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Supporting Information

Contents

1. Basis set convergence

Table 1 shows the optimised energies, in atomic units, for 2-bromothiophene at the B3LYP and CCSD levels of theory.

Table 1. Basis set convergence

Theory	Basis Set	Energy / A.U. (Hartree.)
B3LYP	3-21G	-3111.354
	6-31G(d)	-3124.087
	6-31+G(d)	-3124.116
	6-31+G(d,p)	-3124.121
	6-311G(d)	-3126.59
	6-311G(d,p)	-3126.593
	6-311+G(d,p)	-3126.596
	6-311++G(d,p)	-3126.596
	cc-pVDZ	-3126.566
	cc-pVTZ	-3126.706
	AUG-cc-pVDZ	-3126.579
	AUG-cc-pVTZ	-3126.708
CCSD	STO-3G	-3089.494
	3-21G	-3108.400
	6-31G(d)	-3121.360
	6-31+G(d)	-3121.393
	6-31+G(d,p)	-3121.417
	6-311G(d)	-3123.932
	6-311G(d,p)	-3123.955
	6-311+G(d,p)	-3123.963
	6-311++G(d,p)	-3123.963
	cc-pVDZ	-3123.923
	cc-pVTZ	-3124.294
	AUG-cc-pVDZ	-3123.971

2. Nucleophilic Attack of 2-bromothiophene

Chemical intuition would suggest that the proton at position 3 would be the most easily removed. This is confirmed by calculating the energies of the anions (Table 3). The free Gibbs energy of anion **4** is more negative and hence more stable than **5**, suggesting preferential lithitation at this position.

Table 3. Internal and free Gibbs energies in THF[a]		
Anion	**U / a.u.**	**ΔG / a.u.**
4	-3126.067706	-3126.055707
5	-3126.062513	-3126.050591
[a] Calculated using IEFPCM at the B3LYP/6-311++G(d,p) level.		

Additionally, pKa values were calculated by evaluating the equilibrium constant (1)

$$K_a = \frac{[C_4H_2BrS^-][H^+]}{[C_4H_3BrS]} \qquad (1)$$

using the free-energy change for the reaction (2)

$$C_4H_3BrS \rightleftarrows C_4H_2BrS^- + H^+ . \qquad (2)$$

Standard frequency calculations (B3LYP/cc-pVTZ) were employed to estimate the enthalpic and entropic contributions to the free energies of 2-bromo-thiophene and its deprotonated anion in the gas phase and in solution (the later using the standard integral equation formalism variant of the polarizable continuum model). The gas phase reaction free energy change was corrected to account for the difference in the definition of the standard state in the gas phase and solution (1 atm versus 1 M) by adding $RT\ln(24.46)$ and the corrected $\Delta_r G_g$ was then added to the solvation energy difference between reactants and products to obtain a measure of the free energy change for deprotonation in the solution phase. The difficulty with this procedure is that the solvation energy of H^+ cannot be calculated using the IEFPCM since the proton has no electrons. The standard solution to this problem is to use the experimental value, but we have been unable to find a value for $\Delta_{sol}G(H^+)$ in THF. The generally accepted value for $\Delta_{sol}G(H^+)$ in water is -1112.3 kJ/mol[23]. Using this value one obtains pK_a values of 46, 52 and 50 for deprotonation of 2-bromo-thiophene at the 3, 4 and 5 positions respectively but these values are unlikely to be a good reflection of reality since THF and water are as chalk is to cheese.

An alternative way of proceeding is to calculate the dissociation constant for a substance whose value is experimentally known in THF and then adjusting $\Delta_{sol}G(H^+)$ in THF to obtain agreement with experiment. Using the value for the pK_a of aniline in THF obtained spectroscopically by Garrido and co-workers[24], we estimate $\Delta_{sol}G(H^+)$ in THF to be -1301 kJ mol^{-1} and obtain pK_a values of 13, 19 and 17 for deprotonation of 2-bromo-thiophene at the 3, 4 and 5 positions. As a check on the validity of this approach we then calculated the pK_a of piperazine and obtained 22, which is to be compared with the experimental value of 19. The absolute accuracy of these calculations is therefore doubtful and further complicated by the low permittivity and aprotic nature of THF. Calculations on $LiNH_2$ give a similar conclusion. We calculate $\Delta_{sol}G(Li^+)$ in THF to be - 446 kJ mol^{-1} which results in a dissociation pK of

lithium amide of 35. Our value for the solvation energy of Li^+ is considerably smaller than the value of -566.4 kJ mol^{-1} calculated by Westphal and Pliego in another aprotic solvent, DMSO[25]. Using $\Delta_{sol}G(Li^+)$ DMSO reduces the calculated pK of lithium amide to 14, and the truth probably somewhere in between. Despite the shortcomings in the calculations, these considerations nonetheless suggest lithiation at position 3 should be favoured over position 4.

Atomic charges were calculated. All the methods except for MK show the H^3 atom is relatively more positive than H^4 and thus in the model HD reaction the H^3 atom would be expected to be attacked by the lithium amide preferentially. All methods show that the H^3 atom is more positive than the bromine atom (Br) thus the bromine is unlikely to be attacked.

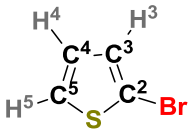


Table 4. Atomic charges (eV) with various methods[a]

Atom	Mulliken	MK	NBO	AIM
S	-0.18	0.10	0.45	0.25
C^2	-0.078	-0.21	0.35	-0.26
C^3	0.16	0.083	0.28	0.030
C^4	-0.56	-0.25	-0.24	0.013
C^5	0.13	-0.18	-0.39	-0.20
H^3	0.19	0.099	0.23	0.055
H^4	0.15	0.17	0.22	0.044
H^5	0.25	0.19	0.23	0.071
Br	-0.051	0.0047	0.13	-0.011

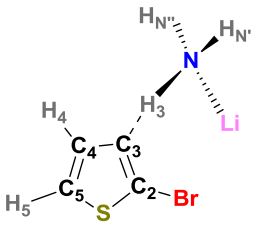
[a] Calculated at the B3LYP/6-311++G(d,p) level.

3. Geometries of the Transition States

3.1 Transition State 1a

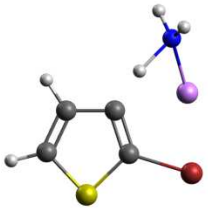
Table 5. Structural data for Transition state 1a

Selected Structural Data



Bond Length / Å		Bond Angle / °	
$S-C_2$	1.751	$S-C_2-C_3$	116.2
C_2-C_3	1.357	C_3-C_2-Br	125.2
C_3-C_4	1.441	$C_2-C_3-C_4$	107.9
C_4-C_5	1.366	$C_3-C_4-C_5$	115.3
C_5-S	1.739	$C_3-C_4-H_4$	122.6
C_2-Br	1.945	C_4-C_5-S	111.8
C_3-H_3	1.389	$C_4-C_5-H_5$	128.8
C_4-H_4	1.084	$C_2-C_3-H_3$	129.7
C_5-H_5	1.081	$H_3-N-H_{N''}$	110.7
H_3-N	1.368	$H_3-N-H_{N'}$	113.4
$N-H_{N''}$	1.017	$H_{N''}-N-H_{N'}$	105.9
$N-H_{N'}$	1.017	H_3-N-Li	65.9
N-Li	1.863	$H_4-C_4-C_3-H_3$	3.0

Cartesian Coordinates



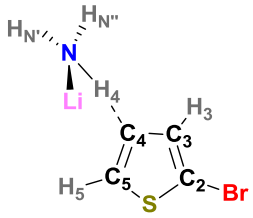
Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-2.297853	3.979407	0.446345
2	6	0	-3.053674	2.856797	0.262869
3	6	0	-0.918034	3.865575	0.046879
4	6	0	-0.727227	2.612762	-0.438077
5	16	0	-2.127218	1.561025	-0.434623
6	1	0	-2.709583	4.886011	0.875240
7	1	0	-4.096787	2.696677	0.495240
8	1	0	-0.001336	4.891033	0.239880
9	35	0	0.947874	1.930859	-1.153657
10	1	0	0.638545	6.744513	0.028238
11	3	0	0.924254	4.501841	-1.260418
12	7	0	1.008611	5.798370	0.074429
13	1	0	1.679856	5.799068	0.838664

