Supporting Information

Theoretical study of C-arylations with Aryl Halides to determine the reaction mechanism, the effect of substituents and heteroatoms

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Content

1. Computational Details

All the calculations were performed considering non-catalyzed (Figure 3a) and catalyzed (Figure 3b) reactions using CuI and *N,N*-dimethyl-ethylenediamine (DMEN), on four different substituted lactams. The calculations were performed using DFT/wB97XD/6-311G(d,p)[1] as a basis set for light atoms and LanL2DZ[2-4] to treat iodine atoms at *Gaussian 09*[5]. All stationary states were confirmed by vibrational frequencies. Intrinsic Reaction Coordinate (IRC)[6] calculations were also performed on the complete set of reactions.

Chemical potential (μ), hardness (η)[7] and electrophilicity index (ω)[8], were calculated using HOMO and LUMO energies. The dual index was extracted from the densities of the HOMO and LUMO cubes from the density. Electrostatic potential, population analysis via NBO[9] using the routines available in *Gaussian 09*[5], and non-covalent interactions (NCI) using NCIplot[10] calculations, were also performed.

2. Cartesian Coordinates of the systems studied in this paper

Cartesian coordinates of ωB97XD/6-311G(d,p). Optimized geometries are given below in standard XYZ format. The first line indicates represents the total number of atoms.

Reactants Non-catalyzed

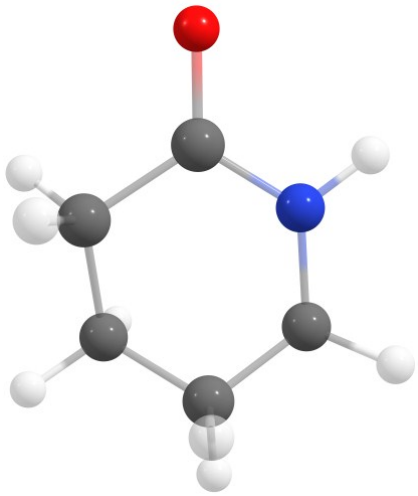

Figure S1: Computed structure C.

16

C	1.158815888	1.372556993	0.878529173
C	2.455762273	0.887890075	0.246601882
C	2.958148458	3.290953179	-0.353106958
C	1.517610663	3.665773891	-0.044337558
C	0.553120863	2.483319475	0.026470995
H	0.472020058	0.528197239	0.976625416
H	4.285845450	1.804945040	-0.323851929
H	1.542179775	4.188081821	0.918973243
H	-0.408427966	2.806873506	0.432496602
N	3.329815438	2.006944003	-0.073498177
O	3.753982251	4.104789142	-0.776371436
H	2.985742115	0.218283136	0.929215114
H	2.225075823	0.314087034	-0.661734869

H	1.360988448	1.751335437	1.886617018
H	0.359244366	2.100207032	-0.982257534
H	1.217342379	4.402832739	-0.790172808

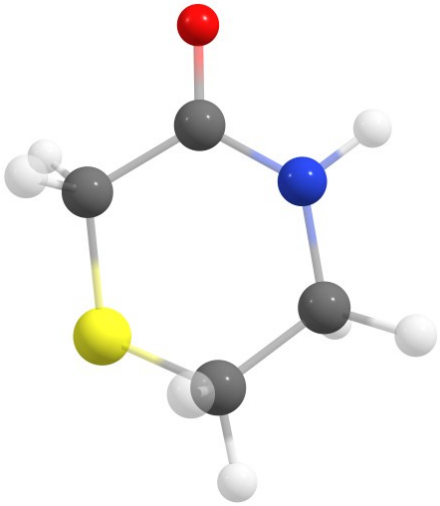

Figure S2: Computed structure S.

14

C	1.173987268	1.285984817	0.924646325
C	2.465959381	0.872862611	0.245770684
C	2.974992557	3.294794715	-0.358644469
C	1.553454410	3.753067960	-0.066373693
H	0.530477199	0.415685664	1.057515969
H	4.280608839	1.808893422	-0.296953846
H	1.563220667	4.247490535	0.909575732
N	3.322729151	2.011920232	-0.053595440
O	3.789808768	4.090385446	-0.776759567
H	3.021979644	0.202532839	0.908737960
H	2.229676898	0.321269049	-0.671671363
H	1.369421522	1.724835796	1.906897858
H	1.301560091	4.501820349	-0.815370493
S	0.262836887	2.476440938	-0.095828445

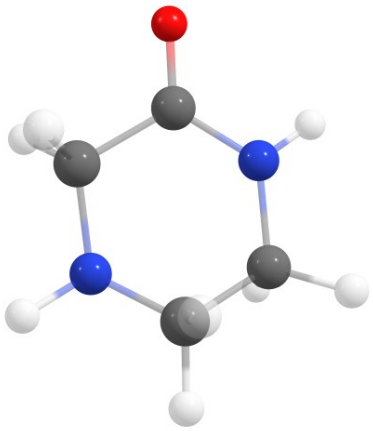

Figure S3: Computed structure NH

15			
C	1.158607276	1.395503050	0.790951651
C	2.469583039	0.880509084	0.223794086
C	2.961888694	3.274587875	-0.335310574
C	1.490113920	3.589955105	-0.112029908
H	0.447179490	0.570018985	0.859314599
H	4.324939647	1.816766643	-0.253079912
H	1.448153027	4.149855560	0.839233836
N	3.353745823	2.001355029	-0.054212146
O	3.743195359	4.135594111	-0.683229462
H	2.956697063	0.214942577	0.941599666
H	2.265174531	0.314446467	-0.692250738
H	1.329685163	1.786869906	1.809933096
H	1.193740793	4.272053895	-0.909232635
N	0.648335879	2.403153038	-0.122325296
H	-0.303577456	2.652318230	0.110294930

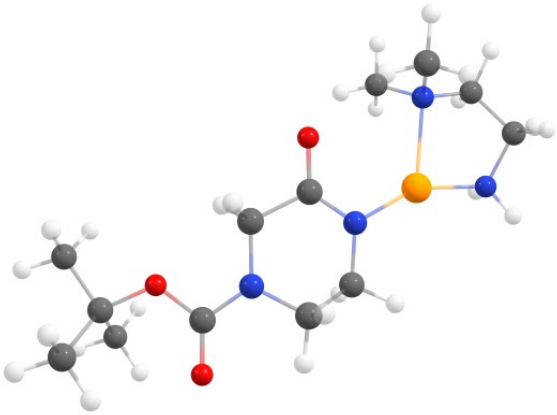

Figure S4: Computed structure N-Boc.

