Supplementary Material

RSC Advances

Stereospecific Alkylation of Substituted Adenines by the Mitsunobu Coupling Reaction under Microwave-Assisted Conditions

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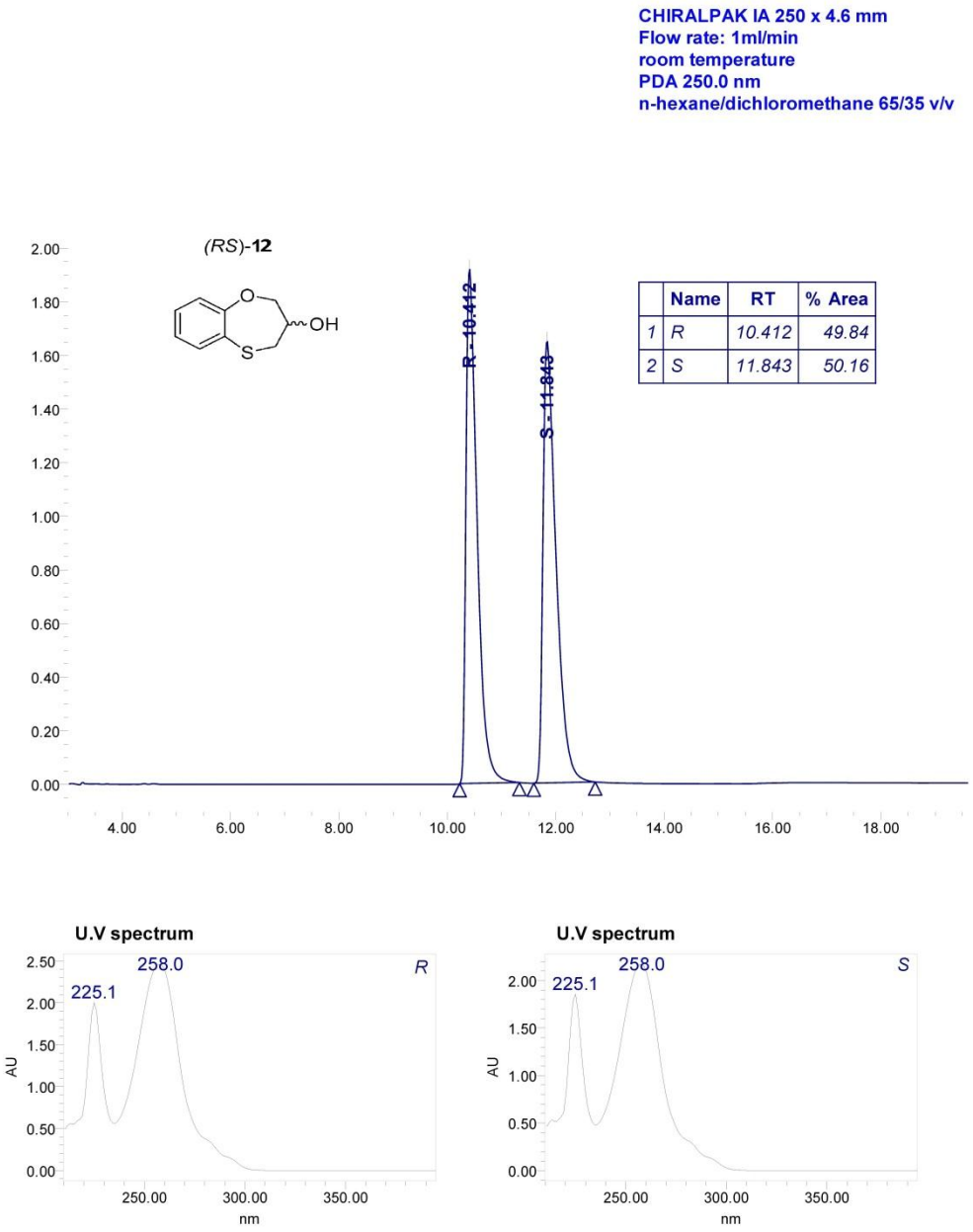

CHIRALPAK IA 250 x 4.6 mm
Flow rate: 1ml/min
room temperature
PDA 250.0 nm
n-hexane/dichloromethane 65/35 v/v
(RS)-12
OH
S
R - 10.412
S - 11.843
Name RT % Area
1 R 10.412 49.84
2 S 11.843 50.16
U.V spectrum
258.0
225.1
R
AU
nm
U.V spectrum
258.0
225.1
S
AU
nm

Figure S1

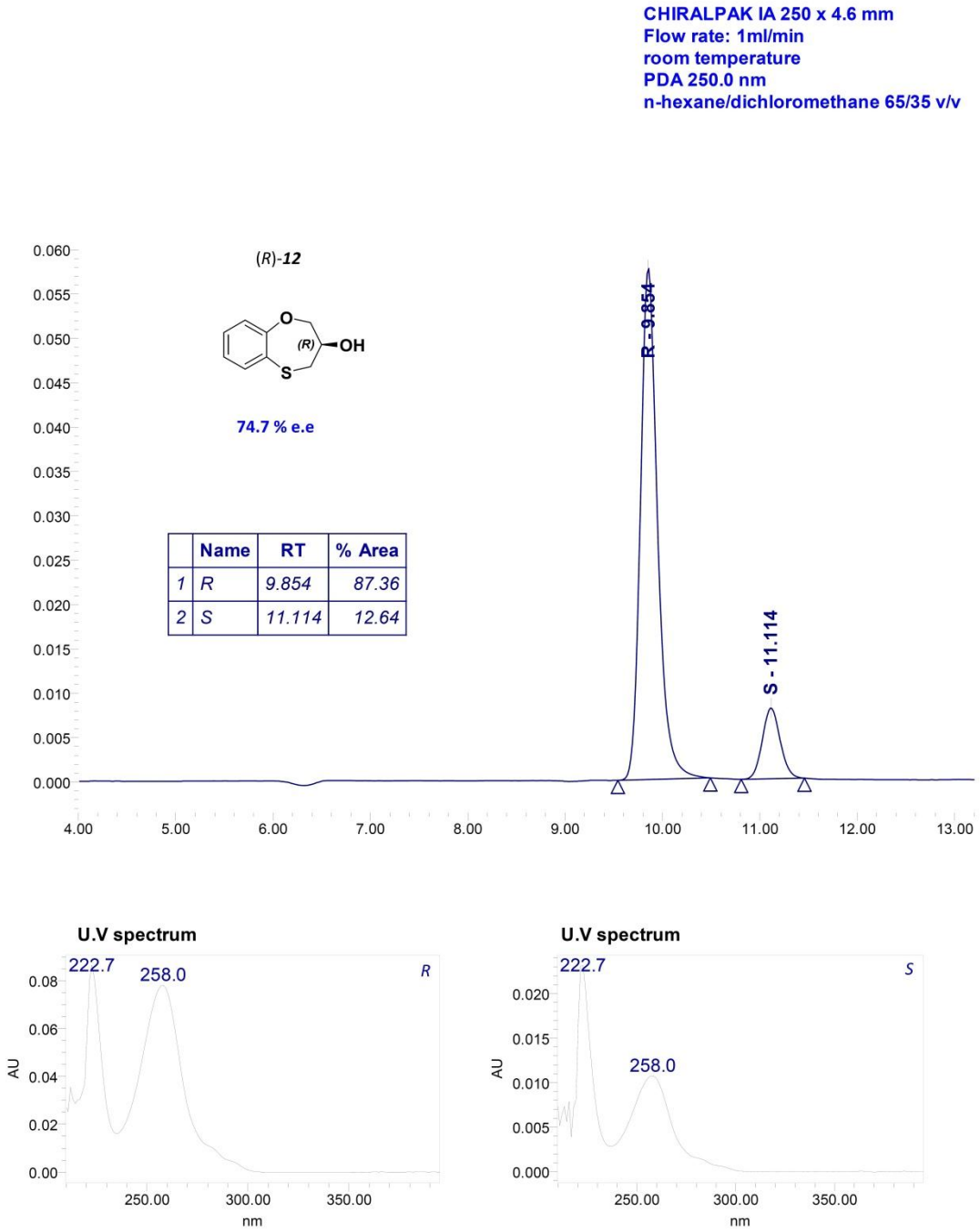

CHIRALPAK IA 250 x 4.6 mm
Flow rate: 1ml/min
room temperature
PDA 250.0 nm
n-hexane/dichloromethane 65/35 v/v
(R)-12
74.7 % e.e
Name RT % Area
1 R 9.854 87.36
2 S 11.114 12.64
R - 9.854
S - 11.114
U.V spectrum
222.7
258.0
R
AU
nm
U.V spectrum
222.7
258.0
S
AU
nm