Calculated at the B3LYP/6-311++G(d,p) level, in vacuum

3.2 Transition State 1b

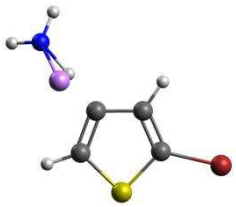
Table 6. Selected structural data for transition state 1b

Selected Structural Data



Bond Length / Å		Bond Angle / °	
$S-C_2$	1.738	$S-C_2-C_3$	112.6
C_2-C_3	1.365	C_3-C_2-Br	127.0
C_3-C_4	1.440	$C_2-C_3-C_4$	113.7
C_4-C_5	1.374	$C_3-C_4-C_5$	110.2
C_5-S	1.753	$C_3-C_4-H_4$	125.8
C_2-Br	1.899	C_4-C_5-S	113.8
C_3-H_3	1.083	$C_4-C_5-H_5$	128.7
C_4-H_4	1.419	$C_2-C_3-H_3$	122.0
C_5-H_5	1.083	$H_4-N-H_{N'}$	112.6
H_4-N	1.354	$H_4-N-H_{N''}$	111.4
$N-H_{N'}$	1.017	$H_6-N-H_{N''}$	105.8
$N-H_{N''}$	1.017	H_4-N-Li	62.4
N-Li	1.862	$H_4-C_4-C_3-H_3$	9.8

Cartesian Coordinates



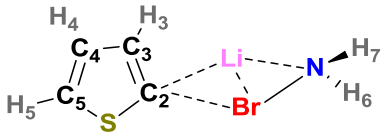
Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-4.593678	2.997609	0.928694
2	6	0	-3.692823	3.540150	0.045109
3	6	0	-2.364889	3.496595	0.599668
4	6	0	-2.306704	2.929206	1.840260
5	16	0	-3.865266	2.414722	2.412797
6	35	0	-0.757032	2.669684	2.906912
7	1	0	-4.023423	3.870312	-1.294786
8	1	0	-1.479157	3.858267	0.091254
9	1	0	-5.657844	2.841546	0.800487
10	1	0	-3.783304	4.754598	-3.035575
11	7	0	-4.508186	4.572521	-2.345853
12	3	0	-4.625680	5.351990	-0.658553
13	1	0	-5.243545	4.076041	-2.842585

Calculated at the B3LYP/6-311++G(d,p) level, in vacuum

3.3 Transition State 1c

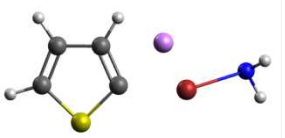
Table 7. Selected structural data for transition state 1c

Selected Structural Data



Bond Length / Å		Bond Angle / °	
$S-C_2$	1.733	$S-C_2-C_3$	109.2
C_2-C_3	1.383	C_3-C_2-Br	117.4
C_3-C_4	1.437	$C_2-C_3-C_4$	114.3
C_4-C_5	1.364	$C_3-C_4-C_5$	112.5
C_5-S	1.745	$C_3-C_4-H_4$	124.1
C_2-Br	2.214	C_4-C_5-S	110.7
C_2-Li	2.610	$C_4-C_5-H_5$	128.4
C_3-H_3	1.090	$C_2-C_3-H_3$	122.6
C_4-H_4	1.083	C_2-Br-N	152.8
C_5-H_5	1.080	$Br-N-H_7$	107.8
$N-H_6$	1.021	$Br-N-H_6$	108.0
$N-H_7$	1.021	Br-N-Li	50.0
N-Li	2.880	C_2-Li-N	102.7
N-Br	2.200	$C_2-Li-Br$	53.7
Li-Br	2.235	Li-Br-N	81.0

Cartesian Coordinates



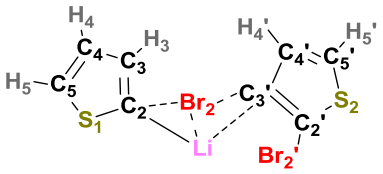
Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-2.422290	3.444021	0.024562
2	6	0	-2.926896	2.193403	-0.179716
3	6	0	-1.026198	3.424777	0.362608
4	6	0	-0.477260	2.158243	0.444010
5	16	0	-1.689720	0.983986	0.049231
6	1	0	-0.480317	4.320494	0.657265
7	1	0	-3.017872	4.346187	-0.045600
8	1	0	-3.938571	1.911737	-0.432361
9	35	0	1.726488	1.994229	0.314939
10	1	0	4.266081	2.891677	0.275109
11	3	0	1.050477	3.500719	-1.191314
12	7	0	3.687090	2.568875	-0.501327
13	1	0	4.147728	1.723893	-0.842016

Calculated at the B3LYP/6-311++G(d,p) level, in vacuum

3.4 Transition State 2 (Four Centre)

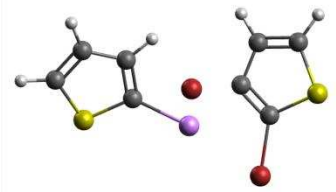
Table 8. Selected structural data for transition state 2

Selected Structural Data



Bond Length / Å		Bond Angle / °	
S_1-C_2	1.741	S_1-C_2-C_3	109.8
C_2-C_3	1.388	C_3-C_2-Br_2	110.1
C_3-C_4	1.422	C_3-C_2-Li	114.1
C_4-C_5	1.373	C_2-C_3-C_4	113.8
C_5-S_1	1.740	C_3-C_4-C_5	112.5
C_2-Br_2	2.657	C_2-C_3-H_3	122.8
C_2-Li	1.996	C_3-C_4-H_4	124.2
C_3-H_3	1.084	C_4-C_5-S	111.3
C_4-H_4	1.083	C_4-C_5-H_5	127.9
C_5-H_5	1.081	C_2-Br_2-C_3'	81.2
Br_2-Li	2.541	C_2-Li-C_3'	114.7
Br_2-C_3'	2.612	Br_2-C_2-Li	64.4
Li-C_3'	2.074	Br_2-C_3'-Li	64.5
S_2-C_2'	1.754	S_2-C_2'-C_3'	113.1
C_2'-C_3'	1.355	S_2-C_2'-Br_2'	120.8
C_3'-C_4'	1.429	C_2'-C_3'-C_4'	111.8
C_4'-C_5'	1.364	C_3'-C_4'-C_5'	112.9
C_5'-S_2	1.743	C_3'-C_4'-H_4'	123.8
C_2'-Br_2'	1.914	C_4'-C_5'-S_2	112.4
C_4'-H_4'	1.082	C_5'-S_2-C_2'	89.6
C_5'-H_5'	1.081	S_2-C_5'-H_5'	119.1

Cartesian Coordinates



Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
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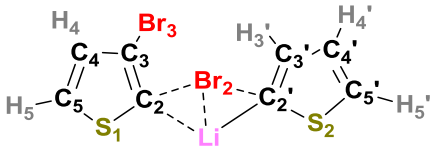
3	16	0	3.114636	0.100711	-1.778103
4	16	0	-0.184560	2.923810	4.402611
5	6	0	1.627283	0.830833	-2.319190
6	6	0	0.816751	1.190982	-1.282567
7	6	0	1.390633	0.911656	-0.003596
8	6	0	2.590644	0.291626	-0.114663
9	6	0	0.268166	2.615544	2.750527
10	6	0	-0.154086	3.663113	1.944382
11	6	0	-0.788208	4.508354	4.013662
12	6	0	-0.689164	4.763418	2.668559
13	3	0	1.727959	1.512154	1.952842
14	1	0	1.452979	0.944635	-3.379604
15	1	0	-0.158954	1.637721	-1.420197
16	1	0	-0.084773	3.635871	0.863343
17	1	0	-1.128898	5.174855	4.793030
18	1	0	-1.002120	5.695805	2.215517

