Supporting Information

Synthesis, X-ray single crystal, conformational analysis and cholinesterase inhibitory activity of a new spiropyrrolidine scaffold tethered benzo[*b*]thiophene analogue

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Acetylcholinesterase (AChE) inhibitory assay [1]

140 μL of 0.1 M sodium phosphate buffer of pH 8 was first added to a 96-wells microplate followed by 20 μL of test samples and 20 μL of 0.09 units/mL acetylcholinesterase enzyme from electric eel (Sigma-Aldrich, CAS Number 9000-81-1). After 15 min of incubation at 25 °C, 10 μL of 10 mM 5,5′-dithiobis-2-nitrobenzoic acid (DTNB, Sigma-Aldrich, CAS Number 69-78-3) was added into each well followed by 10 μL of 14 mM acetylthiocholine iodide (Sigma-Aldrich, CAS Number 1866-15-5). Thirty min after the initiation of enzymatic reaction, absorbance of the colored end-product was measured using StatFax-2100 microplate reader (Awareness Technology, Inc., USA) at 412 nm. Each test was conducted in triplicates. Test samples were prepared in DMSO at an initial concentration of 1 mg/mL (1000 ppm). The concentration of DMSO in final reaction mixture was 1%. At this concentration, DMSO has no inhibitory effect on acetylcholinesterase enzyme. The initial screening was carried out at 50 μg/mL of test samples in 1% DMSO. Absorbance of the test samples was corrected by subtracting the absorbance of their respective blank. Percentage enzyme inhibition is calculated using the following formula

$$\text{Percentage of inhibition} = \frac{\text{Absorbance of control - Absorbance of Sample}}{\text{Absorbance of control}} \text{ X } 100$$

Subsequently, the determination of IC_{50} was carried out using a set of six concentrations (1.56-50 μg/mL).

Reference

1. Kumar, R. S.; Almansour, A. I.,; Arumugam, N.; Althomili, D. M. Q.; Altaf, M.; Basiri, A.; Kotresha D.; Manohar, T.S.; Venketesh, S. Ionic liquid-enabled synthesis, cholinesterase inhibitory activity, and molecular docking study of highly functionalized tetrasubstituted pyrrolidines. *Bioorg. Chem.* **2018**, *77*, 263-268.

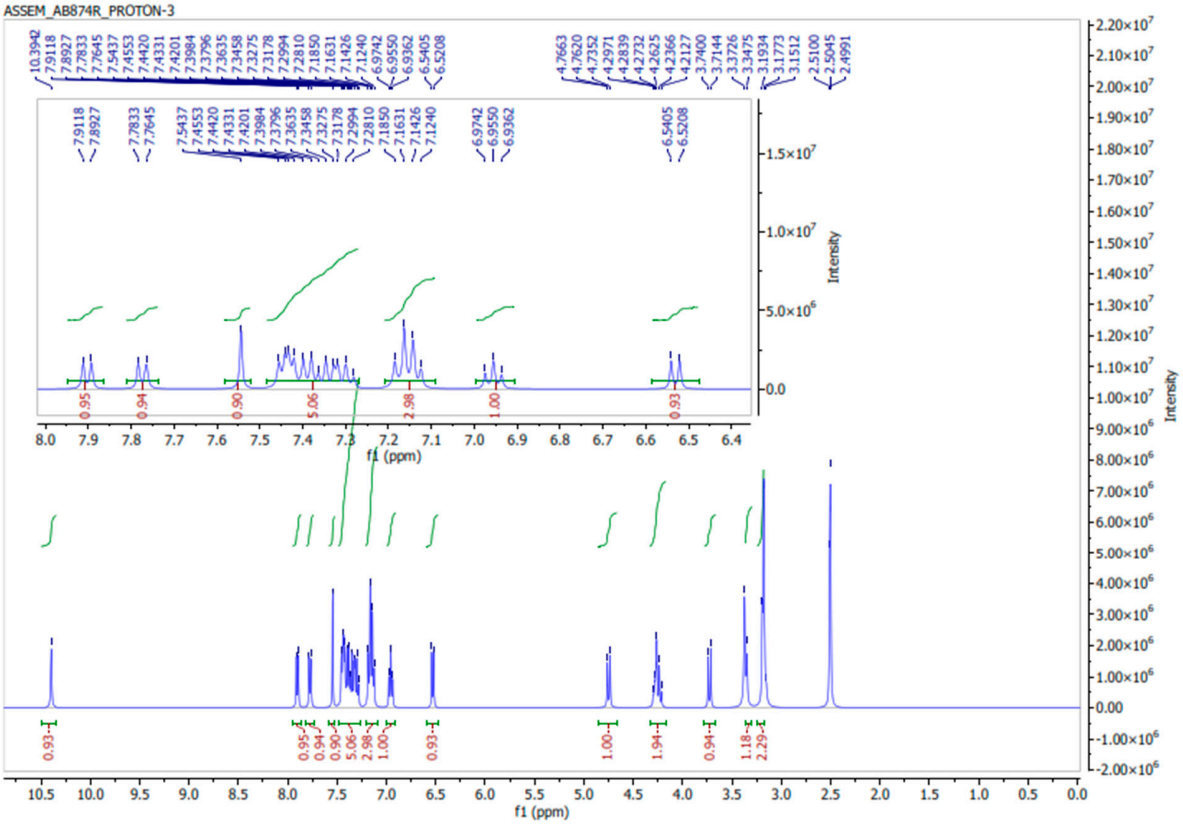


Figure S1. ^{1}H NMR of **5** in DMSO-d_6.