Figure S2

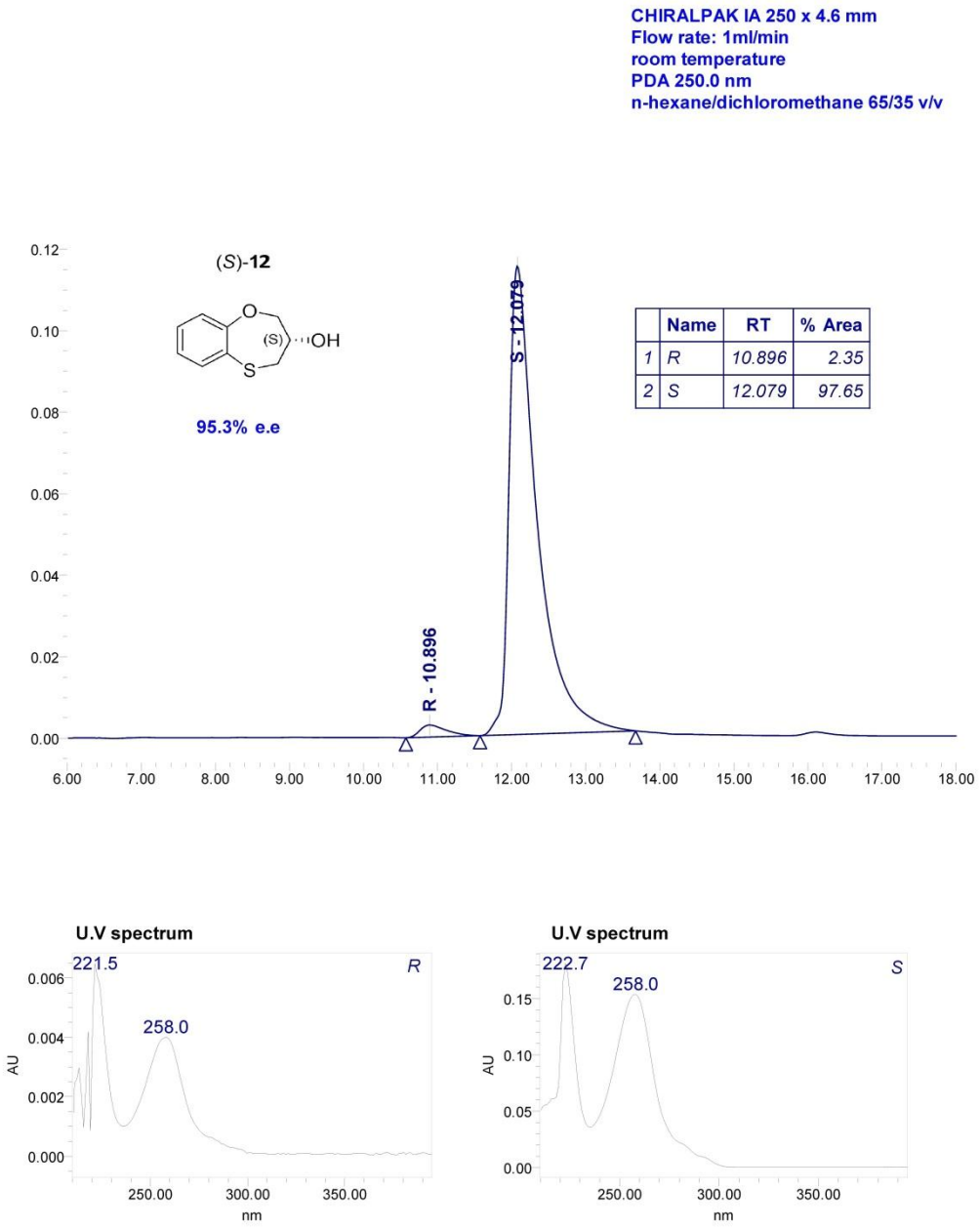

CHIRALPAK IA 250 x 4.6 mm
Flow rate: 1ml/min
room temperature
PDA 250.0 nm
n-hexane/dichloromethane 65/35 v/v
(S)-12
95.3% e.e
S - 12.079
R - 10.896
Name RT % Area
1 R 10.896 2.35
2 S 12.079 97.65
U.V spectrum
221.5
258.0
R
U.V spectrum
222.7
258.0
S
AU
nm

Figure S3

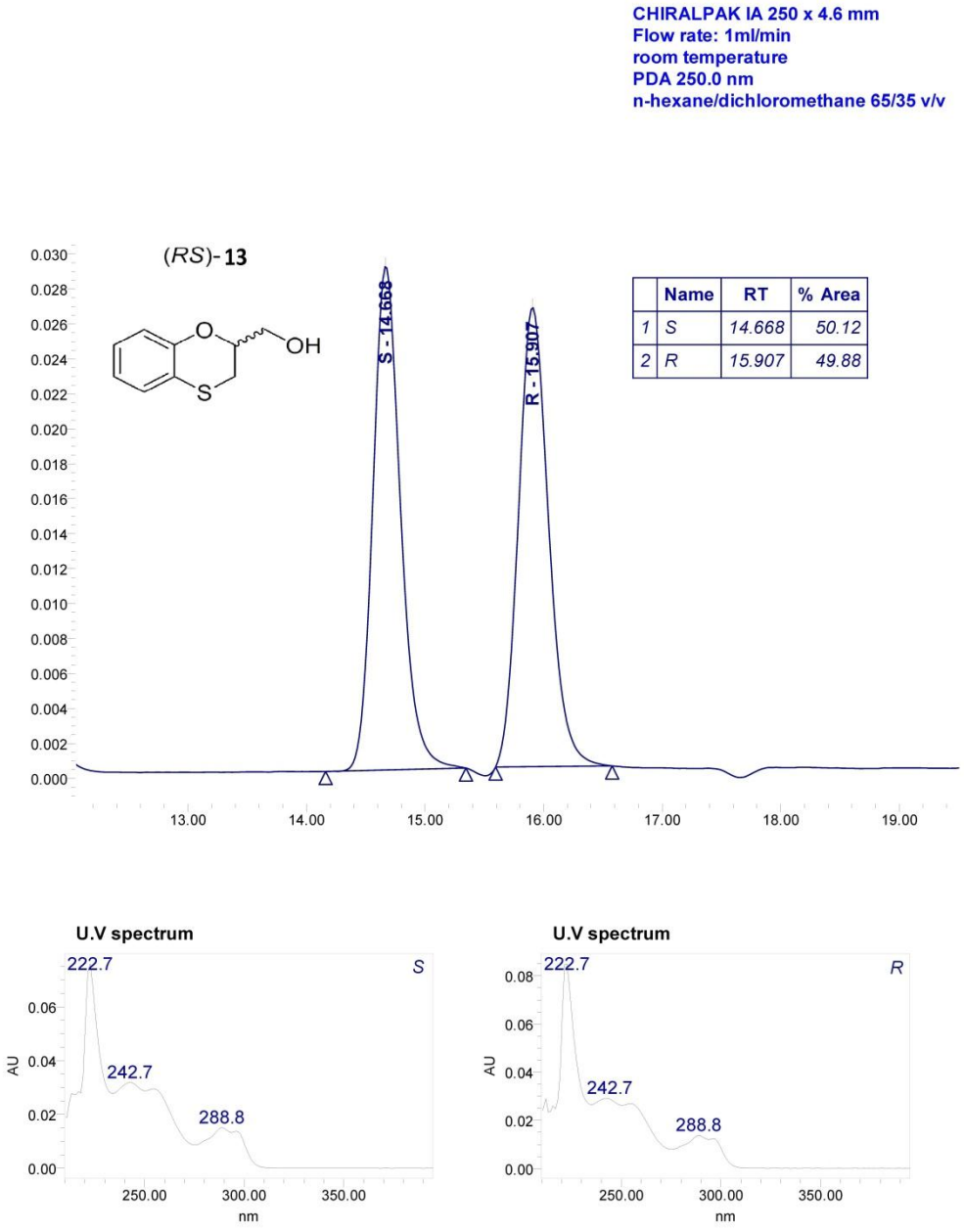

CHIRALPAK IA 250 x 4.6 mm
Flow rate: 1ml/min
room temperature
PDA 250.0 nm
n-hexane/dichloromethane 65/35 v/v
(RS)-13
OH
S
O
S - 14.668
R - 15.907
Name RT % Area
1 S 14.668 50.12
2 R 15.907 49.88
AU
nm
U.V spectrum
222.7
242.7
288.8
S
U.V spectrum
222.7
242.7
288.8
R