Calculated at the B3LYP/6-311++G(d,p) level, in vacuum

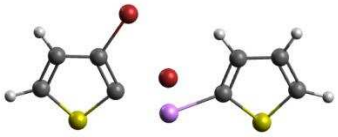
3.5 Transition State 3 (Four Centre)

Table 9. Selected structural data for transition state 3

Selected Structural Data



Cartesian Coordinates



Bond Length / Å		Bond Angle / °	
S_1-C_2	1.748	S_1-C_2-C_3	108.0
C_2-C_3	1.384	C_2-C_3-Br_3	123.4
C_3-C_4	1.420	C_2-C_3-C_4	115.8
C_4-C_5	1.370	C_3-C_4-C_5	111.5
C_5-S_1	1.736	C_4-C_5-S_1	111.5
C_2-Br_2	2.645	C_3-C_4-H_4	124.1
C_2-Li	2.002	C_5-S_1-C_2	93.0
C_3-Br_3	1.908	C_4-C_5-H_5	127.7
C_4-H_4	1.081	C_3-C_2-Br_2	115.3
C_5-H_5	1.080	C_2-Br_2-C_2'	84.7
Br_2-Li	2.621	C_2-Li-C_2'	132.1
Br_2-C_2'	2.768	Br_2-C_2-Li	67.0
Li-C_2'	1.991	Br_2-C_2'-Li	64.4
S_2-C_2'	1.745	Br_2-C_2'-C_3'	111.6
C_2'-C_3'	1.388	S_2-C_2'-C_3'	109.7
C_3'-C_4'	1.419	C_2'-C_3'-C_4'	113.7
C_4'-C_5'	1.375	C_3'-C_4'-C_5'	112.7
C_5'-S_2	1.737	C_3'-C_4'-H_4'	124.1
C_3'-H_3'	1.083	C_4'-C_5'-S_2	111.3
C_4'-H_4'	1.083	C_5'-S_2-C_2'	92.3
C_5'-H_5'	1.081	S_2-C_5'-H_5'	120.7

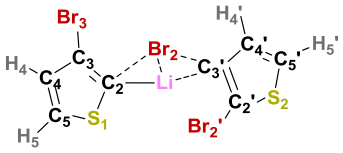
Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	35	0	0.982705	-0.918235	-3.260416
2	35	0	-1.355194	-4.087471	-2.235886
3	16	0	2.956495	-3.918123	-3.138815
4	16	0	0.909638	1.141325	-0.122156
5	6	0	2.253764	-5.405047	-3.694497
6	6	0	0.921005	-5.476666	-3.384504
7	6	0	0.480093	-4.307094	-2.710704
8	6	0	1.460968	-3.377727	-2.411835
9	6	0	0.301009	-0.414967	-0.625118
10	6	0	-1.073454	-0.463042	-0.435461
11	6	0	-1.594378	0.664176	0.251174
12	6	0	-0.643222	1.629623	0.482582
13	3	0	1.421462	-2.032720	-0.929537
14	1	0	2.863846	-6.162350	-4.165411
15	1	0	0.282948	-6.316805	-3.621485
16	1	0	-1.683477	-1.287504	-0.782310
17	1	0	-0.757169	2.557688	1.024116
18	1	0	-2.627559	0.763376	0.559538

Calculated at the B3LYP/6-311++G(d,p) level, in vacuum

3.6 Transition State 4 (Four Centre)

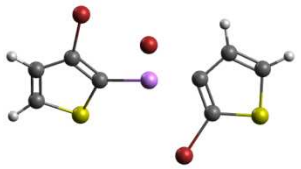
Table 10. Selected structural data for transition state 4

Selected Structural Data



Bond Length / Å		Bond Angle / °	
S_1-C_2	1.747	S_1-C_2-C_3	108.1
C_2-C_3	1.383	C_2-C_3- Br_3	122.2
C_3-C_4	1.416	C_2-C_3-C_4	115.9
C_4-C_5	1.373	C_3-C_4-C_5	111.3
C_5-S_1	1.733	C_3-C_4-H_4	124.3
C_3-Br_3	1.909	C_4-C_5-S_1	111.7
C_4-H_4	1.081	C_4-C_5-H_5	127.5
C_5-H_5	1.081	C_3-C_2-Li	122.1
C_2-Br_2	2.635	C_2-Br_2-C_3'	87.1
C_2-Li	1.990	C_2-Li-C_3'	132.9
Br_2-Li	2.606	Br_2-C_2-Li	66.9
Br_2-C_3'	2.701	Br_2-C_3'-Li	65.2
Li-C_3'	2.019	S_2-C_2'-C_3'	112.4
S_2-C_2'	1.753	S_2-C_2'-Br_2'	120.0
C_2'-C_3'	1.361	C_2'-C_3'-C_4'	112.1
C_3'-C_4'	1.432	C_3'-C_4'-C_5'	112.9
C_4'-C_5'	1.362	C_3'-C_4'-H_4'	123.7
C_5'-S_2	1.746	C_4'-C_5'-S_2	112.2
C_2'-Br_2'	1.898	C_5'-S_2-C_2'	90.1
C_4'-H_4'	1.082	S_2-C_5'-H_5'	119.3
C_5'-H_5'	1.081	Li-C_3'-C_2'	111.1

Cartesian Coordinates



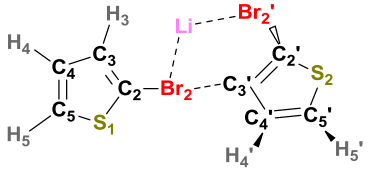
Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	35	0	-0.148085	-1.398314	-3.925373
2	35	0	-0.814673	-4.874524	-2.113245
3	16	0	2.998151	-2.792548	-2.830581
4	16	0	-0.236040	2.754160	-1.151276
5	6	0	3.197778	-4.508972	-2.964172
6	6	0	2.024777	-5.176973	-2.711586
7	6	0	0.970225	-4.274362	-2.429322
8	6	0	1.319452	-2.937194	-2.369476
9	6	0	0.493583	1.192853	-1.469903
10	6	0	-0.427126	0.246817	-1.801088
11	6	0	-1.746122	0.792681	-1.909232
12	6	0	-1.804816	2.109336	-1.564152
13	35	0	2.370893	0.969819	-1.303170
14	1	0	4.169431	-4.938137	-3.162345
15	1	0	1.921799	-6.253368	-2.714435
16	3	0	0.240529	-1.606101	-1.356888
17	1	0	-2.610927	0.217447	-2.212756
18	1	0	-2.672179	2.751081	-1.504527

Calculated at the B3LYP/6-311++G(d,p) level, in vacuum

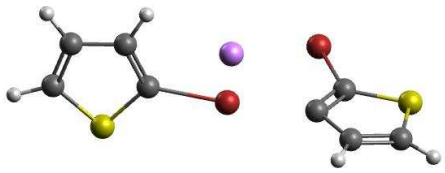
3.7 Transition State 2 (S_N2 Type)

