Revised Version

Supplementary Information

Understanding the mechanism and regioselectivity of the copper(I) catalyzed [2+3] cycloaddition reaction between azide and alkyne: A systematic DFT study[†,‡]

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Contents:

Theoretical background

Along with the global indices, the conceptual DFT defines a number of local indices. In 1984, Parr and Yang [1] proposed within the DFT the f(r) function named frontier function or Fukui function for a molecule, which was defined as:

$$f_K = \left[\frac{\partial \rho(r)}{\partial N}\right]_{v(r)}$$

Parr and Yang assumed that the preferred direction for the approach of a reagent towards the other is the one for which the initial variation of the chemical potential μ for a species is a maximum, and that the preferred direction is the one with the largest f(r) at the reaction site [1]. Using a frozen core approximation, in which valence $\delta\rho = \delta\rho_{valence}$, they proposed:

$$f_k^- = \rho_{HOMO}(r) \qquad for\ electrophilic\ attacks$$

And

$$f_k^+ = \rho_{LUMO}(r) \qquad for\ nucleophilic\ attacks$$

Although, in principle, the electron density of a neutral or $N_{0 \pm 1electron}$ molecule contains all the information needed for the evaluation of the Fukui function f (r), most studies in the literature have been carried out in the so-called finite difference method, in which the Fukui functions f (r) are approximated as [2]:

$$f_k^- = \left[q_k(N) - q_k(N-1)\right] \quad for\ electrophilic\ attacks$$

And

$$f_k^+ = \left[q_k(N+1) - q_k(N)\right] \qquad for\ nucleophilic\ attacks$$

where $q_k(N)$, $q_k(N-1)$ and $q_k(N+1)$ are the atomic charges in the neutral, cationic and anionic species respectively.

Thus, the local electrophilicity [3] ω_k and the local nucleophilicity [4] N_k indices were defined as:

$$\omega_k = \omega f_k^+$$
$$N_k = N f_k^-$$

Analysis of the local electrophilicity ω_k and local nucleophilicity N_k indices in an organic molecule allows for the characterization ofthe most electrophilic and nucleophilic centers in the molecule, and thereby to predict theregio- and chemoselectivity in a polar reaction.

Morell et al.[5-7] have proposed a local reactivity descriptor (LRD) which is called the dual descriptor (DD) Δf(r). The dual descriptor can be condensed over the atomic sites: when $\Delta f_k > 0$ the process is driven by a nucleophilic attack on atom k and then that atom acts as an electrophilic species. Conversely, when $\Delta f_k < 0$ the process is driven by an electrophilic attack over atom k and therefore atom k acts as a nucleophilic species. Thus, the Dual Descriptor was defined as:

$$\Delta f_k(r) = f_k^+ - f_k^-$$

References

1 R.G. Parr, W. Yang; *J. Am. Chem. Soc.* **1984**, *106*, 4049.

2 W. Yang, W.J. Mortier; *J. Am. Chem. Soc.* **1986**, *108*, 5708.

3 L.R. Domingo, M.J. Aurell, P. Perez, R. Contreras; J. *Phys. Chem. A*, **2002**, 106, 6871.

4 P. Pérez, L. R. Domingo, M. Duque-Noreña, E. Chamorro; *J. Mol. Struct. (Theochem)* **2009**, *895*, 86.

5 C. Morell, A., Grand, A. Toro-Labbé,. *J. Phys. Chem. A*, **2005**, *109*, 205.

6 C. Morell, A. Hocquet, A., Grand and B, Jamart-Gregoire, *J. Mol. Struct. (Theochem)*, **2008**, *849*, 46

7 C. Morell, P. Ayers, A. Grand, S. Gutiérrez-Oliva, and A. Toro-Labbé, *Phys. Chem. Chem. Phys.*, **2008**, *10*, 7239.

Table S1. Electrophilic and nucleophilic Fukui functions, local Electrophilicity, ω_k, Nucleophilicity, N_k, and Dual Descriptor Values (in eV).