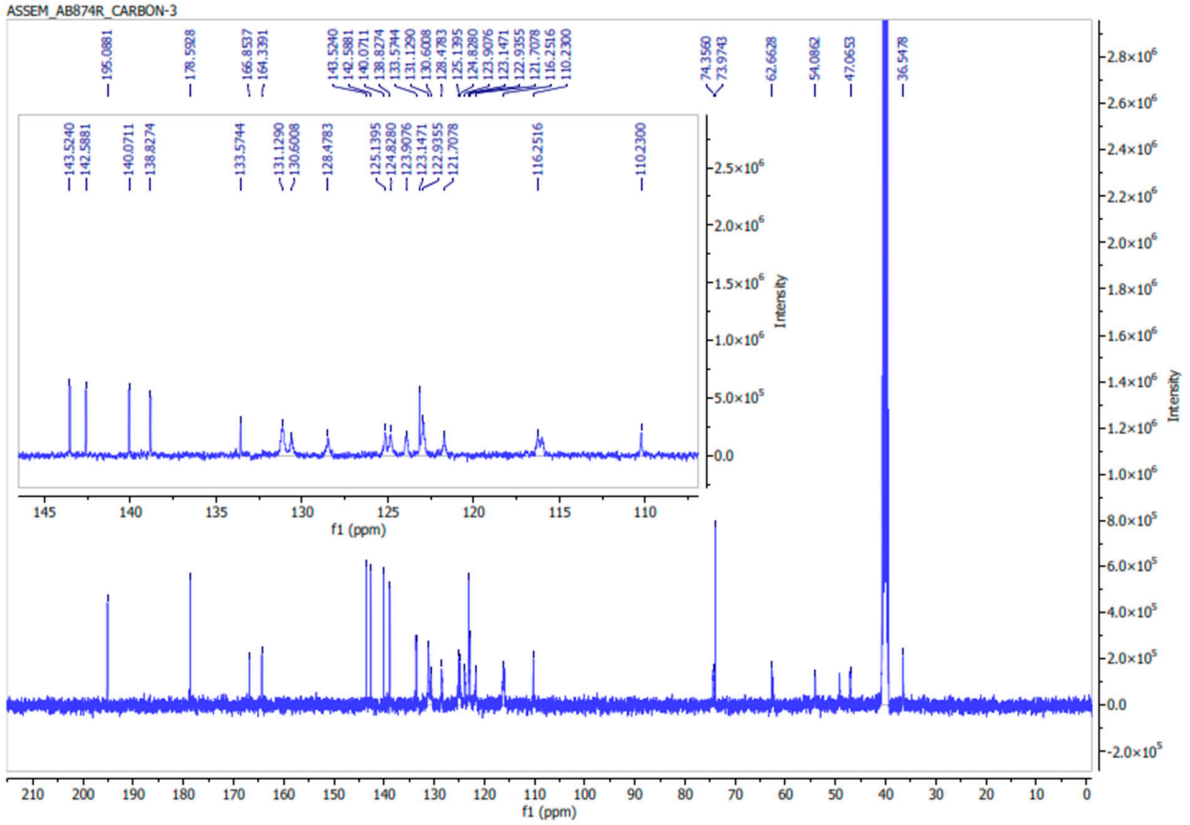


Figure S2. ^{13}C NMR of **5** in DMSO-*d*$_6$.