Figure S4

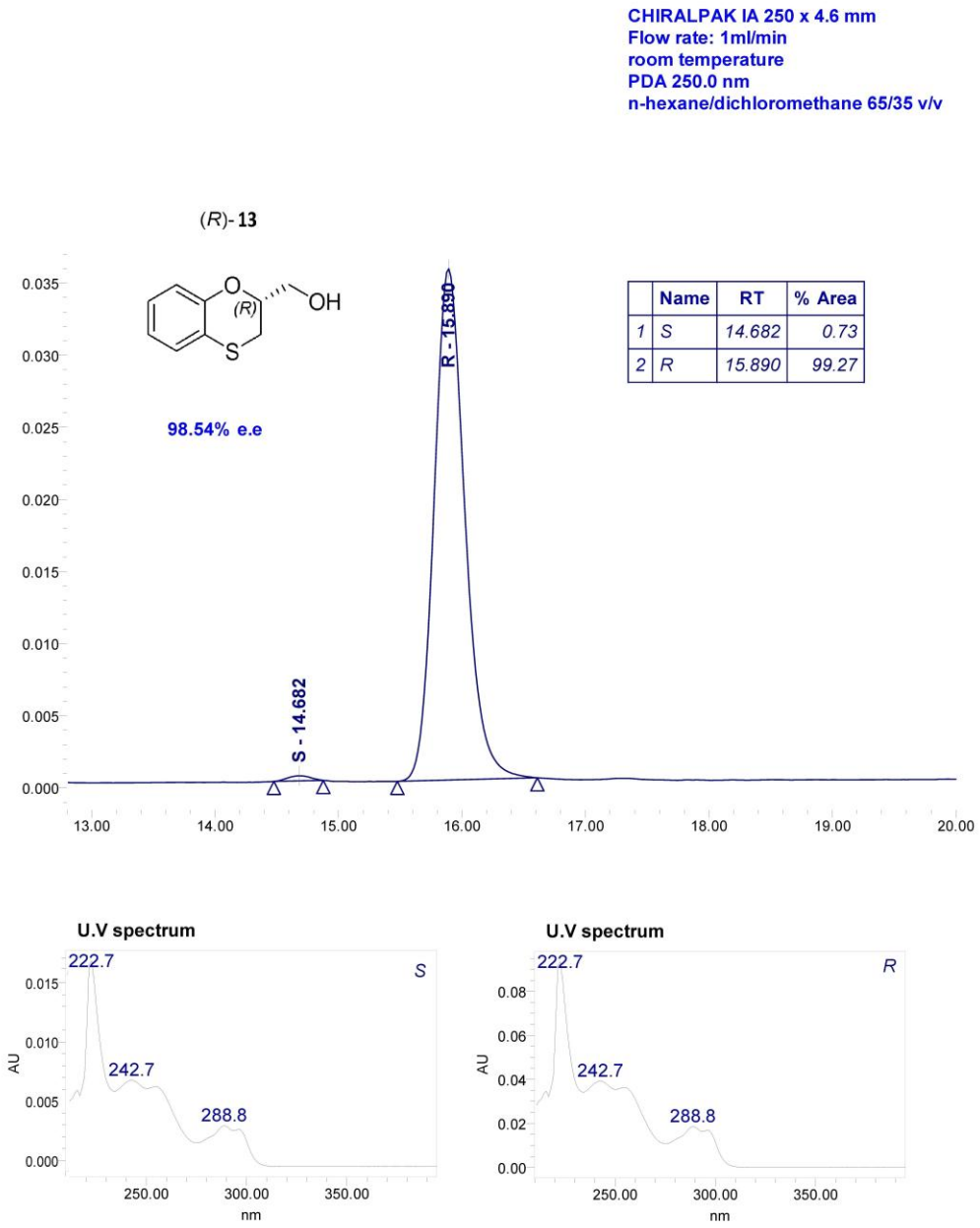

CHIRALPAK IA 250 x 4.6 mm
Flow rate: 1ml/min
room temperature
PDA 250.0 nm
n-hexane/dichloromethane 65/35 v/v
(R)- 13
98.54% e.e
Name RT % Area
1 S 14.682 0.73
2 R 15.890 99.27
S - 14.682
R - 15.890
U.V spectrum
222.7
242.7
288.8
S
U.V spectrum
222.7
242.7
288.8
R
AU
nm