Table 11. Selected structural data for transition state 2

Selected Structural Data



Cartesian Coordinates



Bond Length / Å		Bond Angle / °	
S_1-C_2	1.741	S_1-C_2-C_3	110.4
C_2-C_3	1.371	C_2-C_3- H_3	122.9
C_3-C_4	1.432	C_2-C_3-C_4	113.5
C_4-C_5	1.366	C_3-C_4-C_5	112.9
C_5-S_1	1.741	C_3-C_4-H_4	123.9
C_2-Br_2	2.111	C_4-C_5-S_1	111.0
C_4-H_4	1.083	C_4-C_5-H_5	128.3
C_5-H_5	1.080	C_3-C_2-Br_2	125.9
C_3-H_3	1.084	C_2-Br_2-C_3'	170.8
Br_2-Li	2.313	C_2-Br_2-Li	89.7
Br_2-C_3'	2.375	Br_2-C_3'-C_2'	128.7
Li-Br_2'	2.510	Br_2-Li-Br_2'	113.0
S_2-C_2'	1.759	S_2-C_2'-C_3'	116.3
C_2'-C_3'	1.346	S_2-C_2'-Br_2'	116.8
C_3'-C_4'	1.439	C_2'-C_3'-C_4'	108.2
C_4'-C_5'	1.367	C_3'-C_4'-C_5'	115.2
C_5'-S_2	1.740	C_3'-C_4'-H_4'	122.8
C_2'-Br_2'	1.965	C_4'-C_5'-S_2	111.8
C_4'-H_4'	1.085	C_5'-S_2-C_2'	88.5
C_5'-H_5'	1.082	S_2-C_5'-H_5'	119.4
		Li-Br_2'-C_2'	87.8

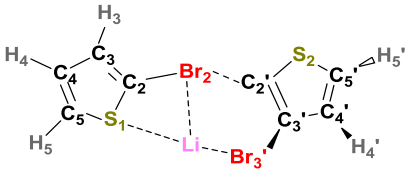
Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	35	0	0.561253	2.315554	0.726457
2	35	0	0.494317	-1.694971	1.030857
3	16	0	1.869014	-1.753851	-1.828665
4	16	0	0.856978	4.553597	3.266798
5	6	0	2.252987	-0.296711	-2.699359
6	6	0	1.894687	0.822158	-2.000107
7	6	0	1.286433	0.576709	-0.719269
8	6	0	1.225389	-0.754315	-0.532063
9	6	0	-0.171173	3.610639	2.224542
10	6	0	-1.483540	3.746967	2.597705
11	6	0	-0.497703	5.130257	4.195581
12	6	0	-1.670996	4.617473	3.719498
13	3	0	0.354859	0.530785	2.183222
14	1	0	2.718541	-0.366779	-3.673151
15	1	0	2.060187	1.820386	-2.390608
16	1	0	-2.298218	3.259785	2.073690
17	1	0	-0.349853	5.811323	5.021271
18	1	0	-2.638425	4.853942	4.146036

Calculated at the B3LYP-D2/6-311++G(d,p) level, in vacuum

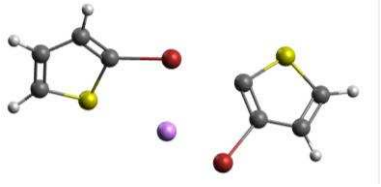
3.8 Transition State 3 (S_N2 Type)

Table 12. Selected structural data for transition state3

Selected Structural Data



Cartesian Coordinates



Bond Length / Å		Bond Angle / °	
S_1-C_2	1.751	S_1-C_2-C_3	110.7
C_2-C_3	1.363	C_2-C_3-H_3	123.1
C_3-C_4	1.436	C_2-C_3-C_4	113.0
C_4-C_5	1.363	C_3-C_4-C_5	113.7
C_5-S_1	1.746	C_3-C_4-H_4	123.5
C_2-Br_1	2.027	C_4-C_5-S_1	110.4
C_4-H_4	1.083	C_4-C_5-H_5	128.8
C_5-H_5	1.080	C_3-C_2-Br_2	133.5
C_3-H_3	1.083	C_2-Br_2-C_2'	162.7
Br_2-Li	2.367	C_2-Br_2-Li	87.2
Br_2-C_2'	2.489	Br_2-C_2'-C_3'	129.5
S_1-Li	2.922	Br_2-Li-Br_3'	112.1
Li-Br_3'	2.487	S_2-C_2'-C_3'	104.9
S_2-C_2'	1.736	S_2-C_2'-Br_2	125.5
C_2'-C_3'	1.356	C_2'-C_3'-C_4'	120.2
C_3'-C_4'	1.430	C_3'-C_4'-C_5'	109.7
C_4'-C_5'	1.364	C_3'-C_4'-H_4'	125.1
C_5'-S_2	1.749	C_4'-C_5'-S_2	110.0
C_3'-Br_3'	2.001	C_5'-S_2-C_2'	95.3
C_4'-H_4'	1.082	S_2-C_5'-H_5'	122.0
C_5'-H_5'	1.081	C_2'-C_3'-Br_3'	122.6

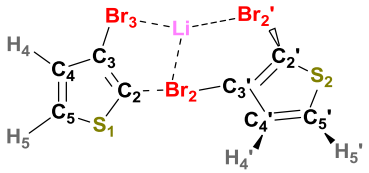
Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	35	0	0.358746	-1.903974	0.588510
2	35	0	-0.912301	1.822272	-0.250387
3	16	0	-3.405371	-1.786081	0.364450
4	16	0	3.112268	-1.648323	-0.964409
5	6	0	-4.409166	-0.411347	-0.035854
6	6	0	-3.632398	0.694515	-0.223965
7	6	0	-1.906464	-0.912728	0.299100
8	6	0	-2.256788	0.356931	-0.024736
9	6	0	3.303883	-2.488120	1.458588
10	6	0	2.361389	-2.210619	0.514345
11	6	0	4.644168	-2.260027	0.997422
12	6	0	4.711790	-1.776791	-0.275591
13	3	0	0.717526	0.012662	-0.752615
14	1	0	-5.485140	-0.488670	-0.105034
15	1	0	-3.999688	1.678939	-0.481538
16	1	0	3.059353	-2.826027	2.457577
17	1	0	5.524673	-2.451005	1.598970
18	1	0	5.585462	-1.548388	-0.867278

Calculated at the B3LYP-D2/6-311++G(d,p) level, in vacuum

3.9 Transition State 4 (S_N2 Type)

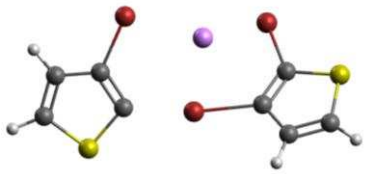
Table 13. Selected structural data for transition state 4

Selected Structural Data



Bond Length / Å		Bond Angle / °	
S_1-C_2	1.733	S_1-C_2-C_3	106.9
C_2-C_3	1.357	C_2-C_3-Br_3	123.4
C_3-C_4	1.429	C_2-C_3-C_4	118.1
C_4-C_5	1.364	C_3-C_4-C_5	110.3
C_5-S_1	1.745	C_3-C_4-H_4	124.8
C_2-Br_2	2.235	C_4-C_5-S_1	110.6
C_4-H_4	1.082	C_4-C_5-H_5	128.0
C_5-H_5	1.081	C_3-C_2-Br_2	125.7
C_3-Br_3	1.969	C_2-Br_2-C_3'	170.3
Br_2-Li	2.377	C_2-Br_2-Li	94.0
Br_3-Li	2.566	Br_2-C_3'-C_2'	126.9
Br_2-C_3'	2.203	Br_2-Li-Br_2'	101.9
Li-Br_2'	2.377	Br_3-Li-Br_2'	138.5
S_2-C_2'	1.754	S_2-C_2'-C_3'	114.6
C_2'-C_3'	1.355	S_2-C_2'-Br_2'	118.6
C_3'-C_4'	1.434	C_2'-C_3'-C_4'	109.7
C_4'-C_5'	1.366	C_3'-C_4'-C_5'	114.4
C_5'-S_2	1.738	C_3'-C_4'-H_4'	122.9
$_2$'-Br_2'	1.936	C_4'-C_5'-S_2	112.0
C_4'-H_4'	1.083	C_5'-S_2-C_2'	89.3
C_5'-H_5'	1.081	S_2-C_5'-H_5'	119.5

