Supporting Information

STUDIES ON ROTATIONAL STABILITY OF 2-ARYL-3-(2-FLUOROPHENYL)QUINAZOLIN-4-ONE DERIVATIVES

Asumi Iida[a], Kazuya Saito[a], Nanami Asada[a], Yuuki Fujimoto[b] and Osamu Kitagawa*[a]

[a]Department of Applied Chemistry, Shibaura Institute of Technology, 3-7-5 Toyosu, Kohto-ku, Tokyo, 135-8548, Japan.

[b]School of Pharmacy, Tokyo University of Pharmacy and Life Sciences, 1432-1, Horinouchi, Hachioji, Tokyo, 192-0392, Japan

E-mail: *kitagawa@shibaura-it.ac.jp*

The Contents of Supporting Information. Copies of ^{1}H-NMR and ^{13}C-NMR spectra of new compounds **2a,b**, crystal structural data of **2a**, and computational studies.

(Contents)

EXPERIMENTAL

General remarks: Melting points were uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz spectrometer. In ^{1}H and ^{13}C NMR spectra, chemical shifts were expressed in δ (ppm) downfield from $CHCl_3$ (7.26 ppm) and $CDCl_3$ (77.0 ppm), respectively. HRMS were recorded on a double focusing magnetic sector mass spectrometer using electrospray ionization. Column chromatography was performed on silica gel (75-150 μm). Medium-pressure liquid chromatography (MPLC) was performed on a 25 x 4 cm i. d. prepacked column (silica gel, 10 μm) with a UV detector. High-performance liquid chromatography (HPLC) was performed on a 25 x 0.4 cm i. d. chiral column with a UV detector.

3-(2-Fluorophenyl)-2-phenylquinazolin-4(3H)-one (2a).

Under N_2 atmosphere, to 2-fluoroaniline (50.0 mg, 0.45 mmol) and *N*-benzoyl anthranilic acid (72.3 mg, 0.3 mmol) in toluene (6.0 mL) was added PCl_3 (62.0 mg, 0.45 mmol) at rt. The mixture was stirred for 30 min at rt and then for 7 h at 130 °C (oil bath). The mixture was poured into water and extracted with AcOEt. The AcOEt extracts were washed with brine, dried over $MgSO_4$, and evaporated to dryness. Purification of the residue by column chromatography (hexane/AcOEt = 10) gave **2a** (46.9 mg, 49%).

2a: white solid; mp 161-163 °C; IR (neat) 1684 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 8.37 (1H, d, J = 7.9 Hz), 7.81-7.84 (2H, m), 7.56 (1H, m), 7.39 (2H, d, J = 7.3 Hz), 7.22-7.32 (4H, m), 7.06-7.15 (3H, m); ^{13}C NMR ($CDCl_3$) δ: 161.6, 157.6 (d, $J_{C\text{-}F}$ = 247.9 Hz), 155.2, 147.4, 135.0, 134.8, 130.8 (d, $J_{C\text{-}F}$ = 8.6 Hz), 130.5, 129.7, 128.3, 128.1, 127.8, 127.4, 127.2, 125.7 (d, $J_{C\text{-}F}$ = 13.3 Hz), 124.5 (d, $J_{C\text{-}F}$ = 3.8 Hz), 120.7, 116.3 (d, $J_{C\text{-}F}$ = 19.1 Hz); MS (*m/z*) 317 (MH^+); HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{20}H_{14}FN_2O_1$ 317.1090; found, 317.1062.

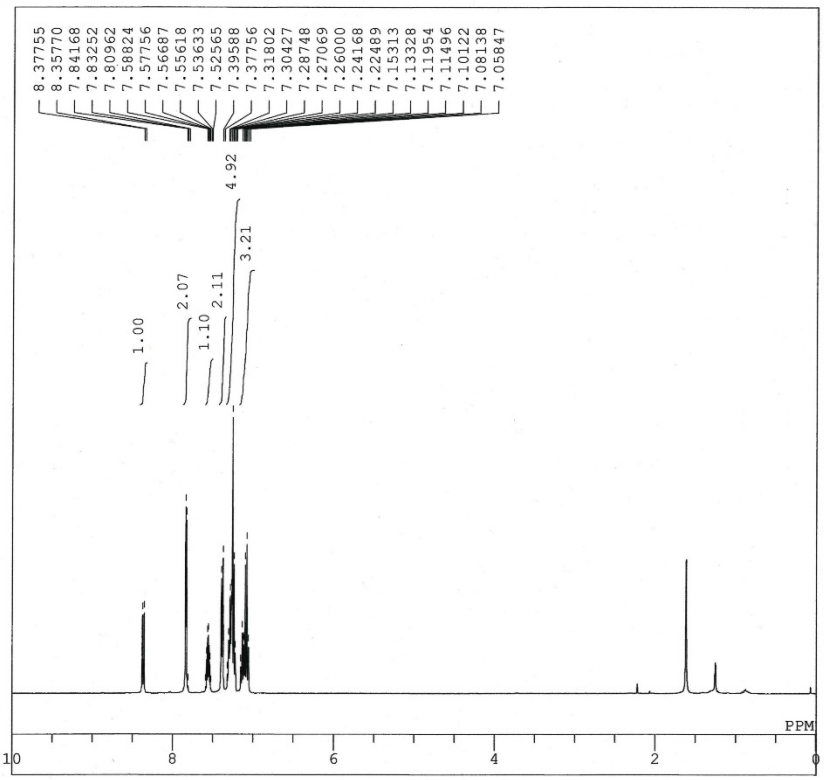
3-(2-Fluorophenyl)-2-(4-methoxyphenyl)quinazolin-4(3H)-one (2b).

Under N_2 atmosphere, to *p*-methoxybenzoyl chloride (187.6 mg, 1.1 mmol) and anthranilic acid (137 mg, 1.0 mmol) in THF (2.0 mL) was added triethylamine (152 mg, 1.5 mmol) at 0 °C, and the mixture was stirred for 40 min at rt. 1N HCl was added to the mixture and then the mixture was filtered.

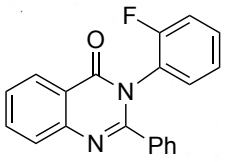
The residue was washed with AcOEt and dried in vacuo. The residue [*N*-(4-methoxy)benzoyl anthranilic acid] was reacted with 2-fluoroaniline (167 mg, 1.5 mmol) in accordance with the procedure for the synthesis of **2a**. Purification of the residue by column chromatography (hexane/AcOEt = 2) gave **2b** (149.7 mg, 44%).

2b: white solid; mp 50-52 °C; IR (neat) 1684 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 8.34 (1H, d, J = 7.9 Hz), 7.78-7.82 (2H, m), 7.52 (1H, m), 7.28-7.35 (3H, m), 7.33 (2H, d, J = 9.2 Hz), 7.29 (1H, m), 6.74 (2H, d, J = 9.2 Hz), 3.74 (3H, s); ^{13}C NMR ($CDCl_3$) δ: 161.7, 160.4, 157.5 (d, J_{C-F} = 249.8 Hz), 154.9, 147.5, 134.8, 130.6 (d, J_{C-F} = 7.6 Hz), 130.5, 130.1, 127.6, 127.2, 127.1, 125.9 (d, J_{C-F} = 13.3 Hz), 124.5 (d, J_{C-F} = 3.8 Hz), 120.4, 116.3 (d, J_{C-F} = 20.0 Hz), 113.4, 55.2; MS (*m/z*) 347 (MH^+); HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{21}H_{16}FN_2O_2$ 347.1196; found, 347.1171.

