Supporting Information

A pathway for aldol additions catalyzed by L-Hydroxyproline-peptides via a β-hydroxyketone hemiaminal intermediate

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Content

Supplementary Computational Data

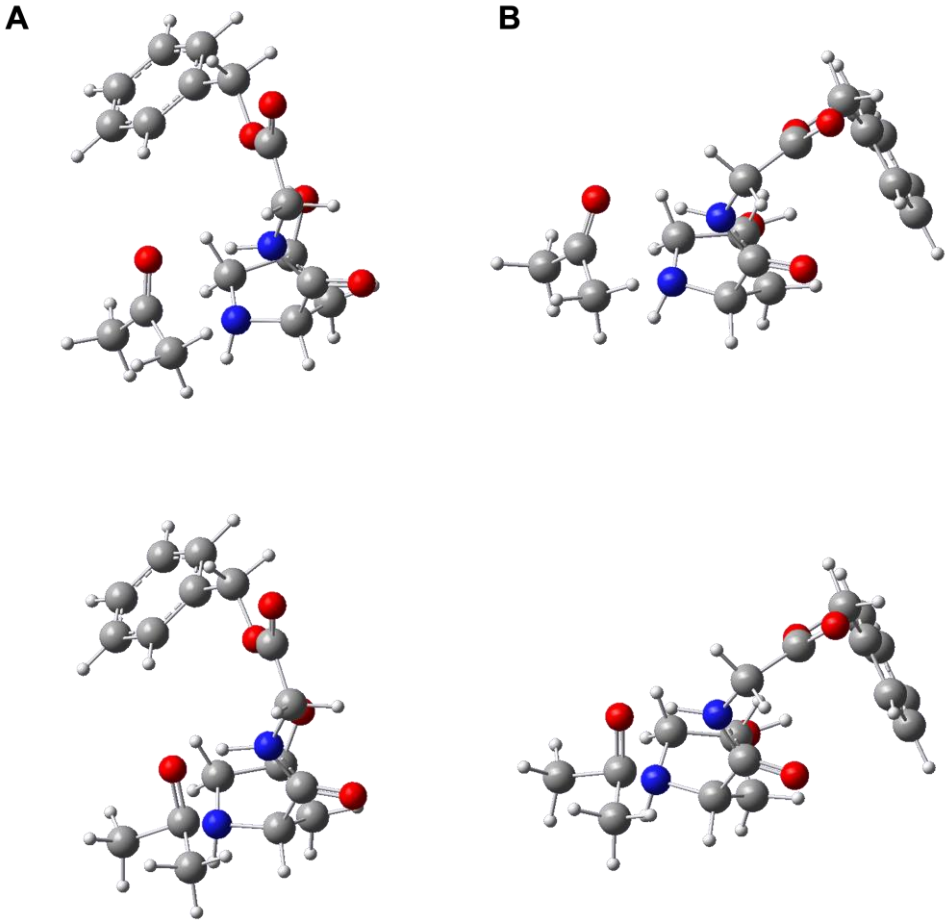

Figure S1. Displacement of atoms in the vibrations associated with the imaginary frequencies calculated at the B3LYP/6-31G(d) level for TS1 (formation of a hemiaminal from catalyst and acetone) with transition structures modeled as in Figure 5A (analogous to catalytic cycles with free amino acids). A: TS1 with a conformer of *cis*-**6**. B: TS1 with a conformer of *trans*-**6**. The top and bottom figures represent two snapshots from the vibration (visualized with GaussView). The displacement of the atoms indicates formation of an N–C bond in TS1, but no displacement of the amide hydrogen atom associated with hydrogen transfer to the carbonyl oxygen of acetone.

Analytical Data

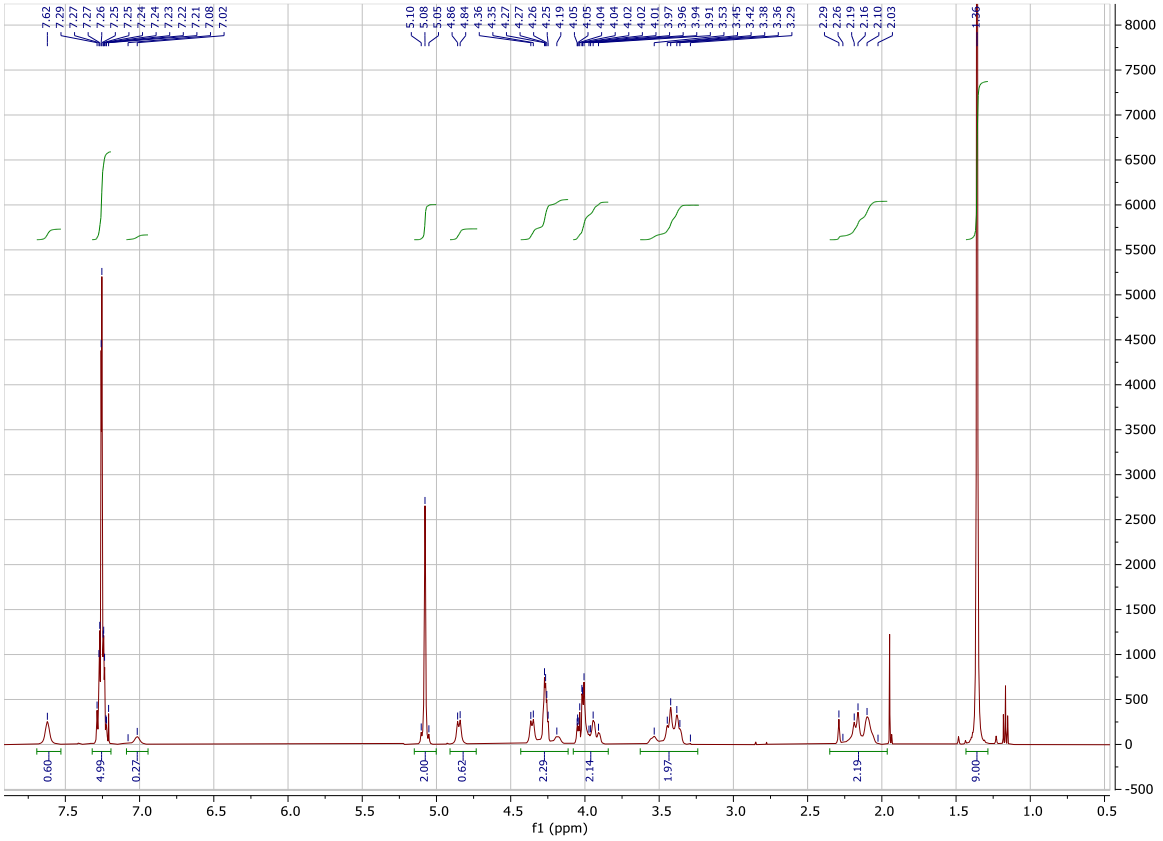

Figure S2. ^{1}H-NMR of *cis*-**4** in $CDCl_3$.

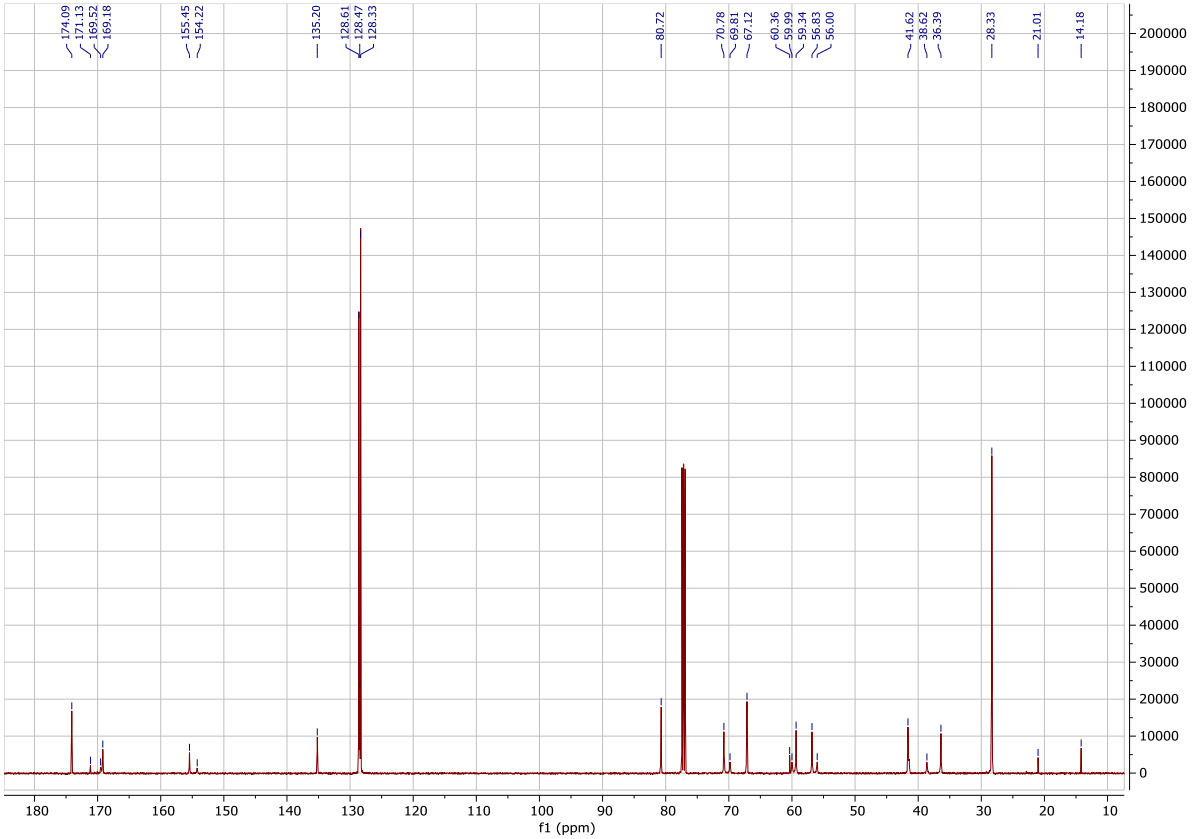

Figure S3. ^{13}C-NMR of *cis*-**4** in $CDCl_3$.

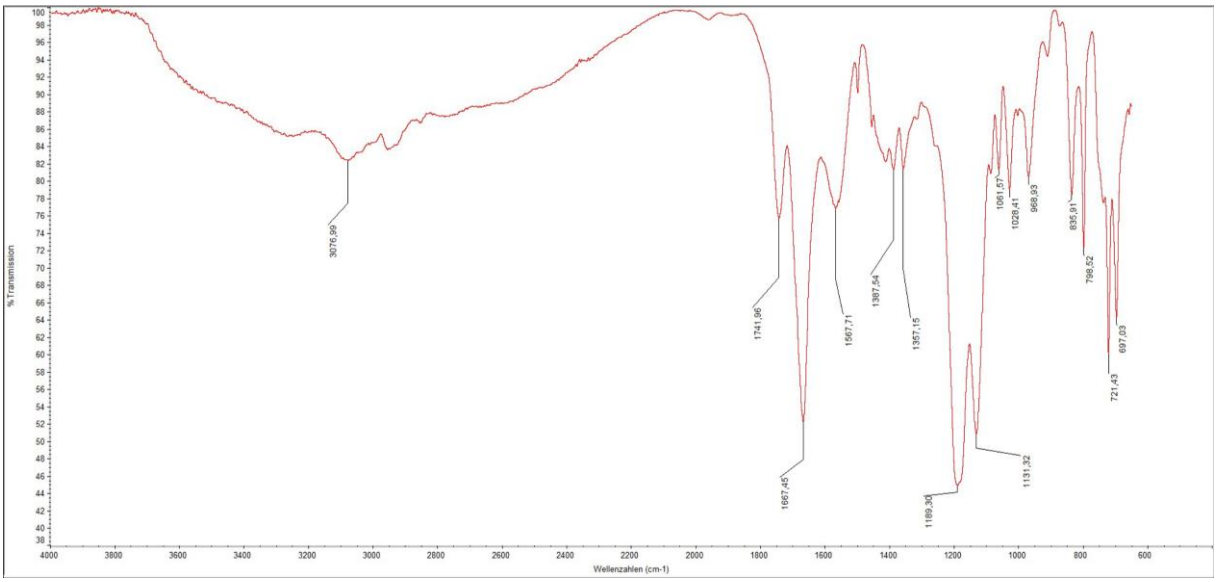

Figure S4. Neat IR of *cis*-**4**.

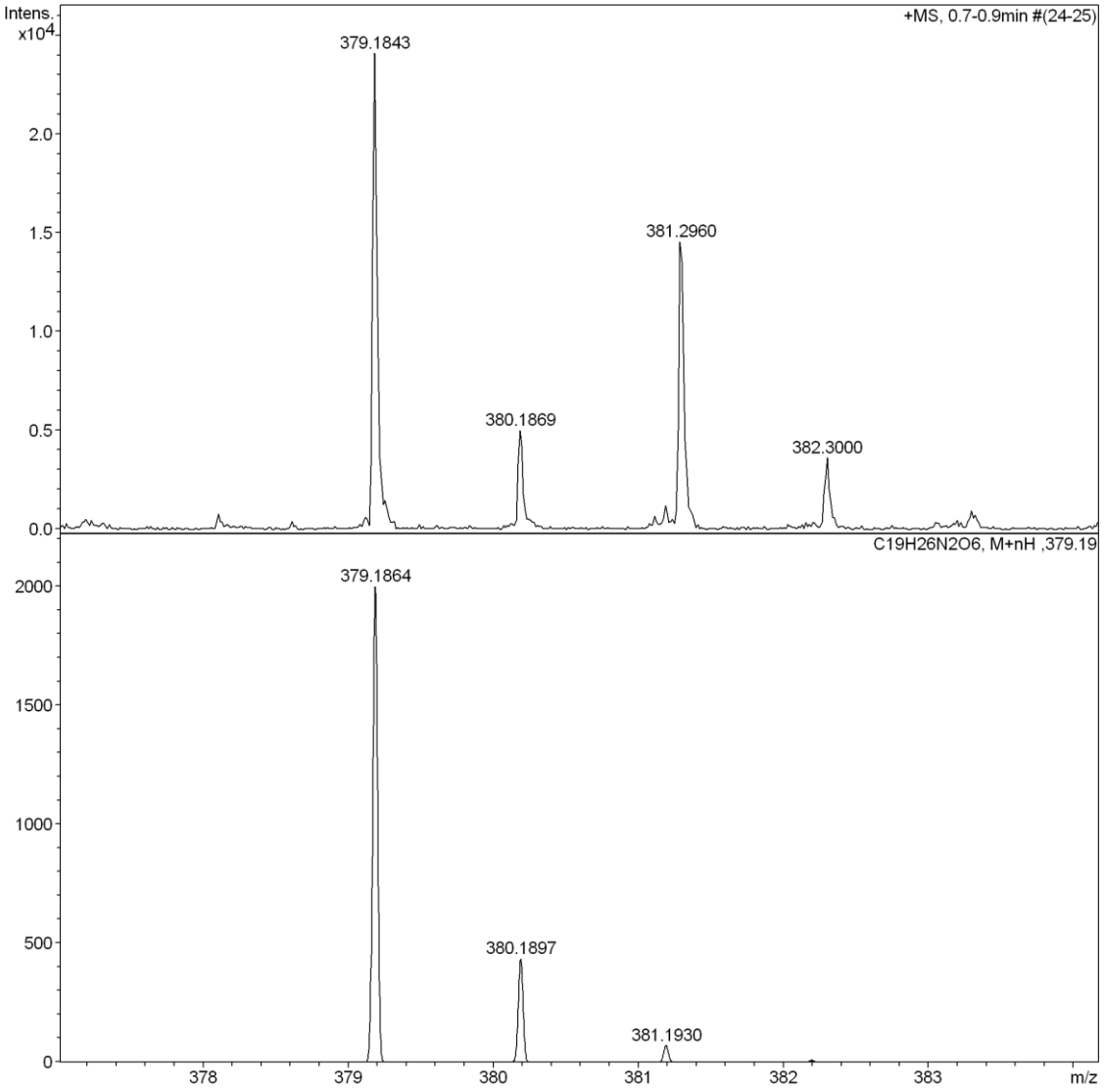

Figure S5. ESI-MS of *cis*-**4**.

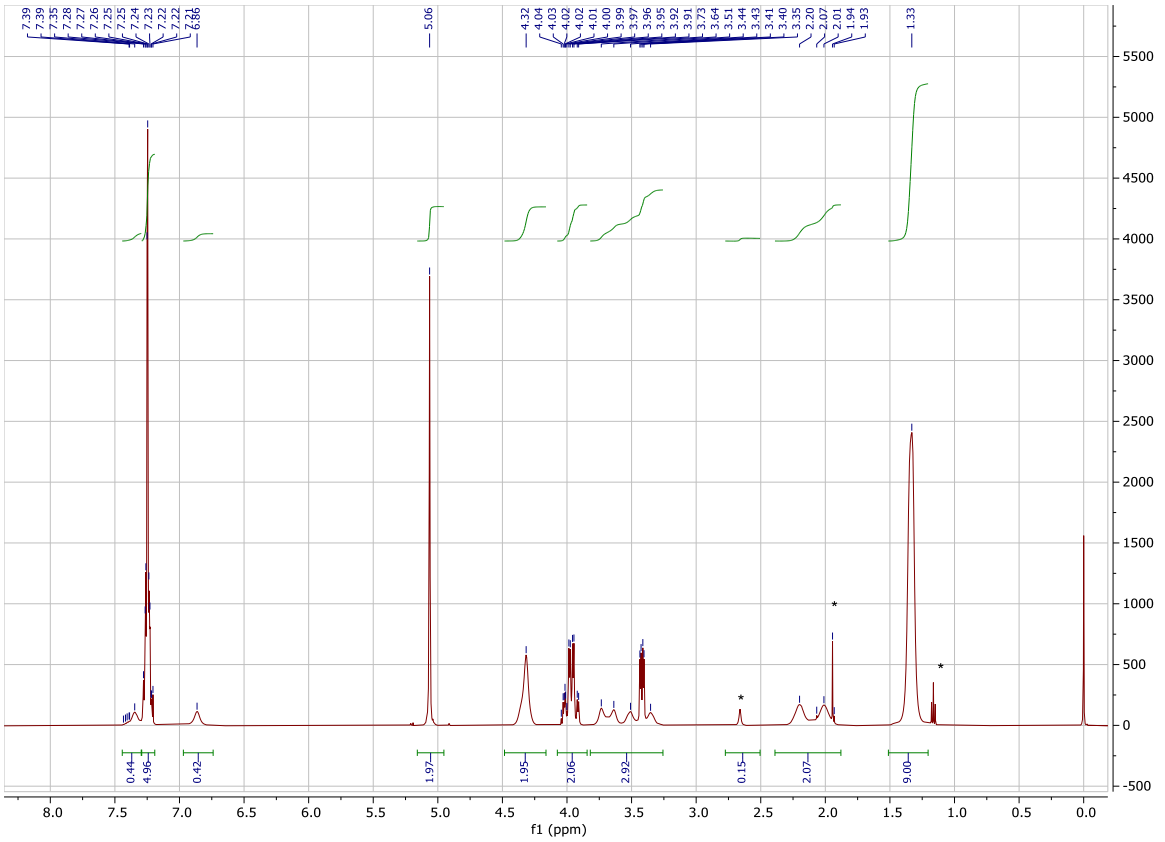

Figure S6. ^{1}H-NMR of *trans*-**4** in $CDCl_3$ (signals due to solvent impurities marked with asterisks *).

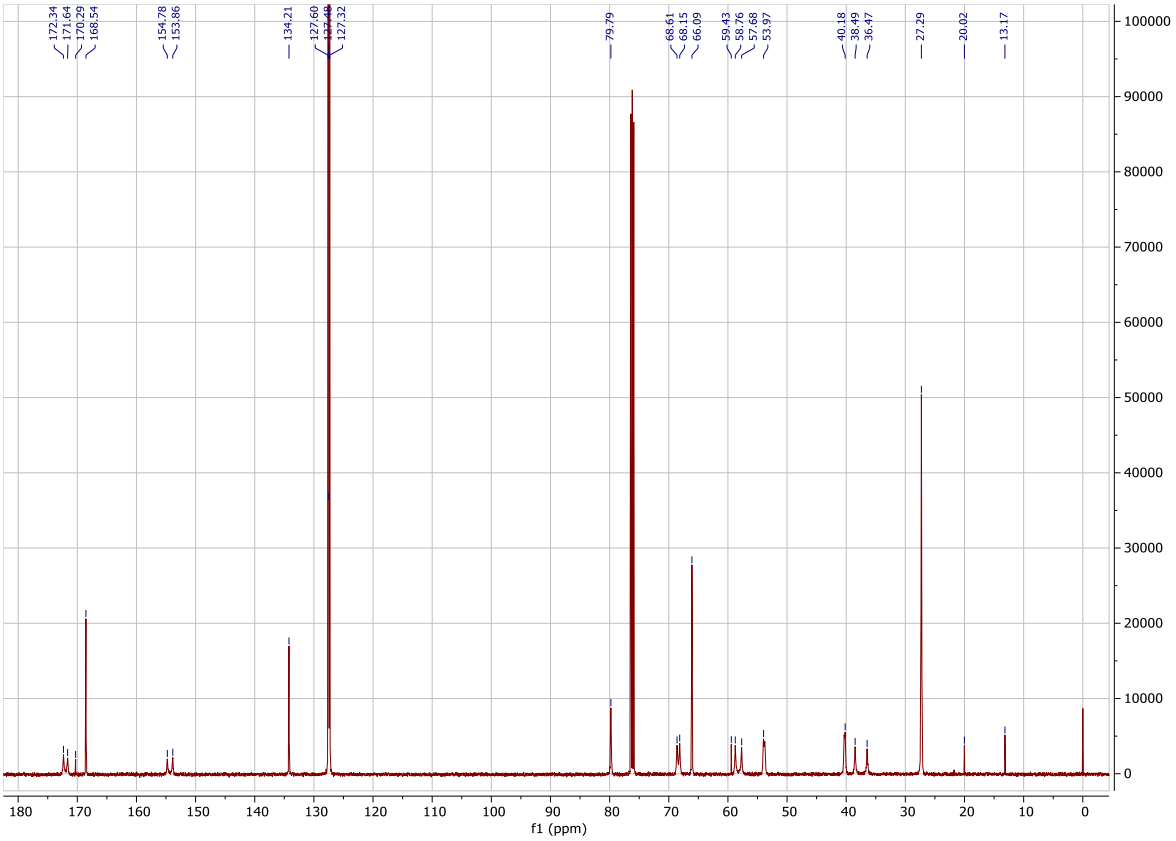

Figure S7. ^{13}C-NMR of *trans*-**4** in $CDCl_3$.

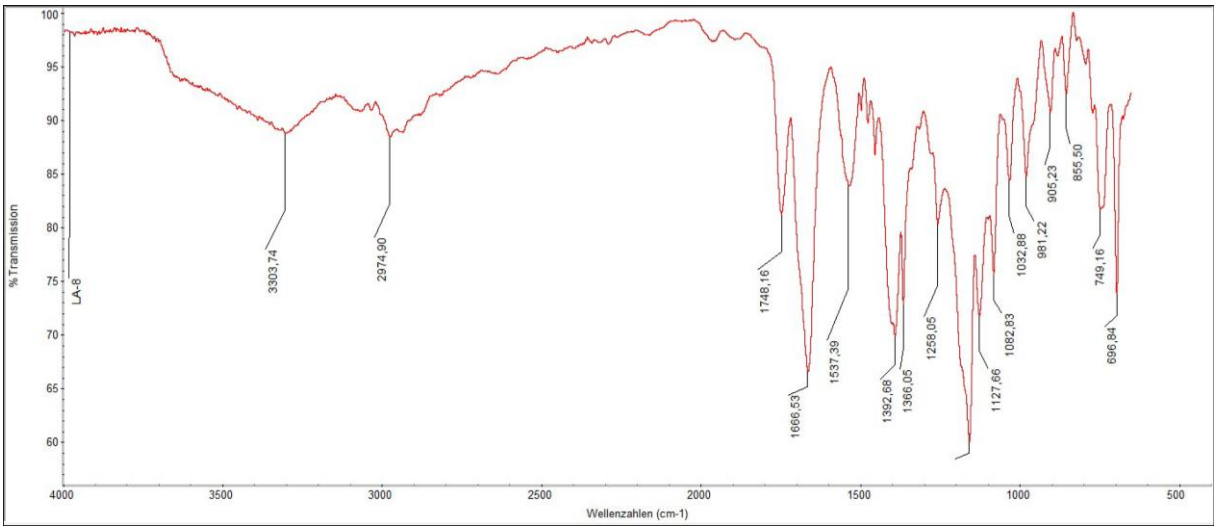

Figure S8. Neat IR of *trans*-**4**.

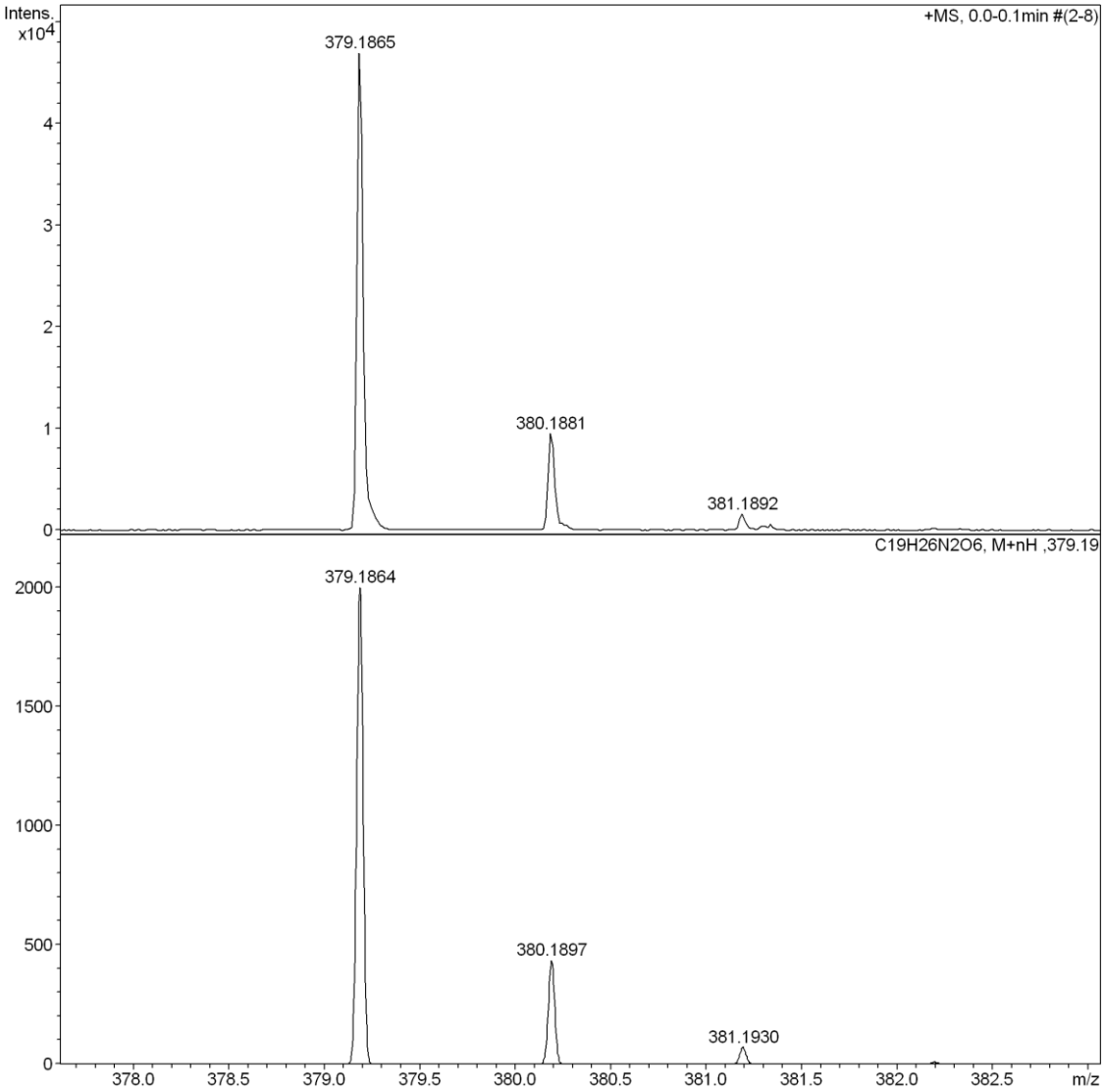

Figure S9. ESI-MS of *trans*-**4**.

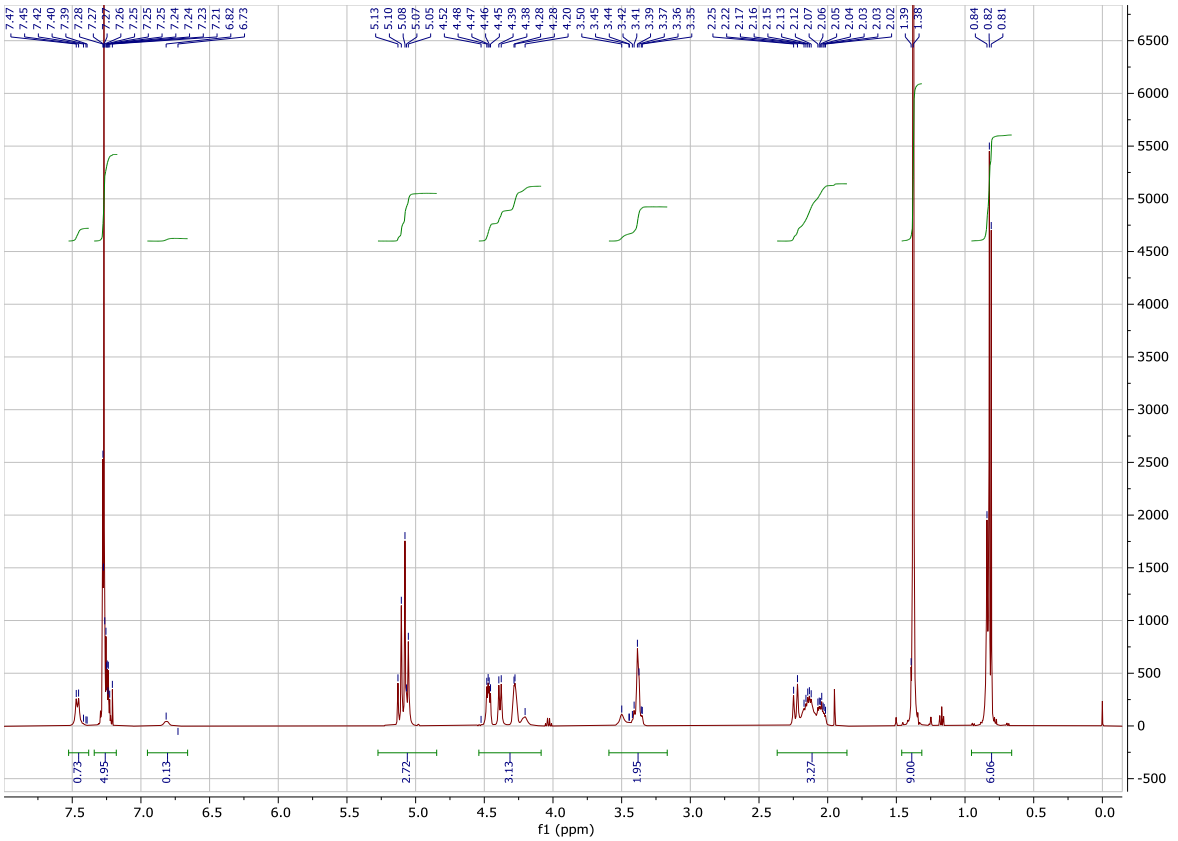

Figure S10. ^{1}H-NMR of *cis*-**5** in $CDCl_3$.

