First Determination of the Rate Constant for Ring-Closure of an Azahexenoyl Radical: 6-Aza-7-ethyl-5-hexenoyl.

Sara H. Kyne,[a,b,c] Ching Yeh Lin, [a,d] Ilhyong Ryu,[a,e] Michelle L. Coote*[a,d] and Carl H. Schiesser*[a,b,c]

Electronic Supplementary Information

Figure S1, derivation of equation 3, experimental and computational details including the preparation of **6**, kinetic data and Gaussian Archive entries (12 pages).

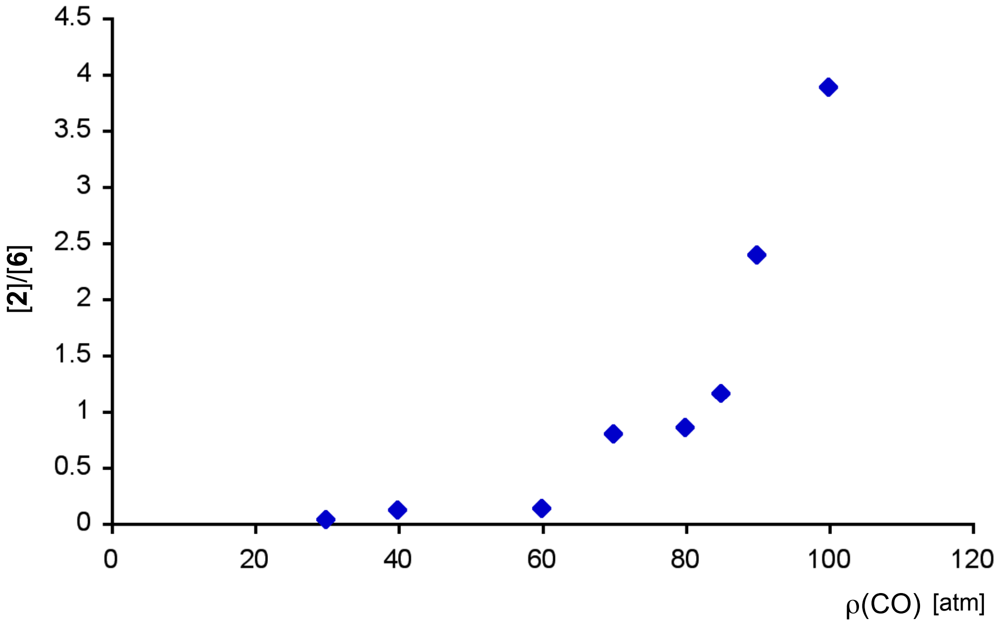

Figure S1. Dependence of [**2**]/[**6**] on carbon monoxide pressure, ρ(CO).

Derivation of equation 3

$$\frac{d[\mathbf{2}]}{dt} = k_c[\mathbf{4}] \quad ; \quad \frac{d[\mathbf{6}]}{dt} = k'_H[\mathbf{5}][Bu_3SnH] \quad \Rightarrow \quad \frac{d[\mathbf{2}]}{d[\mathbf{6}]} = \frac{k_c[\mathbf{4}]}{k'_H[\mathbf{5}][Bu_3SnH]} \qquad ...(2)$$

Steady state approximation:

$$k_{CO}[\mathbf{5}][CO] + k'_H[\mathbf{5}][Bu_3SnH] = k_{-CO}[\mathbf{4}] \quad \Rightarrow \quad [\mathbf{5}] = \frac{k_{-CO}[\mathbf{4}]}{k_{CO}[CO] + k'_H[Bu_3SnH]} \qquad ...(S1)$$

Combining equations (2) and (S1):

$$\frac{d[\mathbf{2}]}{d[\mathbf{6}]} = \frac{k_c(k_{CO}[CO] + k'_H[Bu_3SnH])}{k_{-CO}k'_H[Bu_3SnH]} = \frac{k_c}{k_{-CO}} + \frac{k_c k_{CO}[CO]}{k_{-CO}k'_H[Bu_3SnH]} \qquad ...(S2)$$

Integrating S2, assuming pseudo first order in CO:

$$\boxed{\frac{[\mathbf{2}]}{[\mathbf{6}]} = \frac{k_c}{k_{-CO}} + \frac{k_c k_{CO}}{k_{-CO}k'_H}\,\frac{[CO]}{[\mathbf{6}]}\int \frac{d[\mathbf{6}]}{[Bu_3SnH]} \qquad ...(3)}$$

Experimental Procedure

Standard solutions of Bu_3SnH in benzene were prepared at concentrations listed in Table S1. The radical precursor **1** was added to a Pyrex vial followed by the appropriate volume of the Bu_3SnH standard solution. AIBN (few crystals) was added and the mixture syringed into a 30 mL autoclave and purged with carbon monoxide (3x). The vessel was pressurised with carbon monoxide as detailed in Table S1 and heated at 90° for 60 min. The autoclave was cooled to room temperature, the pressure discharged, and the mixture analysed by GC (Shimadzu GC-18A, DB-1, 30m x 0.250 mm, film thickness 0.25 μm). Ratios of [**2**]/[**6**] were determined by direct integration of GC peaks identified by comparison with authentic standards and are listed in Table S1. Standards (**2** and **6**) were corrected for any difference in response of the GC instrument to **2** and **6**.

