Reaction energy profile and fragment attributed molecular system energy change (FAMSEC)-based protocol designed to uncover reaction mechanism: A case study of the proline catalysed aldol reaction

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Electronic Supporting Information

Table of content

Page

PART S1

Computational details and coordinates for all structures

All calculations were performed in Gaussian 09 Rev. D01 at the RB3LYP/6–311++G(d,p) with Grimme's empirical correction for dispersion (GD3) and RMP2/6–311++G(d,p) levels of theory in solvent (DMSO) using the implicit default solvation model. The B3LYP-optimised local, global and transition state (TS) structures were also optimised at the RMP2 level and frequency calculations were performed on these structures at both levels of theory. None and one imaginary frequency was obtained for minimum energy (local and global) and TS structures, respectively. Topological calculations were performed in AIMAll (ver. 17.11.14) using B3LYP-generated wavefunctions.

RB3LYP Coordinates

2

Atom	X	Y	Z
C1	-0.00462863	0.178140532	0.6151523
O2	-0.0134421	0.517341082	1.7864747
C3	-1.28134278	-0.124580786	-0.1338366
H4	-2.13578709	-0.108943756	0.5416987
H5	-1.42267733	0.624186195	-0.9201481
H6	-1.21074387	-1.096426665	-0.6304427
C7	1.28356795	0.038941613	-0.1618913
H8	1.43279417	-1.013549159	-0.4243945
H9	1.22377847	0.594769111	-1.1018739
C10	2.12848123	0.39012183	0.4292614

Zero-point correction = 0.083228 (Hartree/Particle)
Thermal correction to Energy = 0.088510
Thermal correction to Enthalpy = 0.089454
Thermal correction to Gibbs Free Energy = 0.056063
Sum of electronic and zero-point Energies = –193.146706
Sum of electronic and thermal Energies = –193.141424
Sum of electronic and thermal Enthalpies= –193.140480
Sum of electronic and thermal Free Energies= –193.173871

1a

Atom	X	Y	Z
C1	-0.0945820881	-1.3616508300	-0.8365335880
C2	-0.5190690347	-1.2573374716	0.6302290991
C3	-1.0788227389	0.1706950832	0.7151583197
C4	-0.1246813852	0.9722544295	-0.1992426764
H5	0.3281244270	0.2480799094	-2.1025552561
H6	0.6591109463	-2.1308210435	-1.0132112033
H7	-0.9632543973	-1.5761338223	-1.4696052990
H8	-1.2490175462	-2.0185574329	0.9075498900
H9	0.3511233168	-1.3671245973	1.2850414934
H10	-2.0880936170	0.2049830909	0.2983008665
H11	-1.1155132690	0.5735847011	1.7271909176
H12	-0.6469204573	1.7777075250	-0.7198264624
N13	0.4628012476	-0.0166263775	-1.1345153508
C14	1.0098594764	1.6334091005	0.6007483932
O15	0.8307496198	2.4944067393	1.4355402361
O16	2.2188399062	1.1665470996	0.2925674012
H17	2.0193456037	0.4865838968	-0.4168367709

Zero-point correction = 0.144439 (Hartree/Particle)
Thermal correction to Energy = 0.151574
Thermal correction to Enthalpy = 0.152518
Thermal correction to Gibbs Free Energy = 0.112465
Sum of electronic and zero-point Energies = –401.167135
Sum of electronic and thermal Energies = –401.160000
Sum of electronic and thermal Enthalpies = –401.159056
Sum of electronic and thermal Free Energies = –401.199110

1b

Atom	X	Y	Z
C1	-0.4090342829	-1.2417777602	-1.0365123470
C2	-0.6679877535	-1.5447881579	0.4695639391
C3	-0.3162309883	-0.2234293381	1.2092014177
C4	-0.0898466893	0.7677367134	0.0537820277
H5	1.3839410276	-0.3040841776	-0.8583830776
H6	0.0865113893	-2.0562345172	-1.5651403464
H7	-1.3492538419	-1.0266239834	-1.5514139257
H8	-1.7054929740	-1.8402176315	0.6362186313
H9	-0.0336802727	-2.3620827660	0.8174100463
H10	-1.1028450646	0.1090238381	1.8868095774
H11	0.6032172475	-0.3273668019	1.7897031322
H12	-1.0601281261	1.1753315470	-0.2628674836
N13	0.4290475018	-0.0221423670	-1.0821181369
C14	0.7733566709	1.9810686690	0.3373918600
O15	0.9007085432	2.5009165302	1.4196362013
O16	1.3832903879	2.4938242140	-0.7505225570
H17	1.1744272251	1.9208459692	-1.5127589589

Zero-point correction =	0.144477 (Hartree/Particle)
Thermal correction to Energy =	0.151947
Thermal correction to Enthalpy =	0.152891
Thermal correction to Gibbs Free Energy =	0.111845
Sum of electronic and zero-point Energies =	–401.156469
Sum of electronic and thermal Energies =	–401.149000
Sum of electronic and thermal Enthalpies =	–401.148056
Sum of electronic and thermal Free Energies =	–401.189101

3a

Atom	X	Y	Z
C1	-0.6916850048	-1.9375015508	-1.2185793238
C2	-1.6069619830	-2.3973912377	-0.0787230580
C3	-1.6756783939	-1.1474146077	0.8128553526
C4	-1.6270080967	0.0247043311	-0.2081486431
H5	-1.7704851814	-0.4732417091	-2.2069861297
H6	0.3512071852	-1.9667144146	-0.8932061339
H7	-0.7883639362	-2.5209893400	-2.1346306448
H8	-2.5984753746	-2.6468021265	-0.4697230819
H9	-1.2178388612	-3.2685219087	0.4522526545
H10	-2.5713304507	-1.1019025535	1.4316952680
H11	-0.8035236500	-1.1094406505	1.4685078165
H12	-2.6229400284	0.4422444921	-0.3716703728
N13	-1.0753773719	-0.5240601710	-1.4719324254
C14	-0.7413908516	1.1752989962	0.2726118365
O15	-0.9240760916	1.7908845175	1.3008615327
O16	0.2768470597	1.4393638881	-0.5494302064
H17	0.1495733464	0.7766572727	-1.2886132891
C18	2.3804416706	-0.3210758444	1.0129221934
O19	1.7233567346	-1.3294925621	1.2145379515
C20	3.1570755963	-0.1243680716	-0.2663318614
H21	2.8825172843	-0.8796087298	-1.0021978211
H22	2.9830106501	0.8770626844	-0.6662276427
H23	4.2268303159	-0.2050568301	-0.0454639043
C24	2.4480348022	0.7957037052	2.0249368385
H25	3.4689521540	1.1722585878	2.1262586158
H26	1.8279292207	1.6204998632	1.6594133813
H27	2.0658592563	0.4631039696	2.9895110972

Zero-point correction =	0.228970 (Hartree/Particle)
Thermal correction to Energy =	0.243408
Thermal correction to Enthalpy =	0.244352
Thermal correction to Gibbs Free Energy =	0.184586
Sum of electronic and zero-point Energies =	–594.318801
Sum of electronic and thermal Energies =	–594.304363
Sum of electronic and thermal Enthalpies =	–594.303419
Sum of electronic and thermal Free Energies =	–594.363185

3b

Atom	X	Y	Z
C1	-2.2641727131	0.5704324091	-2.2935412506
C2	-2.0183714657	1.5842351092	-1.1681108589
C3	-0.8059885576	0.9801408678	-0.4439682103
C4	-0.9740779599	-0.5687808272	-0.6636731390
H5	-2.8582022975	-1.0642012062	-1.2137865744
H6	-3.2712514758	0.6079634282	-2.7124366242
H7	-1.5537592881	0.7355269124	-3.1115116773
H8	-1.8282619419	2.5974992927	-1.5286952714
H9	-2.8862263879	1.6138216175	-0.5022746603
H10	0.1252672965	1.3075405241	-0.9106044184
H11	-0.7610090224	1.2544835081	0.6109148953
H12	-0.0230654376	-0.9870289409	-1.0036226683
N13	-2.0144019294	-0.7549819190	-1.6896299842
C14	-1.3453822750	-1.2676302056	0.6389173393
O15	-2.4684636724	-1.6472373097	0.9006609884
O16	-0.3565017639	-1.4231858963	1.5223523830
H17	0.5146478782	-1.0923819410	1.1767835190
C18	2.5928144812	0.4425407195	0.8724470209
O19	1.9985879889	-0.5861617150	0.5635727742
C20	2.0666762043	1.3731017646	1.9301715900
H21	1.7603282723	2.3101156938	1.4538636000
H22	1.2171640502	0.9375330099	2.4539337205
H23	2.8588761693	1.6234335351	2.6401492003
C24	3.8783079403	0.8204182318	0.1938785126
H25	3.8232290415	1.8504326052	-0.1691391111
H26	4.6912234572	0.7862626391	0.9265267231
H27	4.0954134082	0.1396080928	-0.6274778183

Zero-point correction = 0.228937 (Hartree/Particle)
Thermal correction to Energy = 0.243389
Thermal correction to Enthalpy = 0.244334
Thermal correction to Gibbs Free Energy = 0.183671
Sum of electronic and zero-point Energies = –594.317076
Sum of electronic and thermal Energies = –594.302624
Sum of electronic and thermal Enthalpies = –594.301680
Sum of electronic and thermal Free Energies = –594.362342

4a

Atom	X	Y	Z
C1	-0.2142578068	-1.3418801271	-0.6664473997
C2	-1.5993364941	-1.9535653225	-0.9065553140
C3	-2.4317407846	-1.3178920232	0.2147961561
C4	-1.8537336948	0.1227623131	0.3059517752
H5	-0.3465398083	0.7035998494	-0.9764160675
H6	0.3093019067	-1.8825469812	0.1290069959
H7	0.4270260249	-1.3405016675	-1.5488502351
H8	-1.9812426733	-1.6456154512	-1.8848729234
H9	-1.5982367073	-3.0445856784	-0.8650357576
H10	-3.5037840457	-1.3096521626	0.0208739079
H11	-2.2644169649	-1.8526202978	1.1544787088
H12	-2.4658115594	0.8145605046	-0.2778743371
N13	-0.4747751384	0.0473074059	-0.2171946258
C14	-1.8626370569	0.6309580569	1.7456262804
O15	-2.8816372374	0.8780779951	2.3574583669
O16	-0.6586507062	0.7624525769	2.3025529247
H17	0.0073932101	0.5297890487	1.6066048547
C18	2.7366003409	-0.0651676578	0.6869122870
O19	2.1165168599	-0.1564435759	1.7337352907
C20	3.5475739128	-1.2165586342	0.1448892824
H21	3.5698117180	-2.0404322372	0.8570093945
H22	3.1006535318	-1.5566501065	-0.7950054992
H23	4.5651123049	-0.8903302141	-0.0880145211
C24	2.7316702357	1.2037349710	-0.1295742178
H25	3.7288412825	1.6549083488	-0.0870051502
H26	2.5269593588	0.9845679163	-1.1807225829
H27	1.9962399911	1.9063231507	0.2584724064

Zero-point correction = 0.228542 (Hartree/Particle)
Thermal correction to Energy = 0.243192
Thermal correction to Enthalpy = 0.244136
Thermal correction to Gibbs Free Energy = 0.183038
Sum of electronic and zero-point Energies = –594.318198
Sum of electronic and thermal Energies = –594.303549
Sum of electronic and thermal Enthalpies = –594.302604
Sum of electronic and thermal Free Energies = –594.363702

4b

Atom	X	Y	Z
C1	-0.1705743733	2.2625588835	-0.2296233115
C2	-1.6761737669	2.5380035918	0.0194944711
C3	-2.2901023528	1.1345282590	0.2746682983
C4	-1.0790489148	0.1804647631	0.2294733497
H5	-0.3068646154	0.7383195994	-1.5847054566
H6	0.2691896879	2.8933345220	-1.0034665566
H7	0.3989802266	2.4155604209	0.6925745741
H8	-1.8230059502	3.2141048018	0.8641064264
H9	-2.1328889599	3.0030084112	-0.8568177672
H10	-2.8138662671	1.0674281728	1.2299900201
H11	-2.9954616580	0.8632950354	-0.5118461906
H12	-0.6485011465	0.0793254136	1.2320526387
N13	-0.0488869504	0.8401142533	-0.6048232405
C14	-1.3742978437	-1.2264964519	-0.2913608127
O15	-2.3747288993	-1.5187670048	-0.9110364716
O16	-0.4444313465	-2.1536309177	-0.0417117532
H17	0.3372161545	-1.7845212918	0.4494772794
C18	2.3797330493	-0.3848354803	0.4472006969
O19	1.6399069737	-1.0241979952	1.1921448964
C20	2.6822270222	-0.8422165771	-0.9536016125
H21	1.9475290966	-1.5684235454	-1.2967404908
H22	2.7247829471	0.0044841248	-1.6392909278
H23	3.6721920945	-1.3134559482	-0.9451927161
C24	3.0858460230	0.8480144796	0.9339154646
H25	4.1672709971	0.7269121054	0.8181619936
H26	2.7906698696	1.6961909234	0.3104755157
H27	2.8403909027	1.0490004512	1.9756416826

Zero-point correction = 0.229360 (Hartree/Particle)
Thermal correction to Energy = 0.243496
Thermal correction to Enthalpy = 0.244441
Thermal correction to Gibbs Free Energy = 0.186547
Sum of electronic and zero-point Energies = –594.313547
Sum of electronic and thermal Energies = –594.299411
Sum of electronic and thermal Enthalpies = –594.298466
Sum of electronic and thermal Free Energies = –594.356360

5a

Atom	X	Y	Z
C1	-0.0171571315	-1.9617347208	-0.4179515031
C2	-1.5104260512	-2.1161066394	-0.6847728431
C3	-2.1145567745	-1.0140397845	0.1894788547
C4	-1.0800479450	0.1488501252	0.1230439600
H5	0.3431549380	-0.1531409416	-1.3248784554
H6	0.2598532175	-2.3563482371	0.5630904862
H7	0.6209771353	-2.4107147098	-1.1757246461
H8	-1.7246885314	-1.9372197639	-1.7423963487
H9	-1.8774877917	-3.1095480543	-0.4237611380
H10	-3.0968917020	-0.6779127909	-0.1387118297
H11	-2.2054524682	-1.3678063925	1.2198196968
H12	-1.3776079701	0.8826085825	-0.6228925990
N13	0.2084380865	-0.4874363814	-0.3744340564
C14	-1.1222967116	0.8851515543	1.4752560128
O15	-2.0335630020	1.6895119170	1.6199679096
O16	-0.3030363747	0.5738758265	2.4421832989
H17	0.6192000107	0.0398139417	2.1519041614
C18	1.8651856094	-0.1017953435	0.4842933168
O19	1.7094576568	-0.5393201226	1.6910288907
C20	2.8380475301	-0.8893770490	-0.3759160618
H21	2.7271615466	-1.9591519660	-0.2043707467
H22	2.7394021364	-0.6660248145	-1.4397873798
H23	3.8453066734	-0.5990076149	-0.0632659391
C24	1.9416025032	1.4052948871	0.2627397574
H25	2.9179841381	1.7318104600	0.6322268536
H26	1.8744880872	1.6693386528	-0.7941016133
H27	1.1798531848	1.9452293796	0.8226319615

Zero-point correction = 0.229618 (Hartree/Particle)
Thermal correction to Energy = 0.241264
Thermal correction to Enthalpy = 0.242208
Thermal correction to Gibbs Free Energy = 0.192049
Sum of electronic and zero-point Energies = –594.300687
Sum of electronic and thermal Energies = –594.289042
Sum of electronic and thermal Enthalpies = –594.288098
Sum of electronic and thermal Free Energies = –594.338256

5b

Atom	X	Y	Z
C1	-0.4029099281	1.3024110333	-1.3257489985
C2	-1.9174399546	1.1114922786	-1.2901921809
C3	-2.1834922370	0.8312475511	0.1981415825
C4	-0.9399721225	0.0612790829	0.6793408962
H5	0.1943058859	-0.6154258908	-0.9217070965
H6	0.0561870105	1.1769755716	-2.3047158504
H7	-0.1273985150	2.2768937074	-0.9233666977
H8	-2.4507093678	1.9873852726	-1.6609547142
H9	-2.2025856696	0.2523472733	-1.9039702688
H10	-2.2678017114	1.7688597043	0.7506649607
H11	-3.0878022452	0.2499351600	0.3684762229
H12	-0.5325898950	0.4806547448	1.6016662342
N13	0.1122124629	0.2513814606	-0.3926802541
C14	-1.1493198352	-1.4420429328	0.9512781460
O15	-2.2523012523	-1.9540080953	0.9621994976
O16	-0.0446733842	-2.1218056864	1.1794168958
H17	0.8046998199	-1.4830678168	1.2384240659
C18	1.7889211545	0.3746539540	0.3300891472
O19	1.7806308693	-0.4765103396	1.3163419522
C20	1.9013903880	1.8343898516	0.7458282002
H21	1.9060922502	2.5253085689	-0.0977119907
H22	1.1037110631	2.1040017957	1.4408652989
H23	2.8521357775	1.9371285989	1.2747447019
C24	2.6385386973	0.0005673327	-0.8805560437
H25	2.4516086592	0.6421630568	-1.7440071915
H26	3.6876550476	0.1113665282	-0.5934985386
H27	2.4739070320	-1.0445817657	-1.1523679766

Zero-point correction = 0.230689 (Hartree/Particle)
Thermal correction to Energy = 0.242251
Thermal correction to Enthalpy = 0.243195
Thermal correction to Gibbs Free Energy = 0.193182
Sum of electronic and zero-point Energies = –594.302870
Sum of electronic and thermal Energies = –594.291308
Sum of electronic and thermal Enthalpies = –594.290364
Sum of electronic and thermal Free Energies = –594.340377

6a

Atom	X	Y	Z
C1	-0.1603524393	-1.5611266845	0.9399083284
C2	-1.6587996187	-1.7059470406	0.6222442348
C3	-1.7869742887	-1.2988729275	-0.8548002985
C4	-0.7551554935	-0.1738990383	-1.0005381376
H5	0.7958921265	-1.4796061116	-0.8835772537
H6	0.0371684123	-0.9891542427	1.8409757273
H7	0.3593910856	-2.5145947462	0.9964298973
H8	-2.0088865609	-2.7212415294	0.8055698201
H9	-2.2398111414	-1.0291770444	1.2509376054
H10	-1.5259016630	-2.1327896799	-1.5128308850
H11	-2.7813104438	-0.9496536568	-1.1249600856
H12	-0.4340085535	-0.0265851489	-2.0295651408
N13	0.4305112578	-0.7822587489	-0.2340376859
C14	-1.3269921850	1.1783591290	-0.4810370308
O15	-2.2443068597	1.6205342628	-1.1914411544
O16	-0.8618964088	1.6943083531	0.5751585493
H17	0.5754507787	1.3025383786	1.1139162385
C18	1.7006089781	0.0987347134	0.1254193602
O19	1.4371168523	0.8172042996	1.2746771558
C20	1.9993966296	0.9840846083	-1.0835998143
H21	1.2171637880	1.7273717131	-1.2355518816
H22	2.9334213687	1.5112627790	-0.8852576306
H23	2.1232021099	0.3965009921	-1.9960270247
C24	2.8361320230	-0.8757807549	0.4182230516
H25	3.0706191044	-1.4981672330	-0.4477161235
H26	3.7220174294	-0.2921002793	0.6704665720
H27	2.5930037120	-1.5108443624	1.2704136064

Zero-point correction =	0.234574 (Hartree/Particle)
Thermal correction to Energy =	0.246325
Thermal correction to Enthalpy =	0.247270
Thermal correction to Gibbs Free Energy =	0.197264
Sum of electronic and zero-point Energies =	–594.309671
Sum of electronic and thermal Energies =	–594.297919
Sum of electronic and thermal Enthalpies =	–594.296975
Sum of electronic and thermal Free Energies =	–594.346980

6b

Atom	X	Y	Z
C1	-0.3093767288	1.0397269453	-1.4207433194
C2	-1.8304584926	0.9978867458	-1.2953874471
C3	-2.0460736433	1.0078190952	0.2237853641
C4	-0.9464056075	0.0785582145	0.7513967534
H5	0.1604945402	-0.8367186830	-0.6044614963
H6	0.0830306840	0.6544180127	-2.3589974143
H7	0.0677758136	2.0475499194	-1.2583573451
H8	-2.2940884610	1.8436074136	-1.8030670647
H9	-2.2223914799	0.0775699166	-1.7361995974
H10	-1.9090971057	2.0178113930	0.6182649102
H11	-3.0299790730	0.6532052101	0.5271947259
H12	-0.5645824023	0.3675162666	1.7258979511
N13	0.1696130890	0.1627216567	-0.2845289097
C14	-1.3653211282	-1.4238718667	0.8260269206
O15	-2.2686926995	-1.6975288939	1.6340280314
O16	-0.7322979609	-2.1991396262	0.0530376434
H17	1.8432089004	-1.4054178552	0.9529364658
C18	1.5881531700	0.4171985520	0.2664039693
O19	1.7746888382	-0.5094075679	1.3097579027
C20	1.6989050150	1.8018486852	0.8858444600
H21	1.5830808106	2.5890799146	0.1424441601
H22	0.9629832456	1.9436232260	1.6775949174
H23	2.6932337290	1.8914971152	1.3238205334
C24	2.5791611458	0.1974166469	-0.8724772391
H25	2.4522935387	0.9365720409	-1.6640801261
H26	3.5887621219	0.2909511223	-0.4714316655
H27	2.4664801407	-0.8013935996	-1.3030030842

Zero-point correction = 0.234061 (Hartree/Particle)
Thermal correction to Energy = 0.246190
Thermal correction to Enthalpy = 0.247135
Thermal correction to Gibbs Free Energy = 0.195918
Sum of electronic and zero-point Energies = –594.313838
Sum of electronic and thermal Energies = –594.301708
Sum of electronic and thermal Enthalpies = –594.300764
Sum of electronic and thermal Free Energies = –94.3519810

7

Atom	X	Y	Z
C1	0.2982293938	-2.0957021832	-0.4912330199
C2	-0.7260973320	-2.1544267976	0.6378051803
C3	-1.7174141961	-1.0072549374	0.3240957042
C4	-1.1035792293	-0.2288594418	-0.8555576085
H5	0.7575080752	-0.5246842948	-1.7763055902
H6	1.2771671522	-2.4982136219	-0.2562184256
H7	-0.0689391928	-2.5887120491	-1.3921868467
H8	-1.2041425600	-3.1331476852	0.6687251897
H9	-0.2382779542	-1.9803862466	1.5968523904
H10	-2.6997084266	-1.3780026380	0.0303667777
H11	-1.8446451550	-0.3545890537	1.1854061615
H12	-1.4481751480	-0.6472632872	-1.7994757675
N13	0.3910404865	-0.6205093904	-0.8293921071
C14	-1.4619194341	1.2920571162	-0.8883873446
O15	-2.0250069703	1.6865806774	-1.9234707462
O16	-1.2035886527	1.9725327664	0.1477687642
H17	-0.0545122369	1.2328756540	0.9891994773
C18	1.3660682428	0.2619859602	0.0940490550
O19	0.6850505314	0.6038257707	1.2434451571
C20	1.7831044493	1.4575064467	-0.7706280475
H21	0.9308208164	2.0302444661	-1.1299317228
H22	2.3956177425	2.1145931395	-0.1521203414
H23	2.3836824854	1.1309619727	-1.6226875648
C24	2.5818585135	-0.5641720622	0.4890840280
H25	3.0832105609	-1.0018263430	-0.3753236552
H26	3.2822953772	0.1110438584	0.9823836404
H27	2.3139526606	-1.3443577962	1.2008372624

Zero-point correction = 0.235153 (Hartree/Particle)
Thermal correction to Energy = 0.246784
Thermal correction to Enthalpy = 0.247728
Thermal correction to Gibbs Free Energy = 0.198108
Sum of electronic and zero-point Energies = –594.301751
Sum of electronic and thermal Energies = –594.290120
Sum of electronic and thermal Enthalpies = –594.289176
Sum of electronic and thermal Free Energies = –594.338796

8

Atom	X	Y	Z
C1	0.4722714307	-1.7931193190	-0.9699678577
C2	-0.4084548344	-2.3899837540	0.1522703504
C3	-1.3985562225	-1.2621027291	0.5513734610
C4	-1.2529491073	-0.2406661687	-0.5694321616
H5	0.3577413833	0.1187470566	-1.8156092944
H6	1.5325036959	-2.0135683130	-0.8949277460
H7	0.1315259609	-2.1063362616	-1.9558229237
H8	-0.9349600091	-3.2640493246	-0.2303796979
H9	0.1938721403	-2.7147355704	0.9995090589
H10	-2.4267311843	-1.6108980450	0.6183435781
H11	-1.1386506982	-0.8106335601	1.5099483000
H12	-1.7114743236	-0.6581651505	-1.4734605802
N13	0.2396286985	-0.2982596936	-0.8925697359
C14	-1.8843429405	1.1669184142	-0.4665066339
O15	-2.9801121548	1.2193441845	0.1120313904
O16	-1.2627192158	2.1007540316	-1.0592171982
H17	0.1199172494	2.0588027397	-0.0518459130
C18	1.2892098462	0.5044542251	0.0353783839
O19	0.6424706199	1.5721016590	0.6303783040
C20	2.3781341306	0.9466297365	-0.9418450452
H21	1.9705523324	1.6400320807	-1.6823297266
H22	3.1557102360	1.4642788739	-0.3796567208
H23	2.8303524838	0.0966710353	-1.4575571574
C24	1.8405738948	-0.3529445445	1.1673319674
H25	2.4034459947	-1.2162659385	0.8185750861
H26	2.5241135899	0.2856382542	1.7283907884
H27	1.0507270033	-0.6705439186	1.8445977239

Zero-point correction =	0.234647 (Hartree/Particle)
Thermal correction to Energy =	0.246415
Thermal correction to Enthalpy =	0.247359
Thermal correction to Gibbs Free Energy =	0.197330
Sum of electronic and zero-point Energies =	–594.296720
Sum of electronic and thermal Energies =	–594.284952
Sum of electronic and thermal Enthalpies =	–594.284008
Sum of electronic and thermal Free Energies =	–594.334037

9a

Atom	X	Y	Z
C1	0.3840649949	-1.6807530894	-1.1254104814
C2	-0.4296596300	-2.4017196034	0.0076021589
C3	-1.3647230266	-1.3097792510	0.6350233223
C4	-1.2628190561	-0.2419604123	-0.4347763148
H5	-0.1615703227	0.7968619808	-1.5892177371
H6	1.4410339258	-1.9318985223	-1.1383940911
H7	-0.0245704768	-1.9060248712	-2.1105153911
H8	-1.0179709031	-3.2118135273	-0.4248388703
H9	0.2296125906	-2.8396732140	0.7562331855
H10	-2.3865417351	-1.6666041934	0.7588184012
H11	-1.0074045981	-0.9576618061	1.6019462897
H12	-1.7738342961	-0.6641265278	-1.3130267784
N13	0.1733214716	-0.2243149459	-0.8690517737
C14	-1.7122547391	1.2167690212	-0.5345692081
O15	-2.6427349748	1.7256654320	0.0663782109
O16	-0.9778565964	1.7694267751	-1.4763114182
H17	0.5018658321	2.2154649446	0.2179058519
C18	1.2362249533	0.4017566503	0.0863071479
O19	0.6469257400	1.4632234373	0.8069227220
C20	2.3456705639	0.9025168979	-0.8406478492
H21	1.9586718254	1.6555060344	-1.5319281176
H22	3.1430460117	1.3489083176	-0.2449282725
H23	2.7652465233	0.0832161630	-1.4273067950
C24	1.7991649574	-0.5359313787	1.1545645389
H25	2.2807273640	-1.4141821813	0.7291181010
H26	2.5551333010	0.0263715307	1.7041954333
H27	1.0349302998	-0.8467436608	1.8628077349

Zero-point correction = 0.229737 (Hartree/Particle)
Thermal correction to Energy = 0.241029
Thermal correction to Enthalpy = 0.241973
Thermal correction to Gibbs Free Energy = 0.193718
Sum of electronic and zero-point Energies = –594.270035
Sum of electronic and thermal Energies = –594.258743
Sum of electronic and thermal Enthalpies = –594.257799
Sum of electronic and thermal Free Energies = –594.306054

9b

Atom	X	Y	Z
C1	-0.2904715225	0.9838139059	-1.4196713284
C2	-1.8149650931	0.9955604922	-1.2892345895
C3	-2.0271383548	1.0514628972	0.2303058807
C4	-0.9324878909	0.1212379562	0.7653786955
H5	-0.0109712243	-1.1168594758	-0.4546821646
H6	0.0677018400	0.5381292459	-2.3465734295
H7	0.1062718851	1.9979639595	-1.3418893946
H8	-2.2592749475	1.8394684401	-1.8172032231
H9	-2.2394421723	0.0762273606	-1.7022450837
H10	-1.8596541476	2.0657550685	0.6011262606
H11	-3.0192103283	0.7306738217	0.5477791686
H12	-0.5809358965	0.3870550280	1.7591518630
N13	0.1726818060	0.1630038622	-0.2544570093
C14	-1.3561552668	-1.3721986990	0.7848170475
O15	-2.2383952230	-1.7874553696	1.5233606451
O16	-0.6623498087	-2.0625163538	-0.0724158385
H17	1.8882642924	-1.3925524188	0.9393538602
C18	1.5611563603	0.4286486574	0.2696050840
O19	1.7905308224	-0.5077057816	1.3141350033
C20	1.6930762776	1.8076477177	0.9088348054
H21	1.5026324334	2.6012281807	0.1865603497
H22	1.0042721313	1.9185633631	1.7472645407
H23	2.7103859126	1.9237487666	1.2846685743
C24	2.5560984931	0.2267600654	-0.8721019139
H25	2.4343044337	0.9820082839	-1.6496665547
H26	3.5681719695	0.3040784385	-0.4729123532
H27	2.4291032190	-0.7606474124	-1.3238888956

Zero-point correction = 0.229342 (Hartree/Particle)
Thermal correction to Energy = 0.241006
Thermal correction to Enthalpy = 0.241950
Thermal correction to Gibbs Free Energy = 0.192443
Sum of electronic and zero-point Energies = –594.311156
Sum of electronic and thermal Energies = –594.299492
Sum of electronic and thermal Enthalpies = –594.298548
Sum of electronic and thermal Free Energies = –594.348055

10a

Atom	X	Y	Z
C1	0.5114657874	-1.6413051547	-1.2748653443
C2	-0.2645314974	-2.4937815007	-0.2316325121
C3	-1.3103889259	-1.5206633124	0.3650321054
C4	-1.1237636008	-0.2422774071	-0.4783541488
H5	-1.5991368613	1.8429498781	-1.5802733636
H6	1.5711868715	-1.8772173809	-1.3168667209
H7	0.0987974020	-1.8179231343	-2.2727226806
H8	-0.7322100510	-3.3558393303	-0.7105899673
H9	0.4020632976	-2.8752267807	0.5435264316
H10	-2.3328322826	-1.8928056827	0.2802955050
H11	-1.1216331218	-1.3157208973	1.4176800683
H12	-1.7169223291	-0.3713051422	-1.3933000808
N13	0.2872060490	-0.2139892093	-0.9461491176
C14	-1.6515939214	1.0394671019	0.1622730874
O15	-1.9376436977	1.1562182589	1.3282816661
O16	-1.9108389746	2.0572860657	-0.6898630358
H17	0.9690079951	2.1961151620	-0.8810532573
C18	1.3049899153	0.4423071152	-0.0816281577
O19	0.9351360334	1.8232834294	0.0092655666
C20	2.6802562945	0.3389612605	-0.7536415676
H21	2.6082448845	0.6028825337	-1.8116348515
H22	3.3552586729	1.0383176514	-0.2578501897
H23	3.1119764304	-0.6589992474	-0.6695668673
C24	1.3794211188	-0.0379761750	1.3726442635
H25	1.5838010310	-1.1081096210	1.4131826178
H26	2.1879560050	0.4858697471	1.8866438888
H27	0.4481274751	0.1714817722	1.897566662

Zero-point correction =	0.232583 (Hartree/Particle)
Thermal correction to Energy =	0.244807
Thermal correction to Enthalpy =	0.245751
Thermal correction to Gibbs Free Energy =	0.195193
Sum of electronic and zero-point Energies =	–594.290553
Sum of electronic and thermal Energies =	–594.278329
Sum of electronic and thermal Enthalpies =	–594.277385
Sum of electronic and thermal Free Energies =	–594.327943

10b

Atom	X	Y	Z
C1	-0.2608052919	1.0213456904	-1.4225500310
C2	-1.7871631051	0.9962275516	-1.3276666580
C3	-2.0242453754	1.0351967108	0.1872570910
C4	-0.8996048405	0.1326060263	0.7337562740
H5	-0.1836369914	-1.5768179484	-0.4857147364
H6	0.1177070659	0.6106558699	-2.3589359143
H7	0.1018105229	2.0518904404	-1.3290859007
H8	-2.2461009247	1.8332597776	-1.8549923090
H9	-2.1817087136	0.0696657724	-1.7555725005
H10	-1.8785725983	2.0500107754	0.5653743982
H11	-3.0143198036	0.6970051912	0.4931125567
H12	-0.5692875304	0.4490818048	1.7225826512
N13	0.1865414414	0.1875833991	-0.2756571013
C14	-1.3705642127	-1.3209043281	0.8906618703
O15	-2.1903171150	-1.6753473824	1.7100464395
O16	-0.8061247925	-2.1664887088	0.0269190724
H17	1.8898329401	-1.4018251731	0.8501400974
C18	1.5520402004	0.4415116402	0.2520323040
O19	1.8022327142	-0.5354952959	1.2670314038
C20	1.6997271603	1.7958614273	0.9513163871
H21	1.4908551140	2.6149754372	0.2620491100
H22	1.0246693457	1.8742545758	1.8051341596
H23	2.7222942507	1.9061662842	1.3157724709
C24	2.5623679489	0.2927459223	-0.8866791455
H25	2.4505037151	1.0833548720	-1.6304138273
H26	3.5715586671	0.3487023032	-0.4757541811
H27	2.4335102083	-0.6720226354	-1.3847639811

Zero-point correction =	0.232629 (Hartree/Particle)
Thermal correction to Energy =	0.244708
Thermal correction to Enthalpy =	0.245652
Thermal correction to Gibbs Free Energy =	0.195050
Sum of electronic and zero-point Energies =	–594.313014
Sum of electronic and thermal Energies =	–594.300935
Sum of electronic and thermal Enthalpies =	–594.299990
Sum of electronic and thermal Free Energies =	–594.350592

RMP2 structures

2

Atom	X	Y	Z
C1	0.0000002401	0.0000000016	-0.1823577806
O2	-0.0000000282	-0.0000000042	-1.4070023784
C3	0.0059732125	-1.2828331316	0.6152245810
H4	-0.1416589027	-2.1416048267	-0.0400419070
H5	0.9678073510	-1.3749155602	1.1307415356
H6	-0.7725471034	-1.2527026549	1.3829058667
C7	-0.0059731895	1.2828331346	0.6152245820
H8	-0.9678073665	1.3749152644	1.1307415216
H9	0.7725471204	1.2527029009	1.3829058816
H10	0.1416586663	2.1416048761	-0.0400419027

Zero-point correction = 0.084443 (Hartree/Particle)
Thermal correction to Energy = 0.089745
Thermal correction to Enthalpy = 0.090690
Thermal correction to Gibbs Free Energy = 0.056565
Sum of electronic and zero-point Energies = –192.577358
Sum of electronic and thermal Energies = –192.572056
Sum of electronic and thermal Enthalpies = –192.571111
Sum of electronic and thermal Free Energies = –192.605236