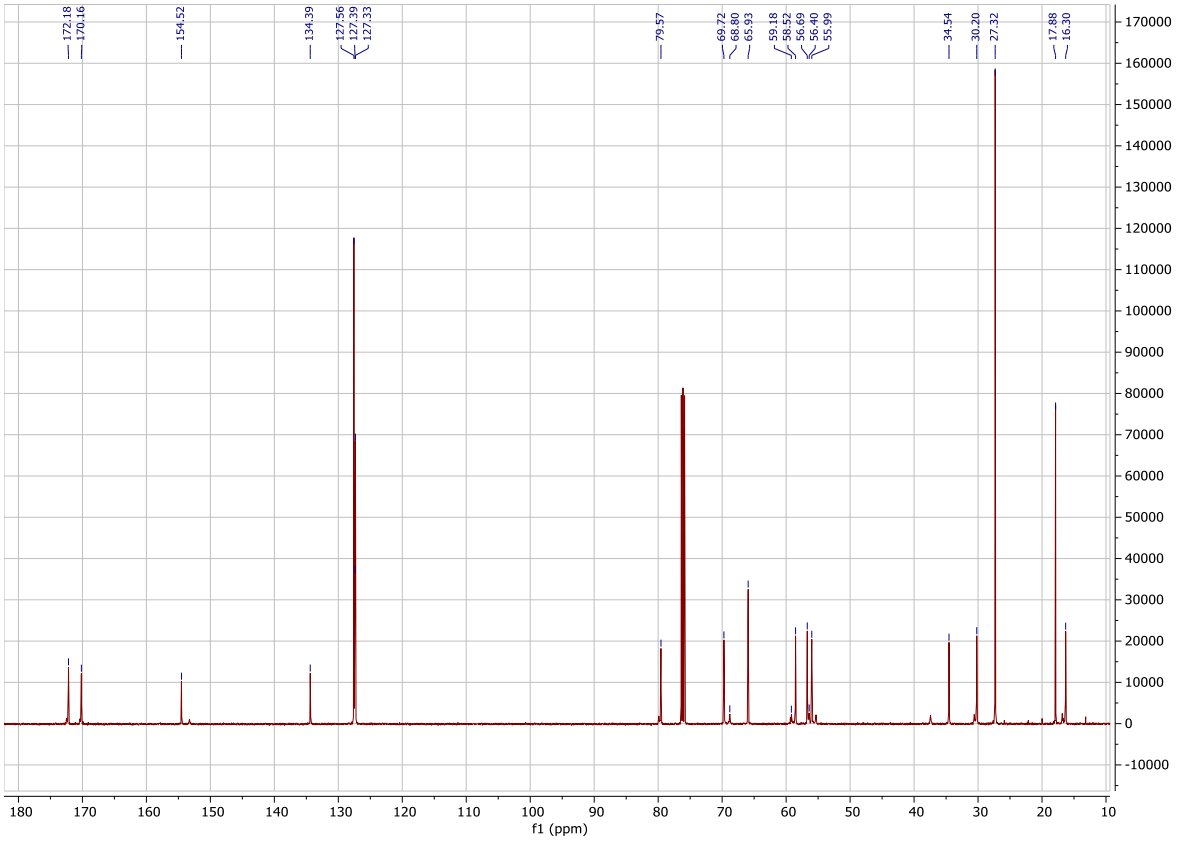

Figure S11. ^{13}C-NMR of *cis*-**5** in $CDCl_3$.

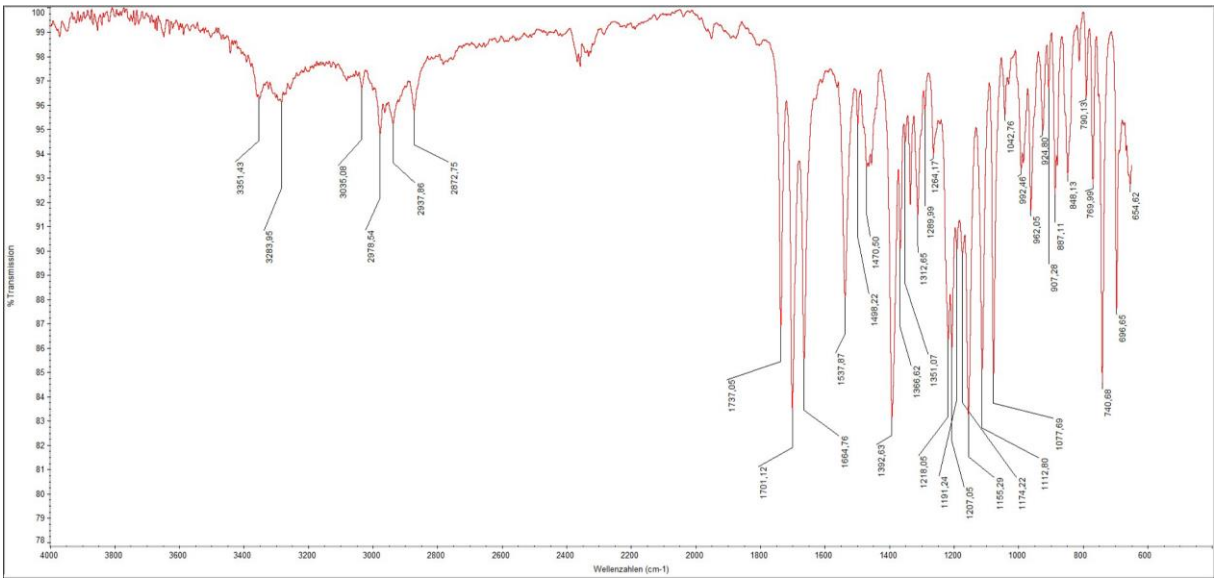

Figure S12. Neat IR of *cis*-**5**.

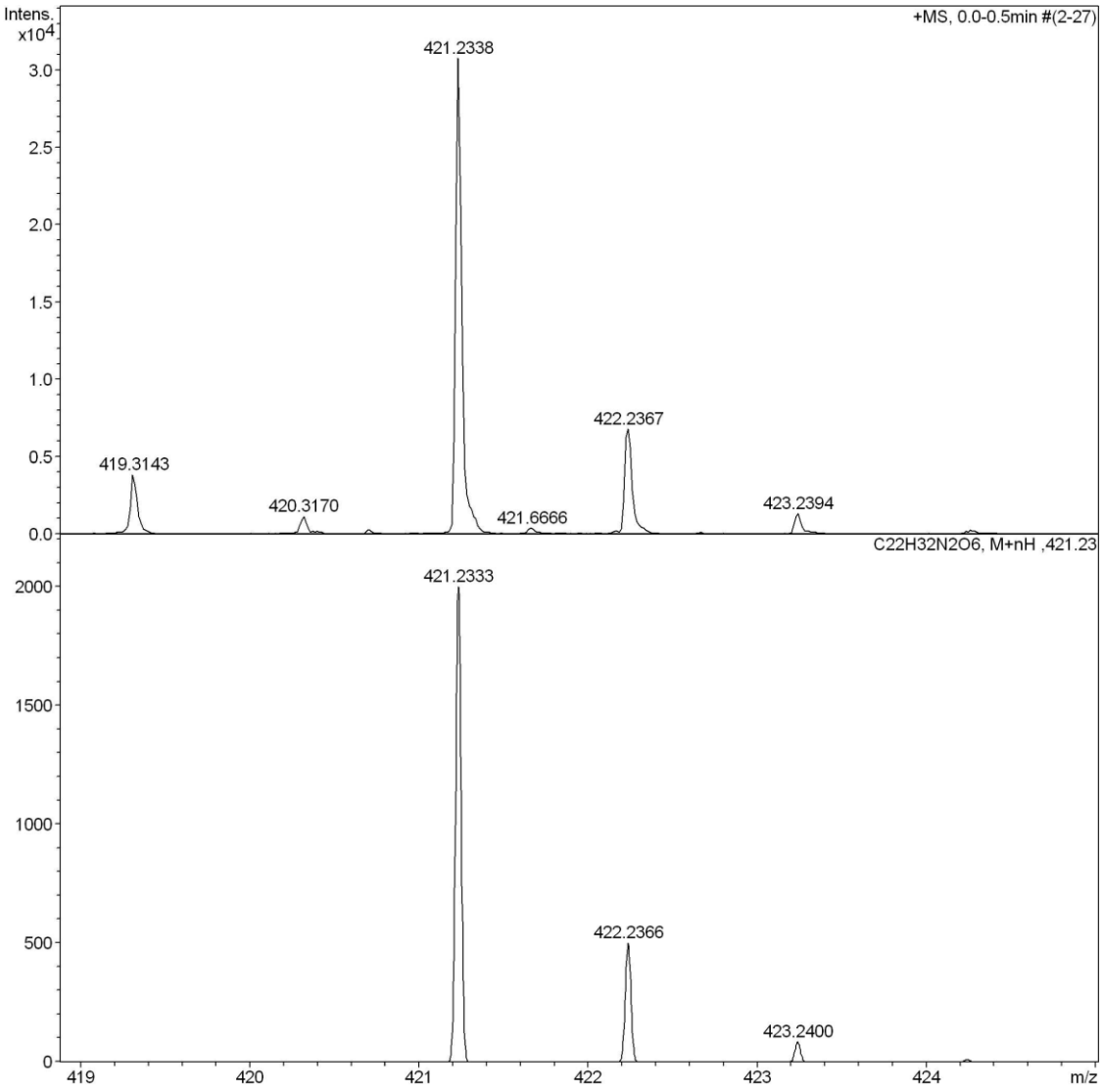

Figure S13. ESI-MS of *cis*-**5**.

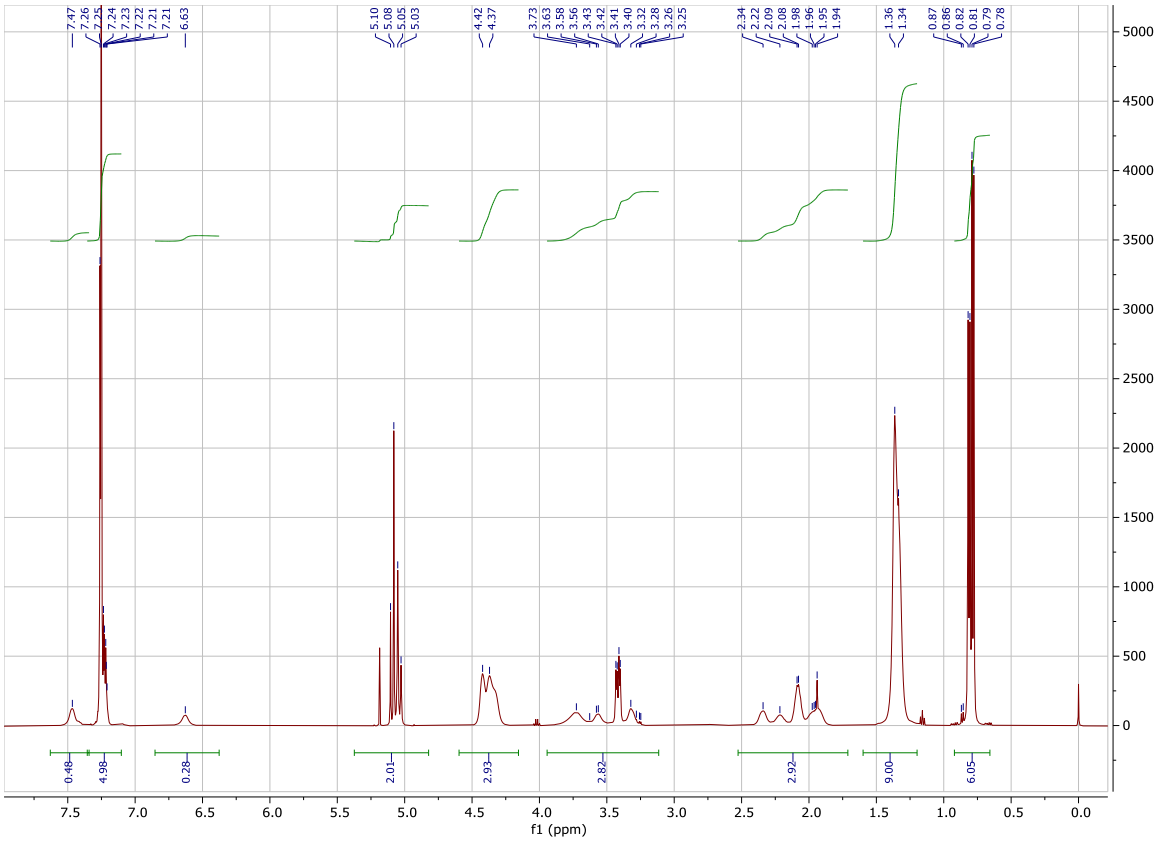

Figure S14. ^{1}H-NMR of *trans*-**5** in $CDCl_3$.

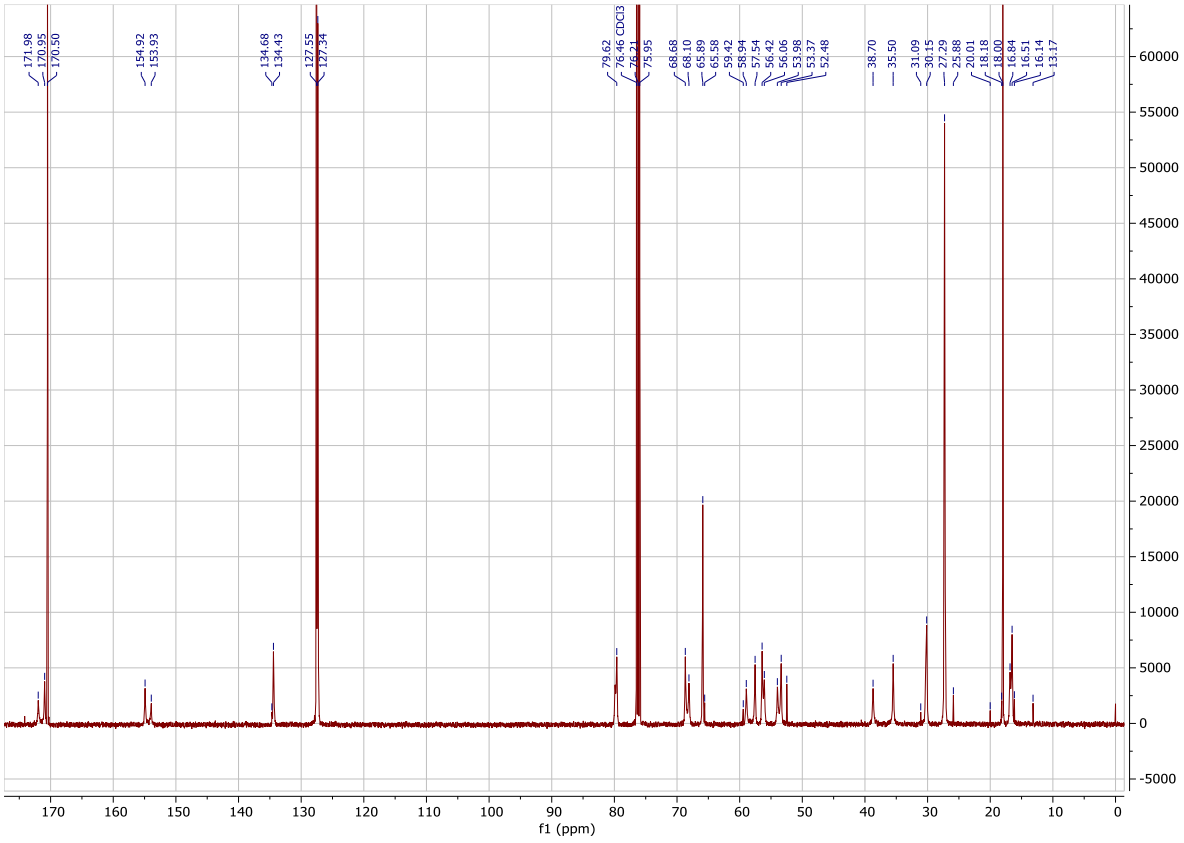

Figure S15. ^{13}C-NMR of *trans*-**5** in $CDCl_3$.

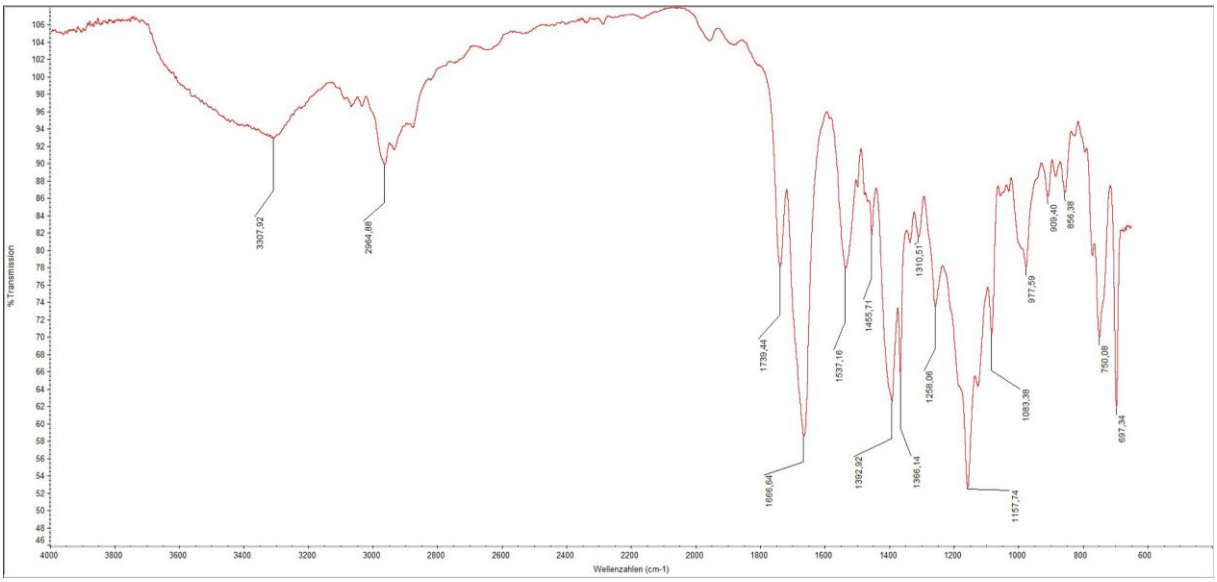

Figure S16. Neat IR of *trans*-**5**.

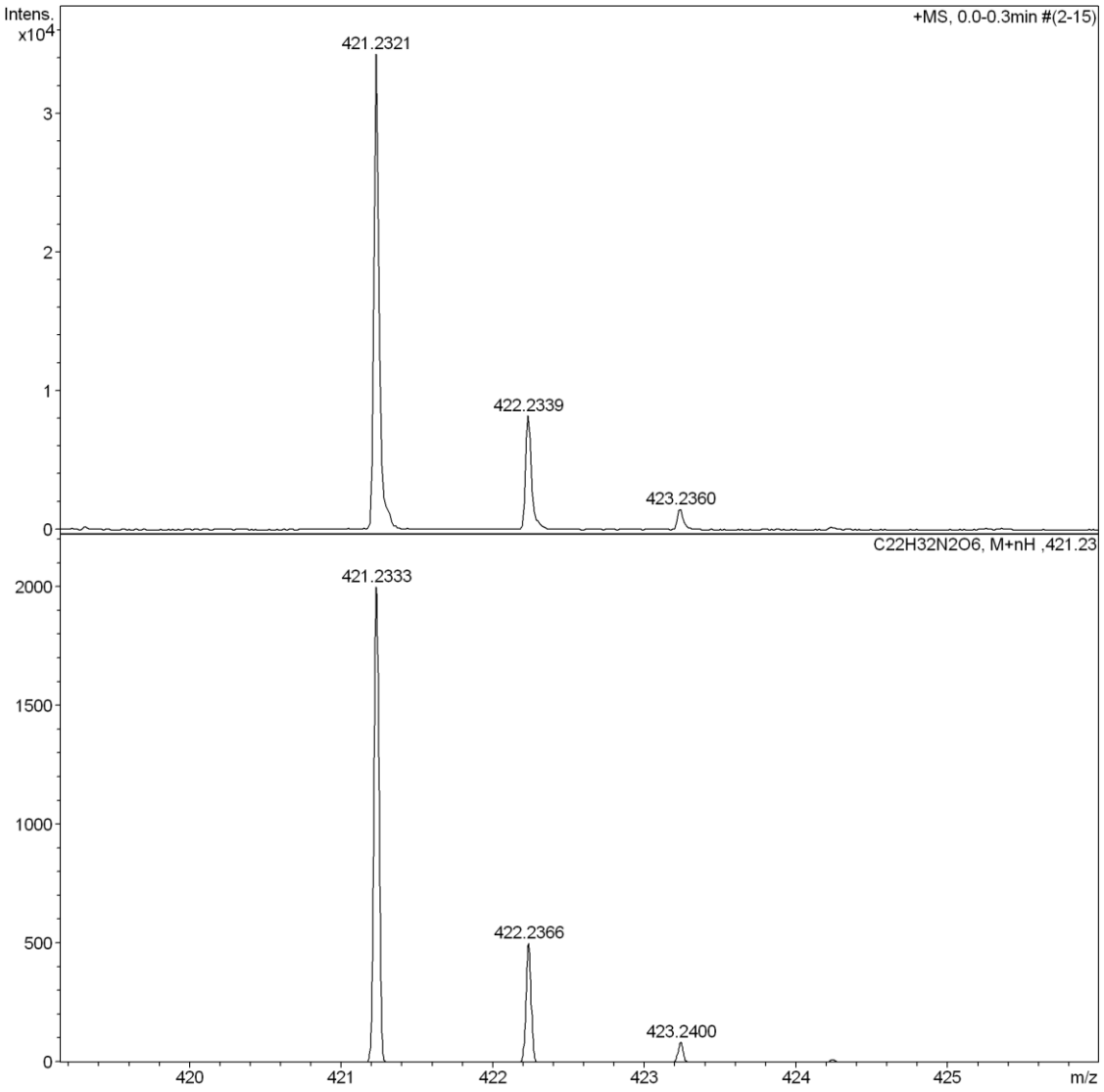

Figure S17. ESI-MS of *trans*-**5**.

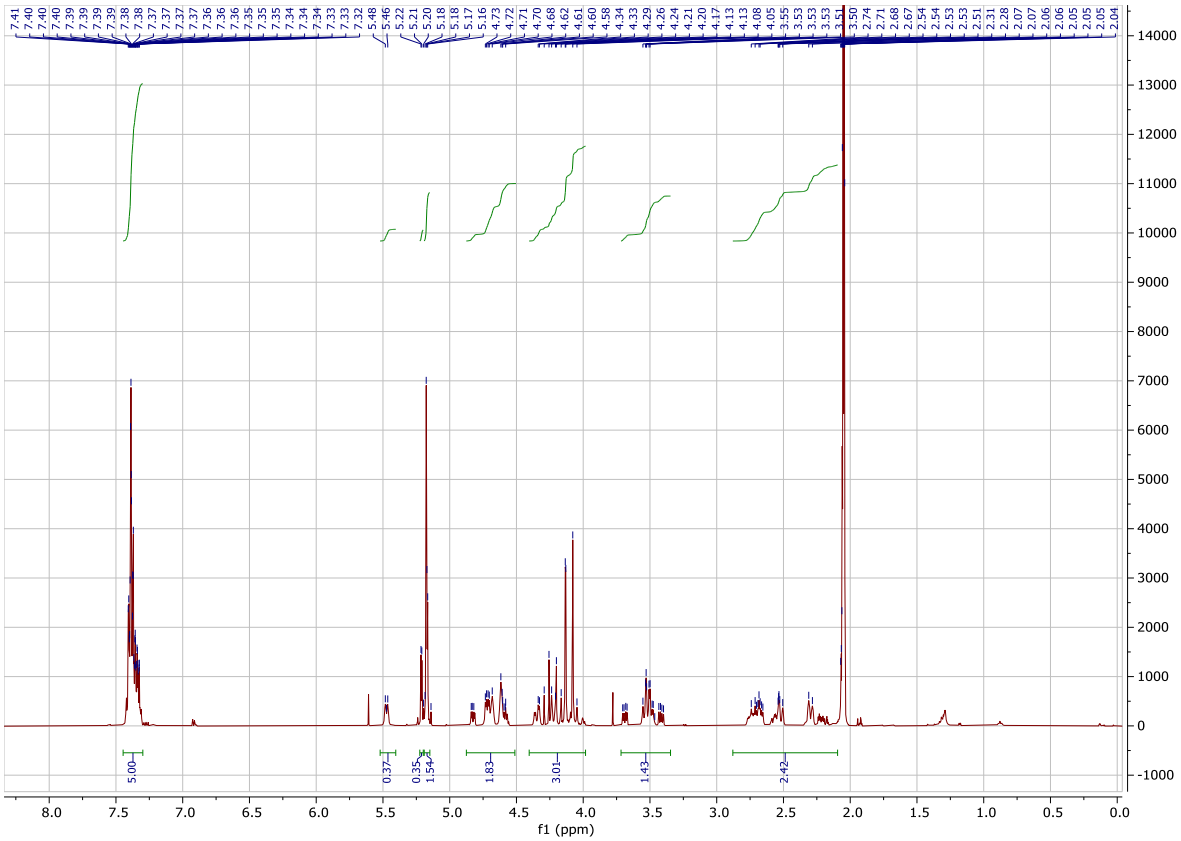

Figure S18. ^{1}H-NMR of *cis*-**6** in $CDCl_3$.

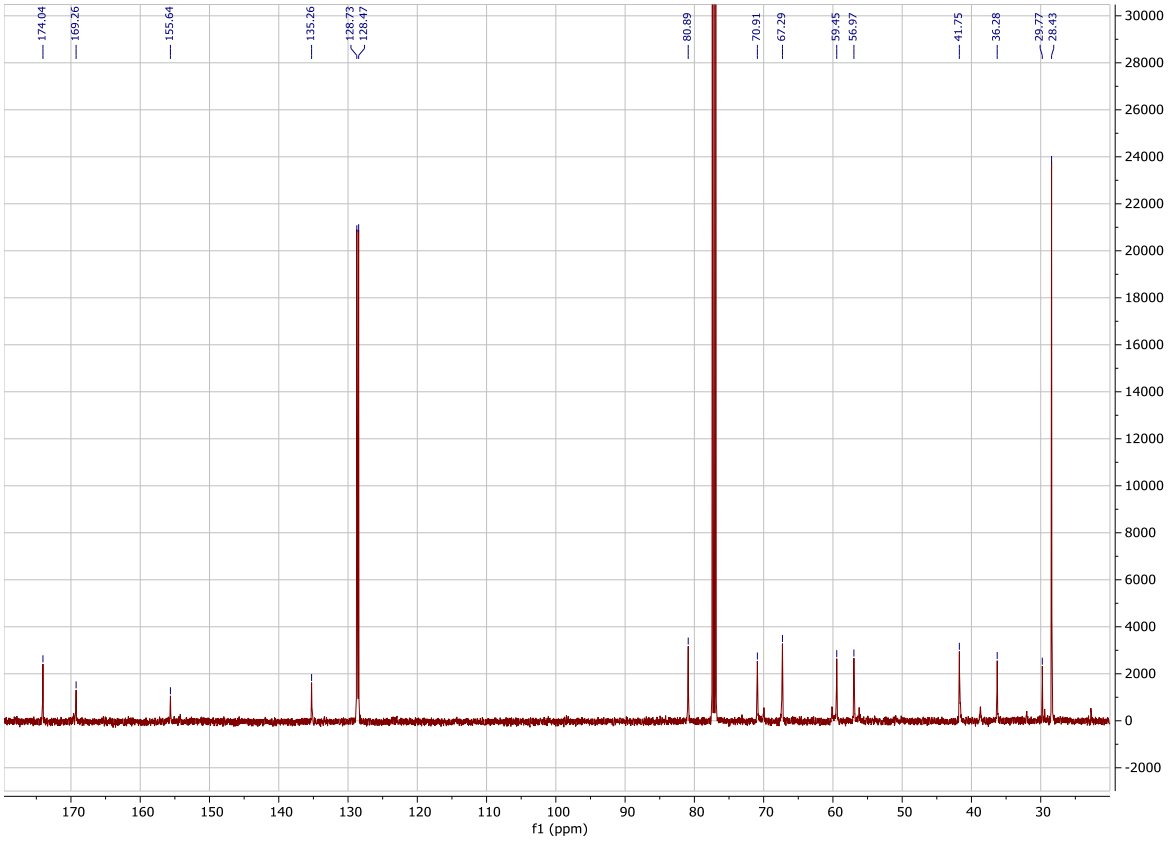

Figure S19. ^{13}C-NMR of *cis*-**6** in $CDCl_3$.