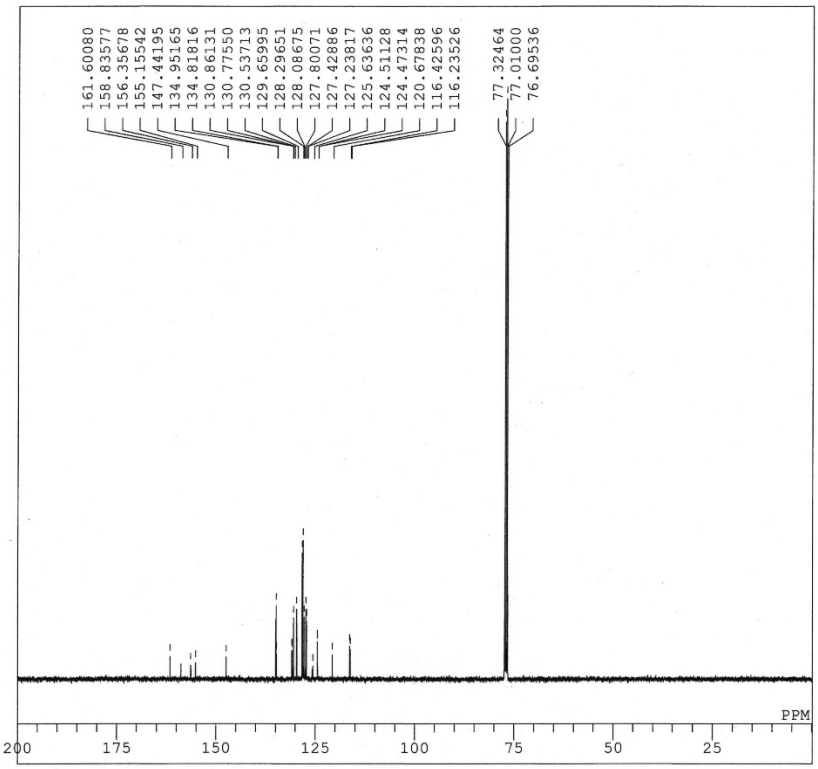
Copies of ^{1}H-NMR and ^{13}C-NMR chart of 2a,b



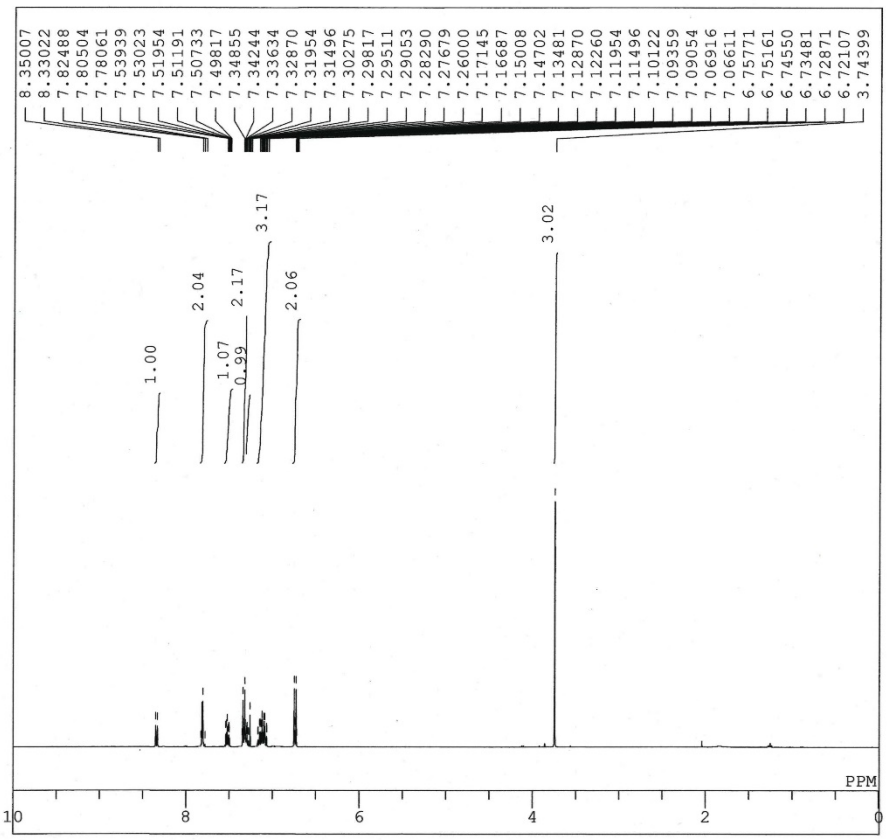

```
DFILE   AI118 37- 20190605-1.als
COMNT   Qn-BOC 1H
DATIM   2019-06-05 10:57:44
OBNUC   1H
EXMOD   single_pulse.ex2
OBFRQ         399.78 MHz
OBSET           5.19 KHz
OBFIN           6.74 Hz
POINT          13107
FREQU        7999.88 Hz
SCANS             32
ACQTM          1.6384 sec
PD             5.0000 sec
PW1              5.29 usec
IRNUC   1H
CTEMP           15.9 c
SLVNT   CDCL3
EXREF           7.26 ppm
BF              0.12 Hz
RGAIN             50
```



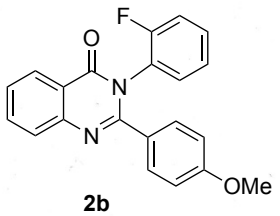
2a



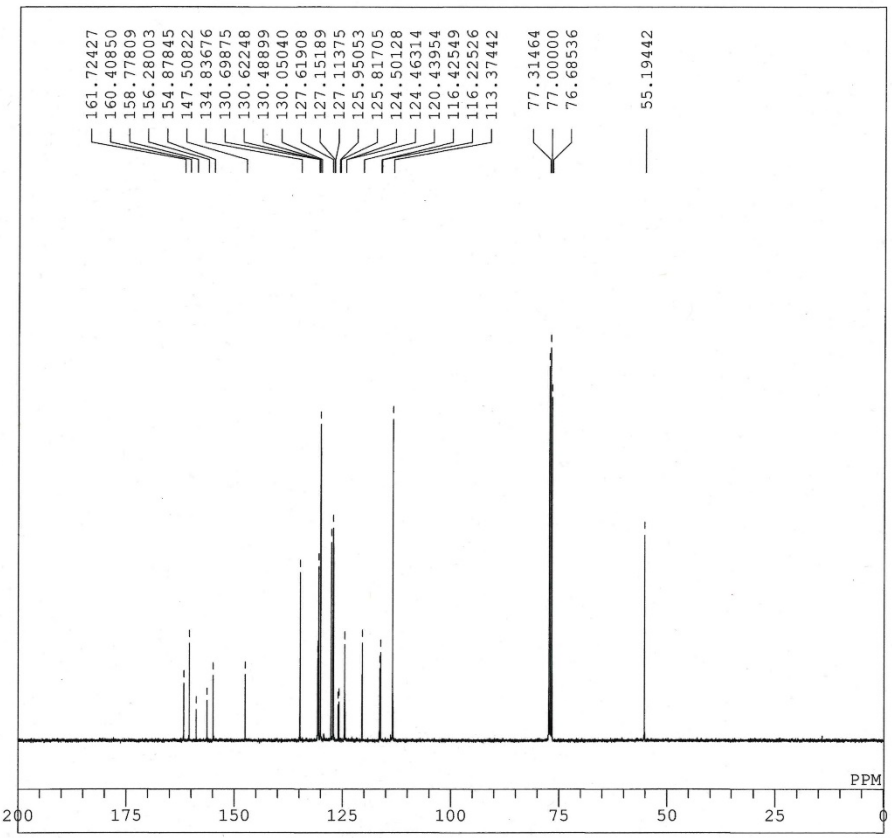

```
DFILE   AI118 20200120-1.jdf
COMNT
DATIM   2020-01-20 10:49:06
OBNUC   13C
EXMOD   single_pulse_dec
OBFRQ         100.53 MHz
OBSET           5.35 KHz
OBFIN           5.86 Hz
POINT          32768
FREQU       31407.03 Hz
SCANS           1024
ACQTM          1.0433 sec
PD             2.0000 sec
PW1              2.87 usec
IRNUC   1H
CTEMP           17.3 c
SLVNT   CDCL3
EXREF          77.01 ppm
BF              1.20 Hz
RGAIN             60
```