1a

Atom	X	Y	Z
C1	-0.0930450355	-1.3525486764	-0.8294345799
C2	-0.4933360795	-1.2349863656	0.6399189512
C3	-1.0852610950	0.1772179399	0.6965711676
C4	-0.1260162716	0.9756594110	-0.2052119551
H5	0.2993832548	0.2504353650	-2.1062773624
H6	0.6603940790	-2.1215823350	-1.0147473898
H7	-0.9759486265	-1.5637056966	-1.4451117267
H8	-1.2025683360	-2.0094040441	0.9400448430
H9	0.3933538838	-1.3055967138	1.2799499658
H10	-2.0845533442	0.1798018560	0.2503335022
H11	-1.1494572102	0.5969938990	1.7025981479
H12	-0.6341555336	1.7911044461	-0.7279251993
N13	0.4627631679	-0.0106441180	-1.1389138639
C14	1.0104448310	1.6014758021	0.6134482664
O15	0.8336039203	2.4519870011	1.4650880665
O16	2.2114663311	1.1116161764	0.3039269229
H17	1.9729320640	0.4621760528	-0.4242577566

Zero-point correction = 0.146422 (Hartree/Particle)
Thermal correction to Energy = 0.153475
Thermal correction to Enthalpy = 0.154420
Thermal correction to Gibbs Free Energy = 0.114528
Sum of electronic and zero-point Energies = –400.050286
Sum of electronic and thermal Energies = –400.043233
Sum of electronic and thermal Enthalpies = –400.042289
Sum of electronic and thermal Free Energies = –400.082180

1b

Atom	X	Y	Z
C1	1.9908283126	-0.8840891838	0.0728809425
C2	2.2108924055	0.6505878302	-0.0762849780
C3	0.7833220463	1.2519092515	-0.0998089025
C4	-0.0702920017	0.0781134971	0.3874849106
H5	0.4196984994	-1.1001098358	-1.1854360616
H6	2.5930362845	-1.4757111915	-0.6192837656
H7	2.2196129921	-1.2049711527	1.0934932825
H8	2.7904396949	1.0403838814	0.7646018485
H9	2.7506300454	0.8880252463	-0.9961776488
H10	0.6789002677	2.1383957011	0.5292651270
H11	0.4832516879	1.5138651954	-1.1194419761
H12	0.0096136273	-0.0005251072	1.4821453456
N13	0.5535547484	-1.1347528549	-0.1717448156
C14	-1.5511372777	0.1306409581	0.0791330605
O15	-2.1958141065	1.1495292204	-0.0377072227
O16	-2.1350556815	-1.0822835363	-0.0175455489
H17	-1.4211815446	-1.7401079194	0.0780264025

Zero-point correction =	0.146368 (Hartree/Particle)
Thermal correction to Energy =	0.153795
Thermal correction to Enthalpy =	0.154739
Thermal correction to Gibbs Free Energy =	0.113870
Sum of electronic and zero-point Energies =	–400.039435
Sum of electronic and thermal Energies =	–400.032008
Sum of electronic and thermal Enthalpies =	–400.031064
Sum of electronic and thermal Free Energies =	–400.071933

3a

Atom	X	Y	Z
C1	-0.6729361151	-1.9319506865	-1.2282175341
C2	-1.6630400586	-2.4396035610	-0.1782814686
C3	-1.7590092337	-1.2358194314	0.7674120007
C4	-1.6607238856	-0.0249137099	-0.1945386097
H5	-1.7434817258	-0.4656658028	-2.2020945144
H6	0.3431197802	-1.9590411008	-0.8225183998
H7	-0.6937165312	-2.4778032337	-2.1740467666
H8	-2.6334065751	-2.6376791956	-0.6475733238
H9	-1.3222292321	-3.3469000399	0.3283541617
H10	-2.6821328818	-1.2081448076	1.3497243801
H11	-0.9100835121	-1.2343877249	1.4569920755
H12	-2.6479882437	0.4076902290	-0.3848512750
N13	-1.0562440556	-0.5166781356	-1.4555007983
C14	-0.7885648137	1.0909446083	0.3748225010
O15	-1.0024980537	1.6385679443	1.4393766403
O16	0.2438914905	1.4066804462	-0.4134697134
H17	0.1116188946	0.7775803903	-1.1801224302
C18	2.3738754420	-0.1949190219	1.0577048382
O19	1.6177723128	-1.1144393047	1.3516419061
C20	3.1184548147	-0.1677369189	-0.2559337520
H21	2.7228342364	-0.9240548760	-0.9353930540
H22	3.0505007333	0.8248725934	-0.7086180954
H23	4.1779542362	-0.3716145851	-0.0635457695
C24	2.6261704422	0.9621834148	1.9925898667
H25	3.7027381063	1.0945462160	2.1399039437
H26	2.2415885151	1.8765996337	1.5304264086
H27	2.1319359135	0.7959866604	2.9504567820

Zero-point correction =	0.231870 (Hartree/Particle)
Thermal correction to Energy =	0.246282
Thermal correction to Enthalpy =	0.247226
Thermal correction to Gibbs Free Energy =	0.187797
Sum of electronic and zero-point Energies =	–592.633705
Sum of electronic and thermal Energies =	–592.619293
Sum of electronic and thermal Enthalpies =	–592.618349
Sum of electronic and thermal Free Energies =	–592.677777

3b

Atom	X	Y	Z
C1	-2.1985833244	0.5602395425	-2.3077718592
C2	-2.0314286486	1.5675205861	-1.1676954048
C3	-0.8196106734	0.9949957466	-0.4228504998
C4	-0.9538140629	-0.5514787472	-0.6440698472
H5	-2.8251351989	-1.0287779632	-1.2020543668
H6	-3.1823482567	0.5823380082	-2.7832473445
H7	-1.4366087451	0.7330323413	-3.0770297188
H8	-1.8667181826	2.5936102902	-1.5085288885
H9	-2.9203364955	1.5446190792	-0.5276406818
H10	0.1101872425	1.3448822706	-0.8822625043
H11	-0.8022092643	1.2693868264	0.6359062698
H12	0.0091700362	-0.9617300085	-0.9629159850
N13	-1.9700325992	-0.7600418148	-1.6884445466
C14	-1.3652451460	-1.2352722447	0.6492831330
O15	-2.5092164113	-1.5727035545	0.8912239183
O16	-0.3929175560	-1.4168295624	1.5515264012
H17	0.4726850206	-1.0970172864	1.2000408724
C18	2.5806644698	0.4246659074	0.8641904378
O19	1.9880441443	-0.6144454315	0.5711328125
C20	2.0907416796	1.3440973386	1.9512941169
H21	1.7343908741	2.2717556014	1.4898401054
H22	1.2844205688	0.8856374838	2.5245949853
H23	2.9198762331	1.6098844613	2.6129992748
C24	3.8338052836	0.8314526646	0.1400302519
H25	3.7523436416	1.8721715084	-0.1867362679
H26	4.6768126381	0.7749890002	0.8369684741
H27	4.0141627325	0.1762179566	-0.7119831383

Zero-point correction =	0.232246 (Hartree/Particle)
Thermal correction to Energy =	0.246582
Thermal correction to Enthalpy =	0.247526
Thermal correction to Gibbs Free Energy =	0.187705
Sum of electronic and zero-point Energies =	–592.629674
Sum of electronic and thermal Energies =	–592.615338
Sum of electronic and thermal Enthalpies =	–592.614394
Sum of electronic and thermal Free Energies =	–592.674215

4a

Atom	X	Y	Z
C1	-0.2316316844	-1.3623380847	-0.6141142402
C2	-1.6180772759	-1.9314004293	-0.9202550070
C3	-2.4571894909	-1.3042986940	0.1968291638
C4	-1.8639709632	0.1229120007	0.3104470782
H5	-0.3564199577	0.6659015936	-0.9742606557
H6	0.2257045247	-1.9137091711	0.2163648025
H7	0.4575828688	-1.3800002554	-1.4619025568
H8	-1.9601730005	-1.5742049737	-1.8979769450
H9	-1.6456340298	-3.0244144139	-0.9102082899
H10	-3.5289940315	-1.2782949802	-0.0090402843
H11	-2.2985560757	-1.8531885059	1.1321952480
H12	-2.4560388199	0.8330039161	-0.2752532088
N13	-0.4755954640	0.0360568086	-0.1870992324
C14	-1.8765744649	0.5980324116	1.7573835288
O15	-2.9008448265	0.8259840788	2.3742745349
O16	-0.6663801453	0.7077421096	2.3099839583
H17	-0.0357494243	0.5012813901	1.5729981181
C18	2.7679813694	-0.0443300717	0.6793362814
O19	2.1560949945	-0.1196161341	1.7387694562
C20	3.5872771199	-1.1972739868	0.1506290419
H21	3.5683704119	-2.0326870064	0.8511684690
H22	3.1872054497	-1.5138457715	-0.8182609890
H23	4.6184418900	-0.8705803041	-0.0171590076
C24	2.7493161243	1.2068521743	-0.1649213126
H25	3.7631140609	1.6187395172	-0.2178312172
H26	2.4470659357	0.9620261527	-1.1878053416
H27	2.0707749048	1.9463506295	0.2606086071

Zero-point correction = 0.231822 (Hartree/Particle)
Thermal correction to Energy = 0.246308
Thermal correction to Enthalpy = 0.247252
Thermal correction to Gibbs Free Energy = 0.187177
Sum of electronic and zero-point Energies = –592.632613
Sum of electronic and thermal Energies = –592.618127
Sum of electronic and thermal Enthalpies = –592.617183
Sum of electronic and thermal Free Energies = –592.677257

4b

Atom	X	Y	Z
C1	-0.7881216404	1.5672720187	-1.1912572882
C2	-2.3202246126	1.5465250623	-0.9315364042
C3	-2.5495829801	0.2731863897	-0.0835734652
C4	-1.1327759017	-0.1143017016	0.3502770063
H5	-0.4292524052	-0.4080435999	-1.5304390700
H6	-0.5272626414	1.7579972690	-2.2351300739
H7	-0.3134794057	2.3361889343	-0.5723225337
H8	-2.6335400779	2.4462533236	-0.3952343431
H9	-2.8829785644	1.5000192052	-1.8673907830
H10	-3.2153905943	0.4382173153	0.7679709397
H11	-2.9620156196	-0.5351292467	-0.6935207379
H12	-0.8230135439	0.4957719107	1.2087499415
N13	-0.2490186993	0.2554202501	-0.7744891982
C14	-0.9426685875	-1.5827329864	0.7035847581
O15	-1.7093002094	-2.4608355091	0.3576663491
O16	0.1544763073	-1.8787458415	1.4150666396
H17	0.7034958823	-1.0704960792	1.5583323953
C18	2.3056196502	0.6183150423	0.6678339392
O19	1.6377551648	0.3552624831	1.6691647294
C20	2.6228379907	2.0400652072	0.2958122575
H21	2.2193288452	2.2421472759	-0.7011698302
H22	2.1965548744	2.7334012965	1.0213503244
H23	3.7085671195	2.1705505326	0.2402767893
C24	2.9042602565	-0.4556953117	-0.2005285952
H25	2.7832302525	-0.2005315566	-1.2552187986
H26	3.9790806883	-0.4996743125	0.0130880414
H27	2.4563184517	-1.4271073714	0.0081370105

Zero-point correction = 0.232156 (Hartree/Particle)
Thermal correction to Energy = 0.246439
Thermal correction to Enthalpy = 0.247383
Thermal correction to Gibbs Free Energy = 0.188899
Sum of electronic and zero-point Energies = –592.627022
Sum of electronic and thermal Energies = –592.612739
Sum of electronic and thermal Enthalpies = –592.611794
Sum of electronic and thermal Free Energies = –592.670279

5a

Atom	X	Y	Z
C1	-0.0325483717	-1.9637505485	-0.3452700522
C2	-1.5145781302	-2.1214369424	-0.6670383306
C3	-2.1378941223	-0.9871932452	0.1477077728
C4	-1.0762219712	0.1529684625	0.0869714884
H5	0.3380739245	-0.2095616549	-1.3352703532
H6	0.1973164002	-2.3169164304	0.6671391990
H7	0.6324333943	-2.4541004081	-1.0570749339
H8	-1.6794155898	-1.9665064470	-1.7385575957
H9	-1.9049963917	-3.1030875775	-0.3872333306
H10	-3.1010926184	-0.6415745101	-0.2322579028
H11	-2.2724851276	-1.3107800949	1.1855182222
H12	-1.3568773511	0.9025938544	-0.6550189356
N13	0.1980440374	-0.4981297975	-0.3668985349
C14	-1.1181682986	0.8606278074	1.4418043944
O15	-1.9988584278	1.6900492112	1.6159693384
O16	-0.3308155346	0.4710881086	2.4321190736
H17	0.5415127835	0.0069390296	2.1359435568
C18	1.9537424010	-0.0984650280	0.5233050832
O19	1.8097773294	-0.5628771884	1.6960932799
C20	2.8593074513	-0.8606275535	-0.4226975188
H21	2.7615743132	-1.9355925883	-0.2649945854
H22	2.6811201843	-0.6090680598	-1.4712260816
H23	3.8877783727	-0.5693344760	-0.1777193298
C24	1.9497135304	1.4055832216	0.3038361872
H25	2.9420282344	1.7715219554	0.5940886770
H26	1.7858928364	1.6631529373	-0.7453926453
H27	1.2126367418	1.9095779626	0.9306538575

Zero-point correction =	0.232998 (Hartree/Particle)
Thermal correction to Energy =	0.244918
Thermal correction to Enthalpy =	0.245863
Thermal correction to Gibbs Free Energy =	0.194664
Sum of electronic and zero-point Energies =	–592.615564
Sum of electronic and thermal Energies =	–592.603643
Sum of electronic and thermal Enthalpies =	–592.602699
Sum of electronic and thermal Free Energies =	–592.653898

5b

Atom	X	Y	Z
C1	-0.4931520269	1.4573344709	-1.2217818524
C2	-1.9920280957	1.1677583604	-1.2342526966
C3	-2.2384966239	0.7440519968	0.2211066828
C4	-0.9427638160	0.0214508839	0.6321460143
H5	0.1724249962	-0.4649615830	-1.0450751722
H6	-0.0150683936	1.4845912554	-2.2033515203
H7	-0.2920769939	2.3932973161	-0.6926675384
H8	-2.5869943715	2.0341296359	-1.5341191055
H9	-2.2033262434	0.3397116257	-1.9196004231
H10	-2.3771189389	1.6276264476	0.8504742399
H11	-3.1038415465	0.0902405269	0.3380375457
H12	-0.5436864473	0.3974131291	1.5817963738
N13	0.0753446700	0.3405329555	-0.4216440016
C14	-1.0600266915	-1.4990879786	0.7609996522
O15	-2.0909586260	-2.1113695925	0.5508092349
O16	0.0691267003	-2.1145259239	1.1036359309
H17	0.8012885942	-1.4285200583	1.2913849098
C18	1.8654727652	0.4269670417	0.4388704554
O19	1.7130847833	-0.2370928495	1.5148674552
C20	2.0209128400	1.9266771127	0.5715785990
H21	2.0143971664	2.4355662128	-0.3944781232
H22	1.2397178543	2.3341524008	1.2193666859
H23	2.9894187158	2.1086960411	1.0515795281
C24	2.6338367473	-0.2132324237	-0.7032683078
H25	2.4635520498	0.2989227630	-1.6538974851
H26	3.7012752030	-0.1458406058	-0.4617852056
H27	2.3725857296	-1.2712891610	-0.7949318761

Zero-point correction = 0.233729 (Hartree/Particle)
Thermal correction to Energy = 0.245487
Thermal correction to Enthalpy = 0.246431
Thermal correction to Gibbs Free Energy = 0.195828
Sum of electronic and zero-point Energies = –592.619637
Sum of electronic and thermal Energies = –592.607878
Sum of electronic and thermal Enthalpies = –592.606934
Sum of electronic and thermal Free Energies = –592.657537

6a

Atom	X	Y	Z
C1	-0.1587304226	-1.5501116033	0.9441872032
C2	-1.6587834289	-1.6533633291	0.6280703560
C3	-1.7555997457	-1.3044659504	-0.8626254362
C4	-0.7258865193	-0.1816944187	-1.0074479727
H5	0.8122382482	-1.4899951641	-0.8698523036
H6	0.0612917559	-0.9872369830	1.8487929634
H7	0.3344638079	-2.5215560705	0.9836390963
H8	-2.0414429511	-2.6504473421	0.8533268527
H9	-2.2137258022	-0.9234932280	1.2217874301
H10	-1.4637074868	-2.1606449899	-1.4815413384
H11	-2.7471509759	-0.9703037594	-1.1696818201
H12	-0.3951818201	-0.0364595726	-2.0369450409
N13	0.4388059679	-0.7824543405	-0.2279879980
C14	-1.3067881229	1.1510698259	-0.4711117251
O15	-2.1752639993	1.6368292109	-1.2205310399
O16	-0.9069633090	1.5937370701	0.6490669196
H17	0.5533935350	1.2533422898	1.1291755628
C18	1.6814733612	0.0923886041	0.1223550770
O19	1.4328429098	0.8051252616	1.2812157179
C20	1.9623542358	0.9864469624	-1.0789168757
H21	1.1715592796	1.7271331769	-1.2162605250
H22	2.8982308908	1.5155406470	-0.8827967851
H23	2.0803911608	0.4026001185	-1.9970139733
C24	2.8234414310	-0.8737654423	0.3961835317
H25	3.0526842126	-1.4808029788	-0.4843634268
H26	3.7074368970	-0.2849632190	0.6512575489
H27	2.5852168904	-1.5234547756	1.2414180009

Zero-point correction =	0.237459 (Hartree/Particle)
Thermal correction to Energy =	0.249096
Thermal correction to Enthalpy =	0.250040
Thermal correction to Gibbs Free Energy =	0.200283
Sum of electronic and zero-point Energies =	–592.633272
Sum of electronic and thermal Energies =	–592.621635
Sum of electronic and thermal Enthalpies =	–592.620691
Sum of electronic and thermal Free Energies =	–592.670448

6b

Atom	X	Y	Z
C1	-0.2947971507	0.9667429939	-1.4289354612
C2	-1.8126522317	0.9731916689	-1.2710534732
C3	-1.9825457500	1.0572281445	0.2488420897
C4	-0.9273797036	0.0770409613	0.7596620032
H5	0.1523536763	-0.8907171017	-0.5528939587
H6	0.0680251107	0.5229542390	-2.3562496825
H7	0.1110209093	1.9734786115	-1.3187930173
H8	-2.2622128427	1.8114011559	-1.8074163359
H9	-2.2375048100	0.0401995620	-1.6546851547
H10	-1.7617266514	2.0715446384	0.5986135049
H11	-2.9771659166	0.7735582285	0.5974178287
H12	-0.5335780486	0.3164011823	1.7467126221
N13	0.1810875674	0.1323998138	-0.2677058831
C14	-1.4115692923	-1.4036659940	0.7626891533
O15	-2.3436935621	-1.6739091547	1.5424018609
O16	-0.7895089744	-2.1661910813	-0.0424724585
H17	1.9280636572	-1.3839303018	0.9173017672
C18	1.5738841259	0.4204927688	0.2707274754
O19	1.7936087095	-0.5083831156	1.3053163348
C20	1.6453024995	1.7992127724	0.9006347620
H21	1.4728749615	2.5887636046	0.1676601637
H22	0.9277042390	1.8985143365	1.7180751205
H23	2.6509762088	1.9252488120	1.3082255802
C24	2.5638991782	0.2398846156	-0.8697093645
H25	2.4153764799	0.9875974946	-1.6521311980
H26	3.5732473505	0.3532096369	-0.4673335705
H27	2.4700102602	-0.7590684924	-1.3094007088

Zero-point correction = 0.236235 (Hartree/Particle)
Thermal correction to Energy = 0.248267
Thermal correction to Enthalpy = 0.249211
Thermal correction to Gibbs Free Energy = 0.198480
Sum of electronic and zero-point Energies = –592.639677
Sum of electronic and thermal Energies = –592.627646
Sum of electronic and thermal Enthalpies = –592.626702
Sum of electronic and thermal Free Energies = –592.677432

7

Atom	X	Y	Z
C1	0.2987398617	-2.0879109216	-0.4996657570
C2	-0.6971932152	-2.1418293263	0.6534579935
C3	-1.6937708661	-0.9987844987	0.3489608870
C4	-1.0947319332	-0.2296613092	-0.8396021560
H5	0.7502773158	-0.5134894282	-1.7842208710
H6	1.2848377734	-2.4962260517	-0.2939249965
H7	-0.1046410924	-2.5674113129	-1.3951301260
H8	-1.1758277320	-3.1222468563	0.6937660124
H9	-0.1878861455	-1.9615104850	1.6017505772
H10	-2.6764958671	-1.3790289944	0.0595461163
H11	-1.8172232368	-0.3414969202	1.2095660770
H12	-1.4510799802	-0.6598057724	-1.7779930921
N13	0.3889959100	-0.6181379593	-0.8304016139
C14	-1.4040147330	1.2947961949	-0.8979477646
O15	-1.8112428289	1.7168971133	-1.9989793822
O16	-1.2417619836	1.9526472929	0.1761418896
H17	-0.0929393129	1.1958346768	0.9779197648
C18	1.3303377288	0.2466114720	0.0827471121
O19	0.6487410917	0.5761290611	1.2400232576
C20	1.7444637654	1.4510382504	-0.7629233918
H21	0.8907591433	2.0199025979	-1.1317119235
H22	2.3461256890	2.1066624261	-0.1288896187
H23	2.3586909918	1.1287437012	-1.6095370203
C24	2.5519296468	-0.5670433375	0.4751757108
H25	3.0508577586	-1.0035095658	-0.3937747642
H26	3.2488036667	0.1193574077	0.9622602537
H27	2.2890485838	-1.3485274547	1.1904868260

Zero-point correction =	0.238064 (Hartree/Particle)
Thermal correction to Energy =	0.249538
Thermal correction to Enthalpy =	0.250483
Thermal correction to Gibbs Free Energy =	0.201319
Sum of electronic and zero-point Energies =	–592.625458
Sum of electronic and thermal Energies =	–592.613983
Sum of electronic and thermal Enthalpies =	–592.613039
Sum of electronic and thermal Free Energies =	–592.662202

8

Atom	X	Y	Z
C1	0.4707044690	-1.7964709736	-0.9629932964
C2	-0.4063219850	-2.3700585879	0.1733404314
C3	-1.3706408213	-1.2229070719	0.5711467345
C4	-1.2333817309	-0.2410862266	-0.5811918380
H5	0.3748174995	0.1118659067	-1.8222426830
H6	1.5326721793	-2.0232418073	-0.8963116290
H7	0.1083460476	-2.1108669773	-1.9432907750
H8	-0.9579072436	-3.2335527581	-0.2041272949
H9	0.2008156051	-2.7033288690	1.0160212041
H10	-2.4026100514	-1.5611607137	0.6671305489
H11	-1.0793564447	-0.7457556081	1.5102987335
H12	-1.6882755857	-0.6958379159	-1.4727656700
N13	0.2493247592	-0.3057624561	-0.8946200615
C14	-1.8463110971	1.1720135846	-0.5182672905
O15	-2.9519654460	1.2466077549	0.0466170645
O16	-1.1931642891	2.0834562472	-1.1212688192
H17	0.0938426464	2.0047546629	-0.0202303601
C18	1.2591754979	0.4740464603	0.0376527944
O19	0.5890662347	1.5088629744	0.6732181318
C20	2.3328730366	0.9767872645	-0.9205000123
H21	1.8988349173	1.6821515711	-1.6372754795
H22	3.0998143097	1.4951367249	-0.3410359962
H23	2.8017100254	0.1513614504	-1.4653828310
C24	1.8418772091	-0.3954529435	1.1409792298
H25	2.4294503769	-1.2324294391	0.7636474955
H26	2.5123301187	0.2552160093	1.7082047293
H27	1.0679797625	-0.7522482631	1.8202469389

Zero-point correction = 0.237697 (Hartree/Particle)
Thermal correction to Energy = 0.249323
Thermal correction to Enthalpy = 0.250267
Thermal correction to Gibbs Free Energy = 0.200337
Sum of electronic and zero-point Energies = –592.620415
Sum of electronic and thermal Energies = –592.608789
Sum of electronic and thermal Enthalpies = –592.607845
Sum of electronic and thermal Free Energies = –592.657775

9a

Atom	X	Y	Z
C1	-1.077507	1.275562	-1.111182
C2	-0.858728	2.312844	0.044262
C3	0.363104	1.792919	0.875418
C4	0.921841	0.802030	-0.123400
H5	0.571315	-0.605621	-1.325369
H6	-2.115598	0.993261	-1.279036
H7	-0.662798	1.641501	-2.053385
H8	-0.633628	3.291509	-0.387085
H9	-1.751484	2.418077	0.663046
H10	1.074270	2.591988	1.094015
H11	0.066792	1.329117	1.818042
H12	1.252141	1.425469	-0.970834
N13	-0.267306	0.096905	-0.698956
C14	2.029449	-0.259242	-0.129733
O15	2.999609	-0.279624	0.618578
O16	1.777783	-1.041590	-1.148899
H17	-1.168481	-2.225095	-1.262060
C18	-1.064122	-0.894620	0.155915
O19	-1.792851	-1.659958	-0.788226
C20	-2.131295	-0.275532	1.054978
H21	-2.847296	0.327147	0.496277
H22	-2.677056	-1.107882	1.506069
H23	-1.695093	0.318101	1.857414
C24	-0.151508	-1.781959	0.996456
H25	0.445928	-1.193144	1.697926
H26	-0.792991	-2.450860	1.575328
H27	0.515509	-2.384502	0.378440

Zero-point correction =	0.232632 (Hartree/Particle)
Thermal correction to Energy =	0.243900
Thermal correction to Enthalpy =	0.244844
Thermal correction to Gibbs Free Energy =	0.196511
Sum of electronic and zero-point Energies =	–592.595620
Sum of electronic and thermal Energies =	–592.584353
Sum of electronic and thermal Enthalpies =	–592.583409
Sum of electronic and thermal Free Energies =	–592.631742

9b

Atom	X	Y	Z
C1	-0.279253	0.956384	-1.419055
C2	-1.800988	0.969247	-1.279547
C3	-1.990485	1.073191	0.237517
C4	-0.917702	0.121378	0.768408
H5	-0.013783	-1.102123	-0.449641
H6	0.078115	0.498359	-2.343134
H7	0.118850	1.972728	-1.342541
H8	-2.248867	1.798846	-1.830844
H9	-2.223679	0.031329	-1.654939
H10	-1.780534	2.093247	0.576361
H11	-2.987439	0.786895	0.579904
H12	-0.551599	0.370158	1.764798
N13	0.180237	0.144914	-0.250453
C14	-1.377628	-1.358328	0.762960
O15	-2.282712	-1.748330	1.496203
O16	-0.697203	-2.058360	-0.099564
H17	1.903641	-1.386072	0.901942
C18	1.555504	0.425362	0.271257
O19	1.797882	-0.513663	1.304465
C20	1.662339	1.797753	0.918290
H21	1.444679	2.593199	0.202736
H22	0.982140	1.882965	1.769161
H23	2.685048	1.931210	1.279933
C24	2.544740	0.249700	-0.872797
H25	2.404997	1.012028	-1.643020
H26	3.558023	0.340401	-0.473726
H27	2.428978	-0.739315	-1.329175

Zero-point correction = 0.231918 (Hartree/Particle)
Thermal correction to Energy = 0.243596
Thermal correction to Enthalpy = 0.244540
Thermal correction to Gibbs Free Energy = 0.194908
Sum of electronic and zero-point Energies = –592.640210
Sum of electronic and thermal Energies = –592.628532
Sum of electronic and thermal Enthalpies = –592.627588
Sum of electronic and thermal Free Energies = –592.677220

10a

Atom	X	Y	Z
C1	0.4947346475	-1.6086895308	-1.3086157010
C2	-0.2248074604	-2.4694914275	-0.2362158966
C3	-1.2700624906	-1.5146086263	0.3865663064
C4	-1.1229381824	-0.2429479982	-0.4678039644
H5	-1.5494674091	1.8023635864	-1.5798433357
H6	1.5565643468	-1.8323117953	-1.4023887731
H7	0.0285279620	-1.7810043322	-2.2853753602
H8	-0.6932028968	-3.3423296809	-0.6987964271
H9	0.4779369682	-2.8314922831	0.5180311234
H10	-2.2894440106	-1.9045329254	0.3183167649
H11	-1.0601188410	-1.3063336882	1.4362016225
H12	-1.7293183818	-0.3984089382	-1.3730681606
N13	0.2721255763	-0.1864524901	-0.9672629642
C14	-1.6516271741	1.0397142951	0.1581361326
O15	-1.9420708947	1.1668197446	1.3264340601
O16	-1.9000038053	2.0470045631	-0.7121208565
H17	1.0148009980	2.1755548563	-0.8879075307
C18	1.2829377779	0.4385306758	-0.0814686907
O19	0.9356808241	1.8206074896	0.0075302837
C20	2.6606640005	0.3092229352	-0.7309894248
H21	2.6036348937	0.5618052474	-1.7946747357
H22	3.3343585837	1.0107500452	-0.2319520564
H23	3.0788514445	-0.6939204696	-0.6236225199
C24	1.3363400802	-0.0404503378	1.3695084937
H25	1.5187807887	-1.1162084015	1.4166429153
H26	2.1607583568	0.4704755462	1.8762659504
H27	0.4100642978	0.1985339401	1.8947727446

Zero-point correction = 0.235564 (Hartree/Particle)
Thermal correction to Energy = 0.247650
Thermal correction to Enthalpy = 0.248594
Thermal correction to Gibbs Free Energy = 0.198381
Sum of electronic and zero-point Energies = –592.618379
Sum of electronic and thermal Energies = –592.606293
Sum of electronic and thermal Enthalpies = –592.605349
Sum of electronic and thermal Free Energies = –592.655562

10b

Atom	X	Y	Z
C1	-0.2469283623	0.9734388674	-1.4249744494
C2	-1.7699572043	0.9715402275	-1.3079515033
C3	-1.9703428630	1.0675857929	0.2070318057
C4	-0.8832106785	0.1204855673	0.7376995217
H5	-0.1958941985	-1.5492104575	-0.4719433383
H6	0.1171945255	0.5449015647	-2.3616139036
H7	0.1296376327	2.0016499650	-1.3390544878
H8	-2.2248208108	1.7987118191	-1.8578724818
H9	-2.1801116860	0.0303454521	-1.6908742152
H10	-1.7563727301	2.0857273679	0.5490852207
H11	-2.9689704089	0.7852643976	0.5484906900
H12	-0.5275181136	0.4037046895	1.7307664218
N13	0.1984836370	0.1426558226	-0.2757552793
C14	-1.4115271633	-1.3139772488	0.8546443855
O15	-2.2710860643	-1.6468412782	1.6480458592
O16	-0.8485136923	-2.1585513084	-0.0127484228
H17	1.9169131560	-1.3876809690	0.8219738930
C18	1.5484773542	0.4371839336	0.2539703316
O19	1.8257296317	-0.5320485067	1.2612721132
C20	1.6544290212	1.7890997450	0.9543379771
H21	1.4036245100	2.6037520687	0.2707311089
H22	0.9924124097	1.8357686378	1.8227111924
H23	2.6818816328	1.9334338406	1.2992256279
C24	2.5540349747	0.3244636435	-0.8861787781
H25	2.4112832114	1.1167662340	-1.6253667704
H26	3.5635270123	0.4106950854	-0.4758176024
H27	2.4508252666	-0.6453649538	-1.3847349162

Zero-point correction = 0.235218 (Hartree/Particle)
Thermal correction to Energy = 0.247268
Thermal correction to Enthalpy = 0.248212
Thermal correction to Gibbs Free Energy = 0.197632
Sum of electronic and zero-point Energies = –592.641242
Sum of electronic and thermal Energies = –592.629192
Sum of electronic and thermal Enthalpies = –592.628248
Sum of electronic and thermal Free Energies = –592.678828

End of PART S1

PART S2

Examples of strategies one might consider in the study of reaction mechanisms and relative stability of molecular systems: potential advantages and insights they can provide.

IQA, in our opinion, is perfectly suited for the purpose of studying reaction mechanisms as it allows computing atomic and interaction energies at any stage of a chemical process. Unfortunately, just by looking at the large energy terms of self-atomic energies or much smaller in value diatomic interaction energies it is difficult, or even impossible, to gain a direct and meaningful insight on their significance when reaction mechanism is of interest. However, the general concept of the FAMSEC method, where changes in energy terms are monitored, provides convenient means of their mathematical and chemical significance by purposely grouping of the IQA-defined terms. To this effect, using intuition and experience, a chemist can identify molecular fragments in order to analyse specific energy changes and interpret them in terms of bringing molecules together, most reactive sites of molecules, bond formation and breaking, etc. with an aim of understanding reaction mechanism.

Examples of strategies and approaches one can take are provided below with pointing on some (not exhaustive) insights one can gain at each consecutive step leading to a final product:

a) A **molecular system** approach – examining of $\Delta E_{\text{self}}^{\text{Tot}}$ and $\Delta E_{\text{int}}^{\text{Tot}}$ values. This will indicate whether self or interaction energies can be seen as responsible for the computed ΔE. It should be highly informative to monitor these three global energy terms throughout a multi-step process as this might reveal some important/interesting trends.

b) An **inter-molecular** approach. In this case two (or more) molecules are treated as separate fragments ($\mathcal{M}$ and $\mathcal{N}$) of the molecular system. Computed inter-fragment $\Delta E_{\text{self}}^{\mathcal{M},\mathcal{N}}$ and $\Delta E_{\text{int}}^{\mathcal{M},\mathcal{N}}$ energy values might be useful in interpreting the formation of (i) global energy minimum adducts, (ii) or local energy minimum structures that are better pre-organised for a chemical bond formation, or (iii) a transitional state (TS) structure, etc.

c) An **inter-fragment** approach where selected two fragments, namely an *m*-atom fragment $\mathcal{G}$ of a molecule $\mathcal{M}$ and another *n*-atom fragment $\mathcal{H}$ of a molecule $\mathcal{N}$, are investigated. One can use either (i) on purpose selected molecular fragments that might play a leading role or be seen as a driving force throughout the process, or (ii) analyse all possible 2-, 3-, 4- (etc.) atom fragments $\mathcal{G}$ and treating remaining atoms of a molecular system as another molecular fragment $\mathcal{H}$. From this approach one can identify $\mathcal{G}$ fragments that experienced, at each step of a chemical process, most (un)favourable change in inter-fragment interactions $\Delta E_{\text{int}}^{\mathcal{G},\mathcal{H}}$. Fragments for which most significant $\Delta E_{\text{int}}^{\mathcal{G},\mathcal{H}} < 0$ is obtained can be seen as driving a process toward a product (or TS) and fragments for which $\Delta E_{\text{int}}^{\mathcal{G},\mathcal{H}} >> 0$ can be seen as opposing a chemical change most.

d) Accounting for all interactions in a **(atom A)-(molecular system)** approach. By computing the $\Delta E_{\text{int}}^{\text{A},\mathcal{R}}$ term, where $\mathcal{R}$ is made of all atoms of a molecular system but an atom A, one can identify atoms that drive (or oppose) a chemical change most.

e) Accounting for all non-bonding interactions in a (**atom A)-(molecular system)** approach. Here, only changes in the long-distance interaction energies are considered in computing the $\Delta E_{\text{int}}^{\text{A},\mathcal{R}}$ term. By doing this (by eliminating interaction energies between the selected atom A and atoms to which A is covalently bonded to) might provide better insight on the role played by A in terms of facilitating/opposing a change.

f) Accounting for all non-bonding interactions in a (**atom A of $\mathcal{M}$)-(atoms of $\mathcal{N}$)** approach. The computed the $\Delta E_{\text{int}}^{\text{A},\mathcal{N}}$ term is possibly a best descriptor one can use in identifying most prominent atoms of $\mathcal{M}$ in driving/opposing the chemical change in terms of interactions (either attractive or repulsive) with all atoms of an oncoming molecule $\mathcal{N}$. Exactly the same approach can be used for atoms of $\mathcal{N}$ and their interactions with entire molecule $\mathcal{M}$. By grouping most prominent atoms of either $\mathcal{M}$ or $\mathcal{N}$ one can identify molecular fragments of $\mathcal{M}$ and $\mathcal{N}$ that play most significant roles.

g) An (**atom A in $\mathcal{M}$)-(molecular fragment $\mathcal{G}$ in $\mathcal{N}$)** approach. Having identified fragments under f) above one can calculate $\Delta E_{\text{int}}^{\text{A},\mathcal{G}}$ to identify individual atoms interacting with the fragment $\mathcal{G}$ of an on-coming molecule most significantly, hence one can understand the role played by the atom A better at any stage of the process.

h) A selected ***n*-atom fragment $\mathcal{G}$** approach. A fragment, selected by chemical intuition or using the above points as guiding rules, can be investigated in order to establish whether this fragment (i) experienced most (un)favourable change in the intra-fragment interactions, $\Delta E_{\text{int}}^{\mathcal{G}}$, or (ii) became most stabilised or strained in the molecular system after a particular transformation by examining *loc*-FAMSEC energy term, or (iii) experienced most/least favourable change in inter-fragment interactions, $\Delta E_{\text{int}}^{\mathcal{G},\mathcal{H}}$; a chemist is free to select any *n*-atom $\mathcal{H}$ fragment, or (iv) (de)stabilised an entire molecular system most on a change from an initial to a final state by computing the *mol*-FAMSEC term, e.g., from monomers to adduct, or form pre-organised molecule to TS, etc.

i) A **2-atom A–B** approach involving atoms between which covalent bonds are being broken and/or formed. By monitoring $\Delta E_{\text{int}}^{\text{A,B}}$ and delocalization index ΔDI(A,B) (and most likely also $\Delta E_{\text{self}}^{\text{A,B}}$ as well as changes in these atoms net charges) along the reaction coordinates one can gain an invaluable insight on the process of covalent bonds formation/braking.