ρCO (atm)	[CO] (M)	[Bu_3SnH] (M)	[**1**] (M)	[**2**]/[**6**]	ln([**2**]/[**6**])
30	0.29	0.022	0.017	0.025	-3.68
40	0.38	0.030	0.023	0.116	-2.15
60	0.57	0.045	0.035	0.128	-2.06
70	0.67	0.052	0.040	0.794	-0.23
80	0.76	0.058	0.045	0.851	-0.16
85	0.81	0.064	0.049	1.155	0.14
90	0.86	0.067	0052	2.388	0.87
100	0.95	0.073	0.052	3.877	1.36

Table S1 Experimental data for the reaction of **1** with Bu_3SnH and CO under varying conditions.

5-Aza-6-ethyl-4-octene (6)

Butanal (500 μL, 5.56 mmol) was cooled to 0 °C, and 3-aminopentane dried over calcium hydride (650 μL, 5.58 mmol) added dropwise over 10 min. The neat mixture was allowed to warm to room temperature (60 min). At this time sodium sulfate (794 mg, 5.58 mmol) was added, and the mixture left to stir overnight. Dry diethyl ether was added to dissolve the mixture, and the white solid filtered off. The solvent was removed *in vacuo* to give a clear oil (558 mg, 71%) that required no further purification.

^1H NMR (400 MHz) δ 0.78 (dd, J = 7.2, 7.7 Hz, 6H), 0.97 (td, J = 0.5, 7.3 Hz, 3H), 1.47 – 1.60 (m, 6H), 2.22 – 2.27 (m, 2H), 2.60 (tt, J = 4.4, 8.6 Hz, 1H), 7.56 (t, J = 5.2 Hz, 1H); ^{13}C NMR (101 MHz) δ 10.93, 13.74, 19.86, 28.64, 37.60, 74.64, 163.48; IR (neat) 1381, 1461, 1665, 2876, 2876, 2935 cm^{-1}; MS (EI) *m/z* (rel intensity) 149 (13), 112 (M-Et^+, 50), 84 (25), 70 (19), 55 (12); HRMS (EI) *m/z* calcd for $C_9H_{19}N$ M^+ 141.1517, found $C_7H_{14}N$ $(M\text{-}Et)^+$ 112.1126, found 112.1158.

(K. A. W. Parry, P. J. Robinson, P. J. Sainsbury and M. J. Waller, *J. Chem. Soc. B*, 1970, 700.)

Computational Details

Standard ab initio molecular orbital theory calculations were performed in Gaussian 03.[1] COSMO-RS calculations were performed in ADF[2] using the implementation of Pye et al.[3] Calculations of partition functions were carried out using our in-house program T-Chem.[4,5] All geometry optimisations, frequency and single point energy calculations on open-shell species were performed using unrestricted wavefunctions, spin contamination is not severe in all radical cases. (maximum 0.7601) Our methodology is based on computational procedures that we have shown to be successful in a previous study of cyclization kinetics,[6] as well as a broad range of other radical processes.[7]

Geometries of all species were optimised at the UMP2/cc-pVDZ level of theory and frequency calculations were also performed at this level. Where relevant, systematic conformational searching at a resolution of 120° was carried out to ensure all conformations were global rather than merely local minimum energy structures. Improved energies were calculated using an ONIOM approximation to the G3 theory, which we have successfully benchmarked for several radical processes.[8] In this procedure, we first define the core of the reaction so as to contain all forming and breaking bonds, and any important primary substituents. Deleted substituents are replaced by hydrogens so as to maintain the correct chemical valency, and the geometries of all resulting species are fully optimised at the same level of theory. In the present work, the reaction core for the cyclization of ***4*** is the corresponding cyclization reaction of the parent system *7* (structures as numbered in the MS). Core for the cyclization of ***11*** is also *7*. The core system is studied at a high level of theory and also a lower level; the full system is studied at the same lower level of theory. In the present work, we use as our low level of theory MP2/cc-pVTZ, and as our high level of theory a modified version of G3(MP2)-CC in which all calculations with the Pople double zeta basis set 6-31G(d) are replaced with the corresponding calculations with the Dunning double zeta basis set cc-pVDZ; all calculations with the Pople triple zeta basis set G3MP2large are replaced with the corresponding calculations with the Dunning triple zeta basis set cc-pVTZ. Given the similarity basis set sizes, this modification is expected to make no difference to the overall results but has instead been made to allow us to make use of previously published calculations on the core system.[9] The full system at the high level of theory is then approximated as the sum of the core system at the high level of theory and the difference in energies of the full and core systems, as calculated at the lower level. In other words, the low level of theory is used only to measure the remote substituent effects, which are generally less computationally demanding than the stretched bonds and potentially delocalised radicals associated with the reaction core.