DFILE AI150 f=14-21 20200116-1.a
COMNT Qn-BOC 1H
DATIM 2020-01-16 10:06:35
OBNUC 1H
EXMOD single_pulse.ex2
OBFRQ 399.78 MHz
OBSET 5.19 KHz
OBFIN 6.74 Hz
POINT 13107
FREQU 7999.88 Hz
SCANS 32
ACQTM 1.6384 sec
PD 5.0000 sec
PW1 5.14 usec
IRNUC 1H
CTEMP 15.6 c
SLVNT CDCL3
EXREF 7.26 ppm
BF 0.12 Hz
RGAIN 36



2b



DFILE AI150 f=14-21 13C 20200116
COMNT
DATIM 2020-01-16 11:26:55
OBNUC 13C
EXMOD single_pulse_dec
OBFRQ 100.53 MHz
OBSET 5.35 KHz
OBFIN 5.86 Hz
POINT 32768
FREQU 31407.03 Hz
SCANS 1024
ACQTM 1.0433 sec
PD 2.0000 sec
PW1 2.87 usec
IRNUC 1H
CTEMP 16.1 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 1.20 Hz
RGAIN 60

X-Ray crystallographic data of 2a

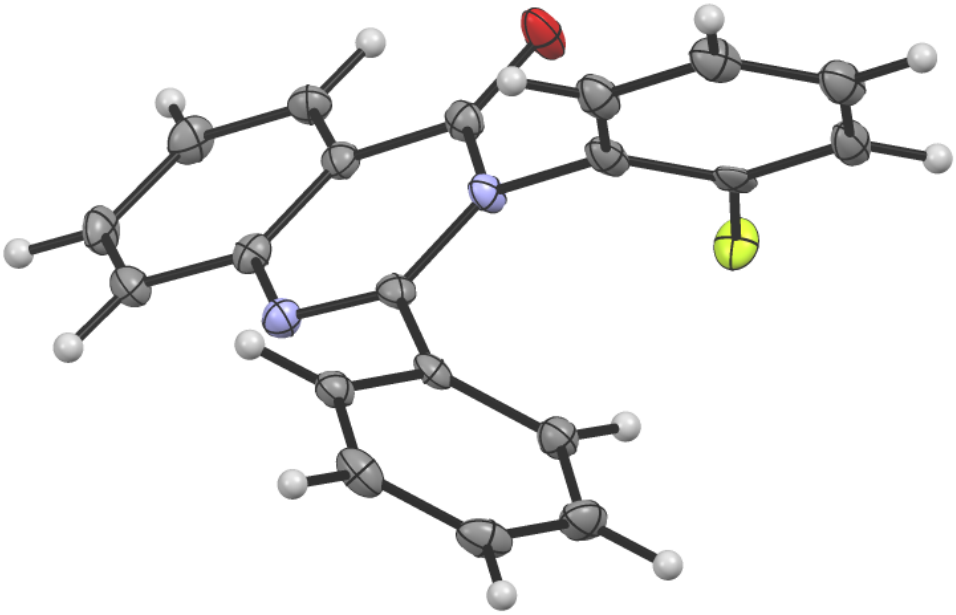


Figure S1. ORTEP drawing of **2a** (CCDC 1989906). Crystallographic data for **2a** at 100 K: formula $C_{20}H_{13}FN_2O$, Fw; 316.32, Triclinic, space group P_1, a=8.0036(5), b=10.0747(5), c=10.8040(5) Å, α=107.641(2)º, β=111.171(2)º, γ=93.594(2)°, V=759.50(7) Å^3, Z=2, D_{calcd}=1.383 Mg/m^3, m(MoKα)=0.71073 Å, R=0.0883, R_w=0.1277.

Table S1. Cartesian coordinates of **2a**.

C1	0.50853(15)	0.18592(11)	0.65644(9)
C2	0.60461(15)	0.10776(10)	0.74364(9)
C3	0.52156(15)	0.03559(11)	0.81571(9)
C4	0.61248(16)	-0.03662(11)	0.89072(9)
H4	0.5489	-0.0856	0.9366
C5	0.79826(17)	-0.03645(11)	0.89791(9)
H5	0.8631	-0.0844	0.9499
C6	0.88910(16)	0.03341(11)	0.82960(9)
H6	1.0163	0.0344	0.8343
C7	0.79115(15)	0.10221(11)	0.75392(9)
C8	0.80183(15)	0.17839(11)	0.58381(9)
C9	0.91614(16)	0.18355(11)	0.50791(10)
H9	1.0425	0.1807	0.5278
C10	0.84104(16)	0.19296(11)	0.40257(9)
H10	0.9157	0.1985	0.3488
C11	0.65470(16)	0.19421(11)	0.37596(9)
H11	0.6043	0.1997	0.3031
C12	0.53887(15)	0.18767(10)	0.45210(9)
C13	0.61530(15)	0.18366(10)	0.56150(9)
C14	0.49322(15)	0.33021(11)	0.70207(9)
C15	0.68435(16)	0.40048(11)	0.74126(9)
H15A	0.7469	0.3514	0.798
H15B	0.7536	0.3989	0.681
C16	0.68760(17)	0.54196(12)	0.78512(10)
H16A	0.6147	0.5902	0.732
H16B	0.6333	0.5442	0.8514
C17	0.87802(17)	0.60572(11)	0.80859(10)
H17	0.9395	0.6132	0.7489
C18	0.97110(17)	0.65297(11)	0.90279(10)
C19	0.89646(19)	0.65390(13)	1.00645(10)
H19A	0.7648	0.6354	0.9913
H19B	0.9279	0.7393	1.045
H19C	0.9482	0.5877	1.0504
C20	1.16586(19)	0.70777(13)	0.91353(12)
H20A	1.2061	0.6993	0.8439
H20B	1.2406	0.6602	0.965
H20C	1.1774	0.7995	0.9387
C21	0.38462(17)	0.32506(12)	0.79483(10)
H21A	0.3616	0.413	0.8171
H21B	0.4535	0.2868	0.8551
H21C	0.2695	0.2721	0.7715
C22	0.40345(16)	0.40419(11)	0.61227(10)
H22	0.4678	0.4171	0.5544
C23	0.24629(18)	0.45276(13)	0.60510(11)
H23A	0.1758	0.4429	0.6606
H23B	0.2037	0.4976	0.5444
C24	0.33882(15)	0.18406(11)	0.40938(9)
H24A	0.3217	0.1923	0.332
H24B	0.2887	0.2559	0.4442
H24C	0.2768	0.1017	0.4243
F1	0.33982(9)	0.03274(7)	0.81376(5)
O1	0.89035(10)	0.16601(8)	0.68682(6)
O2	0.32723(10)	0.13104(8)	0.62270(6)
H_2O	0.3291(19)	0.0493(16)	0.6122(11)

Computational studies

Theoretical calculations to gain the barrier of the N–C axial rotation in quinazolinone **1b**, **2a** and **2b** were performed by using Gaussian 09 program (Rev. D.01).[1] All geometrical optimizations for minimums and transition states, frequency analyses, and intrinsic reaction coordinate (IRC) calculations were carried out by using density functional theory (DFT) with the B3LYP[2] exchange-correlation functional in conjunction with 6-31G(d,p) basis set in the gas phase, at 298.15 K and under 1 atm pressure. The effect of CCl_4 solvent was taken into account by polarizable continuum model (PCM).[3] Visualizations were accomplished using CYLview v1.0.565 β[4] for the stationary point geometries.