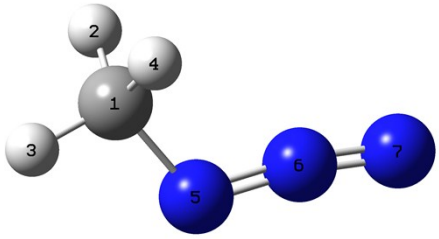
	Number of atom	f_k^+	f_k^-	ω_k	N_k	$\Delta f_k(r)$
Methylazide	N1	0.18	**0.43**	0.22	**0.93**	**-0.24**
	N3	0.40	0.40	0.47	0.88	0.01
Dinuclear Cu(I)-acetylide	C4	0.05	0.08	0.09	0.48	-0.03
	C5	0.01	-0.03	0.02	-	0.04
	Cu6	**0.37**	0.30	**0.66**	0.52	**0.07**
	Cu7	0.37	0.29	0.66	0.50	**0.08**
Reactive complex	N1	0.01	0.13	0.02	0.55	-0.12
	N3	**0.13**	0.28	0.28	**1.17**	**-0.15**
	C4	0.03	**0.02**	0.07	0.11	0.01
	C5	-0.02	0.00	-	0.01	-0.02

Table S2. B3LYP/6-31G(d) and B3LYP/6-311G(d,p) total (E, in a.u.) and relative energies (ΔE, kcal mol^{-1}) of the stationary points involved in the 32CA reaction of methylazide with methylacetylene.

	B3LYP/6-31G(d)		B3LYP/6-311G(d,p)	
	E	ΔE	E	ΔE
Methylazide	-204.093315		-204.148221	
Methylacetylene	-116.653270		-116.690652	
TS14	-320.716560	18.84	-320.805340	21.04
TS15	-320.717077	18.52	-320.805182	21.14
CA14	-320.859635	-70.95	-320.940029	-63.48
CA15	-320.859495	-70.86	-320.939704	-63.28

Cartesian coordinates, energies, and imaginary frequency (transition states) for all optimized geometries.

Methyl azide

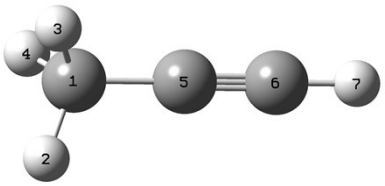


E(Hartree) = -204.093315062

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	7	0	0.391276	-0.630665	-0.000048
2	7	0	-0.717975	-0.096025	0.000111
3	7	0	-1.801285	0.271185	-0.000057
4	6	0	1.554423	0.283851	-0.000006
5	1	0	1.563227	0.917762	-0.893423
6	1	0	1.564295	0.916251	0.894472
7	1	0	2.441839	-0.348587	-0.001054

Propine



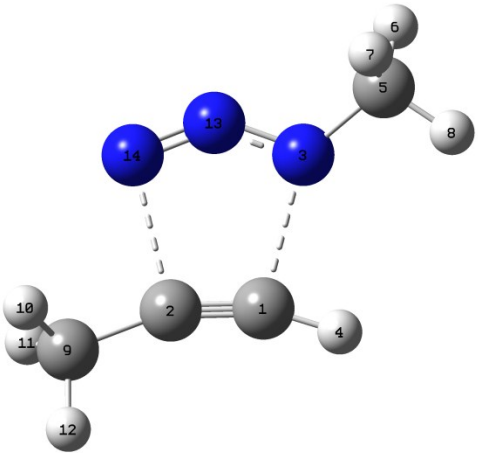
E(Hartree) = -116.65327005

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	0.000000	0.000000	-1.241443
2	1	0	0.000000	1.022446	-1.638037
3	1	0	0.885464	-0.511223	-1.638037
4	1	0	-0.885464	-0.511223	-1.638037
5	6	0	0.000000	0.000000	0.218960