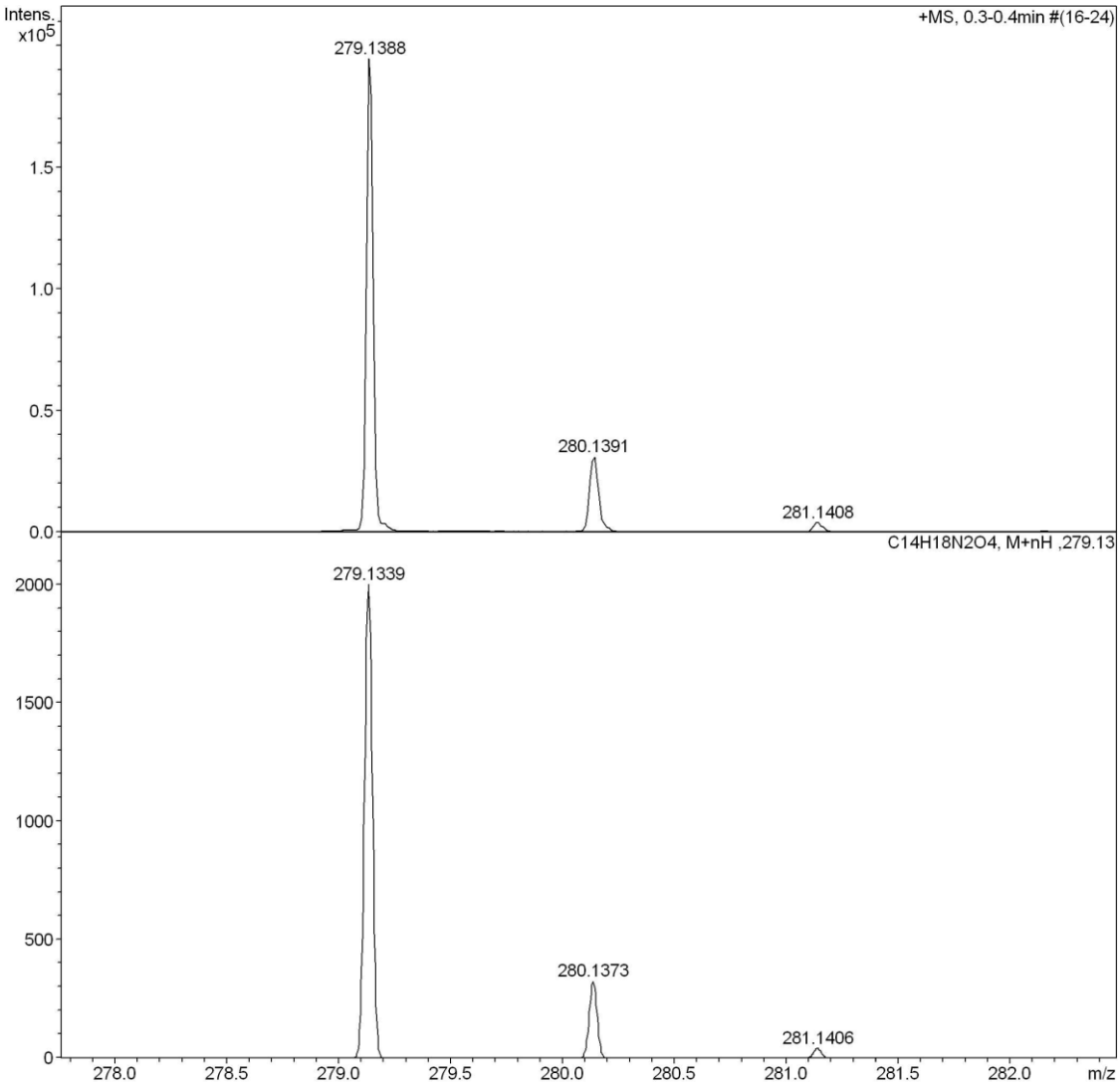

Figure S20. ESI-MS of *cis*-**6**.

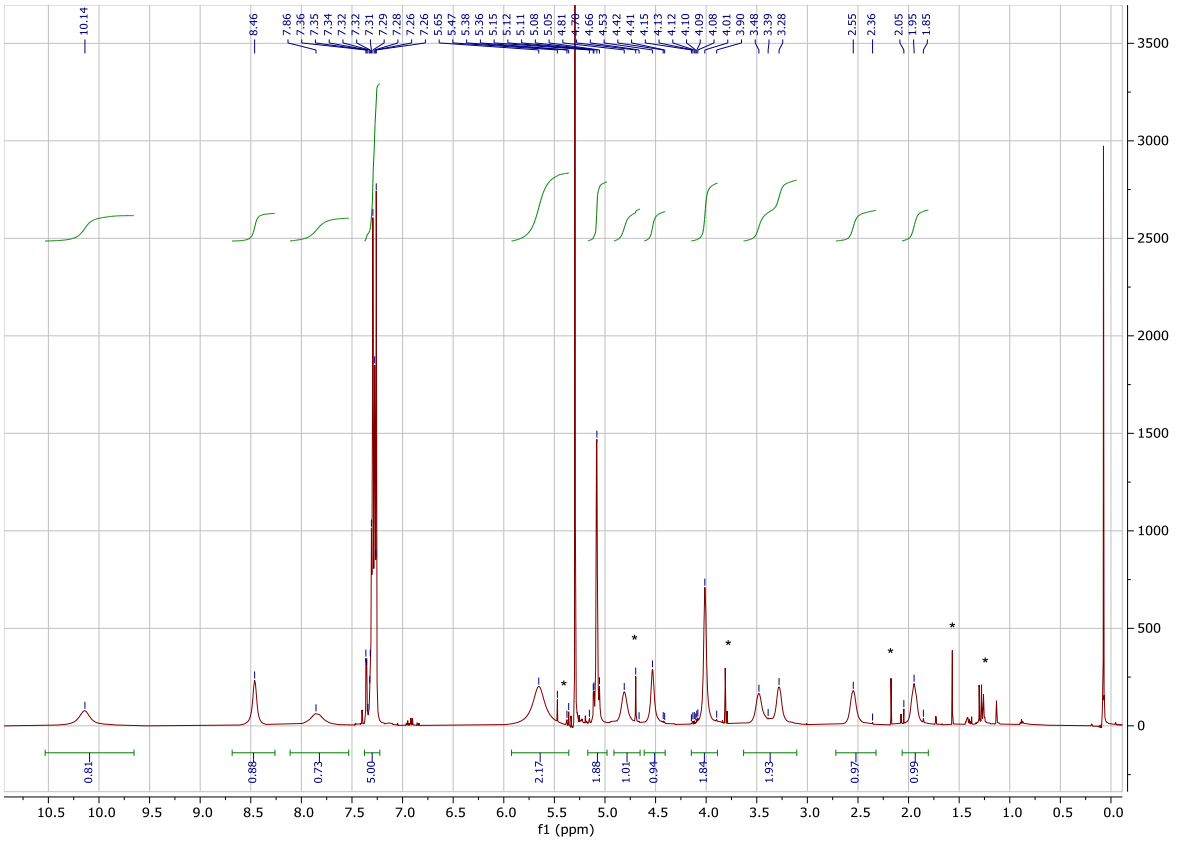

Figure S21. ^{1}H-NMR of *trans*-**6** in $CDCl_3$ (signals due to solvent impurities marked with asterisks *).

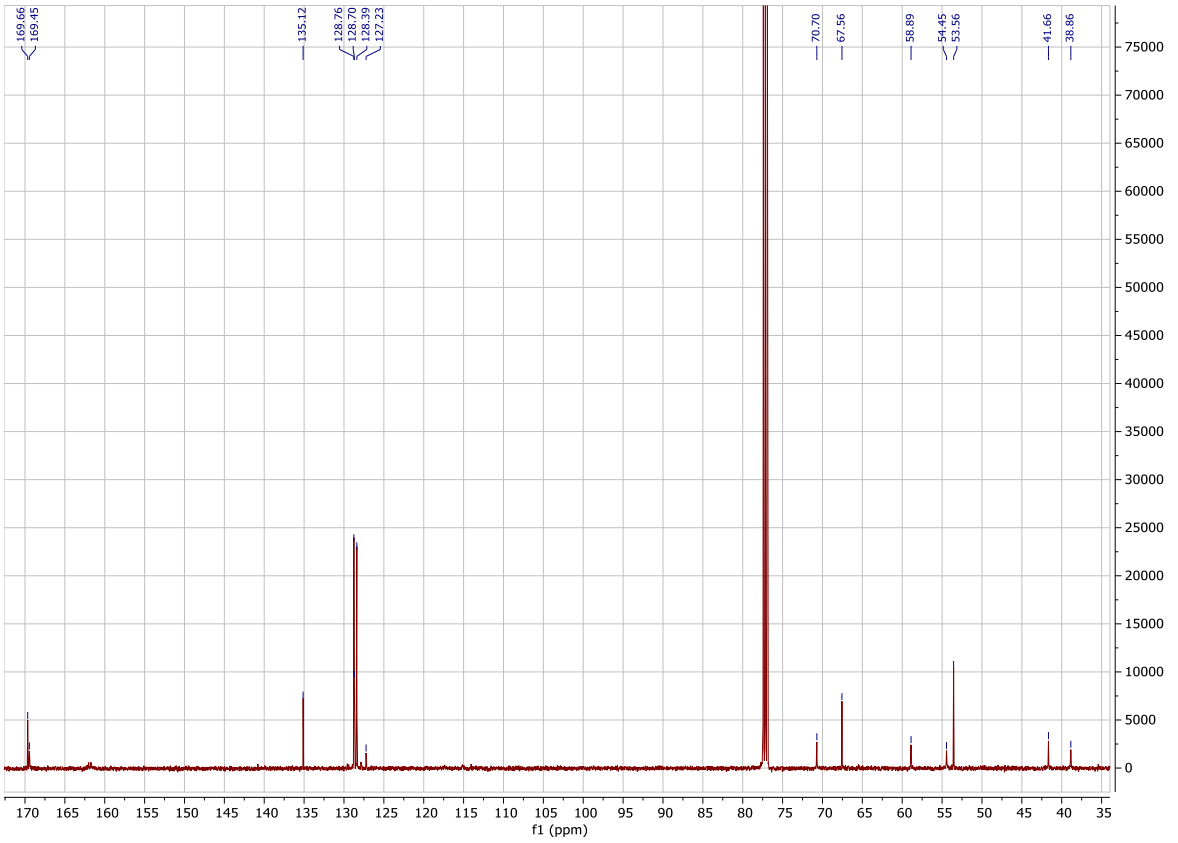

Figure S22. ^{13}C-NMR of *trans*-**6** in $CDCl_3$.

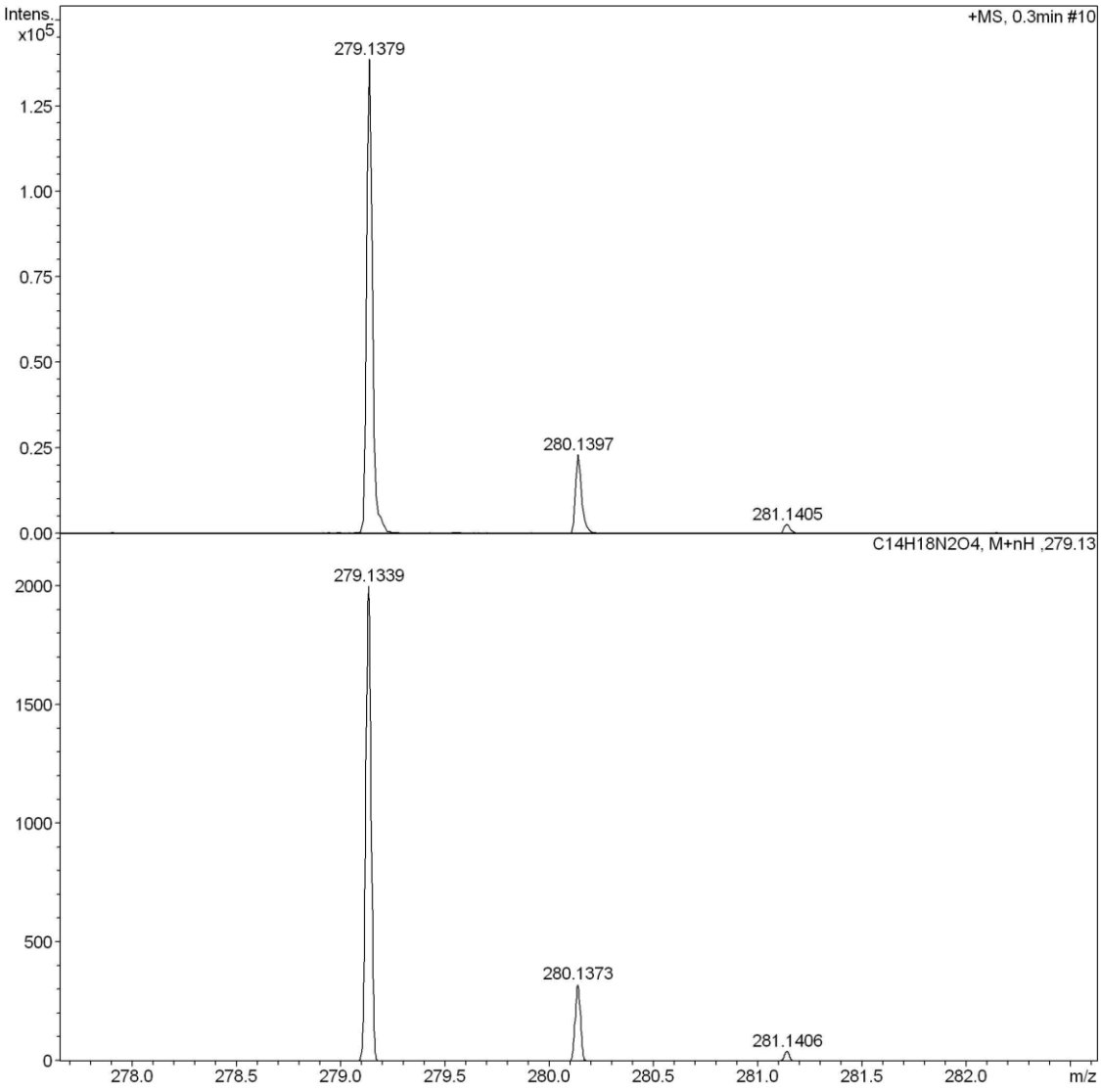

Figure S23. ESI-MS of *trans*-**6**.

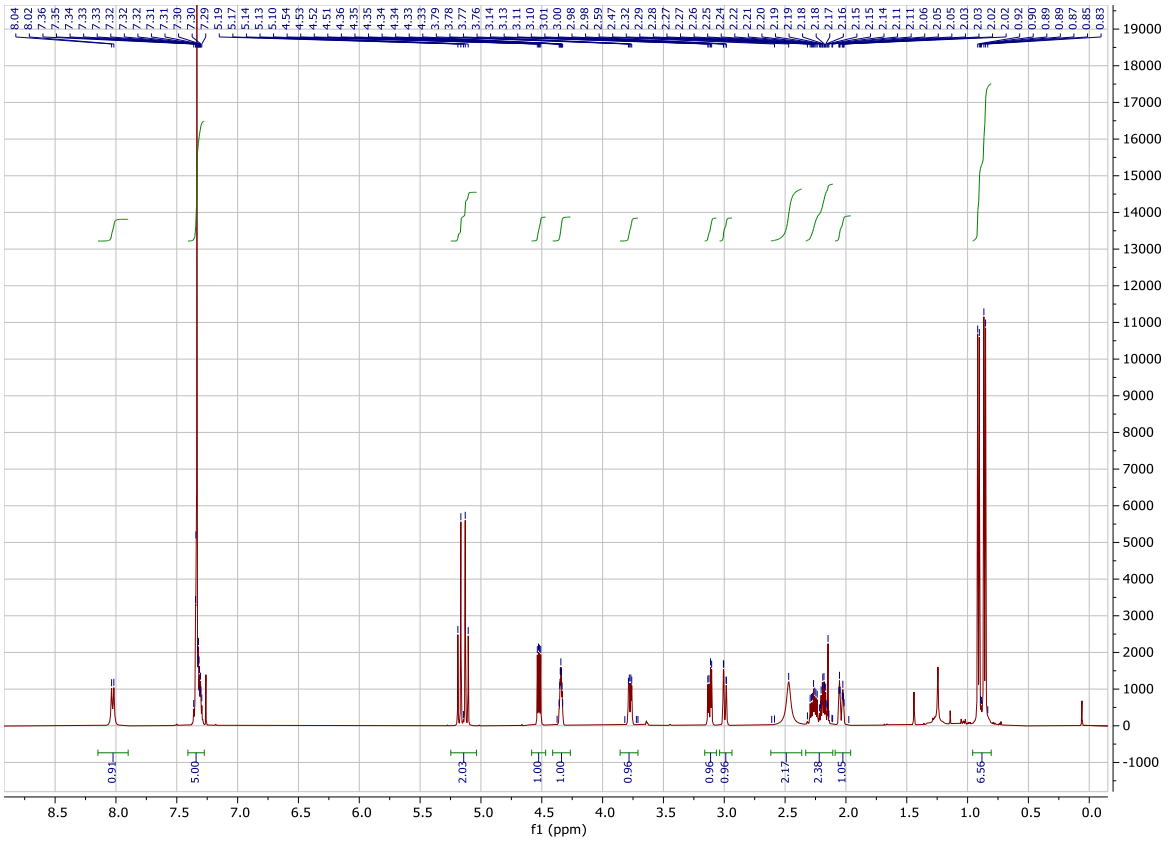

Figure S24. ^{1}H-NMR of *cis*-**7** in $CDCl_3$.

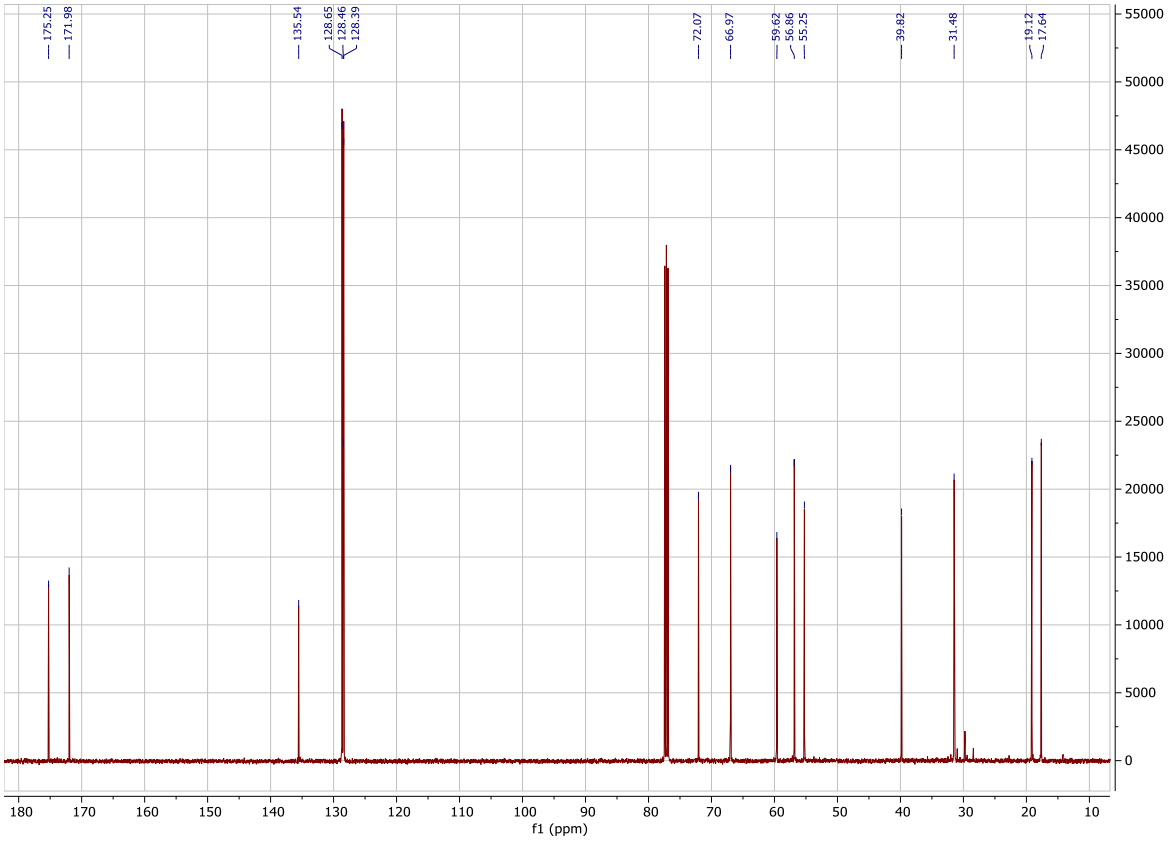

Figure S25. ^{13}C-NMR of *cis*-**7** in $CDCl_3$.

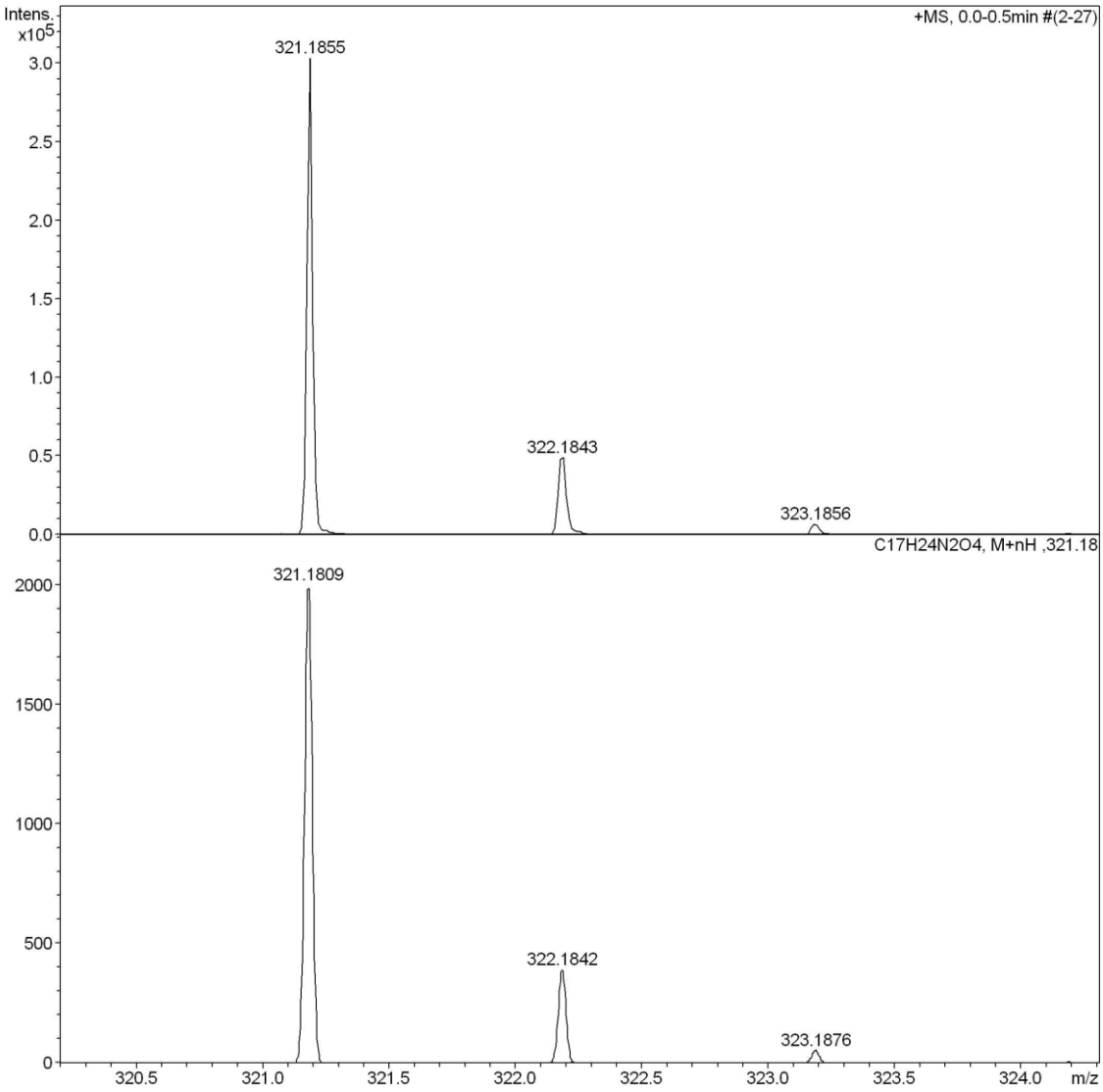

Figure S26. ESI-MS of *cis*-**7**.

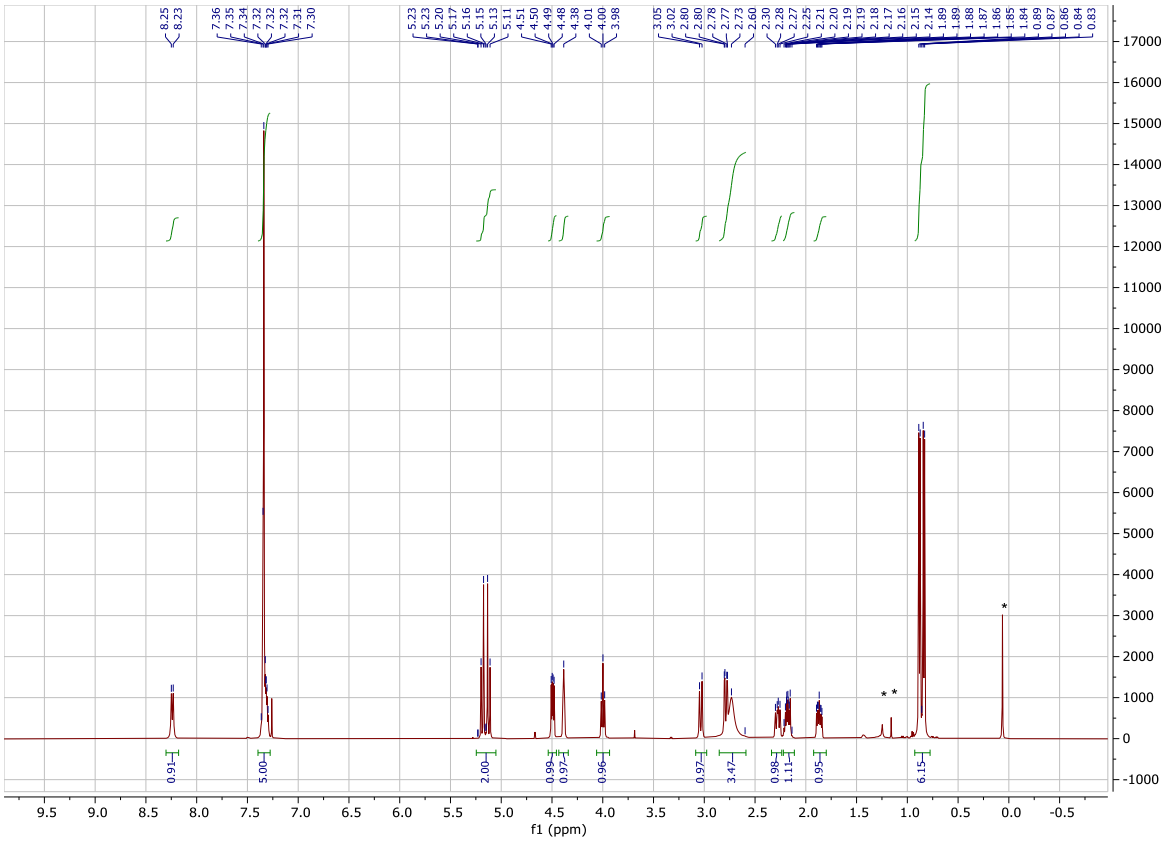

Figure S27. ^{1}H-NMR of *trans*-**7** in $CDCl_3$. (signals due to solvent impurities marked with asterisks *).

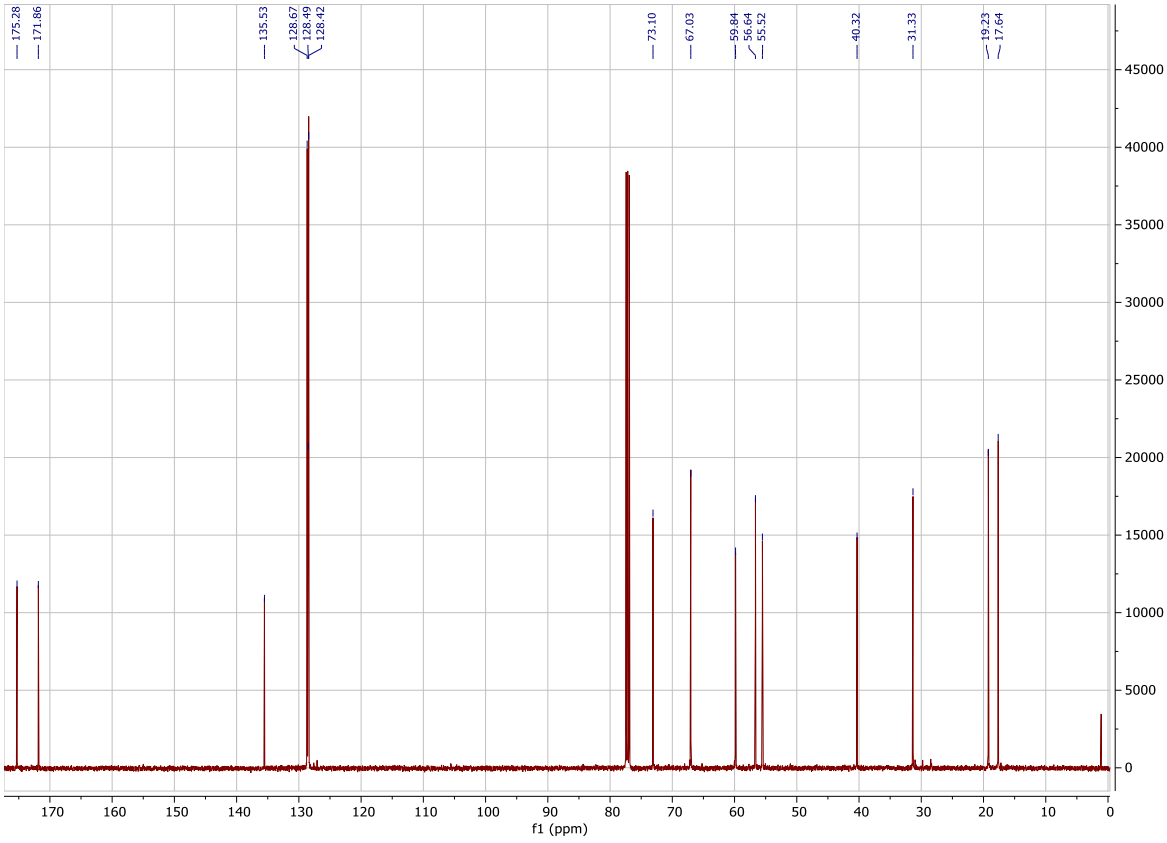

Figure S28. ^{13}C-NMR of *trans*-**7** in $CDCl_3$.