Two transition states for N–C axial rotation were found as clockwise mode (abbreviated as "cw") and anticlockwise mode (abbreviated as "anticw"). Therefore, for the comparison with experimental observations, the total reaction rate constants of rotation (k_{tot}) and activation energies ($\Delta G^{\ddagger}_{tot}$) were calculated as follows:

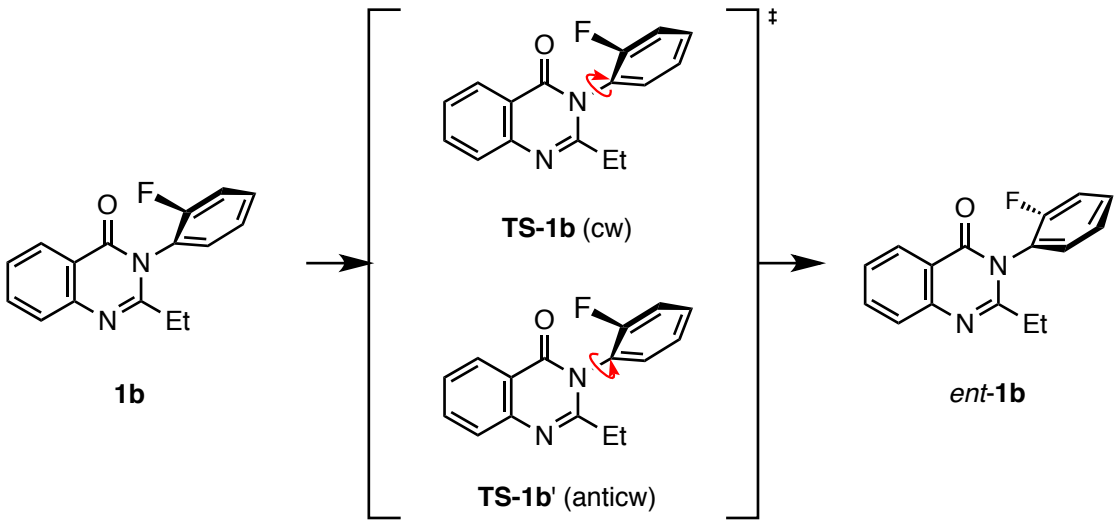
$$k_{cw} = \frac{k_B T}{h} \exp\left(-\frac{\Delta G^{\ddagger}_{cw}}{RT}\right) \qquad k_{anticw} = \frac{k_B T}{h} \exp\left(-\frac{\Delta G^{\ddagger}_{anticw}}{RT}\right) \qquad \text{(equations 1 and 2)}$$

$$k_{tot} = k_{cw} + k_{anticw} \qquad \text{(equation 3)}$$

$$\Delta G^{\ddagger}_{tot} = -RT \cdot \ln\left(\frac{k_B T}{k_{tot} \cdot h}\right) \qquad \text{(equation 4)}$$

where k_B is Boltzmann constant (1.38065 x 10^{-23} J K^{-1}), T is temperature (298.15 K), h is Planck's constant (6.62607 x 10^{-34} J s), and R is gas constant (8.31447 J K^{-1} mol^{-1}).

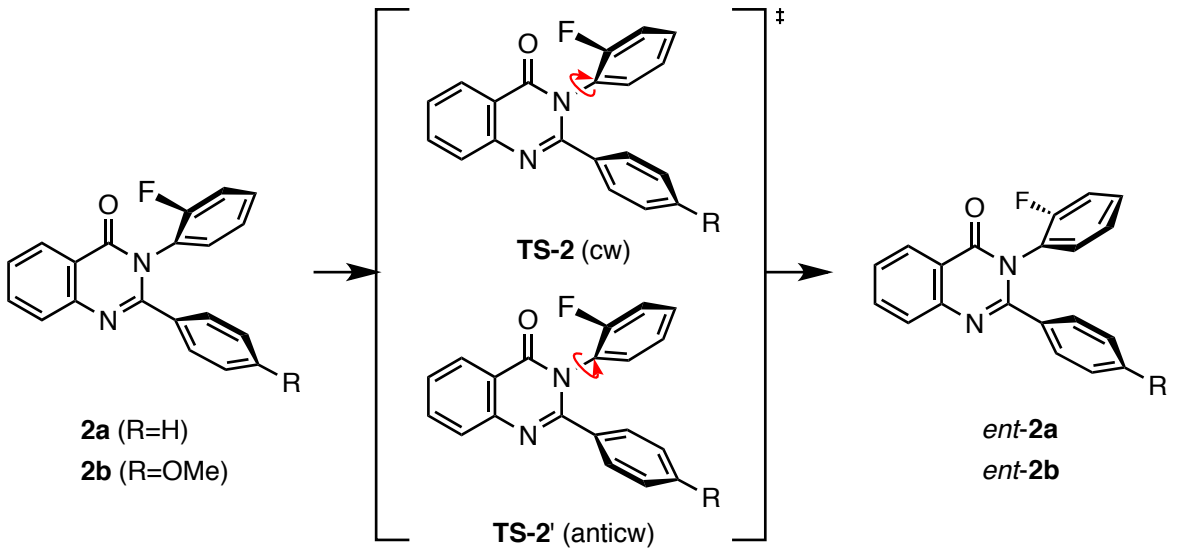
The summary of the calculations, the pictures of all stationary points, and cartesian coordinates are described in the following pages.



Scheme S1. The pathways for the axial rotation of **1b**.

	1b	**TS-1b** (cw)	**TS-1b'** (anticw)	Total of two TSs
$E_0 + E_{ZPE}$ (Hartree/particle)	-901.879838	-901.840094	-901.840476	
$E_0 + H_{corr}$ (Hartree/particle)	-901.878894	-901.83915	-901.839532	
$E_0 + G_{corr}$ (Hartree/particle)	-901.940636	-901.897241	-901.897473	
k (s^{-1})		6.86725×10^{-8}	8.77961×10^{-8}	1.56469×10^{-8}
ΔG (kcal mol^{-1})		27.23079645	27.08521413	26.74278773
Imaginary frequency (cm^{-1})		-52.2104	-64.3236	

Table S2. Energies, reaction rates, and imaginary frequencies (for TS) of each stationary point for quinazolinone **1b** described in Figure S2. Abbreviations are as follows: E_0, electronic energies; E_{ZPE}, zero-point energies; H_{corr}, thermal enthalpies; G_{corr}, thermal free energies; k, reaction rate constant; ΔG, relative free energy referred to **1b**; TS, transition state; cw, clockwise; anticw, anticlockwise.



Scheme S2. The pathways for the axial rotation of **2**.

	2a	**TS-2a** (cw)	**TS-2a'** (anticw)	Total of two TSs
$E_0 + E_{ZPE}$ (Hartree/particle)	-1054.274278	-1054.242083	-1054.241037	
$E_0 + H_{corr}$ (Hartree/particle)	-1054.273334	-1054.241139	-1054.240092	
$E_0 + G_{corr}$ (Hartree/particle)	-1054.339266	-1054.303885	-1054.302899	
k (s^{-1})		3.32858 x 10^{-4}	1.17170 x 10^{-4}	4.50028 x 10^{-4}
ΔG (kcal mol^{-1})		22.20193131	22.82065617	22.02320676
Imaginary frequency (cm^{-1})		-45.8038	-48.3404	

Table S3. Energies, reaction rates, and imaginary frequencies (for TS) of each stationary point for quinazolinone **2a** (R=H) described in Figure S3. Abbreviations are as follows: E_0, electronic energies; E_{ZPE}, zero-point energies; H_{corr}, thermal enthalpies; G_{corr}, thermal free energies; k, reaction rate constant; ΔG, relative free energy referred to **2a**; TS, transition state; cw, clockwise; anticw, anticlockwise.