Figure S5

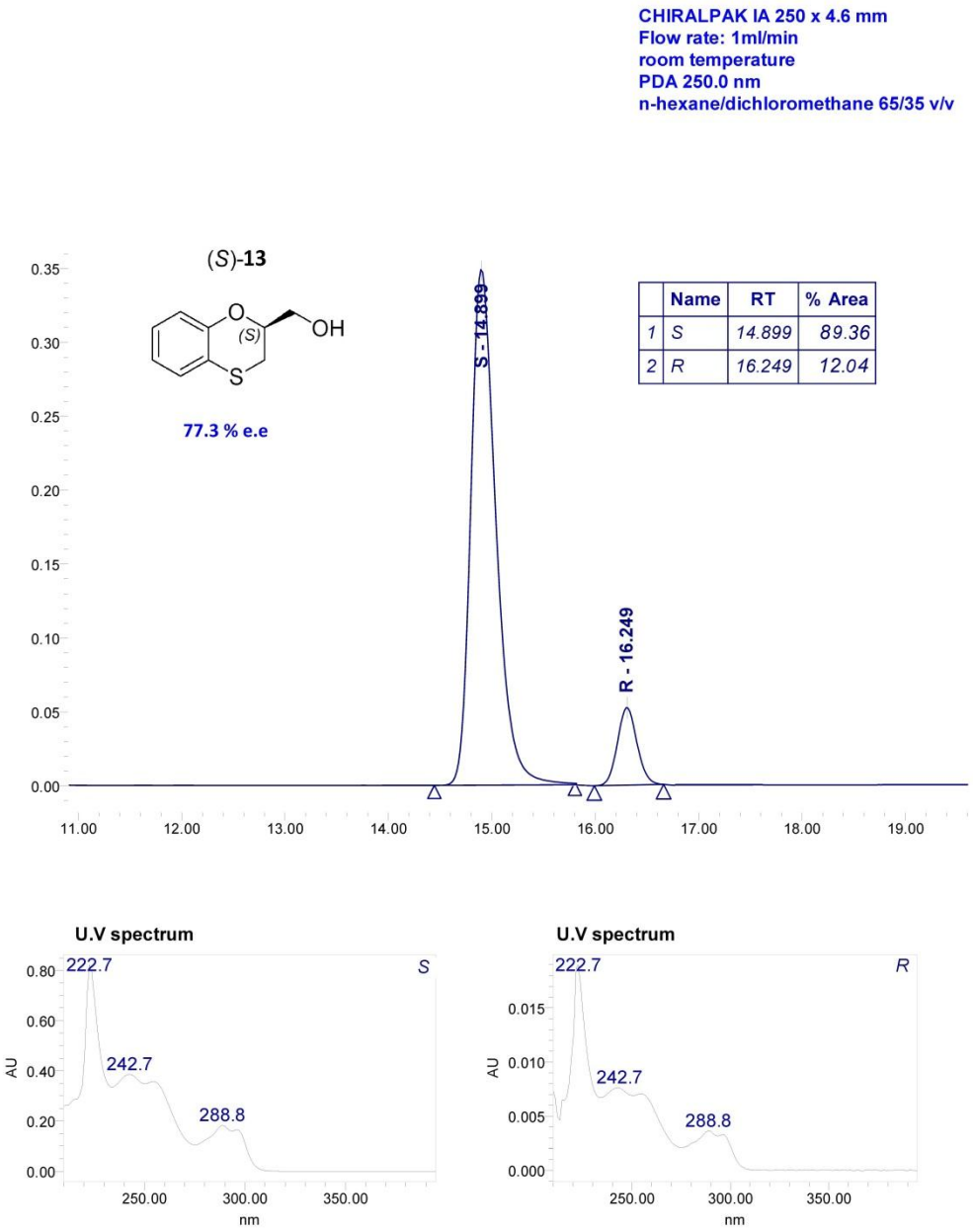

CHIRALPAK IA 250 x 4.6 mm
Flow rate: 1ml/min
room temperature
PDA 250.0 nm
n-hexane/dichloromethane 65/35 v/v
(S)-13
77.3 % e.e
S - 14.899
R - 16.249
Name RT % Area
1 S 14.899 89.36
2 R 16.249 12.04
U.V spectrum
222.7
242.7
288.8
S
U.V spectrum
222.7
242.7
288.8
R
AU
nm

Figure S6

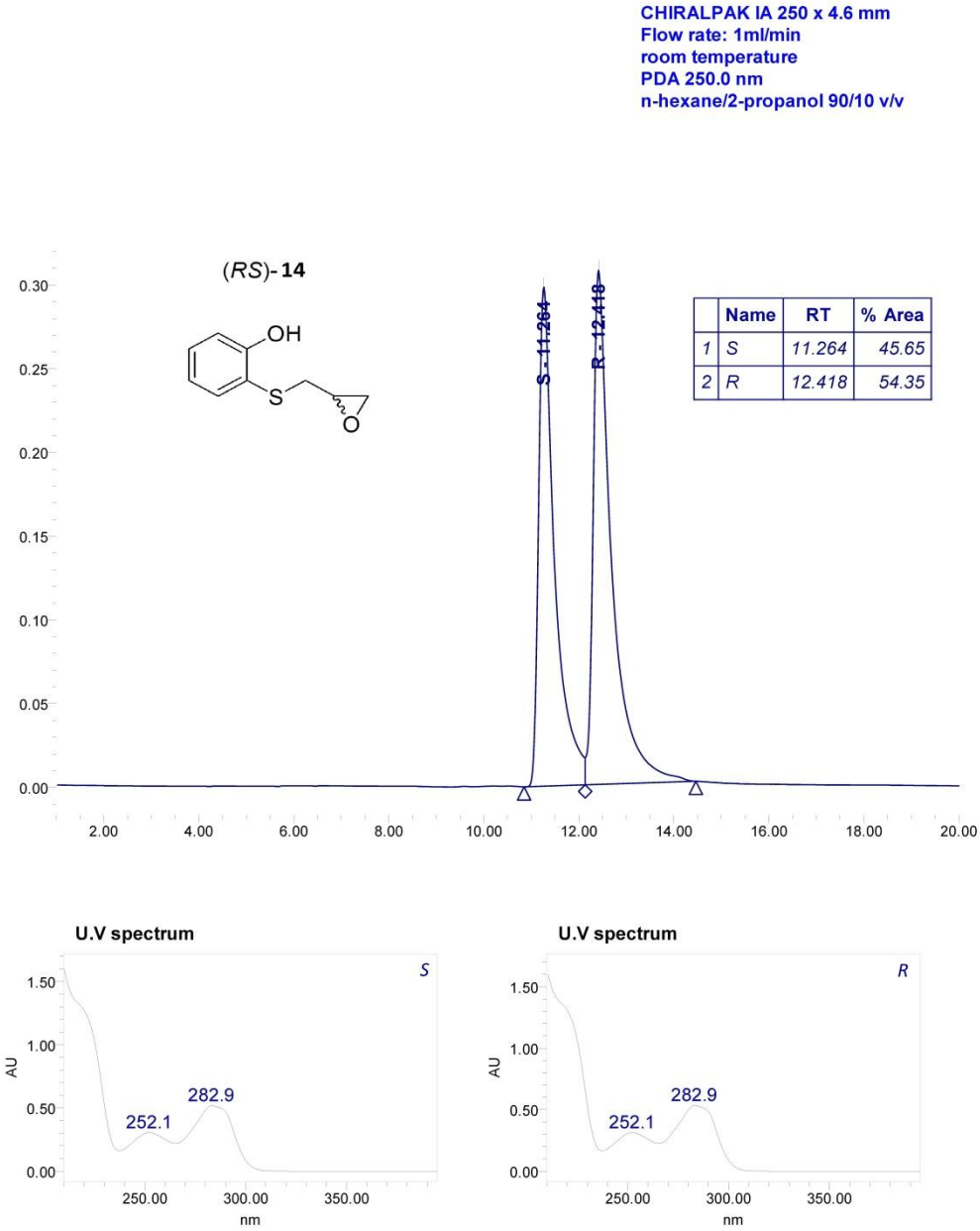

CHIRALPAK IA 250 x 4.6 mm
Flow rate: 1ml/min
room temperature
PDA 250.0 nm
n-hexane/2-propanol 90/10 v/v
(RS)-14
OH
S
O
S - 11.264
R - 12.418
Name RT % Area
1 S 11.264 45.65
2 R 12.418 54.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
2.00 4.00 6.00 8.00 10.00 12.00 14.00 16.00 18.00 20.00
U.V spectrum
S
AU
1.50
1.00
0.50
0.00
252.1
282.9
250.00 300.00 350.00
nm
U.V spectrum
R
AU
1.50
1.00
0.50
0.00
252.1
282.9
250.00 300.00 350.00
nm