48

Cu	-0.252371746	0.461843958	2.256181344
N	1.837098961	-0.070468416	1.538599970
N	-0.752288474	-0.949573447	0.927685739
C	-1.979000862	2.132842367	3.827043547
C	0.402745242	2.439303279	4.090045089
C	-2.157669268	2.741485290	5.203768954
H	-2.350976410	2.844766825	3.075430943
C	0.143554600	3.589176611	5.066557013
N	-1.257870593	3.867092665	5.330911180
H	-3.174277179	3.100299030	5.354464277
H	0.682492694	3.342493318	5.989196565
N	-0.599989537	1.759324003	3.543820930
O	1.603890119	2.208817535	3.879910005
C	1.653172957	-1.088863260	0.518083881
H	1.552849841	-0.592989479	-0.453669396
H	2.513112096	-1.772223010	0.443264913
C	0.381998532	-1.886769469	0.789947172
H	0.471534291	-2.434326949	1.729967620
H	0.218680606	-2.616471811	-0.010392379
H	0.621838657	4.471734030	4.645640343
H	-1.930171550	1.991835024	5.974742300
H	-2.604708227	1.237810711	3.751771417
H	-1.587816577	-1.460923301	1.189131051
H	-0.950532639	-0.539509170	0.019165430
C	2.494847898	-0.585526551	2.736193772
H	1.946097880	-1.446575481	3.127213197
H	3.531963094	-0.898369473	2.529175938
H	2.480637102	0.198891354	3.493934338
C	2.510700662	1.127523277	1.051053138
H	3.540625498	0.921024667	0.716067085
H	1.945745273	1.546641358	0.213934908
H	2.521247667	1.858332590	1.860720719
C	-1.711700675	5.040451112	5.842093492
O	-2.870519833	5.260011145	6.134018143
O	-0.701106620	5.922049952	5.971703553
C	-0.939791388	7.269993419	6.462226521
C	-1.882844493	8.018785788	5.523355165
H	-1.499140932	7.983008749	4.500253720
H	-2.879997139	7.581945524	5.544577607
H	-1.945120585	9.066639398	5.829537651
C	0.452946764	7.889554671	6.426979823
H	1.137417707	7.324109783	7.063149251
H	0.846222828	7.886691134	5.407893611
H	0.413534878	8.921493487	6.784312476
C	-1.470841470	7.227144032	7.893214937

H	-2.462679467	6.779044675	7.924902547
H	-0.795739149	6.644567136	8.525642076
H	-1.523705684	8.243520274	8.293012423

Reactants Catalyzed

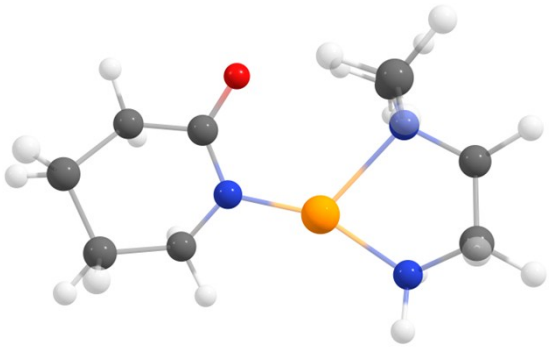

Figure S5: Computed structure C.

34

Cu	-0.318375523	0.548779784	1.906666592
N	1.821080538	-0.297683346	1.845415929
N	-0.748564955	-1.331188694	1.410502986
C	-1.987277517	2.886383096	2.301002641
C	0.343168050	3.171012356	2.645706367
C	-2.324722445	3.576432864	3.623827778
H	-2.111350563	3.604878311	1.473862691
C	-0.085489169	4.596670418	2.974920118
C	-1.253908394	4.631830357	3.973935610
H	-3.320698444	4.027500900	3.569943220
H	0.785842016	5.129538879	3.354047316
N	-0.642944219	2.325930630	2.324027963
O	1.543954297	2.865534545	2.696214817
C	1.670502379	-1.688406816	1.458672880
H	1.718389814	-1.753342945	0.365948371
H	2.474713254	-2.328795850	1.854065368
C	0.317015572	-2.221223196	1.918147537
H	0.257486013	-2.215491021	3.007980381
H	0.184923469	-3.254284678	1.578631383

H	-0.388844406	5.085135151	2.040698849
H	-2.358364116	2.807493177	4.401368648
H	-2.700330006	2.080562464	2.111725083
H	-1.645826542	-1.635851229	1.771422751
H	-0.805880090	-1.433765274	0.400936555
C	2.290036315	-0.138722882	3.217551204
H	1.627819964	-0.670158826	3.906666270
H	3.313730889	-0.529004865	3.348019029
H	2.255892222	0.923159411	3.465039471
C	2.628654985	0.486737944	0.920568093
H	3.673412120	0.136358416	0.873753782
H	2.192800705	0.428500979	-0.080737846
H	2.597068204	1.526031942	1.250761054
H	-1.686902799	5.635990331	3.991623000
H	-0.862820975	4.445721841	4.977686293

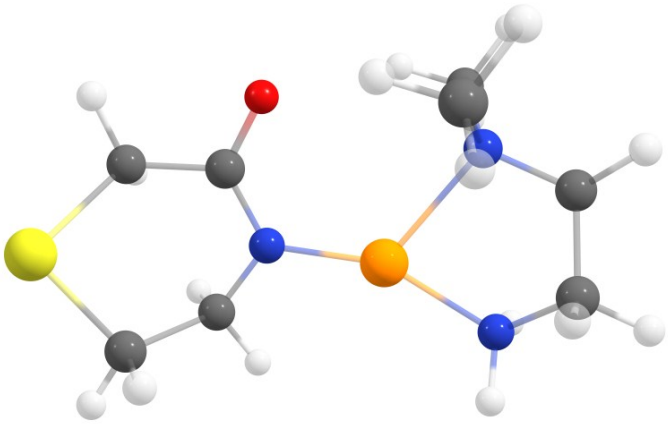

Figure S6: Computed structure S.