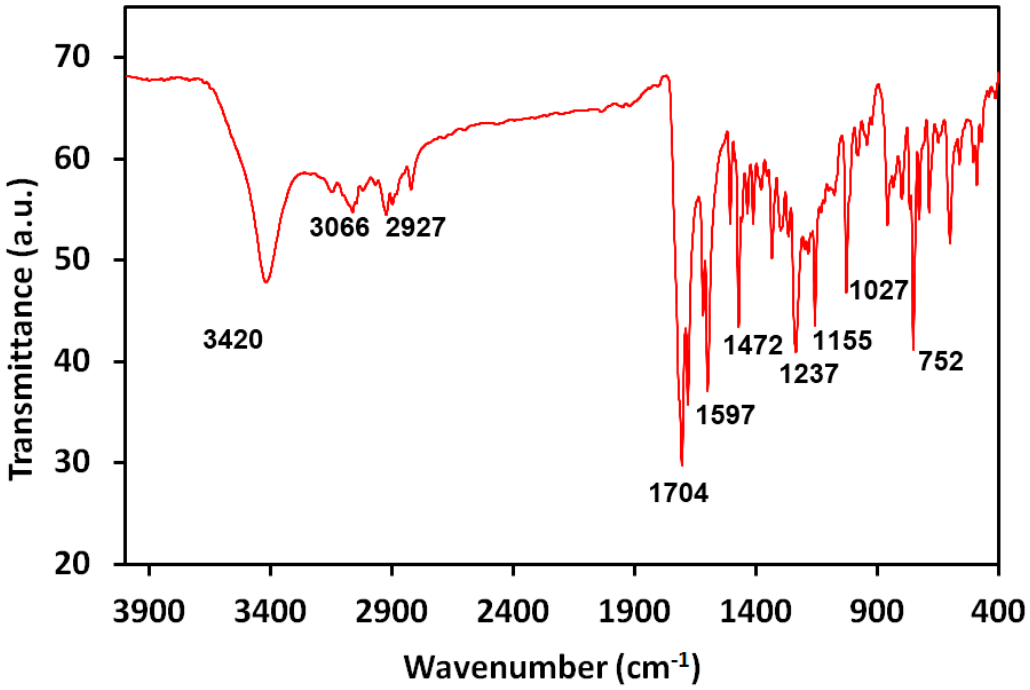


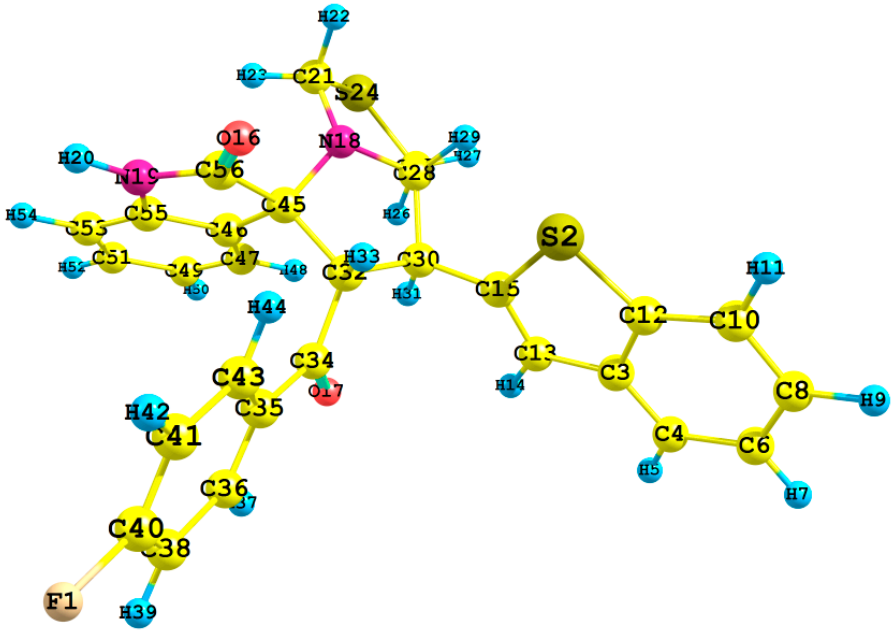
Figure S3. IR of **5** in KBr.

Figure S4: Atom numbering of the optimized structures of conformers A and B (See Table S1).

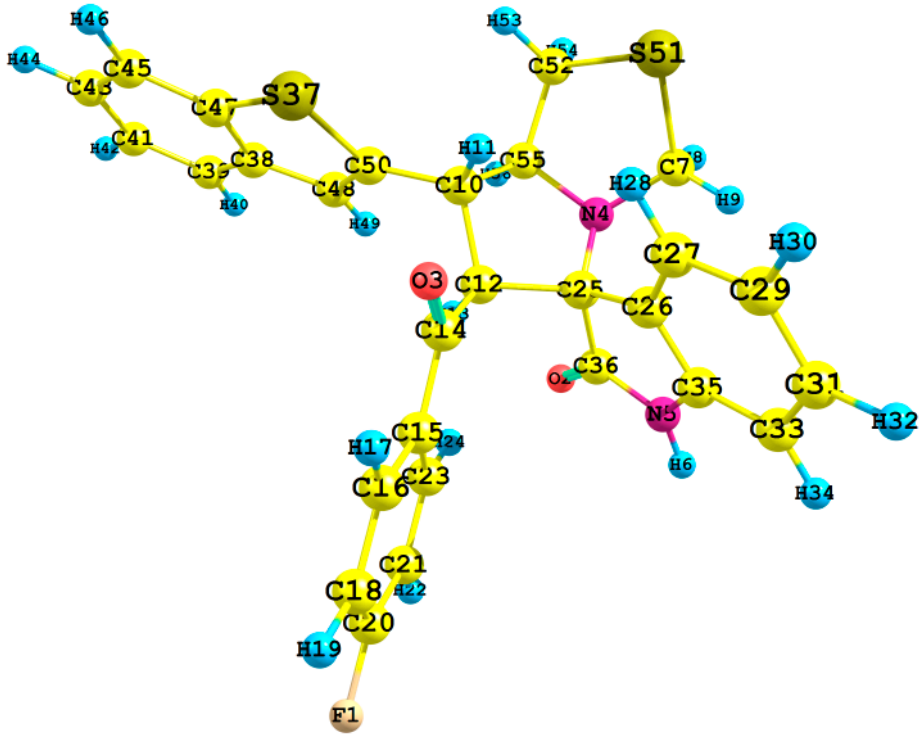
Table S1 Selected bond lengths [Å] and angles [deg] for **5**.

F1-C18	1.352(4)	S1A-C6A	1.735(9)
S1A-C8A	1.755(7)	C1A-C2A	1.393(11)
C1A-C6A	1.396(12)	C1A-C7A	1.465(17)

A



B



C2A-C3A	1.389(12)	C2A-H2A	0.95
C3A-C4A	1.481(11)	C3A-H3A	0.95
C4A-C5A	1.380(11)	C4A-H4A	0.95

C5A-C6A	1.428(10)	C5A-H5A	0.95
C7A-C8A	1.462(17)	C7A-H7AA	0.95
C8A-C12	1.430(8)	S1B-C6B	1.741(8)
S1B-C8B	1.747(8)	C1B-C2B	1.372(12)
C1B-C6B	1.441(11)	C1B-C7B	1.463(13)
C2B-C3B	1.372(12)	C2B-H2B	0.95
C3B-C4B	1.411(11)	C3B-H3B	0.95
C4B-C5B	1.391(11)	C4B-H4B	0.95
C5B-C6B	1.405(10)	C5B-H5B	0.95
C7B-C8B	1.381(11)	C7B-H7BA	0.95
C8B-C12	1.594(8)	O1-C28	1.229(4)
O2-C14	1.218(4)	N1-C11B	1.393(9)
N1-C9	1.437(4)	N1-C21	1.469(4)
N1-C11A	1.577(9)	N2-C28	1.343(4)
N2-C27	1.408(4)	N2-H2	0.88
C9-S2A	1.815(4)	C9-S2B	1.875(4)
C9-H9A	0.99	C9-H9B	0.99
S2A-C10A	1.778(8)	C10A-C11A	1.574(10)
C10A-H10A	0.99	C10A-H10B	0.99
C11A-C12	1.555(10)	C11A-H11A	1
S2B-C10B	1.770(8)	C10B-C11B	1.558(10)
C10B-H10C	0.99	C10B-H10D	0.99
C11B-C12	1.585(10)	C11B-H11B	1.00
C12-C13	1.541(5)	C12-H12	1.00
C13-C14	1.527(4)	C13-C21	1.563(4)
C13-H13	1.00	C14-C15	1.491(4)
C15-C20	1.394(5)	C15-C16	1.400(4)
C16-C17	1.383(5)	C16-H16	0.95
C17-C18	1.375(5)	C17-H17	0.95
C18-C19	1.372(5)	C19-C20	1.386(5)

