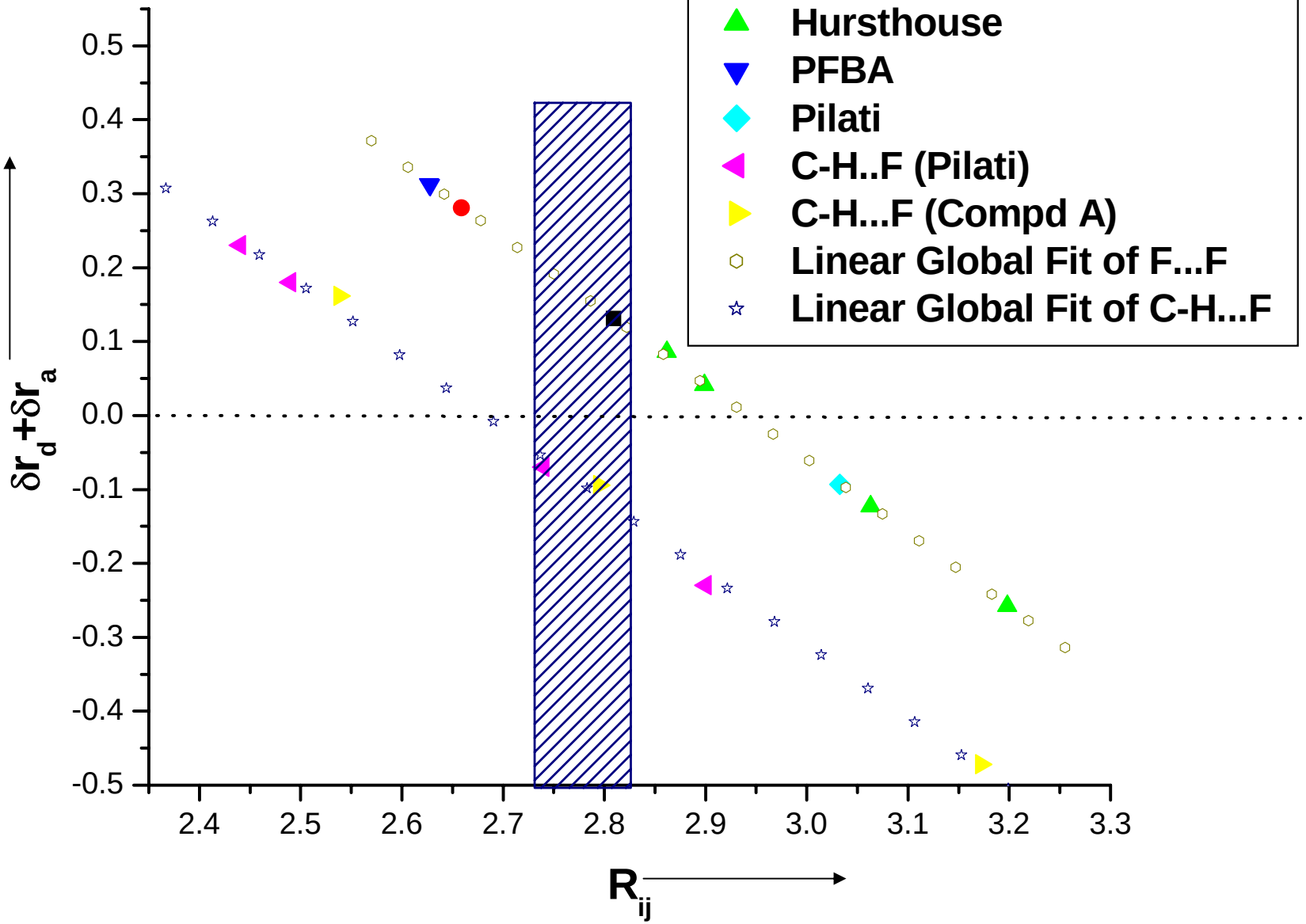
Compound	R_{ij}	ρ_b	$\nabla^2\rho_b$	G(r_{CP})	V(r_{CP})	E(r_{CP})	$\Delta r_D+\Delta r_A$
A	2.809	0.049	1.030	37.752	-24.476	13.276	0.131
B	2.659	0.067	0.926	36.873	-27.869	9.003	0.281
Hursthouse	2.899	0.040	0.700	25.782	-16.884	8.898	0.041
	2.862	0.050	0.820	30.944	-21.264	9.680	0.086
	2.862	0.040	0.800	29.084	-18.535	10.549	0.086
	3.063	0.030	0.500	18.162	-11.553	6.609	-0.123
	3.198	0.020	0.400	14.05	-8.283	5.767	-0.258
Pilati	3.033	0.034	0.600	21.847	-13.969	7.878	-0.093
PFBA	2.627	0.058	1.233	45.668	-30.251	15.417	0.313
	2.628	0.067	1.410	52.858	-35.862	16.996	0.312


Compd A
Compd B
Hursthouse
PFBA
Pilati
$\nabla^2(r_{CP})$= 13.139-7.042 R_{ij} +0.956 R_{ij}^2
R = 0.94
Laplacian
R_{ij}
1.4
1.2
1.0
0.8
0.6
0.4
2.6
2.7
2.8
2.9
3.0
3.1
3.2