Having obtained the geometries, frequencies and energies of each reactant and transition structure, gas-phase rate coefficients were calculated via the standard transition state theory equation (1).[10]

$$k(T) = \kappa(T)\frac{k_B T}{h}\left(c^\circ\right)^{1-m} e^{\left(-\Delta G^{\ddagger}/RT\right)} = \kappa(T)\frac{k_B T}{h}\left(c^\circ\right)^{1-m} \frac{Q_{\ddagger}}{\prod\limits_{\text{reactants}} Q_i} e^{\left(-\Delta E^{\ddagger}/RT\right)} \tag{1}$$

In this equation, $\kappa(T)$ is the tunneling correction factor, T is the absolute temperature, R is the universal gas constant (8.314 J mol^{-1} K^{-1}), k_B is the Boltzmann constant (1.380658 × 10^{-23} J molec^{-1} K^{-1}), h is the Planck's constant (6.6260755 × 10^{-34} J s), c° ($=P/RT$) is the standard unit of concentration (mol L^{-1}) and m is the molecularity of the reaction, $Q_{\ddagger}$ and Q_i are the molecular partition functions of the transition structure and reactant *i* respectively, $\Delta G^{\ddagger}$ is the Gibb's free energy of activation and $\Delta E^{\ddagger}$ is the 0 K, zero-point energy corrected energy barrier for the reaction. The tunneling coefficient $\kappa(T)$ corrects for quantum effects in motion along the reaction path and can be assumed to be unity in the cyclization reactions studied, due to the large masses of the reacting groups. Molecular partition functions (Q_i) and their associated thermodynamic functions (i.e. *H*, *S* and *G*) were calculated using the optimized geometries and frequencies in conjunction with the standard textbook formulae, based on the statistical thermodynamics of an ideal gas under the harmonic oscillator rigid-rotor approximation.[11,12] All scaling factors are set to 1.0.

Solvation energies in benzene were calculated using the new generation method COSMO-RS,[13] as used successfully in our recent study of acrylate propagation kinetics.[14] Among other advantages this method is designed and parameterised to model the temperature dependence of the solvation energies is thus suitable for calculating Arrhenius parameters in solution. COSMO-RS calculations were carried out using the BP/TZVP level since this was the level of theory for which it was parameterised. Geometries were not reoptimized in the solution phase. Free energies of each species in solution were obtained as the sum of the corresponding gas-phase free energy, the calculated free energy of solvation and a correction term, $\Delta nRT\ ln(V)$, to take account of the fact that the solvation energy is computed for the passage from 1 mol L^{-1}(g) to 1 mol L^{-1}(soln).[15] The overall solution phase free energy of activation was then used to calculate the rate coefficient via equation (1) as for the gas-phase calculations. In this equation, the standard unit of concentration ($c°$) has a value of 1 mol L^{-1} for solution-phase free energies. Since the solvation models are parameterized to calculate total free energies of solvation, rather than the individual enthalpic and entropic components, solution-phase Arrhenius parameters were obtained by repeating all calculations at 298, 313, 333, 353 and 363 K and fitting the Arrhenius relationship to the resulting rate data.

References

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Gaussian Archive Entries for 6-aza-7-ethyl-5-hexenoyl radical (4) and its transition state for 6-*endo* cyclization

ONIOM core for (E)-(4)
(E)-6-aza-5-hexenoyl radical (7)[9]

```
1\1\MARCCENTRE-ANET08\POpt\UMP2-FC\CC-pVDZ\C5H8N1O1(2)\HIROSHI\24-Aug-2
004\1\\#MP2/CC-PVDZ SCF=QC OPT=(Z-MATRIX,CALCHFFC,MAXCYCLE=100) NOSY
MM FREQ=NORAMAN\\substrate for 5-exo and 6-endo terminal imine\\0,2\X\C,1,1.\O,2,r1,1,9
0.\C,2,r2,1,a1,3,d1,0\C,4,r3,2,a2,3,d2,0\C,5,r4,4,a3,2,d3,0\C,6,r5,5,a4,4,d4,0\N,7,r6,6,a5,5,d5,0\H
,4,r7,2,a6,3,d6,0\H,4,r8,2,a7,3,d7,0\H,5,r9,4,a8,2,d8,0\H,5,r10,4,a9,2,d9,0\H,6,r11,5,a10,4,d10,0\
H,6,r12,5,a11,4,d11,0\H,7,r13,6,a12,5,d12,0\H,8,r14,7,a13,6,d13,0\\r1=1.19453748\r2=1.528919
29\r3=1.53087448\r4=1.53503018\r5=1.50545665\r6=1.2788313\r7=1.10605284\r8=1.10623587
\r9=1.10605818\r10=1.10425582\r11=1.10321329\r12=1.10684398\r13=1.1101802\r14=1.03098
786\a1=141.64597632\a2=112.16490384\a3=112.01271645\a4=111.5735627\a5=120.76943107\
a6=105.57852011\a7=108.95483181\a8=109.32093934\a9=109.22725409\a10=110.70912533\a1
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.01721501\\Version=DEC-AXP-OSF/1-G98RevA.7\HF=-323.2712395\MP2=-324.2792284\PU
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00e+00\RMSF=8.677e-05\Dipole=-0.3253737,-0.6780411,0.3733075\PG=C01 [X(C5H8N1O1)]
\\@
```