C19-H19	0.95	C20-H20	0.95
C21-C22	1.526(4)	C21-C28	1.556(4)
C22-C23	1.381(5)	C22-C27	1.395(4)
C23-C24	1.399(5)	C23-H23	0.95
C24-C25	1.387(5)	C24-H24	0.95
C25-C26	1.392(5)	C25-H25	0.95
C26-C27	1.384(5)	C26-H26	0.95
O3-C29	1.415(5)	O3-H3O	0.84
C29-H29A	0.98	C29-H29B	0.98
C29-H29C	0.98		
C6A-S1A-C8A	90.7(4)	C2A-C1A-C6A	117.0(8)
C2A-C1A-C7A	126.7(9)	C6A-C1A-C7A	116.2(9)
C3A-C2A-C1A	120.4(8)	C3A-C2A-H2A	119.8
C1A-C2A-H2A	119.8	C2A-C3A-C4A	122.0(7)
C2A-C3A-H3A	119	C4A-C3A-H3A	119
C5A-C4A-C3A	117.4(7)	C5A-C4A-H4A	121.3
C3A-C4A-H4A	121.3	C4A-C5A-C6A	117.9(7)
C4A-C5A-H5A	121.0	C6A-C5A-H5A	121.0
C1A-C6A-C5A	125.1(7)	C1A-C6A-S1A	112.3(6)
C5A-C6A-S1A	122.4(6)	C8A-C7A-C1A	105.7(12)
C8A-C7A-H7AA	127.2	C1A-C7A-H7AA	127.2
C12-C8A-C7A	130.1(8)	C12-C8A-S1A	114.4(5)
C7A-C8A-S1A	115.0(8)	C6B-S1B-C8B	91.3(4)
C2B-C1B-C6B	121.0(8)	C2B-C1B-C7B	129.9(8)
C6B-C1B-C7B	108.9(7)	C3B-C2B-C1B	118.9(8)
C3B-C2B-H2B	120.5	C1B-C2B-H2B	120.5
C2B-C3B-C4B	119.7(8)	C2B-C3B-H3B	120.1
C4B-C3B-H3B	120.1	C5B-C4B-C3B	124.1(7)
C5B-C4B-H4B	118.0	C3B-C4B-H4B	118.0
C4B-C5B-C6B	115.1(6)	C4B-C5B-H5B	122.5

C6B-C5B-H5B	122.5	C5B-C6B-C1B	121.0(7)
C5B-C6B-S1B	125.8(6)	C1B-C6B-S1B	113.1(6)
C8B-C7B-C1B	113.7(7)	C8B-C7B-H7BA	123.2
C1B-C7B-H7BA	123.2	C7B-C8B-C12	132.8(7)
C7B-C8B-S1B	112.5(6)	C12-C8B-S1B	114.7(4)
C11B-N1-C9	118.5(4)	C11B-N1-C21	112.5(4)
C9-N1-C21	118.5(3)	C9-N1-C11A	103.0(4)
C21-N1-C11A	111.7(4)	C28-N2-C27	111.6(3)
C28-N2-H2	124.2	C27-N2-H2	124.2
N1-C9-S2A	117.7(2)	N1-C9-S2B	98.3(2)
N1-C9-H9A	107.9	S2A-C9-H9A	107.9
N1-C9-H9B	107.9	S2A-C9-H9B	107.9
H9A-C9-H9B	107.2	C10A-S2A-C9	91.8(3)
C11A-C10A-S2A	108.6(5)	C11A-C10A-H10A	110.0
S2A-C10A-H10A	110.0	C11A-C10A-H10B	110.0
S2A-C10A-H10B	110.0	H10A-C10A-H10B	108.4
C12-C11A-C10A	118.6(6)	C12-C11A-N1	99.8(5)
C10A-C11A-N1	112.9(6)	C12-C11A-H11A	108.3
C10A-C11A-H11A	108.3	N1-C11A-H11A	108.3
C10B-S2B-C9	87.0(3)	C11B-C10B-S2B	107.1(5)
C11B-C10B-H10C	110.3	S2B-C10B-H10C	110.3
C11B-C10B-H10D	110.3	S2B-C10B-H10D	110.3
H10C-C10B-H10D	108.5	N1-C11B-C10B	104.6(6)
N1-C11B-C12	106.9(6)	C10B-C11B-C12	107.1(6)
N1-C11B-H11B	112.5	C10B-C11B-H11B	112.5
C12-C11B-H11B	112.5	C8A-C12-C13	115.3(4)
C8A-C12-C11A	118.9(5)	C13-C12-C11A	110.0(4)
C13-C12-C11B	97.3(4)	C13-C12-C8B	106.9(3)
C11B-C12-C8B	106.7(5)	C8A-C12-H12	103.4
C13-C12-H12	103.4	C11A-C12-H12	103.4