Cartesian Coordinates



Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	16	0	-4.171020	-1.833009	-1.444368
2	1	0	-3.930549	-2.415518	-3.819579
3	6	0	-3.352936	-2.152080	-2.944387
4	6	0	-2.617975	-1.533859	-0.685224
5	35	0	-2.580730	-1.069136	1.193724
6	6	0	-1.998357	-2.021986	-2.825982
7	6	0	-1.550933	-1.667149	-1.510134
8	1	0	-1.319516	-2.177255	-3.655989
9	3	0	-0.615130	0.321097	0.284313
10	35	0	0.561627	-1.283263	-1.015447
11	35	0	1.393400	1.632153	1.195462
12	6	0	2.575211	-0.580593	-0.345651
13	6	0	2.816012	0.490477	0.452744
14	16	0	4.115296	-1.264932	-0.750130
15	6	0	4.174225	0.804606	0.766556
16	1	0	4.487810	1.630426	1.390818
17	6	0	5.016929	-0.085579	0.167621
18	1	0	6.096078	-0.115586	0.214482

Calculated at the B3LYP-D2/6-311++G(d,p) level, in vacuum

4. Intrinsic Reaction Coordinates

4.1 Four Centre Type

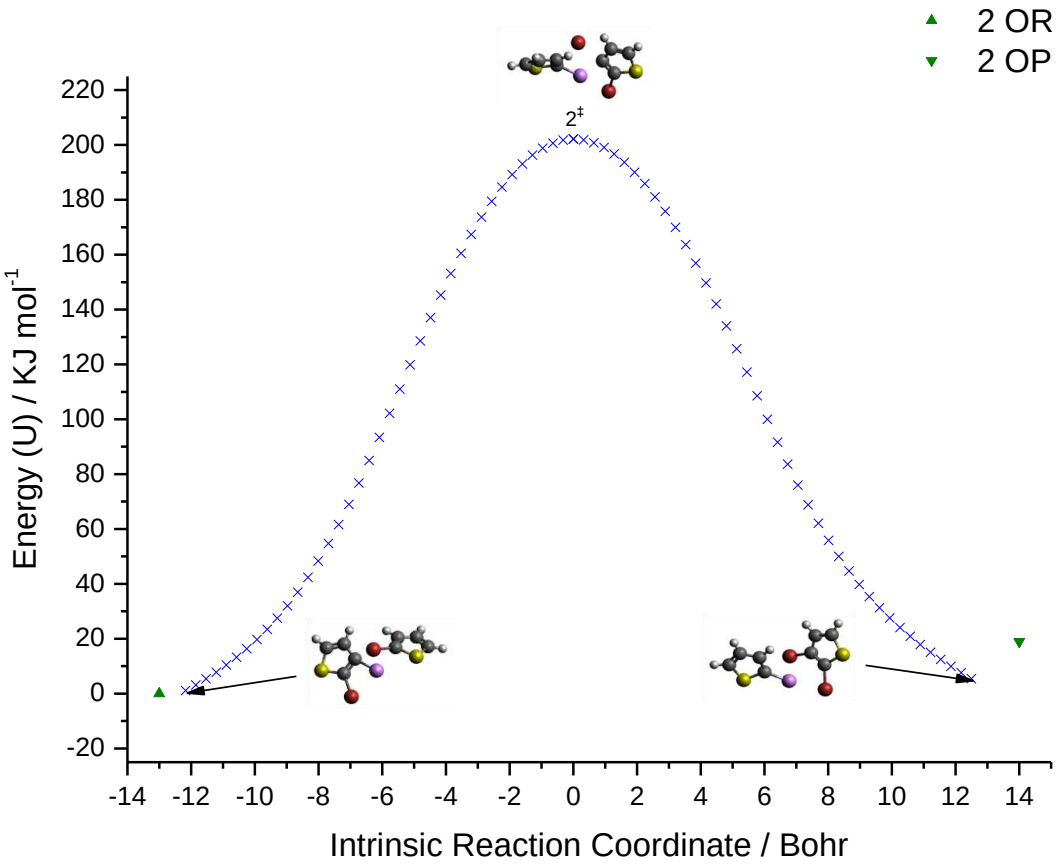


Figure 1. Minimum energy path along the forward and reverse intrinsic reaction coordinates of step 2 (four-centre type), referenced to the optimised starting reagents (2 OR).

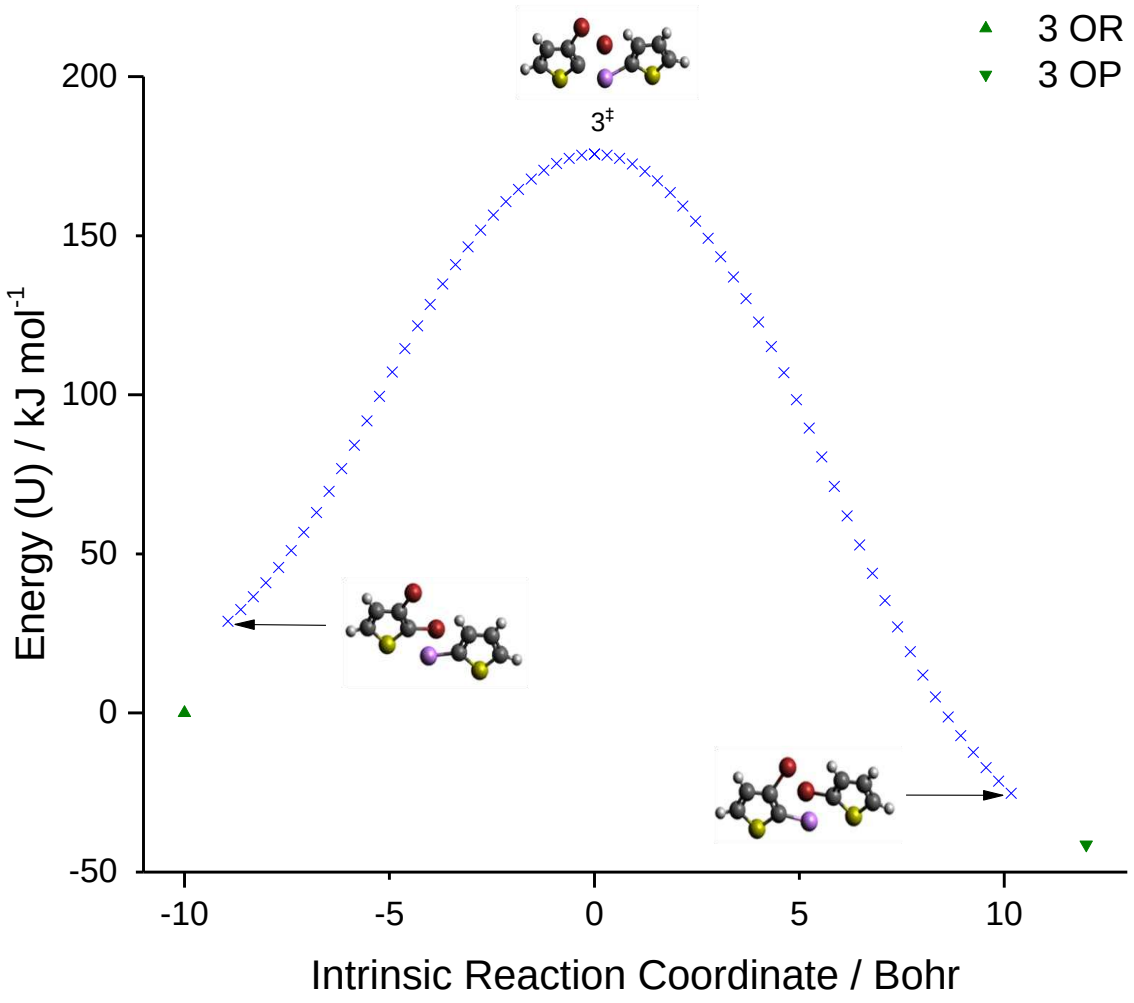


Figure 2. Minimum energy path along the forward and reverse intrinsic reaction coordinates of step 3 (four-centre type), referenced to the optimised starting reagents (3 OR).