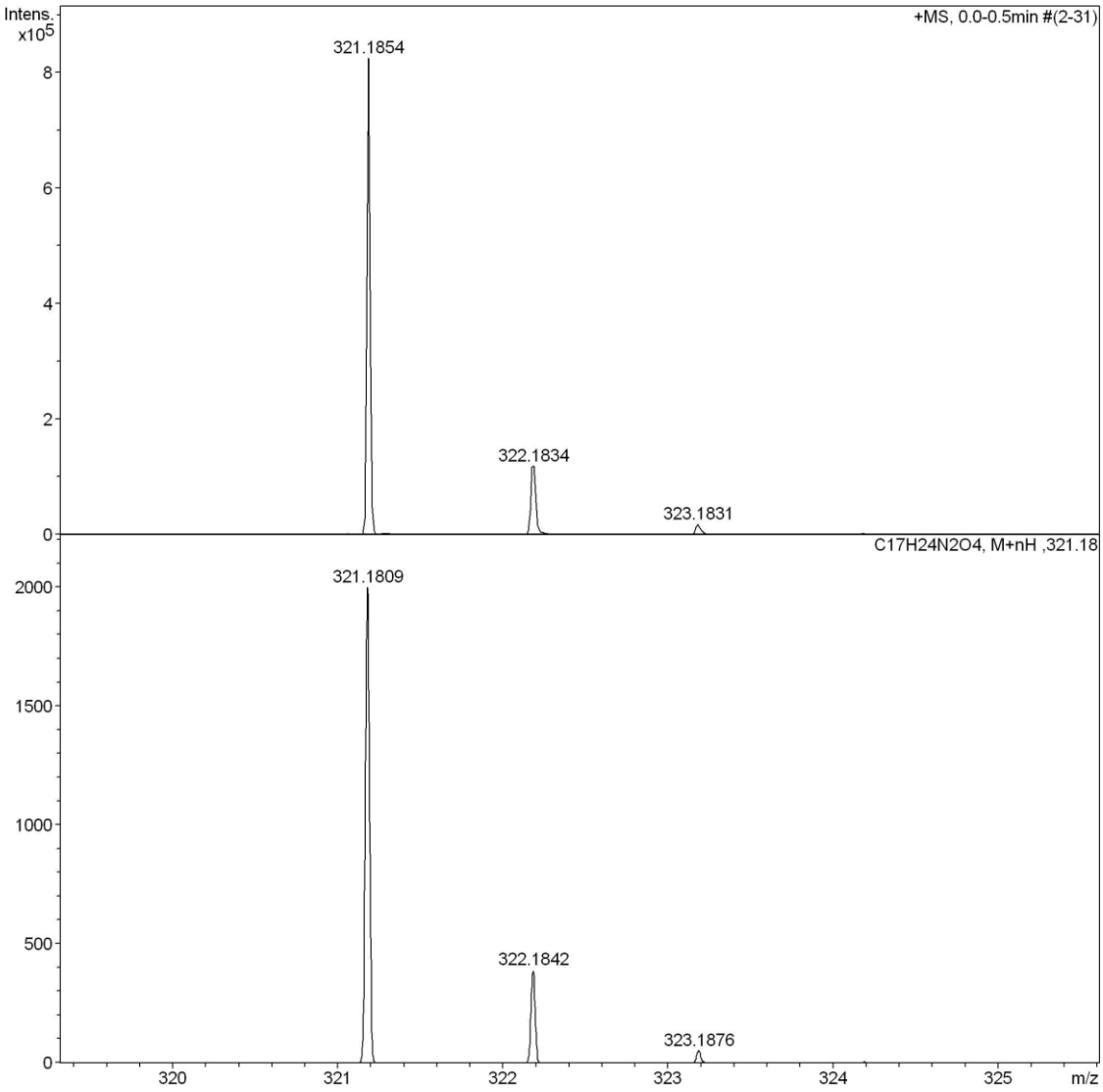

Figure S29. ESI-MS of *trans*-**7**.

Chiral Phase HPLC Data

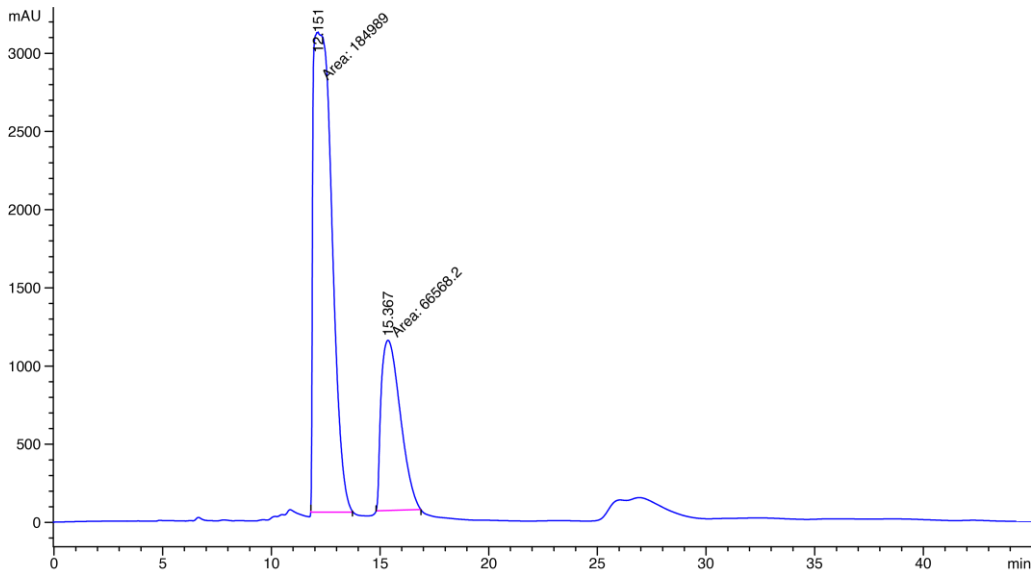

Figure S30. Chiral phase HPLC (Chiralpak AS-H, Daicel). *n*-hexane / isopropanol (70:30) as eluent, UV 254 nm, flow rate 0.7 mL min^{-1} and T = 25 °C. Products of the aldol reaction of **8** with acetone in DMSO/acetone in presence of catalyst *cis*-**2**. The Chromatogram shows (*R*)-**9**, t_R = 12.2 min, and (*S*)-**9**, t_R = 15.4 min, *R*/*S* ratio of 74:26 (*ee* = 48 %).

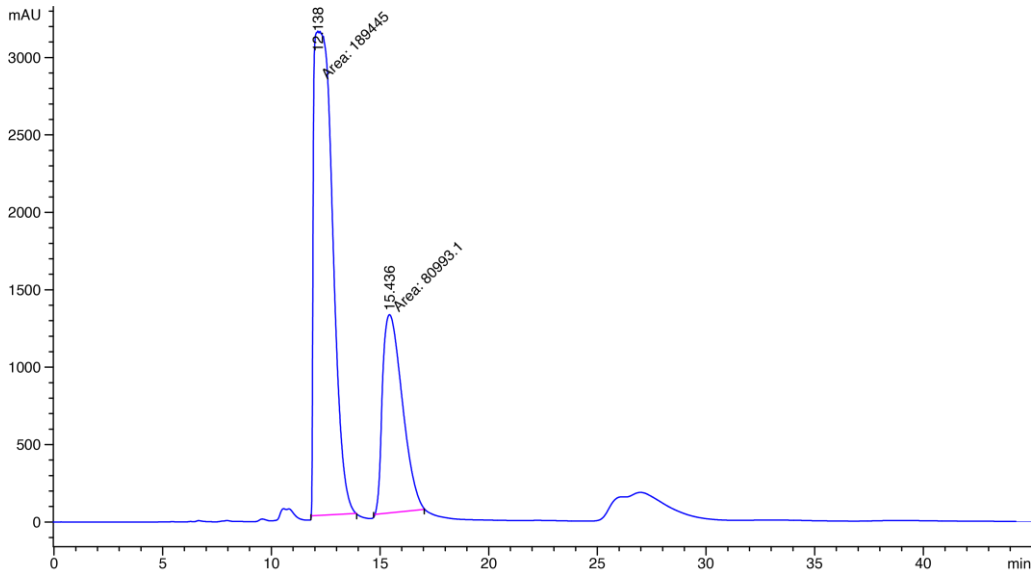

Figure S31. Chiral phase HPLC of (*R*)-**9**, t_R = 12.1 min, and (*S*)-**9**, t_R = 15.4 min, from aldol reaction of **8** with acetone in DMSO/acetone in presence of catalyst *trans*-**2**.

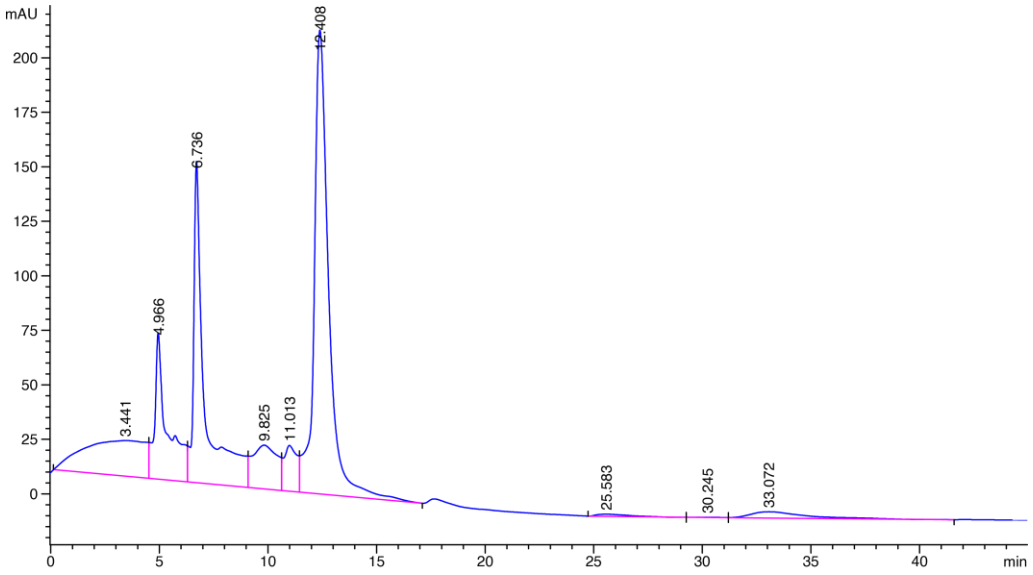

Figure S32. Chiral phase HPLC of (*R*)-**9**, t_R = 12.4 min, from aldol reaction of **8** with acetone in DMSO/acetone in presence of catalyst *cis*-**6**. Peaks at 4.97 min and 6.74 min are from injection and starting material, respectively.

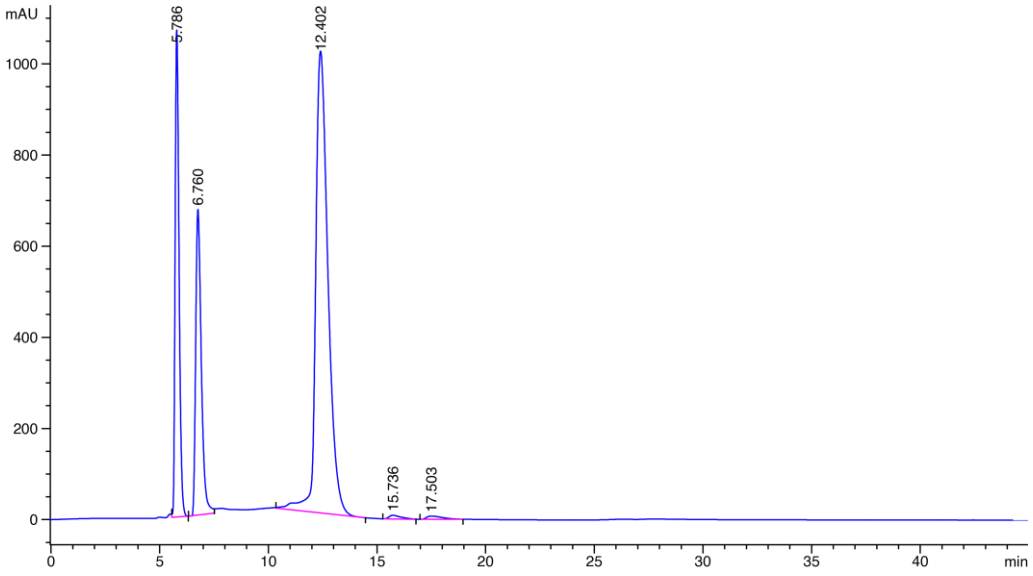

Figure S33. Chiral phase HPLC of (*R*)-**9**, t_R = 12.4 min, from aldol reaction of **8** with acetone in DMSO/acetone in presence of catalyst *trans*-**6**. Peaks at 5.79 min and 6.76 min are from injection and starting material, respectively.

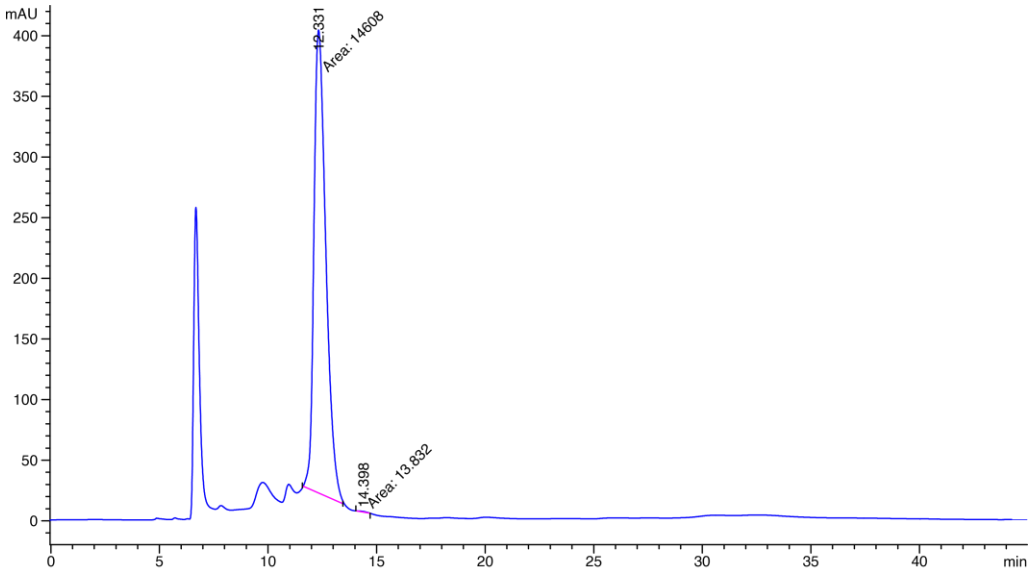

Figure S34. Chiral phase HPLC of (*R*)-**9**, t_R = 12.4 min, from aldol reaction of **8** with acetone in pure acetone as a solvent in presence of catalyst *cis*-**6**. The peak at 6.76 min is from starting material.

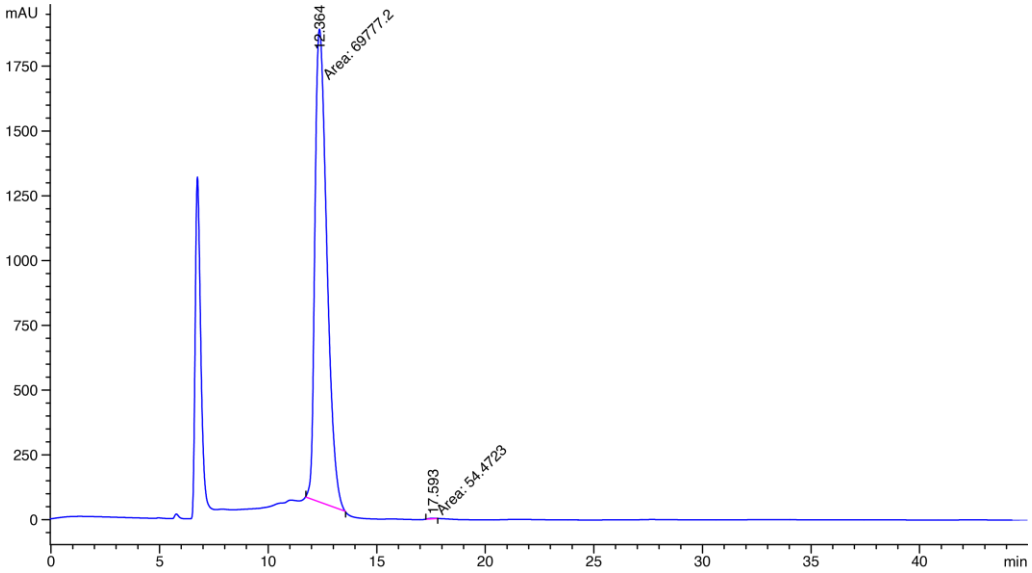

Figure S35. Chiral phase HPLC of (*R*)-**9**, t_R = 12.4 min, from aldol reaction of **8** with acetone in pure acetone as a solvent in presence of catalyst *trans*-**6**. The peak at 6.76 min is from starting material.

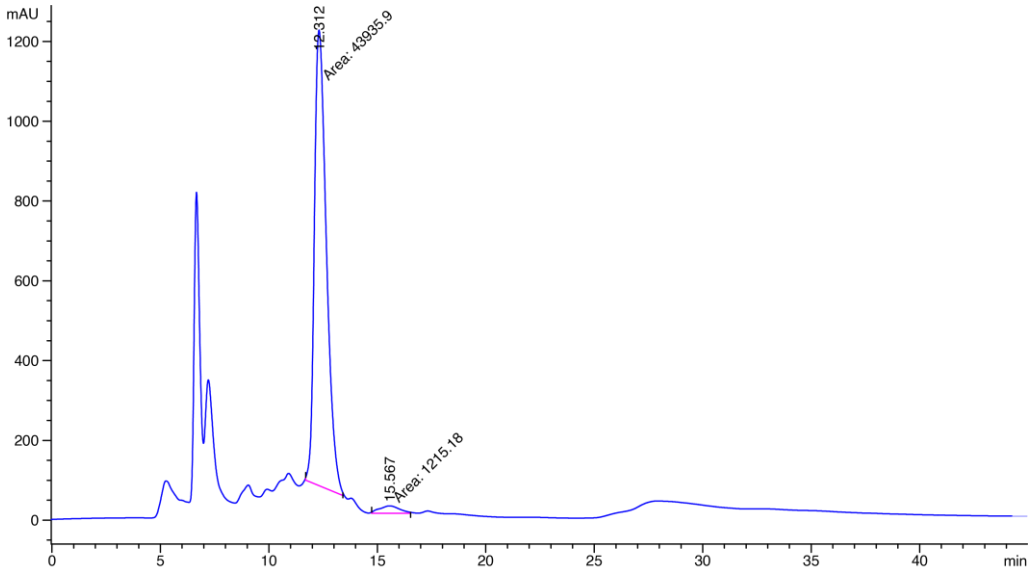

Figure S36. Chiral phase HPLC of (*R*)-**9**, t_R = 12.3 min, and (*S*)-**9**, t_R = 15.6 min, from aldol reaction of **8** with acetone in DMSO/acetone in presence of catalyst *cis*-**7**. Peaks at 5.26 min and 6.66 min are from injection and starting material, respectively.

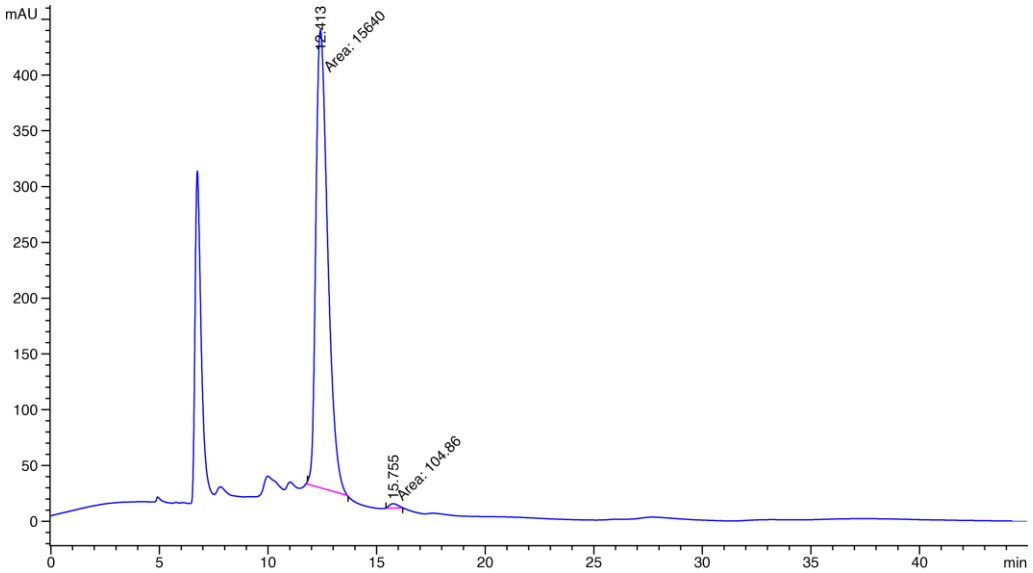

Figure S37. Chiral phase HPLC of (*R*)-**9**, t_R = 12.4 min, and (*S*)-**9**, t_R = 15.8 min, from aldol reaction of **8** with acetone in DMSO/acetone in presence of catalyst *trans*-**7**. The peak at 6.76 min is from starting material.

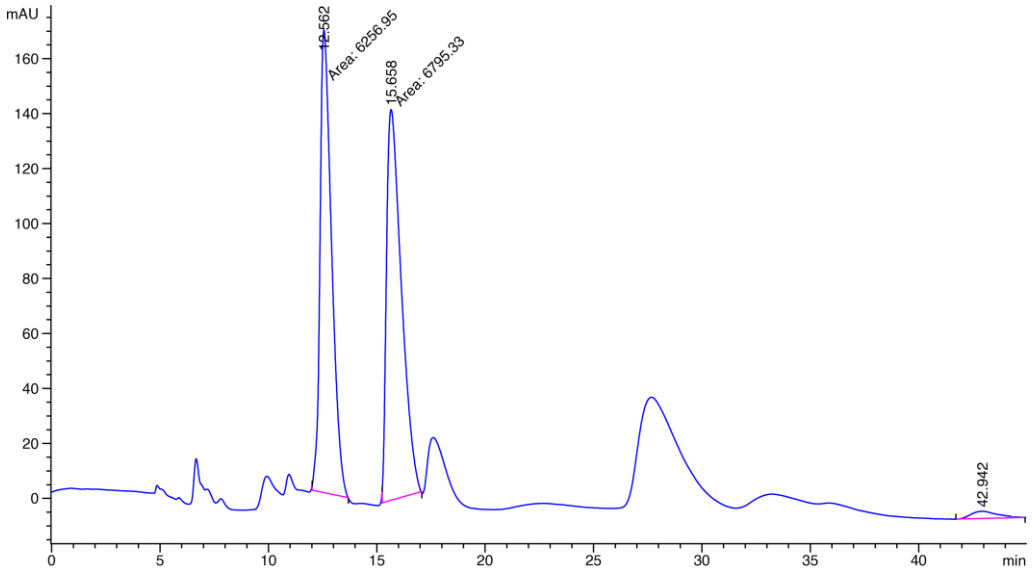

Figure S38. Chiral phase HPLC of (*R*)-**9**, t_R = 12.3 min, and (*S*)-**9**, t_R = 15.6 min, from aldol reaction of **8** with acetone in pure acetone as a solvent in presence of catalyst *cis*-**7**. Additional peaks such as the broad peak at 27.7 min presumably have their origin in by-products formed in the course of an alternative pathway with *cis*-**7** (see main article).

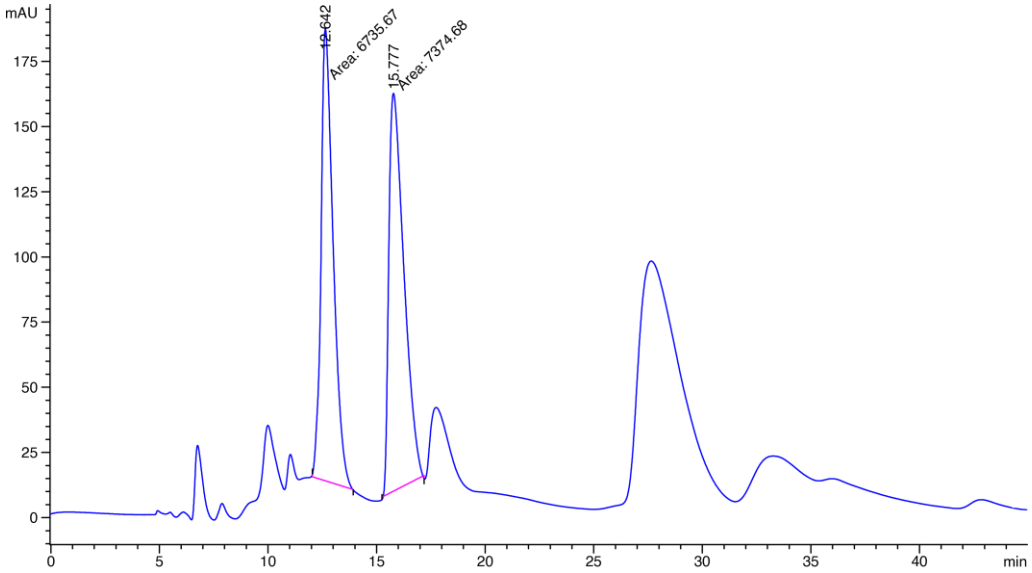

Figure S39. Chiral phase HPLC of (*R*)-**9**, t_R = 12.4 min, and (*S*)-**9**, t_R = 15.8 min, from aldol reaction of **8** with acetone in pure acetone as a solvent in presence of catalyst *trans*-**7**. Additional peaks such as the broad peak at 27.7 min presumably have their origin in by-products formed in the course of an alternative pathway with *trans*-**7** (see main article).

Model Geometries from DFT Calculations

Aldol Reaction Cycle with *cis*-4-Hydroxy-L-proline (*cis*-**2**) as a Catalyst

Table S1. Numbers of conformers of intermediates and transition structures from *cis*-**2**.

	# conformers	# conformers accounting for ≥ 95%
cis-**2**	29	7
TS1 from *cis*-**2**	3	3
Hemiaminal from *cis*-**2**	84	22
TS2 from *cis*-**2**	5	5
Iminium from *cis*-**2**	2	1
TS3 from *cis*-**2**	2	1
Enamine from *cis*-**2**	18	6
$TS4_{pro\ R}$ from *cis*-**2**	5	2
$TS4_{pro\ S}$ from *cis*-**2**	6	2
TS3a from *cis*-**2**	3	3
Bicyclic by-product from *cis*-**2**	3	2

cis-**2** (most abundant conformer; abundance: 73%)
# of imaginary frequencies: 0
Energy: -476.380230 Hartrees
Gibbs Free Energy: -476.265546 Hartrees

N	0.479235	1.256570	0.652731
C	-0.437602	0.849238	-0.502593
C	-1.588769	-0.002640	0.124145
O	-1.315384	-0.469174	1.282078
C	1.848997	0.660165	0.424249
C	0.472296	-0.004196	-1.410859
H	-0.089581	-0.799284	-1.905792
C	1.547039	-0.561179	-0.454639
H	0.943083	0.616546	-2.180211
H	2.445060	-0.880298	-0.988291
H	2.303804	0.413353	1.383690
H	2.454811	1.399733	-0.101686
H	-0.826699	1.743523	-0.986980
O	-2.596052	-0.173219	-0.573057
H	0.012183	0.784271	1.460683
H	0.506765	2.265333	0.813166
O	1.108389	-1.676819	0.303458
H	0.268535	-1.433804	0.754661

TS1 from *cis*-**2** (most abundant conformer; abundance: 49%)
# of imaginary frequencies: 1
Energy: -669.522887 Hartrees
Gibbs Free Energy: -669.333645 Hartrees

C	-0.162730	-1.700823	0.170874
N	0.449038	-0.606026	-0.650815
C	-0.668283	0.351833	-0.988074
C	-1.854120	-0.610626	-1.179333
C	-1.689608	-1.596740	-0.010444
C	2.004476	0.019741	0.136913
C	-1.033470	1.469184	0.028951
O	-2.042535	2.113177	-0.234514
O	-0.279932	1.738929	1.062454
O	1.672782	0.314005	1.355854
H	-0.400728	0.868765	-1.912485
H	-1.755533	-1.138343	-2.134820
H	-2.811442	-0.086380	-1.169834
H	-2.136262	-2.573582	-0.230743
H	0.239100	-2.660610	-0.153203
H	0.109048	-1.521321	1.213888
H	0.755374	-1.000683	-1.540899
H	0.614222	1.115454	1.224045
C	2.923493	-1.190084	-0.010106
H	3.036960	-1.517046	-1.048559
H	3.912605	-0.895203	0.358585
H	2.574120	-2.023338	0.604476
C	2.368621	1.175226	-0.797419
H	3.365604	1.527010	-0.507471
H	2.412202	0.873393	-1.848594
H	1.677342	2.013289	-0.684317
O	-2.211992	-1.074340	1.212557
H	-3.172731	-0.979659	1.106645

Hemiaminal from *cis*-**2** (most abundant conformer; abundance: 20%)
# of imaginary frequencies: 0
Energy: -669.537567 Hartrees
Gibbs Free Energy: -669.345906 Hartrees

C	0.550545	0.375936	0.729572
C	1.409473	-0.787739	1.265926
C	1.312936	-1.826210	0.143774
C	-0.142659	-1.689821	-0.289073
N	-0.435584	-0.234914	-0.201191
C	1.405277	1.412494	-0.021119
H	2.434917	-0.483027	1.492256
H	0.961306	-1.188170	2.181437
H	-0.769132	-2.276975	0.397302
H	-0.298374	-2.062900	-1.304241
H	0.058044	0.895012	1.555408

C	-1.852484	0.132007	0.030736
C	-2.745852	-0.598666	-0.979553
H	-2.434715	-0.381021	-2.005832
H	-2.718353	-1.683977	-0.837480
H	-3.780116	-0.268708	-0.848601
C	-2.038538	1.647122	-0.103598
H	-3.094600	1.891679	0.038643
H	-1.466736	2.193066	0.652091
H	-1.729819	1.991344	-1.094104
O	2.276732	2.070203	0.514440
O	1.099002	1.540720	-1.315933
O	-2.265416	-0.175574	1.371503
O	2.127932	-1.476124	-0.977448
H	3.054622	-1.509958	-0.689642
H	0.397029	0.842383	-1.453308
H	-2.401666	-1.134930	1.437673
H	1.538495	-2.843961	0.486240

TS2 from *cis*-**2** (most abundant conformer; abundance: 40%)
# of imaginary frequencies: 1
Energy: -669.520671 Hartrees
Gibbs Free Energy: -669.331775 Hartrees

C	1.549520	-1.684755	0.068657
C	0.019781	-1.833461	0.066713
N	-0.477952	-0.515281	0.529337
C	0.629209	0.359334	0.975443
C	1.778776	-0.651073	1.183480
C	-1.717338	-0.052916	0.205796
C	1.073998	1.458631	-0.030654
O	0.687121	1.340703	-1.272677
O	1.828080	2.333880	0.388576
O	-1.559855	0.440445	-1.485778
H	0.370326	0.857541	1.912609
H	1.676836	-1.129857	2.163649
H	2.761758	-0.179692	1.125284
H	-0.307412	-2.624381	0.751839
H	-0.338237	-2.069986	-0.938668
H	-0.502391	0.874141	-1.442233
H	-2.183287	1.156579	-1.705014
C	-2.812151	-1.092489	0.079371
H	-3.027226	-1.500593	1.073533
H	-3.723514	-0.633945	-0.310178
H	-2.525949	-1.911909	-0.580816
C	-2.152992	1.227910	0.895183
H	-2.268490	1.031226	1.966695
H	-1.434587	2.040532	0.770693
H	-3.120225	1.556291	0.507727
O	2.057577	-1.262838	-1.193704
H	1.613121	-0.425415	-1.437117
H	2.038731	-2.638171	0.281358