C14-C13-C12	112.6(3)	C14-C13-C21	113.1(2)
C12-C13-C21	104.6(3)	C14-C13-H13	108.8
C12-C13-H13	108.8	C21-C13-H13	108.8
O2-C14-C15	120.6(3)	O2-C14-C13	120.5(3)
C15-C14-C13	118.8(3)	C20-C15-C16	119.0(3)
C20-C15-C14	122.9(3)	C16-C15-C14	118.1(3)
C17-C16-C15	120.9(3)	C17-C16-H16	119.6
C15-C16-H16	119.6	C18-C17-C16	117.8(3)
C18-C17-H17	121.1	C16-C17-H17	121.1
F1-C18-C19	118.2(3)	F1-C18-C17	118.3(3)
C19-C18-C17	123.6(3)	C18-C19-C20	118.1(3)
C18-C19-H19	121.0	C20-C19-H19	121.0
C19-C20-C15	120.7(3)	C19-C20-H20	119.7
C15-C20-H20	119.7	N1-C21-C22	119.1(3)
N1-C21-C28	109.2(2)	C22-C21-C28	101.6(2)
N1-C21-C13	101.7(2)	C22-C21-C13	115.7(2)
C28-C21-C13	109.4(3)	C23-C22-C27	119.9(3)
C23-C22-C21	132.2(3)	C27-C22-C21	107.9(3)
C22-C23-C24	118.5(3)	C22-C23-H23	120.8
C24-C23-H23	120.8	C25-C24-C23	120.6(3)
C25-C24-H24	119.7	C23-C24-H24	119.7
C24-C25-C26	121.5(3)	C24-C25-H25	119.2
C26-C25-H25	119.2	C27-C26-C25	117.0(3)
C27-C26-H26	121.5	C25-C26-H26	121.5
C26-C27-C22	122.5(3)	C26-C27-N2	127.3(3)
C22-C27-N2	110.3(3)	O1-C28-N2	126.7(3)
O1-C28-C21	124.8(3)	N2-C28-C21	108.6(3)
C29-O3-H3O	109.5	O3-C29-H29A	109.5
O3-C29-H29B	109.5	H29A-C29-H29B	109.5
O3-C29-H29C	109.5	H29A-C29-H29C	109.5

H29B-C29-H29C	109.5

Table S2 The calculated geometric parameters of the studied conformers with and without the crystallized methanol molecule[a].

Parameter	**Calc.[b]**	**Calc.[c]**	**Exp.**	**Parameter**	**Calc.[b]**	**Calc.[c]**	**Exp.**
Conformer A				**Conformer A**			
R(1-40)	1.345	1.346	1.352	R(1-20)	1.346	1.346	1.352
R(2-12)	1.758	1.757	1.735	R(2-36)	1.217	1.225	1.230
R(2-15)	1.773	1.774	1.754	R(3-14)	1.224	1.223	1.218

R(3-4)	1.407	1.407	1.392	R(4-7)	1.441	1.442	1.437
R(3-12)	1.416	1.416	1.396	R(4-25)	1.478	1.472	1.469
R(3-13)	1.439	1.438	1.465	R(4-55)	1.472	1.479	1.392
R(4-6)	1.388	1.388	1.389	R(5-35)	1.404	1.408	1.409
R(6-8)	1.406	1.407	1.481	R(5-36)	1.375	1.365	1.342
R(8-10)	1.391	1.391	1.380	R(7-51)	1.866	1.866	1.875
R(10-12)	1.398	1.398	1.428	R(10-12)	1.542	1.543	1.541
R(13-15)	1.361	1.363	1.463	R(10-50)	1.505	1.505	1.593
R(15-30)	1.502	1.500	1.430	R(10-55)	1.543	1.543	1.585
R(16-56)	1.216	1.225	1.230	R(12-14)	1.533	1.531	1.527
R(17-34)	1.225	1.224	1.218	R(12-25)	1.573	1.577	1.563
R(18-21)	1.435	1.442	1.437	R(14-15)	1.494	1.495	1.491
R(18-28)	1.461	1.481	1.577	R(15-16)	1.407	1.407	1.400
R(18-45)	1.464	1.473	1.469	R(15-23)	1.405	1.405	1.394
R(19-55)	1.405	1.407	1.409	R(16-18)	1.388	1.388	1.383
R(19-56)	1.374	1.365	1.342	R(18-20)	1.393	1.393	1.374
R(21-24)	1.885	1.867	1.815	R(20-21)	1.390	1.390	1.371
R(24-25)	1.837	1.836	1.777	R(21-23)	1.394	1.393	1.386
R(25-28)	1.555	1.544	1.573	R(25-26)	1.525	1.528	1.527
R(28-30)	1.551	1.541	1.555	R(25-36)	1.568	1.565	1.556
R(30-32)	1.553	1.544	1.541	R(26-27)	1.390	1.390	1.381
R(32-34)	1.535	1.530	1.527	R(26-35)	1.405	1.404	1.395
R(32-45)	1.567	1.577	1.563	R(27-29)	1.402	1.401	1.400
R(34-35)	1.493	1.495	1.491	R(29-31)	1.395	1.395	1.386
R(35-36)	1.408	1.407	1.400	R(31-33)	1.400	1.400	1.391
R(35-43)	1.406	1.405	1.394	R(33-35)	1.389	1.388	1.384
R(36-38)	1.388	1.388	1.383	R(37-47)	1.755	1.755	1.742
R(38-40)	1.394	1.393	1.374	R(37-50)	1.764	1.765	1.747
R(40-41)	1.390	1.390	1.371	R(38-39)	1.408	1.408	1.372
R(41-43)	1.393	1.393	1.386	R(38-47)	1.418	1.418	1.441
R(45-46)	1.529	1.529	1.527	R(38-48)	1.439	1.439	1.463
R(45-56)	1.569	1.566	1.556	R(39-41)	1.388	1.388	1.372