	2b	**TS-2b** (cw)	**TS-2b'** (anticw)	Total of two TSs
$E_0 + E_{ZPE}$ (Hartree/particle)	-1168.766129	-1168.734244	-1168.732924	
$E_0 + H_{corr}$ (Hartree/particle)	-1168.765185	-1168.7333	-1168.73198	
$E_0 + G_{corr}$ (Hartree/particle)	-1168.837106	-1168.802194	-1168.80079	
k (s^{-1})		5.46944 x 10^{-4}	1.23672 x 10^{-4}	6.70616 x 10^{-4}
ΔG (kcal mol^{-1})		21.90762912	22.78865316	21.78682761
Imaginary frequency (cm^{-1})		-48.6694	-47.1963	

Table S4. Energies, reaction rates, and imaginary frequencies (for TS) of each stationary point for quinazolinone **2b** (R=OMe) described in Figure S4. Abbreviations are as follows: E_0, electronic energies; E_{ZPE}, zero-point energies; H_{corr}, thermal enthalpies; G_{corr}, thermal free energies; k, reaction rate constant; ΔG, relative free energy referred to **2b**; TS, transition state; cw, clockwise; anticw, anticlockwise.

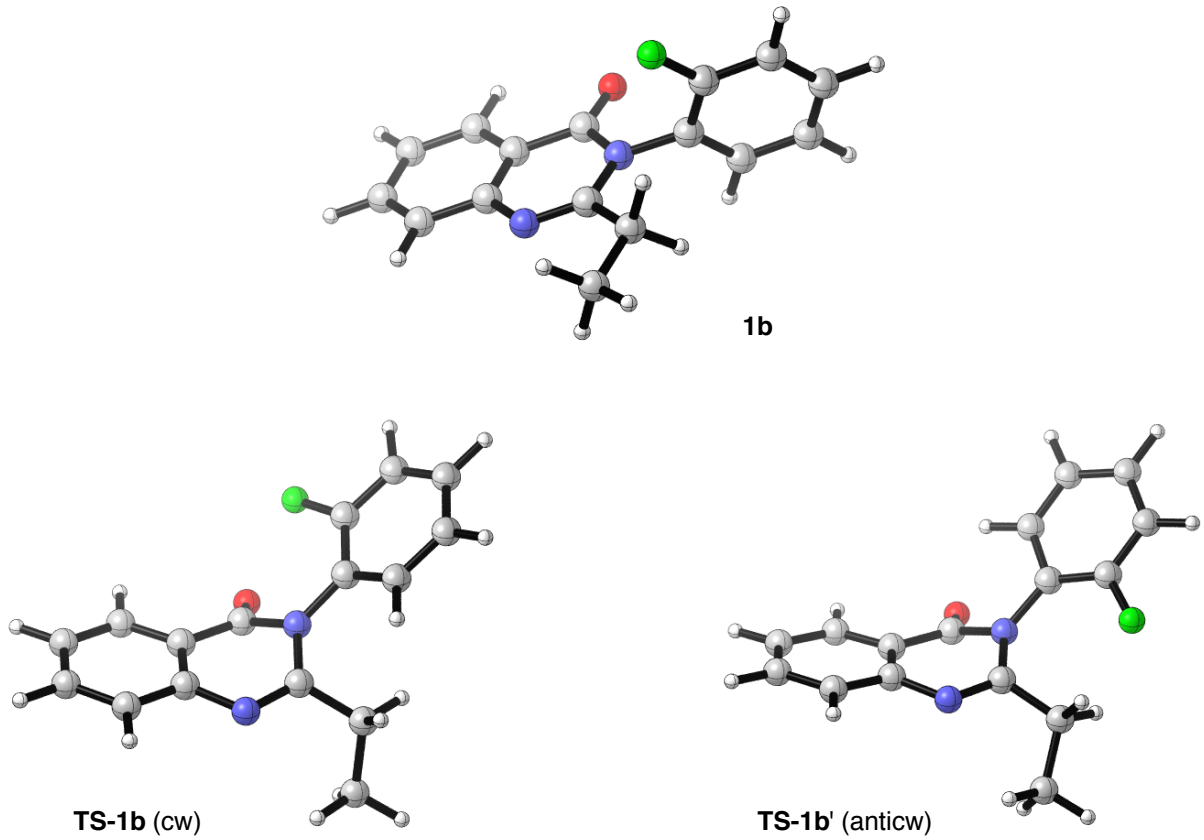


Figure S2. Stationary points for the rotation of **1b**.

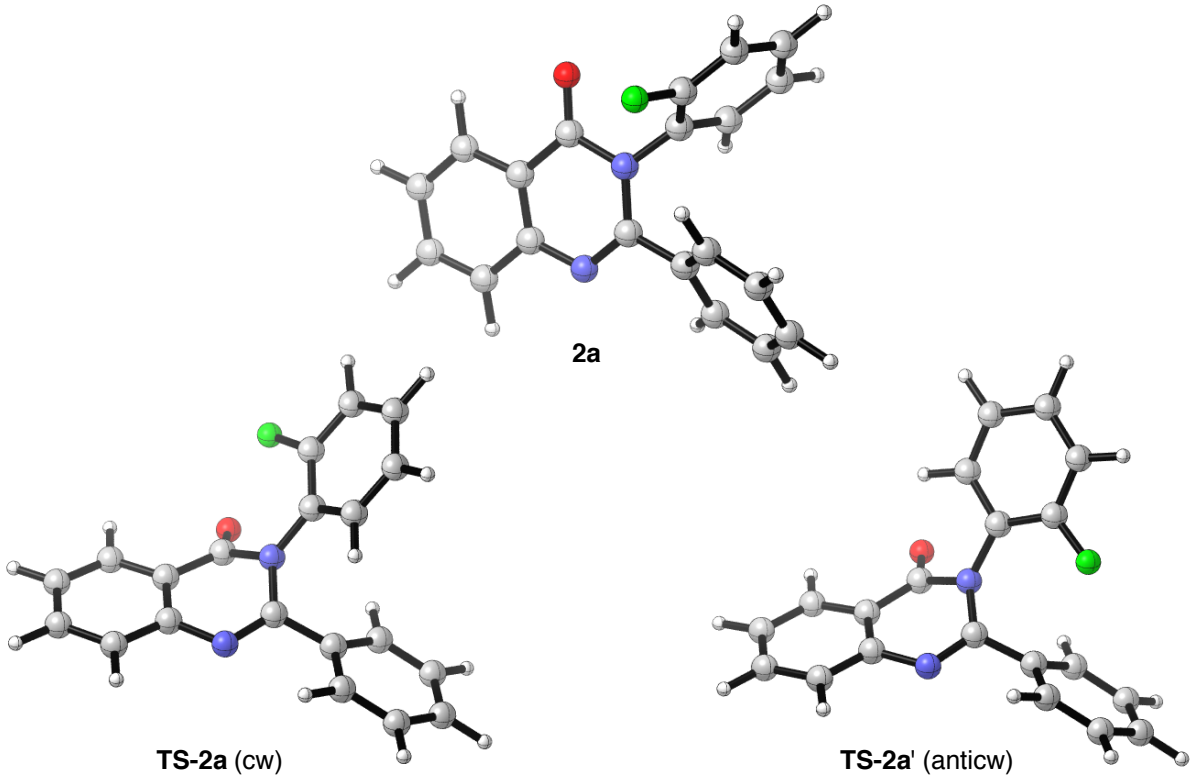


Figure S3. Stationary points for the rotation of **2a**.