6	6	0	0.000000	0.000000	1.426135
7	1	0	0.000000	0.000000	2.492199

TS14



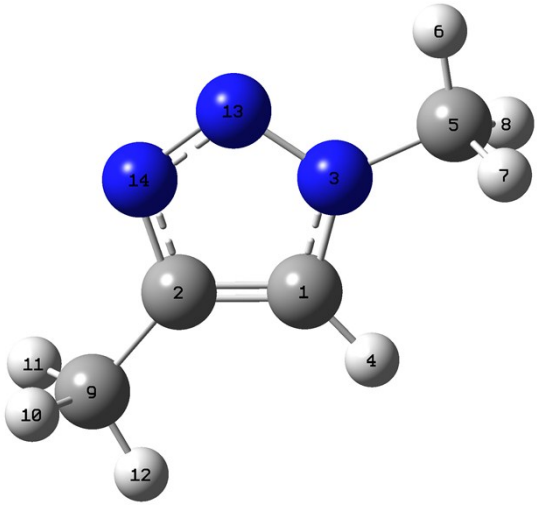
Imaginary Frequency: - 424.22 cm^{-1}

E(Hartree) = -320.71656009

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	0.487394	1.337557	-0.100523
2	6	0	1.410783	0.522122	-0.003895
3	7	0	-1.333364	0.116647	-0.283477
4	1	0	-0.042987	2.258541	-0.198025
5	6	0	-2.690368	0.300780	0.223654
6	1	0	-3.412403	-0.325901	-0.313834
7	1	0	-2.771957	0.102121	1.300074
8	1	0	-2.948619	1.346396	0.039727
9	6	0	2.780003	-0.004344	0.125572
10	1	0	2.881184	-0.606649	1.034668
11	1	0	3.029571	-0.655126	-0.719285
12	1	0	3.513375	0.809409	0.164461
13	7	0	-0.749641	-0.985968	-0.095490
14	7	0	0.343713	-1.397177	-0.017695

CA14

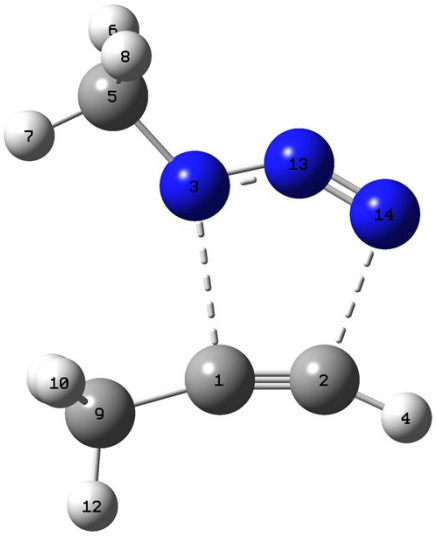


E(Hartree) = -320.85963450

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	-0.014549	-0.930555	-0.000091
2	6	0	-1.106754	-0.088294	-0.000003
3	7	0	1.061279	-0.100403	-0.000003
4	1	0	0.079239	-2.006253	-0.000119
5	6	0	2.476080	-0.421935	0.000080
6	1	0	3.018498	0.524292	-0.000062
7	1	0	2.742360	-0.995596	0.893316
8	1	0	2.742384	-0.995883	-0.892963
9	6	0	-2.568754	-0.407312	0.000099
10	1	0	-3.062708	0.014431	0.882680
11	1	0	-3.063038	0.015653	-0.881703
12	1	0	-2.735865	-1.488724	-0.000604
13	7	0	0.661995	1.190806	-0.000025
14	7	0	-0.642847	1.198261	-0.000122

TS15



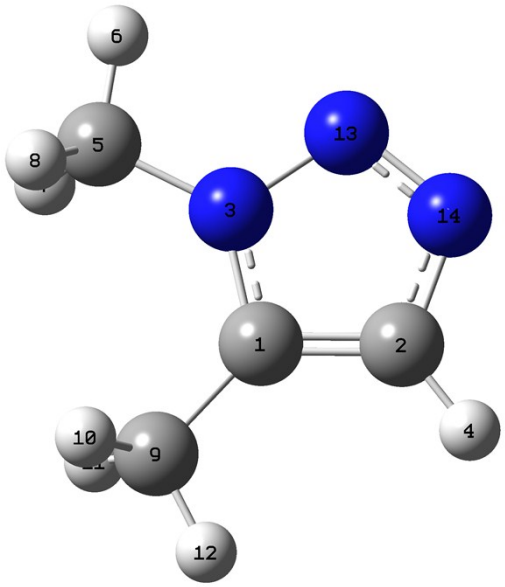
Imaginary Frequency: - 417.12 cm^{-1}

E(Hartree) = -320.71707686

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	1.424277	-0.069331	0.013263
2	6	0	1.457803	1.165713	0.039689
3	7	0	-0.866149	-0.301062	-0.089603
4	1	0	1.932082	2.122596	0.072124
5	6	0	-1.962074	-1.253320	0.052822
6	1	0	-2.700235	-1.160260	-0.754003
7	1	0	-1.517765	-2.249923	-0.008126
8	1	0	-2.475560	-1.163434	1.018954
9	6	0	1.779587	-1.492503	-0.014312
10	1	0	1.364064	-2.026496	0.847059
11	1	0	1.406394	-1.978233	-0.922037
12	1	0	2.870362	-1.610167	0.009258
13	7	0	-1.099202	0.935100	-0.030360
14	7	0	-0.474206	1.932042	0.003963

CA15



E(Hartree) = - 320.85949506

Standard orientation:

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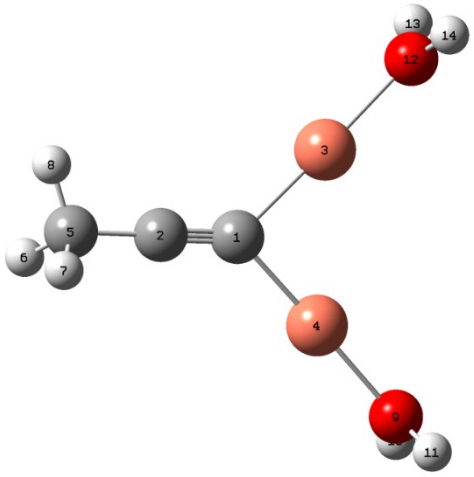
1	6	0	0.307114	-0.694774	0.000023
2	6	0	-0.972146	-1.212975	-0.000003
3	7	0	0.098191	0.652085	0.000005
4	1	0	-1.284711	-2.247865	-0.000084
5	6	0	1.068169	1.729722	0.000001
6	1	0	0.506701	2.664573	-0.000105
7	1	0	1.701127	1.684421	0.892330
8	1	0	1.701292	1.684308	-0.892207
9	6	0	1.657420	-1.332011	0.000094
10	1	0	2.243802	-1.052109	-0.884381
11	1	0	2.243376	-1.052797	0.885069
12	1	0	1.555056	-2.420414	-0.000350
13	7	0	-1.228877	0.940396	0.000232
14	7	0	-1.873597	-0.192466	-0.000374

dinuclear copper-acetylide

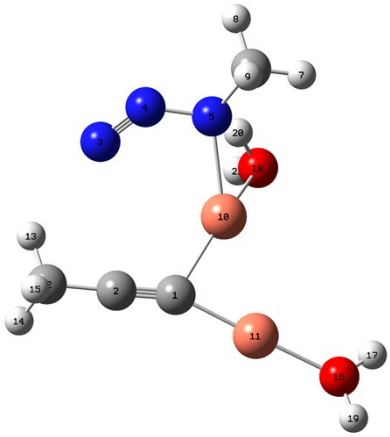


E(Hartree) = -661.22746111

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	-0.069065	1.025164	0.000026
2	6	0	-0.185563	2.272173	0.000047
3	29	0	-1.318768	-0.444032	0.000005
4	29	0	1.386982	-0.233681	-0.000004
5	6	0	-0.333717	3.734833	-0.000025
6	1	0	0.126867	4.181930	0.891087
7	1	0	0.134490	4.182558	-0.886854
8	1	0	-1.395200	4.021644	-0.004532
9	8	0	2.883855	-1.478851	-0.000007
10	1	0	3.361371	-1.758149	0.820447
11	1	0	3.361069	-1.758871	-0.820390
12	8	0	-2.623429	-1.889645	-0.000012
13	1	0	-3.060115	-2.230073	0.820602
14	1	0	-3.060028	-2.230406	-0.820533