R(46-47)	1.389	1.391	1.381	R(41-43)	1.407	1.407	1.412
R(46-55)	1.405	1.404	1.395	R(43-45)	1.390	1.391	1.390
R(47-49)	1.401	1.401	1.400	R(45-47)	1.399	1.398	1.405
R(49-51)	1.395	1.395	1.386	R(48-50)	1.364	1.363	1.382
R(51-53)	1.400	1.400	1.391	R(51-52)	1.835	1.836	1.770
R(53-55)	1.389	1.388	1.384	R(52-55)	1.547	1.545	1.559
	0.969	0.972			0.983	0.982	
A(1-40-38)	118.8	118.8	118.3	A(1-20-18)	118.8	118.9	118.3
A(1-40-41)	119.0	118.9	118.2	A(1-20-21)	118.9	118.9	118.2
A(12-2-15)	91.2	91.1	90.6	A(2-36-5)	126.3	125.2	126.7
A(2-12-3)	111.1	111.4	112.3	A(2-36-25)	126.4	127.0	124.7
A(2-12-10)	127.2	127.1	122.3	A(3-14-12)	119.4	119.6	120.5
A(2-15-13)	111.7	111.7	115.1	A(3-14-15)	120.4	120.5	120.7
A(2-15-30)	121.5	122.6	114.4	A(7-4-25)	121.3	120.7	118.5
A(4-3-12)	118.8	118.9	117.0	A(7-4-55)	112.9	112.9	118.6
A(4-3-13)	129.3	129.4	126.7	A(4-7-8)	111.2	111.1	107.9
A(3-4-5)	119.8	119.8	119.8	A(4-7-9)	112.1	112.1	107.9
A(3-4-6)	119.6	119.6	120.4	A(25-4-55)	112.1	112.0	112.5
A(12-3-13)	111.9	111.7	116.2	A(4-25-12)	103.4	102.8	101.8
A(3-12-10)	121.7	121.6	125.1	A(4-25-26)	116.6	117.7	119.1
A(3-13-14)	123.5	123.5	127.1	A(4-25-36)	108.1	108.7	109.2
A(3-13-15)	114.1	114.1	105.7	A(4-55-10)	104.7	104.4	107.0
A(5-4-6)	120.6	120.6	119.8	A(4-55-52)	109.2	109.1	104.6
A(4-6-7)	119.7	119.8	119.0	A(4-55-56)	110.4	109.8	112.6
A(4-6-8)	120.8	120.7	122.0	A(6-5-35)	125.3	125.4	124.1
A(7-6-8)	119.5	119.5	119.0	A(6-5-36)	122.2	122.3	124.3
A(6-8-9)	119.7	119.7	121.3	A(35-5-36)	112.2	112.3	111.6
A(6-8-10)	120.8	120.8	117.4	A(5-35-26)	109.7	109.5	110.2
A(9-8-10)	119.5	119.5	121.3	A(5-35-33)	128.0	127.9	127.3
A(8-10-11)	120.8	120.7	121.0	A(5-36-25)	107.3	107.8	108.6
A(8-10-12)	118.3	118.4	117.9	A(8-7-9)	109.2	109.2	107.1

A(11-10-12)	120.9	120.9	121.0	A(7-51-52)	86.9	87.2	87.0
A(14-13-15)	122.4	122.3	127.2	A(11-10-12)	107.3	107.6	103.3
A(13-15-30)	126.7	125.7	130.0	A(11-10-50)	109.4	109.4	113.8
A(15-30-28)	116.1	116.1	119.0	A(12-10-50)	114.4	114.3	107.0
A(15-30-31)	106.1	106.4	103.5	A(12-10-55)	102.7	102.1	97.3
A(15-30-32)	113.6	116.0	115.3	A(10-12-13)	108.6	107.9	108.8
A(16-56-19)	126.3	124.9	126.7	A(10-12-14)	112.4	113.0	112.7
A(16-56-45)	126.4	127.3	124.7	A(10-12-25)	103.9	103.1	104.6
A(17-34-32)	119.4	119.7	120.5	A(50-10-55)	114.2	114.3	106.8
A(17-34-35)	120.3	120.4	120.7	A(10-50-37)	119.7	119.7	114.7
A(21-18-28)	113.3	112.8	103.0	A(10-50-48)	128.5	128.2	132.8
A(21-18-45)	121.5	120.6	118.5	A(10-55-52)	114.5	114.9	107.1
A(18-21-22)	111.6	111.1	107.9	A(10-55-56)	109.6	109.4	112.5
A(18-21-23)	111.4	112.1	107.9	A(13-12-14)	110.6	110.6	108.8
A(28-18-45)	113.1	112.0	111.7	A(13-12-25)	106.4	107.1	108.7
A(18-28-25)	109.3	109.3	112.9	A(14-12-25)	114.5	114.7	113.1
A(18-28-29)	109.2	109.6	108.3	A(12-14-15)	120.2	119.9	118.8
A(18-28-30)	105.0	104.1	99.8	A(12-25-26)	117.5	116.1	115.7
A(18-45-32)	100.7	102.7	101.8	A(12-25-36)	109.1	109.9	109.5
A(18-45-46)	117.9	117.7	119.1	A(14-15-16)	117.3	117.3	118.1
A(18-45-56)	108.7	108.8	109.2	A(14-15-23)	123.8	123.7	122.9
A(20-19-55)	125.3	125.4	124.1	A(16-15-23)	118.9	118.9	119.0
A(20-19-56)	122.1	122.2	124.3	A(15-16-17)	118.0	118.0	119.6
A(55-19-56)	112.5	112.4	111.6	A(15-16-18)	121.1	121.1	120.9
A(19-55-46)	109.7	109.5	110.2	A(15-23-21)	120.6	120.6	120.6
A(19-55-53)	127.8	127.8	127.3	A(15-23-24)	121.1	121.1	119.7
A(19-56-45)	107.2	107.8	108.6	A(17-16-18)	120.9	120.9	119.6
A(22-21-23)	109.3	109.3	107.1	A(16-18-19)	122.0	122.0	121.1
A(24-25-26)	109.2	109.7	110.0	A(16-18-20)	118.4	118.4	117.8
A(24-25-27)	109.6	109.6	109.9	A(19-18-20)	119.6	119.6	121.1
A(24-25-28)	107.1	106.9	108.7	A(18-20-21)	122.2	122.2	123.6
A(26-25-27)	108.4	108.4	108.2	A(20-21-22)	119.7	119.6	120.9