All the above provides lots of descriptive (qualitative) as well energetic (quantitative) information from which one should be able to propose fully-supported mechanism of a chemical process and pin-point the origin, on a fundamental atomic and molecular fragment levels, of structural and chemical events.

End of PART S2

PART S3

Data pertaining to lowest and higher energy (**1a** and **1b**, respectively) conformers of S-proline, **1**, and their relative stability.

Table S1. Energies computed for **1a** (lowest energy) and **1b** (higher energy) conformers of **1** (part a) and acetone **2** (part b) at the B3LYP/6-311++G(d,p)/GD3 and MP2/6-311++G(d.p) (italic) levels.

Part a

Proline	E	**Δ**	E_{ZPVE}	**Δ**	H	**Δ**	G	**Δ**	**d(N13,H17)**
1a	-401.3116		-401.1671		-401.1591		-401.1991		1.7864
	-400.1967		*-400.0503*		*-400.0394*		*-400.0822*		*1.7363*
1b	-401.3009	-6.7	-401.1565	-6.7	-401.1481	-6.9	-401.1891	-6.3	2.1251
	-400.1858	*-6.8*	*-400.0503*	*-6.8*	*-400.0311*	*-7.0*	*-400.0719*	*-6.4*	*2.0805*

Part b

	E	E_{ZPVE}	H	G
Acetone	-193.2299	-193.1467	-193.1405	-193.1739
	-192.6618	*-192.5774*	*-192.5711*	*-192.6052*

Note that differences in all energy terms computed for both conformers of proline at both levels of theory are only about 0.1 kcal mol^{-1}.

Classically, the higher stability of **1a** would be attributed to the presence of the significantly shorter H-bond (~ 0.339 Å shorter than in **3b**) between {N13,H17}. This might be the case, but would have to be proven, and this is not an easy (if at all possible) task. Hence, instead of focusing on a single interaction, we decided to analyse the entire molecules.

Inspection of net atomic charges, Q(A), in both conformers (Table S2) instantly reveals that there are significant differences observed for a number of atoms. Unexpectedly, the largest change in Q(A) is observed for H5 and its electron population, N(H5), is smaller in **1a**; hence, H5 in **1a** is more positively charged by 33 me. Comparable $|\Delta Q(\mathrm{A})|$ values are also observed for N13, O15 and O16, but their electron populations increased, relative to **1b**; hence they became more negatively charged.

Table S2. Net atomic charges *Q*(A) and electron populations *N*(A) in **1a** and **1b.** Δ*Q*(A) Δ*N*(A) stand for a difference between values in **1a** and **1b**, *e.g.*, Δ*Q*(A) = {*Q*(A) in **1a**} – {*Q*(A) in **1b**}. All values are in *e*.

	***Q*(A)**			***N*(A)**		
Atom A	**1a**	**1b**	**Δ*Q*(A)**	**1a**	**1b**	**Δ*N*(A)**
C1	0.3219	0.3195	0.0024	5.6781	5.6805	-0.0024
C2	0.0441	0.0291	0.0150	5.9559	5.9709	-0.0150
C3	0.0437	0.0379	0.0058	5.9563	5.9621	-0.0058
C4	0.3016	0.3056	-0.0039	5.6984	5.6944	0.0039
H5	0.3698	0.3369	0.0329	0.6302	0.6631	-0.0329
H6	0.0153	0.0206	-0.0053	0.9847	0.9794	0.0053
H7	0.0025	0.0077	-0.0052	0.9975	0.9923	0.0052
H8	0.0136	0.0012	0.0124	0.9864	0.9988	-0.0124
H9	-0.0015	0.0000	-0.0015	1.0015	1.0000	0.0015
H10	0.0098	0.0121	-0.0023	0.9902	0.9879	0.0023
H11	0.0221	0.0055	0.0166	0.9779	0.9945	-0.0166
H12	0.0505	0.0441	0.0064	0.9495	0.9559	-0.0064
N13	-0.9898	-0.9631	-0.0267	7.9898	7.9631	0.0267
C14	1.5252	1.5184	0.0068	4.4748	4.4816	-0.0068
O15	-1.1940	-1.1726	-0.0214	9.1940	9.1726	0.0214
O16	-1.1375	-1.1096	-0.0279	9.1375	9.1096	0.0279
H17	0.6024	0.6058	-0.0034	0.3976	0.3942	0.0034

Table S3. Full set of intramolecular non-covalent diatomic interaction energies $E_{\mathrm{int}}^{\mathrm{A,B}}$ and their components ($V_{\mathrm{XC}}^{\mathrm{A,B}}$ and $V_{\mathrm{cl}}^{\mathrm{A,B}}$) in the lowest (**1a**) and higher (**1b**) energy conformers of S-proline also showing changes in these energy components on structural transformation from **1a** to **1b**. All values in kcal mol^{-1}.

Atom		$E_{\mathrm{int}}^{\mathrm{A,B}}$		$V_{\mathrm{XC}}^{\mathrm{A,B}}$		$V_{\mathrm{cl}}^{\mathrm{A,B}}$		**1a** *minus* **1b**		
A	**B**	**1a**	**1b**	**1a**	**1b**	**1a**	**1b**	$\Delta E_{\mathrm{int}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{XC}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{cl}}^{\mathrm{A,B}}$
C3	C1	-1.7	-0.8	-5.5	-4.1	3.9	3.3	-0.9	-1.4	0.6
C4	C1	21.8	21.3	-2.8	-4.3	24.6	25.6	0.6	1.6	-1.0
C4	C2	-1.8	-2.4	-5.1	-4.9	3.3	2.6	0.6	-0.2	0.7
H5	C1	28.3	26.5	-1.7	-2.0	29.9	28.5	1.8	0.3	1.5
H5	C2	2.3	1.5	-0.4	-0.2	2.7	1.8	0.8	-0.1	0.9
H5	C3	2.6	2.0	-0.2	-0.4	2.8	2.4	0.6	0.2	0.4
H5	C4	26.0	24.3	-1.8	-2.0	27.8	26.4	1.7	0.3	1.4
H6	C2	-2.1	-2.2	-3.3	-3.2	1.2	0.9	0.1	-0.1	0.2
H6	C3	-0.2	0.0	-0.5	-0.3	0.3	0.3	-0.2	-0.2	0.0
H6	C4	1.1	1.3	-0.4	-0.5	1.6	1.8	-0.2	0.1	-0.2
H6	H5	1.9	1.8	-0.1	-0.3	1.9	2.1	0.1	0.2	-0.2
H7	C2	-2.5	-2.7	-3.5	-3.5	1.0	0.9	0.2	0.0	0.2
H7	C3	-0.2	0.1	-0.5	-0.1	0.2	0.2	-0.3	-0.3	0.0
H7	C4	1.0	0.8	-0.1	-0.5	1.1	1.4	0.2	0.4	-0.2
H7	H5	0.9	1.1	-0.3	-0.5	1.2	1.5	-0.2	0.1	-0.3
H7	H6	-1.9	-1.7	-3.1	-3.1	1.2	1.3	-0.1	0.0	-0.1
H8	C1	-1.2	-1.8	-3.6	-3.6	2.4	1.8	0.6	0.0	0.6
H8	C3	-2.5	-2.8	-3.5	-3.6	1.0	0.8	0.3	0.1	0.2
H8	C4	0.7	0.7	-0.5	-0.2	1.2	0.8	0.1	-0.3	0.4
H8	H5	1.0	0.8	-0.1	0.0	1.0	0.8	0.2	0.0	0.3
H8	H6	0.2	0.1	-0.1	-0.1	0.3	0.2	0.1	0.0	0.1
H8	H7	-0.2	-0.4	-0.4	-0.7	0.3	0.3	0.2	0.2	0.0
H9	C1	-2.1	-1.9	-3.7	-3.6	1.7	1.7	-0.1	-0.1	0.0
H9	C3	-2.9	-2.9	-3.7	-3.7	0.8	0.8	0.0	0.0	0.0
H9	C4	0.2	0.5	-0.3	-0.3	0.6	0.8	-0.2	0.0	-0.2
H9	H5	0.4	0.5	0.0	0.0	0.4	0.5	-0.1	0.0	-0.1
H9	H6	-0.2	-0.3	-0.4	-0.6	0.3	0.3	0.1	0.1	0.0
H9	H7	-0.4	-0.2	-0.5	-0.4	0.1	0.2	-0.2	-0.1	0.0
H9	H8	-2.0	-2.2	-3.2	-3.4	1.2	1.2	0.2	0.2	0.0
H10	C1	0.7	1.0	-0.5	-0.3	1.2	1.3	-0.3	-0.3	-0.1
H10	C2	-2.6	-2.4	-3.6	-3.3	1.0	0.9	-0.2	-0.3	0.1
H10	C4	-2.0	-1.6	-3.9	-3.6	1.8	1.9	-0.4	-0.3	-0.1
H10	H5	0.7	1.1	0.0	0.0	0.8	1.1	-0.4	0.0	-0.4
H10	H6	0.1	0.1	0.0	0.0	0.1	0.1	0.0	0.0	0.0
H10	H7	-0.2	0.1	-0.3	0.0	0.1	0.1	-0.3	-0.3	0.0
H10	H8	-0.1	-0.3	-0.4	-0.6	0.3	0.3	0.2	0.2	0.0
H10	H9	-0.4	0.0	-0.5	-0.2	0.2	0.2	-0.4	-0.4	0.0
H11	C1	1.2	0.9	-0.5	-0.2	1.6	1.0	0.3	-0.3	0.6
H11	C2	-2.1	-2.6	-3.2	-3.5	1.1	0.9	0.5	0.3	0.2
H11	C4	-1.1	-2.1	-3.3	-3.8	2.2	1.6	1.0	0.5	0.6

Table S3 continues

Atom		$E_{\mathrm{int}}^{\mathrm{A,B}}$		$V_{\mathrm{XC}}^{\mathrm{A,B}}$		$V_{\mathrm{cl}}^{\mathrm{A,B}}$		**1a** *minus* **1b**		
A	**B**	**1a**	**1b**	**1a**	**1b**	**1a**	**1b**	$\Delta E_{\mathrm{int}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{XC}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{cl}}^{\mathrm{A,B}}$
H11	H5	1.3	0.5	0.0	-0.2	1.3	0.6	0.8	0.1	0.7
H11	H6	0.1	0.1	-0.1	0.0	0.1	0.1	0.0	0.0	0.0
H11	H7	0.1	0.0	0.0	0.0	0.1	0.1	0.0	0.0	0.0
H11	H8	0.2	-0.1	-0.1	-0.3	0.3	0.2	0.3	0.2	0.1
H11	H9	-0.1	-0.5	-0.4	-0.8	0.3	0.3	0.3	0.4	0.0
H11	H10	-1.7	-1.9	-3.1	-3.2	1.4	1.3	0.2	0.1	0.1
H12	C1	2.9	2.4	-0.2	-0.8	3.1	3.1	0.5	0.6	-0.1
H12	C2	0.1	0.1	-0.4	-0.3	0.5	0.4	0.0	-0.1	0.1
H12	C3	-1.3	-1.8	-3.0	-3.3	1.6	1.5	0.5	0.3	0.2
H12	H5	3.4	2.5	-0.4	-0.5	3.8	3.0	1.0	0.1	0.8
H12	H6	0.2	0.2	-0.1	0.0	0.2	0.2	0.0	0.0	0.0
H12	H7	0.1	-0.4	0.0	-0.6	0.1	0.2	0.5	0.6	-0.1
H12	H8	0.2	0.1	0.0	0.0	0.2	0.1	0.0	0.0	0.1
H12	H9	0.1	0.1	0.0	0.0	0.1	0.1	0.0	0.0	0.0
H12	H10	-0.2	-0.1	-0.6	-0.5	0.4	0.4	-0.1	-0.1	0.0
H12	H11	0.4	-0.2	-0.1	-0.5	0.5	0.3	0.6	0.4	0.2
N13	C2	-16.4	-13.0	-7.8	-7.3	-8.6	-5.8	-3.3	-0.5	-2.8
N13	C3	-15.6	-15.1	-6.4	-7.4	-9.2	-7.7	-0.5	1.0	-1.5
N13	H6	-11.6	-11.9	-5.4	-5.2	-6.2	-6.6	0.3	-0.2	0.4
N13	H7	-10.2	-10.6	-5.6	-5.7	-4.6	-4.9	0.4	0.1	0.3
N13	H8	-4.1	-2.7	-0.6	-0.5	-3.5	-2.2	-1.4	-0.1	-1.3
N13	H9	-1.9	-2.2	-0.5	-0.3	-1.3	-1.9	0.3	-0.3	0.6
N13	H10	-3.0	-3.9	-0.2	-0.7	-2.8	-3.2	0.8	0.4	0.4
N13	H11	-4.7	-2.7	-0.5	-0.5	-4.2	-2.2	-2.0	0.0	-2.0
N13	H12	-15.8	-15.0	-4.8	-5.4	-11.0	-9.7	-0.8	0.6	-1.4
C14	C1	50.7	47.1	-0.2	-0.5	50.9	47.6	3.5	0.3	3.3
C14	C2	6.9	4.7	-0.4	-0.4	7.3	5.1	2.2	0.0	2.2
C14	C3	6.0	5.8	-4.4	-3.3	10.4	9.1	0.2	-1.1	1.3
C14	H5	58.6	60.2	-0.2	-0.3	58.8	60.5	-1.6	0.2	-1.8
C14	H6	3.2	3.5	0.0	-0.1	3.2	3.6	-0.3	0.1	-0.4
C14	H7	2.0	1.9	0.0	0.0	2.0	1.9	0.1	0.0	0.1
C14	H8	3.5	1.5	0.0	0.0	3.6	1.5	2.0	0.0	2.0
C14	H9	-0.8	1.2	-0.2	0.0	-0.6	1.3	-2.0	-0.2	-1.8
C14	H10	3.7	3.7	-0.4	-0.1	4.1	3.8	0.1	-0.3	0.4
C14	H11	4.1	1.4	-0.7	-0.6	4.8	1.9	2.7	-0.2	2.9
C14	H12	11.4	9.4	-4.1	-4.9	15.5	14.3	2.0	0.8	1.2
C14	N13	-188.2	-176.9	-6.0	-5.7	-182.2	-171.1	-11.3	-0.3	-11.1
O15	C1	-32.4	-31.2	-0.1	-0.1	-32.4	-31.1	-1.2	0.0	-1.2
O15	C2	-5.1	-3.7	-0.1	-0.2	-5.0	-3.6	-1.4	0.0	-1.4
O15	C3	-8.3	-7.7	-2.1	-2.7	-6.3	-5.0	-0.7	0.6	-1.2

Table S3 continues

Atom		$E_{\mathrm{int}}^{\mathrm{A,B}}$		$V_{\mathrm{XC}}^{\mathrm{A,B}}$		$V_{\mathrm{cl}}^{\mathrm{A,B}}$		**1a** *minus* **1b**		
A	**B**	**1a**	**1b**	**1a**	**1b**	**1a**	**1b**	$\Delta E_{\mathrm{int}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{XC}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{cl}}^{\mathrm{A,B}}$
O15	C4	-57.6	-58.2	-9.7	-9.5	-47.9	-48.7	0.6	-0.1	0.8
O15	H5	-37.2	-37.7	-0.1	0.0	-37.2	-37.7	0.5	0.0	0.5
O15	H6	-2.1	-2.4	0.0	0.0	-2.1	-2.4	0.4	0.0	0.3
O15	H7	-1.1	-1.3	0.0	0.0	-1.1	-1.2	0.1	0.0	0.1
O15	H8	-2.4	-1.0	0.0	0.0	-2.3	-1.0	-1.3	0.0	-1.3
O15	H9	0.3	-0.8	0.0	0.0	0.3	-0.8	1.1	0.0	1.2
O15	H10	-3.0	-2.9	-0.1	-0.5	-2.9	-2.4	-0.1	0.4	-0.5
O15	H11	-4.9	-2.3	-2.1	-1.4	-2.8	-0.9	-2.7	-0.8	-1.9
O15	H12	-10.8	-9.4	-1.4	-1.0	-9.4	-8.3	-1.4	-0.3	-1.1
O15	N13	109.0	104.0	-0.9	-0.9	109.8	104.9	4.9	0.0	4.9
O16	C1	-40.5	-34.7	-0.2	-0.2	-40.3	-34.5	-5.8	0.0	-5.8
O16	C2	-5.3	-3.2	-0.3	-0.1	-5.0	-3.1	-2.1	-0.2	-1.9
O16	C3	-7.0	-5.9	-0.5	-0.5	-6.4	-5.3	-1.1	0.0	-1.1
O16	C4	-63.6	-61.1	-8.2	-8.4	-55.4	-52.7	-2.5	0.2	-2.7
O16	H5	-47.4	-47.3	-0.1	-0.5	-47.3	-46.8	-0.1	0.4	-0.5
O16	H6	-2.4	-2.5	0.0	0.0	-2.3	-2.5	0.1	0.0	0.2
O16	H7	-1.8	-1.3	-0.1	0.0	-1.7	-1.3	-0.5	-0.1	-0.4
O16	H8	-2.6	-1.0	0.0	0.0	-2.6	-0.9	-1.6	0.0	-1.6
O16	H9	0.4	-0.7	-0.6	0.0	0.9	-0.7	1.1	-0.6	1.7
O16	H10	-2.5	-2.1	-0.1	0.0	-2.4	-2.1	-0.4	-0.1	-0.3
O16	H11	-3.2	-1.1	-0.1	0.0	-3.1	-1.0	-2.1	0.0	-2.1
O16	H12	-9.2	-8.5	-0.5	-0.7	-8.7	-7.8	-0.7	0.2	-0.9
O16	N13	140.9	128.0	-11.9	-7.0	152.8	134.9	12.9	-5.0	17.9
O16	O15	178.9	170.1	-28.4	-28.7	207.3	198.8	8.8	0.3	8.5
H17	C1	27.1	21.6	-0.2	-0.1	27.3	21.7	5.5	-0.1	5.6
H17	C2	3.0	1.7	0.0	-0.1	3.0	1.8	1.2	0.0	1.2
H17	C3	3.8	3.0	0.0	0.0	3.8	3.0	0.8	0.0	0.8
H17	C4	33.6	30.3	-0.5	-0.4	34.1	30.7	3.3	-0.1	3.4
H17	H5	32.2	30.0	-0.1	-0.1	32.4	30.1	2.2	0.0	2.3
H17	H6	1.5	1.5	-0.1	0.0	1.6	1.5	0.0	0.0	0.0
H17	H7	1.2	0.8	-0.1	0.0	1.2	0.8	0.3	-0.1	0.4
H17	H8	1.5	0.6	0.0	0.0	1.5	0.6	1.0	0.0	1.0
H17	H9	-0.4	0.4	0.0	0.0	-0.4	0.4	-0.8	0.0	-0.8
H17	H10	1.3	1.1	0.0	0.0	1.3	1.1	0.2	0.0	0.2
H17	H11	1.8	0.6	0.0	0.0	1.8	0.6	1.2	0.0	1.2
H17	H12	4.8	4.3	0.0	0.0	4.9	4.4	0.5	0.0	0.5
H17	N13	-132.8	-99.4	-19.1	-6.9	-113.8	-92.5	-33.5	-12.2	-21.3
H17	C14	175.6	171.5	-1.0	-0.9	176.6	172.4	4.2	-0.1	4.3
H17	O15	-86.3	-85.3	-0.5	-0.7	-85.8	-84.7	-1.0	0.2	-1.1

Table S4. Diatomic interaction energies $E_{\text{int}}^{\text{A,B}}$ and their components ($V_{\text{XC}}^{\text{A,B}}$ and $V_{\text{cl}}^{\text{A,B}}$) between covalently bonded atoms in the lowest (**1a**) and higher (**1b**) energy conformers of S-proline also showing changes in these energy components on structural transformation from **1a** to **1b**.. All values in kcal mol^{-1}.

Atom		$E_{\text{int}}^{\text{A,B}}$		$V_{\text{XC}}^{\text{A,B}}$		$V_{\text{cl}}^{\text{A,B}}$		**1a** *minus* **1b**		
A	**B**	**1a**	**1b**	**1a**	**1b**	**1a**	**1b**	$\Delta E_{\text{int}}^{\text{A,B}}$	$\Delta V_{\text{XC}}^{\text{A,B}}$	$\Delta V_{\text{cl}}^{\text{A,B}}$
C2	C1	-166.9	-164.4	-182.9	-177.4	15.9	12.9	-2.50	-5.51	3.01
C3	C2	-171.5	-169.0	-182.9	-179.4	11.5	10.5	-2.50	-3.52	1.02
C4	C3	-162.9	-165.3	-177.3	-179.4	14.3	14.1	2.37	2.19	0.18
H6	C1	-148.4	-148.1	-173.9	-174.2	25.5	26.1	-0.34	0.25	-0.59
H7	C1	-149.4	-148.7	-173.1	-173.2	23.7	24.5	-0.69	0.08	-0.77
H8	C2	-153.3	-154.4	-175.2	-175.7	21.9	21.3	1.11	0.52	0.59
H9	C2	-153.6	-154.5	-174.3	-175.7	20.7	21.2	0.91	1.41	-0.49
H10	C3	-153.3	-153.7	-174.4	-175.4	21.1	21.7	0.39	1.01	-0.62
H11	C3	-152.7	-153.3	-174.6	-174.4	21.9	21.1	0.62	-0.19	0.81
H12	C4	-144.0	-141.8	-170.8	-167.1	26.8	25.3	-2.18	-3.66	1.48
N13	C1	-274.8	-273.3	-177.7	-180.7	-97.0	-92.7	-1.45	2.94	-4.39
N13	C4	-269.3	-265.6	-182.0	-184.7	-87.3	-81.0	-3.67	2.64	-6.30
N13	H5	-247.1	-238.2	-161.8	-163.6	-85.3	-74.5	-8.91	1.88	-10.79
C14	C4	-80.3	-82.9	-174.2	-179.9	93.9	97.0	2.66	5.74	-3.08
O15	C14	-862.3	-865.2	-244.1	-247.7	-618.3	-617.5	2.82	3.64	-0.82
O16	C14	-665.4	-632.4	-180.1	-173.5	-485.4	-459.0	-33.00	-6.63	-26.38
H17	O16	-312.1	-317.3	-100.5	-112.7	-211.6	-204.6	5.19	12.23	-7.04
	Total:	-4267	-4228	-2980	-2995	-1288	-1234	-39.2	15.0	-54.2

Table S5. Interaction energies ($E_{\mathrm{int}}^{\mathrm{A},\mathcal{R}}$ in kcal mol^{-1}) between atom A and a molecular fragment $\mathcal{R}$ (made of remaining atoms of S-proline) computed for **1a** and **1b**. $\Delta E_{\mathrm{int}}^{\mathrm{A},\mathcal{R}}$ = { $E_{\mathrm{int}}^{\mathrm{A},\mathcal{R}}$ in **1a**} – { $E_{\mathrm{int}}^{\mathrm{A},\mathcal{R}}$ in **1b**}.

	$E_{\mathrm{int}}^{\mathrm{A},\mathcal{R}}$		$\Delta V_{\mathrm{XC}}^{\mathrm{A},\mathcal{R}}$		$\Delta V_{\mathrm{cl}}^{\mathrm{A},\mathcal{R}}$		**1a** *minus* **1b**		
Atom A	**1a**	**1b**	**1a**	**1b**	**1a**	**1b**	$\Delta E_{\mathrm{int}}^{\mathrm{A},\mathcal{R}}$	$\Delta V_{\mathrm{XC}}^{\mathrm{A},\mathcal{R}}$	$\Delta V_{\mathrm{cl}}^{\mathrm{A},\mathcal{R}}$
C1	-684.7	-683.0	-726.9	-725.3	42.2	42.3	-1.7	-1.6	-0.1
C2	-670.3	-665.7	-743.5	-735.2	73.2	69.5	-4.6	-8.3	3.7
C3	-668.2	-666.2	-739.7	-738.4	71.5	72.3	-2.0	-1.3	-0.8
C4	-697.7	-700.9	-740.9	-749.7	43.3	48.7	3.3	8.7	-5.5
H5	-171.9	-170.4	-167.1	-170.8	-4.9	0.4	-1.5	3.7	-5.2
H6	-160.7	-160.6	-187.5	-187.7	26.9	27.1	-0.1	0.1	-0.2
H7	-162.6	-162.4	-187.8	-188.3	25.2	25.9	-0.2	0.5	-0.7
H8	-161.1	-163.0	-187.7	-188.7	26.6	25.7	2.0	1.0	1.0
H9	-163.3	-163.5	-188.6	-189.0	25.3	25.5	0.2	0.4	-0.2
H10	-162.5	-161.8	-188.2	-188.4	25.7	26.6	-0.7	0.1	-0.8
H11	-161.5	-163.3	-188.8	-189.2	27.3	25.8	1.8	0.4	1.4
H12	-157.9	-158.0	-186.3	-185.6	28.5	27.5	0.2	-0.8	1.0
N13	-945.6	-899.9	-591.4	-582.3	-354.2	-317.5	-45.8	-9.1	-36.7
C14	-1470.3	-1443.1	-616.3	-618.2	-854.1	-824.9	-27.2	1.9	-29.2
O15	-826.2	-835.2	-289.5	-293.5	-536.7	-541.7	9.1	4.1	5.0
O16	-842.7	-820.8	-331.7	-332.5	-511.1	-488.4	-21.9	0.8	-22.7
H17	-244.2	-234.3	-122.2	-122.0	-121.9	-112.4	-9.8	-0.3	-9.6

Insight from a single atom perspective considering the $E_{\mathrm{int}}^{\mathrm{A},\mathcal{R}}$ term. The total interaction energy between an atom A and all remaining atoms in a molecule (they constitute a molecular fragment $\mathcal{R}$) can also be interpreted as how 'friendly' a molecular environment is toward a particular atom and with increase in 'friendliness' atoms are involved in overall stronger (more negative) $E_{\mathrm{int}}^{\mathrm{A},\mathcal{R}}$ intramolecular interactions. A full set of $E_{\mathrm{int}}^{\mathrm{A},\mathcal{R}}$ data provided in Table S5 reveals that, on **1b** to **1a** structural change, 11 out of 17 atoms became involved in stronger interactions with $\mathcal{R}$. Most favourable change in $E_{\mathrm{int}}^{\mathrm{A},\mathcal{R}}$ by –45.8, –27.2, –21.9, and –9.8 kcal mol^{-1} was found for N13, C14, O16 and H17, respectively, whereas O15 experienced most 'unfriendly' change when in **1a**, but only by +9.1 kcal mol^{-1}. Interestingly, C14 and N13 are involved in most attractive interactions with $\mathcal{R}$ in both conformers with, e.g., $E_{\mathrm{int}}^{\mathrm{A},\mathcal{R}}$ of –1470.3 and –945.6 kcal mol^{-1}, respectively, in **1a**.

Insight from a molecular fragment perspective. Treating all 136 unique 2-atom pairs as molecular fragments of **1** on equal footing we found that, on the **1b** → **1a** structural change the {H17,N13} molecular fragment became most stabilised with *loc*-FAMSEC of –18.3 kcal mol^{-1} and also contributed –7.0 kcal mol^{-1} to **1a** stability, as defined by *mol*-FAMSEC. However, the {O16,N13} fragment stabilised **1a** most (*mol*-FAMSEC = –49.7 kcal mol^{-1}) as its interactions with remaining atoms became stronger by –93.5 kcal mol^{-1}.

Often, H-bonds are analysed using a 3-atom molecular fragment involving PD–H···PA (or X–H···Y) where PD = X stands for a proton donor and PA = Y represents a proton acceptor. As expected, significantly stronger O16–H17···N13 H-bond in **1a** contributed –29.7 kcal mol^{-1} (as a molecular fragment {O16,H17,N16}) toward stability of **1a**. However, among all 680 unique 3-atom fragments in **1**, {N13,O15,O16} stabilized **1a** most with *mol*-FAMSEC = –56 kcal mol^{-1} and this is due to most significant change (in stabilising manner) in the interaction energy between this fragment and the remaining atoms of **1** (–111.9 kcal mol^{-1}).

End of PART S3

PART S4

Data pertaining to global minimum adducts of **1a** and **1b** with acetone **2**.

S-proline (**1a** and **1b**) and acetone (**2**) molecules were placed relative to each other in such a way as to facilitate the consecutive C–N bond formation and were energy optimised without any constrain – resultant adducts are shown in Fig. S1.

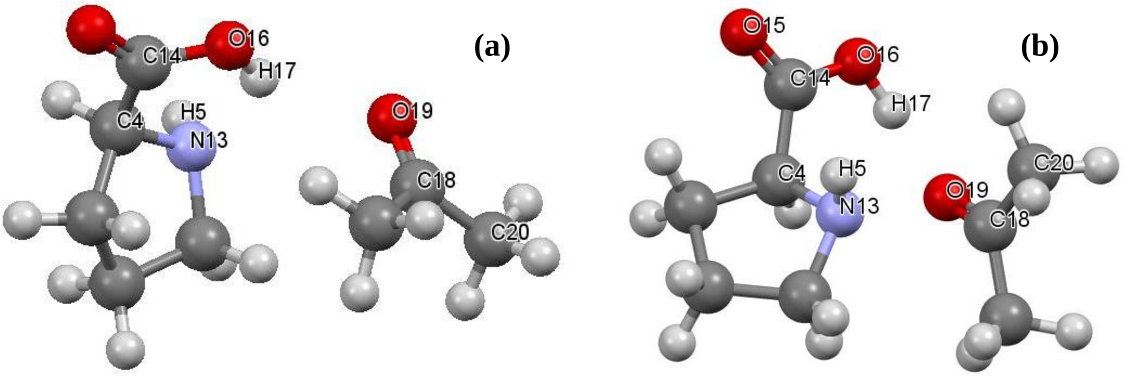

Figure S1. Initial optimised adduct structures used as inputs for search of global minimum structures of adducts: (a) – **1a** plus **2**; (b) – **1b** plus **2**.

In search for a global minimum structure (GMS) of adducts, structures shown in Fig. S1 were used as inputs for a dihedral scan, DA(C4,N13,C18,C20) that resulted in rotating **2** relative to **1** – results obtained are shown in Fig. S2.

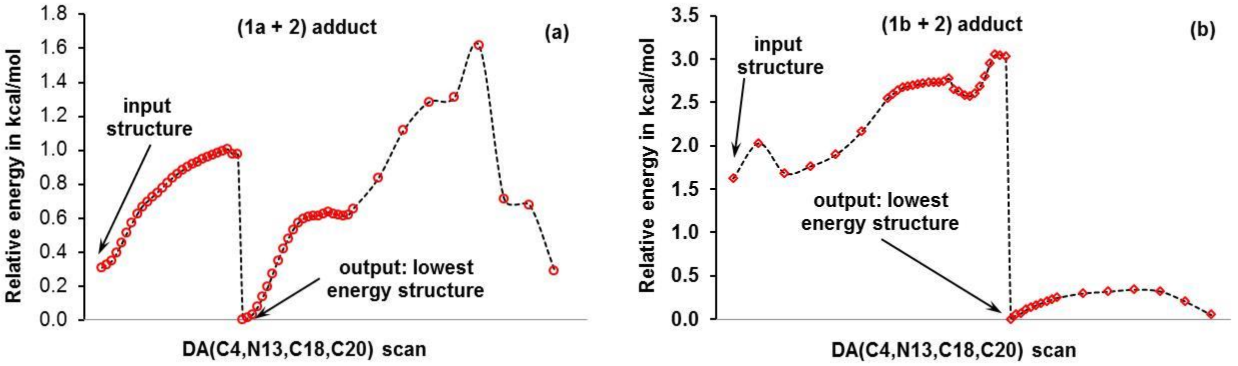

Figure S2. Data obtained from DA(C4,N13,C18,C20) scans in search for GMS of adducts between **1** and **2**. Part (a) – data for **1a** and **2**. Part (b) – data for **1b** and **2**. Energy change was computed relative to energies of GMS of adducts, either **3a** or **3b**.

Data shown in Fig. S2 makes it clear that molecules are free to move relative to each other with rotational energy barrier of about 1.6 kcal mol^{-1} found for **1a** being lower, relative to the **1b**, by about 1.4 kcal mol^{-1}. The lowest energy adducts obtained from the scans shown in Fig. S2 were energy optimised and the resultant GMS of **3a** and **3b**, as molecular graphs, are shown in Fig. S3.

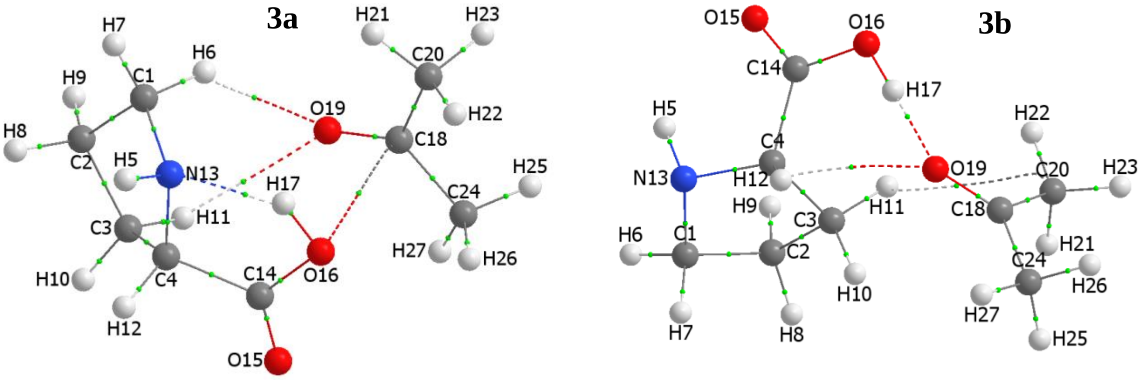

Figure S3. Molecular graphs of the global minimum energy structures **3a** (containing **1a**) and **3b** (containing **1b**) obtained for adducts between **1** and **2**.