RC

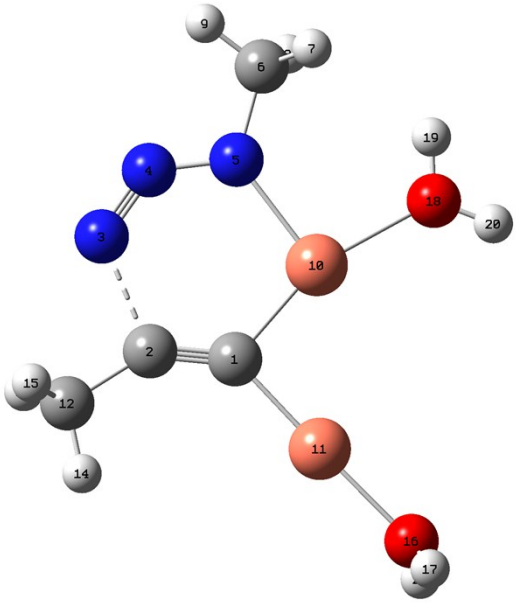


E(Hartree) = -865.32282171

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	0.764755	1.244781	-0.081985
2	6	0	0.193218	2.350187	-0.011102
3	7	0	-2.740172	1.300248	0.399201
4	7	0	-3.037059	0.280218	-0.211059
5	7	0	-2.308869	-0.928468	-0.279854
6	6	0	-2.911687	-1.836405	-1.281618
7	1	0	-2.374091	-2.790754	-1.226857
8	1	0	-3.976465	-2.022887	-1.075058
9	1	0	-2.825810	-1.447570	-2.307994
10	29	0	-0.308242	-0.410633	0.093427
11	29	0	2.205964	0.040099	-0.170991
12	6	0	-0.505609	3.638070	0.087429
13	1	0	-1.536522	3.449883	0.410688
14	1	0	-0.021919	4.300350	0.817540
15	1	0	-0.538306	4.151827	-0.882072
16	8	0	3.672436	-1.246032	-0.211450
17	1	0	3.546464	-2.159890	0.101495
18	8	0	-0.896115	-1.903103	1.661060
19	1	0	4.566139	-1.083600	-0.560903
20	1	0	-1.743806	-1.674670	1.123314
21	1	0	-0.981554	-1.727895	2.617966

TS1



Imaginary Frequency: -328.76 cm^{-1}

E(Hartree) = -865.29799698

Standard orientation:

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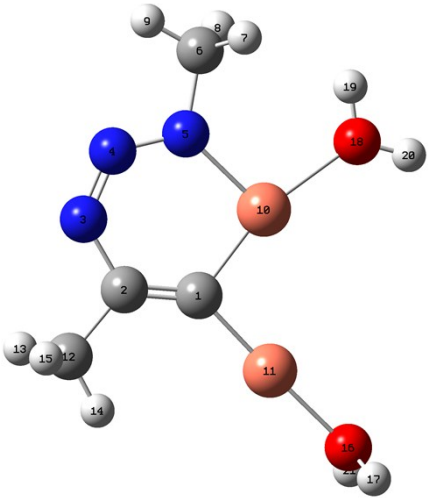
			X	Y	Z
1	6	0	0.465139	0.807646	0.000768
2	6	0	-0.035620	2.010202	0.001664
3	7	0	-1.927311	2.187567	-0.005040
4	7	0	-2.679646	1.192302	-0.005392
5	7	0	-2.436584	-0.132038	-0.013140
6	6	0	-3.681067	-0.933985	0.014166
7	1	0	-3.675930	-1.677166	-0.801437
8	1	0	-3.798135	-1.461757	0.976154
9	1	0	-4.559030	-0.291314	-0.125902
10	29	0	-0.536884	-0.818649	-0.002866
11	29	0	2.156612	-0.016127	0.001049
12	6	0	0.348321	3.458748	0.005487
13	1	0	-0.067255	3.961087	0.887926
14	1	0	1.439844	3.567105	0.008584
15	1	0	-0.062608	3.964285	-0.877292
16	8	0	3.917162	-0.929316	0.000293
17	1	0	4.449381	-0.998712	-0.817263
18	8	0	-0.944320	-2.823817	0.001334
19	1	0	-1.884458	-3.080462	-0.006972
20	1	0	-0.341757	-3.587294	0.021200
21	1	0	4.469256	-0.952676	0.807166

IC



E(Hartree) = -865.32290919

Standard orientation:

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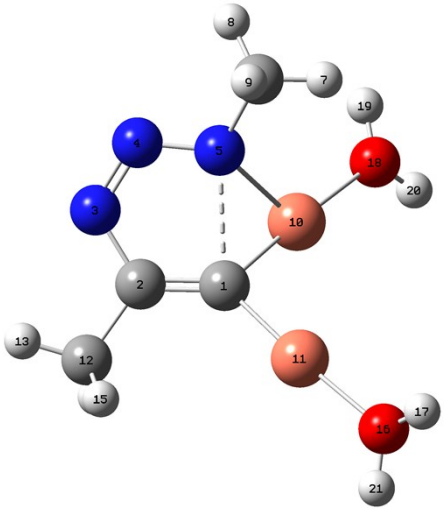
1	6	0	0.422049	0.723670	-0.000137
2	6	0	-0.129030	1.961247	-0.000106
3	7	0	-1.554373	2.271175	-0.000019
4	7	0	-2.514614	1.401985	0.000063
5	7	0	-2.357570	0.060941	0.000109
6	6	0	-3.661973	-0.640375	0.000185
7	1	0	-3.769168	-1.271791	-0.897818
8	1	0	-3.769542	-1.270926	0.898745
9	1	0	-4.476214	0.093903	-0.000339
10	29	0	-0.616154	-0.856252	-0.000068
11	29	0	2.111101	-0.078453	-0.000046
12	6	0	0.648557	3.270474	-0.000028
13	1	0	0.383253	3.864888	0.884756
14	1	0	1.727359	3.082556	-0.001102
15	1	0	0.381590	3.865967	-0.883568
16	8	0	3.869700	-0.992899	0.000258
17	1	0	4.404160	-1.077965	-0.811872
18	8	0	-1.187443	-2.819743	0.000036
19	1	0	-2.144417	-3.004851	0.000024
20	1	0	-0.644535	-3.626862	-0.000900
21	1	0	4.404287	-1.076135	0.812497