A(26-25-28)	111.3	111.2	110.0	A(20-21-23)	118.8	118.7	118.1
A(27-25-28)	111.2	111.0	110.0	A(22-21-23)	121.6	121.6	120.9
A(25-28-29)	107.7	109.2	108.4	A(21-23-24)	118.3	118.3	119.7
A(25-28-30)	114.2	114.7	118.6	A(26-25-36)	101.8	101.5	101.5
A(29-28-30)	111.3	109.9	108.3	A(25-26-27)	131.9	132.0	132.2
A(28-30-31)	109.3	108.5	103.4	A(25-26-35)	108.8	108.9	107.9
A(28-30-32)	104.7	102.1	110.0	A(27-26-35)	119.4	119.2	119.9
A(31-30-32)	106.7	107.4	103.3	A(26-27-28)	120.6	120.7	120.7
A(30-32-33)	108.9	108.1	108.8	A(26-27-29)	119.2	119.1	118.5
A(30-32-34)	111.7	112.9	112.7	A(26-35-33)	122.3	122.7	122.5
A(30-32-45)	104.6	102.5	104.6	A(28-27-29)	120.2	120.2	120.8
A(33-32-34)	110.9	111.1	108.8	A(27-29-30)	119.6	119.5	119.7
A(33-32-45)	105.6	107.0	108.7	A(27-29-31)	120.5	120.7	120.6
A(34-32-45)	114.6	114.7	113.1	A(30-29-31)	119.9	119.8	119.7
A(32-34-35)	120.3	119.9	118.8	A(29-31-32)	119.8	119.8	119.3
A(32-45-46)	118.0	116.0	115.7	A(29-31-33)	121.1	121.0	121.5
A(32-45-56)	109.6	110.2	109.5	A(32-31-33)	119.2	119.2	119.2
A(34-35-36)	117.2	117.4	118.1	A(31-33-34)	121.1	121.2	121.5
A(34-35-43)	123.9	123.7	122.9	A(31-33-35)	117.5	117.4	117.0
A(36-35-43)	118.9	118.9	119.0	A(34-33-35)	121.3	121.4	121.5
A(35-36-37)	118.1	118.0	119.6	A(47-37-50)	91.5	91.4	91.2
A(35-36-38)	121.1	121.1	120.9	A(37-47-38)	110.9	110.9	113.1
A(35-43-41)	120.6	120.6	120.6	A(37-47-45)	127.4	127.5	125.8
A(35-43-44)	121.2	121.0	119.7	A(37-50-48)	111.8	112.1	112.5
A(37-36-38)	120.8	120.9	119.6	A(39-38-47)	118.8	118.7	121.0
A(36-38-39)	122.0	122.0	121.1	A(39-38-48)	129.3	129.1	129.9
A(36-38-40)	118.4	118.4	117.8	A(38-39-40)	119.8	119.7	120.5
A(39-38-40)	119.6	119.6	121.1	A(38-39-41)	119.6	119.7	118.9
A(38-40-41)	122.2	122.2	123.6	A(47-38-48)	111.9	112.2	108.9
A(40-41-42)	119.7	119.7	120.9	A(38-47-45)	121.6	121.7	121.0
A(40-41-43)	118.8	118.7	118.1	A(38-48-49)	122.9	124.0	123.2
A(42-41-43)	121.5	121.6	120.9	A(38-48-50)	113.8	113.5	113.7

A(41-43-44)	118.2	118.4	119.7	A(40-39-41)	120.6	120.6	120.5
A(46-45-56)	101.8	101.4	101.5	A(39-41-42)	119.7	119.8	120.2
A(45-46-47)	132.2	132.0	132.2	A(39-41-43)	120.8	120.8	119.7
A(45-46-55)	108.7	108.9	107.9	A(42-41-43)	119.5	119.5	120.1
A(47-46-55)	119.1	119.1	119.9	A(41-43-44)	119.7	119.7	118.0
A(46-47-48)	120.8	120.7	120.7	A(41-43-45)	120.8	120.8	124.0
A(46-47-49)	119.4	119.2	118.5	A(44-43-45)	119.5	119.5	118.0
A(46-55-53)	122.5	122.7	122.5	A(43-45-46)	120.7	120.7	122.4
A(48-47-49)	119.8	120.1	120.8	A(43-45-47)	118.4	118.4	115.1
A(47-49-50)	119.6	119.5	119.7	A(46-45-47)	120.9	120.9	122.5
A(47-49-51)	120.5	120.7	120.6	A(49-48-50)	123.3	122.6	123.1
A(50-49-51)	119.9	119.8	119.7	A(51-52-53)	109.8	109.6	110.3
A(49-51-52)	119.8	119.8	119.3	A(51-52-54)	109.6	109.6	110.3
A(49-51-53)	121.0	120.9	121.5	A(51-52-55)	106.5	106.8	107.1
A(52-51-53)	119.2	119.2	119.2	A(53-52-54)	108.4	108.4	108.5
A(51-53-54)	121.1	121.2	121.5	A(53-52-55)	111.4	111.4	110.3
A(51-53-55)	117.5	117.4	117.0	A(54-52-55)	111.0	111.0	110.4
A(54-53-55)	121.3	121.4	121.5	A(52-55-56)	108.3	109.1	112.5
	0.942	0.940			0.959	0.959	