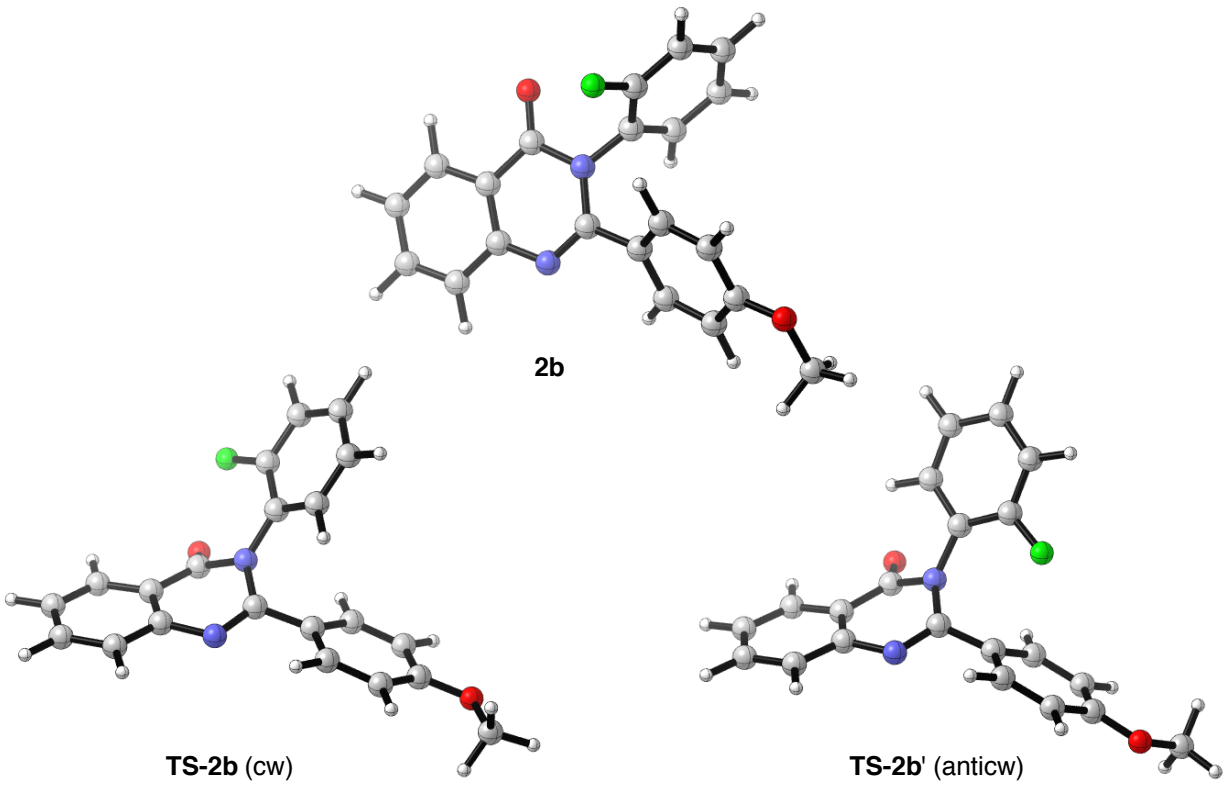
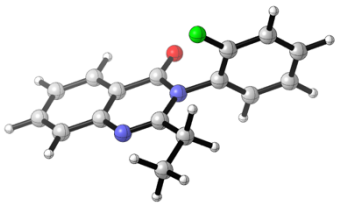


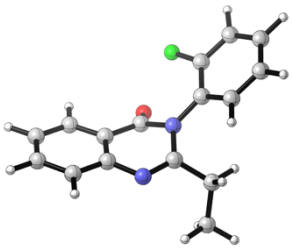
Figure S4. Stationary points for the rotation of **2b**.



1b

C	3.782987751	0.961180340	-0.361822883
C	2.411130231	0.646027630	-0.303560929
C	2.021655924	-0.610064922	0.207637155
C	2.985647936	-1.529516055	0.653248371
C	4.331333764	-1.204209955	0.589563591
C	4.726354480	0.046160905	0.079382972
H	4.071019894	1.929721197	-0.756694085
H	2.647904335	-2.484445237	1.041186752
H	5.080274364	-1.911094739	0.932364701
H	5.781913510	0.297428137	0.031312203
C	0.599750786	-0.948128364	0.272027205
N	1.489975582	1.581231710	-0.748345669
C	0.229843867	1.293875186	-0.695890577
C	-0.788337076	2.310620585	-1.161852539
H	-1.402557291	2.592853492	-0.297720833
H	-1.474954088	1.825435401	-1.865769027
O	0.140809774	-2.000130565	0.697422555
N	-0.257415237	0.071596117	-0.219669560
C	-1.667332378	-0.207579367	-0.169004139
C	-2.448253090	0.320357561	0.858998496
C	-2.274267977	-1.039538557	-1.111425620
C	-3.808062759	0.058620390	0.957731693
C	-3.637648723	-1.319115028	-1.027430673
H	-1.665699706	-1.465105595	-1.902235951
C	-4.401399676	-0.771154160	0.005937792
H	-4.374441758	0.498662679	1.770880128
H	-4.100879768	-1.966711989	-1.764194574
H	-5.462691262	-0.987663495	0.073794657
F	-1.862970593	1.133503494	1.763399224
C	-0.170831349	3.557496560	-1.793170324
H	-0.963966629	4.244451439	-2.102566701
H	0.483494549	4.074368316	-1.088129324

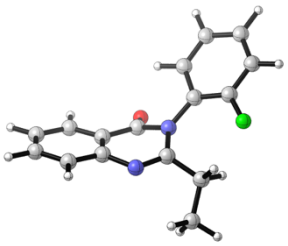
H	0.428725165	3.301504362	-2.670135418



TS-1b (cw)

C	-3.508862822	0.412900583	-1.167774157
C	-2.268357552	0.408833459	-0.510121305
C	-1.894304042	-0.716321193	0.249383918
C	-2.761314072	-1.809204610	0.382922627
C	-3.977384624	-1.803627200	-0.289393030
C	-4.344268291	-0.693324673	-1.067783785
H	-3.797032403	1.292396507	-1.734021999
H	-2.456110106	-2.650933567	0.995739514
H	-4.647188169	-2.653739989	-0.208195408
H	-5.300041888	-0.691586432	-1.583396354
C	-0.575787726	-0.702292468	0.898436029
N	-1.470210363	1.545367569	-0.502126845
C	-0.243644100	1.456966485	-0.112558858
C	0.493288031	2.761696696	0.167101669
H	0.761849738	3.246721191	-0.779013168
H	1.421660348	2.560421115	0.703728199
O	-0.263565908	-1.364999488	1.865341510
N	0.344186485	0.209539378	0.248276622
C	1.715426316	-0.105598044	-0.018341045
C	2.336097714	-1.340063487	0.280145203
C	2.514350431	0.791635359	-0.760446792
C	3.682916275	-1.577410978	0.022961324
C	3.855992151	0.553179282	-1.040083821
H	2.075009127	1.690497849	-1.161944984
C	4.465531970	-0.626724558	-0.620021272
H	4.077247708	-2.544924388	0.314299862
H	4.412965989	1.293329469	-1.605211998
H	5.512904546	-0.822781943	-0.822717944
F	1.654240207	-2.391836547	0.768070234

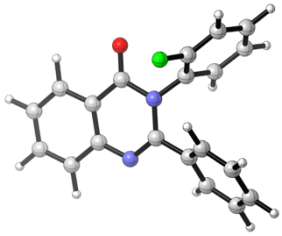
C	-0.377592122	3.727002468	0.987123264
H	0.172061447	4.655870411	1.167684913
H	-1.302466663	3.960388835	0.457702833
H	-0.639171632	3.292540908	1.956684042



TS-1b' (anticw)