ONIOM core for (Z)-(4)
(Z)-6-aza-5-hexenoyl radical (7)

```
 1\1\GINC-X150\FOpt\UMP2-FC\CC-pVDZ\C5H8N1O1(2)\CYL509\03-Mar-2010\0\\#
 MP2/cc-pvdz OPT IOP(2/17=4) Freq=noraman maxdisk=2684354560\\r.z5.freq
 \\0,2\C,0.0247465618,-0.0158871392,0.9935813034\O,1.218398755,-0.05215
 52848,0.9869342317\C,-0.9043030584,-0.1767858559,2.1981822495\C,-2.179
 4819978,-0.945349037,1.8416768581\C,-3.1469048176,-1.0460630623,3.0299
 875681\C,-4.3724375276,-1.8576977329,2.6818367817\N,-5.5933717384,-1.4
 777503059,2.665200869\H,-1.1579510668,0.8519404976,2.515908311\H,-0.34
 54084746,-0.659201077,3.0219374466\H,-1.9114545766,-1.9611456023,1.497
 4018126\H,-2.68093098,-0.4466371466,0.9935234493\H,-3.4529816771,-0.03
 62255994,3.3614597378\H,-2.6286446474,-1.530642262,3.8797418796\H,-4.1
 759524973,-2.907292319,2.3934460019\H,-5.6268306334,-0.4852613162,2.95
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 778917\PUHF=-323.2730658\PMP2-0=-324.2801663\S2=0.763987\S2-1=0.754043
 \S2A=0.75015\RMSD=6.264e-09\RMSF=8.007e-05\Thermal=0.\Dipole=0.1495138
 ,0.2718676,0.6608537\PG=C01 [X(C5H8N1O1)]\\@
```

ONIOM core for transition state (E)-8[9]

```
1\1\CHEMCLUSTER-KNET19\FTS\UMP2-FC\CC-pVDZ\C5H8N1O1(2)\CARLHS\14-Jul-20
04\1\\#MP2/CC-PVDZ OPT=(EF,TS,READFC) GEOM=CHECKPOINT GUESS=READ\\Ryu
endo transition state\\0,2\N\C,1,cn2\O,2,oc3,1,ocn3\C,2,cc4,1,ccn4,3,dih4,0\C,1,cn5,2,cnc5,3,dih
5,0\C,5,cc6,1,ccn6,2,dih6,0\C,6,cc7,5,ccc7,1,dih7,0\H,6,hc8,5,hcc8,1,dih8,0\H,6,hc9,5,hcc9,1,dih
9,0\H,7,hc10,6,hcc10,5,dih10,0\H,7,hc11,6,hcc11,5,dih11,0\H,4,hc12,2,hcc12,1,dih12,0\H,4,hc1
3,2,hcc13,1,dih13,0\H,5,hc14,1,hcn14,2,dih14,0\H,1,hn15,5,hnc15,6,dih15,0\\cn2=1.70686088\o
c3=1.23611776\ocn3=111.47933405\cc4=1.52558592\ccn4=101.92556148\dih4=136.87327196\
cn5=1.26386706\cnc5=129.710325\dih5=-158.05876896\cc6=1.50047474\ccn6=120.08666353\d
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8=106.85020617\dih8=107.10783117\hc9=1.1048931\hcc9=108.40337025\dih9=-139.33977267\
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96256\dih11=-73.85112682\hc12=1.10306881\hcc12=107.27550093\dih12=169.43618507\hc13
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9\dih14=-175.71327735\hn15=1.02561437\hnc15=118.98254545\dih15=-178.89003907\\Versio
n=x86-Linux-G03RevB.04\State=2-A\HF=-323.2415158\MP2=-324.2546109\PUHF=-323.2495
473\PMP2-0=-324.2611595\S2=0.824558\S2-1=0.796502\S2A=0.752374\RMSD=5.280e-09\R
MSF=3.710e-05\Dipole=-1.2946531,0.3964719,-2.0082828\PG=C01 [X(C5H8N1O1)]\\@
```

ONIOM core for transition state (Z)-8[9]

```
1\1\CHEMISTRY CLUSTER KIRKLAND-KNET2\FTS\UMP2-FC\CC-pVDZ\C5H8N1O1(2)\
HIROSHI\15-May-2005\1\\#MP2/CC-PVDZ SCF=DIRECT OPT=(EF,TS,READFC,MAXCYC
LE=100) NOSYMM GEOM=CHECK GUESS=READ FREQ=NUMER\\6-Endo TS another con
formation of imine\\0,2\N\C,1,cn2\O,2,oc3,1,ocn3\C,2,cc4,1,ccn4,3,dih4,0\C,1,cn5,2,cnc5,3,dih5
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=1.19758048\ocn3=119.72204646\cc4=1.54301207\ccn4=104.61503342\dih4=209.79931852\cn
5=1.30060855\cnc5=95.30197177\dih5=-265.9622889\cc6=1.50113609\ccn6=123.35440381\dih
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ux-G03RevB.04\HF=-323.2267141\MP2=-324.2349872\PUHF=-323.2443446\PMP2-0=-324.25
01678\S2=0.973413\S2-1=0.909706\S2A=0.759797\RMSD=5.580e-09\RMSF=3.166e-05\Dipole
=-1.3121116,-0.8623299,-0.0522211\PG=C01 [X(C5H8N1O1)]\\@
```