[a]atom numbering refer to **Fig. S4** [b]without methanol [c]with methanol

Table S3 Natural charge populations at the different atomic sites of the studied conformers.

Atom		**A**	**A with MeOH**			**B**	**B with MeOH**
F	1	-0.3261	-0.3269	F	1	-0.3267	-0.3268
S	2	0.4110	0.4317	O	2	-0.6019	-0.6354
C	3	-0.0841	-0.0854	O	3	-0.5540	-0.5487
C	4	-0.2128	-0.2132	N	4	-0.4981	-0.5029

H	5	0.2422	0.2409	N	5	-0.6327	-0.6200
C	6	-0.2444	-0.2465	H	6	0.4427	0.4451
H	7	0.2418	0.2403	C	7	-0.3864	-0.3876
C	8	-0.2362	-0.2381	H	8	0.2399	0.2411
H	9	0.2425	0.2408	H	9	0.2609	0.2578
C	10	-0.2409	-0.2417	C	10	-0.2940	-0.2898
H	11	0.2473	0.2451	H	11	0.2805	0.2748
C	12	-0.1983	-0.2027	C	12	-0.3150	-0.3142
C	13	-0.2490	-0.2473	H	13	0.2727	0.2758
H	14	0.2564	0.2551	C	14	0.5827	0.5814
C	15	-0.1805	-0.1854	C	15	-0.1677	-0.1673
O	16	-0.5943	-0.6331	C	16	-0.1645	-0.1652
O	17	-0.5588	-0.5525	H	17	0.2676	0.2678
N	18	-0.4958	-0.5015	C	18	-0.3081	-0.3080
N	19	-0.6313	-0.6205	H	19	0.2585	0.2586
H	20	0.4439	0.4449	C	20	0.4457	0.4451
C	21	-0.3742	-0.3868	C	21	-0.3094	-0.3095
H	22	0.2450	0.2418	H	22	0.2592	0.2588
H	23	0.2487	0.2574	C	23	-0.1925	-0.1920
S	24	0.1507	0.1547	H	24	0.2573	0.2548
C	25	-0.6052	-0.6115	C	25	0.0697	0.0708
H	26	0.2359	0.2693	C	26	-0.1072	-0.1020
H	27	0.2623	0.2533	C	27	-0.1918	-0.1881
C	28	-0.0516	-0.0586	H	28	0.2641	0.2641
H	29	0.2547	0.2772	C	29	-0.2552	-0.2504
C	30	-0.2841	-0.2866	H	30	0.2467	0.2478
H	31	0.2821	0.2768	C	31	-0.2129	-0.2135
C	32	-0.3119	-0.3202	H	32	0.2446	0.2455
H	33	0.2794	0.2809	C	33	-0.2777	-0.2751
C	34	0.5839	0.5820	H	34	0.2439	0.2446

C 35	-0.1708	-0.1670	C 35	0.1723	0.1670
C 36	-0.1652	-0.1658	C 36	0.7198	0.7323
H 37	0.2664	0.2670	S 37	0.4506	0.4390
C 38	-0.3090	-0.3083	C 38	-0.0821	-0.0817
H 39	0.2585	0.2583	C 39	-0.2151	-0.2139
C 40	0.4469	0.4450	H 40	0.2412	0.2408
C 41	-0.3089	-0.3094	C 41	-0.2443	-0.2465
H 42	0.2604	0.2588	H 42	0.2413	0.2398
C 43	-0.1886	-0.1906	C 43	-0.2378	-0.2395
H 44	0.2611	0.2553	H 44	0.2421	0.2406
C 45	0.0660	0.0711	C 45	-0.2399	-0.2411
C 46	-0.1007	-0.1016	H 46	0.2468	0.2454
C 47	-0.1868	-0.1873	C 47	-0.2071	-0.2066
H 48	0.2456	0.2622	C 48	-0.2681	-0.2653
C 49	-0.2516	-0.2512	H 49	0.2502	0.2730
H 50	0.2457	0.2470	C 50	-0.1862	-0.1912
C 51	-0.2131	-0.2136	S 51	0.1599	0.1579
H 52	0.2447	0.2451	C 52	-0.6129	-0.6121
C 53	-0.2758	-0.2755	H 53	0.2705	0.2709
H 54	0.2439	0.2444	H 54	0.2519	0.2527
C 55	0.1682	0.1670	C 55	-0.0452	-0.0528
C 56	0.7148	0.7319	H 56	0.2511	0.2717
O 57		-0.7985	O 57		-0.8027
H 58		0.5068	H 58		0.5080
C 59		-0.3106	C 59		-0.3114
H 60		0.1888	H 60		0.1911
H 61		0.2103	H 61		0.2077
H 62		0.1866	H 62		0.1894