32

Cu	-0.281231611	0.591179280	1.859732465
N	1.813514838	-0.288826416	1.842469665
N	-0.771104826	-1.300188300	1.434662706
C	-1.964317278	2.919871242	2.233661925
C	0.375821926	3.208887043	2.573214534
C	-2.391718216	3.356735314	3.632702615
H	-2.088858329	3.766178638	1.541374224
C	-0.014399965	4.633176182	2.961262143
S	-1.320597444	4.706896616	4.244017545
H	-3.422872718	3.716744101	3.630135031
H	0.864190105	5.116460782	3.381558813

N	-0.613377959	2.385341313	2.212920183
O	1.573538972	2.901633450	2.604353541
C	1.642031003	-1.688794174	1.492768670
H	1.687546099	-1.782857875	0.402220096
H	2.438416272	-2.327911949	1.904481545
C	0.282079118	-2.189609031	1.968132503
H	0.223717976	-2.150762743	3.057371140
H	0.136253129	-3.230432484	1.659867943
H	-0.338308348	5.192996572	2.079983428
H	-2.308404534	2.506618594	4.313501999
H	-2.647966002	2.139971332	1.890374463
H	-1.670408641	-1.571038403	1.816565227
H	-0.841348963	-1.441832020	0.430744299
C	2.290208298	-0.105307524	3.210272329
H	1.621348570	-0.607847718	3.914050135
H	3.306814304	-0.510735217	3.345692914
H	2.278641605	0.961790451	3.434692743
C	2.642346054	0.451261785	0.898249635
H	3.678912626	0.076913461	0.868114060
H	2.210106383	0.372618545	-0.103020343
H	2.632518381	1.500234535	1.196346319

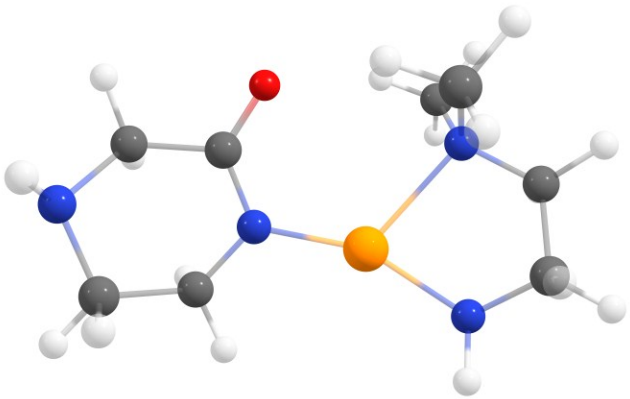

Figure S7: Computed structure NH.

33

Cu	-0.334275990	0.545192089	1.931402654
N	1.813164607	-0.280055777	1.852091494
N	-0.751513933	-1.337933338	1.440832939
C	-1.990009897	2.908932625	2.279912938
C	0.322037374	3.180282880	2.646457196
C	-2.330561619	3.669564197	3.559784525

H	-2.088181818	3.591532694	1.420803130
C	-0.137346198	4.601733448	2.974601050
N	-1.291716278	4.656358320	3.878824393
H	-3.303684025	4.164355318	3.444097959
H	0.700266662	5.131247080	3.426945678
N	-0.659528242	2.322911595	2.345446354
O	1.527743100	2.896495351	2.696627310
C	1.671215742	-1.673567252	1.471188086
H	1.711137429	-1.741815290	0.378385406
H	2.484030441	-2.305495917	1.862321411
C	0.326204605	-2.216714685	1.943099165
H	0.275073788	-2.208181866	3.033351107
H	0.200583774	-3.251871810	1.607764093
H	-0.382602202	5.125278235	2.041845148
H	-2.426511292	2.937871164	4.371737527
H	-2.726532688	2.117117844	2.125763288
H	-1.643409430	-1.651322794	1.807644389
H	-0.814059101	-1.442875235	0.431789503
C	2.293974056	-0.112799870	3.219119992
H	1.642424420	-0.646798905	3.916400915
H	3.321770319	-0.494630631	3.341412744
H	2.254839948	0.949643563	3.463298399
C	2.606099874	0.507397491	0.916921109
H	3.652510883	0.163781362	0.860337996
H	2.160506478	0.443740189	-0.079728116
H	2.571817348	1.547416137	1.244545370
H	-0.956322070	4.488227585	4.816475481

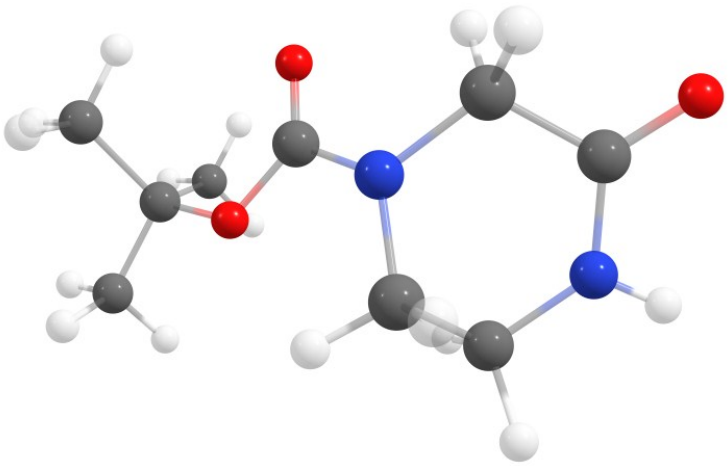

Figure S8: Computed structure N-Boc

30

C	1.303900589	1.099732867	-0.457181128
C	2.600103729	1.624796568	-1.053110965
C	2.624466483	3.230388515	0.881752434
C	1.131286135	2.995288764	1.073911066
H	0.739182860	0.538623259	-1.195555183
H	4.217278843	2.742371519	-0.222391676
H	1.007698059	2.502905600	2.046193275
N	3.241365297	2.519107595	-0.103069648
O	3.224951097	3.992323980	1.608916239
H	3.276630224	0.793922219	-1.271158313
H	2.381076282	2.143505505	-1.994343420
H	1.523169723	0.441793613	0.392059595
H	0.643273124	3.966082181	1.133269624
N	0.515854221	2.219577587	0.016211199
C	-0.602570593	2.704494700	-0.603294513
O	-0.948427503	1.926676011	-1.642769914
C	-2.140451862	2.217938603	-2.435281950
C	-2.140301311	1.090580186	-3.461032202
H	-2.996995673	1.195357869	-4.130625153
H	-1.226585920	1.117133967	-4.059309914
H	-2.204244158	0.119975987	-2.963841173
C	-1.996065611	3.571823603	-3.124290191
H	-1.993299713	4.382011339	-2.397101568
H	-1.066930202	3.604625962	-3.699453631
H	-2.830503482	3.717216995	-3.815295262
C	-3.387155248	2.146826003	-1.558362216
H	-4.276959818	2.232110245	-2.187512314
H	-3.427277086	1.186360220	-1.037947545
H	-3.395344256	2.950459217	-0.823868624
O	-1.189992435	3.699568002	-0.242948751