Figure S7

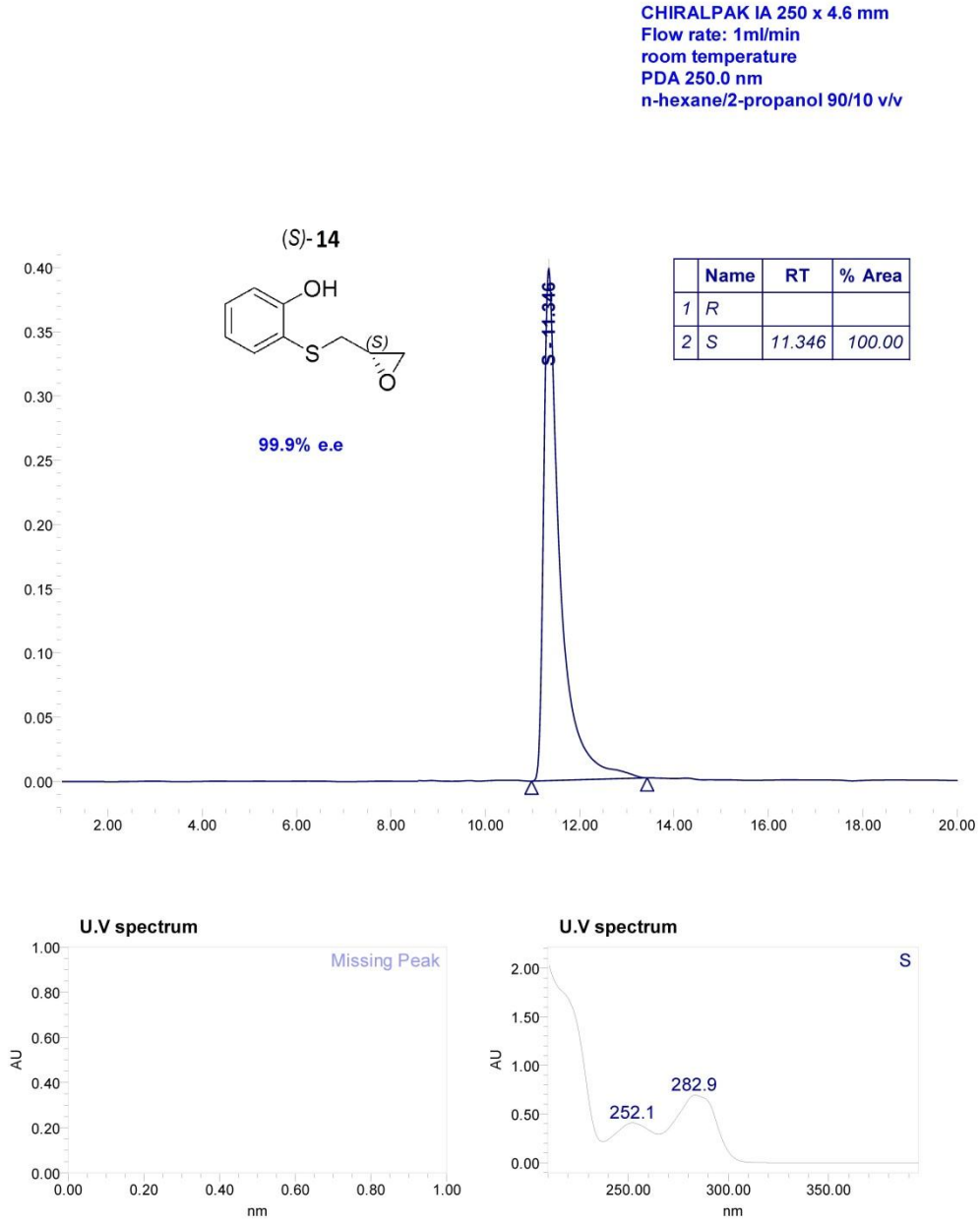

CHIRALPAK IA 250 x 4.6 mm
Flow rate: 1ml/min
room temperature
PDA 250.0 nm
n-hexane/2-propanol 90/10 v/v
(S)-14
OH
S
(S)
O
99.9% e.e
S - 11.346
Name
RT
% Area
1 R
2 S 11.346 100.00
AU
nm
U.V spectrum
Missing Peak
U.V spectrum
S
252.1
282.9

Figure S8

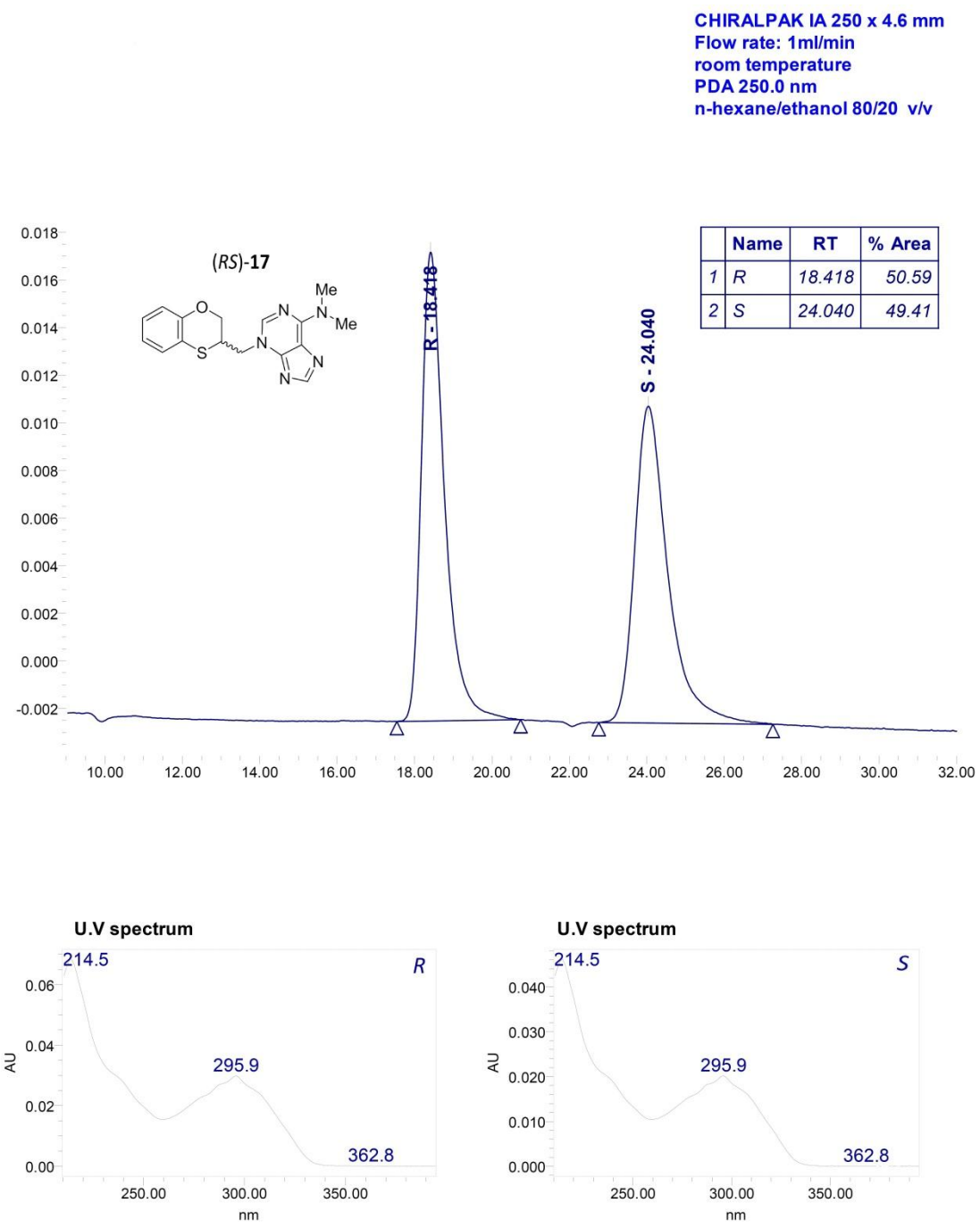

CHIRALPAK IA 250 x 4.6 mm
Flow rate: 1ml/min
room temperature
PDA 250.0 nm
n-hexane/ethanol 80/20 v/v
(RS)-17
Me
N
Me
R - 18.418
S - 24.040
Name RT % Area
1 R 18.418 50.59
2 S 24.040 49.41
0.018
0.016
0.014
0.012
0.010
0.008
0.006
0.004
0.002
0.000
-0.002
10.00 12.00 14.00 16.00 18.00 20.00 22.00 24.00 26.00 28.00 30.00 32.00
U.V spectrum
214.5
R
295.9
362.8
AU
0.06
0.04
0.02
0.00
250.00 300.00 350.00
nm
U.V spectrum
214.5
S
295.9
362.8
AU
0.040
0.030
0.020
0.010
0.000
250.00 300.00 350.00
nm