Molecular graphs in Fig. S3 show that the intramolecular O16H17···N13 H-bond in **1b** has been broken and intermolecular O16H17···O19 H-bond has been formed in **3b**; this makes **3b** well pre-organised for the subsequent proton transfer. None of the GMS of adducts shows suitable placement of C18 of **2** relative to N13 of **1**. This already suggests that adducts must be pre-organised prior the N13–C18 bond formation.

Table S6. Energies (in au) and changes in energies as $E(\mathbf{3}) - E(\mathbf{1}+\mathbf{2})$ (in kcal mol^{-1}) computed for the indicated structures at the B3LYP/6-311++G(d,p)/GD3 and MP2/6-311++G(d.p) (italic) levels.

Structure	E	**Δ**	E_{ZPVE}	**Δ**	H	**Δ**	G	**Δ**
1a + 2	-594.5415		-594.3138		-594.2995		-594.3730	
	-592.8585		*-592.6276*		*-592.6134*		*-592.6874*	
3a	-594.5478	-3.9	-594.3188	-3.1	-594.3034	-2.4	-594.3632	6.1
	-592.8656	*-4.4*	*-592.6337*	*-3.8*	*-592.6183*	*-3.1*	*-592.6778*	*6.0*
1b + 2	-594.5309	–	-594.3032		-594.2885		-594.3630	
	-592.8476		*-592.6168*		*-592.6022*		*-592.6772*	
3b	-594.5460	-9.5	-594.3171	-8.7	-594.3017	-8.2	-594.3623	0.4
	-592.8619	*-9.0*	*-592.6297*	*-8.1*	*-592.6144*	*-7.7*	*-592.6742*	*1.9*
		Energy difference for 3a relative to 3b						
		-1.1		-1.1		-1.1		-0.5
		-2.3		*-2.5*		*-2.5*		*-2.2*

The origin of 3b adduct larger, relative to 3a, gain in stability

Our focus throughout this work is mainly on changes in the interaction energies, $\Delta E_{\text{int}}^{\text{A,B}}$, rather than self-atomic energy changes, $\Delta E_{\text{self}}^{\text{A}}$. This is because $\Delta E_{\text{int}}^{\text{A,B}}$ (i) can be seen as a driving force facilitating (or otherwise) a chemical change, (ii) there are many more diatomic interactions than atoms in a molecule. To this effect, the number of unique atom-pairs in any molecule (or molecular system) is $(n\times(n\text{-}1))/2$ where n is the number of atoms (e.g., n = 27 in **3a** and **3b**) whereas the number of unique diatomic pairs is 351 and interaction energies can vary extensively, and (iii) the $\Delta E_{\text{int}}^{\text{A,B}}$ values are often well over an order in magnitude larger when compared with $\Delta E_{\text{self}}^{\text{A}}$. For instance, 22 atoms (out of 27) experienced $|\Delta E_{\text{self}}^{\text{A}}| < 2$ kcal mol^{-1} and the largest change found on the **3a** formation is +8.3 kcal mol^{-1}. At the same time, the most significant changes $\Delta E_{\text{int}}^{\text{A,B}}$ were found to be –161.3 and +138.3 kcal mol^{-1} for {O19,C14} and {O18,14} atom pairs, respectively.

Relative to monomers **1** and **2**:

A) The total interaction energy change on the formation of adducts **3a** and **3b** (this includes all intra- and inter-molecular diatomic interactions) was computed to be –21.3 (in **3a**) and –46.1 (in **3b**) kcal mol^{-1}; hence, interactions have changed in more stabilizing manner, by –24.8 kcal mol^{-1}, in **3b**.

B) On adducts formation, the total intermolecular interaction energy between atoms of **1** and atoms of **2**, *i.e.*, the intermolecular interaction energy, was found to be –34.3 (in **3a**) and –53.6 (in **3b**) kcal mol^{-1}; hence entire molecules, **1** and **2**, interact stronger when in **3b**, by –19.3 kcal mol^{-1}.

C) From data under A) and B) it follows that intramolecular interactions in **1** and **2** also became stronger on the **3a** and **3b** formation but, at the same time, interactions between molecules played a dominant role in stabilizing the adducts.

D) The intramolecular O16H17···N13 in **1a** was preserved in **3a** but its strength slightly weakened, from $E_{\text{int}}^{\text{N13,H17}}$ of –132.8 kcal mol^{-1} in **1a** to –131.0 kcal mol^{-1} in the adduct **3a**. Totally opposite applies to **3b** as the intramolecular O16H17···N13 bond in **1b** is no longer present in **3b**. Importantly, however, a new inter-molecular O16H17···O19 H-bond was formed in **3b** with $E_{\text{int}}^{\text{H17,O19}}$ of –143.9 kcal mol^{-1}. This is –44.5 kcal mol^{-1} stronger relative to the initial intramolecular O16H17···N13 H-bond in **1b** and also –11.1 kcal mol^{-1} stronger than the intramolecular O16H17···N13 H-bond in the **3a** adduct.

Inspection of all unique 351 diatomic interactions and their energy changes on both adducts formation showed that two molecular fragments, $\mathcal{G}$ = {C1,C4,H5,N13,C14,O15,O16,H17} containing atoms of **1** and $\mathcal{H}$ = {C18,O19} made of atoms of **2**, should be considered. This is because their diatomic intermolecular interaction energies, $E_{\text{int}}^{\text{A,B}}$, in **3a** and **3b** are strongest among all intermolecular interactions (in absolute value, they all are well above 10 kcal mol^{-1} - see Table S7); full set of data, i.e., interaction energies and their components are provided in Tables S8 and S9. Furthermore, it is important to add that nearly all intramolecular interactions in **1a**, **1b** and **2** changed on the **3a** and **3b** formation but much less than 10 kcal mol^{-1}. Clearly, these two fragments, $\mathcal{G}$ and $\mathcal{H}$, that contain 10 atoms in total, can be seen as a driving force towards adducts formation.

Analysis of data in Table S7 leads to several important observations:

1. There are many atom pairs that became involved in strong diatomic interactions with $\left|E_{\text{int}}^{\text{A,B}}\right|$ > 50 kcal mol^{-1}. This demonstrates that formation of adducts **3a** and **3b** is an intermolecular event that cannot be ascribed just to a single ‘obvious’ classical interaction(s).
2. Considering the degree of preparedness for the C–N bond formation, the atoms in question (N13 and C18) are already involved in strong attractive interaction in both adducts with that in **3a** being stronger by about –19 kcal mol^{-1}. Focusing on the proton transfer, H17 and O19 are also involved in highly attractive interaction in **3a** and **3b** but by far more, by about –78.3 kcal mol^{-1} in **3b**. Hence, the two atom pairs, through their interactions, will facilitate the two chemical events but one must note that they are not the strongest among those shown in Table S7.
3. C14 of **1** is involved in the strongest intermolecular diatomic interactions, namely: (i) repulsive with C18 of **2** with $E_{\text{int}}^{\text{C14,C18}}$ = +138.3 kcal mol^{-1} (note that $E_{\text{int}}^{\text{C14,C18}}$ is more repulsive, by +20.5 kcal mol^{-1}, in **3a**) and (ii) attractive with O19 of **2** in both adducts, **3a** and **3b**. Remarkably, $E_{\text{int}}^{\text{C14,O19}}$ of –159.8 kcal mol^{-1} that was computed for the interaction in **3b**, shows that C14 and O19 interact stronger than H17 and O19 of the intermolecular O16H17···O19 H-bond in **3b**.
4. Molecular fragment $\mathcal{G}$ in **3a** shows (i) affinity to C18 of **2,** as it is involved in the overall attractive interactions of $E_{\text{int}}^{\mathcal{G},\text{C18}}$ = –19.5 kcal mol^{-1} and (ii) repulsive character toward O19 of

2, $E_{\text{int}}^{\mathcal{G},\text{O19}}$ = +14.1 kcal mol^{-1}. As a result, fragment $\mathcal{G}$ (formally in **1a**) slightly attracts oncoming **2** through interactions with $\mathcal{H}$ with $E_{\text{int}}^{\mathcal{G},\mathcal{H}}$ of –5.3 kcal mol^{-1}.

5. Exactly opposite trends are observed for the molecular fragment $\mathcal{G}$ in **1b**: (i) $\mathcal{G}$ is involved in the overall repulsive interaction with C18 $E_{\text{int}}^{\mathcal{G},\text{C18}}$ = +18.8 kcal mol^{-1}) but (ii) it shows large affinity to O19 with $E_{\text{int}}^{\mathcal{G},\text{O19}}$ of –62.0 kcal mol^{-1}. Due to the latter (it compensates over the repulsive interaction with C18) the two fragments, $\mathcal{G}$ and $\mathcal{H}$, are involved in highly attractive interaction of $E_{\text{int}}^{\mathcal{G},\mathcal{H}}$ = –43.2 kcal mol^{-1}.

Additional insight one can gain from two FAMSEC-defined terms that also indicate the importance of a molecular environment (placement of atoms relative to each other):

(a) Among 351 unique 2-atom fragments in each adduct, we found that the {O16,O19} fragment is involved in the strongest attractive interactions with remaining atoms of **3** (–287.4 and –396.6 kcal mol^{-1} in **3a** and **3b**, respectively) and this fragment contributed most to adducts stability, –148.3 (in **3a**) and –217.7 (in **3b**) kcal mol^{-1}. Note that both contributions are significantly larger in **3b**.

(b) Among 2925 unique 3-atom fragments in adducts, the {O15,O16,O19} fragment's interactions with remaining atoms of adducts improved most and became stronger by –525.0 (in **3a**) and –604.1 (in **3b**) kcal mol^{-1} and this fragment contribution to adducts stability was most significant, –268.4 (in **3a**) –314.8 (in **3b**) kcal mol^{-1}, in both cases, highly in favour of **3b**.

Table S7. Interaction energies (in kcal mol^{-1}) between atoms of molecular fragments $\mathcal{G}$ made of C1, C4, H5, N13, C14, O15, O16, and H17 (in **1**) and $\mathcal{H}$ = {C18,O19} (in **2**) computed for global minimum energy structures of **3a** and **3b** adducts.

PART A. Data for C18 of $\mathcal{H}$

Atom		**3a**			**3b**		
A	**B**	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$
C18	C1	26.23	-0.04	26.27	19.66	0.00	19.66
C18	C4	24.04	-0.01	24.05	21.87	-0.06	21.93
C18	H5	24.01	0.00	24.01	20.08	0.00	20.08
C18	N13	-76.94	-0.01	-76.92	-58.03	-0.01	-58.02
C18	C14	138.29	-0.13	138.42	117.75	-0.01	117.76
C18	O15	-98.63	-0.11	-98.52	-73.85	-0.01	-73.84
C18	O16	-113.43	-1.72	-111.72	-114.24	-0.18	-114.07
C18	H17	56.95	-0.01	56.96	85.59	-0.25	85.84
		$E_{\text{int}}^{\mathcal{G},\text{C18}}$	$V_{\text{XC}}^{\mathcal{G},\text{C18}}$	$V_{\text{cl}}^{\mathcal{G},\text{C18}}$	$E_{\text{int}}^{\mathcal{G},\text{C18}}$	$V_{\text{XC}}^{\mathcal{G},\text{C18}}$	$V_{\text{cl}}^{\mathcal{G},\text{C18}}$
		-19.5	-2.0	-17.4	18.8	-0.51	19.33

PART B. Data for O19 of $\mathcal{H}$

Atom		**3a**			**3b**		
A	**B**	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$
O19	C1	-34.37	-1.05	-33.32	-25.50	-0.01	-25.49
O19	C4	-29.66	-0.10	-29.56	-30.70	-1.38	-29.32
O19	H5	-29.51	-0.01	-29.50	-26.41	-0.01	-26.39
O19	N13	94.34	-0.11	94.45	76.41	-0.11	76.52
O19	C14	-161.33	-0.30	-161.03	-159.84	-0.18	-159.66
O19	O15	115.09	-0.16	115.25	97.83	-0.17	98.00
O19	O16	125.14	-0.94	126.08	150.04	-8.19	158.23
O19	H17	-65.55	-0.01	-65.54	-143.88	-18.25	-125.62
		$E_{\text{int}}^{\mathcal{G},\text{O19}}$	$V_{\text{XC}}^{\mathcal{G},\text{O19}}$	$V_{\text{cl}}^{\mathcal{G},\text{O19}}$	$E_{\text{int}}^{\mathcal{G},\text{O19}}$	$V_{\text{XC}}^{\mathcal{G},\text{O19}}$	$V_{\text{cl}}^{\mathcal{G},\text{O19}}$
		14.1	-2.7	16.8	-62.0	-28.3	-33.7

PART C. Inter-fragment interaction energies.

Inter-fragment interaction energies					
3a			**3b**		
$E_{\text{int}}^{\mathcal{G},\mathcal{H}}$	$V_{\text{XC}}^{\mathcal{G},\mathcal{H}}$	$V_{\text{cl}}^{\mathcal{G},\mathcal{H}}$	$E_{\text{int}}^{\mathcal{G},\mathcal{H}}$	$V_{\text{XC}}^{\mathcal{G},\mathcal{H}}$	$V_{\text{cl}}^{\mathcal{G},\mathcal{H}}$
-5.3	-4.7	-0.6	-43.2	-28.8	-14.4

Table S8. Full set of intra- and inter-molecular diatomic interaction energies $E_{\text{int}}^{\text{A,B}}$ and their components, $V_{\text{XC}}^{\text{A,B}}$ and $V_{\text{cl}}^{\text{A,B}}$, obtained for the global minimum energy adduct **3a** and changes in these energies on (**1a**+**2**) → **3a**. All values in kcal mol^{-1}.

Atom		**3a**			**3a *minus* (1a+2)**		
A	**B**	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$	$\Delta E_{\text{int}}^{\text{A,B}}$	$\Delta V_{\text{XC}}^{\text{A,B}}$	$\Delta V_{\text{cl}}^{\text{A,B}}$
C2	C1	-167.0	-182.4	15.5	-0.05	0.42	-0.46
C3	C1	-2.1	-5.6	3.5	-0.39	-0.02	-0.36
C3	C2	-171.2	-182.7	11.4	0.24	0.28	-0.04
C4	C1	21.2	-3.0	24.2	-0.68	-0.21	-0.46
C4	C2	-1.8	-4.9	3.2	0.04	0.16	-0.12
C4	C3	-161.8	-175.0	13.2	1.12	2.24	-1.12
H5	C1	27.7	-1.8	29.5	-0.56	-0.12	-0.44
H5	C2	2.4	-0.1	2.6	0.07	0.21	-0.14
H5	C3	2.5	-0.1	2.6	-0.17	0.05	-0.22
H5	C4	25.3	-1.9	27.2	-0.70	-0.09	-0.60
H6	C1	-147.1	-172.1	25.0	1.35	1.86	-0.51
H6	C2	-2.4	-3.5	1.1	-0.23	-0.18	-0.05
H6	C3	-0.1	-0.4	0.3	0.09	0.05	0.04
H6	C4	1.6	-0.1	1.8	0.50	0.29	0.21
H6	H5	1.8	-0.3	2.1	-0.09	-0.29	0.21
H7	C1	-148.3	-174.2	25.8	1.03	-1.09	2.12
H7	C2	-2.1	-3.2	1.1	0.36	0.35	0.01
H7	C3	-0.2	-0.5	0.3	0.04	0.00	0.03
H7	C4	1.2	-0.4	1.6	0.20	-0.30	0.49
H7	H5	1.7	-0.3	2.0	0.76	-0.04	0.79
H7	H6	-1.5	-2.9	1.4	0.35	0.18	0.17
H8	C1	-2.3	-3.8	1.5	-1.09	-0.18	-0.92
H8	C2	-153.8	-174.5	20.7	-0.54	0.67	-1.20
H8	C3	-3.0	-3.8	0.8	-0.56	-0.33	-0.23
H8	C4	0.2	-0.3	0.5	-0.56	0.19	-0.76
H8	H5	0.0	-0.1	0.0	-1.00	0.00	-0.99
H8	H6	-0.3	-0.5	0.2	-0.52	-0.41	-0.11
H8	H7	-0.2	-0.4	0.2	-0.01	0.02	-0.03
H9	C1	-1.4	-3.5	2.0	0.62	0.25	0.37
H9	C2	-153.3	-174.9	21.7	0.34	-0.64	0.98
H9	C3	-2.7	-3.5	0.8	0.20	0.20	0.00
H9	C4	0.5	-0.5	1.0	0.26	-0.16	0.41
H9	H5	0.9	0.0	1.0	0.53	0.00	0.53
H9	H6	-0.1	-0.4	0.3	0.12	0.07	0.05
H9	H7	0.2	-0.1	0.3	0.54	0.43	0.11
H9	H8	-2.1	-3.2	1.1	-0.11	-0.03	-0.08
H10	C1	0.9	-0.5	1.4	0.19	0.02	0.17
H10	C2	-2.3	-3.3	1.0	0.30	0.28	0.02
H10	C3	-153.8	-175.6	21.8	-0.50	-1.22	0.72
H10	C4	-1.8	-3.6	1.8	0.22	0.23	-0.02

Table S8 continues

Atom		**3a**			**3a *minus* (1a+2)**		
A	**B**	$E_{\mathrm{int}}^{\mathrm{A,B}}$	$V_{\mathrm{XC}}^{\mathrm{A,B}}$	$V_{\mathrm{cl}}^{\mathrm{A,B}}$	$\Delta E_{\mathrm{int}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{XC}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{cl}}^{\mathrm{A,B}}$
H10	H5	1.0	0.0	1.0	0.28	-0.01	0.29
H10	H6	0.1	0.0	0.1	0.04	0.01	0.04
H10	H7	0.1	-0.1	0.1	0.23	0.25	-0.02
H10	H8	-0.2	-0.5	0.2	-0.10	-0.04	-0.05
H10	H9	0.2	-0.1	0.2	0.54	0.45	0.08
H11	C1	1.4	-0.3	1.7	0.22	0.15	0.07
H11	C2	-2.3	-3.5	1.1	-0.24	-0.25	0.02
H11	C3	-152.2	-173.2	21.0	0.56	1.43	-0.87
H11	C4	-1.4	-3.5	2.1	-0.25	-0.19	-0.06
H11	H5	1.4	0.0	1.4	0.05	0.01	0.04
H11	H6	0.0	-0.1	0.2	-0.03	-0.08	0.05
H11	H7	0.1	0.0	0.1	0.08	0.01	0.07
H11	H8	-0.3	-0.5	0.2	-0.53	-0.40	-0.13
H11	H9	-0.1	-0.4	0.3	0.00	-0.06	0.06
H11	H10	-1.6	-3.0	1.4	0.08	0.05	0.02
H12	C1	2.8	-0.2	3.0	-0.07	-0.03	-0.04
H12	C2	0.3	-0.2	0.5	0.19	0.19	-0.01
H12	C3	-1.5	-3.0	1.5	-0.17	-0.03	-0.14
H12	C4	-144.2	-170.6	26.5	-0.14	0.15	-0.29
H12	H5	3.3	-0.4	3.7	-0.15	-0.10	-0.05
H12	H6	0.2	0.0	0.2	0.05	0.02	0.03
H12	H7	0.2	0.0	0.2	0.07	-0.02	0.09
H12	H8	0.0	-0.1	0.1	-0.13	-0.01	-0.12
H12	H9	0.1	0.0	0.2	0.08	0.00	0.08
H12	H10	-0.2	-0.6	0.4	0.05	0.02	0.03
H12	H11	0.1	-0.3	0.4	-0.28	-0.25	-0.03
N13	C1	-273.4	-177.7	-95.7	1.39	0.05	1.34
N13	C2	-16.3	-8.0	-8.2	0.10	-0.23	0.33
N13	C3	-14.0	-5.9	-8.1	1.53	0.48	1.05
N13	C4	-266.6	-182.2	-84.4	2.69	-0.16	2.85
N13	H5	-245.9	-162.3	-83.7	1.16	-0.49	1.65
N13	H6	-12.5	-5.6	-6.9	-0.83	-0.15	-0.68
N13	H7	-11.8	-5.3	-6.5	-1.63	0.35	-1.98
N13	H8	-1.6	-0.7	-0.9	2.53	-0.09	2.62
N13	H9	-3.6	-0.7	-2.9	-1.69	-0.16	-1.53
N13	H10	-3.8	-0.4	-3.4	-0.73	-0.18	-0.55
N13	H11	-4.4	-0.2	-4.2	0.31	0.33	-0.02
N13	H12	-15.7	-5.0	-10.8	0.11	-0.15	0.26
C14	C1	50.2	-0.2	50.4	-0.47	0.00	-0.48
C14	C2	7.2	-0.3	7.5	0.30	0.04	0.26

Table S8 continues

Atom		**3a**			**3a *minus* (1a+2)**		
A	**B**	$E_{\mathrm{int}}^{\mathrm{A,B}}$	$V_{\mathrm{XC}}^{\mathrm{A,B}}$	$V_{\mathrm{cl}}^{\mathrm{A,B}}$	$\Delta E_{\mathrm{int}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{XC}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{cl}}^{\mathrm{A,B}}$
C14	C3	4.9	-4.4	9.3	-1.10	0.02	-1.12
C14	C4	-82.7	-176.4	93.8	-2.39	-2.23	-0.16
C14	H5	57.1	-0.2	57.3	-1.54	-0.04	-1.50
C14	H6	3.5	0.0	3.5	0.27	-0.01	0.28
C14	H7	3.7	0.0	3.8	1.75	0.00	1.75
C14	H8	0.6	0.0	0.6	-2.90	0.02	-2.91
C14	H9	2.1	0.0	2.2	2.94	0.18	2.77
C14	H10	4.1	-0.1	4.2	0.37	0.26	0.11
C14	H11	3.7	-1.1	4.8	-0.39	-0.34	-0.06
C14	H12	11.0	-4.3	15.3	-0.35	-0.13	-0.22
C14	N13	-186.4	-5.8	-180.5	1.78	0.16	1.62
O15	C1	-32.1	-0.1	-32.0	0.32	0.01	0.32
O15	C2	-5.3	-0.2	-5.2	-0.23	-0.06	-0.17
O15	C3	-7.5	-2.3	-5.2	0.87	-0.18	1.05
O15	C4	-56.9	-9.6	-47.3	0.70	0.07	0.63
O15	H5	-36.4	-0.1	-36.3	0.83	-0.01	0.84
O15	H6	-2.3	0.0	-2.3	-0.22	0.01	-0.23
O15	H7	-2.4	0.0	-2.4	-1.28	-0.01	-1.27
O15	H8	-0.4	0.0	-0.3	2.00	0.00	2.01
O15	H9	-1.4	0.0	-1.4	-1.75	0.03	-1.78
O15	H10	-2.9	-0.3	-2.7	0.02	-0.18	0.20
O15	H11	-4.2	-1.1	-3.1	0.73	1.01	-0.28
O15	H12	-10.5	-1.2	-9.3	0.31	0.14	0.18
O15	N13	108.0	-0.9	108.9	-0.96	-0.01	-0.95
O15	C14	-862.2	-244.1	-618.1	0.19	-0.03	0.22
O16	C1	-40.3	-0.2	-40.0	0.25	-0.03	0.28
O16	C2	-5.3	-0.1	-5.2	0.03	0.18	-0.14
O16	C3	-6.2	-0.5	-5.7	0.75	0.00	0.76
O16	C4	-63.0	-8.2	-54.8	0.53	-0.04	0.58
O16	H5	-46.1	-0.2	-45.9	1.34	-0.02	1.35
O16	H6	-2.6	-0.1	-2.5	-0.26	-0.09	-0.17
O16	H7	-2.9	0.0	-2.9	-1.15	0.06	-1.22
O16	H8	-0.5	0.0	-0.5	2.14	0.01	2.13
O16	H9	-1.5	0.0	-1.5	-1.89	0.53	-2.43
O16	H10	-2.6	0.0	-2.6	-0.14	0.05	-0.19
O16	H11	-3.0	-0.1	-2.9	0.21	-0.02	0.23
O16	H12	-9.1	-0.5	-8.6	0.09	-0.01	0.10
O16	N13	140.4	-11.6	152.0	-0.50	0.32	-0.81
O16	C14	-662.8	-178.7	-484.1	2.66	1.44	1.22
O16	O15	179.7	-28.0	207.7	0.82	0.43	0.39

Table S8 continues

Atom		**3a**			**3a *minus* (1a+2)**		
A	**B**	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$	$\Delta E_{\text{int}}^{\text{A,B}}$	$\Delta V_{\text{XC}}^{\text{A,B}}$	$\Delta V_{\text{cl}}^{\text{A,B}}$
H17	C1	26.8	-0.2	27.0	-0.32	0.00	-0.32
H17	C2	3.0	-0.1	3.1	0.06	-0.03	0.08
H17	C3	3.3	0.0	3.3	-0.53	-0.01	-0.53
H17	C4	33.0	-0.5	33.6	-0.53	0.01	-0.54
H17	H5	31.2	-0.1	31.3	-1.08	0.00	-1.08
H17	H6	1.6	-0.1	1.7	0.11	-0.02	0.13
H17	H7	1.9	0.0	1.9	0.77	0.06	0.71
H17	H8	0.3	0.0	0.3	-1.25	0.00	-1.25
H17	H9	0.9	0.0	0.9	1.29	0.02	1.27
H17	H10	1.5	0.0	1.5	0.14	0.00	0.14
H17	H11	1.7	0.0	1.7	-0.12	0.00	-0.12
H17	H12	4.8	0.0	4.8	-0.04	0.01	-0.05
H17	N13	-131.0	-18.2	-112.7	1.88	0.84	1.04
H17	C14	175.6	-1.0	176.6	0.01	0.04	-0.03
H17	O15	-86.5	-0.5	-86.0	-0.25	0.00	-0.25
H17	O16	-314.4	-100.7	-213.7	-2.26	-0.23	-2.03
C18	C1	26.2	0.0	26.3	26.23	-0.04	26.27
C18	C2	3.6	0.0	3.6	3.58	-0.01	3.59
C18	C3	3.1	-0.1	3.2	3.11	-0.06	3.16
C18	C4	24.0	0.0	24.1	24.04	-0.01	24.05
C18	H5	24.0	0.0	24.0	24.01	0.00	24.01
C18	H6	1.2	-0.1	1.3	1.17	-0.14	1.31
C18	H7	2.2	0.0	2.2	2.21	0.00	2.21
C18	H8	0.6	0.0	0.6	0.60	0.00	0.60
C18	H9	0.6	0.0	0.6	0.64	-0.01	0.65
C18	H10	1.9	0.0	1.9	1.92	-0.01	1.93
C18	H11	1.4	-0.1	1.6	1.42	-0.15	1.56
C18	H12	4.1	0.0	4.1	4.08	0.00	4.09
C18	N13	-76.9	0.0	-76.9	-76.94	-0.01	-76.92
C18	C14	138.3	-0.1	138.4	138.29	-0.13	138.42
C18	O15	-98.6	-0.1	-98.5	-98.63	-0.11	-98.52
C18	O16	-113.4	-1.7	-111.7	-113.43	-1.72	-111.72
C18	H17	56.9	0.0	57.0	56.95	-0.01	56.96
O19	C1	-34.4	-1.1	-33.3	-34.37	-1.05	-33.32
O19	C2	-4.8	-0.2	-4.6	-4.77	-0.21	-4.56
O19	C3	-5.2	-1.2	-4.0	-5.23	-1.18	-4.05
O19	C4	-29.7	-0.1	-29.6	-29.66	-0.10	-29.56
O19	H5	-29.5	0.0	-29.5	-29.51	-0.01	-29.50
O19	H6	-5.4	-3.7	-1.7	-5.37	-3.66	-1.71
O19	H7	-3.0	-0.1	-2.9	-2.98	-0.06	-2.93

Table S8 continues

Atom		**3a**			**3a *minus* (1a+2)**		
A	**B**	$E_{\mathrm{int}}^{\mathrm{A,B}}$	$V_{\mathrm{XC}}^{\mathrm{A,B}}$	$V_{\mathrm{cl}}^{\mathrm{A,B}}$	$\Delta E_{\mathrm{int}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{XC}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{cl}}^{\mathrm{A,B}}$
O19	H8	-0.9	0.0	-0.9	-0.93	-0.03	-0.90
O19	H9	-0.9	-0.1	-0.7	-0.86	-0.15	-0.72
O19	H10	-2.6	-0.1	-2.6	-2.64	-0.06	-2.58
O19	H11	-5.9	-3.9	-2.0	-5.89	-3.85	-2.04
O19	H12	-5.1	0.0	-5.1	-5.07	-0.01	-5.06
O19	N13	94.3	-0.1	94.4	94.34	-0.11	94.45
O19	C14	-161.3	-0.3	-161.0	-161.33	-0.30	-161.03
O19	O15	115.1	-0.2	115.2	115.09	-0.16	115.25
O19	O16	125.1	-0.9	126.1	125.14	-0.94	126.08
O19	H17	-65.6	0.0	-65.5	-65.55	-0.01	-65.54
O19	C18	-723.5	-257.3	-466.3	0.82	1.47	-0.64
C20	C1	-0.4	0.0	-0.4	-0.40	-0.04	-0.36
C20	C2	0.0	0.0	0.0	-0.04	0.00	-0.04
C20	C3	0.0	0.0	0.0	-0.03	-0.01	-0.03
C20	C4	-0.3	0.0	-0.3	-0.35	0.00	-0.34
C20	H5	-0.4	0.0	-0.4	-0.40	0.00	-0.40
C20	H6	-0.3	-0.2	0.0	-0.26	-0.25	-0.01
C20	H7	0.0	0.0	0.0	-0.02	0.00	-0.02
C20	H8	0.0	0.0	0.0	0.00	0.00	0.00
C20	H9	0.0	0.0	0.0	-0.01	0.00	-0.01
C20	H10	0.0	0.0	0.0	-0.01	0.00	-0.01
C20	H11	0.0	0.0	0.0	-0.04	-0.02	-0.02
C20	H12	0.0	0.0	0.0	-0.05	0.00	-0.05
C20	N13	1.3	0.0	1.3	1.29	-0.04	1.33
C20	C14	-1.6	0.0	-1.6	-1.61	-0.03	-1.58
C20	O15	0.8	0.0	0.8	0.79	-0.03	0.82
C20	O16	0.5	-1.7	2.2	0.48	-1.68	2.16
C20	H17	-1.5	-0.1	-1.5	-1.52	-0.06	-1.46
C20	C18	-167.3	-187.5	20.2	0.18	-0.08	0.26
C20	O19	-15.5	-11.8	-3.8	-0.08	0.16	-0.24
H21	C1	0.5	-0.2	0.6	0.48	-0.17	0.65
H21	C2	0.1	0.0	0.1	0.07	-0.02	0.09
H21	C3	0.1	0.0	0.1	0.08	0.00	0.08
H21	C4	0.7	0.0	0.7	0.66	0.00	0.66
H21	H5	0.6	0.0	0.6	0.65	0.00	0.65
H21	H6	-0.5	-0.5	0.0	-0.49	-0.53	0.04
H21	H7	0.0	0.0	0.1	0.05	-0.01	0.05
H21	H8	0.0	0.0	0.0	0.00	-0.01	0.01
H21	H9	0.0	0.0	0.0	0.02	0.00	0.02
H21	H10	0.0	0.0	0.0	0.04	0.00	0.05

Table S8 continues

Atom		**3a**			**3a *minus* (1a+2)**		
A	**B**	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$	$\Delta E_{\text{int}}^{\text{A,B}}$	$\Delta V_{\text{XC}}^{\text{A,B}}$	$\Delta V_{\text{cl}}^{\text{A,B}}$
H21	H11	0.00	0.0	0.0	0.04	0.00	0.04
H21	H12	0.00	0.1	0.0	0.11	0.00	0.11
H21	N13	0.00	-2.1	-0.1	-2.12	-0.07	-2.06
H21	C14	0.01	4.3	0.0	4.28	0.00	4.28
H21	O15	0.00	-2.9	0.0	-2.94	0.00	-2.93
H21	O16	-0.01	-4.1	-0.1	-4.06	-0.10	-3.96
H21	H17	0.00	1.9	0.0	1.90	-0.03	1.93
H21	C18	0.01	5.1	-3.3	-0.54	-0.03	-0.50
H21	O19	-0.01	-8.8	-2.0	0.62	0.17	0.45
H21	C20	0.03	-153.0	-174.6	0.22	0.27	-0.04
H22	C1	0.00	1.1	0.0	1.06	0.00	1.06
H22	C2	0.00	0.1	0.0	0.14	0.00	0.14
H22	C3	0.00	0.1	0.0	0.11	-0.01	0.11
H22	C4	0.00	0.9	0.0	0.93	-0.01	0.94
H22	H5	0.00	1.0	0.0	0.99	0.00	0.99
H22	H6	0.00	0.0	0.0	0.03	-0.01	0.04
H22	H7	0.00	0.1	0.0	0.08	0.00	0.08
H22	H8	0.00	0.0	0.0	0.02	0.00	0.02
H22	H9	0.00	0.0	0.0	0.03	0.00	0.03
H22	H10	0.00	0.1	0.0	0.06	0.00	0.06
H22	H11	0.00	0.1	0.0	0.05	-0.01	0.06
H22	H12	0.00	0.2	0.0	0.15	0.00	0.15
H22	N13	-0.01	-3.2	0.0	-3.20	-0.01	-3.19
H22	C14	0.01	5.1	0.0	5.13	-0.04	5.17
H22	O15	-0.01	-3.6	0.0	-3.55	-0.03	-3.52
H22	O16	-0.01	-6.6	-2.0	-6.58	-1.99	-4.59
H22	H17	0.00	2.4	0.0	2.42	-0.02	2.45
H22	C18	0.01	5.2	-4.0	0.38	0.61	-0.23
H22	O19	-0.01	-8.9	-1.1	0.26	0.20	0.06
H22	C20	0.03	-151.0	-172.4	-0.66	-0.72	0.06
H22	H21	0.00	-1.1	-2.9	-0.03	0.07	-0.09
H23	C1	0.00	1.1	0.0	1.08	0.00	1.08
H23	C2	0.00	0.1	0.0	0.14	0.00	0.14
H23	C3	0.00	0.1	0.0	0.12	0.00	0.12
H23	C4	0.00	1.0	0.0	0.97	0.00	0.97
H23	H5	0.00	1.0	0.0	1.05	0.00	1.05
H23	H6	0.00	0.0	0.0	0.03	-0.02	0.04
H23	H7	0.00	0.1	0.0	0.08	0.00	0.08
H23	H8	0.00	0.0	0.0	0.02	0.00	0.02
H23	H9	0.00	0.0	0.0	0.03	0.00	0.03