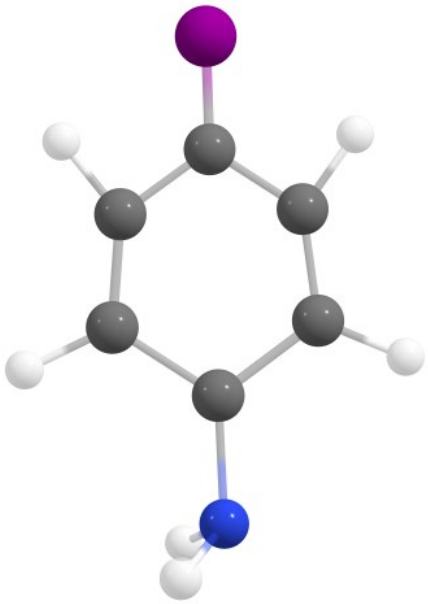

Figure S9: Computed structure 4-iodoaniline.

14

C	7.575460000	0.642641000	-0.666648000
C	8.760471000	0.926905000	-0.283378000
C	9.447393000	2.024685000	-0.412205000
C	8.853360000	3.143278000	-1.078509000
C	7.527236000	2.828443000	-1.508547000
C	7.045426000	1.642563000	-1.261953000
H	8.901964000	-0.056838000	0.145461000
H	6.919147000	3.562860000	-2.035954000
I	6.971580000	-0.537911000	-0.472389000
H	6.123540000	1.105498000	-1.441578000
N	9.486497000	4.416653000	-1.295108000
H	10.343376000	4.311692000	-1.830222000
H	9.756059000	4.844401000	-0.414121000
H	10.461108000	2.076375000	-0.012411000

Transition states Non-Catalyzed

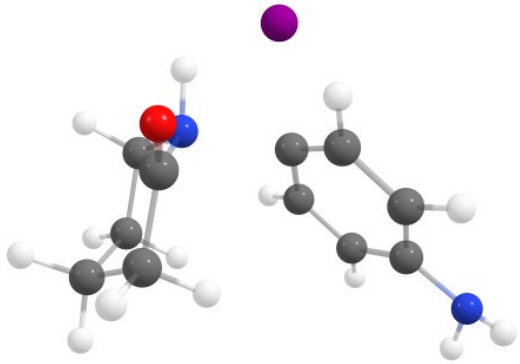

Figure S10: Computed structure TS-C.

30

C	2.310419826	-1.809324278	-0.196560127
C	2.162398848	-1.430513353	1.271856737
C	1.806166011	0.948302971	0.598448609
C	1.972624763	0.581060369	-0.847422605
H	1.342131936	-2.103417064	-0.607118358
H	2.351274067	1.456885473	-1.372725266
N	1.454136630	-0.144410334	1.455516004
C	-0.497204121	-0.341357012	1.317768251
C	-0.899587665	-1.429878996	0.571253587
C	-1.935334441	-1.262636639	-0.342444708
C	-2.547162752	-0.021627664	-0.530646155
C	-2.092806853	1.055481283	0.235795603
C	-1.059076010	0.909821318	1.151285315
H	-0.482910221	-2.413535400	0.739005797
H	-2.561260061	2.028693802	0.130468796
O	1.860031524	2.057794238	1.051562370
H	1.604901810	-2.176232176	1.843802589
H	-0.723723412	1.755880683	1.736019407
N	-3.631308593	0.121927968	-1.399728414
H	-3.661267121	-0.547872176	-2.152027841
H	-3.781471570	1.060689826	-1.734075570
H	-2.289448463	-2.128209198	-0.893226198
I	-0.334795188	-1.030353624	3.910936175
H	1.479893777	0.155529570	2.430280235
C	2.868089243	-0.650504537	-1.016901192
H	3.886404624	-0.411132982	-0.690889461
H	0.964136378	0.360773893	-1.223216527
H	2.927169115	-0.921215245	-2.073039877
H	2.966744096	-2.680632997	-0.256256536
H	3.147997480	-1.336481503	1.739329718

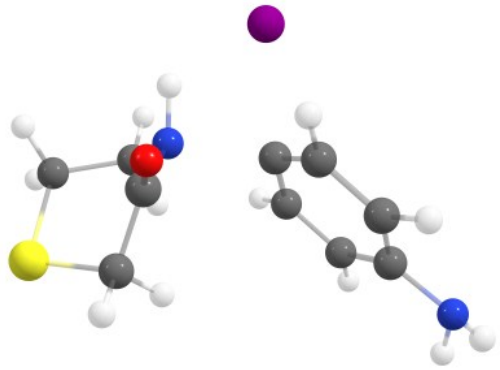

Figure S11: Computed structure TS-S.

28
symmetry c1

C	3.377388943	-1.542753250	0.576446578
C	1.918575821	-1.610389934	0.995671098
C	1.755995938	0.773254492	0.355044519
H	3.770730303	-2.553712712	0.467387190
N	1.364792423	-0.269974550	1.251021383
C	-0.597563941	-0.315907654	1.218139457
C	-1.109627191	-1.349355068	0.463837857
C	-2.201294275	-1.082064766	-0.358982324
C	-2.749048313	0.198153968	-0.449377007
C	-2.173577098	1.215551426	0.319905599
C	-1.085274385	0.973836260	1.144817573
H	-0.751769203	-2.364316455	0.565194921
H	-2.586960231	2.218154439	0.285391303
O	1.798194485	1.909255120	0.730666635
H	1.329512895	-2.084428417	0.208007706
H	-0.652371448	1.772923159	1.730488436
N	-3.881263307	0.443137405	-1.225889845
H	-4.019386438	-0.196135851	-1.992234759
H	-4.001239564	1.401674627	-1.512188527
H	-2.646649202	-1.901339687	-0.913882293
I	-0.315125057	-1.067655709	3.823791742
H	1.467309423	0.019567421	2.224881716
H	3.970991385	-1.017909121	1.327402690
H	1.784477850	-2.183291570	1.914024558
C	2.037679761	0.291046638	-1.036997396
H	1.187900142	-0.291320648	-1.403189106
H	2.207462317	1.151285939	-1.679499477
S	3.569284161	-0.720876137	-1.051189613

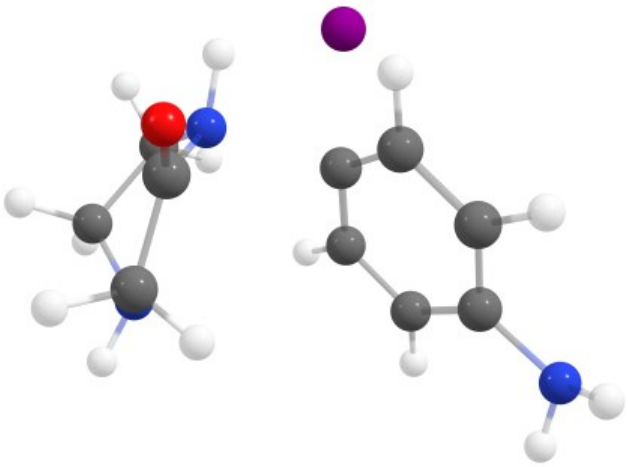

Figure S12: Computed structure TS-NH.