Figure S9

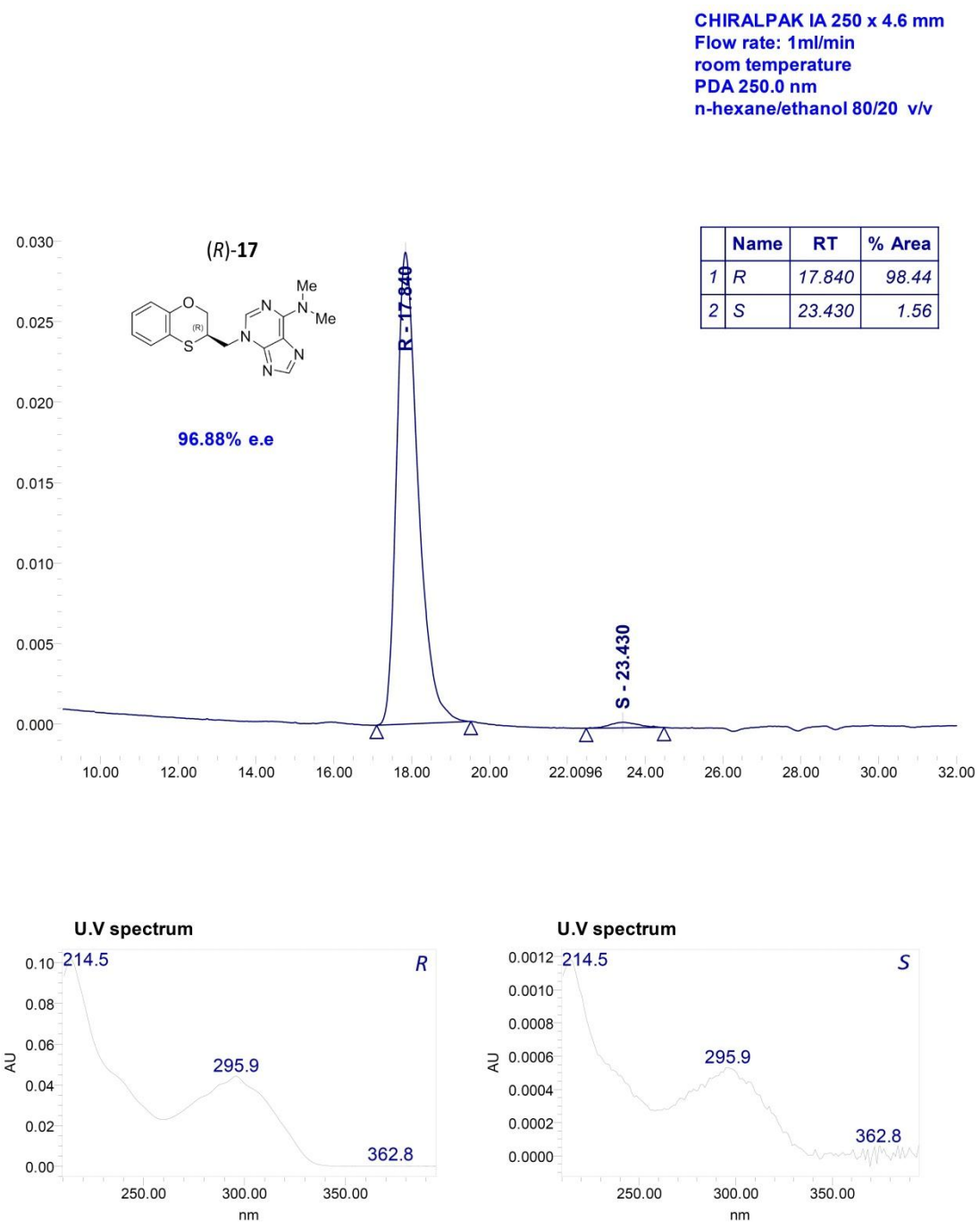
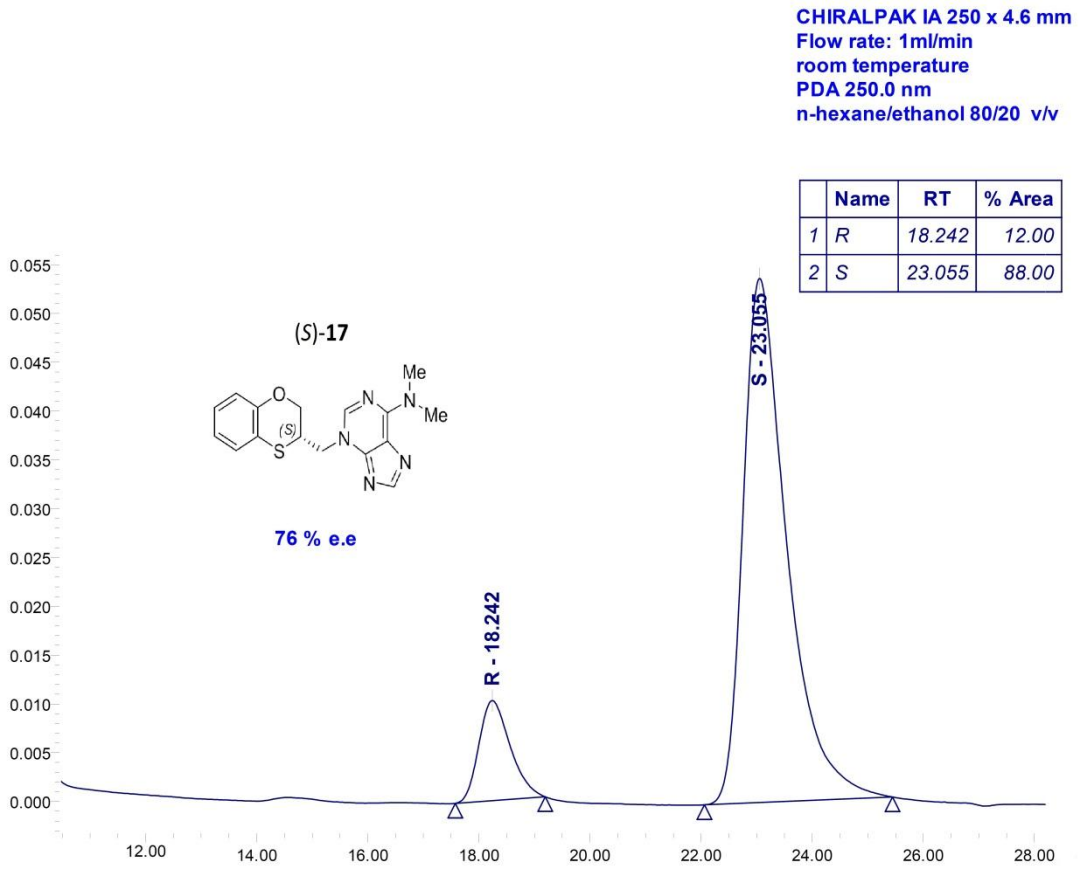

CHIRALPAK IA 250 x 4.6 mm
Flow rate: 1ml/min
room temperature
PDA 250.0 nm
n-hexane/ethanol 80/20 v/v
(R)-17
96.88% e.e
R - 17.840
S - 23.430
Name RT % Area
1 R 17.840 98.44
2 S 23.430 1.56
U.V spectrum
214.5
295.9
362.8
AU
nm
U.V spectrum
214.5
295.9
362.8
AU
nm