Iminium from *cis*-**2** (most abundant conformer; abundance: 100%)
# of imaginary frequencies: 0
Energy: -593.108981 Hartrees
Gibbs Free Energy: -592.943141 Hartrees

C	0.328976	0.551767	0.845165
C	1.540307	-0.291027	1.279868
C	1.584896	-1.479408	0.296670
C	0.091297	-1.788275	0.089449
N	-0.600269	-0.479170	0.266405
C	0.673558	1.662501	-0.221643
O	1.296721	1.275506	-1.251923
O	0.296740	2.815881	0.061523
H	2.469976	0.281773	1.253198
H	1.390593	-0.657088	2.301297
H	-0.292594	-2.479609	0.846998
H	-0.107133	-2.190951	-0.904788
H	2.081423	-2.347450	0.739509
H	-0.174868	1.021238	1.689223
C	-1.853412	-0.289722	-0.010515
C	-2.519160	1.031369	0.195131
H	-1.828516	1.849801	0.394703
H	-3.112308	1.266572	-0.695656
H	-3.232089	0.930605	1.024814
C	-2.680203	-1.419402	-0.545867
H	-3.738219	-1.154474	-0.532399
H	-2.393368	-1.629106	-1.584588
H	-2.532094	-2.338381	0.029180
O	2.248380	-1.189692	-0.911637
H	1.938796	-0.279114	-1.179575

TS3 from *cis*-**2** (most abundant conformer; abundance: 99%)
# of imaginary frequencies: 1
Energy: -593.077094 Hartrees
Gibbs Free Energy: -592.913949 Hartrees

C	0.309759	0.479180	0.907463
C	1.583523	-0.289682	1.265843
C	1.696558	-1.366041	0.172514
C	0.225105	-1.765684	-0.069229
N	-0.561147	-0.570541	0.311119
C	0.508374	1.602931	-0.152090
O	-0.559110	2.259530	-0.507600
O	1.625588	1.821056	-0.631616
H	2.462090	0.356690	1.301160
H	1.456026	-0.762711	2.244614
H	-0.068342	-2.612476	0.561994
H	0.064785	-2.031236	-1.116540
H	2.267250	-2.236241	0.509885
H	-0.172543	0.903909	1.792771
C	-1.865143	-0.382694	0.089204
C	-2.493773	0.818497	0.489084
H	-1.579362	1.707277	-0.150765
H	-3.556264	0.886946	0.274642
C	-2.590455	-1.423503	-0.718650
H	-3.630009	-1.131098	-0.869507
H	-2.118331	-1.577993	-1.695375
H	-2.574744	-2.386701	-0.194461
H	-2.224307	1.218285	1.469443
O	2.324816	-0.888804	-1.009281
H	2.227753	0.086859	-1.022541

Enamine from *cis*-**2** (most abundant conformer; abundance: 31%)
# of imaginary frequencies: 0

Energy: -593.094165 Hartrees
Gibbs Free Energy: -592.927035 Hartrees

C	-1.257201	-1.720875	-0.368647
C	0.263701	-1.776470	-0.248693
N	0.633837	-0.359880	-0.148825
C	-0.357250	0.497316	-0.805012
C	-1.474006	-0.487400	-1.246201
C	-0.877473	1.600334	0.138213
O	-1.880967	-1.448428	0.902511
O	-1.398436	1.191795	1.302246
O	-0.836347	2.782145	-0.145775
C	1.951629	0.071165	0.013355
C	2.356795	1.335477	-0.233219
C	2.915668	-0.967748	0.537173
H	-1.679959	-2.634500	-0.797472
H	0.587544	-2.338686	0.632344
H	0.688938	-2.267461	-1.138541
H	0.072763	1.018413	-1.668387
H	-2.483368	-0.080831	-1.142335
H	-1.325492	-0.758609	-2.294906
H	-1.636845	-2.150116	1.529213
H	-1.452664	0.199473	1.328694
H	1.692855	2.118202	-0.579829
H	3.388894	1.610851	-0.048518
H	2.592042	-1.359305	1.509587
H	3.005056	-1.823795	-0.142649
H	3.908210	-0.529360	0.660903

$TS4_{pro\ R}$ from *cis*-**2** (most abundant conformer; abundance: 89%)
# of imaginary frequencies: 1
Energy: -1143.170376 Hartrees
Gibbs Free Energy: -1142.905113 Hartrees

C	-2.694411	2.176724	0.712901
C	-1.823060	1.167419	1.450626
N	-2.372619	-0.140425	1.011862
C	-3.763714	0.008289	0.529652
C	-4.073880	1.505752	0.775957
C	-4.014714	-0.366633	-0.952056
O	-3.003905	-0.586809	-1.776809
O	-5.172389	-0.456658	-1.320722
C	-1.712577	-1.298129	1.114867
C	-2.445654	-2.579457	0.820658
C	-0.317152	-1.308765	1.289689
H	-0.770724	1.265252	1.196505
H	-1.938110	1.258681	2.536991
H	-2.691105	3.149784	1.215158
H	-4.769644	1.905739	0.036903
H	-4.510279	1.636577	1.771449
H	-4.436775	-0.631071	1.106023
H	-1.798323	-3.435322	1.015258
H	-3.336871	-2.669405	1.451338
H	-2.772488	-2.628257	-0.223850
H	0.141893	-2.274539	1.473724
H	0.167059	-0.485201	1.799852
H	-2.067862	-0.348581	-1.427844
O	-0.618357	0.073787	-1.111056
C	0.167698	-0.842425	-0.664699
C	1.616287	-0.515378	-0.449288
C	2.051533	0.818364	-0.466285
C	3.396086	1.125903	-0.295988
C	4.305509	0.081906	-0.115157
C	3.903047	-1.255587	-0.106245
C	2.554998	-1.545106	-0.276158
N	5.721980	0.397133	0.061823
O	6.062101	1.583520	0.049054
O	6.512862	-0.537692	0.217048
H	0.011281	-1.870497	-1.021106
H	1.327654	1.609235	-0.628577
H	3.745852	2.150511	-0.308190
H	4.636606	-2.040574	0.026620
H	2.227015	-2.580901	-0.278088
O	-2.276728	2.351164	-0.638345
H	-1.539363	1.735852	-0.822160

$TS4_{pro\ S}$ from *cis*-**2** (most abundant conformer; abundance: 57%)
# of imaginary frequencies: 1
Energy: -1143.168629 Hartrees
Gibbs Free Energy: -1142.902869 Hartrees

C	4.222827	-0.829991	-0.689427
C	3.261047	-1.592984	0.212441
N	2.469071	-0.512186	0.855547
C	3.211569	0.768797	0.827939
C	4.566026	0.389137	0.178600
C	2.537621	1.923376	0.048746
O	1.508965	1.683704	-0.749450
O	2.988956	3.044667	0.193357
C	1.286404	-0.706210	1.438805
C	0.659526	0.422756	2.209699
C	0.543850	-1.873418	1.154607
H	2.625748	-2.275657	-0.346326
H	3.795577	-2.152010	0.988790
H	5.111232	-1.427525	-0.920808
H	4.986180	1.212445	-0.401109
H	5.284317	0.108192	0.955476
H	3.353543	1.147021	1.842838
H	1.356251	0.824074	2.953258
H	0.369533	1.247186	1.547842
H	-0.234719	0.073473	2.726406
H	-0.350325	-2.023082	1.749953
H	1.078881	-2.792174	0.943360
H	1.268351	0.698581	-0.893593
O	0.839415	-0.726384	-1.345467
C	-0.047281	-1.440689	-0.733533
C	-1.429183	-0.884167	-0.507077
C	-1.713498	0.471088	-0.732872
C	-3.002100	0.965125	-0.555007
C	-4.010818	0.086986	-0.158943
C	-3.762877	-1.271253	0.056362
C	-2.471044	-1.746275	-0.123206
N	-5.366986	0.599253	0.027115
O	-5.571264	1.799436	-0.175915
O	-6.246146	-0.191992	0.380230
H	-0.080644	-2.507542	-0.996873
H	-0.926429	1.140214	-1.059974
H	-3.231474	2.009632	-0.724717

H	-4.570529	-1.929094	0.351266
H	-2.266008	-2.801781	0.034181
O	3.598055	-0.427461	-1.903846
H	2.659663	-0.710857	-1.882676

TS3a from *cis*-**2** (most abundant conformer; abundance: 56%)
# of imaginary frequencies: 1
Energy: -593.092489 Hartrees
Gibbs Free Energy: -592.924941 Hartrees

C	-1.650565	-0.312954	0.064571
N	-0.469000	-0.663329	0.590401
C	0.356987	0.482848	1.002357
C	1.746727	-0.104194	1.226410
C	1.850907	-1.153172	0.110710
C	0.418542	-1.726369	0.039338
C	0.258061	1.457895	-0.238533
O	-0.817040	1.326200	-0.908219
O	1.215352	2.219341	-0.471665
H	2.565749	-1.948712	0.341256
H	2.523098	0.660845	1.156670
H	1.809522	-0.578373	2.211075
H	-0.035023	0.989451	1.886963
H	0.311937	-2.617788	0.666239
H	0.162217	-1.986862	-0.987818
C	-2.271528	-1.156326	-1.012003
H	-2.482657	-2.160807	-0.625480
H	-3.213181	-0.713421	-1.340446
H	-1.607682	-1.254600	-1.873965
C	-2.611441	0.515641	0.875470
H	-3.209928	1.146988	0.216685
H	-3.291504	-0.178858	1.388216
H	-2.128722	1.138201	1.627691
O	2.242287	-0.578552	-1.137727
H	2.168232	0.391111	-1.068926

Bicyclic by-product from *cis*-**2** (most abundant conformer; abundance: 66%)
# of imaginary frequencies: 0
Energy: -593.111007 Hartrees
Gibbs Free Energy: -592.941668 Hartrees

C	1.435532	-0.292196	0.014990
N	0.289040	-0.606789	-0.842248
C	-0.471167	0.649906	-0.996177
C	-1.961887	0.277244	-0.922650
C	-1.953616	-0.971780	-0.031426
C	-0.676520	-1.676568	-0.489071
C	-0.009855	1.515690	0.175220
O	1.063790	0.948447	0.748252
O	-0.489043	2.562490	0.556883
H	-2.845140	-1.596965	-0.168690
H	-2.565320	1.096707	-0.520651
H	-2.342367	0.029288	-1.918932
H	-0.233889	1.181228	-1.926838
H	-0.889761	-2.270361	-1.386629
H	-0.290329	-2.354531	0.271245
C	1.786527	-1.326023	1.075240
H	2.026789	-2.287699	0.612353
H	2.666919	-0.985774	1.627529
H	0.963802	-1.458011	1.781687
C	2.647384	0.072423	-0.846612
H	3.456558	0.473004	-0.227884
H	3.008145	-0.820356	-1.366696
H	2.376438	0.820554	-1.598173
O	-1.776029	-0.635280	1.347690
H	-2.523256	-0.077008	1.617724

Aldol Reaction Cycle with *trans*-4-Hydroxy-L-proline (*trans*-**2**) as a Catalyst

Table S2. Numbers of conformers of intermediates and transition structures from *trans*-**2**.

	# conformers	# conformers accounting for ≥ 95%
trans-**2**	15	2
TS1 from *trans*-**2**	4	4
Hemiaminal from *trans*-**2**	86	10
TS2 from *trans*-**2**	6	6
Iminium from *trans*-**2**	3	3
TS3 from *trans*-**2**	3	3
Enamine from *trans*-**2**	21	16
$TS4_{pro\ R}$ from *trans*-**2**	9	3
$TS4_{pro\ S}$ from *trans*-**2**	9	3
TS3a from *trans*-**2**	3	3
Bicyclic by-product from *trans*-**2**	3	3

trans-**2** (most abundant conformer; abundance: 51%)
# of imaginary frequencies: 0
Energy: -476.378610 Hartrees
Gibbs Free Energy: -476.267294 Hartrees

C	1.807478	-0.281035	0.553320
C	1.269180	1.150333	0.545800
N	0.185682	1.156097	-0.466869
C	-0.368345	-0.222882	-0.524287
C	0.519702	-1.105584	0.397333
C	-1.837187	-0.201801	-0.081818
O	2.662691	-0.405743	-0.585210
O	-2.305579	1.029035	0.149625
O	-2.516381	-1.202168	0.046144
H	2.347853	-0.522482	1.478468
H	0.854653	1.397445	1.529608
H	2.033007	1.889519	0.294532
H	0.574756	1.402501	-1.372619
H	-0.350600	-0.595585	-1.552782
H	0.046893	-1.249702	1.374838
H	0.703899	-2.095353	-0.028839
H	2.928781	-1.336711	-0.653660
H	-1.509835	1.614509	-0.028023

TS1 from *trans*-**2** (most abundant conformer; abundance: 36%)
# of imaginary frequencies: 1
Energy: -669.521088 Hartrees
Gibbs Free Energy: -669.333173 Hartrees

C	0.693959	-1.146982	-0.903029
N	-0.029644	-0.597862	0.274336
C	0.731255	0.654917	0.631551
C	2.212546	0.326609	0.251540
C	2.159574	-1.024096	-0.497166
C	-1.898049	-0.552164	0.019624
C	0.308769	1.994068	-0.030230
O	1.020512	2.956573	0.233699
O	-0.737073	2.089233	-0.809092
O	-2.058976	0.071638	-1.101506
H	0.620223	0.815517	1.705438
H	2.843064	0.248706	1.141193
H	2.626015	1.118472	-0.375672
H	2.834001	-1.049159	-1.361289
H	0.398951	-2.178329	-1.094491
H	0.445926	-0.526864	-1.768304
H	0.123581	-1.252224	1.045032
H	-1.366191	1.191854	-0.957488
C	-2.234971	-2.038519	-0.003445
H	-1.871696	-2.574296	0.878721
H	-3.328009	-2.122554	-0.017285
H	-1.854084	-2.512550	-0.910844
C	-2.335710	0.152439	1.303897
H	-3.430957	0.113534	1.338938
H	-1.953073	-0.335582	2.205630
H	-2.043194	1.204583	1.303096
O	2.405685	-2.132786	0.372899
H	3.297519	-2.030969	0.742524

Hemiaminal from *trans*-**2** (most abundant conformer; abundance: 42%)
# of imaginary frequencies: 0
Energy: -669.539715 Hartrees
Gibbs Free Energy: -669.347235 Hartrees

C	0.906226	0.176391	-0.446586
C	0.939931	1.734379	-0.406384
C	-0.288093	2.125043	0.430835
C	-0.465455	0.906713	1.332857
N	-0.154491	-0.277529	0.491645
C	2.255597	-0.438491	-0.050420
H	1.852781	2.092826	0.078706
H	0.910793	2.170146	-1.408906
H	-1.455838	0.849178	1.780183
H	0.265826	0.959985	2.148481

H	-0.131507	3.048124	1.000377
H	0.674862	-0.165697	-1.457463
C	-1.279177	-1.011827	-0.167263
C	-2.448256	-1.204982	0.810797
H	-2.111178	-1.604146	1.772950
H	-2.989812	-0.270682	0.984718
H	-3.155336	-1.913577	0.370070
C	-0.766800	-2.381793	-0.628779
H	-1.560018	-2.896003	-1.179235
H	0.095499	-2.289171	-1.295516
H	-0.482305	-2.997590	0.229589
O	3.307311	-0.156079	-0.589634
O	2.170647	-1.327324	0.947165
O	-1.734607	-0.350244	-1.346592
O	-1.486173	2.247679	-0.357117
H	-1.342080	2.934173	-1.029147
H	1.200115	-1.312448	1.188893
H	-1.871619	0.592745	-1.106130

TS2 from *trans*-**2** (most abundant conformer; abundance: 19%)
# of imaginary frequencies: 1
Energy: -669.516629 Hartrees
Gibbs Free Energy: -669.329596 Hartrees

C	0.490502	0.650729	0.775169
C	1.932780	0.134995	0.851549
C	2.033612	-0.793539	-0.366513
C	0.656810	-1.472691	-0.418228
N	-0.244035	-0.542970	0.292312
C	0.368821	1.928566	-0.115645
O	-0.579308	2.001303	-0.986859
O	1.186133	2.828424	0.107956
H	2.648848	0.957634	0.838821
H	2.079456	-0.459788	1.760105
H	0.708403	-2.433952	0.105638
H	0.326217	-1.653101	-1.445674
H	2.182583	-0.192968	-1.275153
H	0.125322	0.929334	1.767935
H	-1.434282	1.045712	-1.154508
C	-1.587617	-0.664352	0.287722
O	-2.211352	0.216584	-1.211790
H	-1.976242	-0.331517	-1.981232
C	-2.358306	0.167868	1.292098
H	-2.109334	-0.169919	2.304444
H	-2.123836	1.230147	1.207805
H	-3.429481	0.038165	1.132867
C	-2.151916	-2.044622	0.032204
H	-3.231170	-1.983404	-0.114363
H	-1.705758	-2.528540	-0.839430
H	-1.953487	-2.674206	0.907708
O	3.029480	-1.802008	-0.274984
H	3.893270	-1.368955	-0.365873

Iminium from *trans*-**2** (most abundant conformer; abundance: 38%)
# of imaginary frequencies: 0
Energy: -593.098012 Hartrees
Gibbs Free Energy: -592.934016 Hartrees

C	-0.211963	0.706986	-0.714323
C	-1.670068	0.287687	-0.888997
C	-1.895046	-0.686794	0.275411
C	-0.568471	-1.454408	0.356593
N	0.440740	-0.531283	-0.221301
C	-0.008813	1.905291	0.325188
O	-0.833379	2.832591	0.175928
O	0.953141	1.791269	1.115370
H	-2.317619	1.164611	-0.855054
H	-1.826889	-0.246979	-1.833155
H	-0.631270	-2.353053	-0.265961
H	-0.285960	-1.738662	1.371441
H	-2.053706	-0.123868	1.205023
H	0.247509	1.008142	-1.657324
C	1.717189	-0.752455	-0.175132
C	2.721800	0.174845	-0.775415
H	2.312353	1.125504	-1.103802
H	3.503174	0.368990	-0.033149
H	3.203402	-0.338300	-1.618278
C	2.236784	-2.004321	0.467274
H	3.279086	-2.169320	0.189772
H	2.189511	-1.901633	1.559522
H	1.649706	-2.884678	0.191266
O	-2.932875	-1.634636	0.083731
H	-3.778053	-1.166557	0.174986

TS3 from *trans*-**2** (most abundant conformer; abundance: 35%)
# of imaginary frequencies: 1
Energy: -593.071756 Hartrees
Gibbs Free Energy: -592.910135 Hartrees

C	0.122396	0.693435	0.734510
C	1.634538	0.513430	0.858833
C	1.977890	-0.455153	-0.282763
C	0.793905	-1.430592	-0.288235
N	-0.335772	-0.629672	0.216856
C	-0.294141	1.854352	-0.226588
O	-1.535506	1.864739	-0.630757
O	0.533140	2.704787	-0.542650
H	2.152913	1.470068	0.783186
H	1.885294	0.035507	1.811995
H	1.007372	-2.264282	0.391963
H	0.580579	-1.832457	-1.280851
H	2.006246	0.095051	-1.233316
H	-0.341386	0.879677	1.709448
C	-1.616384	-0.996861	0.183831
C	-2.621547	-0.118357	0.657334
H	-2.224692	0.957608	-0.130936
H	-3.638596	-0.494915	0.594784
C	-1.961448	-2.284372	-0.513279
H	-3.038299	-2.452916	-0.486738
H	-1.629915	-2.279440	-1.558002
H	-1.466202	-3.128551	-0.018946
H	-2.418206	0.411177	1.591075
O	3.170641	-1.200387	-0.100717
H	3.917842	-0.597225	-0.240532

Enamine from *trans*-**2** (most abundant conformer; abundance: 12%)

# of imaginary frequencies: 0
Energy: -593.088367 Hartrees
Gibbs Free Energy: -592.923017 Hartrees

C	-1.926773	-1.173614	-0.321134
C	-1.605896	0.250547	-0.777108
N	-0.230376	0.515441	-0.273540
C	0.332738	-0.696477	0.330287
C	-0.544161	-1.831235	-0.241519
C	1.798711	-0.896108	-0.058261
O	-2.535188	-1.072165	0.967144
O	2.157542	-0.307006	-1.212021
O	2.573472	-1.579826	0.576939
C	0.108250	1.771894	0.274616
C	1.025351	1.929794	1.248041
C	-0.561422	2.959915	-0.374585
H	-2.592483	-1.686441	-1.026919
H	-1.638954	0.330417	-1.868946
H	-2.335100	0.945325	-0.355746
H	0.268083	-0.684917	1.425103
H	-0.207700	-2.109976	-1.246965
H	-0.525244	-2.725363	0.386578
H	-2.697417	-1.974598	1.287242
H	1.384163	0.233180	-1.496101
H	1.532536	1.106720	1.738356
H	1.302738	2.928223	1.566559
H	-0.469051	2.917522	-1.466575
H	-1.631879	3.007483	-0.142184
H	-0.104462	3.888023	-0.024127

$TS4_{pro\ R}$ from *trans*-**2** (most abundant conformer; abundance: 40%)
# of imaginary frequencies: 1
Energy: -1143.166140 Hartrees
Gibbs Free Energy: -1142.903509 Hartrees

C	3.241573	2.067345	-0.091502
C	2.056481	1.400914	-0.800761
N	2.399948	-0.041203	-0.814203
C	3.770689	-0.275299	-0.322175
C	4.415243	1.119401	-0.384602
C	3.849649	-0.881570	1.104718
O	2.750603	-1.101192	1.797096
O	4.957301	-1.153416	1.539061
C	1.600182	-0.994121	-1.294886
C	2.137319	-2.394333	-1.419912
C	0.224307	-0.750011	-1.476611
H	1.113075	1.568203	-0.287550
H	1.991462	1.768523	-1.831937
H	3.050592	2.101565	0.990089
H	5.247752	1.212843	0.315244
H	4.780530	1.316005	-1.397969
H	4.294708	-0.979784	-0.971051
H	2.488450	-2.779769	-0.455778
H	1.360823	-3.062867	-1.793567
H	2.982608	-2.426281	-2.116812
H	-0.328920	-1.500476	-2.032523
H	-0.110162	0.267408	-1.647694
H	1.831125	-0.753731	1.428589
O	0.445908	-0.284312	1.195648
C	-0.314049	-0.994233	0.437121
C	-1.760432	-0.593884	0.309532
C	-2.176140	0.676374	0.735066
C	-3.511335	1.051100	0.646340
C	-4.432250	0.135634	0.131754
C	-4.049175	-1.139940	-0.289272
C	-2.709339	-1.496484	-0.195159
N	-5.838775	0.520431	0.037985
O	-6.161421	1.651556	0.412826
O	-6.641089	-0.302418	-0.413016
H	-0.189873	-2.089914	0.445768
H	-1.439715	1.357523	1.146938
H	-3.846219	2.028144	0.971539
H	-4.790937	-1.828082	-0.674418
H	-2.396946	-2.487747	-0.512592
O	3.392447	3.377378	-0.610800
H	4.027094	3.847710	-0.047168

$TS4_{pro\ S}$ from *trans*-**2** (most abundant conformer; abundance: 40%)
# of imaginary frequencies: 1
Energy: -1143.164118 Hartrees
Gibbs Free Energy: -1142.901036 Hartrees

C	4.407698	-0.365000	-0.459608
C	3.258333	-1.289511	-0.038367
N	2.309699	-0.398896	0.676224
C	2.864280	0.958848	0.835605
C	4.368754	0.759400	0.587451
C	2.266181	2.008138	-0.137266
O	1.419693	1.631531	-1.077010
O	2.614483	3.168895	-0.004536
C	1.153313	-0.806545	1.194467
C	0.369169	0.140586	2.059501
C	0.579618	-2.026418	0.767502
H	2.768767	-1.765032	-0.884720
H	3.634451	-2.048886	0.657084
H	4.202446	0.047039	-1.457349
H	4.854008	1.683022	0.266300
H	4.851943	0.404616	1.503765
H	2.674830	1.336974	1.841578
H	0.942526	0.413157	2.952943
H	0.122696	1.067815	1.529110
H	-0.562385	-0.326268	2.379638
H	-0.250369	-2.394024	1.362295
H	1.251222	-2.808622	0.428645
H	1.174032	0.621582	-1.161204
O	0.704937	-0.741905	-1.601139
C	-0.147679	-1.476713	-0.968656
C	-1.519220	-0.926293	-0.637137
C	-1.815364	0.430103	-0.836593
C	-3.088226	0.926956	-0.572429
C	-4.071124	0.048740	-0.116046
C	-3.812855	-1.311449	0.074728
C	-2.536356	-1.787936	-0.192052
N	-5.410620	0.562656	0.161423
O	-5.623940	1.765453	-0.016303
O	-6.268444	-0.229413	0.562441
H	-0.226134	-2.524788	-1.302619
H	-1.045900	1.096100	-1.209662

H	-3.325822	1.972946	-0.720837
H	-4.601372	-1.969181	0.417931
H	-2.325550	-2.845588	-0.057475
O	5.605497	-1.122024	-0.472618
H	6.290105	-0.584910	-0.902231

TS3a from *trans*-**2** (most abundant conformer; abundance: 35%)
# of imaginary frequencies: 1
Energy: -593.090458 Hartrees
Gibbs Free Energy: -592.923746 Hartrees

C	-1.495238	-0.795630	0.148464
N	-0.221597	-0.642491	0.508037
C	0.180905	0.749473	0.790149
C	1.706313	0.731087	0.745149
C	2.014049	-0.353485	-0.300418
C	0.911444	-1.397366	-0.070532
C	-0.486607	1.612153	-0.357164
O	-1.407456	1.009106	-1.000653
O	-0.070539	2.771069	-0.509428
H	1.914340	0.068252	-1.310330
H	2.095927	1.716324	0.480464
H	2.127314	0.426372	1.709769
H	-0.198372	1.105496	1.750802
H	1.257916	-2.133558	0.663786
H	0.629518	-1.923866	-0.981908
C	-1.892496	-1.906378	-0.781210
H	-1.684581	-2.879078	-0.319486
H	-2.961704	-1.853152	-0.992522
H	-1.344114	-1.851792	-1.724729
C	-2.594222	-0.252405	1.020049
H	-3.437808	0.064976	0.405140
H	-2.935809	-1.074958	1.664445
H	-2.283881	0.574308	1.657538
O	3.271903	-0.993104	-0.152097
H	3.956279	-0.363146	-0.428719

Bicyclic by-product from *trans*-**2** (most abundant conformer; abundance: 41%)
# of imaginary frequencies: 0
Energy: -593.107501 Hartrees
Gibbs Free Energy: -592.939081 Hartrees

C	-1.447726	-0.617119	0.006667
N	-0.159464	-0.607326	0.696656
C	0.221586	0.816993	0.832995
C	1.734393	0.900465	0.594799
C	2.004591	-0.293296	-0.336764
C	1.009706	-1.350694	0.181661
C	-0.595106	1.525790	-0.250388
O	-1.504989	0.671381	-0.747569
O	-0.472142	2.666904	-0.641061
H	1.754973	-0.023194	-1.369286
H	2.026907	1.864992	0.172314
H	2.273062	0.759762	1.539580
H	-0.063140	1.240162	1.804751
H	1.478882	-1.900623	1.011196
H	0.738453	-2.084112	-0.577262
C	-1.657072	-1.723826	-1.015803
H	-1.563993	-2.705436	-0.542297
H	-2.664981	-1.640173	-1.431157
H	-0.941983	-1.652313	-1.839366
C	-2.590713	-0.563909	1.023987
H	-3.547074	-0.390195	0.521247
H	-2.642118	-1.513979	1.564471
H	-2.427485	0.235980	1.752938
O	3.351704	-0.730371	-0.388983
H	3.620199	-0.969334	0.514248

Aldol Reaction Cycle with *cis*-4-Hyp-Gly-OBn (*cis*-**6**) as a Catalyst

Table S3. Numbers of conformers of intermediates and transition structures from *cis*-**6**.