C	3.500431188	0.667479479	1.180061484
C	2.255191364	0.546158956	0.540906057
C	1.987485127	-0.589863180	-0.241397886
C	2.964471779	-1.580387749	-0.422770941
C	4.188454059	-1.457536600	0.220866424
C	4.448642884	-0.336058119	1.028041400
H	3.702120997	1.556212340	1.768678460
H	2.733897261	-2.435914047	-1.048523245
H	4.946189833	-2.225093497	0.100126492
H	5.409927328	-0.244898175	1.525063077
C	0.647408221	-0.738976064	-0.814764615
N	1.345200180	1.587411985	0.563693163
C	0.129323703	1.412837471	0.167844960
C	-0.674703386	2.678614103	-0.092808514
H	-1.170400404	3.000312532	0.826228148
H	-1.462035797	2.462494134	-0.813912164
O	0.360187196	-1.566526649	-1.665069227
N	-0.351982566	0.119377516	-0.220729635
C	-1.645960545	-0.477223571	0.064973887
C	-2.810224148	0.192592935	0.482177998
C	-1.764623264	-1.887555373	0.047524036
C	-4.000417250	-0.460676858	0.792377126
C	-2.944008855	-2.551734958	0.358722790
H	-0.915379701	-2.487045659	-0.236217033
C	-4.086446736	-1.842573869	0.726267801
H	-4.838520107	0.157987988	1.094161669

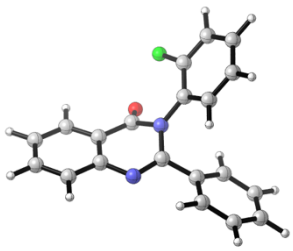
H	-2.957360281	-3.635857842	0.314744908
H	-5.015229168	-2.349898224	0.964144706
F	-2.856711566	1.534568212	0.641131693
C	0.208237426	3.820359014	-0.615852797
H	-0.415709912	4.698658841	-0.809715106
H	0.978651750	4.089500465	0.107681246
H	0.706001393	3.542816465	-1.549924361



2a

C	3.367182173	0.951700134	1.103676842
C	2.156874202	0.688324074	0.431581819
C	1.789971664	-0.652424397	0.185972286
C	2.615996923	1.706678269	0.609077059
C	3.802581860	1.431048842	1.270228914
C	4.176208472	-0.096345495	1.513810524
H	3.636242943	1.985793543	1.291258357
H	2.302810395	-2.724027510	0.400903371
H	4.444078850	-2.242105123	1.599939327
H	5.107054638	0.114654318	2.032013848
C	0.560935455	-0.935323031	-0.554916101
N	1.352328115	1.752203047	0.061622810
C	0.248995098	1.511354516	-0.577173041
O	0.162716359	-2.049396060	-0.865394273
N	-0.156780388	0.226637953	-0.954054733
C	-1.228205620	0.002675286	-1.888964382
C	-2.441084374	-0.529942198	-1.454572934
C	-1.054900171	0.253050971	-3.250382105
C	-3.478794668	-0.803992852	-2.333144608
C	-2.088316043	-0.009118784	-4.150137343
H	-0.106596171	0.652850259	-3.594330197
C	-3.294664733	-0.541468785	-3.691833765
H	-4.405181149	-1.214002162	-1.946753109

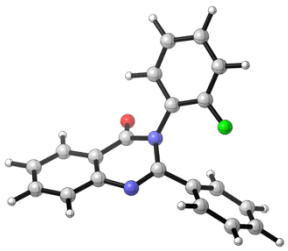
H	-1.946462480	0.193525110	-5.206354242
H	-4.098377259	-0.752438295	-4.389970158
F	-2.617442354	-0.738820135	-0.133716526
C	-0.636641348	2.668678641	-0.883969309
C	-1.996315588	2.663360586	-0.538436217
C	-0.072745373	3.824882822	-1.440953030
C	-2.779744144	3.793746212	-0.764928622
H	-2.431688114	1.788876346	-0.067707764
C	-0.863172871	4.947553067	-1.679295550
H	0.985345406	3.832902172	-1.679756436
C	-2.218714509	4.933887636	-1.343821631
H	-3.828357320	3.784623131	-0.483572198
H	-0.419892780	5.834303320	-2.122241378
H	-2.833501654	5.810469964	-1.525127856



TS-2a (cw)

C	2.936976004	2.320581920	-1.174450632
C	2.005708060	1.513758612	-0.500012396
C	2.468221630	0.478132515	0.336789967
C	3.841257515	0.272346841	0.525097951
C	4.753353599	1.062163112	-0.164589739
C	4.296657930	2.080747451	-1.017347091
H	2.571726856	3.128931084	-1.799135212
H	4.166935182	-0.516421123	1.195092113
H	5.818714287	0.897442789	-0.039162932
H	5.014794560	2.700356427	-1.546144545
C	1.471769256	-0.375820911	1.000704857
N	0.652005157	1.812419134	-0.550002108
C	-0.201111952	0.936347644	-0.126183413
O	1.669541047	-1.034577245	1.999271452
N	0.192872125	-0.356560888	0.317328998
C	-0.555221984	-1.537032517	-0.021933085

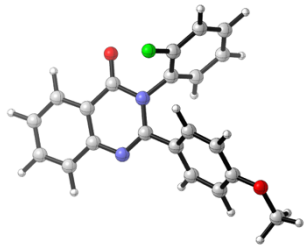
C	-0.197452127	-2.855188357	0.334932712
C	-1.672207643	-1.434249466	-0.878992336
C	-0.970295896	-3.957912400	-0.018952297
C	-2.439150813	-2.533206898	-1.249605789
H	-1.951447522	-0.470199983	-1.274799394
C	-2.108172696	-3.810279962	-0.800967259
H	-0.626674695	-4.929373076	0.319685842
H	-3.291620513	-2.379810411	-1.903182696
H	-2.701372562	-4.675496907	-1.077023640
F	0.941213245	-3.143808551	0.991238408
C	-1.603070725	1.389448688	0.072343080
C	-2.360035319	0.935597628	1.164175614
C	-2.142156668	2.364692408	-0.780928772
C	-3.635939528	1.446872893	1.392178050
H	-1.942239133	0.195932653	1.838859821
C	-3.422957131	2.863072106	-0.555444096
H	-1.544442512	2.723039658	-1.611550755
C	-4.173479397	2.406023569	0.531008100
H	-4.209158941	1.097878283	2.245606091
H	-3.835033965	3.611140556	-1.225943755
H	-5.170580732	2.798105723	0.707514883



TS-2a' (anticw)

C	3.536871546	1.215680721	0.968382492
C	2.378289396	0.712278571	0.351333857
C	2.478108925	-0.408645713	-0.496079223
C	3.724855318	-0.997065316	-0.756331618
C	4.861602691	-0.496899330	-0.135933161
C	4.760990887	0.604156600	0.732888748
H	3.451181955	2.089500023	1.605554063
H	3.770346986	-1.849775222	-1.425316907
H	5.828515986	-0.953516701	-0.321427254

H	5.654790513	0.992120021	1.212416923
C	1.246729141	-0.997844669	-1.031206665
N	1.178604285	1.391900845	0.454818519
C	0.082708524	0.835471672	0.047467112
O	1.215216178	-1.885226216	-1.868583314
N	0.041538906	-0.519844324	-0.397822833
C	-0.929977707	-1.524710227	-0.001775962
C	-2.259693744	-1.292264934	0.387662552
C	-0.501981283	-2.866180698	0.112171973
C	-3.114127104	-2.310185370	0.805433427
C	-1.345083661	-3.889759719	0.525528855
H	0.513786847	-3.122467740	-0.146883895
C	-2.669585342	-3.622351190	0.870886782
H	-4.124875797	-2.027670212	1.078963214
H	-0.952680398	-4.899736943	0.582996605
H	-3.338186043	-4.413920078	1.192126686
F	-2.795053999	-0.055072367	0.407736232
C	-1.056094656	1.756977240	-0.192618858
C	-1.324943937	2.789646053	0.715275745
C	-1.753531209	1.706616997	-1.409162371
C	-2.297242129	3.742776858	0.422611080
H	-0.765537502	2.835342285	1.643251861
C	-2.711749251	2.672983852	-1.705638558
H	-1.536062129	0.916294023	-2.120640881
C	-2.991725304	3.688588052	-0.788689745
H	-2.510269384	4.531882501	1.137525041
H	-3.239761876	2.633310073	-2.653619453
H	-3.744460632	4.436856581	-1.018442068