29

C	2.929029000	-1.590015000	0.106436000
C	2.160480000	-1.436609000	1.412440000
C	1.716593000	0.822233000	0.444803000
H	3.179542000	-2.643183000	-0.027414000
N	1.410174000	-0.158325000	1.430824000
C	-0.540907000	-0.372925000	1.239680000
C	-0.872955000	-1.351039000	0.330889000
C	-1.929764000	-1.102535000	-0.537419000
C	-2.613059000	0.115861000	-0.524313000
C	-2.200444000	1.093116000	0.385684000
C	-1.147654000	0.865287000	1.262287000
H	-0.359401000	-2.300761000	0.298425000
H	-2.716299000	2.046768000	0.427298000
O	1.718901000	1.987860000	0.724699000
H	1.438740000	-2.243004000	1.547590000
H	-0.844384000	1.630661000	1.963576000
N	-3.717266000	0.328589000	-1.352360000
H	-3.730084000	-0.229601000	-2.191244000
H	-3.917783000	1.296688000	-1.547618000
H	-2.230599000	-1.883499000	-1.228258000
I	-0.368624000	-1.319340000	3.792652000
H	1.388981000	0.259802000	2.358324000
H	3.876841000	-1.025245000	0.151728000
H	2.828105000	-1.455710000	2.274749000
C	1.910320000	0.293122000	-0.956595000
H	1.012117000	0.585563000	-1.511354000
H	2.763531000	0.848022000	-1.374993000
N	2.062396000	-1.149898000	-0.971837000
H	2.386494000	-1.466696000	-1.874102000

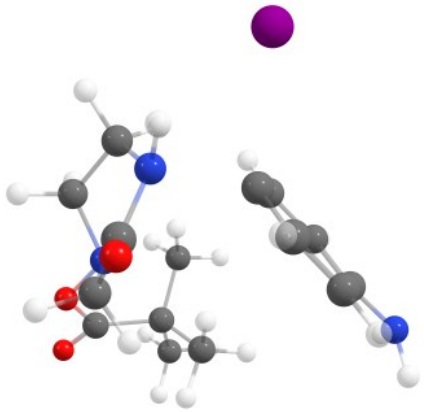

Figure S13: Computed structure TS-N-Boc.

44

C	3.304356000	-1.516451000	-0.181796000
C	2.467700000	-1.491305000	1.093000000
C	1.922062000	0.815804000	0.320028000
H	3.559947000	-2.547859000	-0.423548000
N	1.632018000	-0.276751000	1.181338000
C	-0.291183000	-0.683438000	0.929028000
C	-0.572581000	-1.871681000	0.297007000
C	-1.636491000	-1.895873000	-0.595889000
C	-2.370745000	-0.744132000	-0.886523000
C	-2.022431000	0.441437000	-0.233448000
C	-0.969528000	0.486304000	0.673216000
H	-0.057029000	-2.791227000	0.533021000
H	-2.586120000	1.349166000	-0.421251000
O	1.749997000	1.943373000	0.685883000
H	1.807984000	-2.355840000	1.147954000
H	-0.717382000	1.409512000	1.177118000
N	-3.455549000	-0.790933000	-1.758693000
H	-3.438725000	-1.542620000	-2.428821000
H	-3.709686000	0.088242000	-2.179263000
H	-1.898803000	-2.838355000	-1.065106000
I	-0.106735000	-1.220598000	3.648881000
H	1.517840000	0.040004000	2.146349000
H	4.241330000	-0.952740000	-0.061029000
H	3.114486000	-1.527506000	1.969753000
C	2.359110000	0.468137000	-1.081222000
H	1.605752000	0.863959000	-1.766412000
H	3.303821000	0.994580000	-1.272988000
N	2.507390000	-0.967955000	-1.273330000
O	3.297229000	-1.105273000	-2.448090000

C	2.783511000	-1.775267000	-3.540436000
C	1.360408000	-2.348136000	-3.540707000
C	1.141121000	-2.977715000	-4.923128000
H	1.872266000	-3.761945000	-5.124396000
H	0.139650000	-3.415108000	-4.961393000
H	1.226537000	-2.233100000	-5.716342000
C	0.320422000	-1.233264000	-3.334936000
H	0.494533000	-0.401439000	-4.024023000
H	-0.675251000	-1.633112000	-3.546606000
H	0.310124000	-0.865413000	-2.311675000
C	1.218895000	-3.443145000	-2.470140000
H	1.302688000	-3.034380000	-1.465579000
H	0.234175000	-3.909215000	-2.565764000
H	1.971277000	-4.224754000	-2.608515000
O	3.535395000	-1.856126000	-4.463523000

Transition states Catalyzed

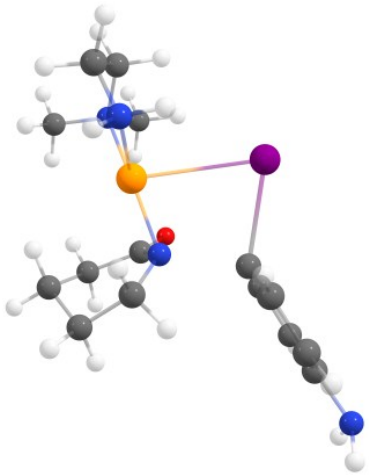

Figure S14: Computed structure TS-C

48

Cu	-0.512245000	-0.337307000	0.501439000
N	1.055852000	-1.275094000	1.384321000
N	-1.652953000	-2.087127000	0.992166000
C	-2.499157000	1.633830000	0.033882000
C	-0.023759000	1.786177000	-0.067431000
C	-2.462784000	2.752161000	1.072649000
H	-3.087610000	1.970800000	-0.827074000
C	-0.023067000	2.645846000	1.202284000
C	-1.296565000	2.555839000	2.028847000
H	-2.340194000	3.718235000	0.570003000
H	0.871799000	2.372226000	1.766643000