Table S8 continues

Atom		**3a**			**3a *minus* (1a+2)**		
A	**B**	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$	$\Delta E_{\text{int}}^{\text{A,B}}$	$\Delta V_{\text{XC}}^{\text{A,B}}$	$\Delta V_{\text{cl}}^{\text{A,B}}$
H23	H10	0.1	0.0	0.1	0.06	0.00	0.06
H23	H11	0.1	0.0	0.1	0.06	0.00	0.06
H23	H12	0.2	0.0	0.2	0.16	0.00	0.16
H23	N13	-3.3	0.0	-3.3	-3.35	0.00	-3.35
H23	C14	5.5	0.0	5.5	5.51	0.00	5.51
H23	O15	-3.7	0.0	-3.7	-3.73	-0.01	-3.73
H23	O16	-5.2	-0.1	-5.1	-5.22	-0.11	-5.11
H23	H17	2.7	0.0	2.7	2.73	0.00	2.73
H23	C18	4.6	-4.7	9.3	0.08	-0.53	0.61
H23	O19	-9.1	-1.3	-7.9	-0.71	-0.13	-0.58
H23	C20	-150.2	-171.5	21.3	1.23	1.27	-0.04
H23	H21	-1.2	-3.0	1.8	-0.03	-0.04	0.01
H23	H22	-1.1	-3.1	2.0	0.12	0.10	0.01
C24	C1	-0.2	0.0	-0.2	-0.24	-0.01	-0.23
C24	C2	0.0	0.0	0.0	-0.04	0.00	-0.04
C24	C3	-0.1	0.0	-0.1	-0.06	-0.01	-0.05
C24	C4	-0.3	0.0	-0.3	-0.33	-0.01	-0.32
C24	H5	-0.3	0.0	-0.3	-0.30	0.00	-0.30
C24	H6	-0.1	0.0	0.0	-0.05	-0.03	-0.02
C24	H7	0.0	0.0	0.0	-0.01	0.00	-0.01
C24	H8	0.0	0.0	0.0	0.00	0.00	0.00
C24	H9	0.0	0.0	0.0	-0.01	0.00	-0.01
C24	H10	0.0	0.0	0.0	-0.02	0.00	-0.02
C24	H11	-0.1	0.0	0.0	-0.05	-0.04	-0.01
C24	H12	-0.1	0.0	-0.1	-0.06	0.00	-0.06
C24	N13	0.8	0.0	0.8	0.83	0.00	0.83
C24	C14	-2.9	-0.1	-2.8	-2.93	-0.12	-2.81
C24	O15	1.6	-1.0	2.5	1.57	-0.96	2.53
C24	O16	0.8	-1.0	1.7	0.76	-0.97	1.74
C24	H17	-0.7	0.0	-0.7	-0.71	-0.01	-0.70
C24	C18	-168.0	-187.8	19.8	-0.53	-0.43	-0.10
C24	O19	-15.1	-11.8	-3.3	0.29	0.15	0.14
C24	C20	-4.1	-5.0	0.9	0.04	0.05	-0.01
C24	H21	-0.4	-0.5	0.1	0.00	0.01	-0.01
C24	H22	-0.7	-0.8	0.1	-0.25	-0.28	0.03
C24	H23	-0.3	-0.4	0.1	0.27	0.31	-0.04
H25	C1	0.7	0.0	0.7	0.72	0.00	0.72
H25	C2	0.1	0.0	0.1	0.10	0.00	0.10
H25	C3	0.1	0.0	0.1	0.09	0.00	0.10
H25	C4	0.7	0.0	0.7	0.74	0.00	0.74

Table S8 continues

Atom		**3a**			**3a *minus* (1a+2)**		
A	**B**	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$	$\Delta E_{\text{int}}^{\text{A,B}}$	$\Delta V_{\text{XC}}^{\text{A,B}}$	$\Delta V_{\text{cl}}^{\text{A,B}}$
H25	H5	0.7	0.0	0.7	0.71	0.00	0.71
H25	H6	0.0	0.0	0.0	0.04	0.00	0.04
H25	H7	0.1	0.0	0.1	0.06	0.00	0.06
H25	H8	0.0	0.0	0.0	0.01	0.00	0.01
H25	H9	0.0	0.0	0.0	0.02	0.00	0.02
H25	H10	0.1	0.0	0.1	0.05	0.00	0.05
H25	H11	0.0	0.0	0.0	0.04	0.00	0.04
H25	H12	0.1	0.0	0.1	0.13	0.00	0.13
H25	N13	-2.2	0.0	-2.2	-2.24	0.00	-2.24
H25	C14	5.3	0.0	5.3	5.25	-0.01	5.26
H25	O15	-4.1	-0.1	-4.0	-4.11	-0.06	-4.05
H25	O16	-4.0	0.0	-4.0	-4.04	-0.04	-4.00
H25	H17	1.8	0.0	1.8	1.82	0.00	1.82
H25	C18	3.7	-4.0	7.8	-1.11	0.55	-1.66
H25	O19	-7.5	-1.1	-6.5	1.66	0.20	1.46
H25	C20	-0.7	-0.9	0.2	-0.32	-0.38	0.06
H25	H21	0.1	-0.1	0.2	-0.11	-0.04	-0.07
H25	H22	0.1	-0.1	0.2	-0.16	-0.10	-0.06
H25	H23	-0.1	-0.4	0.3	0.01	0.05	-0.04
H25	C24	-152.2	-173.6	21.4	-1.84	-1.85	0.01
H26	C1	1.3	0.0	1.3	1.25	0.00	1.25
H26	C2	0.2	0.0	0.2	0.18	0.00	0.18
H26	C3	0.2	0.0	0.2	0.16	0.00	0.17
H26	C4	1.3	0.0	1.3	1.26	-0.03	1.29
H26	H5	1.3	0.0	1.3	1.26	0.00	1.26
H26	H6	0.1	0.0	0.1	0.06	-0.01	0.07
H26	H7	0.1	0.0	0.1	0.10	0.00	0.10
H26	H8	0.0	0.0	0.0	0.02	0.00	0.02
H26	H9	0.0	0.0	0.0	0.03	0.00	0.03
H26	H10	0.1	0.0	0.1	0.09	0.00	0.09
H26	H11	0.1	0.0	0.1	0.07	-0.01	0.08
H26	H12	0.2	0.0	0.2	0.22	0.00	0.22
H26	N13	-3.9	0.0	-3.9	-3.92	-0.01	-3.91
H26	C14	8.9	-0.2	9.1	8.86	-0.20	9.06
H26	O15	-9.2	-2.2	-6.9	-9.16	-2.24	-6.92
H26	O16	-8.9	-2.0	-6.9	-8.92	-2.02	-6.90
H26	H17	3.1	0.0	3.2	3.14	-0.01	3.16
H26	C18	7.0	-4.6	11.7	2.55	-0.43	2.98
H26	O19	-11.6	-1.3	-10.3	-3.13	-0.12	-3.01
H26	C20	-0.3	-0.3	0.1	0.35	0.39	-0.04

Table S8 continues

Atom		**3a**			**3a *minus* (1a+2)**		
A	**B**	$E_{\mathrm{int}}^{\mathrm{A,B}}$	$V_{\mathrm{XC}}^{\mathrm{A,B}}$	$V_{\mathrm{cl}}^{\mathrm{A,B}}$	$\Delta E_{\mathrm{int}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{XC}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{cl}}^{\mathrm{A,B}}$
H26	H21	0.3	0.0	0.3	0.12	0.03	0.08
H26	H22	0.1	-0.3	0.4	0.26	0.17	0.09
H26	H23	0.3	0.0	0.4	0.15	0.02	0.13
H26	C24	-148.4	-169.5	21.1	2.97	3.23	-0.27
H26	H25	-1.0	-3.1	2.0	0.23	0.17	0.06
H27	C1	0.7	0.0	0.7	0.70	0.00	0.70
H27	C2	0.1	0.0	0.1	0.10	0.00	0.10
H27	C3	0.1	0.0	0.1	0.08	-0.01	0.09
H27	C4	0.7	0.0	0.7	0.71	0.00	0.72
H27	H5	0.7	0.0	0.7	0.70	0.00	0.70
H27	H6	0.0	0.0	0.0	0.04	0.00	0.04
H27	H7	0.1	0.0	0.1	0.05	0.00	0.05
H27	H8	0.0	0.0	0.0	0.01	0.00	0.01
H27	H9	0.0	0.0	0.0	0.02	0.00	0.02
H27	H10	0.0	0.0	0.0	0.05	0.00	0.05
H27	H11	0.0	0.0	0.0	0.01	-0.03	0.05
H27	H12	0.1	0.0	0.1	0.12	0.00	0.12
H27	N13	-2.2	0.0	-2.2	-2.21	0.00	-2.21
H27	C14	5.0	0.0	5.0	5.04	-0.01	5.05
H27	O15	-3.8	-0.1	-3.7	-3.80	-0.13	-3.67
H27	O16	-4.1	0.0	-4.1	-4.10	-0.04	-4.07
H27	H17	1.9	0.0	1.9	1.86	0.00	1.86
H27	C18	5.1	-3.4	8.4	-0.59	-0.10	-0.49
H27	O19	-8.9	-2.1	-6.8	0.49	0.06	0.44
H27	C20	-0.4	-0.5	0.1	0.02	0.01	0.01
H27	H21	0.1	-0.1	0.2	-0.02	0.01	-0.02
H27	H22	0.2	-0.1	0.2	-0.05	-0.03	-0.02
H27	H23	0.2	0.0	0.2	0.04	0.03	0.01
H27	C24	-153.2	-174.8	21.6	0.01	0.09	-0.08
H27	H25	-1.3	-2.9	1.7	-0.18	0.02	-0.20
H27	H26	-0.9	-2.9	2.0	0.24	0.03	0.21
				Total:	**-21.3**	**-15.9**	**-5.4**

Table S9. Full set of intra- and inter-molecular diatomic interaction energies $E_{\mathrm{int}}^{\mathrm{A,B}}$ and their components, $V_{\mathrm{XC}}^{\mathrm{A,B}}$ and $V_{\mathrm{cl}}^{\mathrm{A,B}}$, obtained for the global minimum energy adduct **3b** and changes in these energies on (**1b**+**2**) → **3b**. All values in kcal mol^{-1}.

Atom		**3b**			**3b *minus* (1b + 2)**		
A	**B**	$E_{\mathrm{int}}^{\mathrm{A,B}}$	$V_{\mathrm{XC}}^{\mathrm{A,B}}$	$V_{\mathrm{cl}}^{\mathrm{A,B}}$	$\Delta E_{\mathrm{int}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{XC}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{cl}}^{\mathrm{A,B}}$
C2	C1	-166.7	-181.8	15.1	-2.27	-4.40	2.13
C3	C1	-2.8	-5.6	2.8	-1.98	-1.50	-0.48
C3	C2	-171.8	-183.1	11.3	-2.84	-3.72	0.88
C4	C1	22.4	-3.4	25.8	1.12	0.97	0.16
C4	C2	-1.4	-4.5	3.1	1.00	0.47	0.53
C4	C3	-158.6	-170.2	11.6	6.67	9.21	-2.54
H5	C1	27.9	-1.8	29.7	1.37	0.13	1.24
H5	C2	2.1	-0.2	2.3	0.54	0.01	0.52
H5	C3	1.8	-0.1	1.9	-0.25	0.28	-0.52
H5	C4	26.9	-1.8	28.7	2.61	0.25	2.36
H6	C1	-148.4	-173.8	25.5	-0.29	0.35	-0.65
H6	C2	-2.4	-3.3	0.9	-0.12	-0.10	-0.03
H6	C3	-0.3	-0.5	0.2	-0.28	-0.18	-0.10
H6	C4	1.0	-0.5	1.5	-0.31	0.01	-0.32
H6	H5	1.4	-0.3	1.7	-0.42	-0.02	-0.40
H7	C1	-149.7	-172.9	23.2	-1.02	0.29	-1.31
H7	C2	-2.9	-3.7	0.8	-0.27	-0.19	-0.07
H7	C3	-0.4	-0.5	0.2	-0.45	-0.38	-0.07
H7	C4	0.6	-0.2	0.8	-0.26	0.30	-0.56
H7	H5	0.6	-0.4	1.0	-0.49	0.07	-0.55
H7	H6	-2.0	-3.2	1.1	-0.30	-0.10	-0.20
H8	C1	-1.4	-3.4	2.0	0.36	0.19	0.18
H8	C2	-153.5	-175.0	21.5	0.89	0.64	0.25
H8	C3	-2.9	-3.6	0.8	-0.10	-0.04	-0.05
H8	C4	0.5	-0.5	0.9	-0.22	-0.29	0.07
H8	H5	0.8	0.0	0.8	0.07	0.00	0.07
H8	H6	0.1	-0.1	0.2	0.03	0.03	0.01
H8	H7	-0.2	-0.4	0.2	0.22	0.26	-0.05
H9	C1	-2.3	-3.7	1.5	-0.37	-0.12	-0.25
H9	C2	-153.8	-174.5	20.6	0.70	1.23	-0.53
H9	C3	-3.1	-3.8	0.7	-0.21	-0.12	-0.10
H9	C4	0.2	-0.2	0.4	-0.29	0.10	-0.39
H9	H5	-0.1	-0.1	0.0	-0.62	-0.08	-0.54
H9	H6	-0.2	-0.4	0.2	0.10	0.15	-0.05
H9	H7	-0.4	-0.5	0.1	-0.22	-0.16	-0.05
H9	H8	-2.1	-3.2	1.1	0.06	0.12	-0.06
H10	C1	0.7	-0.3	1.0	-0.34	-0.09	-0.25
H10	C2	-2.5	-3.5	1.0	-0.13	-0.19	0.07
H10	C3	-153.5	-174.5	20.9	0.15	0.95	-0.79
H10	C4	-2.1	-3.6	1.6	-0.44	-0.09	-0.35

Table S9 continues

Atom		**3b**			**3b *minus* (1b+2)**		
A	**B**	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$	$\Delta E_{\text{int}}^{\text{A,B}}$	$\Delta V_{\text{XC}}^{\text{A,B}}$	$\Delta V_{\text{cl}}^{\text{A,B}}$
H10	H5	0.8	0.0	0.8	-0.33	0.01	-0.34
H10	H6	0.1	0.0	0.1	-0.03	0.01	-0.04
H10	H7	-0.1	-0.2	0.1	-0.21	-0.24	0.03
H10	H8	-0.2	-0.5	0.3	0.11	0.14	-0.02
H10	H9	-0.4	-0.5	0.1	-0.40	-0.34	-0.06
H11	C1	0.6	-0.5	1.1	-0.23	-0.31	0.07
H11	C2	-2.3	-3.3	1.0	0.24	0.14	0.10
H11	C3	-153.4	-174.7	21.3	-0.07	-0.27	0.20
H11	C4	-1.8	-3.2	1.5	0.37	0.54	-0.17
H11	H5	0.7	0.0	0.7	0.27	0.15	0.12
H11	H6	0.0	-0.1	0.1	-0.07	-0.05	-0.01
H11	H7	0.0	0.0	0.0	-0.04	-0.01	-0.03
H11	H8	0.1	-0.1	0.2	0.24	0.20	0.04
H11	H9	-0.3	-0.5	0.2	0.21	0.26	-0.05
H11	H10	-2.0	-3.2	1.2	-0.11	0.00	-0.10
H12	C1	2.3	-0.2	2.5	-0.02	0.60	-0.62
H12	C2	0.2	-0.2	0.4	0.03	0.02	0.01
H12	C3	-2.1	-3.2	1.1	-0.33	0.08	-0.41
H12	C4	-145.0	-170.1	25.1	-3.15	-3.01	-0.14
H12	H5	2.4	-0.3	2.6	-0.10	0.21	-0.31
H12	H6	0.1	0.0	0.2	-0.06	0.02	-0.08
H12	H7	0.0	0.0	0.1	0.40	0.53	-0.13
H12	H8	0.1	0.0	0.1	-0.04	-0.01	-0.03
H12	H9	0.0	0.0	0.1	-0.07	0.00	-0.08
H12	H10	-0.4	-0.7	0.3	-0.33	-0.25	-0.08
H12	H11	0.1	-0.1	0.2	0.27	0.32	-0.05
N13	C1	-275.2	-183.2	-92.0	-1.88	-2.50	0.62
N13	C2	-15.5	-8.3	-7.2	-2.50	-1.03	-1.47
N13	C3	-11.8	-6.1	-5.7	3.33	1.32	2.01
N13	C4	-268.5	-188.2	-80.4	-2.90	-3.50	0.60
N13	H5	-239.8	-159.4	-80.4	-1.67	4.22	-5.89
N13	H6	-10.7	-5.3	-5.4	1.19	-0.06	1.25
N13	H7	-8.6	-5.8	-2.8	1.98	-0.05	2.03
N13	H8	-3.2	-0.8	-2.4	-0.44	-0.23	-0.21
N13	H9	-1.5	-0.8	-0.7	0.67	-0.48	1.15
N13	H10	-2.5	-0.2	-2.2	1.41	0.46	0.95
N13	H11	-2.8	-0.4	-2.4	-0.06	0.10	-0.16
N13	H12	-13.1	-5.2	-7.9	1.92	0.16	1.76
C14	C1	50.7	-0.3	51.0	3.57	0.16	3.41
C14	C2	6.6	-0.2	6.9	1.93	0.13	1.80

Table S9 continues

Atom		**3b**			**3b *minus* (1b+2)**		
A	**B**	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$	$\Delta E_{\text{int}}^{\text{A,B}}$	$\Delta V_{\text{XC}}^{\text{A,B}}$	$\Delta V_{\text{cl}}^{\text{A,B}}$
C14	C3	1.1	-5.1	6.2	-4.68	-1.79	-2.89
C14	C4	-81.0	-178.3	97.3	1.98	1.64	0.34
C14	H5	71.2	-0.6	71.8	10.96	-0.26	11.21
C14	H6	2.7	0.0	2.7	-0.82	0.03	-0.85
C14	H7	0.8	0.0	0.8	-1.14	0.01	-1.15
C14	H8	2.1	0.0	2.2	0.63	-0.02	0.66
C14	H9	-1.0	0.0	-1.0	-2.22	-0.01	-2.21
C14	H10	3.1	-0.3	3.4	-0.60	-0.22	-0.38
C14	H11	0.3	-1.1	1.4	-1.09	-0.53	-0.56
C14	H12	7.6	-4.0	11.6	-1.77	0.94	-2.71
C14	N13	-178.1	-5.6	-172.4	-1.20	0.10	-1.29
O15	C1	-39.3	-0.1	-39.2	-8.08	-0.03	-8.05
O15	C2	-5.0	-0.2	-4.8	-1.20	-0.03	-1.18
O15	C3	-4.9	-1.1	-3.8	2.82	1.58	1.24
O15	C4	-66.0	-8.9	-57.2	-7.85	0.64	-8.49
O15	H5	-66.7	-5.9	-60.9	-29.00	-5.82	-23.17
O15	H6	-2.0	0.0	-2.0	0.45	0.03	0.43
O15	H7	-0.8	-0.1	-0.7	0.48	-0.04	0.52
O15	H8	-1.7	0.0	-1.6	-0.65	-0.02	-0.63
O15	H9	1.0	-0.3	1.3	1.82	-0.28	2.10
O15	H10	-2.3	-0.1	-2.2	0.59	0.38	0.21
O15	H11	-1.1	-0.2	-0.9	1.19	1.18	0.02
O15	H12	-7.5	-0.8	-6.8	1.88	0.30	1.58
O15	N13	129.5	-5.3	134.7	25.45	-4.37	29.82
O15	C14	-858.1	-243.0	-615.2	7.02	4.70	2.32
O16	C1	-30.9	-0.1	-30.8	3.81	0.17	3.65
O16	C2	-4.6	-0.1	-4.5	-1.43	0.01	-1.44
O16	C3	-4.7	-1.4	-3.3	1.14	-0.89	2.03
O16	C4	-54.2	-8.9	-45.3	6.85	-0.57	7.42
O16	H5	-37.7	-0.1	-37.6	9.58	0.40	9.18
O16	H6	-1.7	0.0	-1.7	0.79	-0.02	0.81
O16	H7	-0.2	0.0	-0.2	1.15	0.02	1.13
O16	H8	-1.3	0.0	-1.2	-0.29	0.00	-0.29
O16	H9	0.4	0.0	0.4	1.13	0.01	1.13
O16	H10	-2.1	0.0	-2.0	0.02	-0.02	0.04
O16	H11	-1.3	-1.2	-0.1	-0.27	-1.15	0.88
O16	H12	-7.6	-1.3	-6.3	0.84	-0.63	1.48
O16	N13	98.4	-0.7	99.1	-29.57	6.25	-35.82
O16	C14	-665.1	-176.7	-488.4	-32.64	-3.27	-29.38
O16	O15	180.6	-29.3	209.9	10.49	-0.62	11.11

Table S9 continues

Atom		**3b**			**3b *minus* (1b+2)**		
A	**B**	$E_{\mathrm{int}}^{\mathrm{A,B}}$	$V_{\mathrm{XC}}^{\mathrm{A,B}}$	$V_{\mathrm{cl}}^{\mathrm{A,B}}$	$\Delta E_{\mathrm{int}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{XC}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{cl}}^{\mathrm{A,B}}$
H17	C1	16.3	0.0	16.3	-5.32	0.13	-5.45
H17	C2	2.5	0.0	2.5	0.74	0.05	0.70
H17	C3	1.4	-0.1	1.5	-1.56	-0.06	-1.50
H17	C4	21.5	-0.4	22.0	-8.72	-0.04	-8.68
H17	H5	18.7	0.0	18.7	-11.35	0.11	-11.46
H17	H6	0.9	0.0	0.9	-0.63	0.00	-0.63
H17	H7	0.0	0.0	0.0	-0.81	0.01	-0.82
H17	H8	0.6	0.0	0.6	0.07	0.01	0.06
H17	H9	-0.1	0.0	-0.1	-0.52	0.00	-0.52
H17	H10	0.9	0.0	0.9	-0.21	0.00	-0.21
H17	H11	0.1	-0.1	0.1	-0.55	-0.05	-0.49
H17	H12	2.8	-0.3	3.1	-1.55	-0.27	-1.28
H17	N13	-51.3	0.0	-51.2	48.11	6.86	41.25
H17	C14	174.1	-0.7	174.8	2.65	0.17	2.48
H17	O15	-87.0	-0.5	-86.5	-1.70	0.16	-1.86
H17	O16	-320.5	-97.2	-223.3	-3.15	15.54	-18.69
C18	C1	19.7	0.0	19.7	19.66	0.00	19.66
C18	C2	3.0	0.0	3.0	2.99	-0.02	3.00
C18	C3	1.3	-0.2	1.5	1.28	-0.22	1.49
C18	C4	21.9	-0.1	21.9	21.87	-0.06	21.93
C18	H5	20.1	0.0	20.1	20.08	0.00	20.08
C18	H6	1.1	0.0	1.1	1.13	0.00	1.13
C18	H7	-0.3	0.0	-0.3	-0.34	0.00	-0.34
C18	H8	0.5	0.0	0.5	0.52	0.00	0.52
C18	H9	0.1	0.0	0.1	0.07	0.00	0.08
C18	H10	-0.7	-0.3	-0.3	-0.66	-0.34	-0.32
C18	H11	0.2	-0.1	0.2	0.18	-0.07	0.25
C18	H12	2.5	-0.1	2.6	2.54	-0.10	2.64
C18	N13	-58.0	0.0	-58.0	-58.03	-0.01	-58.02
C18	C14	117.8	0.0	117.8	117.75	-0.01	117.76
C18	O15	-73.9	0.0	-73.8	-73.85	-0.01	-73.84
C18	O16	-114.2	-0.2	-114.1	-114.24	-0.18	-114.07
C18	H17	85.6	-0.2	85.8	85.59	-0.25	85.84
O19	C1	-25.5	0.0	-25.5	-25.50	-0.01	-25.49
O19	C2	-4.0	-0.1	-3.9	-3.96	-0.08	-3.88
O19	C3	-3.1	-1.2	-1.9	-3.09	-1.20	-1.89
O19	C4	-30.7	-1.4	-29.3	-30.70	-1.38	-29.32
O19	H5	-26.4	0.0	-26.4	-26.41	-0.01	-26.39
O19	H6	-1.5	0.0	-1.5	-1.48	0.00	-1.47
O19	H7	0.4	0.0	0.4	0.40	0.00	0.40

Table S9 continues

Atom		**3b**			**3b *minus* (1b+2)**		
A	**B**	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$	$\Delta E_{\text{int}}^{\text{A,B}}$	$\Delta V_{\text{XC}}^{\text{A,B}}$	$\Delta V_{\text{cl}}^{\text{A,B}}$
O19	H8	-0.7	0.0	-0.7	-0.75	0.00	-0.74
O19	H9	-0.1	0.0	-0.1	-0.12	-0.01	-0.11
O19	H10	-0.8	-1.0	0.2	-0.81	-0.96	0.15
O19	H11	-0.7	-0.2	-0.5	-0.75	-0.22	-0.53
O19	H12	-6.3	-2.9	-3.4	-6.34	-2.90	-3.44
O19	N13	76.4	-0.1	76.5	76.41	-0.11	76.52
O19	C14	-159.8	-0.2	-159.7	-159.84	-0.18	-159.66
O19	O15	97.8	-0.2	98.0	97.83	-0.17	98.00
O19	O16	150.0	-8.2	158.2	150.04	-8.19	158.23
O19	H17	-143.9	-18.3	-125.6	-143.88	-18.25	-125.62
O19	C18	-706.3	-249.9	-456.4	18.04	8.83	9.22
C20	C1	-0.3	0.0	-0.3	-0.27	-0.01	-0.27
C20	C2	-0.1	0.0	-0.1	-0.08	-0.03	-0.05
C20	C3	-0.4	-0.4	0.0	-0.44	-0.41	-0.03
C20	C4	-0.3	0.0	-0.3	-0.28	-0.02	-0.27
C20	H5	-0.3	0.0	-0.3	-0.26	0.00	-0.26
C20	H6	0.0	0.0	0.0	-0.02	0.00	-0.02
C20	H7	0.0	0.0	0.0	0.00	0.00	0.00
C20	H8	0.0	0.0	0.0	-0.01	0.00	-0.01
C20	H9	0.0	0.0	0.0	0.00	0.00	0.00
C20	H10	-0.2	-0.2	0.0	-0.24	-0.22	-0.02
C20	H11	-0.8	-0.8	0.1	-0.75	-0.82	0.07
C20	H12	-0.1	0.0	0.0	-0.06	-0.01	-0.04
C20	N13	0.7	0.0	0.7	0.67	-0.01	0.68
C20	C14	-1.3	0.0	-1.3	-1.34	-0.01	-1.33
C20	O15	1.0	0.0	1.0	0.97	-0.01	0.98
C20	O16	0.6	-0.4	1.0	0.57	-0.40	0.97
C20	H17	-0.5	-0.1	-0.4	-0.52	-0.15	-0.37
C20	C18	-168.6	-190.0	21.3	-1.16	-2.58	1.42
C20	O19	-15.9	-11.3	-4.6	-0.49	0.63	-1.12
H21	C1	1.0	0.0	1.0	1.04	0.00	1.04
H21	C2	0.1	0.0	0.2	0.15	-0.02	0.16
H21	C3	-0.2	-0.3	0.1	-0.22	-0.30	0.09
H21	C4	1.1	0.0	1.1	1.10	-0.02	1.13
H21	H5	1.1	0.0	1.1	1.07	0.00	1.07
H21	H6	0.1	0.0	0.1	0.06	0.00	0.06
H21	H7	0.0	0.0	0.0	-0.01	0.00	-0.01
H21	H8	0.0	0.0	0.0	0.02	0.00	0.02
H21	H9	0.0	0.0	0.0	-0.01	0.00	-0.01
H21	H10	-0.2	-0.2	0.0	-0.22	-0.22	0.01

Table S9 continues

Atom		**3b**			**3b** ***minus*** **(1b+2)**		
A	**B**	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$	$\Delta E_{\text{int}}^{\text{A,B}}$	$\Delta V_{\text{XC}}^{\text{A,B}}$	$\Delta V_{\text{cl}}^{\text{A,B}}$
H21	H11	-0.4	-0.4	0.0	-0.41	-0.37	-0.04
H21	H12	0.1	0.0	0.1	0.14	-0.01	0.15
H21	N13	-3.0	0.0	-3.0	-3.01	-0.01	-2.99
H21	C14	6.3	0.0	6.3	6.32	0.00	6.32
H21	O15	-4.1	0.0	-4.1	-4.10	0.00	-4.10
H21	O16	-6.0	0.0	-6.0	-6.00	-0.01	-5.99
H21	H17	3.9	0.0	3.9	3.94	0.00	3.95
H21	C18	6.0	-4.9	10.9	0.34	-1.60	1.94
H21	O19	-11.0	-1.2	-9.8	-1.64	0.96	-2.60
H21	C20	-149.1	-170.4	21.3	4.13	4.48	-0.35
H22	C1	0.7	0.0	0.7	0.74	0.00	0.74
H22	C2	0.1	0.0	0.1	0.10	-0.01	0.11
H22	C3	-0.1	-0.2	0.0	-0.15	-0.19	0.04
H22	C4	0.8	0.0	0.8	0.77	-0.01	0.79
H22	H5	0.7	0.0	0.7	0.74	0.00	0.74
H22	H6	0.0	0.0	0.0	0.04	0.00	0.04
H22	H7	0.0	0.0	0.0	-0.01	0.00	-0.01
H22	H8	0.0	0.0	0.0	0.01	0.00	0.01
H22	H9	0.0	0.0	0.0	0.00	0.00	0.00
H22	H10	0.0	0.0	0.0	-0.03	-0.01	-0.02
H22	H11	-0.6	-0.6	0.0	-0.59	-0.58	-0.01
H22	H12	0.1	0.0	0.1	0.10	0.00	0.10
H22	N13	-2.1	0.0	-2.1	-2.12	0.00	-2.12
H22	C14	4.1	0.0	4.1	4.08	-0.02	4.10
H22	O15	-2.7	0.0	-2.7	-2.70	-0.02	-2.68
H22	O16	-4.9	-1.1	-3.8	-4.92	-1.12	-3.80
H22	H17	2.4	-0.2	2.6	2.43	-0.18	2.61
H22	C18	5.8	-3.3	9.2	0.99	1.26	-0.27
H22	O19	-9.7	-1.7	-8.0	-0.45	-0.42	-0.03
H22	C20	-152.8	-174.4	21.6	-2.45	-2.69	0.24
H22	H21	-0.7	-2.8	2.1	0.36	0.12	0.24
H23	C1	1.0	0.0	1.0	0.98	0.00	0.98
H23	C2	0.1	0.0	0.2	0.15	0.00	0.15
H23	C3	0.1	0.0	0.1	0.06	-0.02	0.08
H23	C4	1.1	0.0	1.1	1.05	0.00	1.05
H23	H5	1.0	0.0	1.0	1.00	0.00	1.00
H23	H6	0.1	0.0	0.1	0.06	0.00	0.06
H23	H7	0.0	0.0	0.0	-0.01	0.00	-0.01
H23	H8	0.0	0.0	0.0	0.02	0.00	0.02
H23	H9	0.0	0.0	0.0	0.00	0.00	0.00

Table S9 continues

Atom		**3b**			**3b *minus* (1b+2)**		
A	**B**	$E_{\mathrm{int}}^{\mathrm{A,B}}$	$V_{\mathrm{XC}}^{\mathrm{A,B}}$	$V_{\mathrm{cl}}^{\mathrm{A,B}}$	$\Delta E_{\mathrm{int}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{XC}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{cl}}^{\mathrm{A,B}}$
H23	H10	0.0	0.0	0.0	-0.02	-0.01	0.00
H23	H11	-0.1	-0.1	0.0	-0.09	-0.05	-0.03
H23	H12	0.1	0.0	0.1	0.14	0.00	0.14
H23	N13	-2.8	0.0	-2.8	-2.81	0.00	-2.81
H23	C14	5.9	0.0	5.9	5.85	0.00	5.85
H23	O15	-3.8	0.0	-3.8	-3.81	0.00	-3.81
H23	O16	-5.5	0.0	-5.5	-5.54	-0.02	-5.52
H23	H17	3.6	0.0	3.6	3.63	-0.01	3.64
H23	C18	5.7	-4.4	10.1	1.24	-0.18	1.42
H23	O19	-10.2	-1.1	-9.1	-1.72	0.06	-1.79
H23	C20	-150.7	-172.2	21.4	0.66	0.61	0.05
H23	H21	-0.7	-3.1	2.4	0.44	-0.14	0.58
H23	H22	-0.7	-2.8	2.1	0.51	0.43	0.09
C24	C1	-0.1	0.0	-0.1	-0.07	0.00	-0.07
C24	C2	0.0	0.0	0.0	0.00	0.00	0.00
C24	C3	0.0	0.0	0.0	-0.03	-0.01	-0.01
C24	C4	0.0	0.0	0.0	-0.03	-0.01	-0.02
C24	H5	-0.1	0.0	-0.1	-0.05	0.00	-0.05
C24	H6	0.0	0.0	0.0	0.00	0.00	0.00
C24	H7	0.0	0.0	0.0	0.01	0.00	0.01
C24	H8	0.0	0.0	0.0	0.01	0.00	0.01
C24	H9	0.0	0.0	0.0	0.00	0.00	0.00
C24	H10	0.0	0.0	0.0	-0.02	-0.04	0.02
C24	H11	0.0	0.0	0.0	-0.02	-0.01	-0.01
C24	H12	0.0	0.0	0.0	0.00	-0.01	0.01
C24	N13	0.2	0.0	0.2	0.18	0.00	0.18
C24	C14	0.2	0.0	0.2	0.22	0.00	0.22
C24	O15	0.0	0.0	0.0	-0.01	0.00	-0.01
C24	O16	-0.6	-0.1	-0.5	-0.58	-0.09	-0.49
C24	H17	0.5	-0.1	0.6	0.48	-0.11	0.58
C24	C18	-167.4	-190.2	22.8	0.15	-2.80	2.95
C24	O19	-17.3	-11.4	-5.9	-1.95	0.50	-2.45
C24	C20	-3.6	-4.7	1.1	0.48	0.28	0.20
C24	H21	-0.3	-0.5	0.2	0.11	-0.01	0.11
C24	H22	-0.3	-0.4	0.2	0.13	0.07	0.06
C24	H23	-0.5	-0.8	0.2	0.08	-0.01	0.09
H25	C1	0.8	0.0	0.8	0.83	0.00	0.84
H25	C2	0.1	0.0	0.1	0.12	0.00	0.12
H25	C3	0.1	0.0	0.1	0.06	-0.01	0.08
H25	C4	0.9	0.0	0.9	0.88	0.00	0.88

Table S9 continues

Atom		**3b**			**3b *minus* (1b+2)**		
A	**B**	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$	$\Delta E_{\text{int}}^{\text{A,B}}$	$\Delta V_{\text{XC}}^{\text{A,B}}$	$\Delta V_{\text{cl}}^{\text{A,B}}$
H25	H5	0.8	0.0	0.8	0.84	0.00	0.84
H25	H6	0.0	0.0	0.0	0.05	0.00	0.05
H25	H7	0.0	0.0	0.0	-0.02	0.00	-0.02
H25	H8	0.0	0.0	0.0	0.02	0.00	0.02
H25	H9	0.0	0.0	0.0	0.00	0.00	0.00
H25	H10	0.0	0.0	0.0	-0.05	-0.02	-0.02
H25	H11	0.0	0.0	0.0	0.01	0.00	0.02
H25	H12	0.1	0.0	0.1	0.10	0.00	0.10
H25	N13	-2.4	0.0	-2.4	-2.44	0.00	-2.44
H25	C14	4.4	0.0	4.4	4.39	0.00	4.39
H25	O15	-2.9	0.0	-2.9	-2.92	0.00	-2.91
H25	O16	-4.0	0.0	-4.0	-3.96	-0.01	-3.95
H25	H17	2.6	0.0	2.6	2.62	-0.01	2.63
H25	C18	5.4	-4.5	9.8	0.52	0.11	0.41
H25	O19	-9.9	-1.1	-8.8	-0.65	0.18	-0.83
H25	C20	-0.6	-0.7	0.2	-0.15	-0.22	0.07
H25	H21	0.0	-0.4	0.4	-0.22	-0.40	0.18
H25	H22	0.3	0.0	0.3	0.01	-0.01	0.02
H25	H23	0.3	-0.1	0.4	0.49	0.39	0.09
H25	C24	-150.5	-172.0	21.5	-0.15	-0.31	0.16
H26	C1	0.9	0.0	0.9	0.94	0.00	0.94
H26	C2	0.1	0.0	0.1	0.13	0.00	0.13
H26	C3	0.1	0.0	0.1	0.08	0.00	0.09
H26	C4	1.0	0.0	1.0	0.98	0.00	0.98
H26	H5	0.9	0.0	0.9	0.94	0.00	0.94
H26	H6	0.1	0.0	0.1	0.05	0.00	0.05
H26	H7	0.0	0.0	0.0	-0.03	0.00	-0.03
H26	H8	0.0	0.0	0.0	0.01	0.00	0.01
H26	H9	0.0	0.0	0.0	0.00	0.00	0.00
H26	H10	0.0	0.0	0.0	-0.03	0.00	-0.03
H26	H11	0.0	0.0	0.0	0.02	0.00	0.02
H26	H12	0.1	0.0	0.1	0.11	0.00	0.11
H26	N13	-2.7	0.0	-2.7	-2.73	0.00	-2.73
H26	C14	4.8	0.0	4.8	4.83	0.00	4.83
H26	O15	-3.2	0.0	-3.2	-3.22	0.00	-3.22
H26	O16	-4.3	0.0	-4.3	-4.33	-0.01	-4.32
H26	H17	2.9	0.0	2.9	2.86	-0.01	2.87
H26	C18	5.8	-4.9	10.6	1.27	-0.68	1.94
H26	O19	-10.8	-1.2	-9.5	-2.33	-0.09	-2.25
H26	C20	-0.4	-0.5	0.1	0.26	0.25	0.02

Table S9 continues

Atom		**3b**			**3b *minus* (1b+2)**		
A	**B**	$E_{\mathrm{int}}^{\mathrm{A,B}}$	$V_{\mathrm{XC}}^{\mathrm{A,B}}$	$V_{\mathrm{cl}}^{\mathrm{A,B}}$	$\Delta E_{\mathrm{int}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{XC}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{cl}}^{\mathrm{A,B}}$
H26	H21	0.4	0.0	0.5	0.23	0.01	0.22
H26	H22	0.3	0.0	0.3	0.48	0.44	0.04
H26	H23	0.0	-0.4	0.4	-0.19	-0.39	0.20
H26	C24	-149.4	-170.9	21.5	1.97	1.89	0.08
H26	H25	-0.8	-3.1	2.3	0.46	0.11	0.35
H27	C1	0.8	0.0	0.8	0.77	0.00	0.77
H27	C2	0.1	0.0	0.1	0.11	0.00	0.11
H27	C3	0.1	0.0	0.1	0.07	0.00	0.07
H27	C4	0.8	0.0	0.8	0.81	0.00	0.81
H27	H5	0.8	0.0	0.8	0.77	0.00	0.77
H27	H6	0.0	0.0	0.0	0.04	0.00	0.04
H27	H7	0.0	0.0	0.0	-0.02	0.00	-0.02
H27	H8	0.0	0.0	0.0	0.01	0.00	0.01
H27	H9	0.0	0.0	0.0	0.00	0.00	0.00
H27	H10	0.0	0.0	0.0	-0.03	0.00	-0.03
H27	H11	0.0	0.0	0.0	0.01	0.00	0.01
H27	H12	0.1	0.0	0.1	0.09	0.00	0.09
H27	N13	-2.2	0.0	-2.2	-2.22	0.00	-2.22
H27	C14	4.1	0.0	4.1	4.06	0.00	4.06
H27	O15	-2.7	0.0	-2.7	-2.69	0.00	-2.69
H27	O16	-3.7	0.0	-3.7	-3.68	-0.01	-3.68
H27	H17	2.5	0.0	2.5	2.47	0.00	2.47
H27	C18	6.7	-3.3	10.1	1.08	-0.07	1.15
H27	O19	-11.0	-2.1	-8.8	-1.59	0.04	-1.63
H27	C20	-0.3	-0.5	0.1	0.06	0.01	0.05
H27	H21	0.4	0.0	0.4	0.22	0.07	0.15
H27	H22	0.2	-0.1	0.3	-0.03	-0.06	0.03
H27	H23	0.3	0.0	0.4	0.12	0.00	0.12
H27	C24	-152.9	-174.7	21.8	0.38	0.25	0.13
H27	H25	-0.7	-2.8	2.1	0.36	0.14	0.22
H27	H26	-0.7	-2.8	2.2	0.47	0.08	0.39
				Total:	**-46.1**	**-9.1**	**-37.0**

End of PART S4

PART S5

Data pertaining to multi-step processes leading to the CN-bond formation.