	# conformers	# conformers accounting for ≥ 95%
cis-**6**	69	21
TS1 from *cis*-**6**	6	6
Hemiaminal from *cis*-**6**	95	17
TS2 from *cis*-**6**	13	5
Iminium from *cis*-**6**	36	18
TS3 from *cis*-**6**	8	4
Enamine from *cis*-**6**	47	14
$TS4_{pro\ R}$ from *cis*-**6**	4	1
$TS4_{pro\ S}$ from *cis*-**6**	8	1
TS3a from *cis*-**6**	7	4
Bicyclic by-product from *cis*-**6**	32	18

cis-**6** (most abundant conformer; abundance: 29%)
# of imaginary frequencies: 0
Energy: -954.755276 Hartrees
Gibbs Free Energy: -954.501423 Hartrees

C	-4.272290	-1.353943	0.742596
C	-4.686476	-1.365266	-0.737152
N	-4.208410	-0.069105	-1.267009
C	-4.098502	0.906019	-0.158436
C	-4.486048	0.122770	1.122054
C	-2.675282	1.484041	-0.037992
O	-2.950483	-1.828573	0.977000
N	-1.824602	1.072087	-1.010941
O	-2.366246	2.255822	0.872076
C	-0.404586	1.269954	-0.923133
C	0.289377	0.089747	-0.243923
O	-0.286519	-0.857467	0.261430
O	1.616073	0.236646	-0.273325
C	3.856822	-0.470392	0.211764
C	4.505898	0.296334	1.188345
C	5.850639	0.640046	1.041043
C	6.559784	0.218815	-0.086841
C	5.920624	-0.547208	-1.065290
C	4.575910	-0.889664	-0.915325
C	2.403739	-0.822607	0.362286
H	-4.914540	-2.015438	1.330618
H	-4.229556	-2.203828	-1.273275
H	-5.779278	-1.464149	-0.813779
H	-4.806970	0.276410	-2.009966
H	-4.765102	1.764430	-0.301229
H	-3.901162	0.421617	1.994700
H	-5.544666	0.290110	1.346798
H	-2.290469	-1.282360	0.510023
H	-2.218911	0.363901	-1.628335
H	0.035836	1.418980	-1.913621
H	-0.210015	2.170119	-0.332097
H	3.955879	0.621944	2.067974
H	6.344772	1.231974	1.806443
H	7.607625	0.482726	-0.200795
H	6.469477	-0.880652	-1.941630
H	4.080711	-1.488796	-1.675742
H	2.155629	-1.766818	-0.128432
H	2.101570	-0.884345	1.410581

TS1 from *cis*-**6** (most abundant conformer; abundance: 37%)
# of imaginary frequencies: 1
Energy: -1147.857625 Hartrees
Gibbs Free Energy: -1147.524478 Hartrees

C	2.857754	-0.196291	-0.568724
C	4.086753	-0.528673	0.285905
C	3.614342	-0.266893	1.721470
C	2.770224	1.003986	1.543755
N	2.116474	0.878635	0.200998
C	1.924698	-1.411357	-0.779233
H	4.432952	-1.552857	0.134464
H	4.902380	0.155596	0.032704
H	3.415349	1.887804	1.548739
H	2.012799	1.106338	2.322163
H	4.448554	-0.072790	2.403992
H	3.142549	0.183073	-1.549245
H	0.646387	-0.193510	-1.773413
C	1.634066	2.151238	-0.613330
H	0.883718	0.777350	-0.010443
C	2.509876	2.536869	-1.803079
H	3.546370	2.734116	-1.507601
H	2.492556	1.776259	-2.587690
H	2.105574	3.456627	-2.238764
C	1.469004	3.328018	0.352771
H	0.904434	4.103769	-0.173986
H	0.890703	3.034186	1.233498
H	2.423069	3.759925	0.673462
O	2.145323	-2.505529	-0.242947
O	0.407962	1.579107	-0.954103
O	2.856661	-1.342772	2.263873
H	2.597832	-1.930637	1.525639
N	0.880792	-1.180809	-1.606145

C	-0.168946	-2.162388	-1.778131
C	-1.315579	-2.101770	-0.767391
O	-2.313804	-2.783741	-0.877377
O	-1.081582	-1.237513	0.230888
C	-3.211497	-0.117893	0.756455
C	-2.880132	1.109069	0.161730
C	-3.889382	1.993393	-0.222960
C	-5.233178	1.670576	-0.011072
C	-5.566227	0.451340	0.581749
C	-4.558527	-0.440372	0.957314
C	-2.133557	-1.069939	1.220796
H	-0.611143	-2.057085	-2.772677
H	0.268121	-3.162274	-1.715050
H	-1.837974	1.367265	-0.014581
H	-3.625809	2.940146	-0.687435
H	-6.014873	2.363969	-0.309578
H	-6.608044	0.188451	0.744097
H	-4.821603	-1.393889	1.409172
H	-1.599566	-0.677968	2.089825
H	-2.549834	-2.048514	1.467914

Hemiaminal from *cis*-**6** (most abundant conformer; abundance: 38%)
# of imaginary frequencies: 0
Energy: -1147.919087 Hartrees
Gibbs Free Energy: -1147.582728 Hartrees

C	3.156534	0.485028	0.906743
C	4.151230	1.657815	0.793333
C	4.280875	1.900161	-0.720936
C	4.194284	0.469298	-1.274044
N	3.218909	-0.211565	-0.402436
C	1.706369	0.958403	1.088436
H	5.117753	1.344337	1.201241
H	3.828520	2.554553	1.328710
H	5.191305	-0.002101	-1.237704
H	3.860660	0.475179	-2.316298
H	5.239705	2.359132	-0.982107
H	3.422154	-0.179568	1.735563
C	3.226906	-1.687043	-0.372426
C	4.464257	-2.294926	0.307724
H	4.396484	-3.387301	0.296864
H	5.380689	-2.004940	-0.215198
H	4.540901	-1.973529	1.351014
C	3.081213	-2.216587	-1.806618
H	3.960256	-1.995973	-2.420005
H	2.203821	-1.768236	-2.285677
H	2.949717	-3.302209	-1.775095
O	1.267327	1.983718	0.548228
O	2.115341	-2.121299	0.412186
O	3.271451	2.758348	-1.235451
H	2.451993	2.561525	-0.729243
H	1.298588	-1.761611	0.006762
N	0.923394	0.159534	1.858328
H	1.299554	-0.760352	2.061262
C	-0.514670	0.294011	1.836584
C	-1.140050	-0.366117	0.606343
O	-0.538158	-1.051520	-0.203279
O	-2.445068	-0.102486	0.543009
C	-4.616160	-0.270905	-0.465486
C	-5.041899	0.937471	-1.033222
C	-6.370994	1.345852	-0.914490
C	-7.288768	0.546867	-0.227116
C	-6.873262	-0.660411	0.340181
C	-5.542833	-1.065907	0.221207
C	-3.180287	-0.698699	-0.577149
H	-0.781868	1.352600	1.840095
H	-4.329594	1.557810	-1.571887
H	-6.691027	2.283139	-1.361068
H	-8.324751	0.862084	-0.137843
H	-7.584341	-1.286851	0.871488
H	-5.221225	-2.006984	0.660783
H	-3.066948	-1.783588	-0.514578
H	-2.716955	-0.351341	-1.503599
H	-0.945132	-0.161512	2.733347

TS2 from *cis*-**6** (most abundant conformer; abundance: 50%)
# of imaginary frequencies: 1
Energy: -1147.878413 Hartrees
Gibbs Free Energy: -1147.549060 Hartrees

C	3.106209	0.700237	1.099468
C	3.231510	2.181760	0.703107
C	3.173333	2.168529	-0.835186
C	3.936255	0.877141	-1.196857
N	3.854249	0.021532	0.011699
C	1.616089	0.297639	1.241228
O	0.952070	0.926604	2.090056
H	2.437807	2.783962	1.147005
H	4.199785	2.575028	1.032005
H	4.986350	1.082889	-1.426767
H	3.475805	0.385469	-2.058632
H	3.687045	3.035019	-1.259041
H	3.595481	0.504366	2.056589
H	1.952182	-1.564141	-0.220328
C	4.263823	-1.241247	0.038461
O	2.677776	-2.338724	-0.663634
H	2.663486	-2.188822	-1.624254
C	4.298141	-1.959923	1.362740
H	5.114269	-1.548935	1.970625
H	3.362956	-1.850498	1.913143
H	4.485032	-3.021472	1.201289
C	5.252485	-1.700685	-1.001835
H	5.308762	-2.789267	-1.005989
H	5.005230	-1.355369	-2.006929
H	6.241800	-1.301205	-0.741546
O	1.862872	2.223262	-1.374941
H	1.296237	1.506274	-1.025642
N	1.172317	-0.661164	0.424756
C	-0.234289	-0.962187	0.533468
C	-1.106884	0.058657	-0.191556
O	-0.700674	0.981175	-0.876011
O	-2.409826	-0.199095	0.004307
C	-4.744379	0.218553	-0.341038
C	-5.426306	0.724277	0.773307
C	-6.708947	0.270643	1.086061
C	-7.322779	-0.695774	0.285143
C	-6.650548	-1.205339	-0.829026
C	-5.368491	-0.749251	-1.139347

C	-3.354329	0.691755	-0.664633
H	-0.435410	-1.941340	0.080627
H	-0.583148	-1.005900	1.573566
H	-4.950936	1.478490	1.395880
H	-7.229287	0.672995	1.950850
H	-8.322435	-1.047285	0.525589
H	-7.125625	-1.953658	-1.457407
H	-4.847983	-1.144001	-2.008686
H	-3.151192	0.660894	-1.738265
H	-3.175266	1.709446	-0.308118

Iminium from *cis*-**6** (most abundant conformer; abundance: 21%)
# of imaginary frequencies: 0
Energy: -1071.456944 Hartrees
Gibbs Free Energy: -1071.151068 Hartrees

C	-3.262574	-0.335834	1.198491
C	-4.172573	-1.562770	1.010148
C	-4.510063	-1.597935	-0.496234
C	-4.661059	-0.100961	-0.824795
N	-3.719517	0.589876	0.100731
C	-1.732031	-0.616537	1.085903
O	-1.013602	-0.252415	2.050308
H	-3.684051	-2.484626	1.332256
H	-5.091304	-1.436672	1.593559
H	-5.671349	0.268199	-0.617187
H	-4.400961	0.113486	-1.861746
H	-5.460217	-2.109690	-0.678432
H	-3.438728	0.161897	2.152030
C	-3.350480	1.824382	-0.043475
C	-2.378296	2.479787	0.879218
H	-1.467445	2.687281	0.301814
H	-2.785764	3.443768	1.201760
H	-2.094357	1.871368	1.736290
C	-3.878702	2.630018	-1.193062
H	-3.603536	3.679248	-1.080931
H	-3.450121	2.261278	-2.133705
H	-4.967310	2.550795	-1.273958
O	-3.531968	-2.226562	-1.286480
H	-2.638394	-1.888185	-0.948776
N	-1.374491	-1.199769	-0.045002
C	0.050088	-1.397394	-0.175465
C	0.829321	-0.102360	-0.413103
O	0.366655	0.964526	-0.767630
O	2.151228	-0.305713	-0.218592
C	4.439069	0.403730	-0.237574
C	5.214959	-0.102802	-1.288316
C	6.527300	-0.522848	-1.063910
C	7.077666	-0.440563	0.217666
C	6.311823	0.064056	1.272112
C	5.000450	0.483976	1.043846
C	3.018016	0.835854	-0.476479
H	0.503920	-1.883922	0.699567
H	0.254969	-2.044089	-1.039877
H	4.789242	-0.165072	-2.287050
H	7.119884	-0.910241	-1.888171
H	8.100030	-0.764116	0.393214
H	6.736696	0.134177	2.269711
H	4.407139	0.879751	1.864781
H	2.722655	1.649926	0.191377
H	2.861074	1.165206	-1.507305

TS3 from *cis*-**6** (most abundant conformer; abundance: 59%)
# of imaginary frequencies: 1
Energy: -1071.436258 Hartrees
Gibbs Free Energy: -1071.131413 Hartrees

C	-3.399538	0.392192	-1.027267
C	-4.045576	1.759254	-0.789687
C	-3.843169	2.035058	0.714025
C	-3.976954	0.631866	1.347305
N	-3.639873	-0.320460	0.263896
C	-1.863689	0.432061	-1.256543
O	-1.213775	1.484495	-1.036229
H	-3.598927	2.541483	-1.406329
H	-5.114293	1.698467	-1.019138
H	-4.999771	0.437552	1.689467
H	-3.294309	0.527123	2.193784
H	-4.620331	2.694351	1.111814
H	-3.882684	-0.156913	-1.838741
C	-3.491613	-1.633309	0.411370
C	-3.171157	-2.451953	-0.712643
H	-2.096120	-1.801758	-1.192776
H	-3.074575	-3.511595	-0.488109
C	-3.528772	-2.188228	1.808024
H	-3.396330	-3.270327	1.791781
H	-2.742586	-1.743219	2.429325
H	-4.488805	-1.962756	2.287206
H	-3.766466	-2.270261	-1.612213
O	-2.599176	2.645736	1.004891
H	-1.958748	2.321355	0.325674
N	-1.345808	-0.737995	-1.645296
C	0.100347	-0.803769	-1.681317
C	0.744366	-0.730607	-0.296919
O	0.177149	-0.932365	0.758348
O	2.058488	-0.452740	-0.400232
C	4.234018	-0.075169	0.531163
C	4.635283	1.262517	0.414516
C	5.956218	1.581802	0.097061
C	6.892038	0.563680	-0.105578
C	6.501710	-0.772722	0.010340
C	5.179020	-1.088697	0.326554
C	2.804967	-0.416275	0.852413
H	0.401108	-1.760580	-2.126781
H	0.534699	-0.010858	-2.300494
H	3.909200	2.055826	0.575761
H	6.256055	2.622715	0.012324
H	7.921790	0.811187	-0.348603
H	7.226397	-1.567795	-0.142169
H	4.877334	-2.129357	0.418875
H	2.717629	-1.393600	1.334775
H	2.343018	0.330930	1.503231

Enamine from *cis*-**6** (most abundant conformer; abundance: 35%)
# of imaginary frequencies: 0
Energy: -1071.471141 Hartrees
Gibbs Free Energy: -1071.163645 Hartrees

C	-4.907526	-1.860902	0.012788
C	-5.484581	-0.454617	-0.192909
N	-4.310147	0.414533	-0.042166
C	-3.251330	-0.227111	0.731205
C	-3.848702	-1.609778	1.102105
C	-1.969836	-0.402823	-0.106666
N	-0.815274	-0.066389	0.497058
O	-1.998405	-0.876903	-1.252203
C	-4.331143	1.789108	-0.242430
C	-5.566396	2.329315	-0.925768
C	-3.322046	2.616857	0.111783
H	-5.931628	-0.360625	-1.186025
H	-6.260423	-0.237900	0.558938
H	-5.678145	-2.562040	0.344721
H	-3.102459	-2.407563	1.143083
H	-4.329509	-1.540188	2.083131
H	-3.019584	0.357687	1.632466
H	-5.697986	1.889104	-1.921818
H	-6.476588	2.110805	-0.354338
H	-5.488886	3.412620	-1.040619
H	-3.400546	3.677526	-0.096818
H	-2.405796	2.278580	0.580429
H	-0.803123	0.326772	1.431707
O	-4.358018	-2.402596	-1.179513
H	-3.577099	-1.850110	-1.409643
C	0.474537	-0.251873	-0.133964
H	0.638324	-1.302944	-0.399658
C	1.562823	0.200917	0.823802
O	1.347287	0.645501	1.935858
O	2.770474	0.044567	0.279432
C	3.910281	0.446338	1.108560
H	3.876614	-0.137718	2.031452
H	3.788530	1.502932	1.358815
C	5.164578	0.191140	0.321681
C	7.485238	-0.298915	-1.175708
C	5.702098	1.189635	-0.501010
C	5.801978	-1.054814	0.388083
C	6.956453	-1.300140	-0.356755
C	6.856842	0.947059	-1.246652
H	5.215625	2.160625	-0.554619
H	5.393196	-1.833261	1.027788
H	7.444505	-2.268836	-0.295255
H	7.267177	1.729690	-1.878685
H	8.386086	-0.487676	-1.753154
H	0.549351	0.324574	-1.063588

$TS4_{pro\ R}$ from *cis*-**6** (most abundant conformer; abundance: 100%)
# of imaginary frequencies: 1
Energy: -1621.544021 Hartrees
Gibbs Free Energy: -1621.136323 Hartrees

C	-1.528412	-4.082294	-1.060222
C	-2.068638	-3.393306	0.185843
N	-0.841634	-2.934199	0.884731
C	0.312325	-3.803814	0.539713
C	-0.272976	-4.785882	-0.512151
C	1.570042	-3.102571	-0.017817
N	1.424610	-1.904497	-0.617354
O	2.641985	-3.709090	0.053569
C	-0.825732	-1.948532	1.782197
C	0.420437	-1.710182	2.589138
C	-1.888175	-1.015082	1.831692
H	-2.725102	-2.563120	-0.057939
H	-2.602577	-4.098061	0.834514
H	-2.245534	-4.810279	-1.453930
H	0.445045	-5.018526	-1.300817
H	-0.559380	-5.722810	-0.023697
H	0.651893	-4.342724	1.427806
H	1.214394	-1.252092	1.986108
H	0.197787	-1.043252	3.423665
H	0.812401	-2.649632	2.992811
H	-1.869476	-0.325470	2.670258
H	-2.887406	-1.346269	1.574537
H	0.509894	-1.422065	-0.645293
O	-1.059170	-0.657819	-0.764341
C	-1.432228	0.079265	0.223410
C	-2.729686	0.840897	0.102636
C	-3.642622	0.511630	-0.910113
C	-4.833138	1.215090	-1.048435
C	-5.099539	2.263403	-0.164698
C	-4.203029	2.623209	0.844707
C	-3.019279	1.906398	0.969498
N	-6.346822	3.010345	-0.304628
O	-7.128108	2.681365	-1.202356
O	-6.565233	3.936723	0.482043
H	-0.656952	0.672736	0.736051
H	-3.397949	-0.293753	-1.594133
H	-5.546178	0.970674	-1.825866
H	-4.436385	3.447989	1.506129
H	-2.309368	2.178886	1.745939
O	-1.229399	-3.149104	-2.089478
H	-1.260497	-2.245126	-1.708827
C	2.564494	-1.252431	-1.212569
H	2.213771	-0.519823	-1.946219
H	3.189364	-1.978052	-1.741181
C	3.442524	-0.519518	-0.198593
O	3.177972	-0.355845	0.975846
O	4.552408	-0.070585	-0.804848
C	5.503144	0.694454	0.002994
H	6.468096	0.472033	-0.455048
H	5.481137	0.304242	1.021283
C	5.200852	2.170756	-0.038535
C	4.625164	4.915992	-0.142265
C	5.682464	2.959205	-1.092620
C	4.428288	2.772731	0.964235
C	4.142936	4.138380	0.913640
C	5.395916	4.324025	-1.146503
H	6.287996	2.501700	-1.871532
H	4.048785	2.165274	1.780695
H	3.546601	4.595254	1.698733
H	5.777353	4.925289	-1.967217
H	4.404781	5.979331	-0.180649

$TS4_{pro\ S}$ from *cis*-**6** (most abundant conformer; abundance: 100%)
# of imaginary frequencies: 1
Energy: -1621.538348 Hartrees
Gibbs Free Energy: -1621.128521 Hartrees

C	5.033389	-0.942121	0.583138
C	3.864097	-1.899277	0.833976
N	2.698703	-1.018421	1.144005
C	3.090635	0.403487	1.082018
C	4.610765	0.349060	1.301397
C	2.721866	1.103530	-0.245881
N	2.071203	0.391857	-1.182200
O	3.021221	2.295419	-0.373009
C	1.517707	-1.463858	1.532714
C	0.469506	-0.482869	1.973500
C	1.181128	-2.847296	1.342036
H	3.642820	-2.505833	-0.042570
H	4.053125	-2.539553	1.700371
H	5.108069	1.239168	0.910549
H	4.825085	0.272207	2.372523
H	2.593363	0.966859	1.873316
H	-0.453170	-1.005622	2.225071
H	0.804280	0.070029	2.859023
H	0.250577	0.249255	1.187700
H	0.357178	-3.185504	1.966374
H	2.021989	-3.535785	1.380213
H	1.860275	-0.623335	-1.079654
O	1.486432	-2.329233	-1.180323
C	0.676121	-2.968642	-0.385845
C	-0.805679	-2.579091	-0.412453
C	-1.216992	-1.461347	-1.148324
C	-2.555890	-1.089429	-1.204902
C	-3.495394	-1.862804	-0.522716
C	-3.124381	-3.004446	0.194939
C	-1.780527	-3.353909	0.239743
N	-4.899322	-1.469346	-0.559762
O	-5.200101	-0.420624	-1.141349
O	-5.727771	-2.198075	-0.005110
H	0.729868	-4.078544	-0.427704
H	-0.469993	-0.884922	-1.678324
H	-2.876731	-0.223130	-1.769366
H	-3.878795	-3.593312	0.701617
H	-1.484508	-4.243594	0.790133
O	5.139608	-0.763039	-0.828176
H	5.876934	-0.152649	-0.992167
C	1.728060	1.033226	-2.431091
H	1.360062	0.263480	-3.117399
C	0.658407	2.120951	-2.340710
O	0.543384	2.999411	-3.172413
O	-0.154703	1.965492	-1.284577
C	-1.202551	2.966890	-1.118586
H	-1.989223	2.765361	-1.850774
H	-0.770003	3.946062	-1.338242
C	-1.714617	2.878562	0.293185
C	-2.650293	2.729202	2.935032
C	-2.981681	2.350886	0.567731
C	-0.917896	3.329150	1.356449
C	-1.380441	3.252355	2.669855
C	-3.449507	2.279208	1.882675
H	-3.606207	1.991125	-0.246313
H	0.069176	3.736158	1.150090
H	-0.755518	3.606003	3.485325
H	-4.436117	1.870486	2.082667
H	-3.013653	2.674531	3.957577
H	2.602643	1.500622	-2.893757
H	5.964828	-1.351514	0.991800

TS3a from *cis*-**6** (most abundant conformer; abundance: 84%)
# of imaginary frequencies: 1
Energy: -1071.444335 Hartrees
Gibbs Free Energy: -1071.135149 Hartrees

C	-3.335354	1.734494	-0.049738
N	-3.901836	0.545261	-0.154027
C	-3.686106	-0.414367	0.956481
C	-4.100740	-1.765915	0.364228
C	-3.732213	-1.646630	-1.126700
C	-4.071275	-0.178575	-1.439455
C	-2.167106	-0.378059	1.324718
O	-1.781423	-1.194095	2.195128
H	-4.337753	-2.314913	-1.744181
H	-3.576291	-2.586729	0.856399
H	-5.180103	-1.920616	0.473037
H	-4.275449	-0.152209	1.837936
H	-5.112670	-0.066455	-1.759778
H	-3.421701	0.219235	-2.218987
C	-3.020334	2.533662	-1.282544
H	-3.934878	2.722979	-1.857157
H	-2.584148	3.495402	-1.008211
H	-2.317659	2.000726	-1.927610
C	-3.405476	2.511665	1.234165
H	-2.488218	3.086286	1.374229
H	-4.234285	3.228141	1.133339
H	-3.584630	1.898721	2.115562
O	-2.385186	-1.983351	-1.420132
H	-1.763650	-1.356229	-0.996736
N	-1.484914	0.521313	0.632915
C	-0.082797	0.622265	0.929328
C	0.760283	-0.203690	-0.037546
O	0.328181	-1.012443	-0.840037
O	2.070052	0.059255	0.114940
C	4.388248	-0.291766	-0.383716
C	5.067924	-0.907133	0.676148
C	6.364145	-0.513467	1.011246
C	6.995822	0.500995	0.286515
C	6.326821	1.118923	-0.772893
C	5.029483	0.723670	-1.104662
C	2.983975	-0.704288	-0.728989
H	0.264201	1.661590	0.864649
H	0.159949	0.259979	1.941865
H	4.579218	-1.699445	1.238182
H	6.882202	-1.000155	1.833016
H	8.006673	0.805368	0.543865
H	6.815213	1.905134	-1.342008
H	4.511016	1.203635	-1.931301
H	2.742853	-0.494246	-1.774305
H	2.812565	-1.767846	-0.542720

Bicyclic by-product from *cis*-**6** (most abundant conformer; abundance: 14%)
# of imaginary frequencies: 0
Energy: -1071.480691 Hartrees
Gibbs Free Energy: -1071.169596 Hartrees

C	-2.280388	1.580306	-0.019843
N	-3.564428	0.856066	-0.119256
C	-3.637690	-0.012438	1.088556
C	-4.439996	-1.266547	0.692177
C	-4.848782	-0.994695	-0.771983
C	-3.736051	-0.058838	-1.262509
C	-2.172079	-0.277123	1.452710
N	-1.428412	0.626727	0.758259
O	-1.740832	-1.127324	2.228231
H	-5.804930	-0.463015	-0.799212
H	-3.803101	-2.157712	0.743273
H	-5.300240	-1.439472	1.343128
H	-4.103210	0.523414	1.924638
H	-4.009469	0.487298	-2.169112
H	-2.835484	-0.661853	-1.476546
C	-1.669276	1.919208	-1.380338
H	-2.387359	2.500626	-1.966469
H	-0.775366	2.537190	-1.249474
H	-1.390315	1.024533	-1.939443
C	-2.489880	2.867119	0.798590
H	-1.531252	3.351048	1.015540
H	-3.109902	3.569850	0.233571
H	-2.987453	2.653747	1.749479
O	-5.045411	-2.150540	-1.569755
H	-4.219460	-2.662588	-1.557669
C	0.000023	0.701325	0.916148
C	0.761421	-0.157682	-0.096195
O	0.257511	-0.895147	-0.917840
O	2.081854	0.010068	0.070211
C	4.373532	-0.478485	-0.439742
C	5.013324	-1.211648	0.568584
C	6.331360	-0.924118	0.926102
C	7.023985	0.100866	0.275899
C	6.394565	0.835813	-0.731941
C	5.075775	0.546509	-1.086737
C	2.946988	-0.776305	-0.808138
H	0.351096	1.734791	0.842211
H	0.261945	0.339937	1.916923
H	4.476710	-2.012082	1.072373
H	6.818437	-1.501244	1.707216
H	8.051516	0.322888	0.550715
H	6.930551	1.630626	-1.243248
H	4.588059	1.117258	-1.873367
H	2.723840	-0.498971	-1.841528
H	2.699306	-1.831887	-0.670851

Aldol Reaction Cycle with *trans*-4-Hyp-Gly-OBn (*trans*-**6**) as a Catalyst

Table S4. Numbers of conformers of intermediates and transition structures from *trans*-**6**.

	# conformers	# conformers accounting for ≥ 95%
trans-**6**	84	27
TS1 from *trans*-**6**	5	5
Hemiaminal from *trans*-**6**	93	16
TS2 from *trans*-**6**	20	14
Iminium from *trans*-**6**	42	25
TS3 from *trans*-**6**	6	5
Enamine from *trans*-**6**	99	54
$TS4_{pro\ R}$ from *trans*-**6**	9	5
$TS4_{pro\ S}$ from *trans*-**6**	15	3
TS3a from *trans*-**6**	5	3
Bicyclic by-product from *trans*-**6**	23	12

trans-**6** (most abundant conformer; abundance: 24%)
# of imaginary frequencies: 0
Energy: -954.752156 Hartrees
Gibbs Free Energy: -954.501349 Hartrees

C	-5.570720	-0.396818	0.925524
C	-4.430442	-1.363141	0.567069
N	-3.862043	-0.842758	-0.691984
C	-3.926429	0.633585	-0.565991
C	-4.976951	0.964439	0.542323
C	-2.554327	1.245423	-0.243102
O	-6.712187	-0.614785	0.086348
N	-1.511089	0.408712	-0.413543
O	-2.436137	2.421496	0.116037
C	-0.145667	0.806330	-0.177139
C	0.773582	-0.384988	-0.377487
O	0.398190	-1.498309	-0.691998
O	2.048225	-0.041640	-0.161888
C	4.393928	-0.526771	-0.038959
C	4.897509	-0.502326	1.268356
C	6.149352	0.054085	1.535008
C	6.911081	0.591476	0.493937
C	6.417375	0.569940	-0.812977
C	5.164730	0.013293	-1.076620
C	3.037201	-1.108540	-0.321203
H	-5.855547	-0.449320	1.985079
H	-3.660725	-1.339340	1.349647
H	-4.757632	-2.400197	0.444132
H	-4.487725	-1.119421	-1.445947
H	-4.223635	1.064044	-1.528142
H	-4.495390	1.436176	1.403194
H	-5.760413	1.638684	0.188016
H	-7.068030	-1.492557	0.301265
H	-1.716973	-0.548432	-0.686835
H	0.165083	1.611318	-0.855936
H	-0.011364	1.193330	0.841067
H	4.307279	-0.923515	2.078669
H	6.531338	0.064673	2.552048
H	7.887475	1.021453	0.699830
H	7.008075	0.982579	-1.626113
H	4.782957	-0.005898	-2.094578
H	2.959397	-1.493076	-1.341120
H	2.781704	-1.912188	0.373993

TS1 from *trans*-**6** (most abundant conformer; abundance: 51%)
# of imaginary frequencies: 1
Energy: -1147.854678 Hartrees
Gibbs Free Energy: -1147.523902 Hartrees

C	-1.933973	-0.051656	1.111409
C	-1.443491	-1.256844	1.940322
C	-1.072301	-2.320845	0.898084
C	-2.108868	-2.072108	-0.204010
N	-2.176749	-0.591472	-0.285016
C	-0.960953	1.150503	1.185866
H	-0.618185	-0.975719	2.595068
H	-2.259951	-1.638651	2.564480
H	-3.081047	-2.484677	0.094561
H	-1.822971	-2.492571	-1.168907
H	-0.070328	-2.127932	0.501420
H	-2.884025	0.310066	1.514634
H	-1.454652	1.786687	-0.725513
C	-3.246257	0.114168	-1.223475
H	-1.563848	-0.019427	-1.214582
C	-4.212817	1.030417	-0.475163
H	-4.870935	0.474315	0.201792
H	-3.690913	1.808910	0.086448
H	-4.841845	1.529983	-1.219116
C	-4.008067	-0.920518	-2.054904
H	-4.629906	-0.374556	-2.771533
H	-3.321449	-1.550592	-2.625906
H	-4.665289	-1.553247	-1.448737
O	-0.289548	1.332085	2.205973
O	-2.277654	0.786395	-1.977852
O	-1.033630	-3.653380	1.372220
H	-1.886577	-3.848079	1.796077

N	-0.952056	2.015903	0.148047
C	-0.115859	3.194098	0.202790
C	1.392992	2.951039	0.183659
O	2.188745	3.778913	0.581921
O	1.726279	1.768820	-0.352808
C	3.293124	-0.052559	-0.431821
C	3.973042	-0.671164	-1.485842
C	4.139765	-2.059063	-1.506306
C	3.617797	-2.840443	-0.474837
C	2.930989	-2.229582	0.580274
C	2.773152	-0.843942	0.603470
C	3.145139	1.444979	-0.387622
H	-0.357152	3.824829	-0.658722
H	-0.319051	3.775697	1.106378
H	4.375982	-0.065828	-2.294197
H	4.671914	-2.526581	-2.330162
H	3.743510	-3.919549	-0.490124
H	2.522939	-2.833541	1.386271
H	2.235719	-0.369553	1.420727
H	3.611826	1.877479	0.501282
H	3.583853	1.919961	-1.269854

Hemiaminal from *trans*-**6** (most abundant conformer; abundance: 25%)
# of imaginary frequencies: 0
Energy: -1147.913697 Hartrees
Gibbs Free Energy: -1147.581225 Hartrees

C	-3.057181	-0.937309	0.417765
C	-3.879695	-2.063494	-0.258863
C	-4.990219	-1.292891	-0.983866
C	-4.215325	-0.080979	-1.511454
N	-3.236001	0.264255	-0.440310
C	-1.596725	-1.364892	0.589003
H	-3.266548	-2.604980	-0.989325
H	-4.268195	-2.781310	0.466743
H	-3.681070	-0.340071	-2.433823
H	-4.886465	0.749326	-1.730603
H	-5.439070	-1.880580	-1.791084
H	-3.457177	-0.769946	1.422267
C	-3.464033	1.519738	0.264683
C	-3.435275	2.710673	-0.704344
H	-4.211923	2.640672	-1.468980
H	-3.594873	3.641510	-0.149587
H	-2.461018	2.772199	-1.198809
C	-2.423856	1.743961	1.371910
H	-2.610117	2.711892	1.849140
H	-2.486615	0.977347	2.148211
H	-1.409313	1.750961	0.963831
O	-1.269367	-2.171100	1.462892
O	-4.788869	1.421296	0.875188
O	-6.050712	-0.917809	-0.110412
H	-5.765119	-0.110475	0.365687
H	-5.014413	2.264597	1.301128
N	-0.743754	-0.845433	-0.328574
H	-1.129698	-0.113690	-0.916779
C	0.671901	-1.101300	-0.316181
C	1.492129	0.153502	-0.035024
O	1.036897	1.256164	0.195577
O	2.801652	-0.130273	-0.092327
C	5.120230	0.471660	0.018951
C	5.794850	-0.052608	1.129344
C	7.093762	-0.547174	1.000946
C	7.731445	-0.521428	-0.242144
C	7.066717	0.000847	-1.354758
C	5.767837	0.494623	-1.223253
C	3.714017	0.985400	0.154276
H	0.872554	-1.842340	0.463324
H	5.300963	-0.070023	2.097938
H	7.608492	-0.948124	1.869704
H	8.743954	-0.902738	-0.342461
H	7.560306	0.027164	-2.322298
H	5.252854	0.903902	-2.089089
H	3.513648	1.372483	1.156667
H	3.492859	1.771792	-0.571768
H	1.013985	-1.527510	-1.267127