(E)-6-aza-7-ethyl-5-hexenoyl radical (4)

```
 1\1\GINC-V166\FOpt\UMP2-FC\CC-pVDZ\C10H18N1O1(2)\CYL509\01-Mar-2010\0\
 \#mp2/cc-pvdz OPT=(GDIIS)\\r.14 confsearch\\0,2\C,-0.6107967553,1.2490
 9522,1.0864097998\O,0.4947430235,1.4798082406,0.6973951585\C,-1.038801
 0401,0.1883338556,2.101479346\C,-2.3638024947,-0.4747656548,1.71505674
 76\C,-2.833361305,-1.485876489,2.7720404923\C,-4.1131912963,-2.1582434
 49,2.3570407411\N,-5.2085279507,-1.9775254901,3.0100606361\H,-1.152709
 7192,0.7236699228,3.0625420296\H,-0.2229747362,-0.5498813274,2.2165549
 7\H,-2.2500090873,-0.98125135,0.7384553112\H,-3.1351211852,0.304285279
 1,1.5805902204\H,-3.0071909668,-0.9832509981,3.7384819582\H,-2.0480167
 66,-2.2524154836,2.9171134882\H,-4.0726813514,-2.7958902194,1.44533179
 39\C,-6.4012398126,-2.6522791647,2.5000140625\C,-7.4417527389,-1.58764
 14002,2.1273591801\H,-6.159900555,-3.2499920789,1.588636893\C,-6.92836
 36291,-3.6009717686,3.5844403314\C,-6.9706287047,-0.6523752485,1.01256
 00894\H,-8.3687549046,-2.1055632696,1.8192441975\H,-7.6794917818,-1.00
 53369326,3.0362401205\H,-7.7567489196,0.0707378695,0.7395689721\H,-6.0
 800962843,-0.084372816,1.327231777\H,-6.7058909367,-1.2234432894,0.105
 1058937\C,-5.9361800585,-4.7072872422,3.946332912\H,-7.1698101155,-2.9
 999010688,4.4800212562\H,-7.8745916044,-4.0448403356,3.2237068072\H,-6
 .3612809794,-5.3947573247,4.6960715017\H,-5.6679220915,-5.3019850916,3
 .0552567124\H,-5.0085676944,-4.2811432549,4.3616101155\\Version=EM64L-
 G03RevE.01\State=2-A\HF=-518.45557\MP2=-520.1892554\PUHF=-518.4590449\
 PMP2-0=-520.1914701\S2=0.763405\S2-1=0.753625\S2A=0.750133\RMSD=6.269e
 -09\RMSF=2.846e-06\Thermal=0.\Dipole=-0.30357,-0.7029947,0.160288\PG=C
 01 [X(C10H18N1O1)]\\@
```

Transition state 8 for 6-*endo* cyclization of (E)-6-aza-7-ethyl-5-hexenoyl radical (4)

```
 1\1\GINC-V179\FTS\UMP2-FC\CC-pVDZ\C10H18N1O1(2)\CYL509\08-Mar-2010\0\\
 #mp2/cc-pvdz OPT=(TS,calcfc,noeigentest,maxcyc=200,z-matrix,GDIIS) max
 disk=5368709120\\r.ts.e15 confsearch\\0,2\N,-0.0450262628,-0.015918915
 6,-0.0185046346\C,-0.0263431294,0.0616889389,1.671255852\O,1.131620281
 4,0.0498230059,2.130196272\C,-1.0705801166,1.1170553797,2.0066837241\C
 ,-0.9956642137,0.3495355367,-0.7553976895\C,-2.2527169112,0.9691853217
 ,-0.2227483405\C,-2.3953778262,0.8262280321,1.2963205266\H,-2.23197297
 67,2.0340199137,-0.5303844437\H,-3.107379298,0.5218959667,-0.762760792
 4\H,-3.2005701012,1.4931609261,1.6489955081\H,-2.6976591019,-0.2093468
 245,1.5319112781\H,-1.203639972,1.1055294092,3.101475694\H,-0.69903234
 74,2.1311857907,1.7370857131\H,-0.914750692,0.2145114808,-1.8498858059
 \C,1.1947049251,-0.5925525359,-0.578708536\C,0.9073594065,-1.873619092
 3,-1.3661879061\C,1.9634890618,0.4649780095,-1.3785299469\H,1.78072700
```

```
89,-0.8364053722,0.325116702\C,0.2610785829,-2.9638110715,-0.50831857\
H,0.2732114994,-1.6407820423,-2.2444924491\H,1.8697402144,-2.235307154
5,-1.7720640283\C,2.228748518,1.7409958189,-0.57351694\H,2.9218764549,
0.0084536553,-1.6870182092\H,1.4149161106,0.698527256,-2.3132324823\H,
0.0741048583,-3.8756008716,-1.0991337259\H,0.917218111,-3.2270556276,0
.3377210048\H,-0.697306569,-2.6225412585,-0.0843641002\H,2.9177860081,
2.4115455348,-1.1127096909\H,1.2941617555,2.2953599043,-0.3868795183\H
,2.6591867192,1.493196025,0.4102054931\\Version=EM64L-G03RevE.01\State
=2-A\HF=-518.4267122\MP2=-520.1703573\PUHF=-518.4353851\PMP2-0=-520.17
75446\S2=0.838192\S2-1=0.80738\S2A=0.752921\RMSD=8.663e-09\RMSF=3.634e
-06\Thermal=0.\Dipole=-1.1123288,0.2592602,-1.8044417\PG=C01 [X(C10H18
N1O1)]\\@
```