Figure S10



	Name	RT	% Area
1	R	18.242	12.00
2	S	23.055	88.00

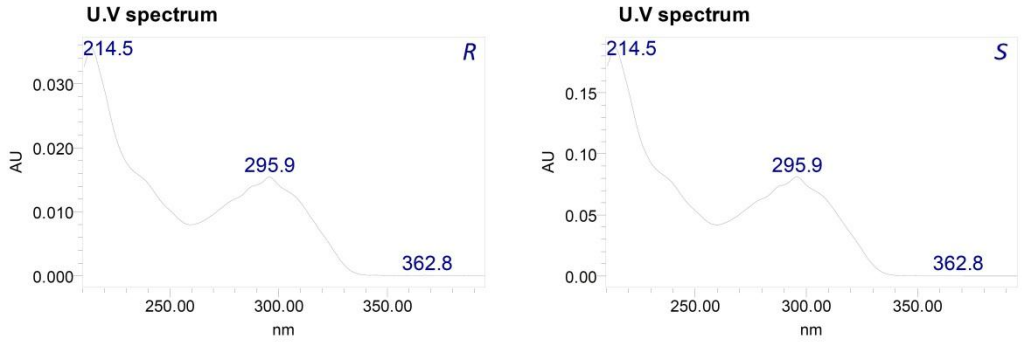
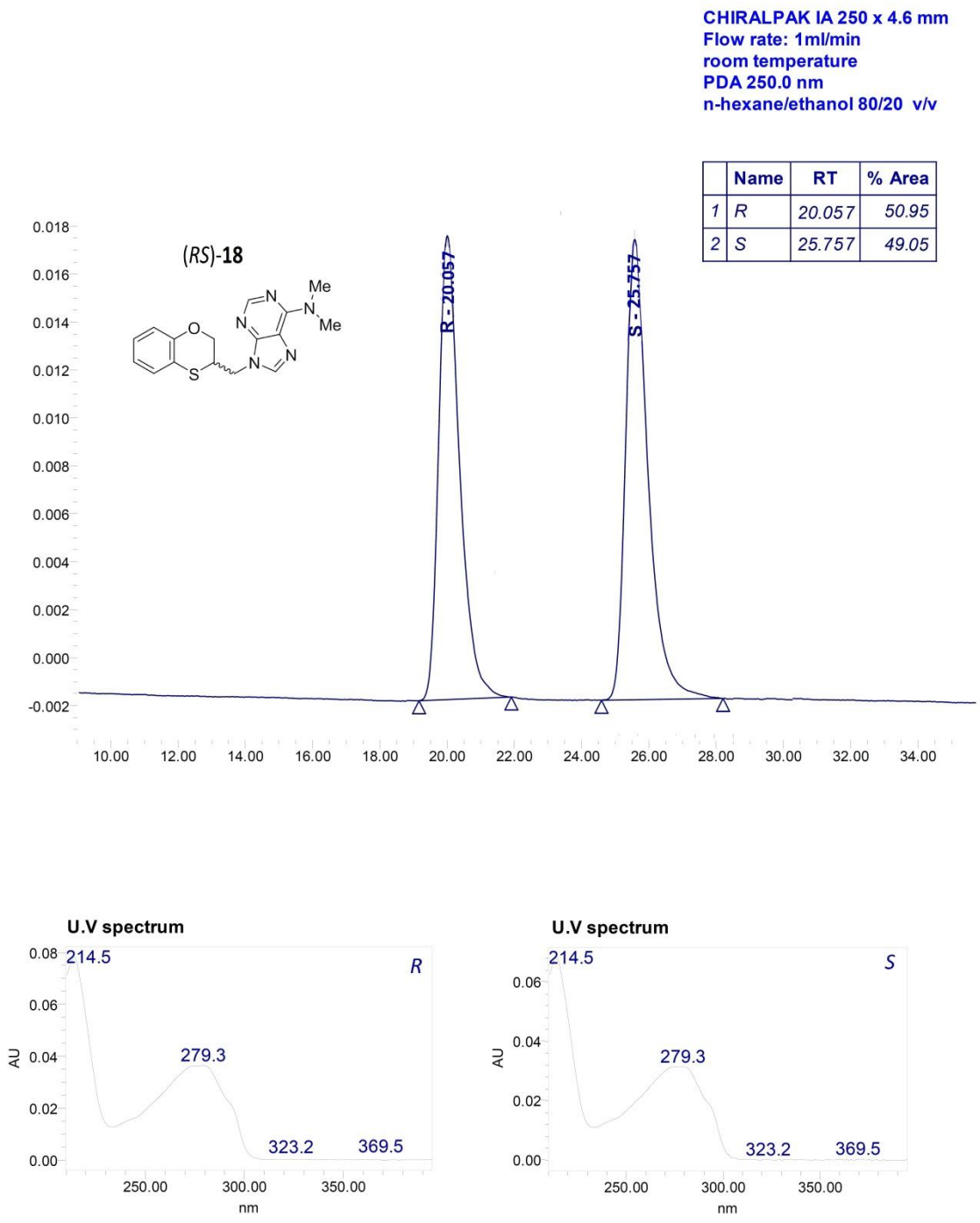


Figure S11



	Name	RT	% Area
1	R	20.057	50.95
2	S	25.757	49.05

Figure S12

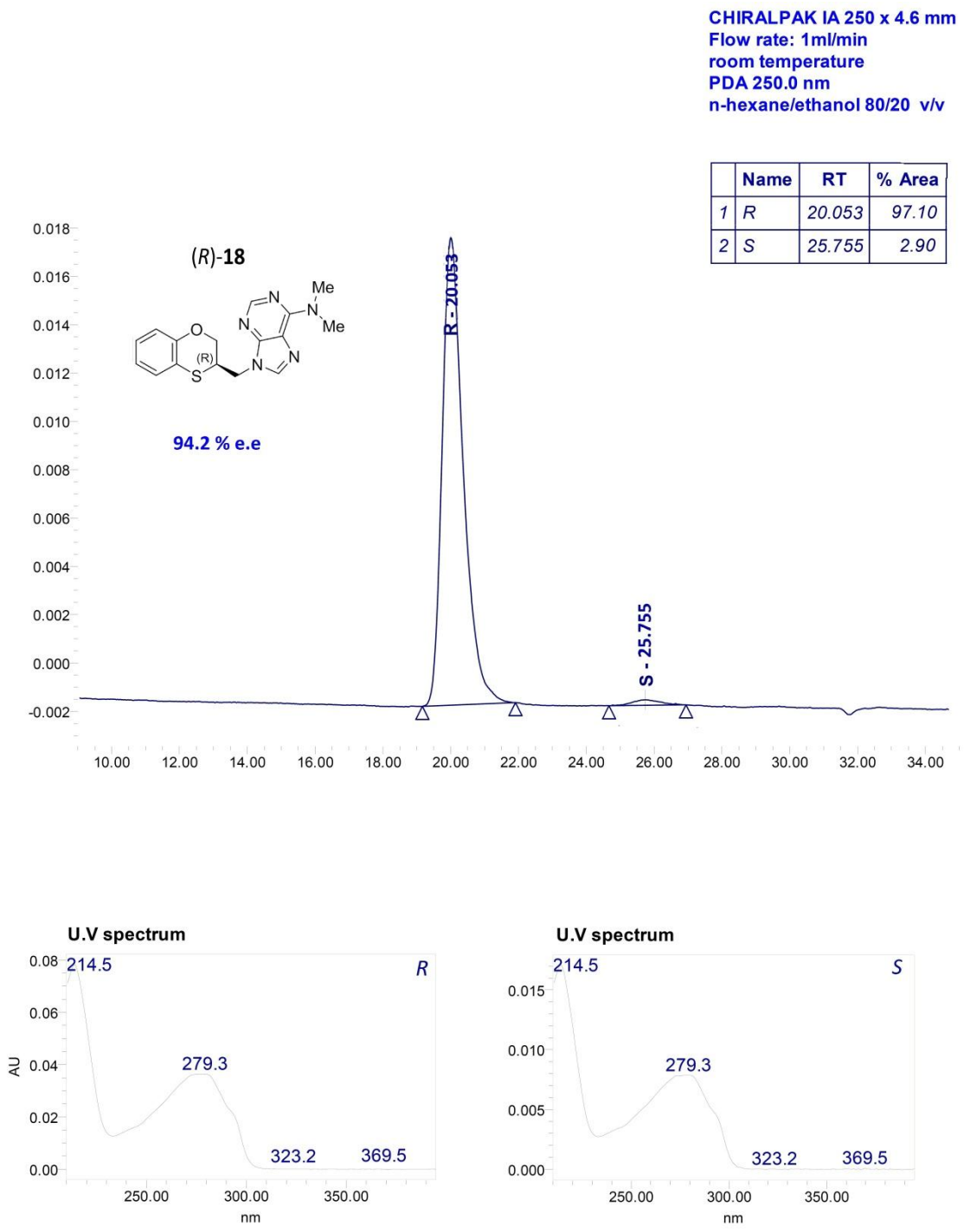
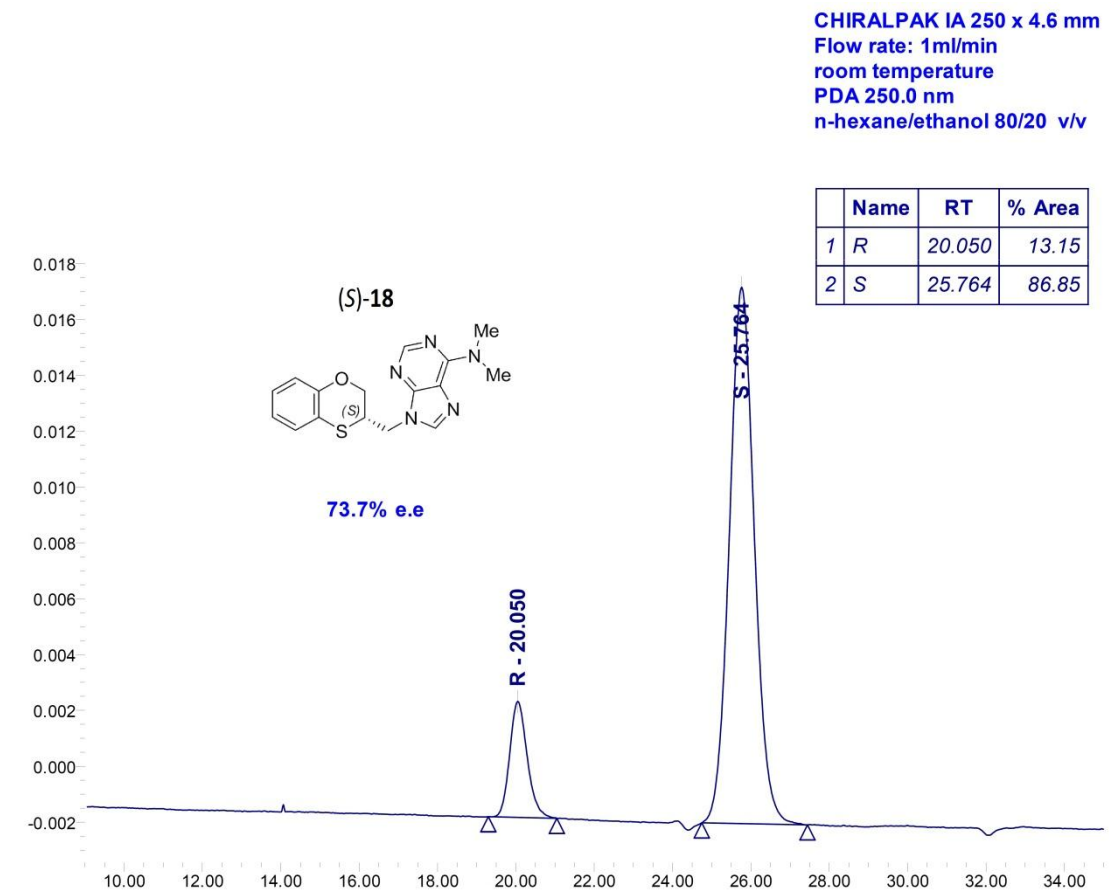