A structural re-arrangement from 3a and 3b to pre-organised for the C–N bond formation and H-transfer structures, 4a and 4b.

Data obtained from d(N13,C18) scans performed on GMS of **3a** and **3b** adducts is shown in Fig. S4. Structures at the local minima and those pertaining to products after CN-bond formation were energy optimised without any constrain. Transitional state structures (**5a** and **5b**) and their energies were obtained by applying Berny protocol.

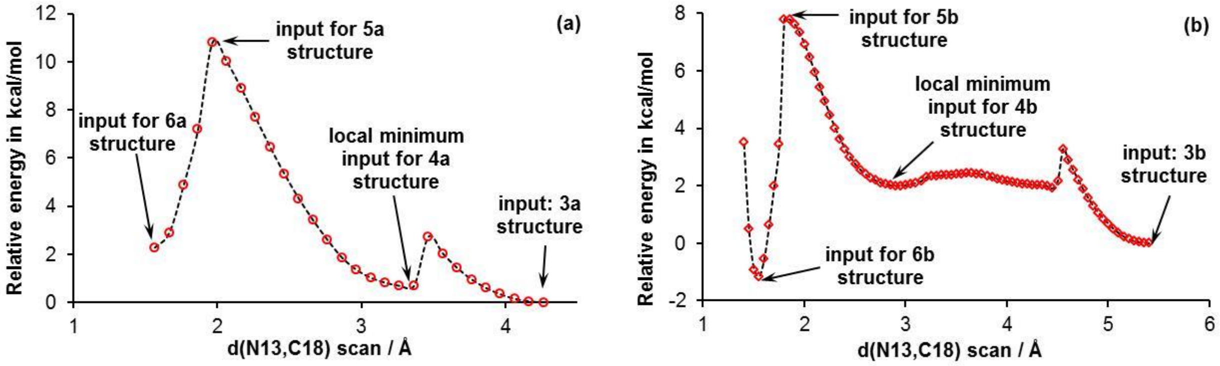

Figure S4. B3LYP data obtained from the d(N13,C18) scans performed on GMS of **3a** and **3b** adducts.

To facilitate interpretation of energies included in Table S10, analysis for selected structures (based on the MP2 data as it is a higher level of theory relative to B3LYP) follows:

1) ***Local minimum structures* 4a *and* 4b**. Both GMS adducts (**3a** and **3b**) had to overcome a small energy barrier (of about 3 kcal mol^{-1}, see Fig. S4) to attained local minimum structures **4a** and **4b** that are much better pre-organised for the C18N13-bond formation accompanied by the H17 transfer from O16 to O19 (Fig. S5). **4a** is higher in energy then **3a** by +0.7, +0.7 and +0.3 kcal mol^{-1} obtained for ΔE_{ZPVE}, ΔH and ΔG, respectively. Note that these energy changes (shown as Δ in Table S10) represent differences between consecutive structures, e.g., $\Delta H = H(\mathbf{4a}) - H(\mathbf{3a})$ = 0.7 kcal mol^{-1}. For **4b** we obtained +1.7, +1.5 and +2.5 kcal mol^{-1} for ΔE_{ZPVE}, ΔH and ΔG, respectively. The energy of **4a** is lower than that of **4b** by –2.9, –2.6 and –4.6 kcal mol^{-1} obtained for ΔE_{ZPVE}, ΔH and ΔG, respectively.

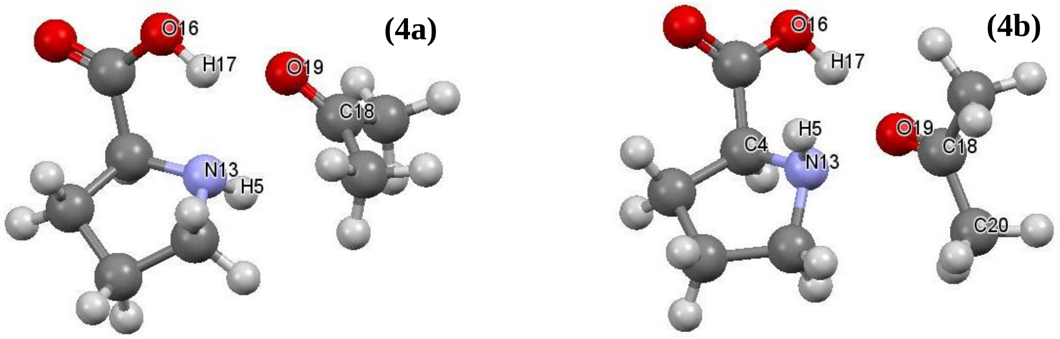

Figure S5. Ball-and-stick representation of energy optimised local minimum B3LYP structures **4a** (d(N13,C18) =3.338 Å. d(N17,O19) =2.222 Å) and **4b** (d(N13,C18) =2.9278 Å. d(H17,O19) =1.6806 Å).

2) ***Transitional state (TS) structures* 5a *and* 5b**. To attain the TS structure (Fig. S6), the pre-organised (local minimum) **4a** and **4b** structures had to climb an energy barrier of 10.7 (ΔE_{ZPVE}), 9.1 (ΔH) and 14.7 (ΔG) kcal mol^{-1} in the case of **4a** and significantly smaller energy barriers of 4.6 (ΔE_{ZPVE}), 3.1 (ΔH) and 8.0 (ΔG) kcal mol^{-1} in the case of **4b**. As a result, on an absolute scale, the energy of TS(**5a**) structure is higher than that of TS(**5b**) (computed as, e.g., (ΔH) =H(**5a**) – H(**5b**)) by 2.6 (ΔE_{ZPVE}), 2.7 (ΔH) and 2.3 (ΔG) kcal mol^{-1}.

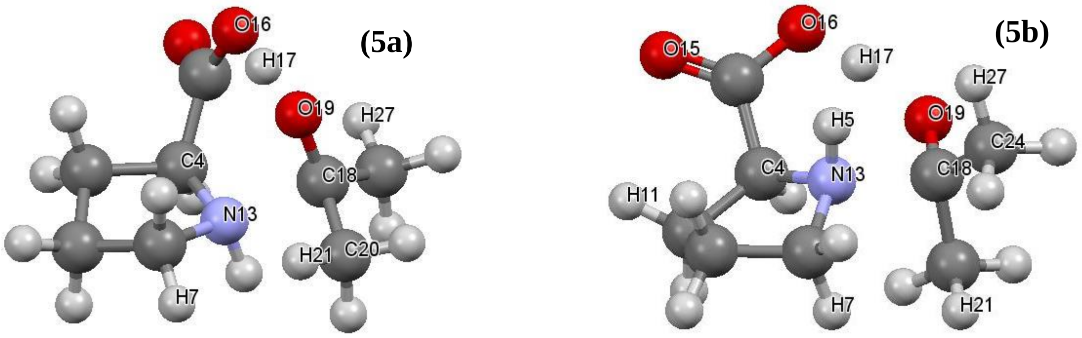

Figure S6. Ball-and-stick representation of B3LYP TS structures **5a** (d(N13,C18) = 1.9055 Å, d(O16,O19) = 2.4194 Å, d(O16,H17) = 1.1045 Å, d(H17,O19) = 1.3178 Å) and **5b** (d(N13,C18) = 1.8300 Å, d(O16,O19) = 2.4612 Å, d(O16,H17) = 1.0644 Å, d(H17,O19) = 1.4042 Å,.

Table S10. B3LYP/6-311++G(d,p)/GD3 energies (in au) and associated energy changes (in kcal mol^{-1}) between consecutive steps from **3a** and **3b**, followed by **4a** and **4b** (local minimum structures), **5a** and **5b** (TS structures) to **6a** and **6b** (products on CN-bond formation). Δ stands for an energy difference (in kcal mol^{-1}) between consecutive structures, *e.g.*, *E*(**5a**) – *E*(**4a**) or *G*(**6b**) – *G*(**5b**). Energy differences between structures containing **1a** and **1b** as, e.g. Δ*E*(**4**) = *E*(**4a**) – *E*(**4b**), are also provided (values in kcal mol^{-1}). Data obtained at the MP2/6-311++G(d,p) level is printed in italic.

Structure	***E***	**Δ**	E_{ZPVE}	**Δ**	***H***	**Δ**	***G***	**Δ**
	Structures containing **1a**							
3a	-594.5478		-594.3188		-594.3034		-594.3632	
	-592.8656		*-592.6337*		*-592.6183*		*-592.6778*	
4a	-594.5467	0.6	-594.3182	0.4	-594.3026	0.5	-594.3637	-0.3
	-592.8644	*0.7*	*-592.6326*	*0.7*	*-592.6172*	*0.7*	*-592.6773*	*0.3*
5a	-594.5303	11.0	-594.3007	11.4	-594.2881	9.6	-594.3383	15.6
	-592.8486	*10.0*	*-592.6156*	*10.7*	*-592.6027*	*9.1*	*-592.6539*	*14.7*
6a	-594.5442	2.2	-594.3097	5.7	-594.2970	4.0	-594.3470	10.2
	-592.8707	*-13.9*	*-592.6333*	*-11.1*	*-592.6207*	*-11.3*	*-592.6704*	*-10.4*
	Structures containing **1b**							
3b	-594.5460		-594.3171		-594.3017		-594.3623	
	-592.8619		*-592.6297*		*-592.6144*		*-592.6742*	
4b	-594.5428	3.1	-594.3136	3.3	-594.2985	3.1	-594.3564	4.2
	-592.8592	*1.7*	*-592.6270*	*1.7*	*-592.6118*	*1.6*	*-592.6703*	*2.5*
5b	-594.5336	7.8	-594.3029	8.9	-594.2904	7.1	-594.3404	13.8
	-592.8534	*3.6*	*-592.6196*	*4.6*	*-592.6069*	*3.1*	*-592.6575*	*8.0*
6b	-594.5479	-1.2	-594.3138	2.0	-594.3008	0.6	-594.3520	6.5
	-592.8759	*-14.1*	*-592.6397*	*-12.6*	*-592.6267*	*-12.4*	*-592.6774*	*-12.5*
		Energy difference for 4a relative to 4b						
		-2.5		-2.9		-2.6		-4.6
		-3.3		*-3.5*		*-3.4*		*-4.4*
		Energy difference for 5a relative to 5b						
		2.0		1.4		1.4		1.3
		3.0		*2.6*		*2.7*		*2.3*
		Energy difference for 6a relative to 6b						
		2.3		2.6		2.4		3.1
		3.3		*4.0*		*3.8*		*4.4*

Table S11. Net atomic charges, *Q*(A) and differences, Δ*Q*(A), computed for the indicated structures - values in *e*.

	Q(A)		Δ*Q*(A)	*Q*(A)		Δ*Q*(A)		
Atom	**3a**	**4a**	**4a – 3a**	**3b**	**4b**	**4b – 3b**	**3a – 3b**	**4a – 4b**
C1	0.3162	0.3241	0.0080	0.3313	0.3252	-0.0061	-0.0151	-0.0011
C2	0.0437	0.0450	0.0014	0.0388	0.0306	-0.0082	0.0049	0.0144
C3	0.0375	0.0414	0.0039	0.0265	0.0298	0.0033	0.0110	0.0116
C4	0.2955	0.3112	0.0157	0.3101	0.3071	-0.0030	-0.0146	0.0041
H5	0.3643	0.3604	-0.0039	0.3547	0.3342	-0.0205	0.0096	0.0262
H6	0.0224	0.0014	-0.0210	0.0115	0.0150	0.0035	0.0109	-0.0136
H7	0.0181	0.0162	-0.0019	-0.0069	-0.0018	0.0050	0.0250	0.0181
H8	-0.0064	-0.0036	0.0028	0.0024	-0.0032	-0.0056	-0.0088	-0.0005
H9	0.0065	0.0072	0.0006	-0.0076	-0.0069	0.0008	0.0141	0.0140
H10	0.0135	0.0185	0.0050	0.0051	0.0003	-0.0048	0.0083	0.0182
H11	0.0245	0.0031	-0.0214	0.0054	0.0150	0.0096	0.0191	-0.0119
H12	0.0494	0.0426	-0.0068	0.0339	0.0309	-0.0030	0.0155	0.0117
N13	-0.9855	-0.9831	0.0025	-0.9705	-0.9332	0.0373	-0.0150	-0.0499
C14	1.5236	1.5242	0.0005	1.5233	1.5278	0.0045	0.0003	-0.0037
O15	-1.1914	-1.1960	-0.0045	-1.1828	-1.1778	0.0050	-0.0086	-0.0182
O16	-1.1387	-1.1419	-0.0032	-1.1612	-1.1566	0.0046	0.0225	0.0147
H17	0.6051	0.6213	0.0162	0.6302	0.6298	-0.0004	-0.0251	-0.0085
C18	0.9662	0.9685	0.0023	0.9400	0.9547	0.0146	0.0261	0.0138
O19	-1.1579	-1.1537	0.0042	-1.1516	-1.1619	-0.0103	-0.0063	0.0082
C20	-0.0158	-0.0170	-0.0013	-0.0158	-0.0091	0.0067	0.0000	-0.0080
H21	0.0303	0.0343	0.0040	0.0557	0.0502	-0.0055	-0.0253	-0.0159
H22	0.0407	0.0405	-0.0001	0.0400	0.0369	-0.0031	0.0007	0.0036
H23	0.0399	0.0382	-0.0017	0.0509	0.0426	-0.0083	-0.0110	-0.0044
C24	-0.0200	-0.0147	0.0053	-0.0103	-0.0017	0.0086	-0.0096	-0.0130
H25	0.0295	0.0420	0.0125	0.0484	0.0408	-0.0075	-0.0189	0.0012
H26	0.0585	0.0352	-0.0233	0.0537	0.0440	-0.0098	0.0048	-0.0088
H27	0.0302	0.0355	0.0053	0.0442	0.0375	-0.0067	-0.0140	-0.0020

Note that (i) N13 is not the most negatively charged atom in all structures and its charge decreased on **3a** → **4a** by 25m*e* and **3b** → **4b** by 373m*e*, (ii) C18 is most positively charged in all structures and became more positively charged due to a loss of electrons on **3a** → **4a** by 23m*e* and **3b** → **4b** by 146m*e*, and (iii) many atoms experienced significant change in net atomic charges on both structural changes, **3a** → **4a** and **3b** → **4b**.

Table S12. Top 30 atom-pairs for which most significant increase/decrease in the net 2-atom fragment charge (in e) took place on the pre-organisation from: **3a** to **4a** – part a, **3b** to **4b** – part b. $\Delta\Delta Q$(A,B) = {ΔQ(A,B) in **4**} – {ΔQ(A,B) in **3**} where ΔQ(A,B) is a difference in net atomic charges between atoms A and B.

Part A: change from **3a** to **4a**.

Charge difference increased			**Charge difference decreased**		
Atom A	**Atom B**	**$\Delta\Delta Q$(A,B)**	**Atom A**	**Atom B**	**$\Delta\Delta Q$(A,B)**
H26	H17	0.0395	H25	H5	-0.0164
H26	C4	0.0391	O15	H6	-0.0165
H17	H11	0.0376	O15	H11	-0.0169
H17	H6	0.0372	O16	H6	-0.0178
H11	C4	0.0372	O16	H11	-0.0182
H6	C4	0.0367	H26	O15	-0.0188
H25	H11	0.0340	H25	H12	-0.0193
H25	H6	0.0335	H5	C4	-0.0196
H26	C1	0.0313	C20	H6	-0.0197
H11	C1	0.0294	H26	O16	-0.0201
H6	C1	0.0290	C20	H11	-0.0202
H27	H11	0.0268	H26	H7	-0.0214
H27	H6	0.0263	H26	C20	-0.0221
H26	C18	0.0257	H26	H25	-0.0222
H21	H11	0.0254	N13	H6	-0.0235
H11	C3	0.0253	H8	H6	-0.0238
H21	H6	0.0250	N13	H11	-0.0239
H6	C3	0.0249	H26	H9	-0.0239
H26	C14	0.0238	H11	H8	-0.0242
C18	H11	0.0238	O19	H6	-0.0252
C18	H6	0.0233	O19	H11	-0.0256
H17	H12	0.0230	H26	N13	-0.0258
H11	C2	0.0228	H26	H8	-0.0261
H12	C4	0.0225	C24	H6	-0.0263
H6	C2	0.0224	C24	H11	-0.0267
C14	H11	0.0220	H26	H21	-0.0273
C14	H6	0.0215	H26	O19	-0.0275
H22	H11	0.0213	H27	H26	-0.0280
H22	H6	0.0209	H26	H10	-0.0283
H17	O15	0.0207	H26	C24	-0.0286
Atom-pairs of special interest					
O19	H17	0.0120	C18	N13	-0.0001

Part B: change from **3b** to **4b**.

Charge difference increased			**Charge difference decreased**		
Atom A	**Atom B**	**ΔΔ*Q*(A,B)**	**Atom A**	**Atom B**	**ΔΔ*Q*(A,B)**
O19	N13	0.0476	H5	C3	-0.0238
C18	H5	0.0351	H6	H5	-0.0240
O16	N13	0.0327	O16	H5	-0.0251
O15	N13	0.0323	O15	H5	-0.0255
C14	H5	0.0250	H7	H5	-0.0255
O19	C18	0.0249	C20	H5	-0.0272
H26	C18	0.0244	N13	H11	-0.0277
H23	C18	0.0229	C24	N13	-0.0287
C18	C2	0.0228	C24	H5	-0.0291
H25	C18	0.0222	H11	H5	-0.0301
H27	C18	0.0213	C20	N13	-0.0306
C18	C1	0.0207	N13	H7	-0.0323
C18	H8	0.0202	C14	N13	-0.0328
H21	C18	0.0201	N13	H6	-0.0339
H17	H5	0.0201	N13	C3	-0.0340
O19	H11	0.0199	N13	H9	-0.0366
C18	H10	0.0194	H17	N13	-0.0377
C24	O19	0.0189	N13	C4	-0.0404
H22	C18	0.0177	N13	H12	-0.0404
C18	H12	0.0177	H22	N13	-0.0404
C18	C4	0.0177	N13	H10	-0.0421
C20	O19	0.0170	H21	N13	-0.0428
O19	H7	0.0154	N13	H8	-0.0429
H11	H8	0.0152	N13	C1	-0.0434
C18	H17	0.0150	H27	N13	-0.0440
O19	C14	0.0148	H25	N13	-0.0449
H11	H10	0.0144	N13	C2	-0.0455
H26	C14	0.0143	H23	N13	-0.0456
C18	H9	0.0139	H26	N13	-0.0471
O19	H6	0.0138	N13	H5	-0.0578
Atom-pairs of special interest					
O19	H17	0.0099	C18	N13	-0.0227

Table S13. Top 10 atom-pairs with strongest attractive/repulsive diatomic intermolecular interactions in: **3a** – part A, **3b** – part B. Interaction energies are in kcal mol^{-1}.

Part A: data for **3a**.

Strongest attractive interactions					**Strongest repulsive interactions**				
Atom A	**Atom B**	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$	**Atom A**	**Atom B**	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$
O19	C14	-161.3	-0.3	-161.0	H23	C14	5.5	0.0	5.5
C18	O16	-113.4	-1.7	-111.7	H26	C14	8.9	-0.2	9.1
C18	O15	-98.6	-0.1	-98.5	C18	H5	24.0	0.0	24.0
C18	N13	-76.9	0.0	-76.9	C18	C4	24.0	0.0	24.0
O19	H17	-65.6	0.0	-65.6	C18	C1	26.2	0.0	26.2
O19	C1	-34.4	-1.1	-33.3	C18	H17	56.9	0.0	56.9
O19	C4	-29.7	-0.1	-29.6	O19	N13	94.3	-0.1	94.4
O19	H5	-29.5	0.0	-29.5	O19	O15	115.1	-0.2	115.3
H26	O15	-9.2	-2.2	-7.0	O19	O16	125.1	-0.9	126.0
H26	O16	-8.9	-2.0	-6.9	C18	C14	138.3	-0.1	138.4

All interactions and components			
	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$
Total:	-34.3	-26.7	-7.6

Part B: data for **3b**.

Strongest attractive interactions					**Strongest repulsive interactions**				
Atom A	**Atom B**	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$	**Atom A**	**Atom B**	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$
O19	C14	-159.8	-0.2	-159.6	H23	C14	5.9	0.0	5.9
O19	H17	-143.9	-18.3	-125.6	H21	C14	6.3	0.0	6.3
C18	O16	-114.2	-0.2	-114.0	C18	C1	19.7	0.0	19.7
C18	O15	-73.9	0.0	-73.9	C18	H5	20.1	0.0	20.1
C18	N13	-58.0	0.0	-58.0	C18	C4	21.9	-0.1	22.0
O19	C4	-30.7	-1.4	-29.3	O19	N13	76.4	-0.1	76.5
O19	H5	-26.4	0.0	-26.4	C18	H17	85.6	-0.2	85.8
O19	C1	-25.5	0.0	-25.5	O19	O15	97.8	-0.2	98.0
O19	H12	-6.3	-2.9	-3.4	C18	C14	117.8	0.0	117.8
H21	O16	-6.0	0.0	-6.0	O19	O16	150.0	-8.2	158.2

All interactions and components			
	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$
Total:	-53.6	-40.7	-12.9

Table S14. Top 10 atom-pairs with strongest attractive/repulsive diatomic intermolecular interactions in: **4a** – part A, **4b** – part B. Interaction energies are in kcal mol^{-1}.

Part A: data for **4a**.

Strongest attractive interactions					Strongest repulsive interactions				
Atom A	**Atom B**	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$	**Atom A**	**Atom B**	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$
O19	C14	-139.6	-0.1	-139.5	H26	C14	3.8	0.0	3.8
C18	O16	-104.5	-0.1	-104.4	H25	C14	4.5	0.0	4.5
C18	N13	-103.4	-0.9	-102.5	C18	C4	26.0	0.0	26.0
O19	H17	-102.7	-3.8	-98.9	C18	C1	31.0	-0.4	31.4
C18	O15	-69.9	0.0	-69.9	C18	H5	33.2	0.0	33.2
O19	H5	-38.7	0.0	-38.7	C18	H17	73.4	-0.1	73.5
O19	C1	-37.9	-0.6	-37.3	O19	O15	88.9	-0.1	89.0
O19	C4	-32.0	0.0	-32.0	C18	C14	108.1	0.0	108.1
H25	N13	-4.7	-0.1	-4.6	O19	N13	119.8	-3.0	122.8
H27	N13	-4.7	-1.1	-3.6	O19	O16	135.0	-4.3	139.3

All interactions and components			
	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$
Total:	-23.9	-23.0	-0.9

Sum of all intermolecular interactions

Part B: data for **4b**.

Strongest attractive interactions					Strongest repulsive interactions				
Atom A	**Atom B**	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$	**Atom A**	**Atom B**	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$
O19	C14	-165.3	-0.2	-165.1	H25	C14	5.3	0.0	5.3
O19	H17	-146.5	-18.3	-128.2	H26	C14	5.7	0.0	5.7
C18	O16	-120.5	-0.3	-120.2	C18	C1	30.6	-0.1	30.7
C18	N13	-112.2	-4.7	-107.4	C18	H5	31.2	0.0	31.2
C18	O15	-78.8	0.0	-78.8	C18	C4	31.4	-0.2	31.6
O19	C4	-40.4	-1.4	-38.9	C18	H17	90.3	-0.3	90.6
O19	H5	-36.5	-0.1	-36.4	O19	O15	100.2	-0.2	100.4
O19	C1	-35.9	-0.1	-35.8	O19	N13	120.1	-4.0	124.1
O19	H12	-6.7	-3.1	-3.5	C18	C14	127.2	0.0	127.2
H27	O16	-5.9	-2.0	-3.9	O19	O16	153.1	-8.1	161.2

All interactions and components			
	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$
Total:	-70.3	-55.4	-14.9

Table S15. Top 10 atom-pairs for which most significant increase/decrease in the intermolecular diatomic interaction energy (in kcal mol^{-1}) that took place on the pre-organisation from: **3a** to **4a** – part A, **3b** to **4b** – part B. $\Delta E_{\text{int}}^{\text{A,B}}$ = { $E_{\text{int}}^{\text{A,B}}$ in **4**} – { $E_{\text{int}}^{\text{A,B}}$ in **3**}.

Part A: from **3a** to **4a**.

Strongest attractive interactions					**Strongest repulsive interactions**				
Atom A	**Atom B**	$\Delta E_{\text{int}}^{\text{A,B}}$	$\Delta V_{\text{XC}}^{\text{A,B}}$	$\Delta V_{\text{cl}}^{\text{A,B}}$	**Atom A**	**Atom B**	$\Delta E_{\text{int}}^{\text{A,B}}$	$\Delta V_{\text{XC}}^{\text{A,B}}$	$\Delta V_{\text{cl}}^{\text{A,B}}$
O19	H17	-37.1	-3.8	-33.3	H26	O16	5.4	2.0	3.4
C18	C14	-30.2	0.1	-30.3	O19	H11	5.8	3.8	2.0
C18	N13	-26.4	-0.9	-25.5	H26	O15	6.7	2.2	4.5
O19	O15	-26.1	0.1	-26.2	C18	O16	8.9	1.6	7.3
O19	H5	-9.2	0.0	-9.2	C18	H5	9.2	0.0	9.2
H26	C14	-5.1	0.2	-5.3	O19	O16	9.9	-3.3	13.2
O19	C1	-3.6	0.4	-4.0	C18	H17	16.5	-0.1	16.6
H25	N13	-2.5	-0.1	-2.4	O19	C14	21.8	0.2	21.6
H27	N13	-2.4	-1.1	-1.3	O19	N13	25.4	-2.9	28.3
O19	C4	-2.3	0.1	2.4	C18	O15	28.8	0.1	28.7

All interactions and components			
	$\Delta E_{\text{int}}^{\text{A,B}}$	$\Delta V_{\text{XC}}^{\text{A,B}}$	$\Delta V_{\text{cl}}^{\text{A,B}}$
Total:	10.4	3.8	6.6

Part B: from **3b** to **4b**.

Strongest attractive interactions					**Strongest repulsive interactions**				
Atom A	**Atom B**	$\Delta E_{\text{int}}^{\text{A,B}}$	$\Delta V_{\text{XC}}^{\text{A,B}}$	$\Delta V_{\text{cl}}^{\text{A,B}}$	**Atom A**	**Atom B**	$\Delta E_{\text{int}}^{\text{A,B}}$	$\Delta V_{\text{XC}}^{\text{A,B}}$	$\Delta V_{\text{cl}}^{\text{A,B}}$
C18	N13	-54.1	-4.7	-49.4	H21	O16	1.7	0.0	1.7
O19	C1	-10.4	0.0	-10.4	H23	O16	1.8	0.0	1.8
O19	H5	-10.0	0.0	-10.0	O19	O15	2.4	0.0	2.4
O19	C4	-9.7	-0.1	-9.6	O19	O16	3.1	0.1	3.0
C18	O16	-6.3	-0.2	-6.1	C18	H17	4.7	-0.1	4.8
O19	C14	-5.5	0.0	-5.5	C18	C14	9.4	0.0	9.4
C18	O15	-4.9	0.0	-4.9	C18	C4	9.5	-0.1	9.6
H25	N13	-3.1	-1.0	-2.0	C18	C1	11.0	-0.1	11.1
O19	H17	-2.6	0.0	-2.6	C18	H5	11.2	0.0	11.2
C24	N13	-2.6	-2.9	0.3	O19	N13	43.7	-3.9	47.6

All interactions and components			
	$\Delta E_{\text{int}}^{\text{A,B}}$	$\Delta V_{\text{XC}}^{\text{A,B}}$	$\Delta V_{\text{cl}}^{\text{A,B}}$
Total:	-16.7	-14.7	-2.0

Data in Table S16 can be used to pin-point individual atoms that played most important role in the **3** to **4** pre-organisation process. There are just few atoms interactions of which changed most significantly. It is clear that this is not the C18 atom of **2** that attracts entire **1** (even though it is to form a bond with N13 at the later stage of a process) as we found $E_{\mathrm{int}}^{\mathrm{C18},\mathbf{1}}$ of +7.8 (in **4a**) and +11.2 kcal mol^{-1} (in **4b**). Importantly, note that C18 is involved in strongest repulsive interactions with **1** in both pre-organised adducts, **4a** and **4b**. There is however a significant difference when the trend in $E_{\mathrm{int}}^{\mathrm{C18},\mathbf{1}}$ is considered on the **3** → **4** change, namely the interaction between C18 and all atoms of **1** (i) became repulsive as it changed from very weak attractive in **3a** (–0.7 kcal mol^{-1}) to repulsive in **4a** (+7.8 kcal mol^{-1}) whereas (ii) opposite trend is seen for **3b** → **4b** as it became less repulsive by –15.3 kcal mol^{-1} in the latter.

Focusing on atoms of **1** we found that:

a) O16 in **3a** attracts **2** by far the most with $E_{\mathrm{int}}^{\mathrm{O16},\mathbf{2}}$ of –20 kcal mol^{-1} whereas H17 and C14 of **3b** interact most favourably with **2** with $E_{\mathrm{int}}^{\mathrm{H17},\mathbf{2}}$ and $E_{\mathrm{int}}^{\mathrm{C14},\mathbf{2}}$ of –40.4 and –13.7 kcal mol^{-1}, respectively.

b) After the pre-organisation process, H17, C14 and N13 in **4a** can be seen as keeping **1** and **2** in close proximity as their interactions with **2** of –17.0, –11.8 and –5.8 kcal mol^{-1}, respectively, are dominating. Interestingly, these atoms place the same role in **4b** but their interactions with **1** are stronger in **4b** (we obtained –38.4, –24.6 and –9.1 kcal mol^{-1}, respectively, for H17, N13 and C14). Furthermore, there is no atom of **1b** in **4b** that is repelling **2** by more than 2.9 kcal mol^{-1} whereas there are two atoms of **1a** in **4a** (O15 and O16) that are involved in repulsive interactions (with **2**) larger than +6 kcal mol^{-1}.

Considering atoms of **2**, it is very clear that this is the O19 that attracts **1** most (and by far) in both structures of **3** and **4**. Moreover, $E_{\mathrm{int}}^{\mathrm{O19},\mathbf{2}}$ of –78.9 and –69.3 kcal mol^{-1} in **3b** and **4b**, respectively, are about three times stronger when compared with the same interactions in **3a** and **3b**.

All the above nicely indicates the origin of much higher affinity between **1** and **2** observed for structures containing **1b** (the higher energy conformer of S-proline). It is clear that just few atoms are responsible for intermolecular interaction energy $E_{\mathrm{int}}^{\mathbf{1},\mathbf{2}}$ of (i) –53.6 kcal mol^{-1} in **3b** being stronger, relative to **3a**, by nearly –30 kcal mol^{-1} and (ii) –70.3 kcal mol^{-1} in **4b** being stronger, relative to **4a**, by as much as –46 kcal mol^{-1}. It is reasonable to suggest that such large difference in affinity between **1** and **2** (in favour of **4b**) can be linked with significantly lower energy barrier at a TS computed for **5b**.

Table S16. Interaction energy and its components (in kcal mol^{-1}) between atoms of **1** (S-proline) and entire molecule **2** (acetone) as well as atoms of **2** and entire molecule **1** in adducts **3** and pre-organised structures **4**.

Part A. Interaction energies.