N	-1.199849000	1.178263000	-0.472808000
O	1.031561000	1.708041000	-0.698046000
C	0.697029000	-2.700110000	1.345239000
H	0.809581000	-3.027960000	0.309239000
H	1.378748000	-3.298074000	1.968073000
C	-0.748214000	-2.939021000	1.778320000
H	-0.877732000	-2.688428000	2.833928000
H	-0.971275000	-4.005794000	1.670496000
H	0.129558000	3.677028000	0.865325000
H	-3.422384000	2.782358000	1.596363000
H	-3.035998000	0.771623000	0.447492000
H	-2.552800000	-2.004404000	1.447995000
H	-1.817378000	-2.488070000	0.072257000
C	1.239906000	-0.794304000	2.754811000
H	0.320174000	-0.907762000	3.330713000
H	2.049649000	-1.335430000	3.267119000
H	1.487872000	0.267243000	2.728621000
C	2.268896000	-1.014744000	0.592839000
H	3.144955000	-1.510240000	1.035656000
H	2.116717000	-1.370016000	-0.426407000
H	2.432039000	0.061757000	0.528649000
C	-2.434700000	2.767498000	-4.410080000
C	-1.079940000	2.779160000	-4.066239000
C	-3.250974000	1.815502000	-3.805715000
H	-0.414442000	3.501474000	-4.530233000
H	-4.300494000	1.750596000	-4.077481000
C	-0.548951000	1.882517000	-3.150365000
C	-2.741415000	0.912484000	-2.874407000
H	0.496085000	1.906714000	-2.879513000
H	-3.388484000	0.159546000	-2.443775000
C	-1.396533000	0.965475000	-2.553155000
N	-2.937887000	3.637446000	-5.394952000
H	-2.405012000	4.489813000	-5.482663000
H	-3.917320000	3.850051000	-5.278604000
I	-0.464852000	-1.366225000	-2.483538000
H	-1.298100000	3.306770000	2.823544000
H	-1.373208000	1.574189000	2.515285000

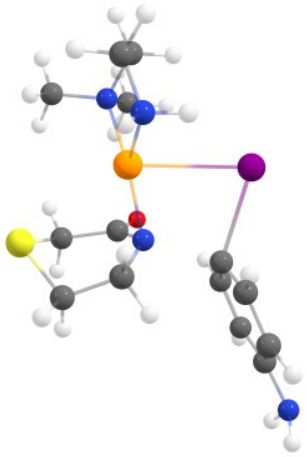

Figure S15: Computed structure TS-S

46

Cu	-0.457200280	-0.254077453	0.510264703
N	1.091102193	-1.244496728	1.370476972
N	-1.668338542	-1.926952157	1.032395581
C	-2.385301249	1.766999957	0.005026993
C	0.108125684	1.785741510	-0.150145221
C	-2.336797116	2.821196143	1.101725193
H	-2.929288475	2.201495399	-0.843187933
C	0.259135497	2.604884856	1.144612279
S	-1.081636704	2.437838797	2.353255772
H	-2.097615249	3.806811434	0.693722824
H	1.193489804	2.292441733	1.609245244
N	-1.114110555	1.253908209	-0.508489309
O	1.125275549	1.704402791	-0.839335210
C	0.654015279	-2.649433638	1.359368684
H	0.725735476	-2.997940878	0.326430984
H	1.315925703	-3.273780573	1.977297901
C	-0.791850649	-2.801935716	1.826485417
H	-0.887143459	-2.513917467	2.875816660
H	-1.072023522	-3.858024229	1.753618969
H	0.365456910	3.657237029	0.866961559
H	-3.307229528	2.888321139	1.595289528
H	-2.982159485	0.917462230	0.352326841
H	-2.548007250	-1.775689984	1.509617313
H	-1.878978503	-2.348858118	0.131667525
C	1.334629251	-0.762829177	2.732514074
H	0.419107299	-0.792527324	3.324048469
H	2.110673708	-1.358464193	3.235787541
H	1.662958984	0.275685268	2.689229428
C	2.299059809	-1.064947136	0.549518087
H	3.156446096	-1.599763637	0.982574236

H	2.106691845	-1.427752979	-0.460243732
H	2.522201869	-0.000726306	0.464132218
C	-2.496525644	2.740674749	-4.440364185
C	-1.130866318	2.758767981	-4.143777096
C	-3.294159702	1.814013222	-3.773835732
H	-0.479582493	3.461470382	-4.655482722
H	-4.352856673	1.744328056	-4.005682742
C	-0.570698581	1.892308108	-3.215748927
C	-2.754890625	0.941477850	-2.830731949
H	0.483607109	1.919940760	-2.984133739
H	-3.389173636	0.207756489	-2.350787652
C	-1.398304588	0.995880763	-2.562968642
N	-3.031035364	3.576572408	-5.436706201
H	-2.498640786	4.421859857	-5.577960913
H	-4.005945987	3.795896084	-5.298153733
I	-0.485683736	-1.355044470	-2.468683692

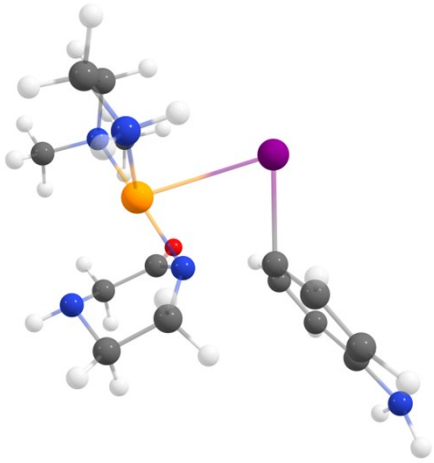

Figure S16: Computed structure TS-NH

47

Cu	-0.516237359	-0.255013734	0.536239172
N	1.036346244	-1.206804332	1.432352699
N	-1.674433103	-1.987465523	0.978692943
C	-2.438379155	1.691677687	-0.040020902
C	0.020883139	1.799250527	-0.142002310
C	-2.343908173	2.592820313	1.192903111
H	-2.948166387	2.238687633	-0.841977122
C	0.002244021	2.549825355	1.195258992
N	-1.177276925	2.206347198	1.977189996
H	-2.276534120	3.647909290	0.876556326
H	0.912927250	2.269899560	1.727175723
N	-1.156020986	1.208924952	-0.553953926
O	1.075295319	1.786256733	-0.776798170