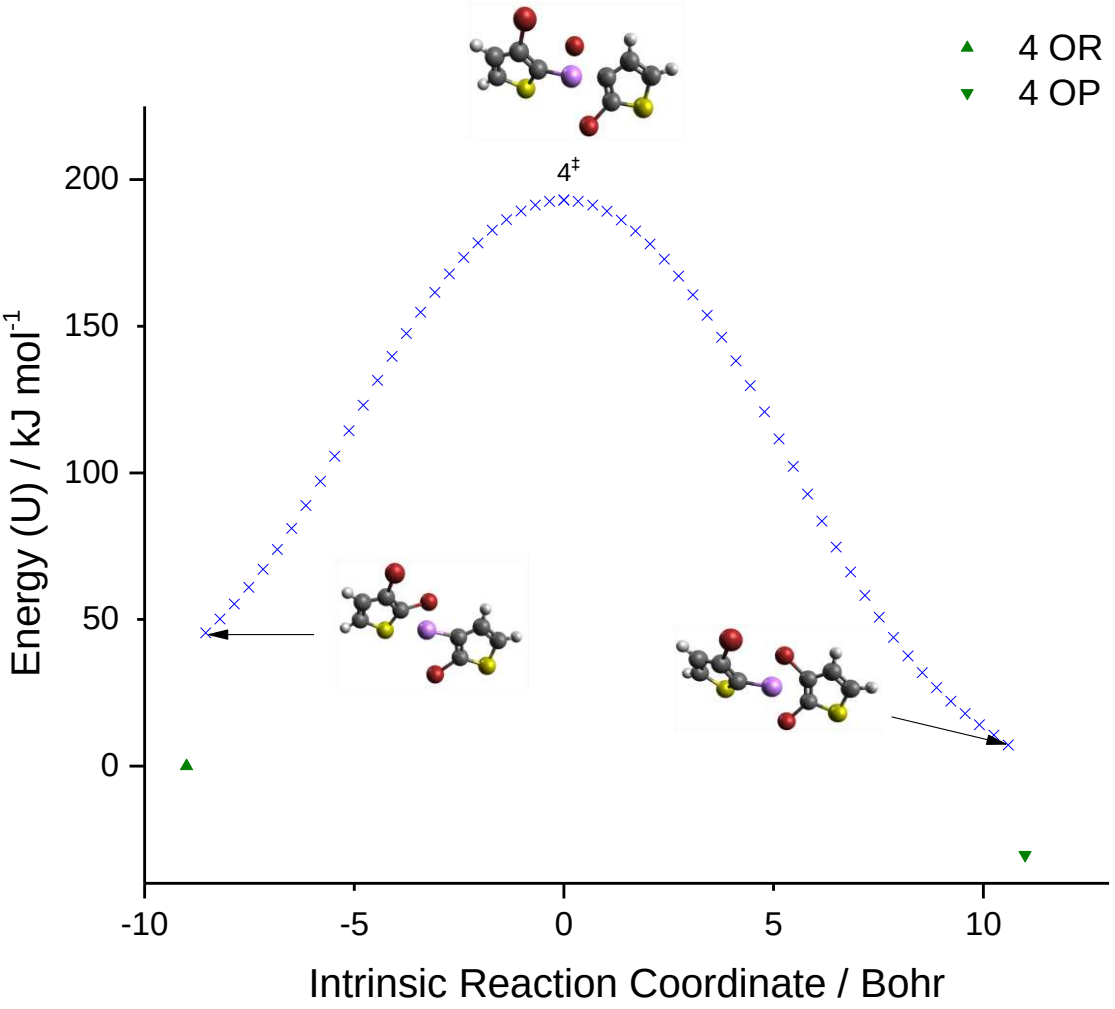


Figure 3. Minimum energy path along the forward and reverse intrinsic reaction coordinates of step 4 (four-centre type), referenced to the optimised starting reagents (4 OR).

4.2 S_N2 Type

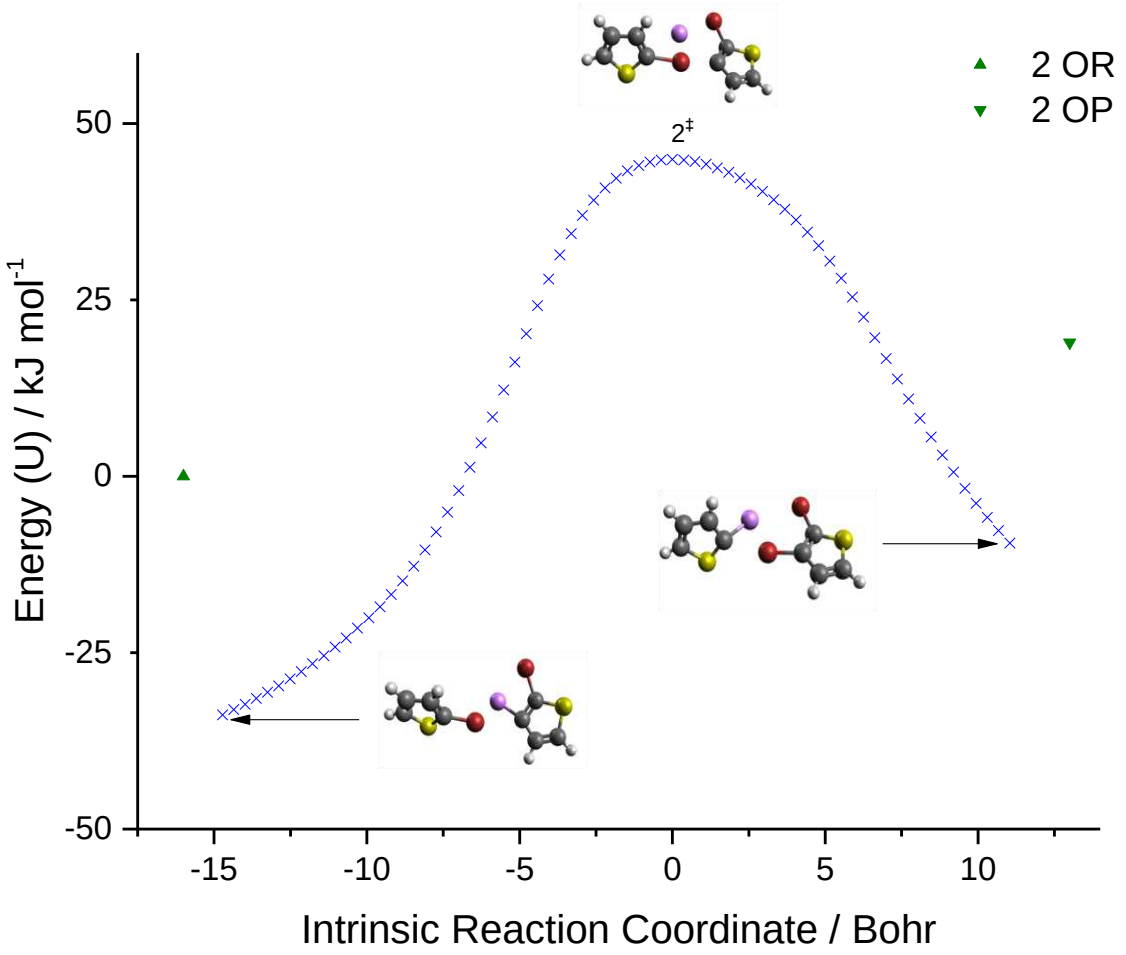


Figure 4. Minimum energy path along the forward and reverse intrinsic reaction coordinates of step 2 (S_N2 type), referenced to the optimised starting reagents (2 OR).