C-H...F
van der Waals fit
Global fit of C-H...F and C-H....O
C-H...O(Compound A)
C-H...C(aromatic, Compound A)
C-H...C(Compound B)
C-H...O(aromatic, Compound B)
$(\Delta r_d+\Delta r_a)_{green}$= 2.45-0.93$R_{ij}$, R=-0.99
$(\Delta r_d+\Delta r_a)_{red}$= 3.01-1.01$R_{ij}$, R=-1.0
C-H…F, a weak, but directional H bond
$\Delta r_D+\Delta r_A$
R_{ij}
0.4
0.2
0.0
-0.2
-0.4
-0.6
-0.8
2.2
2.4
2.6
2.8
3.0
3.2
3.4
3.6
3.8

$(\Delta r_D + \Delta r_A)_{C\text{-}H\ldots F} = 2.617 - 0.976 R_{ij}, R = -1.00$

$(\Delta r_D + \Delta r_A)_{F\ldots F} = 2.943 - 1.000 R_{ij}, R = -1.00$



Conclusions and future directions

1. Hydrogen bonds classified using a universal fit.

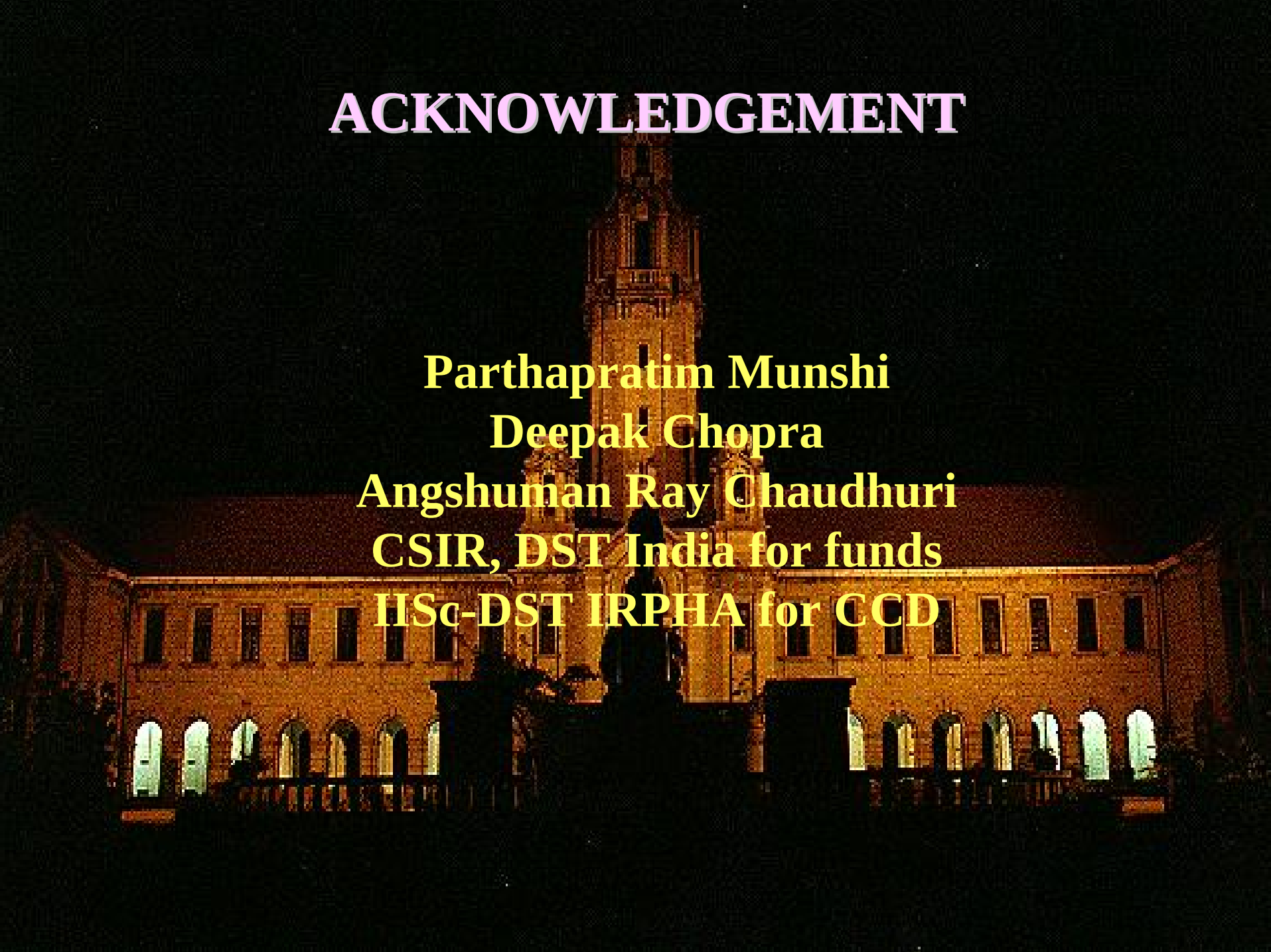
2. Limit of a hydrogen bond featured in C-H…O and C-H…π contacts.

3. Insights into the ubiquitous C-F…F-C contacts.

4. Evaluation of the nature of the interaction.

5. Calculation of electrostatic potentials leading to surface characteristics.

ACKNOWLEDGEMENT



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