C	0.660391283	-2.627235165	1.374441721
H	0.786128766	-2.948708264	0.337866782
H	1.323922878	-3.238447059	2.004163547
C	-0.794798214	-2.850850765	1.780646115
H	-0.940697668	-2.599389229	2.833746740
H	-1.028069949	-3.914854828	1.666683439
H	0.066778428	3.626793573	0.964150629
H	-3.248571680	2.483971935	1.795607729
H	-3.063070956	0.821235750	0.185136144
H	-2.577656824	-1.885354412	1.423591984
H	-1.832341430	-2.388176194	0.057531174
C	1.198445734	-0.741895650	2.810925897
H	0.257685372	-0.818882494	3.356924654
H	1.973739300	-1.315627178	3.340850472
H	1.484487829	0.309764134	2.799173749
C	2.265031875	-0.956727309	0.663395666
H	3.128941633	-1.464373500	1.116494133
H	2.126076470	-1.304153049	-0.360594699
H	2.444371691	0.117754333	0.607890058
C	-2.475712510	2.749476798	-4.462291936
C	-1.113701252	2.765012500	-4.149008114
C	-3.276412844	1.801586294	-3.831290480
H	-0.459862327	3.485287782	-4.632475630
H	-4.332760686	1.736106446	-4.075489778
C	-0.560960238	1.875565543	-3.239346867
C	-2.744160276	0.903707014	-2.908155824
H	0.488650273	1.908435393	-2.986910046
H	-3.382286325	0.157582474	-2.452944611
C	-1.391359465	0.956976102	-2.617678071
N	-3.002625409	3.612043371	-5.442422373
H	-2.473850510	4.465419352	-5.545073340
H	-3.979295239	3.824330820	-5.303539222
I	-0.448666935	-1.344337060	-2.501317534
H	-1.167180440	2.712012054	2.854127203

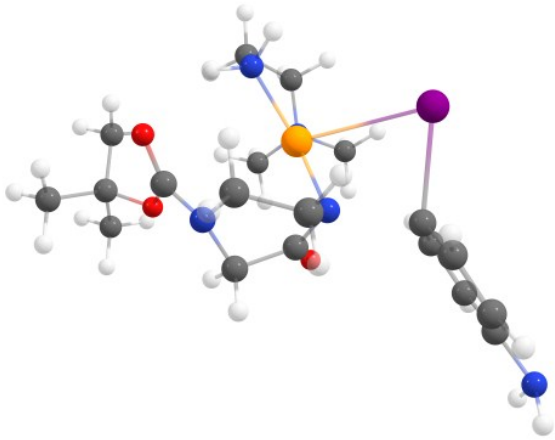

Figure S17: Computed structure TS-N-Boc

62

N	-2.096238000	2.602442000	2.107838000
C	-1.162184000	3.271046000	1.205656000
C	-3.288942000	2.051749000	1.470657000
C	-0.710422000	2.290839000	0.108886000
H	-0.290162000	3.610824000	1.752285000
H	-1.655904000	4.137791000	0.753192000
C	-1.727826000	2.084406000	3.307837000
C	-3.045960000	1.892201000	-0.030908000
H	-3.501700000	1.088354000	1.930183000
H	-4.152940000	2.701168000	1.647457000
N	-1.694679000	1.431304000	-0.330180000
O	0.446751000	2.288707000	-0.279080000
O	-0.506173000	2.492863000	3.683758000
O	-2.434441000	1.332070000	3.960157000
H	-3.744846000	1.144209000	-0.411677000
H	-3.253172000	2.834185000	-0.553265000
Cu	-1.202275000	0.003895000	0.881276000
C	-0.091278000	2.442066000	5.083911000
C	1.266896000	3.131209000	5.050181000
C	0.053016000	1.002882000	5.572739000
C	-1.082913000	3.228423000	5.935943000
H	1.703622000	3.146956000	6.051381000
H	1.166997000	4.159142000	4.695699000
H	1.946740000	2.599000000	4.380792000
H	-0.903202000	0.483571000	5.544793000
H	0.782197000	0.461927000	4.964955000
H	0.421651000	1.010725000	6.601797000
H	-2.054021000	2.734118000	5.963267000
H	-1.206479000	4.237612000	5.535234000
H	-0.702838000	3.309329000	6.957179000
N	0.773144000	-0.798867000	1.139716000

C	1.554041000	0.096179000	1.989385000
C	0.478744000	-2.080204000	1.773032000
C	1.416607000	-0.959817000	-0.161308000
H	0.997586000	0.344023000	2.892928000
H	2.523339000	-0.346497000	2.270470000
H	1.720033000	1.029750000	1.450619000
C	-0.537725000	-1.927916000	2.904630000
H	0.054173000	-2.730744000	1.003120000
H	1.390397000	-2.564746000	2.158925000
H	1.547736000	0.032074000	-0.594654000
H	2.396739000	-1.455677000	-0.079343000
H	0.769439000	-1.540601000	-0.820932000
N	-1.737491000	-1.215754000	2.423689000
H	-0.109650000	-1.350946000	3.726129000
H	-0.780931000	-2.918701000	3.299773000
H	-2.438888000	-1.876740000	2.108883000
H	-2.151843000	-0.666028000	3.174407000
C	-1.661973000	1.001606000	-2.360436000
C	-2.689600000	1.678992000	-2.991794000
C	-0.362671000	1.084357000	-2.828450000
C	-2.396624000	2.488568000	-4.085999000
H	-3.717207000	1.567413000	-2.674210000
C	-0.091617000	1.886990000	-3.926036000
H	0.434979000	0.539289000	-2.350843000
C	-1.095723000	2.614955000	-4.566940000
H	-3.210956000	3.005601000	-4.584832000
H	0.930340000	1.944529000	-4.287983000
N	-0.813202000	3.382501000	-5.710505000
H	0.133470000	3.730941000	-5.733053000
H	-1.465798000	4.137907000	-5.856811000
I	-2.360706000	-1.351865000	-1.754517000

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4. Fukui Functions

We have calculated the Fukui nucleophilic functions for the catalyzed and non-catalyzed systems. It can be seen that the catalyzed systems activate the lactam nitrogen specially at C and NBoc, in agreement with the results of MEP (Figure 4).