Atom A of 1	$E_{\text{int}}^{\text{A},\mathbf{2}}$					
	3a	**4a**	$\Delta_{\mathbf{4a-3a}}$	**3b**	**4b**	$\Delta_{\mathbf{4b-3b}}$
C1	-3.5	-2.1	1.4	-0.9	1.2	2.1
C2	-0.5	-0.2	0.3	-0.3	0.0	0.3
C3	-1.6	-0.2	1.4	-2.4	-0.2	2.1
C4	-1.0	-1.3	-0.2	-3.5	-1.8	1.7
H5	-0.8	0.4	1.2	-1.3	2.4	3.7
H6	-4.8	-2.1	2.7	-0.1	-0.2	-0.1
H7	-0.4	-1.6	-1.2	0.0	-2.1	-2.1
H8	-0.2	-0.1	0.1	-0.1	0.0	0.1
H9	-0.1	0.0	0.1	0.0	-0.1	0.0
H10	-0.4	-0.1	0.3	-2.1	0.1	2.2
H11	-4.3	0.1	4.4	-2.4	-0.1	2.3
H12	-0.2	-0.2	0.0	-3.2	-3.3	-0.1
N13	2.5	-5.8	-8.3	3.9	-24.6	-28.5
C14	6.5	-11.8	-18.3	-13.7	-9.1	4.5
O15	-8.5	6.1	14.6	5.5	2.9	-2.6
O16	-20.0	11.9	31.8	7.3	2.9	-4.4
H17	3.1	-17.0	-20.0	-40.4	-38.4	2.0
	$E_{\text{int}}^{\mathbf{1},\mathbf{2}}$					
	-34.3	-23.9	10.4	-53.6	-70.3	-16.7

Atom A of 2	$E_{\text{int}}^{\text{A},\mathbf{1}}$					
	3a	**4a**	$\Delta_{\mathbf{4a-3a}}$	**3b**	**4b**	$\Delta_{\mathbf{4b-3b}}$
C18	-0.7	7.8	8.5	26.5	11.2	-15.3
O19	-19.6	-25.8	-6.2	-78.9	-69.3	9.6
C20	-2.2	-1.2	1.0	-2.0	-1.9	0.1
H21	-1.2	0.2	1.4	-0.1	-2.6	-2.4
H22	-2.1	-1.1	1.0	-1.5	-0.1	1.4
H23	-0.3	0.3	0.6	0.7	0.1	-0.6
C24	-1.7	-2.4	-0.7	0.1	-3.4	-3.5
H25	-0.6	0.3	0.8	0.5	-1.3	-1.8
H26	-5.3	-0.7	4.6	0.6	-0.2	-0.8
H27	-0.6	-1.2	-0.6	0.6	-2.9	-3.4
	$E_{\text{int}}^{\mathbf{1},\mathbf{2}}$					
	-34.3	-23.9	10.4	-53.6	-70.3	-16.7

Table S16 continues

Part B. Exchange-correlation component of the interaction energies.

Atom A of 1	$V_{\mathrm{XC}}^{\mathrm{A},\mathbf{2}}$					
	3a	**4a**	$\Delta_{\mathbf{4a}-\mathbf{3a}}$	**3b**	**4b**	$\Delta_{\mathbf{4b}-\mathbf{3b}}$
C1	-1.3	-1.9	-0.6	0.0	-1.3	-1.2
C2	-0.2	-0.1	0.1	-0.2	-0.2	0.0
C3	-1.3	0.0	1.2	-2.4	-0.2	2.2
C4	-0.2	-0.1	0.0	-1.5	-1.7	-0.2
H5	0.0	-0.6	-0.5	0.0	-0.2	-0.2
H6	-4.6	-2.4	2.3	0.0	-0.2	-0.2
H7	-0.1	-1.3	-1.2	0.0	-2.1	-2.1
H8	0.0	0.0	0.0	0.0	0.0	0.0
H9	-0.2	0.0	0.1	0.0	0.0	0.0
H10	-0.1	0.0	0.1	-1.8	0.0	1.8
H11	-4.1	0.0	4.1	-2.1	0.0	2.1
H12	0.0	0.0	0.0	-3.0	-3.4	-0.3
N13	-0.3	-7.3	-7.1	-0.1	-15.2	-15.0
C14	-0.8	-0.1	0.7	-0.2	-0.3	0.0
O15	-3.7	-0.1	3.6	-0.2	-0.2	0.0
O16	-9.6	-4.7	4.9	-10.0	-11.3	-1.3
H17	-0.2	-4.2	-4.0	-19.0	-19.2	-0.2
	$V_{\mathrm{XC}}^{\mathbf{1},\mathbf{2}}$					
	-26.7	-23.0	3.8	-40.7	-55.4	-14.7

Atom A of 2	$V_{\mathrm{XC}}^{\mathrm{A},\mathbf{1}}$					
	3a	**4a**	$\Delta_{\mathbf{4a}-\mathbf{3a}}$	**3b**	**4b**	$\Delta_{\mathbf{4b}-\mathbf{3b}}$
C18	-2.4	-2.0	0.4	-1.3	-6.0	-4.8
O19	-11.9	-13.3	-1.4	-33.7	-35.6	-1.9
C20	-2.2	-1.1	1.1	-2.1	-2.1	0.0
H21	-0.9	-0.1	0.8	-1.0	-2.8	-1.8
H22	-2.1	-1.4	0.7	-2.2	-0.2	1.9
H23	-0.2	-0.1	0.1	-0.1	-0.2	0.0
C24	-2.2	-2.3	-0.2	-0.3	-4.0	-3.7
H25	-0.1	-0.2	0.0	-0.1	-1.3	-1.3
H26	-4.5	-0.9	3.6	0.0	-0.3	-0.3
H27	-0.2	-1.6	-1.4	0.0	-2.9	-2.9
	$V_{\mathrm{XC}}^{\mathbf{1},\mathbf{2}}$					
	-26.7	-23.0	3.8	-40.7	-55.4	-14.7

Table S16 continues

Part C. Classical component of the interaction energies.

Atom A of 1	$V_{\mathrm{cl}}^{\mathrm{A},\mathbf{2}}$					
	3a	**4a**	$\Delta_{\mathbf{4a-3a}}$	**3b**	**4b**	$\Delta_{\mathbf{4b-3b}}$
C1	-2.2	-0.1	2.1	-0.8	2.5	3.4
C2	-0.3	-0.1	0.3	-0.1	0.1	0.3
C3	-0.3	-0.1	0.2	0.0	0.0	0.0
C4	-0.8	-1.1	-0.3	-2.0	-0.1	1.9
H5	-0.8	0.9	1.8	-1.3	2.7	3.9
H6	-0.2	0.3	0.4	-0.1	0.0	0.1
H7	-0.3	-0.3	0.0	0.0	0.0	0.0
H8	-0.2	-0.1	0.1	-0.1	0.0	0.2
H9	0.1	0.0	-0.1	0.0	0.0	0.0
H10	-0.3	-0.1	0.2	-0.3	0.1	0.3
H11	-0.2	0.1	0.3	-0.3	-0.1	0.2
H12	-0.2	-0.2	0.0	-0.2	0.1	0.2
N13	2.7	1.5	-1.2	4.1	-9.4	-13.5
C14	7.3	-11.7	-19.0	-13.4	-8.9	4.6
O15	-4.7	6.2	11.0	5.7	3.1	-2.6
O16	-10.4	16.6	26.9	17.4	14.2	-3.1
H17	3.2	-12.8	-16.0	-21.4	-19.2	2.2
	$V_{\mathrm{cl}}^{\mathbf{1},\mathbf{2}}$					
	-7.6	-0.9	6.7	-12.9	-14.9	-2.0

Atom A of 2	$V_{\mathrm{cl}}^{\mathrm{A},\mathbf{1}}$					
	3a	**4a**	$\Delta_{\mathbf{4a-3a}}$	**3b**	**4b**	$\Delta_{\mathbf{4b-3b}}$
C18	1.7	9.8	8.1	27.8	17.2	-10.5
O19	-7.7	-12.5	-4.8	-45.2	-33.8	11.5
C20	0.0	-0.1	-0.1	0.0	0.2	0.1
H21	-0.3	0.3	0.6	0.8	0.2	-0.6
H22	0.0	0.3	0.3	0.7	0.1	-0.5
H23	-0.1	0.4	0.5	0.8	0.2	-0.5
C24	0.5	0.0	-0.6	0.3	0.6	0.3
H25	-0.5	0.4	0.9	0.6	0.1	-0.5
H26	-0.8	0.2	0.9	0.7	0.1	-0.5
H27	-0.4	0.3	0.7	0.6	0.1	-0.5
	$V_{\mathrm{cl}}^{\mathbf{1},\mathbf{2}}$					
	-7.6	-0.9	6.7	-12.9	-14.9	-2.0

From the pre-organised for the C–N bond formation and H-transfer structures, 4a and 4b, to transition state structures 5a and 5b.

In search for the origin of the small difference in the $E_{\mathrm{int}}^{\mathrm{Tot}}$ values computed for **5a** and **5b**, we decomposed the total interaction energy to contributions made by all covalent and non-covalent interactions in **4** and **5**. This approach revealed that on the **4** to **5** change:

1. Covalent interactions (bonds) became largely weakened in **5** relative to **4**, by about 162.7 and 136.8 kcal mol^{-1} in **5a** and **5b**, respectively. The most affected C18–O19 bond experienced the energy decrease by about 128 kcal mol^{-1} in both **5a** and **5b** structures.
2. Non-covalent intra- and intermolecular interactions became much stronger in **5**, by about –171 and –148 kcal mol^{-1} in **5a** and **5b**, respectively.
3. The largest and of stabilizing nature change is observed for intermolecular interactions. They became stronger by –211 and –168 kcal mol^{-1} in **5a** and **5b**, respectively, and the main contribution came from interactions between atoms of the $\mathcal{G}$ and $\mathcal{H}$ molecular fragments (we obtained $\Delta E_{\mathrm{int}}^{\mathcal{G},\mathcal{H}}$ of –181.2 and –146.4 kcal mol^{-1} for changes from **4a** to **5a** and **4b** to **5b**, respectively.

It is important to stress that {H17,O19} and {N13,C18} atom-pairs experienced most significant strengthening in their di-atomic interactions among all possible 351 2-atom fragments and, as a consequence, these fragments of molecular system became most stabilized in **5a** and **5b**.

Clearly, there is not a single cause that can be linked with the small observed difference in energy barriers computed for transitional states **5a** and **5b**. In this instance, it is a result of combined large increases and decreases in interaction energies between all atoms.

Table S17. Net atomic charges, Q(A) and differences, ΔQ(A), computed for the indicated structures - values in *e*.

	Q(A)		ΔQ(A)	Q(A)		ΔQ(A)		
Atom	**4a**	**5a**	**5a – 4a**	**4b**	**5b**	**5b – 4b**	**4a – 4b**	**5a – 5b**
C1	0.3241	0.2933	-0.0309	0.3252	0.2887	-0.0365	-0.0011	0.0046
C2	0.0450	0.0496	0.0046	0.0306	0.0490	0.0184	0.0144	0.0007
C3	0.0414	0.0443	0.0029	0.0298	0.0423	0.0125	0.0116	0.0020
C4	0.3112	0.2501	-0.0612	0.3071	0.2493	-0.0578	0.0041	0.0008
H5	0.3604	0.3865	0.0260	0.3342	0.3865	0.0523	0.0262	-0.0001
H6	0.0014	0.0435	0.0421	0.0150	0.0468	0.0318	-0.0136	-0.0033
H7	0.0162	0.0400	0.0237	-0.0018	0.0382	0.0400	0.0181	0.0018
H8	-0.0036	0.0072	0.0109	-0.0032	0.0239	0.0271	-0.0005	-0.0167
H9	0.0072	0.0228	0.0157	-0.0069	0.0091	0.0159	0.0140	0.0138
H10	0.0185	0.0299	0.0114	0.0003	0.0134	0.0131	0.0182	0.0164
H11	0.0031	0.0129	0.0098	0.0150	0.0442	0.0291	-0.0119	-0.0313
H12	0.0426	0.0591	0.0165	0.0309	0.0696	0.0387	0.0117	-0.0105
N13	-0.9831	-0.8774	0.1056	-0.9332	-0.8693	0.0639	-0.0499	-0.0081
C14	1.5242	1.5779	0.0538	1.5278	1.5704	0.0426	-0.0037	0.0076
O15	-1.1960	-1.1976	-0.0016	-1.1778	-1.1814	-0.0037	-0.0182	-0.0162
O16	-1.1419	-1.1872	-0.0453	-1.1566	-1.1712	-0.0146	0.0147	-0.0161
H17	0.6213	0.6252	0.0039	0.6298	0.6287	-0.0012	-0.0085	-0.0034
C18	0.9685	0.8658	-0.1027	0.9547	0.8701	-0.0846	0.0138	-0.0043
O19	-1.1537	-1.2064	-0.0527	-1.1619	-1.2280	-0.0662	0.0082	0.0216
C20	-0.0170	0.0128	0.0298	-0.0091	0.0122	0.0213	-0.0080	0.0006
H21	0.0343	0.0255	-0.0089	0.0502	0.0078	-0.0424	-0.0159	0.0177
H22	0.0405	0.0148	-0.0257	0.0369	0.0142	-0.0227	0.0036	0.0006
H23	0.0382	0.0321	-0.0061	0.0426	0.0300	-0.0126	-0.0044	0.0021
C24	-0.0147	0.0101	0.0248	-0.0017	0.0090	0.0108	-0.0130	0.0011
H25	0.0420	0.0309	-0.0111	0.0408	0.0090	-0.0318	0.0012	0.0219
H26	0.0352	0.0156	-0.0196	0.0440	0.0261	-0.0178	-0.0088	-0.0105
H27	0.0355	0.0199	-0.0156	0.0375	0.0135	-0.0240	-0.0020	0.0064

Table S18. Top 30 atom-pairs for which most significant increase/decrease in the net 2-atom fragment charge (in e) took place on reaching the transitional state (TS) from: **4a** to **5a** – part a, **4b** to **5b** – part b. $\Delta\Delta Q$(A,B) = {ΔQ(A,B) in **5**} – {ΔQ(A,B) in **4**} where ΔQ(A,B) is a difference in net atomic charges between atoms A and B.

Part A: change from **4a** to **5a**.

Charge difference increased			**Charge difference decreased**		
Atom A	**Atom B**	**$\Delta\Delta Q$(A,B)**	**Atom A**	**Atom B**	**$\Delta\Delta Q$(A,B)**
O19	N13	0.1584	N13	H8	-0.0948
C18	C14	0.1565	N13	H11	-0.0959
O16	N13	0.1510	H23	C18	-0.0966
C14	C4	0.1149	N13	C2	-0.1010
O15	N13	0.1073	C18	O15	-0.1011
O19	C14	0.1065	H17	N13	-0.1018
O16	C14	0.0991	N13	C3	-0.1027
O19	H6	0.0948	H6	C4	-0.1032
O16	H6	0.0874	C18	C3	-0.1056
H5	C4	0.0872	C18	H17	-0.1066
C14	C1	0.0847	C18	C2	-0.1073
C20	O19	0.0825	H23	N13	-0.1117
H22	C14	0.0795	C18	H11	-0.1125
O19	H5	0.0788	C18	H8	-0.1136
C24	O19	0.0776	C18	H10	-0.1141
O19	H7	0.0764	H21	N13	-0.1145
C20	O16	0.0751	H25	N13	-0.1168
H26	C14	0.0734	C18	H9	-0.1184
O16	H5	0.0714	C18	H12	-0.1192
C24	O16	0.0702	H27	N13	-0.1212
H27	C14	0.0694	H26	N13	-0.1252
O19	H12	0.0693	C18	H7	-0.1264
O16	H7	0.0691	C24	C18	-0.1275
O19	H9	0.0684	C18	H5	-0.1287
H17	C4	0.0650	H22	N13	-0.1313
H25	C14	0.0649	C20	C18	-0.1325
O19	H10	0.0641	N13	C1	-0.1365
O19	H8	0.0636	C18	H6	-0.1448
H21	C14	0.0627	N13	C4	-0.1668
O19	H11	0.0625	C18	N13	-0.2083
Atom-pairs of special interest					
O19	H17	0.0566	C18	N13	-0.2083

Part B: change from **4b** to **5b**.

Charge difference increased			**Charge difference decreased**		
Atom A	**Atom B**	**$\Delta\Delta Q$(A,B)**	**Atom A**	**Atom B**	**$\Delta\Delta Q$(A,B)**
O19	N13	0.1300	H23	N13	-0.0765
C18	C14	0.1272	H7	C1	-0.0765
O19	H5	0.1185	C20	C4	-0.0791
H5	C4	0.1102	C18	O15	-0.0810
O19	C14	0.1087	H26	N13	-0.0817
O19	H7	0.1062	C18	H17	-0.0834
O19	H12	0.1048	H8	C4	-0.0849
C14	C4	0.1004	H22	N13	-0.0865
O19	H6	0.0979	H11	C4	-0.0869
O19	H11	0.0953	H27	N13	-0.0879
H21	H5	0.0947	H6	C4	-0.0896
O19	H8	0.0932	C24	C18	-0.0954
H5	C1	0.0889	H25	N13	-0.0956
C20	O19	0.0874	H12	C4	-0.0965
H21	C14	0.0850	C18	C3	-0.0971
O19	C2	0.0845	C18	H10	-0.0977
H25	H5	0.0841	H7	C4	-0.0978
O19	H9	0.0821	N13	C1	-0.1004
O19	H10	0.0793	C18	H9	-0.1005
C14	C1	0.0791	C18	C2	-0.1030
O19	C3	0.0786	C20	C18	-0.1059
O16	N13	0.0785	H21	N13	-0.1063
C24	O19	0.0769	C18	H8	-0.1117
H27	H5	0.0764	C18	H11	-0.1137
H22	H5	0.0750	C18	H6	-0.1164
H25	C14	0.0743	N13	C4	-0.1217
H26	H5	0.0701	C18	H12	-0.1233
O15	N13	0.0675	C18	H7	-0.1246
O16	H5	0.0669	C18	H5	-0.1369
H27	C14	0.0666	C18	N13	-0.1485
Atom-pairs of special interest					
O19	H17	0.0516	C18	N13	-0.1483

Table S19. Top 10 atom-pairs with strongest attractive/repulsive diatomic intermolecular interactions in: **5a** – part A, **5b** – part B. Interaction energies are in kcal mol^{-1}.

Part A: data for **5a**.

Strongest attractive interactions					**Strongest repulsive interactions**				
Atom A	**Atom B**	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$	**Atom A**	**Atom B**	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$
O19	H17	-217.0	-44.9	-172.1	H25	C14	5.7	0.0	5.7
C18	N13	-207.6	-74.2	-133.4	C18	H12	5.8	-0.1	5.9
O19	C14	-193.9	-0.4	-193.5	C18	C4	30.0	-0.9	30.9
C18	O16	-125.6	-0.8	-124.8	C18	C1	36.9	-1.2	38.1
C18	O15	-81.4	-0.1	-81.3	C18	H5	45.7	-0.7	46.4
O19	H5	-50.0	-0.3	-49.7	C18	H17	101.6	-0.8	102.4
O19	C1	-45.7	-1.5	-44.2	O19	O15	111.9	-0.3	112.2
O19	C4	-36.5	-0.3	-36.2	O19	N13	127.9	-13.1	141.1
O19	H6	-9.4	-3.6	-5.8	C18	C14	137.4	-0.3	137.7
C24	N13	-8.1	-6.1	-2.0	O19	O16	171.9	-16.9	188.8

All interactions and components			
	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$
Total:	-235.0	-196.2	-38.8

Part B: data for **5b**.

Strongest attractive interactions					**Strongest repulsive interactions**				
Atom A	**Atom B**	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$	**Atom A**	**Atom B**	$E_{\text{int}}^{\text{A,B}}$	$V_{\text{XC}}^{\text{A,B}}$	$V_{\text{cl}}^{\text{A,B}}$
C18	N13	-224.8	-85.8	-139.0	C18	H6	4.7	0.0	4.7
O19	H17	-198.0	-36.2	-161.8	C18	H12	7.7	-0.6	8.3
O19	C14	-197.4	-0.5	-196.9	C18	C4	33.6	-1.2	34.8
C18	O16	-119.0	-0.7	-118.3	C18	C1	34.3	-0.9	35.2
C18	O15	-78.7	0.0	-78.7	C18	H5	52.4	-0.9	53.3
O19	H5	-60.1	-0.3	-59.8	C18	H17	92.6	-0.5	93.1
O19	C4	-43.3	-2.8	-40.5	O19	O15	113.4	-0.3	113.7
O19	C1	-38.2	-0.5	-37.7	O19	N13	129.7	-13.5	143.2
O19	H12	-14.3	-3.6	-10.7	C18	C14	133.4	-0.1	133.5
C24	N13	-8.4	-6.7	-1.7	O19	O16	172.0	-15.1	187.1

All interactions and components			
	$\Delta E_{\text{int}}^{\text{A,B}}$	$\Delta V_{\text{XC}}^{\text{A,B}}$	$\Delta V_{\text{cl}}^{\text{A,B}}$
Total:	-238.1	-197.5	-40.6

Table S20. Top 10 atom-pairs for which most significant increase/decrease in the intermolecular diatomic interaction energy (in kcal mol^{-1}) took place on reaching the transitional state from: **4a** to **5a** – part A, **4b** to **5b** – part B. $\Delta E_{\mathrm{int}}^{\mathrm{A,B}} = \{ E_{\mathrm{int}}^{\mathrm{A,B}}$ in **5**$\} - \{ E_{\mathrm{int}}^{\mathrm{A,B}}$ in **4**$\}$.

Part A: from **4a** to **5a**.

Strongest attractive interactions					**Strongest repulsive interactions**				
Atom A	**Atom B**	$\Delta E_{\mathrm{int}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{XC}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{cl}}^{\mathrm{A,B}}$	**Atom A**	**Atom B**	$\Delta E_{\mathrm{int}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{XC}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{cl}}^{\mathrm{A,B}}$
O19	H17	-114.3	-41.1	-73.2	C20	C14	3.6	0.0	3.6
C18	N13	-104.2	-73.2	-31.0	C18	C4	4.0	-0.9	4.9
O19	C14	-54.3	-0.3	-54.0	C18	H6	5.6	-0.1	5.7
C18	O16	-21.1	-0.7	-20.4	C18	C1	5.9	-1.0	6.9
C18	O15	-11.5	0.0	-11.5	O19	N13	8.2	-10.1	18.3
O19	H5	-11.3	-0.3	-11.0	C18	H5	12.5	-0.7	13.2
O19	H6	-9.1	-2.3	-6.8	O19	O15	22.9	-0.3	23.2
C24	N13	-8.5	-4.3	-4.2	C18	H17	28.2	-0.6	28.8
C20	N13	-8.2	-5.1	-3.1	C18	C14	29.3	-0.2	29.5
O19	C1	-7.8	-1.0	-6.8	O19	O16	36.8	-12.6	49.4

All interactions and components			
	$\Delta E_{\mathrm{int}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{XC}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{cl}}^{\mathrm{A,B}}$
Total:	–211.1	-173.3	-37.8

Part B: from **4b** to **5b**.

Strongest attractive interactions					**Strongest repulsive interactions**				
Atom A	**Atom B**	$\Delta E_{\mathrm{int}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{XC}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{cl}}^{\mathrm{A,B}}$	**Atom A**	**Atom B**	$\Delta E_{\mathrm{int}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{XC}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{cl}}^{\mathrm{A,B}}$
C18	N13	-112.6	-81.1	-31.5	H21	N13	3.4	0.5	2.9
O19	H17	-51.5	-18.0	-33.5	C18	C1	3.6	-0.8	4.4
O19	C14	-32.1	-0.3	-31.8	C18	H7	4.2	-0.2	4.4
O19	H5	-23.6	-0.2	-23.4	H27	O16	4.8	1.8	3.0
O19	H12	-7.6	-0.4	-7.2	C18	H12	5.0	-0.4	5.4
C20	N13	-6.9	-4.3	-2.6	C18	C14	6.2	-0.1	6.3
C24	N13	-6.0	-3.8	-2.2	O19	N13	9.6	-9.5	19.1
O19	H7	-4.9	0.0	-4.9	O19	O15	13.2	-0.1	13.3
H25	C14	-3.5	0.0	-3.5	O19	O16	18.9	-7.0	25.9
H21	C14	-3.3	0.0	-3.3	C18	H5	21.2	-0.8	22.0

All interactions and components			
	$\Delta E_{\mathrm{int}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{XC}}^{\mathrm{A,B}}$	$\Delta V_{\mathrm{cl}}^{\mathrm{A,B}}$
Total:	-167.8	-142.1	-25.7

Table S21. Interaction energy and its components (in kcal mol^{-1}) between atoms of **1** (S-proline) and entire molecule **2** (acetone) as well as atoms of **2** and entire molecule **1** in pre-organised structures **4** and transition state structures **5**.

Part A. Interaction energies

Atom A of 1	$E_{\text{int}}^{\text{A},\mathbf{2}}$					
	4a	**5a**	$\Delta_{\mathbf{5a-4a}}$	**4b**	**5b**	$\Delta_{\mathbf{5b-4b}}$
C1	-2.1	-5.2	-3.1	1.2	-1.8	-3.1
C2	-0.2	-1.2	-1.0	0.0	-0.9	-0.8
C3	-0.2	-0.7	-0.6	-0.2	-1.0	-0.8
C4	-1.3	-2.3	-1.0	-1.8	-6.1	-4.3
H5	0.4	3.2	2.8	2.4	-1.9	-4.4
H6	-2.1	-4.7	-2.6	-0.2	-1.5	-1.3
H7	-1.6	-3.4	-1.8	-2.1	-4.8	-2.7
H8	-0.1	-0.3	-0.2	0.0	-0.3	-0.3
H9	0.0	-0.3	-0.3	-0.1	0.0	0.0
H10	-0.1	-0.5	-0.4	0.1	-0.3	-0.3
H11	0.1	0.1	0.0	-0.1	-0.6	-0.5
H12	-0.2	-0.8	-0.6	-3.3	-7.8	-4.6
N13	-5.8	-120.0	-114.1	-24.6	-131.9	-107.3
C14	-11.8	-33.3	-21.5	-9.1	-45.9	-36.7
O15	6.1	14.8	8.7	2.9	23.8	20.9
O16	11.9	19.4	7.5	2.9	36.6	33.7
H17	-17.0	-100.0	-83.0	-38.4	-93.8	-55.4
	$E_{\text{int}}^{\mathbf{1},\mathbf{2}}$					
	-23.9	-235.0	-211.1	-70.3	-238.1	-167.8

Atom A of 2	$E_{\text{int}}^{\text{A},\mathbf{1}}$					
	4a	**5a**	$\Delta_{\mathbf{5a-4a}}$	**4b**	**5b**	$\Delta_{\mathbf{5b-4b}}$
C18	7.8	-32.3	-40.1	11.2	-43.4	-54.6
O19	-25.8	-174.9	-149.1	-69.3	-167.6	-98.3
C20	-1.2	-8.6	-7.4	-1.9	-9.1	-7.2
H21	0.2	-2.7	-2.9	-2.6	-3.2	-0.6
H22	-1.1	-1.6	-0.5	-0.1	-3.2	-3.1
H23	0.3	0.4	0.1	0.1	0.4	0.3
C24	-2.4	-9.2	-6.8	-3.4	-8.8	-5.4
H25	0.3	0.3	0.0	-1.3	-2.3	-1.1
H26	-0.7	-1.3	-0.6	-0.2	0.4	0.6
H27	-1.2	-5.2	-3.9	-2.9	-1.3	1.6
	$E_{\text{int}}^{\mathbf{1},\mathbf{2}}$					
	-23.9	-235.0	-211.1	-70.3	-238.1	-167.8

Table S21 continues

Part B. Exchange-correlation component of the interaction energies.

Atom A of 1	$V_{\mathrm{XC}}^{\mathrm{A},\mathbf{2}}$					
	4a	**5a**	$\Delta_{\mathbf{5a}-\mathbf{4a}}$	**4b**	**5b**	$\Delta_{\mathbf{5b}-\mathbf{4b}}$
C1	-1.9	-6.0	-4.1	-1.3	-4.8	-3.5
C2	-0.1	-0.7	-0.6	-0.2	-0.7	-0.6
C3	0.0	-0.4	-0.4	-0.2	-0.5	-0.3
C4	-0.1	-2.7	-2.6	-1.7	-5.4	-3.7
H5	-0.6	-2.7	-2.2	-0.2	-3.2	-3.0
H6	-2.4	-4.8	-2.4	-0.2	-1.7	-1.5
H7	-1.3	-3.1	-1.9	-2.1	-5.0	-3.0
H8	0.0	-0.1	0.0	0.0	-0.1	-0.1
H9	0.0	-0.1	-0.1	0.0	-0.1	0.0
H10	0.0	-0.1	0.0	0.0	-0.1	-0.1
H11	0.0	0.0	0.0	0.0	-0.1	0.0
H12	0.0	-0.4	-0.4	-3.4	-6.6	-3.2
N13	-7.3	-102.8	-95.4	-15.2	-115.0	-99.8
C14	-0.1	-2.8	-2.7	-0.3	-0.7	-0.4
O15	-0.1	-0.8	-0.7	-0.2	-0.4	-0.2
O16	-4.7	-22.5	-17.8	-11.3	-16.2	-4.9
H17	-4.2	-46.2	-42.0	-19.2	-37.0	-17.9
	$V_{\mathrm{XC}}^{\mathbf{1},\mathbf{2}}$					
	-23.0	-196.2	-173.3	-55.4	-14.9	-238.1

Atom A of 2	$V_{\mathrm{XC}}^{\mathrm{A},\mathbf{1}}$					
	4a	**5a**	$\Delta_{\mathbf{5a}-\mathbf{4a}}$	**4b**	**5b**	$\Delta_{\mathbf{5b}-\mathbf{4b}}$
C18	-2.0	-80.1	-78.1	-6.0	-91.7	-85.7
O19	-13.3	-81.8	-68.5	-35.6	-73.1	-37.5
C20	-1.1	-9.1	-8.0	-2.1	-9.8	-7.7
H21	-0.1	-3.6	-3.5	-2.8	-3.6	-0.8
H22	-1.4	-2.1	-0.7	-0.2	-3.7	-3.4
H23	-0.1	-1.0	-0.9	-0.2	-1.0	-0.9
C24	-2.3	-9.7	-7.4	-4.0	-9.1	-5.0
H25	-0.2	-1.0	-0.8	-1.3	-2.8	-1.5
H26	-0.9	-1.8	-0.9	-0.3	-1.0	-0.7
H27	-1.6	-6.1	-4.5	-2.9	-1.8	1.1
	$V_{\mathrm{XC}}^{\mathbf{1},\mathbf{2}}$					
	-23.0	-196.2	-173.3	-55.4	-14.9	-238.1

Table S16 continues

Part C. Classical component of the interaction energies.

Atom A of 1	$V_{\mathrm{cl}}^{\mathrm{A},\mathbf{2}}$					
	4a	**5a**	$\Delta_{\mathbf{5a-4a}}$	**4b**	**5b**	$\Delta_{\mathbf{5b-4b}}$
C1	-0.1	0.8	1.0	2.5	2.9	0.4
C2	-0.1	-0.4	-0.4	0.1	-0.1	-0.2
C3	-0.1	-0.3	-0.2	0.0	-0.5	-0.5
C4	-1.1	0.4	1.5	-0.1	-0.7	-0.6
H5	0.9	5.9	5.0	2.7	1.3	-1.4
H6	0.3	0.1	-0.2	0.0	0.2	0.2
H7	-0.3	-0.3	0.0	0.0	0.2	0.3
H8	-0.1	-0.2	-0.1	0.0	-0.2	-0.2
H9	0.0	-0.2	-0.2	0.0	0.0	0.1
H10	-0.1	-0.4	-0.3	0.1	-0.1	-0.2
H11	0.1	0.1	0.0	-0.1	-0.5	-0.5
H12	-0.2	-0.4	-0.2	0.1	-1.2	-1.3
N13	1.5	-17.2	-18.7	-9.4	-16.9	-7.5
C14	-11.7	-30.5	-18.8	-8.9	-45.2	-36.4
O15	6.2	15.7	9.4	3.1	24.2	21.0
O16	16.6	41.9	25.3	14.2	52.8	38.6
H17	-12.8	-53.8	-41.0	-19.2	-56.8	-37.5
	$V_{\mathrm{cl}}^{\mathbf{1,2}}$					
	-0.9	-38.7	-37.8	-14.9	-40.6	-25.7

Atom A of 2	$V_{\mathrm{cl}}^{\mathrm{A},\mathbf{1}}$					
	4a	**5a**	$\Delta_{\mathbf{5a-4a}}$	**4b**	**5b**	$\Delta_{\mathbf{5b-4b}}$
C18	9.8	47.8	38.0	17.2	48.3	31.1
O19	-12.5	-93.1	-80.7	-33.8	-94.5	-60.7
C20	-0.1	0.5	0.6	0.2	0.6	0.4
H21	0.3	0.9	0.6	0.2	0.4	0.1
H22	0.3	0.5	0.2	0.1	0.5	0.3
H23	0.4	1.4	1.0	0.2	1.4	1.2
C24	0.0	0.5	0.6	0.6	0.3	-0.3
H25	0.4	1.3	0.9	0.1	0.5	0.4
H26	0.2	0.5	0.3	0.1	1.3	1.2
H27	0.3	1.0	0.6	0.1	0.6	0.5
	$V_{\mathrm{cl}}^{\mathbf{1,2}}$					
	-0.9	-38.7	-37.8	-14.9	-40.6	-25.7

End of PART S5

PART S6

Data pertaining to multi-step processes leading from **6a** and **6b** to the first proton transfer.

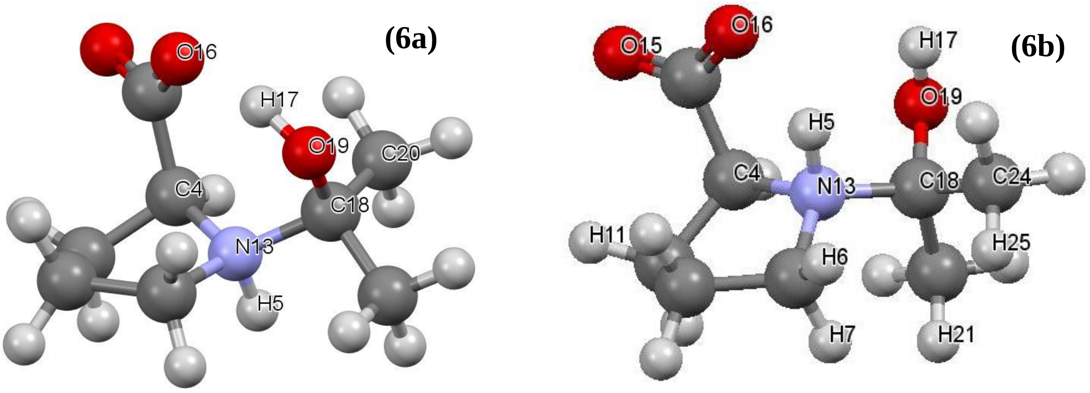

Figure S7. Ball-and-stick representation of **6a (**d(N13,C18) = 1.58697 Å, d(H17,O19) of 1.00186 Å, d(H5,O16) = 3.86653 Å, d(O16,H17) = 1.58424 Å) and **6b** (d(N13,C18) = 1.54295 Å, d(H17,O19) = 0.96689, Å d(H5,O16) = 1.75657 Å) structures.

In search for the GMS of **6a** and **6b**, a dihedral scan DA(C4,N13,C18,O19) was performed - data obtained are shown in Fig. S8.

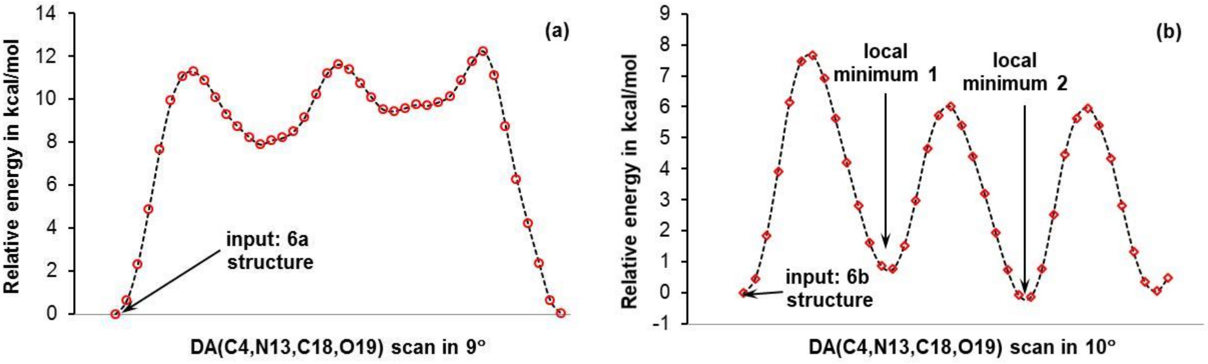

Figure S8. B3LYP data obtained from the DA(C4,N13,C18,O19) scan performed on **6a** (part a) and **6b** (part b).