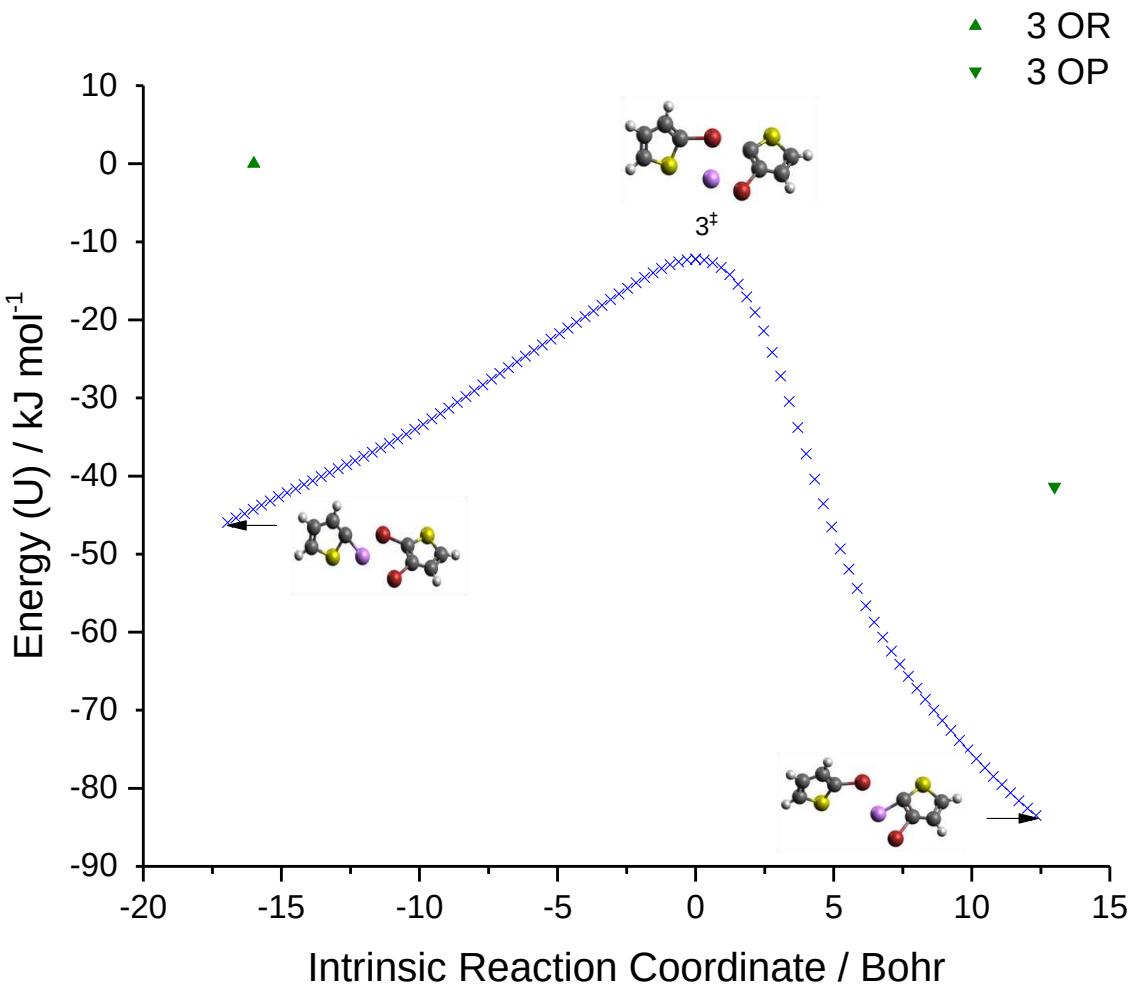


Figure 5. Minimum energy path along the forward and reverse intrinsic reaction coordinates of step 3 (S_N2 type), referenced to the optimised starting reagents (3 OR).

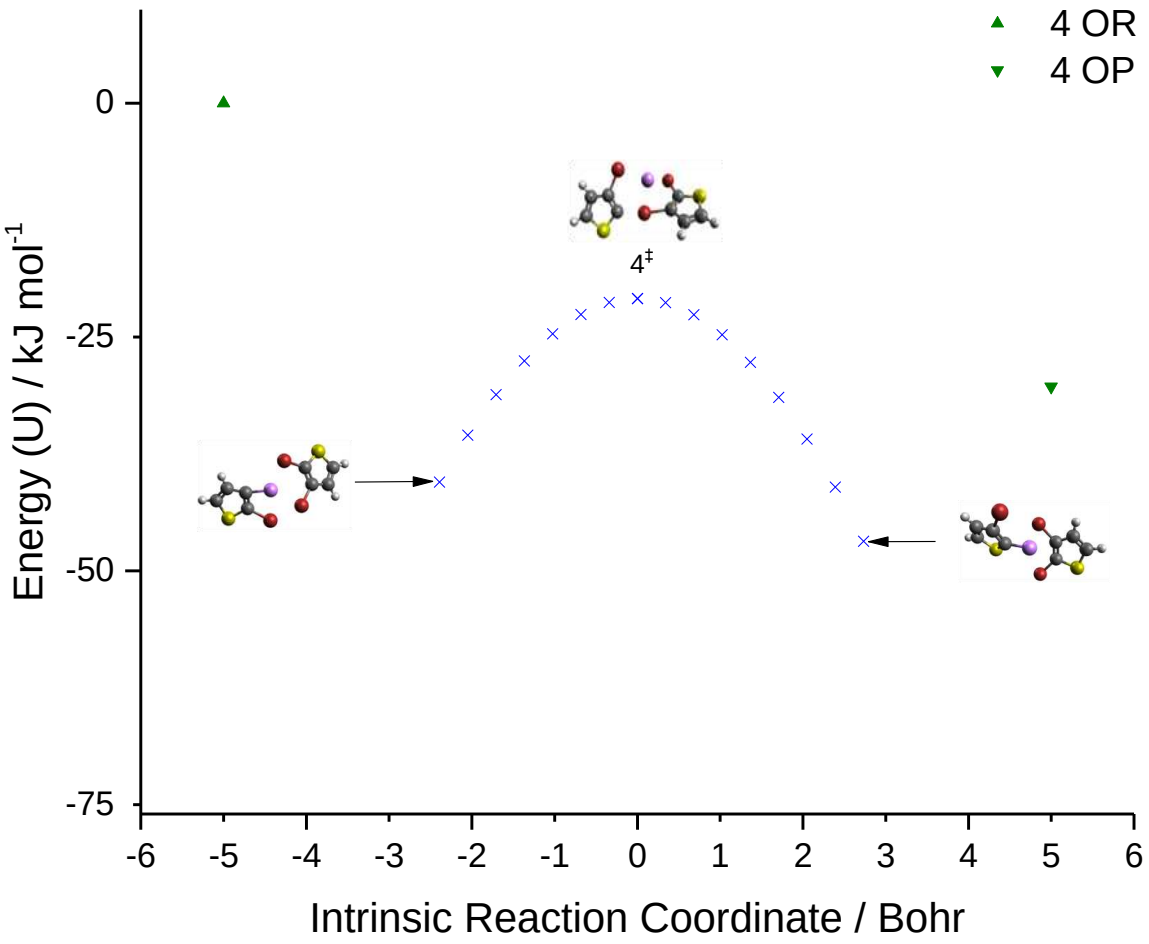


Figure 6. Minimum energy path along the forward and reverse intrinsic reaction coordinates of step 4 (S_N2 type), referenced to the optimised starting reagents (4 OR).