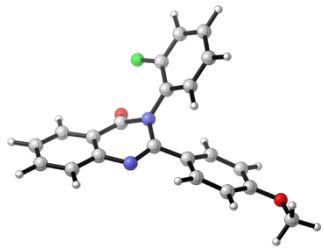


2b

C	3.806865875	1.619110805	-0.150352426
C	2.603403818	0.888972763	-0.074844167

C	2.665493453	-0.515943764	0.048700066
C	3.905512498	-1.173603006	0.102291908
C	5.079593565	-0.440791808	0.029188832
C	5.024729609	0.959528733	-0.100563436
H	3.747331785	2.698602130	-0.240065716
H	3.913541129	-2.254163884	0.195823474
H	6.040309277	-0.944105460	0.071192365
H	5.947189784	1.529982778	-0.158130170
C	1.423651791	-1.288020598	0.070061700
N	1.402831345	1.575909606	-0.087478103
C	0.292329544	0.903153148	-0.046448653
O	1.350780070	-2.508137663	0.124018350
N	0.245864089	-0.496857325	-0.033088743
C	-0.967924585	-1.227560440	-0.287851377
C	-1.589583034	-1.940519465	0.736175881
C	-1.509092808	-1.290963897	-1.572305586
C	-2.731835880	-2.696178296	0.516233651
C	-2.661346724	-2.039320976	-1.813774335
H	-1.019458366	-0.750006234	-2.375441698
C	-3.267136913	-2.744130118	-0.772074139
H	-3.181430377	-3.229506898	1.346313894
H	-3.077774967	-2.078209618	-2.814752589
H	-4.160243211	-3.332161723	-0.957701353
F	-1.085379793	-1.849057199	1.983803237
C	-0.978577995	1.666983578	0.023667703
C	-1.971617440	1.379379372	0.977725163
C	-1.155742498	2.774627937	-0.812446892
C	-3.109905466	2.164605956	1.072208437
H	-1.835284764	0.557604679	1.671547142
C	-2.303457970	3.562387603	-0.738102632
H	-0.380743453	3.020821629	-1.530280690
C	-3.290967349	3.256636295	0.207877179
H	-3.872935010	1.957728374	1.814924227
H	-2.414656561	4.404187412	-1.410413350
O	-4.447256811	3.954142766	0.372991320
C	-4.682246506	5.084042105	-0.460891900
H	-4.724435433	4.800350202	-1.519223414
H	-5.649714276	5.484194947	-0.156488354

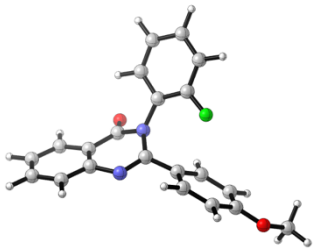
H	-3.912491793	5.852415872	-0.322404687



TS-2b (cw)

C	-3.343906213	-1.844125830	-1.065882135
C	-2.274071747	-1.179241416	-0.443096955
C	-2.537218643	-0.039756566	0.344655840
C	-3.850867436	0.408128591	0.536931794
C	-4.898427906	-0.244926650	-0.101273711
C	-4.639014029	-1.366784437	-0.906093924
H	-3.135305183	-2.732358382	-1.653049718
H	-4.023014793	1.273082718	1.168936980
H	-5.917199658	0.106483270	0.027134926
H	-5.462695047	-1.878408470	-1.395212686
C	-1.396243942	0.662500876	0.950410318
N	-0.994634049	-1.710389837	-0.489083214
C	0.006666851	-0.975407760	-0.120011745
O	-1.456641012	1.395225238	1.914866130
N	-0.154209355	0.390038805	0.252608760
C	0.762854496	1.409824697	-0.178526292
C	0.634169199	2.787634729	0.101179671
C	1.821427834	1.076304472	-1.051117685
C	1.561637786	3.727395436	-0.340543324
C	2.741881509	2.012370653	-1.509278525
H	1.929904235	0.056582316	-1.386521923
C	2.634852967	3.350968382	-1.137207652
H	1.389757137	4.760092169	-0.056781033
H	3.537620184	1.683620282	-2.169769888
H	3.349972508	4.090426434	-1.481511475
F	-0.420472924	3.296009610	0.765064175
C	1.313394343	-1.640851992	0.084137654
C	2.192843085	-1.236859312	1.106988913
C	1.648732958	-2.766313274	-0.680210857

C	3.365781971	-1.933159462	1.347840340
H	1.943562140	-0.381556874	1.725756905
C	2.831177687	-3.466996899	-0.455044460
H	0.967012497	-3.092479144	-1.457757203
C	3.699209509	-3.051493692	0.565061061
H	4.041371483	-1.635499149	2.142532157
H	3.064030498	-4.327517473	-1.069994640
O	4.874903838	-3.658606314	0.874501271
C	5.264159388	-4.807580347	0.127755292
H	5.394724985	-4.570244465	-0.934629463
H	6.219311892	-5.125759229	0.546067862
H	4.534374947	-5.619021462	0.231097841



TS-2b' (anticw)

C	3.294208656	-1.772782305	-1.171372299
C	2.253548152	-1.107177588	-0.498910856
C	2.568683407	-0.079976393	0.413742118
C	3.905638688	0.250846632	0.682079032
C	4.924285377	-0.408567493	0.007983077
C	4.612410243	-1.413614672	-0.925016446
H	3.042511964	-2.572745668	-1.859665301
H	4.114671686	1.036343624	1.400506018
H	5.960797466	-0.150611782	0.200174470
H	5.414062794	-1.927469458	-1.447330274
C	1.473199772	0.694081468	1.005105215
N	0.949949399	-1.549545435	-0.614215634
C	-0.021723719	-0.829346011	-0.147702957
O	1.612327710	1.523052436	1.890566702
N	0.195662926	0.486271809	0.367281232
C	-0.554837686	1.678397228	0.014974594
C	-1.904885790	1.734522311	-0.371102527
C	0.134389645	2.909950615	-0.051972901

C	-2.535844879	2.919718405	-0.743179052
C	-0.484586772	4.098095595	-0.418648997
H	1.181295190	2.945698654	0.207949510
C	-1.835900366	4.116935722	-0.763156505
H	-3.583045288	2.857746706	-1.018635878
H	0.103776926	5.009536793	-0.441131934
H	-2.331147105	5.038780733	-1.049099884
F	-2.681810552	0.634091043	-0.431310775
C	-1.307138179	-1.524575841	0.068427387
C	-1.753560259	-2.487498824	-0.852779652
C	-2.007964552	-1.369024323	1.270946852
C	-2.881417830	-3.247118707	-0.591167654
H	-1.202508395	-2.629383399	-1.775832389
C	-3.132179322	-2.141384619	1.554694215
H	-1.665423324	-0.642900543	2.001251246
C	-3.580046787	-3.081800035	0.617101348
H	-3.242934971	-3.981638689	-1.302982748
H	-3.644121440	-2.005825130	2.499354213
O	-4.669104414	-3.880519645	0.782419265
C	-5.422492513	-3.759527574	1.984357801
H	-6.238555255	-4.477663282	1.899445445
H	-4.816139966	-4.003182664	2.864828191
H	-5.837355414	-2.751033724	2.098492551

References in Supporting Information

1) Gaussian 09, Revision D.01, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Keith, T.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J. and Fox, D. J. Gaussian, Inc., Wallingford CT, 2013.
2) (a) Lee, C. T.; Yang, W. T.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785. b) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648. c) Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098.
3) Tomasi, J.; Mennucci, B.; Cammi, R. *Chem. Rev.* **2005**, *105*, 2999.
4) CYLview, 1.0b; Legault, C. Y., Université de Sherbrooke, 2009 (http://www.cylview.org).