From Fig. S8(a) it is clear that **6a** is indeed the GMS. There are two local minima of comparable to **6b** energies seen in Fig. S8(b). Energy of local minimum 1 structure is about 1 kcal mol^{-1} higher relative to **6b**. Due to being slightly higher in energy and not ideally pre-organised for the proton transfer (Fig. S9(a)), it was no longer considered. Energies of the local minimum 2 structure (Fig. S8(b)) and **6b** are the same. Comparing these two structures makes it clear that **6b** is not only best pre-organised for the H-transfer but also for the subsequent water elimination step.

Moreover, the interatomic distance d(H5,O16) = 1.79507 Å in the local minimum 2 structure is longer, by 0.0385 Å, relative to that observed in **6b**; hence, **6b** was selected for further studies.

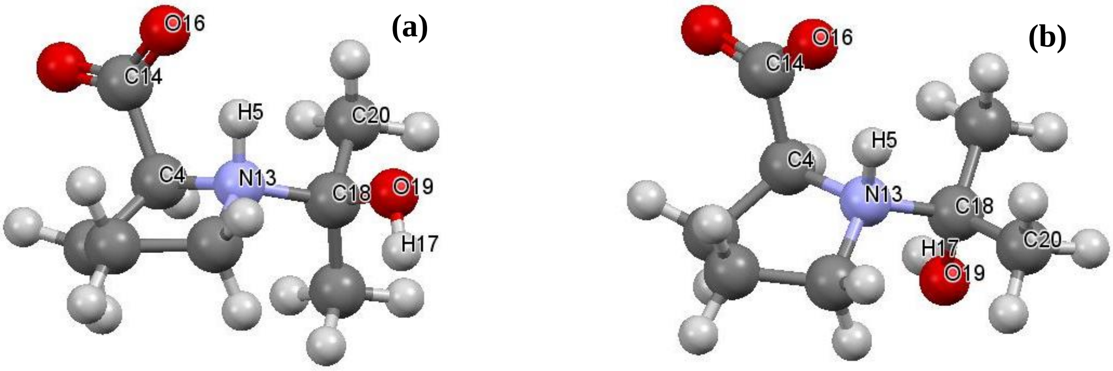

Figure S9. Ball-and-stick representation of energy optimised local minimum 1 (part a) and local minimum 2 (part b) structures obtained from the DA(C4,N13,C18,O19) scan shown in Fig. S8(b).

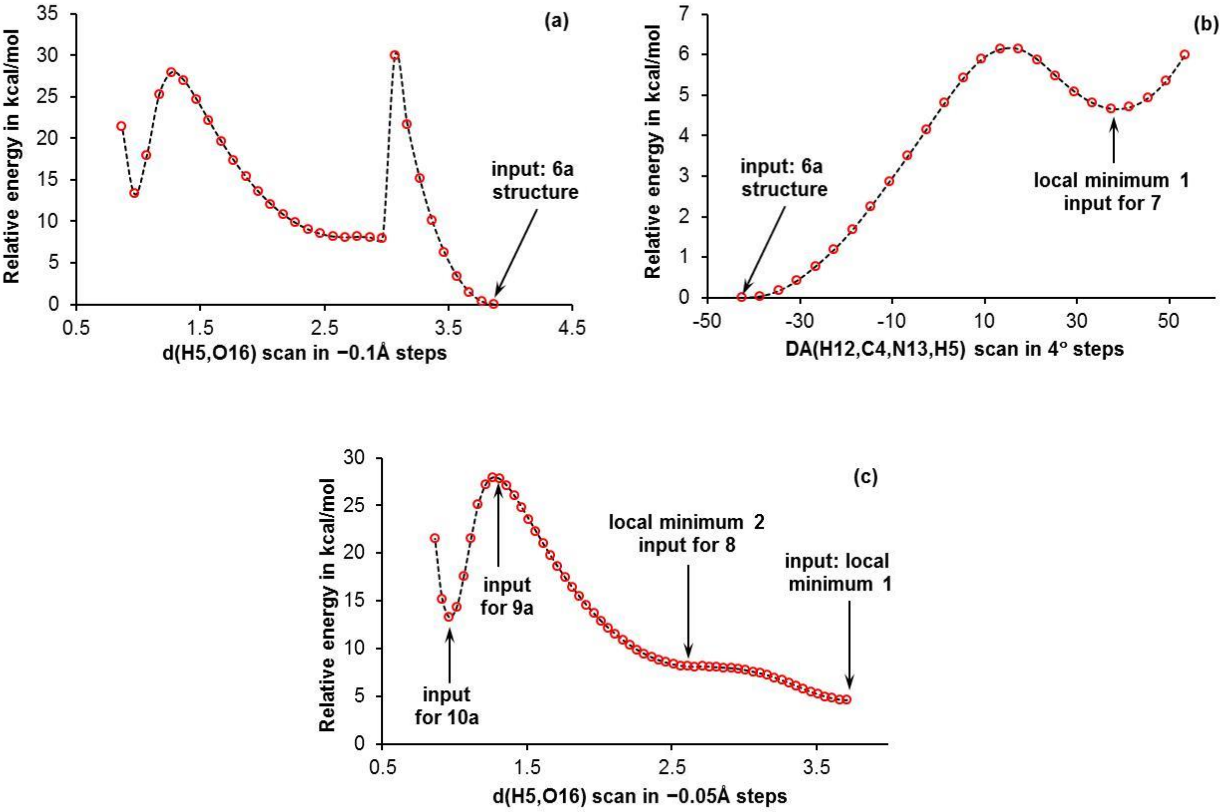

Figure S10. B3LYP data obtained from the indicated scans performed on **6a**.

Scan along the reaction coordinates performed on **6a** (by decreasing the interatomic distance between H5 and O16) shows (Fig. S10(a)) a sharp initial rise in energy with a barrier of 30 kcal mol^{-1}. Because a large structural change took place after overcoming this energy barrier, we concluded that **6a** must undergo an initial pre-organisation first.

Indeed a smooth increase in energy is observed in Fig. S10(b) where, after overcoming an energy barrier of only about 6 kcal mol^{-1}, a local minimum 1 is observed – this structure was energy optimised without any constrain to give structure **7** (shown in Fig. S11) that was subjected to the d(H5,O16) scan. Data obtained (Fig. S10(c)) shows (i) an additional local minimum 2 (it was energy optimised to give structure **8** shown in Fig. S11), (ii) data point corresponding to the structure that was subjected to the Berny optimisation (to obtain a transitional state structure **9a**) and (iii) data point corresponding to the structure that was subjected to full energy optimisation without any constrain in order to obtain product of the proton transfer **10a**.

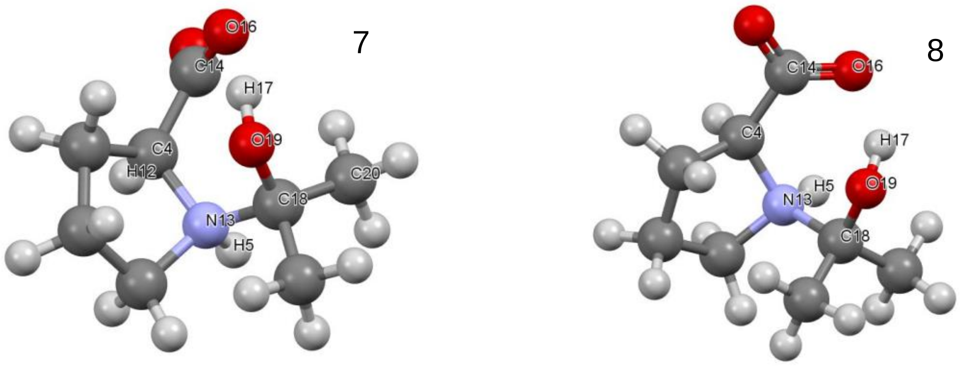

Figure S11. Ball-and-stick representation of structures **7** and **8** obtained from energy optimised local minimum structures 1 and 2, respectively; these minima are shown in Figs. S10(b) and (c).

Scan along the reaction coordinates performed on **6b** is shown in Fig. S12 and transitional state structures of **9a** and **9b** are shown in Fig. S13.

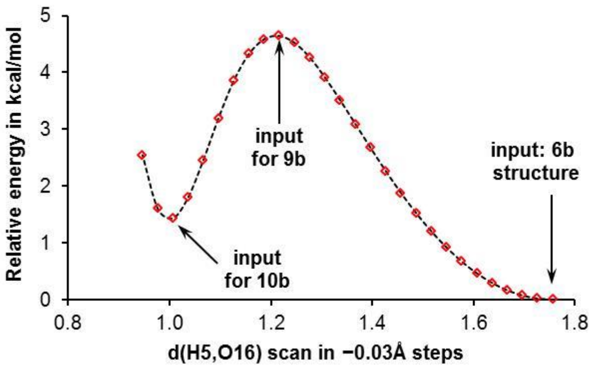

Figure S12. B3LYP data obtained from the d(H5,O16) scan performed on **6b**.

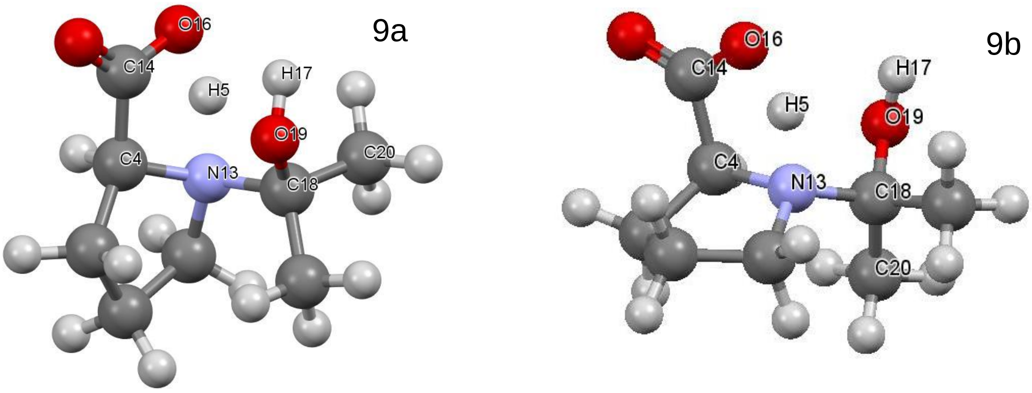

Figure S13. Ball-and-stick representation of transitional state structures **9a (**d(H5,O16) = 1.27470 Å, d(H5,N13) = 1.29366 Å) and **9b** (d(H5,O16) = 0.99901 Å, d(H5,N13) = 1.81499 Å).

Table S22. B3LYP/6-311++G(d,p)/GD3 energies (in au) and associated energy changes (in kcal mol^{-1}) between consecutive steps from **6a** and **6b**, followed by **7** and **8** (local minima structures with **1a**), **9a** and **9b** (TS structures) to **10a** and **10b** (products on H-transfer). Energy differences between structures that originated from **1a** and **1b** as, e.g. Δ*E*(**9**) = *E*(**9a**) – *E*(**9b**), are also provided (values in kcal mol^{-1}). Data obtained at the MP2/6-311++G(d,p) level is printed in italic.

Structure	***E***	**Δ**	***E*$_{\mathbf{ZPVE}}$**	**Δ**	***H***	**Δ**	***G***	**Δ**
	Structures that originated from **1a**							
6a	-594.5442		-594.3097		-594.2970		-594.3470	
	-592.8707		*-592.6333*		*-592.6207*		*-592.6704*	
7	-594.5369	4.6	-594.3018	5.0	-594.2892	4.9	-594.3388	5.1
	-592.8635	*4.5*	*-592.6255*	*4.9*	*-592.6130*	*4.8*	*-592.6622*	*5.2*
8	-594.5314	3.5	-594.2967	3.2	-594.2840	3.2	-594.3340	3.0
	-592.8581	*3.4*	*-592.6204*	*3.2*	*-592.6078*	*3.3*	*-592.6578*	*2.8*
9a	-594.4958	22.3	-594.2659	19.3	-594.2536	19.1	-594.3022	20.0
	-592.8283	*18.7*	*-592.5956*	*15.6*	*-592.5834*	*15.3*	*-592.6317*	*16.3*
10a	-594.5231	–17.2	-594.2906	-15.5	-594.2774	-14.9	-594.3279	-16.2
	-592.8539	*–16.1*	*-592.6184*	*–14.3*	*-592.6053*	*–13.8*	*-592.6556*	*–14.9*
	Structures that originated from **1b**							
6b	-594.5479		-594.3138		-594.3008		-594.3520	
	-592.8759		*-592.6397*		*-592.6267*		*-592.6774*	
9b	-594.5405	4.6	-594.3112	1.7	-594.2985	1.4	-594.3481	2.5
	-592.8721	*2.4*	*-592.6402*	*–0.3*	*-592.6276*	*–0.6*	*-592.6772*	*0.1*
10b	-594.5456	–3.2	-594.3130	–1.2	-594.3000	–0.9	-594.3506	–1.6
	-592.8765	*–2.7*	*-592.6412*	*–0.6*	*-592.6282*	*–0.4*	*-592.6788*	*–1.0*
		Energy difference for 6a relative to 6b						
		2.3		2.6		2.4		3.1
		3.3		*4.0*		*3.8*		*4.4*
		Energy difference for 9a relative to 9b						
		25.8		25.8		25.8		25.6
		24.3		*24.0*		*24.0*		*24.2*
		Energy difference for 10a relative to 10b						
		11.8		11.5		11.8		11.1
		10.9		*10.3*		*10.6*		*10.2*

Comments related to consecutive structural changes from 6a, via 7 and 8, to 9a.

From 6a to 7

The total energy of all (bonded and non-bonded) 371 intramolecular interactions weakened in **7**, hence decreased, by 14.1 kcal mol^{-1}. Selected data for covalent bonds is included in Table S23.

Table S23. Top 6 atom-pairs for which most significant increase/decrease in covalent bond strength (as measured by the interatomic interaction energy change in kcal mol^{-1}) took place on the pre-organisation from **6a** to **7**. $\Delta E_{\text{int}}^{\text{A,B}} = \{ E_{\text{int}}^{\text{A,B}}$ in **7**$\} - \{ E_{\text{int}}^{\text{A,B}}$ in **6a**$\}$.

Strengthened bonds			**Weakened bonds**		
Atom A	**Atom B**	$\Delta E_{\text{int}}^{\text{A,B}}$	**Atom A**	**Atom B**	$\Delta E_{\text{int}}^{\text{A,B}}$
N13	C1	-6.8	O19	H17	2.3
C2	C1	-1.4	C3	C2	2.4
H11	C3	-1.0	N13	C4	3.3
H6	C1	-1.0	O15	C14	6.1
H12	C4	-0.8	O16	C14	6.7
C14	C4	-0.7	C18	N13	8.8
Sum of all changes in the intermolecular interactions					
Attractive:		-13.4	Repulsive:		+34.2
	Total:	+20.8			

Note that covalent bonds weakened in total by 20.8 kcal mol^{-1}. This is a result of some bonds that became either weaker (in total by 34.2 kcal mol^{-1}) or stronger (in total by –13.4 kcal mol^{-1}) The link N13–C18 became strained (hence weakened) most in terms of interatomic interaction energy, by 8.8 kcal mol^{-1}.

The molecular systems **6a** and **6b** were considered in discussions that follow as made of two molecular fragments, $\mathcal{K}$ and $\mathcal{L}$, that are shown in Fig. S14.

Figure S14. Schematic partitioning of entire **6** to two molecular fragments $\mathcal{K}$ and $\mathcal{L}$.

The same fragments apply to the **7** and **8** structures. Atom-pairs for which most significant increase/decrease in the interfragment diatomic interaction energy (in kcal mol^{-1}) took place on the pre-organisation from **6a** to **7** are shown in Table S24.

Table S24. Top 10 atom-pairs for which most significant increase/decrease in the inter-fragment diatomic interaction energy (in kcal mol^{-1}) took place on the pre-organisation from **6a** to **7.** $\Delta E_{\text{int}}^{\text{A,B}} = \{ E_{\text{int}}^{\text{A,B}}$ in **7**$\} - \{ E_{\text{int}}^{\text{A,B}}$ in **6a**$\}$. Atom A belongs to the fragment $\mathcal{K}$ (**1a** minus H17) and atom B belongs to the fragment $\mathcal{L}$ (**2** + H17).

Strengthened interactions			Weakened interactions		
Atom A	**Atom B**	$\Delta E_{\text{int}}^{\text{A,B}}$	**Atom A**	**Atom B**	$\Delta E_{\text{int}}^{\text{A,B}}$
O19	C14	-7.8	C18	H10	1.3
H21	O16	-4.0	C24	H5	1.5
O19	C4	-3.5	H21	C14	1.6
C24	H6	-3.2	O19	C1	3.2
O19	H9	-2.8	H17	C14	3.7
C18	H6	-2.5	O19	O15	4.3
H17	H6	-2.5	C18	O16	4.6
O19	H10	-2.4	H17	N13	5.1
C18	O15	-2.4	C18	N13	8.8
O19	N13	-2.3	O19	H6	9.9
Sum of all changes in the intermolecular interactions					
Attractive:		-65.4	Repulsive:		+64.8
	Total:	–0.6			

The inter-fragment interaction energy, *i.e*, between all atoms of the molecular fragment $\mathcal{K}$ = {atoms of **1a** minus H17} and all atoms of the molecular fragment $\mathcal{L}$ = {atoms of **2** plus H17}, $E_{\text{int}}^{\mathcal{K},\mathcal{L}}$, essentially remained the same in **7** as $\Delta E_{\text{int}}^{\mathcal{K},\mathcal{L}}$ = –0.6 kcal mol^{-1}. Note that this also includes the interaction energy between N13 and all atoms of $\mathcal{L}$; hence this also includes the N13–C18-covalent bond interaction energy. When only non-bonded interactions between $\mathcal{K}$ and $\mathcal{L}$ are considered (excluding interaction energy between N13 and C18), they became stronger in **7** by –13.1 kcal mol^{-1}.

Considering interaction energies between (i) individual atoms of $\mathcal{K}$ and entire molecular fragment $\mathcal{L}$ as well as(ii) individual atoms of $\mathcal{L}$ and entire molecular fragment $\mathcal{K}$ (see data in Table S25) we note that:

Table S25. Interaction energies (in kcal mol^{-1}) between atoms of a molecular fragment $\mathcal{K}$ and entire molecular fragment $\mathcal{L}$ and atoms of $\mathcal{L}$ and entire molecular fragment $\mathcal{K}$ in **6a** and **7**.

Atom A of $\mathcal{K}$	$E_{\text{int}}^{\text{A},\mathcal{L}}$			**Atom A od $\mathcal{L}$**	$E_{\text{int}}^{\text{A},\mathcal{K}}$		
	6a	**7**	$\Delta_{\mathbf{7-6a}}$		**6a**	**7**	$\Delta_{\mathbf{7-6a}}$
C1	18.2	18.6	0.4	H17	-82.5	-77.9	4.7
C2	2.5	0.8	-1.7	C18	-190.3	-181.6	8.7
C3	2.8	0.6	-2.2	O19	30.7	22.6	-8.1
C4	17.8	17.0	-0.9	C20	-12.7	-12.6	0.1
H5	38.3	37.1	-1.1	H21	-6.3	-9.0	-2.8
H6	-1.4	-3.0	-1.6	H22	-2.5	-2.6	-0.1
H7	1.7	2.7	1.0	H23	-3.6	-3.1	0.5
H8	1.6	1.3	-0.3	C24	-11.7	-13.5	-1.8
H9	1.1	-1.5	-2.6	H25	-2.5	-3.1	-0.6
H10	1.0	1.3	0.4	H26	-1.7	-1.7	0.0
H11	2.2	-0.3	-2.5	H27	-4.1	-5.3	-1.2
H12	2.2	3.4	1.2		$E_{\text{int}}^{\mathcal{K},\mathcal{L}}$		
N13	-285.0	-272.5	12.5		-287.2	-287.8	-0.6
C14	101.9	100.6	-1.3				
O15	-55.2	-57.6	-2.4				
O16	-136.8	-136.4	0.4				
	$E_{\text{int}}^{\mathcal{K},\mathcal{L}}$						
	-287.2	-287.8	-0.6				

- In the case of atoms of $\mathcal{K}$, their interaction energies with $\mathcal{L}$, on average, changed slightly ($\Delta E_{\text{int}}^{\text{A},\mathcal{L}}$ = –0.6±1.3 kcal mol^{-1}) except for N13 that experienced the largest unfavourable change with $\Delta E_{\text{int}}^{\text{N13},\mathcal{L}}$ = 12.5 kcal mol^{-1}.
- In the case of atoms of $\mathcal{L}$, largest changes in the $E_{\text{int}}^{\text{A},\mathcal{K}}$ energy term were found for C18, O19 and H17 (the C18–OH fragment of $\mathcal{L}$) of +8.7, –8.1 and +4.7 kcal mol^{-1}, respectively.

From 7 to 8

We noted that the energy of all (bonded and non-bonded) 371 intramolecular interactions marginally improved (by –1.3 kcal mol^{-1}); covalent bonds strengthened by –11.6 kcal mol^{-1} (this is a result of some bonds that became either weaker (in total by 22.8 kcal mol^{-1}) or stronger (in total by –34.3 kcal mol^{-1}) whereas non-bonded weakened by +18.0 kcal mol^{-1}. The link N13–C18 became somewhat more strained (hence weakened) by 2.6 kcal mol^{-1}. The C18–O19 covalent bond became strained the most, its energy decreased by 8.7 kcal mol^{-1}.

Table S26. Interaction energies (in kcal mol^{-1}) between atoms of a molecular fragment $\mathcal{K}$ and entire molecular fragment $\mathcal{L}$ and atoms of $\mathcal{L}$ and entire molecular fragment $\mathcal{K}$ in **7** and **8**.

Atom A of $\mathcal{K}$	$E_{\mathrm{int}}^{\mathrm{A},\mathcal{L}}$			**Atom A of $\mathcal{L}$**	$E_{\mathrm{int}}^{\mathrm{A},\mathcal{K}}$		
	7	**8**	$\Delta_{\mathbf{8}-\mathbf{7}}$		**7**	**8**	$\Delta_{\mathbf{8}-\mathbf{7}}$
C1	18.6	19.6	0.9	H17	-77.9	-67.3	10.6
C2	0.8	-0.1	-0.9	C18	-181.6	-181.0	0.6
C3	0.6	0.9	0.3	O19	22.6	30.0	7.4
C4	17.0	18.9	2.0	C20	-12.6	-12.1	0.5
H5	37.1	39.0	1.9	H21	-9.0	-2.8	6.2
H6	-3.0	-2.2	0.8	H22	-2.6	-2.1	0.5
H7	2.7	3.2	0.6	H23	-3.1	-3.6	-0.5
H8	1.3	1.5	0.2	C24	-13.5	-13.5	0.0
H9	-1.5	-1.6	0.0	H25	-3.1	-6.1	-3.0
H10	1.3	1.8	0.5	H26	-1.7	-1.9	-0.3
H11	-0.3	-2.6	-2.3	H27	-5.3	-6.8	-1.4
H12	3.4	3.0	-0.4		$E_{\mathrm{int}}^{\mathcal{K},\mathcal{L}}$		
N13	-272.5	-273.6	-1.1		-287.8	-267.1	20.6
C14	100.6	88.0	-12.6				
O15	-57.6	-47.1	10.5				
O16	-136.4	-116.0	20.4				
	$E_{\mathrm{int}}^{\mathcal{K},\mathcal{L}}$						
	-287.8	-267.1	20.6				

Looking at data in Table S26 one can note that:

- Inter-fragment interaction energy between molecular fragments $\mathcal{K}$ and $\mathcal{L}$, $E_{\mathrm{int}}^{\mathcal{K},\mathcal{L}}$, weakened by 20.6 kcal mol^{-1}. Note that this also includes the interaction energy between N13 and all atoms of $\mathcal{L}$; hence this also includes the N13C18-covalent bond interaction energy. When only non-bonded interactions between $\mathcal{K}$ and $\mathcal{L}$ are considered (excluding interaction energy between N13 and C18), they became weaker in **8** by +21.7 kcal mol^{-1}.
- N13 of $\mathcal{K}$ are involved in strongest (by far) interactions with $\mathcal{L}$ in **7** and **8**, namely –272.5 and –273.6 kcal mol^{-1}, respectively; these interactions became slightly more attractive in **8**, by –1.1 kcal mol^{-1}.

- Considering atoms of $\mathcal{K}$, C14, O15 and O16 (functional COO^{-} group) experienced largest change in their interaction energies with $\mathcal{L}$ by –12.6, 10.5 and 20.4 kcal mol^{-1}, respectively.
- Considering atoms of $\mathcal{L}$, largest unfavourable changes in the $E_{\text{int}}^{\text{A},\mathcal{K}}$ energy term was found for H17 of +10.6 kcal mol^{-1}.
- Notably, interactions between C18 and $\mathcal{K}$ remained nearly the same, $\Delta E_{\text{int}}^{\text{C18},\mathcal{K}}$ = 0.6 kcal mol^{-1}. C18 of $\mathcal{L}$ is involved in strongest (by far) interactions with $\mathcal{K}$ in **7** and **8**, namely –181.6 and –180.0 kcal mol^{-1}, respectively.

From 8 to 9a

It is important to note that:

- Energy of all (bonded and non-bonded) 371 intramolecular interactions weakened drastically (by +32.0 kcal mol^{-1}). Covalent bonds were influenced most by the **8** to **9a** change and became weaker by +145.1 kcal mol^{-1}. This has been partly compensated by very significant strengthening of all non-bonded interactions (–111.3 kcal mol^{-1}).
- To illustrate an extent of changes in $E_{\text{int}}^{\text{A,B}}$ among covalent bonds, we obtained the total energy of –74.3/+219.4 kcal mol^{-1} for all bonds that strengthened/weakened. Most strengthened/weakened covalent bonds are N13–C18 (the link) and C14–O16 followed by C18–O19 with the change in their interaction energy of –28.4, +93.7 and +50.9 kcal mol^{-1}, respectively.
- Focusing on non-bonded interactions, the most strengthened was between O16 and on-coming H5, $\Delta E_{\text{int}}^{\text{O16,H17}}$ of –144.4 kcal mol^{-1}.

Looking at data in Table S27 one can note that:

- Inter-fragment interaction between molecular fragments $\mathcal{K}$ and $\mathcal{L}$ hardly changed (less than 1 kcal mol^{-1} but numerous atoms' interactions, either with $\mathcal{K}$ or $\mathcal{L}$, changed a lot (inter-fragment interactions between non-bonded atoms weakened by 22.7 kcal mol^{-1}).
- Considering atoms of $\mathcal{K}$, N13, C14 and O16 experienced largest change in their interaction energies with $\mathcal{L}$ by –22.9, –12.3 and +42.0 kcal mol^{-1}, respectively.
- Considering atoms of $\mathcal{L}$, H17, C18 and O19 (the C–OH fragment) experienced largest changes in the $E_{\text{int}}^{\text{A},\mathcal{K}}$ energy term of +46.2, –18.4 and –16.4 kcal mol^{-1}, respectively.

From the data discussed it follows that due to structural re-arrangement from **6a** to **8** (a better suited structure for the intramolecular proton transfer) a small increase in E is observed at each step. However, a wide spread and of moderate changes in interaction energies took place involving nearly entirely the atoms of the $\mathcal{G}$ and $\mathcal{H}$ fragments.

On the **8** to **9a** change with large change in E, extremely large changes took place and they were mainly located on covalent bonds. This means that the skeleton of a molecule became highly strained on reaching the TS (**9a**).

Table S27. Interaction energies (in kcal mol^{-1}) between atoms of a molecular fragment $\mathcal{K}$ and entire molecular fragment $\mathcal{L}$ and atoms of $\mathcal{L}$ and entire molecular fragment $\mathcal{K}$ in **8** and **9a**.

Atom A of $\mathcal{K}$	$E_{\text{int}}^{\text{A},\mathcal{L}}$			**Atom A of $\mathcal{L}$**	$E_{\text{int}}^{\text{A},\mathcal{K}}$		
	8	**9a**	$\Delta_{\mathbf{9a-8}}$		**8**	**9a**	$\Delta_{\mathbf{9a-8}}$
C1	19.6	19.7	0.1	H17	-67.3	-21.0	46.2
C2	-0.1	-1.5	-1.4	C18	-181.0	-199.4	-18.4
C3	0.9	0.1	-0.8	O19	30.0	13.6	-16.4
C4	18.9	18.3	-0.6	C20	-12.1	-14.3	-2.2
H5	39.0	43.1	4.1	H21	-2.8	-7.7	-4.8
H6	-2.2	-3.1	-0.9	H22	-2.1	-1.8	0.3
H7	3.2	1.9	-1.3	H23	-3.6	-6.9	-3.3
H8	1.5	1.1	-0.4	C24	-13.5	-13.9	-0.4
H9	-1.6	-2.2	-0.7	H25	-6.1	-6.1	0.0
H10	1.8	1.6	-0.2	H26	-1.9	-2.5	-0.6
H11	-2.6	-4.7	-2.1	H27	-6.8	-7.9	-1.2
H12	3.0	2.7	-0.3		$E_{\text{int}}^{\mathcal{K},\mathcal{L}}$		
N13	-273.6	-296.5	-22.9		-267.1	-267.9	-0.7
C14	88.0	75.7	-12.3				
O15	-47.1	-50.1	-3.0				
O16	-116.0	-74.0	42.0				
	$E_{\text{int}}^{\mathcal{K},\mathcal{L}}$						
	-267.1	-267.9	-0.7				

An overall change from 6a to 9a and from 6b to 9b

In search for the origin of such large energy differences observed at TSs (**9a** and **9b**) we noted the following:

- Total interaction energy changed highly unfavourably in **9a** (by +47.5 kcal mol^{-1}) but opposite trend applies to **9b** (–8.6 kcal mol^{-1}). This illustrates how interactions are working against the change from **6a** to **9a**. On the other hand, one might suggest that interactions drive the change from **6b** to **9b**. This is strongly supported by an ‘absence’ of a TS at the higher MP2 level as on the **6b** to **9b** we obtained –0.3, –0.6 and +0.1 kcal mol^{-1} for ΔE_{corr}, ΔH and ΔG, respectively.

- The $E_{\text{int}}^{\text{O16,H5}}$ term is –211.1 (in **9a**) and –227.4 (in **9b**) kcal mol^{-1}. In both cases they are strongest among all non-covalent interactions and largely assist (facilitate) reaching the TS. To this effect, interaction between O16 and H5 became stronger, relative to **6**, by –165.1 (in **9a**) and –108.3 (in **9b**) kcal mol^{-1}. This shows how extensive structural change had to take place on **6a** to **9a** to bring these atoms so much closer, hence make the interaction so much stronger.
- Overall, covalent bonds’ strength weakened by +154.3 (in **9a**) and +92.7 (in **9b**) kcal mol^{-1}. N13–C1, N13–C18 and N13–C4 as well as C14–O15 strengthened in **9a** and **9b** by between –10 and –22 kcal mol^{-1}. Next, C14–O16 and N15–H5 became weaker in **9a** and **9b** by between 97 and 43 kcal mol^{-1}. Moreover C18–C19 and O19–H17 became weaker in **9a** by 59 and 10 kcal mol^{-1}, respectively, but much smaller effect is observed in **9b** with 9 and 2 kcal mol^{-1}, respectively. It is clear that due H5 being in a process of departing from N15, some density shared between them was utilised to increase density between N13 and all three neighbouring atoms it is covalently bonded to (these interactions (bonds) became stronger). What is somewhat surprising is that the network of covalent bonds effected is reaching as far as O15 in $\mathcal{K}$ and H17 in $\mathcal{L}$. Clearly, a molecular skeleton (a framework of all covalently bonded atoms) in **9a** became by far more strained than in **9b**.
- Inter-fragment (between $\mathcal{K}$ and $\mathcal{L}$) interactions changed by 36.3 (in **9a**) and 3.6 (in **9b**) kcal mol^{-1}. This indicates that $\mathcal{L}$ had to re-position itself relative to $\mathcal{K}$ significantly on **6a** to **9a** and to achieve that a significant energy barrier (working against strong inter-fragment interactions) had to be overcome.

However, one can wonder what would be a classic organic chemist explanation of such small (at B3LYP) or none (at MP2) energy required for the intramolecular H5-transfer, hence the step from **6b** to **10b**. We decided to make use of our approach to gain an insight on a fundamental level. Firstly, we note that H5 is involved in attractive interactions only with 4 atoms, namely: N13 to which it is bonded to in **6b**, O15 and O16 of the COO functional group of $\mathcal{K}$ and O19 in $\mathcal{L}$. Due to the fact that on a proton transfer process H5 is heading not only towards O16 but rather in the direction of the entire COO group, it makes sense to partition $\mathcal{K}$ to two fragments, one containing COO atoms (we will call it $\mathcal{C}$) and remaining atoms of $\mathcal{K}$

with exclusion of N13 (let us call it $\mathcal{D}$). We considered specifically selected for the purpose interactions:

a) $E_{\text{int}}^{\text{H5,N13}}/E_{\text{int}}^{\text{H5,O16}}$ is –127.1/–59.6 (in **6b**) and –101.9/–113.7 (in **9b**) kcal mol^{-1}. Clearly, the attraction to O16 in **6b** is not sufficient to easily overcome attraction to N13.

b) H5 is being attracted by atoms of $\mathcal{C}$ with $E_{\text{int}}^{\text{H5},\mathcal{C}}$ of –32.7 (in **6b**) and –74.0 (in **9b**) kcal mol^{-1} and this is not sufficient for the proton transfer either.

c) H5 is being repelled by atoms of $\mathcal{L}$ with $E_{\text{int}}^{\text{H5},\mathcal{L}}$ of +46.2 (in **6b**) and +43.5 (in **9b**) kcal mol^{-1}. By repelling H5, atoms of $\mathcal{L}$ facilitate its transfer to O16.

d) H5 is also being repelled by atoms of $\mathcal{D}$ with $E_{\text{int}}^{\text{H5},\mathcal{D}}$ of +42.8 (in **6b**) and +43.3 (in **9b**) kcal mol^{-1}. Also in this case atoms of $\mathcal{D}$ assist in the transfer process of H5.

Latter two terms, by repelling H5 can be seen as counteracting the H5 attraction to N13 by pushing H5 towards O16 (or $\mathcal{C}$ in general). As a result, nearly perfect balance in interaction energies is obtained, i.e. resulting in weakening (energy-wise) the overall bonding strength between N13 and H5. Hence, an estimate of the effective (or corrected) interaction energy between H5 and N13 can be obtained by summing up $E_{\text{int}}^{\text{H5,N13}}$, $E_{\text{int}}^{\text{H5},\mathcal{L}}$ and $E_{\text{int}}^{\text{H5},\mathcal{D}}$ giving a product of –38.3 (in **6b**) and –15.1 (in **9b**) kcal mol^{-1}. From this it follows that the attractive interaction between H5 and $\mathcal{C}$ in **6b** is nearly as strong as the corrected (effective) attraction between N13 and H5. In case of **9b**, the $E_{\text{int}}^{\text{H5},\mathcal{C}}$ term of –74.0 kcal mol^{-1} represents much larger attraction than effective interaction (of –15.1 kcal mol^{-1}) between N13 and H5.

End of PART S6