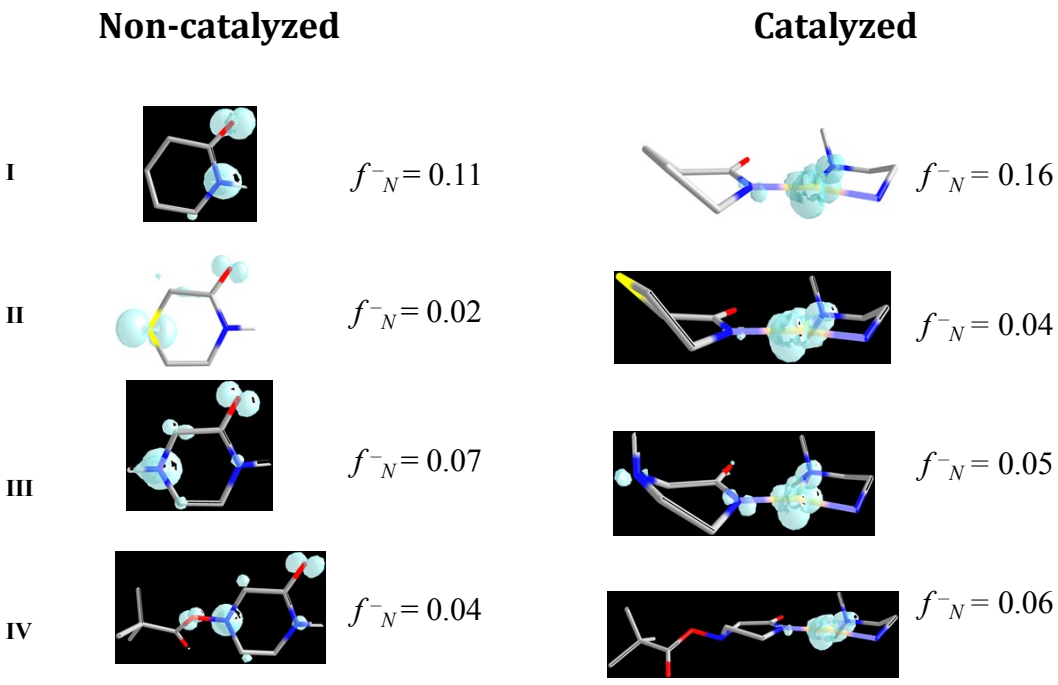
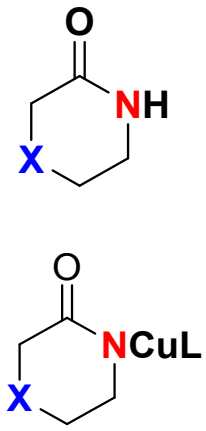


Figure S18. Nucleophilic Fukui functions for the catalyzed and non-catalyzed lactam systems

4. Solvation effects

For the eight lactams and the aryl iodine, we have calculated the effect of the Toluene solvation using a continuum model, SCRF with the SMD method, at wB97XD/6-311G(d,p) level of calculation. When analyzing the geometries and the energies of the systems, they do not differ much from the gas phase calculations (1-2 kcal/mol).

The DFT reactivity indexes are quite different, their values are lower due to the stabilization of the molecular orbitals into the solvent electric field. Specially at the Cu-complex, the changes are almost negligible. All the values and they are listed in Table 1.S.

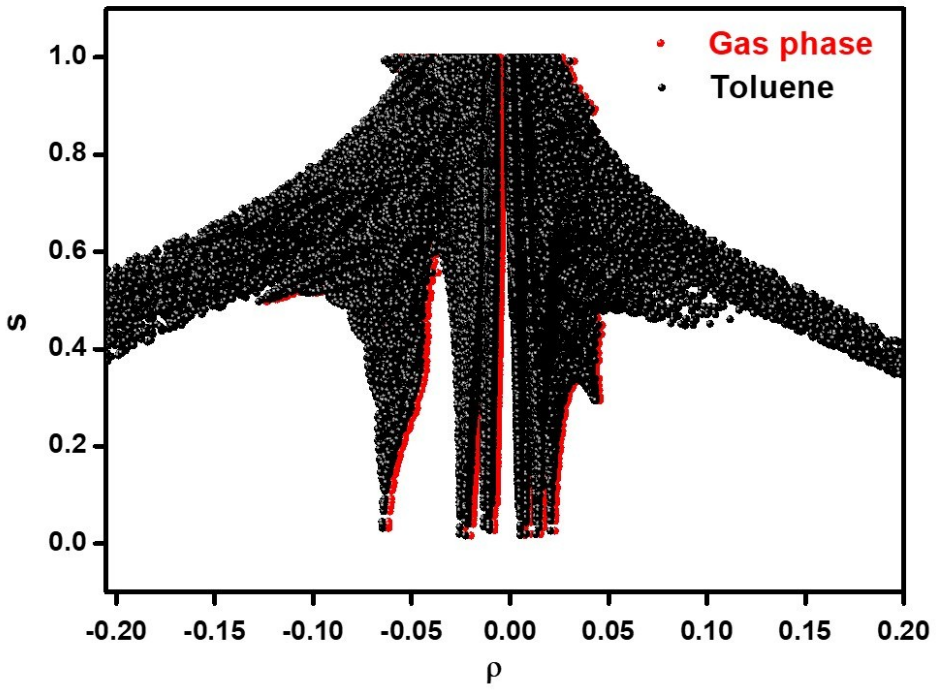


System	μ	η	ω
Non-Catalyzed			
C S N-Boc O	-3.0 -3.1 -3.0 -3.0	11.6 10.3 11.6 11.4	0.4 0.5 0.4 0.4
Catalyzed (Cu Complex)			
C	-2.0	8.8	0.2
S	-2.1	8.8	0.2
N-Boc	-2.1	8.8	0.2
O	-2.0	8.8	0.2

Table 1.S. Chemical potential, hardness and electrophilic indexes using toluene, on the non-catalyzed and catalyzed lactams.

The NCI calculations were performed in gas phase, and the solvent effect was evaluated using the Self-Consistent Reaction Field (SCRF) method by applying the Solvation Model based on Density (SMD)[1] using toluene (DCM $\varepsilon = 2.379$).

The NCI analysis shows that the solvent does not have important effect in the magnitude of the non-covalent interactions, both analyses have similar behavior, which can be seen in the 2D NCI plot. (Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. *J. Phys. Chem. B* 2009, *113* (18), 6378–6396)


Gas phase
Toluene
1.0
0.8
0.6
0.4
0.2
0.0
S
-0.20
-0.15
-0.10
-0.05
0.00
0.05
0.10
0.15
0.20
ρ