(Z)-6-aza-7-ethyl-5-hexenoyl radical (4)

```
1\1\GINC-V1483\FOpt\UMP2-FC\CC-pVDZ\C10H18N1O1(2)\CYL509\15-Mar-2010\0
\\#MP2/cc-pvdz OPT=(GDIIS)\\r.z14 confsearch\\0,2\C,0.6703129111,-0.61
00561535,1.5955483336\O,1.8150420411,-0.9188974112,1.7386856223\C,-0.4
468573316,-0.66629962,2.6392851546\C,-1.7806917715,-1.1045062953,2.028
6070235\C,-2.9198344897,-1.0931939606,3.0609081127\C,-4.2004108402,-1.
6111793281,2.4411272483\N,-5.3370121238,-1.0322178169,2.2487493035\H,-
0.5323913129,0.3621880024,3.0374796392\H,-0.1325463642,-1.3276899898,3
.4684679727\H,-1.6749352906,-2.1200609356,1.6042829795\H,-2.0317659124
,-0.4357084167,1.1861695036\H,-3.0398415275,-0.0774343895,3.4702140493
\H,-2.6474170149,-1.7587920153,3.9028262888\H,-4.1299323262,-2.6493118
215,2.0663430429\C,-5.5315315709,0.3541049826,2.6901727097\C,-6.983802
7337,0.4944688931,3.1605102229\H,-4.8803233846,0.6137955944,3.55072267
3\C,-5.1746580014,1.3025824177,1.5296412101\C,-7.2711976861,-0.3743126
905,4.3861933131\H,-7.1813308559,1.5583474387,3.3909233065\H,-7.655620
8758,0.202288468,2.3351914111\H,-8.3170575818,-0.2705395038,4.71915860
86\H,-7.0875917295,-1.43540061,4.1509419284\H,-6.6170681325,-0.0932823
689,5.2306907236\C,-5.976140672,1.0613742267,0.2467462929\H,-5.3176712
473,2.3433201895,1.876646279\H,-4.0952245258,1.1870673653,1.3147803023
\H,-5.6160392903,1.7166173256,-0.5637465317\H,-5.880626793,0.014381289
5,-0.081439175\H,-7.0473774136,1.2736429626,0.395330201\\Version=EM64L
-G03RevE.01\State=2-A\HF=-518.4455053\MP2=-520.1812642\PUHF=-518.44898
66\PMP2-0=-520.1834789\S2=0.763386\S2-1=0.753588\S2A=0.750132\RMSD=6.4
44e-10\RMSF=5.581e-07\Thermal=0.\Dipole=-0.1700641,0.2266215,0.6037804
\PG=C01 [X(C10H18N1O1)]\\@
```

Transition state 8 for 6-*endo* cyclization of (Z)-6-aza-7-ethyl-5-hexenoyl radical (4)

```
1\1\GINC-V178\FTS\UMP2-FC\CC-pVDZ\C10H18N1O1(2)\CYL509\09-Mar-2010\0\\
#mp2/cc-pvdz OPT=(TS,calcfc,noeigentest,maxcyc=200,z-matrix,GDIIS) max
disk=5368709120\\r.ts.z15 confsearch\\0,2\N,-0.3658556166,-0.202368998
1,-0.1354030505\C,0.1569770055,-0.0541720317,1.7478534932\O,1.32953275
15,0.0192021601,2.0020698467\C,-0.9165588608,-0.8412142226,2.534078868
3\C,-0.3689914505,-1.493695183,-0.0684317441\C,-1.437364419,-2.3492569
398,0.5525411051\C,-1.0886450561,-2.2988850474,2.0646447226\H,-2.45333
62354,-1.9607498601,0.3802196747\H,-1.3938127814,-3.3882002684,0.18552
20123\H,-1.8690961358,-2.8090586456,2.6618036458\H,-0.1386087141,-2.83
83556718,2.2347055283\H,-0.590279134,-0.8138376533,3.5887405474\H,-1.8
793147725,-0.3061831785,2.4624450163\H,0.6145036329,-1.9782905809,-0.1
893062503\C,-1.6387871998,0.5357994898,-0.2268593982\C,-1.4116306075,1
.9999939869,0.1763737912\C,-2.1313295712,0.3747439099,-1.678907743\H,-
2.4298501057,0.1249254598,0.4345683155\C,-0.316233227,2.7023431916,-0.
6286089348\H,-2.3700124284,2.5415703819,0.0827732195\H,-1.1464756483,2
.0244533038,1.2482304578\C,-3.4006318619,1.1679990563,-1.9991366242\H,
-1.3117915572,0.65805985,-2.3622520496\H,-2.3131600893,-0.7021225236,-
1.8516710419\H,-0.1651356281,3.7313160921,-0.2616733758\H,0.6336608635
,2.1533369293,-0.5378972149\H,-0.5750791958,2.7654711446,-1.6993966453
\H,-3.779655289,0.903179108,-3.0002518113\H,-4.2008739282,0.9524488061
,-1.2690615937\H,-3.218989977,2.2548515786,-1.9897841314\\Version=EM64
L-G03RevE.01\State=2-A\HF=-518.3949278\MP2=-520.1357499\PUHF=-518.4121
```

```
149\PMP2-0=-520.1505877\S2=0.972906\S2-1=0.910416\S2A=0.759576\RMSD=9.
575e-09\RMSF=2.124e-06\Thermal=0.\Dipole=-1.1661411,-0.784123,0.118505
5\PG=C01 [X(C10H18N1O1)]\\@
```