5. Gibbs Energy Profile Diagrams

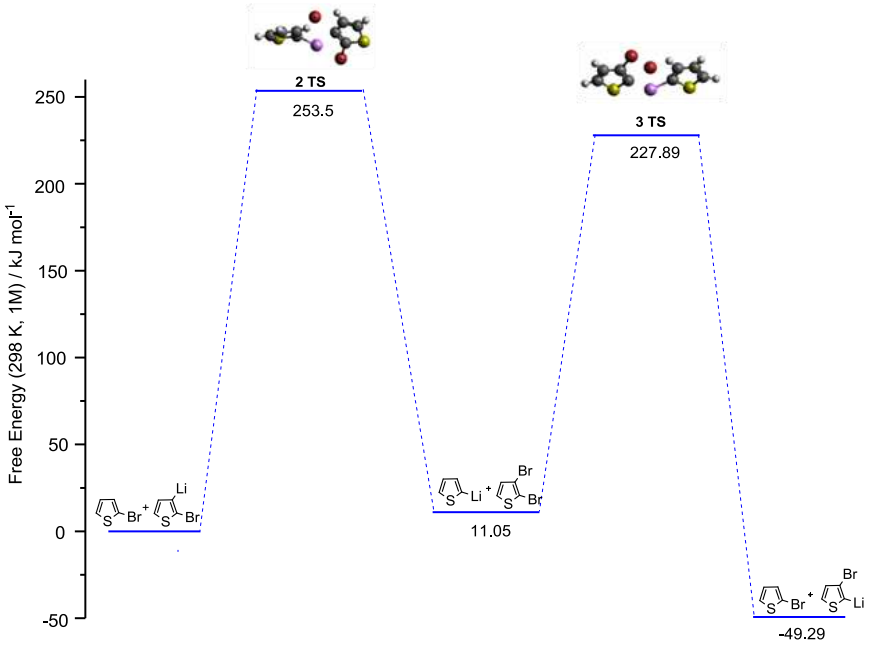


Figure 7. Relative Gibbs energy profile for the four-centre mechanism steps 2 and 3. For clarity, the wells in the entrance and exit channels are not shown.

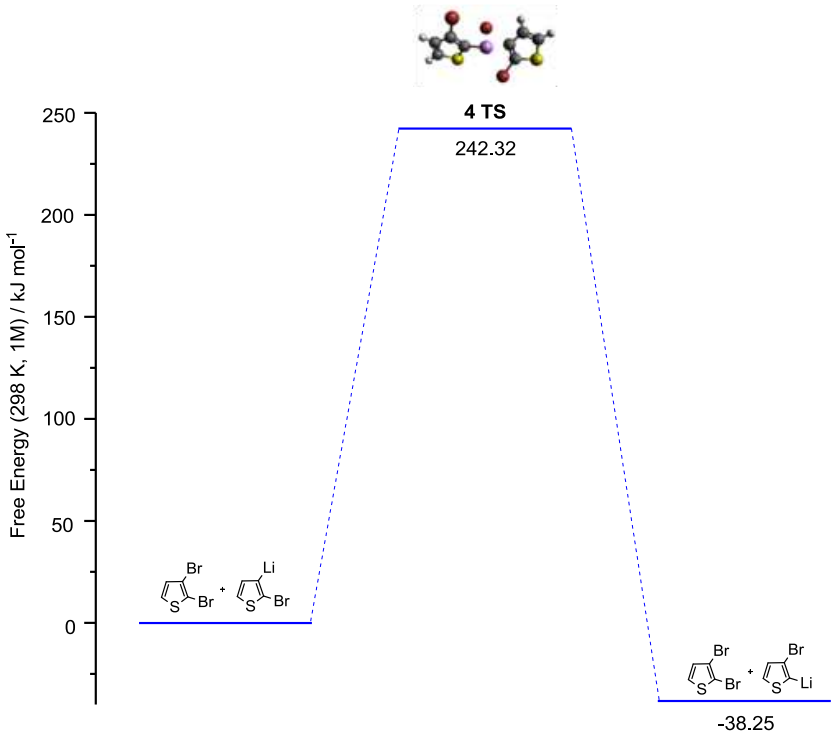


Figure 8. Relative Gibbs energy profile for the four-centre mechanism step 4. For clarity, the wells in the entrance and exit channels are not shown.

6. Activation Energies

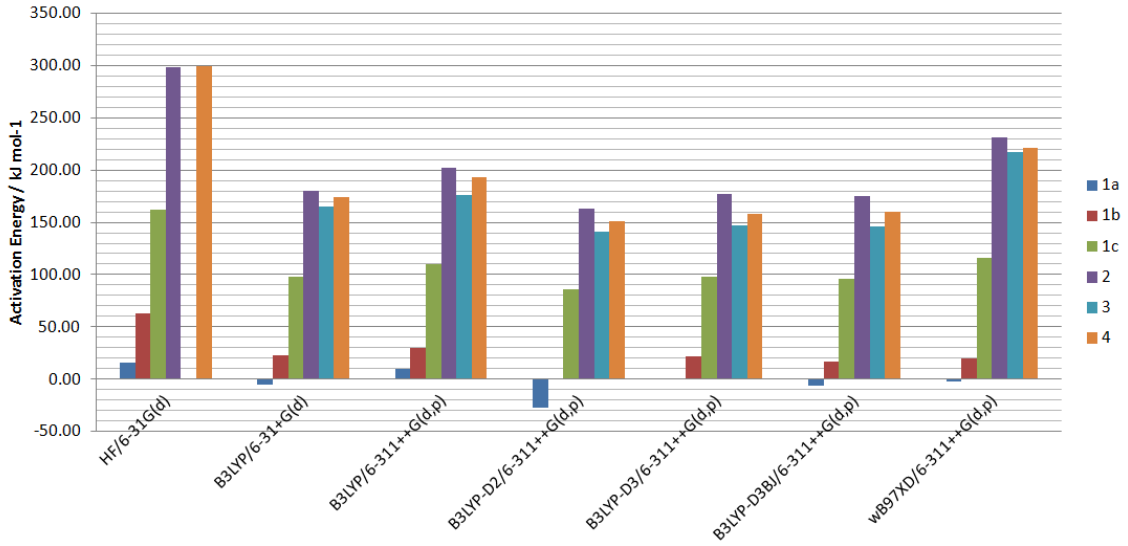


Figure 9. Chart comparing the activation energies *vs* theory level for the lithium-proton exchanges and lithium-bromine (four-centre type) exchange transition states.

Table 14. Activation energies (kJ mol^{-1}) for steps 1a-4 at various theory levels, in vacuum; lithium-proton exchanges and the lithium-halogen (four-centre type) exchange steps

Step	HF/ 6-31G(d)	B3LYP/ 6-31+G(d)	B3LYP/ 6-311++G(d,p)	B3LYP-D2/ 6-311++G(d,p)	B3LYP-D3/ 6-311++G(d,p)	B3LYP-D3BJ/ 6-311++G(d,p)	wB97XD/ 6-311++G(d,p)
1a	15.40	-4.896	9.810	-27.33	0.5300	-6.14	-2.100
1b	63.25	22.93	30.26	1.260	21.92	17.02	19.46
1c	162.1	98.29	110.1	85.99	98.33	95.60	116.2
2	298.4	180.5	202.2	163.0	177.0	174.8	230.8
3	-	165.0	175.6	140.8	146.6	146.4	217.6
4	299.2	173.9	193.1	151.1	158.0	160.3	221.5

[-] No activation energy available due to the transition state being unobtainable after multiple attempts

7. Internal Energies of Reaction

Table 15. Internal energies of reaction (kJ mol^{-1}) for steps 1a-4 at various theory levels, in vacuum; lithium-proton exchanges and the lithium-halogen (four-centre type) exchange steps

Step	HF/ 6-31G(d)	B3LYP/ 6-31+G(d)	B3LYP/ 6-311++G(d,p)	B3LYP-D2/ 6-311++G(d,p)	B3LYP-D3/ 6-311++G(d,p)	B3LYP-D3BJ/ 6-311++G(d,p)	wB97XD/ 6-311++G(d,p)
1a	-6.720	13.60	20.35	8.810	19.07	17.28	14.95
1b	41.86	43.98	49.71	48.38	48.16	47.31	42.97
1c	106.5	131.39	115.87	117.8	116.6	120.1	116.1
2	26.62	4.150	11.36	19.16	7.330	9.360	6.970
3	-70.17	-41.92	-50.04	-58.37	-48.80	-48.06	-47.52
4	-43.55	-37.76	-38.7	-39.21	-41.47	-38.70	-40.55

Table 15 Continued

Step	MP2/ 6-311++G(d,p)	CCSD/ 6-311++G(d,p)
1a	12.92	11.68
1b	39.90	40.93
1c	134.5	120.9
2	4.120	8.640
3	-44.06	-47.48
4	-39.95	-38.84