TS2 from *trans*-**6** (most abundant conformer; abundance: 22%)
# of imaginary frequencies: 1
Energy: -1147.871667 Hartrees
Gibbs Free Energy: -1147.544792 Hartrees

C	3.081120	2.106608	-0.516685
C	3.943298	0.908759	-0.939293
N	3.770035	-0.076501	0.149622
C	2.884229	0.460675	1.216727
C	3.023452	1.975613	1.011935
C	4.224083	-1.319297	0.081605
C	1.394165	0.034622	1.127940
O	0.612570	0.603511	1.920834
O	2.754644	-2.248653	-1.045104
H	3.263873	0.155085	2.194689
H	3.966241	2.339310	1.435998
H	2.190504	2.510670	1.470201
H	2.070475	1.998479	-0.932698
H	4.990925	1.221901	-1.005888
H	3.636540	0.480356	-1.896509
H	1.950339	-1.634429	-0.502988
H	2.653526	-3.160035	-0.723023
C	5.332546	-1.630956	-0.887657
H	6.270535	-1.222135	-0.488003
H	5.444843	-2.710132	-0.994733
H	5.158121	-1.198333	-1.872691
C	4.123439	-2.189330	1.308627
H	4.850922	-1.840719	2.053086
H	3.128638	-2.160228	1.754613
H	4.369366	-3.222418	1.057788
O	3.696785	3.292141	-0.998311
H	3.074948	4.023179	-0.855185
N	1.075125	-0.882049	0.216894
C	-0.331667	-1.199132	0.143493
C	-1.175016	-0.074045	-0.457337
O	-0.763675	0.858290	-1.118782
O	-2.482699	-0.275722	-0.190232
C	-4.802397	0.298553	-0.359646
C	-5.554558	-0.574102	-1.156988
C	-6.840964	-0.956278	-0.772662
C	-7.389231	-0.467553	0.416102
C	-6.647161	0.404221	1.217300

C	-5.361106	0.784301	0.829868
C	-3.408181	0.692457	-0.764122
H	-0.467339	-2.076773	-0.502705
H	-0.766435	-1.446073	1.120393
H	-5.130633	-0.952657	-2.084140
H	-7.415688	-1.630854	-1.401358
H	-8.391897	-0.761321	0.714589
H	-7.070687	0.790586	2.140325
H	-4.786011	1.465435	1.452644
H	-3.282788	0.688262	-1.850419
H	-3.141750	1.685463	-0.392088

Iminium from *trans*-**6** (most abundant conformer; abundance: 13%)
# of imaginary frequencies: 0
Energy: -1071.443229 Hartrees
Gibbs Free Energy: -1071.138514 Hartrees

C	-3.280147	-0.823762	0.491048
C	-4.080239	-1.869238	-0.318503
C	-5.226265	-1.084538	-0.968749
C	-4.576505	0.257925	-1.280688
N	-3.695634	0.481442	-0.108310
C	-1.750661	-1.094278	0.405551
O	-1.343984	-1.987029	1.198030
H	-3.444021	-2.297774	-1.100031
H	-4.441358	-2.686527	0.310495
H	-5.308684	1.057911	-1.379188
H	-3.954093	0.199937	-2.178988
H	-5.599406	-1.564188	-1.881791
H	-3.583139	-0.821954	1.540156
C	-3.308856	1.641418	0.317494
C	-2.468807	1.773624	1.543842
H	-1.414801	1.647814	1.255876
H	-2.603512	2.765476	1.981710
H	-2.697118	1.011054	2.292004
C	-3.686569	2.895481	-0.410563
H	-3.818320	2.746399	-1.482939
H	-4.625102	3.287212	0.005003
H	-2.918645	3.655427	-0.246995
O	-6.288313	-0.814203	-0.056348
H	-6.679491	-1.664831	0.200623
N	-1.129928	-0.408267	-0.531573
C	0.274418	-0.718594	-0.645582
C	1.179460	0.211103	0.158028
O	0.829482	1.066327	0.950692
O	2.480326	-0.039029	-0.118032
C	4.828903	0.319920	0.178416
C	5.488496	-0.698383	0.879156
C	6.753607	-1.131795	0.478679
C	7.373346	-0.549069	-0.629850
C	6.723867	0.467862	-1.334626
C	5.458953	0.898816	-0.931109
C	3.455918	0.769740	0.598168
H	0.526167	-1.739565	-0.312476
H	0.605987	-0.638922	-1.691321
H	5.008947	-1.150918	1.743955
H	7.256125	-1.919998	1.032642
H	8.359563	-0.883054	-0.940629
H	7.203278	0.927173	-2.194782
H	4.956291	1.692578	-1.478740
H	3.295912	0.637242	1.671771
H	3.280745	1.821373	0.353807

TS3 from *trans*-**6** (most abundant conformer; abundance: 42%)
# of imaginary frequencies: 1
Energy: -1071.426912 Hartrees
Gibbs Free Energy: -1071.124039 Hartrees

C	-3.274420	0.269066	-1.126201
C	-3.893491	1.652164	-0.946046
C	-3.752025	1.921358	0.560360
C	-4.008342	0.549677	1.198963
N	-3.619889	-0.421805	0.158016
C	-1.721299	0.303629	-1.289083
O	-1.113223	1.389430	-1.228365
H	-3.382036	2.398594	-1.555819
H	-4.957916	1.632316	-1.204705
H	-5.075863	0.448557	1.428402
H	-3.435540	0.393406	2.115658
H	-2.725223	2.242560	0.771837
H	-3.722369	-0.282357	-1.956945
C	-3.535822	-1.733293	0.338713
C	-3.123853	-2.581394	-0.736737
H	-2.000457	-1.980263	-1.080128
H	-3.089743	-3.639349	-0.486238
C	-3.729060	-2.266498	1.731533
H	-3.662505	-3.354663	1.734439
H	-2.971414	-1.865262	2.415787
H	-4.709671	-1.976369	2.126095
H	-3.624563	-2.400998	-1.692733
O	-4.690185	2.841680	1.097843
H	-4.419068	3.731023	0.820348
N	-1.175093	-0.907495	-1.477740
C	0.268458	-0.947809	-1.496074
C	0.911782	-0.680301	-0.134892
O	0.352717	-0.738202	0.942009
O	2.225475	-0.407583	-0.279983
C	4.407028	0.077628	0.582045
C	5.328437	-0.971721	0.469062
C	6.652006	-0.718263	0.104788
C	7.067902	0.590988	-0.150652
C	6.156383	1.644352	-0.039405
C	4.833838	1.387311	0.325411
C	2.975644	-0.199366	0.952105
H	0.594462	-1.948713	-1.809198
H	0.697648	-0.235028	-2.211120
H	5.007231	-1.990962	0.670368
H	7.357948	-1.540288	0.023900
H	8.098669	0.790076	-0.431019
H	6.475957	2.664719	-0.232648
H	4.126518	2.208448	0.414745
H	2.880617	-1.096353	1.570297
H	2.524915	0.638231	1.491372

Enamine from *trans*-**6** (most abundant conformer; abundance: 6%)
# of imaginary frequencies: 0
Energy: -1071.465517 Hartrees

Gibbs Free Energy: -1071.159728 Hartrees

C	-4.114937	-1.636670	-0.841791
C	-4.326717	-0.160837	-1.211072
N	-3.601656	0.553249	-0.153577
C	-3.504291	-0.261250	1.065457
C	-4.173973	-1.605260	0.693059
C	-2.061458	-0.475037	1.557575
N	-1.089630	-0.230617	0.654369
O	-1.840600	-0.892566	2.697460
C	-3.601331	1.950857	-0.063721
C	-3.902299	2.684060	-1.349692
C	-3.303161	2.624282	1.067144
H	-3.934992	0.080892	-2.202401
H	-5.406935	0.064281	-1.205745
H	-3.122177	-1.957523	-1.173919
H	-3.693782	-2.464227	1.167796
H	-5.224756	-1.590163	1.007918
H	-4.036951	0.209433	1.901126
H	-3.832500	3.762657	-1.193074
H	-3.195276	2.406239	-2.141234
H	-4.908896	2.459348	-1.722466
H	-3.275419	3.707826	1.054093
H	-3.057497	2.141968	2.006307
H	-1.337342	0.182691	-0.238020
O	-5.020445	-2.530887	-1.463266
H	-5.916497	-2.301332	-1.164557
C	0.311983	-0.375251	0.968341
H	0.568761	-1.418355	1.190622
H	0.585529	0.208488	1.856715
C	1.142542	0.099593	-0.210620
O	0.675607	0.557524	-1.236490
O	2.447108	-0.052557	0.034896
C	3.357343	0.379108	-1.027729
H	3.170481	1.438226	-1.221812
H	3.116802	-0.188316	-1.930066
C	4.763593	0.128866	-0.560562
C	7.375463	-0.351448	0.343402
C	5.398889	-1.087960	-0.840385
C	5.450468	1.103454	0.175372
C	6.749679	0.865652	0.626169
C	6.698512	-1.328291	-0.391286
H	4.874167	-1.847581	-1.414810
H	4.965781	2.052204	0.392714
H	7.274067	1.629779	1.193184
H	7.182862	-2.274193	-0.617230
H	8.388374	-0.536081	0.690560

TS4$_{pro\ R}$ from *trans*-**6** (most abundant conformer; abundance: 76%)
# of imaginary frequencies: 1
Energy: -1621.540562 Hartrees
Gibbs Free Energy: -1621.134199 Hartrees

C	0.766600	-4.606713	1.000644
C	1.542711	-3.592904	0.151160
N	0.530895	-3.051628	-0.791974
C	-0.752122	-3.781424	-0.682747
C	-0.365317	-5.065887	0.067719
C	-1.869106	-3.003206	0.050736
N	-1.531802	-1.862514	0.684566
O	-3.006892	-3.480604	0.039094
C	0.775253	-2.090649	-1.674194
C	-0.296046	-1.713309	-2.659178
C	1.941009	-1.280463	-1.555619
H	1.976124	-2.788222	0.738686
H	2.323858	-4.113389	-0.416043
H	0.343298	-4.102459	1.879758
H	-1.219794	-5.503075	0.588579
H	0.035771	-5.804093	-0.634915
H	-1.146659	-4.004751	-1.675545
H	0.069840	-0.931674	-3.326229
H	-0.591875	-2.574082	-3.269318
H	-1.192259	-1.340155	-2.147480
H	2.190249	-0.715203	-2.450011
H	2.810688	-1.727760	-1.082533
H	-0.573776	-1.450149	0.646997
O	0.927194	-0.614881	0.788140
C	1.379120	-0.027765	-0.271115
C	2.657293	0.784188	-0.128436
C	3.469069	0.602768	0.999741
C	4.633124	1.343900	1.165736
C	4.976103	2.281463	0.188410
C	4.180970	2.492961	-0.941142
C	3.022530	1.739497	-1.089229
N	6.194256	3.068223	0.355284
O	6.885793	2.871772	1.359607
O	6.481563	3.895411	-0.515889
H	0.655733	0.525131	-0.905082
H	3.159905	-0.118984	1.747742
H	5.268303	1.212641	2.033019
H	4.470982	3.234482	-1.674912
H	2.390197	1.898979	-1.959036
O	1.661195	-5.632291	1.397813
H	1.212807	-6.171682	2.068448
C	-2.562729	-1.062657	1.298242
H	-2.099022	-0.365048	2.002280
H	-3.261000	-1.689835	1.859579
C	-3.362701	-0.248268	0.280089
O	-3.112799	-0.165984	-0.905953
O	-4.381357	0.372167	0.895705
C	-5.243278	1.229473	0.081077
H	-6.217295	1.153177	0.566829
H	-5.298787	0.806236	-0.922641
C	-4.747837	2.653083	0.063008
C	-3.813307	5.299841	0.056884
C	-5.110902	3.538074	1.087404
C	-3.912137	3.108742	-0.966107
C	-3.448066	4.425353	-0.969882
C	-4.646057	4.854033	1.086718
H	-5.764345	3.194678	1.886004
H	-3.624301	2.425644	-1.759962
H	-2.803950	4.768944	-1.774735
H	-4.936982	5.531334	1.884982
H	-3.453788	6.325251	0.052755

TS4$_{pro\ S}$ from *trans*-**6** (most abundant conformer; abundance: 49%)
# of imaginary frequencies: 1
Energy: -1621.536567 Hartrees

Gibbs Free Energy: -1621.127698 Hartrees

C	-2.839922	2.194773	0.071593
C	-1.639711	2.133801	-0.881959
N	-0.454027	2.341830	-0.008150
C	-0.867484	2.595086	1.390467
C	-2.326748	3.052055	1.239744
C	-0.779140	1.361739	2.321522
N	-0.368712	0.195191	1.783533
O	-1.104626	1.518496	3.501176
C	0.787346	2.416241	-0.459954
C	1.893153	2.783266	0.487910
C	1.087670	1.963441	-1.783920
H	-1.552063	1.184981	-1.405471
H	-1.704363	2.960048	-1.599063
H	-3.081266	1.183789	0.425112
H	-2.886121	2.920709	2.167623
H	-2.360858	4.107018	0.947795
H	-0.243838	3.370786	1.837330
H	2.855079	2.746725	-0.023184
H	1.748616	3.797869	0.877591
H	1.929464	2.100510	1.344402
H	2.037393	2.324431	-2.170403
H	0.284843	2.072325	-2.508503
H	-0.130674	0.103771	0.775012
O	0.246560	-0.352201	-0.889573
C	1.196234	0.132896	-1.631428
C	2.641401	-0.147054	-1.219758
C	2.911331	-0.763944	0.008413
C	4.215086	-1.062831	0.391457
C	5.257647	-0.747602	-0.480820
C	5.021933	-0.152014	-1.723619
C	3.712455	0.139237	-2.083368
N	6.629778	-1.057244	-0.090757
O	6.821326	-1.586592	1.008510
O	7.539752	-0.774709	-0.876637
H	1.108281	-0.047114	-2.722938
H	2.078728	-1.022817	0.651639
H	4.430489	-1.537131	1.340933
H	5.851764	0.067159	-2.383763
H	3.518545	0.591362	-3.052891
O	-3.937041	2.750051	-0.635010
H	-4.734037	2.609964	-0.099602
C	-0.349607	-1.012413	2.578624
H	-0.631653	-0.747435	3.602664
C	-1.286782	-2.117398	2.103180
O	-1.153547	-3.275562	2.447319
O	-2.261903	-1.669562	1.299926
C	-3.161176	-2.672288	0.751163
H	-3.878648	-2.957968	1.525861
H	-2.565834	-3.555039	0.500155
C	-3.849361	-2.094048	-0.457322
C	-5.139937	-1.108028	-2.746135
C	-5.241689	-2.167167	-0.573968
C	-3.102528	-1.517624	-1.497022
C	-3.748396	-1.023581	-2.631090
C	-5.885653	-1.681802	-1.715590
H	-5.826478	-2.606922	0.230508
H	-2.021387	-1.435171	-1.408531
H	-3.164199	-0.575653	-3.430740
H	-6.967467	-1.746784	-1.793863
H	-5.638033	-0.725887	-3.633071
H	0.653548	-1.449785	2.618601

TS3a from *trans*-**6** (most abundant conformer; abundance: 47%)
# of imaginary frequencies: 1
Energy: -1071.437036 Hartrees
Gibbs Free Energy: -1071.130564 Hartrees

C	-3.034099	1.900648	-0.129081
N	-3.717099	0.772747	-0.126316
C	-3.617076	-0.102071	1.065928
C	-4.283338	-1.404620	0.625400
C	-3.920888	-1.494069	-0.864782
C	-3.981884	-0.034359	-1.337165
C	-2.094147	-0.275646	1.394716
O	-1.814546	-1.135939	2.267663
H	-2.893604	-1.866370	-0.974203
H	-3.914706	-2.244635	1.217291
H	-5.373057	-1.345136	0.724653
H	-4.116669	0.340031	1.930863
H	-4.989917	0.190485	-1.703563
H	-3.264225	0.182078	-2.128443
C	-2.645930	2.540575	-1.431738
H	-3.535625	2.742395	-2.039835
H	-2.131542	3.485793	-1.252270
H	-1.985563	1.884552	-2.005025
C	-2.994711	2.789577	1.080257
H	-2.014631	3.262948	1.161290
H	-3.736277	3.586795	0.921356
H	-3.225644	2.281490	2.014278
O	-4.816260	-2.256248	-1.659734
H	-4.664286	-3.192763	-1.456164
N	-1.311755	0.532432	0.705387
C	0.090117	0.484424	1.018036
C	0.892362	-0.349946	0.022687
O	0.443366	-1.166041	-0.757656
O	2.212224	-0.082266	0.140689
C	4.512926	-0.423891	-0.428661
C	5.083578	0.645149	-1.132097
C	6.385875	1.063587	-0.853970
C	7.132716	0.414456	0.132767
C	6.572766	-0.653602	0.838504
C	5.269876	-1.069040	0.558079
C	3.100894	-0.857871	-0.713351
H	0.529112	1.490481	1.032260
H	0.275282	0.035428	2.009287
H	4.504963	1.149185	-1.902685
H	6.818382	1.891818	-1.408604
H	8.147928	0.736767	0.347707
H	7.150777	-1.164489	1.603693
H	4.836618	-1.902178	1.106460
H	2.822273	-0.677564	-1.755303
H	2.949913	-1.919216	-0.497409

Bicyclic by-product from *trans*-**6** (most abundant conformer; abundance: 32%)
# of imaginary frequencies: 0
Energy: -1071.482906 Hartrees

Gibbs Free Energy: -1071.171538 Hartrees

C	-2.247196	1.294685	0.554474
N	-3.508337	0.674426	0.095526
C	-3.606483	-0.623967	0.818732
C	-4.393949	-1.578736	-0.104392
C	-4.739948	-0.699240	-1.326214
C	-3.582409	0.298800	-1.338837
C	-2.147854	-1.018580	1.075626
N	-1.401098	0.102133	0.872769
O	-1.723768	-2.120739	1.414591
H	-4.813174	-1.274659	-2.252068
H	-3.771358	-2.431926	-0.392276
H	-5.301335	-1.965771	0.364764
H	-4.098030	-0.493012	1.789742
H	-3.792686	1.171314	-1.961973
H	-2.664358	-0.189839	-1.702590
C	-1.601909	2.196438	-0.498980
H	-2.315959	2.968621	-0.800914
H	-0.727668	2.703470	-0.078438
H	-1.285026	1.637014	-1.380613
C	-2.515546	2.096843	1.840046
H	-1.576275	2.451005	2.278448
H	-3.138368	2.967174	1.611749
H	-3.032283	1.487375	2.587382
O	-5.992358	-0.030711	-1.174147
H	-5.858682	0.622668	-0.464752
C	0.022561	0.105488	1.082231
C	0.817468	-0.205308	-0.188359
O	0.342190	-0.528728	-1.257355
O	2.130456	-0.086946	0.058023
C	4.438957	-0.207544	-0.579985
C	5.134725	-1.277940	-0.002704
C	6.440240	-1.107110	0.460552
C	7.063464	0.138680	0.349932
C	6.377663	1.211409	-0.225787
C	5.072181	1.037533	-0.688121
C	3.025600	-0.387631	-1.058882
H	0.359447	1.063146	1.489635
H	0.268202	-0.666474	1.820212
H	4.652053	-2.248748	0.080725
H	6.971360	-1.945205	0.903208
H	8.081044	0.271784	0.706926
H	6.859875	2.180630	-0.318115
H	4.540777	1.872114	-1.139189
H	2.781134	0.290041	-1.880826
H	2.829798	-1.412558	-1.383990

Partial Aldol Reaction Cycle with *cis*-4-Hyp-NHMe (*cis*-**12**) as a Catalyst

Table S5. Numbers of conformers of intermediates and transition structures from *cis*-**12**.

	# conformers	# conformers accounting for ≥ 95%
cis-**12**	17	4
$TS1_{pro\ S}$, configuration A from *cis*-**12** and **10**	4	1
(*S*)-hemiaminal from *cis*-**12** and **10**	89	4
TS2 from (*S*)-hemiaminal from *cis*-**12** and **10**	3	2
Enamine from *cis*-**12**	9	2
$TS1_{pro\ R}$, configuration B from *cis*-**12** and **10**	6	1
(*R*)-hemiaminal from *cis*-**12** and **10**	92	20
TS2 from (*R*)-hemiaminal from *cis*-**12** and **10**	5	2
$TS1_{pro\ S}$, configuration C from *cis*-**12** and **10**	4	1
$TS1_{pro\ R}$, configuration D from *cis*-**12** and **10**	5	1

cis-**12** (most abundant conformer; abundance: 68%)
# of imaginary frequencies: 0
Energy: -495.823151 Hartrees
Gibbs Free Energy: -495.675102 Hartrees

C	0.091668	-0.956443	0.173831
C	0.956772	-0.316490	1.310128
C	2.101261	0.373770	0.548996
C	2.330455	-0.626819	-0.593845
N	0.982157	-1.075653	-1.010138
C	-1.101815	-0.056113	-0.154366
H	0.397309	0.381288	1.939681
H	1.354364	-1.107594	1.954316
H	2.912042	-1.485664	-0.231301
H	2.864845	-0.185517	-1.439896
H	2.990952	0.513055	1.171095
H	-0.263840	-1.947079	0.480598
O	-0.931451	1.030275	-0.737383
O	1.736618	1.666076	0.071364
H	0.846492	1.581462	-0.335203
N	-2.308709	-0.490221	0.248342
H	-2.371697	-1.407998	0.668201
C	-3.540934	0.263960	0.066236
H	-4.133252	-0.139690	-0.762683
H	-4.137746	0.223697	0.981238
H	-3.280808	1.299312	-0.154529
H	0.641429	-0.426165	-1.716672

$TS1_{pro\ S}$, configuration A from *cis*-**12** and **10** (most abundant conformer; abundance: 98%)
# of imaginary frequencies: 1
Energy: -882.118016 Hartrees
Gibbs Free Energy: -881.809314 Hartrees

N	0.189674	-0.733275	0.274840
C	0.435287	-2.133789	-0.218760
C	1.935510	-2.179420	-0.542836
C	2.527381	-1.323160	0.589182
C	1.514702	-0.179913	0.786163
C	1.879605	1.081484	-0.016132
N	1.553209	2.243458	0.569084
C	1.736705	3.528119	-0.093206
O	2.451748	1.001405	-1.115357
O	2.222435	-1.675166	-1.835223
H	2.350558	-0.702624	-1.752438
H	2.296580	-3.211757	-0.507693
H	3.526324	-0.955207	0.346171
H	2.592998	-1.913757	1.507872
H	1.387330	0.081855	1.834558
H	-0.188154	-0.103113	-0.512029
H	-0.184546	-2.330914	-1.093241
H	0.184787	-2.840489	0.575703
H	0.903683	2.187233	1.347254
H	2.700105	3.533859	-0.605672
H	1.721590	4.318203	0.659506
H	0.945115	3.714747	-0.828460
C	-2.769115	-0.577419	-2.045173
C	-2.520003	0.189125	-0.737263
C	-2.298480	-0.823189	0.460889
C	-1.040700	-0.452339	1.276630
C	-0.883939	-1.246499	2.563489
C	-3.734916	1.086776	-0.431474
O	-0.984415	0.905182	1.500102
O	-1.364900	1.004267	-0.878436
H	-1.169002	1.238709	0.438723
H	-1.907912	-1.205861	-2.302893

H	-2.924169	0.130140	-2.867874
H	-3.651930	-1.225357	-1.974713
H	-3.867349	1.819749	-1.235808
H	-3.576119	1.631108	0.506423
H	-4.660609	0.504742	-0.335923
H	-2.235664	-1.860259	0.111698
H	-3.141787	-0.785538	1.159095
H	-0.939103	-2.326183	2.398510
H	0.051999	-1.009899	3.078440
H	-1.706085	-0.964835	3.227591

(*S*)-hemiaminal from *cis*-**12** and **10** (most abundant conformer; abundance: 74%)
# of imaginary frequencies: 0
Energy: -882.145144 Hartrees
Gibbs Free Energy: -881.832833 Hartrees

C	1.477493	-0.528226	0.666602
C	2.231935	-1.755829	0.072675
C	1.168143	-2.451259	-0.792229
C	-0.079552	-2.247188	0.071938
N	0.056034	-0.838629	0.458654
C	1.851335	0.738885	-0.115654
H	2.546092	-2.417890	0.885700
H	3.120480	-1.482466	-0.503516
H	-1.000221	-2.421424	-0.490839
H	-0.063974	-2.945915	0.926853
H	1.388247	-3.508556	-0.963528
H	1.735959	-0.392166	1.724573
C	-0.916703	-0.239726	1.397359
C	-2.312825	-0.151684	0.731276
H	-2.715032	-1.159365	0.577357
H	-2.960424	0.322513	1.478006
O	-0.465779	1.069950	1.726949
O	1.395857	0.941886	-1.260617
O	1.038758	-1.850450	-2.078478
H	1.007723	-0.880485	-1.932953
N	2.740320	1.559396	0.464005
H	3.015360	1.364018	1.417754
C	3.251756	2.772860	-0.157779
H	2.723396	3.660282	0.209204
H	3.109117	2.696129	-1.235836
H	4.316734	2.876912	0.064320
C	-1.003591	-0.997955	2.730939
H	-0.019051	-1.034659	3.210079
H	-1.692560	-0.484929	3.408817
H	-1.358827	-2.022986	2.589163
C	-2.419354	0.651488	-0.611236
C	-2.390925	-0.255025	-1.849519
H	-3.201385	-0.991791	-1.813004
H	-2.520531	0.350541	-2.753670
H	-1.442039	-0.792532	-1.932542
C	-3.712484	1.472766	-0.597518
H	-3.695373	2.198245	0.223559
H	-3.831672	2.018239	-1.539832
H	-4.582132	0.820948	-0.459537
O	-1.353831	1.631056	-0.732290
H	-0.707107	1.620875	0.948699
H	-0.538665	1.166920	-1.023077

TS2 from (*S*)-hemiaminal from *cis*-**12** and **10** (most abundant conformer; abundance: 66%)
# of imaginary frequencies: 1
Energy: -882.096822 Hartrees
Gibbs Free Energy: -881.789730 Hartrees

N	0.898766	-0.942765	-0.169175
C	2.114027	-1.791509	-0.151646
C	3.224919	-0.809847	0.241925
C	2.508731	0.056448	1.288833
C	1.083033	0.246764	0.721118
C	0.949053	1.599306	0.010132
N	-0.098248	2.326837	0.424694
C	-0.345147	3.666355	-0.089981
O	1.797745	1.989189	-0.811001
O	3.702825	-0.064439	-0.863435
H	3.082404	0.688513	-1.005446
H	4.077817	-1.347603	0.665179
H	3.021858	1.005674	1.455672
H	2.453331	-0.477845	2.242028
H	0.325571	0.179116	1.497195
H	-0.368469	-1.945656	2.056608
H	2.282649	-2.231188	-1.135840
H	2.011436	-2.590907	0.593127
H	-0.859095	1.802874	0.893340
H	0.573788	4.255693	-0.038626
H	-1.112027	4.141698	0.524060
H	-0.683045	3.648401	-1.133382
C	-3.256478	1.213264	-0.686386
C	-2.556592	-0.009140	-0.060758
C	-1.362449	-0.402771	-1.018114
C	-0.289094	-1.378876	-0.569651
C	-0.383835	-2.772958	-1.118545
C	-3.594137	-1.155703	0.013586
O	-1.143840	-1.910022	1.473080
O	-2.056671	0.314790	1.207085
H	-1.568705	-0.833321	1.518103
H	-2.574954	2.064996	-0.774961
H	-4.092767	1.514729	-0.045719
H	-3.653015	0.991104	-1.684757
H	-4.410514	-0.848404	0.678111
H	-3.153141	-2.068446	0.419603
H	-4.022515	-1.377340	-0.971884
H	-0.859841	0.521956	-1.308409
H	-1.777065	-0.830790	-1.938579
H	0.173782	-3.495712	-0.521931
H	0.007901	-2.786867	-2.144882
H	-1.431673	-3.073318	-1.156146

Enamine from *cis*-**12** (most abundant conformer; abundance: 59%)
# of imaginary frequencies: 0
Energy: -612.540204 Hartrees
Gibbs Free Energy: -612.338545 Hartrees

C	0.129331	-0.083982	0.836891
C	-0.184587	-1.524700	1.314160
C	-1.179806	-2.066110	0.270237
C	-2.011231	-0.817855	-0.059116
N	-1.080713	0.298635	0.104110

C	1.378604	-0.073099	-0.069086
H	-0.666379	-1.472392	2.295982
H	0.704230	-2.155220	1.401647
H	-2.396738	-0.865886	-1.084231
H	-2.873728	-0.712133	0.619496
H	-1.807340	-2.859656	0.685309
H	0.299538	0.572606	1.697244
C	-1.498628	1.606349	-0.108805
C	-2.733847	1.914333	-0.566369
H	-2.997001	2.950422	-0.745853
O	1.393278	-0.651585	-1.167765
O	-0.544664	-2.620802	-0.872366
H	0.112385	-1.953778	-1.177146
N	2.460029	0.559701	0.421823
H	2.379368	1.059658	1.296611
C	3.730725	0.614526	-0.289181
H	3.926394	-0.352366	-0.757535
H	4.525100	0.840782	0.423980
H	3.720686	1.384551	-1.069144
C	-0.493674	2.697473	0.181326
H	-0.230936	2.738595	1.245844
H	0.438648	2.555471	-0.377711
H	-0.908707	3.669207	-0.094671
H	-3.490971	1.169269	-0.780647

$TS1_{pro\ R}$, configuration B from *cis*-**12** and **10** (most abundant conformer; abundance: 100%)
# of imaginary frequencies: 1
Energy: -882.113168 Hartrees
Gibbs Free Energy: -881.803729 Hartrees