(E)-5-Dimethylhydrazonopentanoyl Radical (11)

```
1\1\GINC-X136\FOpt\UMP2-FC\CC-pVDZ\C7H13N2O1(2)\CYL509\27-Mar-2010\0\\
#MP2/CC-PVDZ OPT IOP(2/17=4) FREQ=NORAMAN MAXDISK=1342177280\\r.5dmhp.
freq\\0,2\C,-4.1663781051,-0.4183167333,0.1934610418\O,-4.1061699797,-
0.3791943537,1.3872339119\C,-2.9872496181,-0.4633569521,-0.7766234613\
H,-3.1113040963,-1.3806293483,-1.3808175395\H,-3.1179041235,0.37977681
8,-1.4788255996\C,-1.6222109905,-0.4178991605,-0.082009069\H,-1.549176
0577,-1.2670164279,0.6221886289\H,-1.5531255222,0.4999115274,0.5286562
546\C,-0.463067651,-0.4572069249,-1.08353741\H,-0.4975055748,0.4157546
851,-1.7571747564\H,-0.5548095808,-1.3677744877,-1.7081857491\C,0.8799
946566,-0.4601263403,-0.4015727878\H,1.0894481175,-1.3046262031,0.2788
376141\N,1.6994636503,0.4749881866,-0.6397526415\N,2.9576619981,0.4779
540846,-0.0810543908\C,3.3906953496,1.8562830571,0.119432446\H,4.47389
40303,1.8716571683,0.317983966\H,3.1796205242,2.417290416,-0.801428964
9\H,2.8639153486,2.349078486,0.9646273896\C,3.1804744145,-0.3782007689
,1.0713776485\H,2.4311416631,-0.2022608795,1.8757630958\H,3.1338760973
,-1.44017833,0.7802280977\H,4.1878611365,-0.1750815554,1.4627550441\\V
ersion=AM64L-G03RevC.02\State=2-A\HF=-456.3379228\MP2=-457.8057298\PUH
F=-456.3414989\PMP2-0=-457.8081748\S2=0.766196\S2-1=0.755868\S2A=0.750
216\RMSD=7.006e-09\RMSF=1.050e-06\Dipole=0.7347418,-0.258314,-0.071674
6\PG=C01 [X(C7H13N2O1)]\\@
```

Transition state 12 for 5-*exo* cyclization of (E)-5-Dimethylhydrazonopentanoyl Radical (11)

```
1\1\GINC-X149\FTS\UMP2-FC\CC-pVDZ\C7H13N2O1(2)\CYL509\27-Mar-2010\0\\#
mp2/cc-pvdz OPT=(TS,calcfc,noeigentest,maxcyc=200,GDIIS) IOP(2/17=4) F
req=noraman maxdisk=4026531840\\r.ts.5exo.freq\\0,2\C,-2.188858091,-0.
0173927118,-1.1247745868\C,-2.1680944953,-0.2124710553,0.3998996699\C,
-0.731829745,-0.1245477212,0.8753048878\C,-1.2459520746,-1.0513148822,
-1.7521064343\H,-3.2100925882,-0.1129864483,-1.5295841207\H,-1.8225675
767,0.9975783954,-1.3466259048\H,-2.5672652553,-1.2086062811,0.6624009
349\H,-2.7962645637,0.5445098263,0.9006739588\H,-0.4099313437,-0.79739
22685,1.6833480241\H,-0.8666189006,-0.7627599044,-2.7482360348\H,-1.75
30781856,-2.0300283455,-1.8461830707\C,-0.0788184048,-1.2987593215,-0.
7933253505\O,1.0786417213,-1.4994768018,-1.0436806209\N,-0.0658873426,
0.9312873515,0.5232347739\N,1.1659865744,1.1600713313,1.02651947\C,2.0
063848656,1.8999000778,0.0935805884\H,2.8323936206,2.3778699419,0.6440
157475\H,2.4298794377,1.2496878187,-0.6982841699\H,1.3838647608,2.6740
683884,-0.3762097392\C,1.8379804978,0.1400665422,1.821275855\H,1.96310
34012,-0.8113271404,1.2697403066\H,2.8268999127,0.5308261011,2.1023675
064\H,1.2718699957,-0.052387535,2.747741514\\Version=EM64L-G03RevE.01\
State=2-A\HF=-456.3172505\MP2=-457.782424\PUHF=-456.3353496\PMP2-0=-45
7.7981043\S2=0.996635\S2-1=0.928866\S2A=0.761663\RMSD=9.443e-09\RMSF=4
.837e-06\Thermal=0.\Dipole=-0.2044978,-0.02054,0.2148887\PG=C01 [X(C7H
13N2O1)]\\@
```