TS2



Imaginary Frequency: -185.73 cm^{-1}

E(Hartree) = -865. 30153680

Standard orientation:

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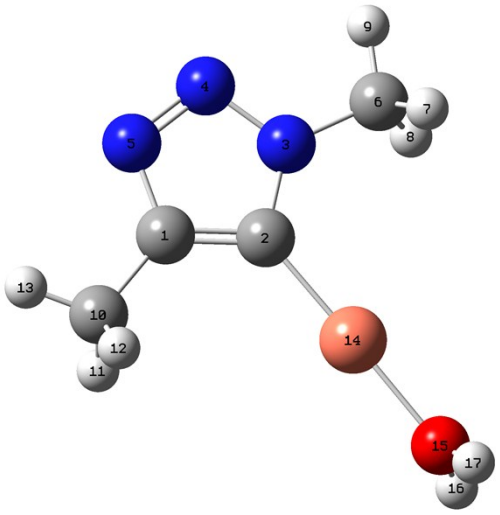
			X	Y	Z
1	6	0	-0.226614	0.641091	-0.160092
2	6	0	0.241945	1.906241	-0.449060
3	7	0	1.552702	2.331657	-0.104519
4	7	0	2.248673	1.491183	0.635785
5	7	0	1.715712	0.263729	0.836097
6	6	0	2.323334	-0.438997	1.996316
7	1	0	2.078551	-1.507388	1.941204
8	1	0	3.414863	-0.310443	1.993362
9	1	0	1.934398	-0.044561	2.945079
10	29	0	0.748910	-0.948293	-0.572204
11	29	0	-1.918636	-0.099093	0.209316
12	6	0	-0.604945	3.012634	-1.055034
13	1	0	-0.045907	3.953876	-1.015081
14	1	0	-0.856175	2.797765	-2.102206
15	1	0	-1.548579	3.124320	-0.504094
16	8	0	-3.634804	-0.966587	0.664379
17	1	0	-3.812116	-1.469084	1.486575
18	8	0	1.668544	-2.637571	-1.081212
19	1	0	2.633843	-2.744202	-0.974059
20	1	0	1.285816	-3.275273	-1.711258
21	1	0	-4.454472	-0.649330	0.234575

Copper-Triazolyl

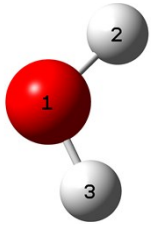


E(Hartree) = -592.79161005

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms)		
			X	Y	Z
1	6	0	-1.395398	1.098493	-0.001128
2	6	0	-0.471649	0.023276	0.000336
3	7	0	-1.305206	-1.082751	0.001274
4	7	0	-2.659573	-0.739149	0.000037
5	7	0	-2.696583	0.608640	-0.001486
6	6	0	-0.940256	-2.502068	0.000496
7	1	0	-0.361768	-2.749002	-0.895572
8	1	0	-0.344316	-2.744773	0.886101
9	1	0	-1.859093	-3.093136	0.010740
10	6	0	-1.124980	2.579180	0.000269
11	1	0	-0.588928	2.893127	0.905892
12	1	0	-0.513309	2.879435	-0.860532
13	1	0	-2.068283	3.135642	-0.043278
14	29	0	1.424713	0.017351	0.000160
15	8	0	3.355004	0.045967	-0.000618
16	1	0	3.901213	0.068042	0.806263
17	1	0	3.901014	0.039278	-0.807912

Water

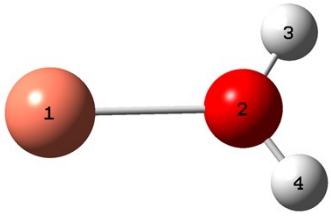


E(Hartree) = -76.40801899

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	8	0	-0.791897	0.432781	0.000000
2	1	0	0.168103	0.432781	0.000000
3	1	0	-1.112351	1.337717	0.000000

Copper-Water



E(Hartree) = - 272.54997945

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	29	0	0	0	0.556252
2	8	0	0	0	-1.50408
3	1	0	0	0.81386	-2.04933
4	1	0	0	-0.81386	-2.04933