N	-0.063201	0.555225	-0.024224
C	0.271770	1.795579	0.758092
C	1.425728	2.505851	-0.005521
C	1.533405	1.712052	-1.326776
C	1.080808	0.286233	-0.987298
C	2.215150	-0.588621	-0.417439
N	2.065536	-1.906213	-0.633280
C	3.025613	-2.881982	-0.136268
O	3.211979	-0.098447	0.138428
O	2.629252	2.531705	0.737774
H	3.010294	1.627301	0.667418
H	1.164626	3.549873	-0.195416
H	2.545013	1.748339	-1.735666
H	0.847531	2.127826	-2.072161
H	0.646526	-0.223559	-1.846258
H	-0.897454	0.706878	-0.693482
H	0.607734	1.525160	1.759607
H	-0.627898	2.408066	0.836570
H	1.112302	-2.210935	-0.831104
H	2.927706	-3.035086	0.945966
H	4.038527	-2.533759	-0.346709
H	2.855477	-3.831382	-0.646835
C	-3.753343	1.358918	-0.116558
C	-3.042201	-0.000878	-0.183071
C	-2.145891	-0.213723	1.101135
C	-0.726173	-0.699238	0.721721
C	0.079330	-1.125083	1.942786
C	-4.089681	-1.126498	-0.277784
O	-0.796333	-1.674404	-0.254175
O	-2.208700	-0.041713	-1.334653
H	-1.474871	-1.118249	-0.967999
H	-4.399882	1.436389	0.766633
H	-3.025499	2.178957	-0.075998
H	-4.370751	1.502223	-1.010948
H	-4.774354	-1.120511	0.579972
H	-3.593343	-2.102904	-0.311077
H	-4.680106	-1.008989	-1.193900
H	-2.082009	0.697756	1.707527
H	-2.573057	-0.985355	1.750894
H	-0.024655	-0.407744	2.761762
H	1.141275	-1.263599	1.734574
H	-0.326148	-2.082564	2.282067

(*R*)-hemiaminal from *cis*-**12** and **10** (most abundant conformer; abundance: 19%)
# of imaginary frequencies: 0
Energy: -882.138566 Hartrees
Gibbs Free Energy: -881.827984 Hartrees

C	-1.125768	-0.139998	-0.755009
C	-1.608788	-1.465092	-1.365583
C	-1.945473	-2.328917	-0.139586
C	-0.841064	-1.917432	0.853037
N	-0.556358	-0.493453	0.569204
C	-2.279769	0.860334	-0.521075
H	-0.786657	-1.923927	-1.925358
H	-2.460958	-1.347025	-2.039008
H	-1.180707	-2.062308	1.884140
H	0.041913	-2.556440	0.696076
H	-1.879819	-3.400496	-0.357218
H	-0.374653	0.345953	-1.387119
C	0.809776	0.000432	0.850038
C	1.882203	-0.725091	-0.034986
H	2.175010	-1.653024	0.466399
H	1.406698	-1.019475	-0.977972
O	0.806785	1.410735	0.585763
O	-3.477444	0.524552	-0.582727
O	-3.258446	-2.094489	0.358290
H	-3.505285	-1.181792	0.091105
N	-1.889719	2.113365	-0.227582
H	-0.907195	2.213506	0.026644
C	-2.834555	3.143030	0.177073
H	-2.345231	4.117231	0.113593
H	-3.192785	2.991584	1.203680
H	-3.697359	3.131674	-0.492389
C	1.072264	-0.186565	2.350135
H	0.316067	0.365635	2.916164
H	1.024125	-1.240605	2.639670
H	2.059259	0.194535	2.620144
C	3.172226	0.025563	-0.437415
C	3.984521	0.587210	0.735550
H	3.413688	1.336771	1.289177
H	4.280217	-0.210152	1.425313
H	4.901685	1.060724	0.363821
C	4.046087	-0.891071	-1.303134
H	4.914262	-0.340483	-1.684205
H	4.415420	-1.743408	-0.722424
H	3.477893	-1.271545	-2.158087
O	2.699621	1.129392	-1.269303

H	1.431123	1.577852	-0.157082
H	3.441729	1.739882	-1.416869

TS2 from (*R*)-hemiaminal from *cis*-**12** and **10** (most abundant conformer; abundance: 71%)
# of imaginary frequencies: 1
Energy: -882.087485 Hartrees
Gibbs Free Energy: -881.788188 Hartrees

N	-0.250183	0.276877	-0.165944
C	0.208902	1.646982	-0.491567
C	-0.702215	2.542479	0.350378
C	-2.029463	1.768610	0.369191
C	-1.599463	0.290313	0.451549
C	-2.587755	-0.609668	-0.312279
N	-3.590025	-1.108209	0.441629
C	-4.659815	-1.915192	-0.130135
O	-2.486188	-0.793956	-1.524612
O	-0.773346	3.817121	-0.262870
H	-1.199869	4.424711	0.361998
H	-0.298888	2.621788	1.369550
H	-2.548080	1.958389	-0.576964
H	-2.689088	2.045931	1.194622
H	-1.497565	-0.029230	1.494758
H	0.753880	0.124382	2.428409
H	0.038820	1.856400	-1.554956
H	1.265977	1.738708	-0.239816
H	-3.583671	-0.957489	1.441127
H	-4.996316	-1.468789	-1.068788
H	-5.491949	-1.945544	0.574757
H	-4.324685	-2.939136	-0.332013
C	4.186377	0.050482	-1.284680
C	3.173123	-0.408807	-0.219670
C	1.810993	-0.705147	-0.998708
C	0.535027	-0.777760	-0.205216
C	0.012944	-2.133710	0.158350
C	3.690677	-1.710562	0.438281
O	1.372580	-0.540538	2.085505
O	2.999314	0.599353	0.716570
H	2.213154	0.098238	1.493590
H	3.861933	0.995533	-1.735326
H	4.316620	-0.690019	-2.084023
H	5.160004	0.218648	-0.810086
H	3.854943	-2.510942	-0.294397
H	2.990161	-2.064377	1.199476
H	4.646201	-1.499376	0.933713
H	1.697153	0.072778	-1.758488
H	1.908933	-1.660001	-1.527192
H	-0.674445	-2.117261	1.003508
H	-0.506514	-2.549952	-0.714963
H	0.849868	-2.788024	0.401992

$TS1_{pro\ S}$, configuration C from *cis*-**12** and **10** (most abundant conformer; abundance: 98%)
# of imaginary frequencies: 1
Energy: -882.109260 Hartrees
Gibbs Free Energy: -881.801257 Hartrees

N	0.017260	-0.711380	0.040726
C	-0.686283	-1.953659	0.518798
C	-1.783693	-2.270248	-0.532536
C	-1.579499	-1.197526	-1.632057
C	-0.908534	-0.005863	-0.920448
C	-1.942641	0.883987	-0.220159
N	-1.925705	2.183443	-0.560885
C	-2.895202	3.135128	-0.028590
O	-2.769138	0.422122	0.582060
O	-3.082475	-2.269513	0.031571
H	-3.213935	-1.358076	0.371071
H	-1.642786	-3.271041	-0.947287
H	-2.523923	-0.933058	-2.113659
H	-0.897504	-1.569123	-2.403921
H	-0.295614	0.583280	-1.602959
H	0.871319	-1.030232	-0.520282
H	-1.144814	-1.767819	1.489863
H	0.056563	-2.742146	0.626723
H	-1.229920	2.521149	-1.211604
H	-2.693940	3.353212	1.025411
H	-3.904212	2.724030	-0.112975
H	-2.827978	4.057892	-0.605286
C	2.882601	0.809516	-1.933426
C	2.871578	0.268010	-0.496542
C	1.798848	1.035582	0.377581
C	0.925964	0.047490	1.184311
C	0.050394	0.711049	2.235201
C	4.267520	0.450989	0.130590
O	1.674386	-0.962831	1.705795
O	2.552008	-1.118027	-0.518607
H	2.255290	-1.241069	0.745457
H	1.910705	0.657392	-2.419085
H	3.636982	0.279793	-2.526715
H	3.111231	1.882281	-1.961070
H	5.010610	-0.116786	-0.441421
H	4.268433	0.078664	1.161149
H	4.573475	1.504929	0.147446
H	1.176093	1.701862	-0.230976
H	2.293984	1.677499	1.114806
H	-0.488299	1.578632	1.847411
H	-0.663632	0.009473	2.673378
H	0.716418	1.054070	3.032747

$TS1_{pro\ R}$, configuration D from *cis*-**12** and **10** (most abundant conformer; abundance: 100%)
# of imaginary frequencies: 1
Energy: -882.114023 Hartrees
Gibbs Free Energy: -881.805675 Hartrees

N	0.145849	-0.918641	0.035523
C	0.694634	-2.179590	-0.590085
C	2.213684	-1.982567	-0.628307
C	2.470104	-1.208712	0.677120
C	1.264856	-0.242288	0.799561
C	1.584383	1.116468	0.167139
N	1.777709	2.132581	1.020837
C	2.173170	3.467166	0.584246
O	1.698653	1.229834	-1.064064
O	2.658957	-1.304087	-1.790189
H	2.314446	-0.385154	-1.748176
H	2.722297	-2.950208	-0.625888
H	3.429133	-0.685148	0.666885

H	2.467072	-1.896486	1.528260
H	0.958381	-0.121522	1.837746
H	-0.244690	-0.313228	-0.753431
H	0.261635	-2.308817	-1.580688
H	0.416738	-3.030354	0.033900
H	1.620457	1.982932	2.008591
H	2.743613	3.945666	1.382042
H	1.297353	4.082016	0.349704
H	2.793019	3.380188	-0.309251
C	-1.924194	2.320918	-0.603223
C	-2.339332	0.849189	-0.448695
C	-1.854951	0.283239	0.947316
C	-1.281599	-1.144535	0.788682
C	-1.076447	-1.888419	2.099561
C	-3.877186	0.747099	-0.534155
O	-2.009303	-1.882923	-0.101109
O	-1.758201	0.078165	-1.485354
H	-2.040415	-1.135312	-0.934719
H	-2.316360	2.944633	0.210509
H	-0.832987	2.416783	-0.616340
H	-2.304522	2.715866	-1.552902
H	-4.373158	1.365625	0.225342
H	-4.196811	-0.290945	-0.391110
H	-4.213865	1.077462	-1.523976
H	-1.117842	0.946319	1.417067
H	-2.691512	0.215744	1.651962
H	-0.516587	-1.306866	2.837783
H	-0.577443	-2.849735	1.945346
H	-2.066444	-2.092769	2.517591
H	2.699306	-1.831887	-0.670851

Partial Aldol Reaction Cycle with *trans*-4-Hyp-NHMe (*trans*-**12**) as a Catalyst

Table S6. Numbers of conformers of intermediates and transition structures from *trans*-**12**.

	# conformers	# conformers accounting for ≥ 95%
trans-**12**	20	4
$TS1_{pro\ S}$, configuration A from *trans*-**12** and **10**	6	6
(*S*)-hemiaminal from *trans*-**12** and **10**	97	10
TS2 from (*S*)-hemiaminal from *trans*-**12** and **10**	3	3
Enamine from *trans*-**12**	6	6
$TS1_{pro\ R}$, configuration B from *trans*-**12** and **10**	6	3
(*R*)-hemiaminal from *trans*-**12** and **10**	94	6
TS2 from (*R*)-hemiaminal from *trans*-**12** and **10**	4	2
$TS1_{pro\ S}$, configuration C from *trans*-**12** and **10**	5	3
$TS1_{pro\ R}$, configuration D from *trans*-**12** and **10**	5	2

trans-**12** (most abundant conformer; abundance: 43%)
# of imaginary frequencies: 0
Energy: -495.821304 Hartrees
Gibbs Free Energy: -495.674184 Hartrees

C	-2.187791	0.076101	0.644519
C	-1.422366	-1.244580	0.532460
N	-0.523976	-1.079419	-0.628447
C	-0.111731	0.346759	-0.621879
C	-1.093978	1.108531	0.324031
C	1.349980	0.538712	-0.184661
O	-3.207708	0.041460	-0.360495
N	2.061241	-0.604142	-0.097142
O	1.799339	1.669056	0.038035
H	-2.630096	0.229643	1.638527
H	-0.824903	-1.404519	1.438400
H	-2.079739	-2.106836	0.393843
H	-1.073584	-1.245198	-1.468394
H	-0.170551	0.743192	-1.640992
H	-0.583625	1.422353	1.240189
H	-1.508010	2.008265	-0.141067
H	-3.606927	0.925020	-0.402812
H	1.536386	-1.447915	-0.309179
C	3.461673	-0.662083	0.272518
H	3.606497	-1.280814	1.165295
H	3.797849	0.354323	0.483808
H	4.068074	-1.077362	-0.540752

$TS1_{pro\ S}$, configuration A from *trans*-**12** and **10** (most abundant conformer; abundance: 30%)
# of imaginary frequencies: 1
Energy: -882.110653 Hartrees
Gibbs Free Energy: -881.803691 Hartrees

N	-0.274683	-0.516290	0.008070
C	-0.861397	-1.413193	1.064919
C	-2.393295	-1.241623	0.962696
C	-2.600237	-0.840551	-0.498312
C	-1.420088	0.087320	-0.783579
C	-1.746955	1.557034	-0.406580
N	-0.740593	2.355839	0.002188
C	-1.000510	3.755449	0.314273
O	-2.905890	1.960922	-0.541445
O	-3.101731	-2.433351	1.253272
H	-3.119019	-2.548016	2.216800
H	-2.722034	-0.426241	1.620817
H	-3.548499	-0.333518	-0.674565
H	-2.550954	-1.737228	-1.125066
H	-1.108847	0.096097	-1.831004
H	0.294885	0.246599	0.427527
H	-0.449380	-1.148738	2.040043
H	-0.609718	-2.450393	0.840726
H	0.225729	2.023848	0.081213
H	-0.076015	4.202951	0.682774
H	-1.774900	3.845496	1.082649
H	-1.335447	4.303683	-0.573156
C	2.787129	0.159671	2.044817
C	2.695400	0.111516	0.512856
C	2.114434	-1.286612	0.040443
C	0.944247	-1.113461	-0.951417
C	0.480680	-2.393552	-1.626736
C	4.094545	0.315386	-0.097063
O	1.184303	-0.127824	-1.853305
O	1.842890	1.156210	0.057877
H	1.562468	0.668620	-1.135660

H	1.797839	0.035608	2.502632
H	3.186158	1.128834	2.365313
H	3.440503	-0.630397	2.435057
H	4.487716	1.296357	0.193314
H	4.037010	0.278631	-1.190954
H	4.801490	-0.455652	0.234566
H	1.807530	-1.904999	0.892114
H	2.883806	-1.858821	-0.489584
H	0.277746	-3.204599	-0.922684
H	-0.406517	-2.215384	-2.242003
H	1.285095	-2.721549	-2.291784

(*S*)-hemiaminal from *trans*-**12** and **10** (most abundant conformer; abundance: 64%)
# of imaginary frequencies: 0
Energy: -882.139947 Hartrees
Gibbs Free Energy: -881.829120 Hartrees

C	1.220013	-0.046075	-0.622325
C	2.033632	1.136423	-1.239662
C	1.981979	2.256583	-0.183336
C	1.598801	1.500026	1.089919
N	0.675729	0.422008	0.675636
C	2.098642	-1.304924	-0.482361
H	1.603323	1.471218	-2.188269
H	3.063378	0.830007	-1.439768
H	2.502888	1.036541	1.504991
H	1.176230	2.145470	1.858452
H	2.933785	2.789542	-0.082432
H	0.397866	-0.325004	-1.285859
C	-0.782773	0.678885	0.674992
C	-1.504597	-0.701515	0.564341
H	-0.802007	-1.436757	0.162946
H	-1.735649	-1.034607	1.583224
O	-1.189854	1.484623	-0.452464
O	2.786336	-1.699144	-1.430188
O	0.935629	3.218327	-0.439210
H	1.111112	3.637055	-1.298212
N	2.017449	-1.924160	0.714404
H	1.434578	-1.458390	1.402620
C	2.742731	-3.134948	1.049715
H	3.275586	-3.466886	0.157379
H	2.054840	-3.923747	1.372685
H	3.466863	-2.952546	1.852041
C	-1.204650	1.398692	1.965119
H	-2.294469	1.389777	2.038822
H	-0.794815	0.899745	2.849227
H	-0.884394	2.444630	1.966940
C	-2.780902	-0.809940	-0.309990
C	-3.254676	-2.268257	-0.304100
H	-3.557641	-2.582083	0.700590
H	-4.113608	-2.383231	-0.974637
H	-2.458015	-2.935208	-0.651722
C	-3.926441	0.108267	0.150673
H	-3.639610	1.160413	0.075689
H	-4.215508	-0.101235	1.187621
H	-4.803588	-0.053840	-0.485978
O	-2.446260	-0.519694	-1.680129
H	-0.575325	2.254386	-0.499336
H	-2.015420	0.357616	-1.639268

TS2 from (*S*)-hemiaminal from *trans*-**12** and **10** (most abundant conformer; abundance: 47%)
# of imaginary frequencies: 1
Energy: -882.090137 Hartrees
Gibbs Free Energy: -881.785931 Hartrees

N	0.527217	0.688742	0.647907
C	1.263773	1.940702	0.940732
C	1.638647	2.467758	-0.440025
C	1.958387	1.188661	-1.225399
C	1.043450	0.087507	-0.621073
C	1.840595	-1.213900	-0.468344
N	2.225758	-1.568908	0.778702
C	3.030717	-2.748141	1.059929
O	2.126542	-1.844475	-1.488340
O	0.488427	3.155670	-0.939902
H	0.631052	3.356230	-1.879176
H	2.495427	3.149309	-0.392092
H	3.014066	0.935338	-1.086088
H	1.788397	1.308293	-2.298331
H	0.173137	-0.118865	-1.255092
H	-1.227194	2.369509	-0.397703
H	2.160413	1.711783	1.525774
H	0.651320	2.647628	1.495516
H	1.935850	-0.991656	1.556275
H	3.206594	-3.266623	0.117308
H	2.507055	-3.417416	1.749859
H	3.992270	-2.465348	1.501247
C	-2.251093	-2.521351	-0.916933
C	-2.297817	-1.052260	-0.443023
C	-1.264485	-0.963553	0.790050
C	-0.661154	0.369620	1.153870
C	-1.137424	1.007459	2.427915
C	-3.724416	-0.745254	0.082775
O	-1.958646	1.804803	-0.082301
O	-1.940971	-0.208487	-1.468836
H	-1.993072	0.987281	-0.813682
H	-1.262524	-2.750427	-1.332519
H	-2.993796	-2.670424	-1.709686
H	-2.463382	-3.234795	-0.109640
H	-4.431061	-0.820963	-0.752892
H	-3.781540	0.272609	0.479882
H	-4.043876	-1.445150	0.866083
H	-0.444802	-1.649438	0.566316
H	-1.757288	-1.347902	1.688796
H	-0.979007	2.084178	2.465774
H	-0.604286	0.544738	3.270123
H	-2.202469	0.809684	2.549879

Enamine from *trans*-**12** (most abundant conformer; abundance: 26%)
# of imaginary frequencies: 0
Energy: -612.534846 Hartrees
Gibbs Free Energy: -612.333686 Hartrees

C	-0.122769	-0.311042	-0.890360
C	0.749484	-1.588521	-0.879111
C	1.590718	-1.451547	0.399015
C	1.854173	0.060181	0.460783

N	0.594721	0.636771	-0.024805
C	-1.563355	-0.616427	-0.434602
H	1.418832	-1.583712	-1.748273
H	0.156678	-2.505411	-0.917339
H	2.090763	0.400954	1.472066
H	2.708763	0.307321	-0.192259
H	1.001480	-1.755326	1.270376
H	-0.211918	0.078537	-1.911932
C	0.431574	2.015719	-0.209819
C	-0.522265	2.553453	-0.998655
H	-0.622284	3.631079	-1.060001
O	-2.344086	-1.180551	-1.207214
O	2.759025	-2.251066	0.445132
H	3.302066	-2.029050	-0.329878
N	-1.857488	-0.279667	0.839326
H	-1.146007	0.236067	1.342923
C	-3.162927	-0.480010	1.442152
H	-3.699061	0.469424	1.559251
H	-3.060740	-0.948744	2.425789
H	-3.740699	-1.134694	0.788310
C	1.366313	2.893505	0.588913
H	1.278315	2.694752	1.664280
H	2.415488	2.728966	0.315401
H	1.133001	3.946452	0.416680
H	-1.230489	1.964732	-1.570291

$TS1_{pro\ R}$, configuration B from *trans*-**12** and **10** (most abundant conformer; abundance: 50%)
# of imaginary frequencies: 1
Energy: -882.108132 Hartrees
Gibbs Free Energy: -881.799278 Hartrees

C	1.226669	0.689365	-0.716173
C	1.427624	2.223498	-0.684839
C	0.401712	2.787769	0.312174
C	0.081237	1.581037	1.197401
N	0.025720	0.471763	0.201150
C	2.514653	-0.059080	-0.284723
H	1.280804	2.672204	-1.669214
H	2.441211	2.437742	-0.342464
H	0.888141	1.382783	1.908121
H	-0.864952	1.668894	1.731793
H	0.804148	3.621453	0.898001
H	0.922203	0.328267	-1.697825
C	-0.348968	-0.999985	0.666968
C	-1.850103	-0.929765	1.038163
H	-2.097508	-1.904597	1.472166
H	-2.014903	-0.192343	1.831992
O	-0.187744	-1.778611	-0.468863
O	3.394627	0.494974	0.378662
O	-0.747989	3.195353	-0.430682
H	-1.361840	3.633259	0.181451
N	2.610473	-1.320915	-0.756724
H	1.724774	-1.758865	-1.013447
C	3.733323	-2.176242	-0.401952
H	3.742686	-3.039427	-1.070273
H	3.670893	-2.530622	0.635607
H	4.665470	-1.619610	-0.518703
H	-0.812111	0.582349	-0.475462
C	0.510859	-1.457410	1.837189
H	1.580941	-1.376004	1.640893
H	0.277295	-0.890869	2.743664
H	0.280801	-2.509661	2.027432
C	-2.747786	-0.637218	-0.233223
C	-3.565371	-1.895143	-0.584382
H	-2.894946	-2.740884	-0.776206
H	-4.249269	-2.179268	0.225960
H	-4.156623	-1.713552	-1.489528
C	-3.703153	0.533792	0.050494
H	-4.354088	0.333195	0.911002
H	-3.138870	1.452028	0.253533
H	-4.335712	0.718652	-0.825662
O	-1.907939	-0.301877	-1.325400
H	-0.943709	-1.273482	-1.106116

(*R*)-hemiaminal from *trans*-**12** and **10** (most abundant conformer; abundance: 48%)
# of imaginary frequencies: 0
Energy: -882.138541 Hartrees
Gibbs Free Energy: -881.828119 Hartrees

C	-1.768022	0.499292	0.403448
C	-2.273912	1.852647	-0.158680
C	-0.993693	2.512888	-0.684974
C	-0.273776	1.308002	-1.299615
N	-0.550520	0.161249	-0.385307
C	-2.877047	-0.556732	0.335155
H	-2.777061	2.452719	0.602635
H	-2.973165	1.688675	-0.987710
H	-0.678360	1.092537	-2.296498
H	0.794890	1.497700	-1.402022
H	-1.206286	3.288864	-1.427703
H	-1.524775	0.634767	1.461443
C	0.589824	-0.320152	0.392215
C	1.698886	-0.861381	-0.573893
H	1.553574	-1.944482	-0.645170
H	1.545578	-0.474850	-1.584131
O	1.068129	0.788875	1.199423
O	-3.843261	-0.497285	1.103780
O	-0.232642	3.130552	0.347662
H	0.277484	2.422021	0.794943
N	-2.727078	-1.476815	-0.641720
H	-1.856548	-1.417433	-1.159588
C	-3.684113	-2.531233	-0.916873
H	-4.054833	-2.465428	-1.945919
H	-4.521573	-2.413789	-0.227251
H	-3.235164	-3.520141	-0.770064
C	0.175655	-1.454277	1.346032
H	-0.518275	-1.103328	2.113847
H	-0.289675	-2.278897	0.797958
H	1.070045	-1.834180	1.846724
C	3.179579	-0.587959	-0.203169
C	4.076535	-1.649677	-0.851440
H	3.817754	-2.646265	-0.479517
H	3.962629	-1.645096	-1.941173
H	5.132004	-1.456997	-0.623998
C	3.634317	0.819506	-0.620395
H	3.596784	0.929306	-1.709830
H	3.001217	1.588468	-0.171070
H	4.670857	0.993902	-0.305614

O	3.275035	-0.715797	1.243739
H	1.922779	0.496099	1.583986
H	4.189825	-0.511503	1.501206

TS2 from (*R*)-hemiaminal from *trans*-**12** and **10**
(most abundant conformer; abundance: 92%)
# of imaginary frequencies: 1
Energy: -882.095282 Hartrees
Gibbs Free Energy: -881.792582 Hartrees

N	-0.318067	0.079597	-0.344125
C	0.123244	1.280954	-1.081667
C	-0.231695	2.401455	-0.109565
C	-1.628197	1.965142	0.363851
C	-1.570205	0.406611	0.380633
C	-2.786828	-0.202725	-0.331746
N	-3.798240	-0.578118	0.479899
C	-5.054327	-1.100434	-0.041416
O	-2.834122	-0.281566	-1.560075
O	0.669348	2.423626	0.986977
H	1.485399	1.922879	0.726512
H	-0.261402	3.377327	-0.612060
H	-2.386063	2.311417	-0.345760
H	-1.864877	2.368241	1.350481
H	-1.483411	0.034176	1.403194
H	0.582985	0.112196	2.257354
H	-0.466636	1.352225	-2.001870
H	1.180371	1.243420	-1.320423
H	-3.678864	-0.522966	1.481885
H	-4.938040	-2.125947	-0.410098
H	-5.404015	-0.473877	-0.865905
H	-5.796290	-1.092028	0.758365
C	3.814607	0.147021	-1.496254
C	3.030998	-0.397854	-0.290685
C	1.725147	-1.155577	-0.840764
C	0.422293	-0.987866	-0.086476
C	-0.237721	-2.236682	0.427044
C	3.903794	-1.435336	0.451839
O	1.201485	-0.577935	1.964263
O	2.719741	0.653297	0.580477
H	2.019593	0.075190	1.397772
H	3.240492	0.915151	-2.027547
H	4.065465	-0.646542	-2.210726
H	4.747102	0.605980	-1.149381
H	4.221316	-2.252606	-0.207599
H	3.354278	-1.864503	1.295848
H	4.798828	-0.938664	0.843292
H	1.540167	-0.839272	-1.872665
H	1.939221	-2.226182	-0.887078
H	-1.032532	-2.045360	1.148012
H	-0.672985	-2.764150	-0.433897
H	0.505765	-2.884082	0.889974

$TS1_{pro\ S}$, configuration C from *trans*-**12** and **10** (most abundant conformer; abundance: 66%)
# of imaginary frequencies: 1
Energy: -882.104131 Hartrees
Gibbs Free Energy: -881.797866 Hartrees

N	0.069493	0.679011	0.309916
C	0.590587	1.890908	1.014506
C	1.095116	2.743908	-0.149871
C	1.754839	1.713400	-1.083416
C	1.120126	0.334053	-0.727381
C	2.198392	-0.614426	-0.185749
N	2.322013	-1.784890	-0.851477
C	3.344394	-2.774802	-0.540474
O	2.904842	-0.288736	0.771268
O	0.013430	3.333307	-0.872137
H	-0.422604	3.974247	-0.286591
H	1.803550	3.509050	0.188484
H	2.832278	1.684165	-0.911881
H	1.574351	1.980721	-2.126396
H	0.601099	-0.104617	-1.579441
H	-0.804540	0.972500	-0.232508
H	1.413307	1.592703	1.666496
H	-0.211173	2.342394	1.596824
H	1.739446	-1.950378	-1.661247
H	3.781088	-2.520598	0.425214
H	4.132334	-2.778554	-1.301736
H	2.895501	-3.770377	-0.487825
C	-2.352899	-1.039594	-2.083858
C	-2.512686	-0.722575	-0.588659
C	-1.348358	-1.396901	0.246560
C	-0.726822	-0.398436	1.248093
C	0.191754	-1.034380	2.279016
C	-3.869849	-1.267728	-0.097934
O	-1.689414	0.364488	1.847701
O	-2.480783	0.681714	-0.395763
H	-2.265759	0.664003	0.916453
H	-1.413763	-0.629510	-2.475244
H	-3.173966	-0.585678	-2.650978
H	-2.356800	-2.120320	-2.274473
H	-4.685936	-0.772043	-0.636857
H	-3.991333	-1.064431	0.972088
H	-3.959128	-2.350927	-0.252506
H	-0.575624	-1.828847	-0.399734
H	-1.738431	-2.227992	0.845127
H	0.941370	-1.691543	1.835650
H	0.693464	-0.277020	2.886956
H	-0.441436	-1.632538	2.941500

$TS1_{pro\ R}$, configuration D from *trans*-**12** and **10** (most abundant conformer; abundance: 50%)
# of imaginary frequencies: 1
Energy: -882.108924 Hartrees
Gibbs Free Energy: -881.800829 Hartrees

C	1.467172	-1.547066	-1.085765
C	2.884717	-1.089377	-0.772198
C	2.713170	0.419508	-0.581402
C	1.371074	0.549435	0.166581
N	0.540443	-0.611543	-0.333751
H	3.565410	-1.323977	-1.600015
H	1.524783	0.413098	1.237137
H	3.535326	0.880969	-0.027292
H	1.252417	-1.443006	-2.151351
C	-0.427390	-1.385279	0.720280
C	-1.569593	-0.385850	1.008504
H	-2.104112	-0.757238	1.890810

H	-1.157392	0.589737	1.293831
O	-0.884037	-2.472311	0.013780
H	-0.244171	-0.316903	-1.001700
C	0.353675	-1.821406	1.949205
H	1.273778	-2.344126	1.677188
H	0.603911	-0.979975	2.602370
H	-0.285905	-2.504346	2.515976
C	-2.541570	-0.268465	-0.234442
C	-3.797523	-1.133067	0.020005
H	-3.514770	-2.174489	0.208256
H	-4.376235	-0.775318	0.882091
H	-4.445163	-1.107472	-0.864513
C	-2.981716	1.193160	-0.428445
H	-2.122266	1.824098	-0.675003
H	-3.696810	1.257151	-1.258154
H	-3.466326	1.596919	0.470745
O	-1.871409	-0.735145	-1.387078
H	-1.411367	-1.944576	-0.774955
O	3.300928	-1.745740	0.423621
H	4.180786	-1.408220	0.658205
H	2.633950	0.908670	-1.558108
C	0.715065	1.896241	-0.151204
O	0.296480	2.139309	-1.285216
N	0.701027	2.789876	0.858496
H	1.028786	2.511100	1.773047
C	0.198492	4.146633	0.683961
H	0.545433	4.758704	1.517591
H	-0.896713	4.164977	0.657563
H	0.575619	4.562132	-0.253615
H	1.261607	-2.571940	-0.784663