Transition state 12 for 6-*endo* cyclization of (E)-5-Dimethylhydrazonopentanoyl Radical (11)

```
1\1\GINC-X144\FTS\UMP2-FC\CC-pVDZ\C7H13N2O1(2)\CYL509\27-Mar-2010\0\\#
mp2/cc-pvdz OPT=(TS,calcfc,noeigentest,maxcyc=200,GDIIS) IOP(2/17=4) F
req=noraman maxdisk=4026531840\\r.ts.6endo.freq\\0,2\C,-1.5821258004,-
0.0311105765,-1.8642323302\C,-1.5076921522,-0.1288748729,-0.3721999861
\C,0.9468203619,0.0099566471,-1.873841387\C,-0.3285455495,0.5960269598
,-2.4847910811\H,-2.4173019616,-0.2915334341,0.2271017883\H,-1.7476551
848,-1.0603807905,-2.2404403488\H,-2.4967967906,0.5318371149,-2.123117
9924\H,1.8408193003,0.4062051235,-2.384317531\H,0.9668387501,-1.095198
64,-2.0007513061\H,-0.3416035583,1.6834719858,-2.2935849584\H,-0.35626
91975,0.4531230378,-3.5783794673\C,1.085170182,0.3816267641,-0.4027986
41\O,2.0517380604,0.0655743619,0.3127060529\N,-0.4178756955,-0.0279099
```

```
211,0.2588192533\N,-0.539714615,-0.1664123652,1.6797527577\C,0.0373706
815,1.0181406671,2.3406878357\H,1.1266777235,1.104305796,2.1961303227\
H,-0.4613097039,1.9161218384,1.9447577216\H,-0.2010546475,0.9296493814
,3.4131723923\C,0.1465923786,-1.4040631681,2.094504527\H,0.0027926068,
-1.5008663645,3.182777931\H,-0.3462233294,-2.2588088298,1.6042202358\H
,1.2216077756,-1.3982151061,1.8508106652\\Version=EM64L-G03RevE.01\Sta
te=2-A\HF=-456.3044573\MP2=-457.7787778\PUHF=-456.3133227\PMP2-0=-457.
7861342\S2=0.840874\S2-1=0.809325\S2A=0.753024\RMSD=5.755e-09\RMSF=1.3
75e-05\Thermal=0.\Dipole=-1.8428631,-0.2595769,-0.435893\PG=C01 [X(C7H
13N2O1)]\\@
```

Table S2 Calculated gas phase energies (Hartree) for imine and hydrazone cyclization reactions.[*]

	core[†]				full	
	MP2 /cc-pVDZ	MP2 /cc-pVTZ	CCSD(T) /cc-pVDZ	G3(MP2)-CC	MP2 /cc-pVTZ	ONIOM G3(MP2)-CC
(E)-**4**	-324.27923	-324.59758	-324.37873	-324.69709	-520.71166	-520.81116
TS (E)-**8**	-324.25461	-324.57786	-324.35850	-324.68175	-520.69788	-520.80177
(Z)-**4**	-324.27789	-324.59589	-324.37760	-324.69560	-520.70344	-520.80315
TS (E)-**8**	-324.23499	-324.55462	-324.34653	-324.66617	-520.66050	-520.77204
(E)-**11**	-324.27923	-324.59758	-324.37873	-324.69709	-458.26145	-458.36095
TS (E)-5-exo **12**	-324.25223	-324.57219	-324.36233	-324.68228	-458.23909	-458.34919
TS (E)-6-endo **12**	-324.25461	-324.57786	-324.35850	-324.68175	-458.23855	-458.34244

---

[*] Both (E) and (Z) stereoisomer are carried out in the imine reaction. For hydrazone cyclization reaction, only the preferred pathway (E) is carried out.

[†] Core system (6-aza-5-hexenoyl) geometries and MP2/cc-pVDZ and CCSD(T)/cc-pVDZ energies are taken from Ref 9.

Table S3 Calculated reaction entropies ($\Delta S^{\ddagger}$), enthalpies($\Delta H^{\ddagger}$) and free energies ($\Delta G^{\ddagger}$) and the rate constants (k) in gas phase and solution phase for imine (90°) and hydrazone (80°) cyclization.

	$\Delta S_{gas}^{\ddagger}$ (J mol^{-1}K^{-1})	$\Delta H_{gas}^{\ddagger}$ (kJ mol^{-1})	$\Delta G_{gas}^{\ddagger}$ (kJ mol^{-1})	k_{gas} (s^{-1})	$\Delta G_{soln}^{\ddagger}$ (kJ mol^{-1})	k_{soln} (s^{-1})
(E)-**4** → TS (E)-**8**	-68.3	26.3	51.1	3.3×10^{5}	42.0	6.8×10^{6}
(Z)-**4** → TS (Z)-**8**	-69.2	78.0	103.2	1.1×10^{-2}	104.4	7.4×10^{-3}
(E)-**11** → TS (E)-5-exo **12**	-40.1	27.0	41.2	6.0×10^{6}	47.1	8.1×10^{5}
(E)-**11** → TS (E)-6-endo **12**	-54.4	43.3	62.5	4.1×10^{3}	60.1	9.6×10^{3}

[‡] Solvation energies are obtained using optimised gas phase geometries with BP/TZVP COSMO-RS.