CHIRALPAK IA 250 x 4.6 mm
Flow rate: 1ml/min
room temperature
PDA 250.0 nm
n-hexane/ethanol 80/20 v/v
Name RT % Area
1 R 20.053 97.10
2 S 25.755 2.90
(R)-18
94.2 % e.e
R - 20.053
S - 25.755
AU
nm
U.V spectrum
214.5
279.3
323.2
369.5
R
S

Figure S13


CHIRALPAK IA 250 x 4.6 mm
Flow rate: 1ml/min
room temperature
PDA 250.0 nm
n-hexane/ethanol 80/20 v/v
Name RT % Area
1 R 20.050 13.15
2 S 25.764 86.85
(S)-18
73.7% e.e
R - 20.050
S - 25.764
AU
nm

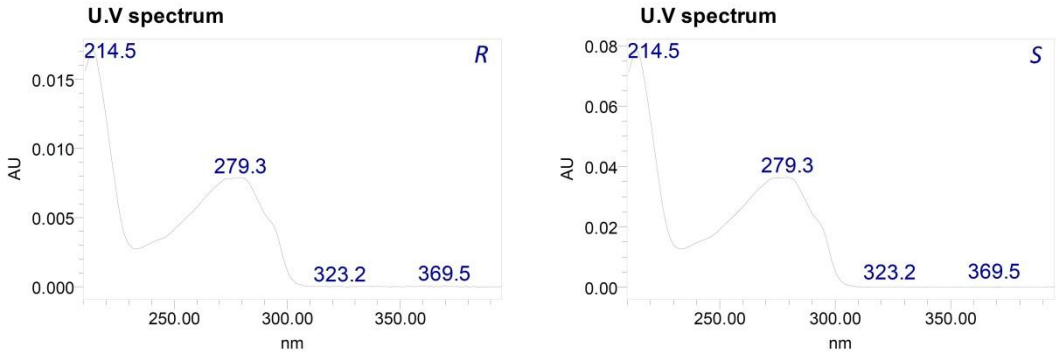
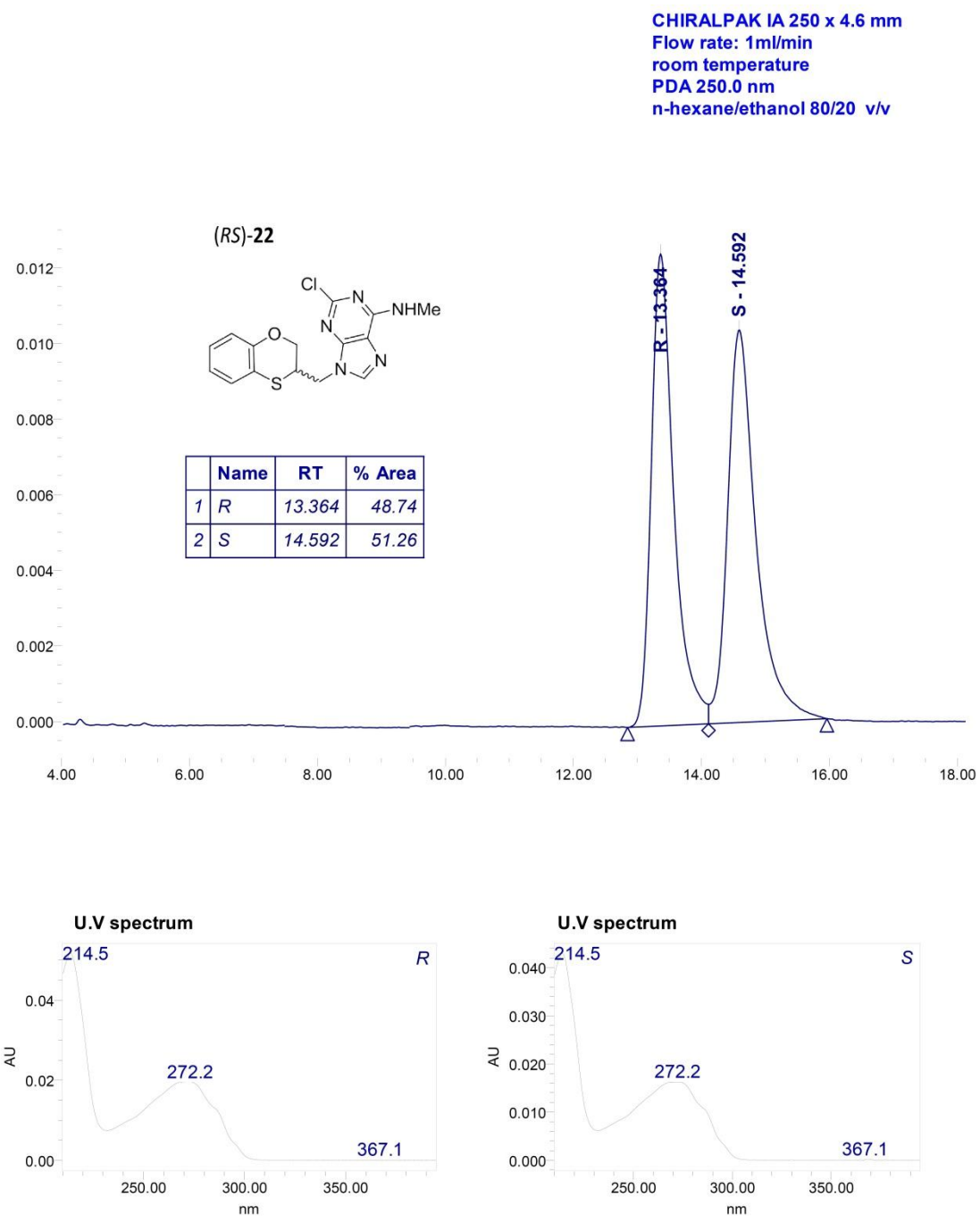
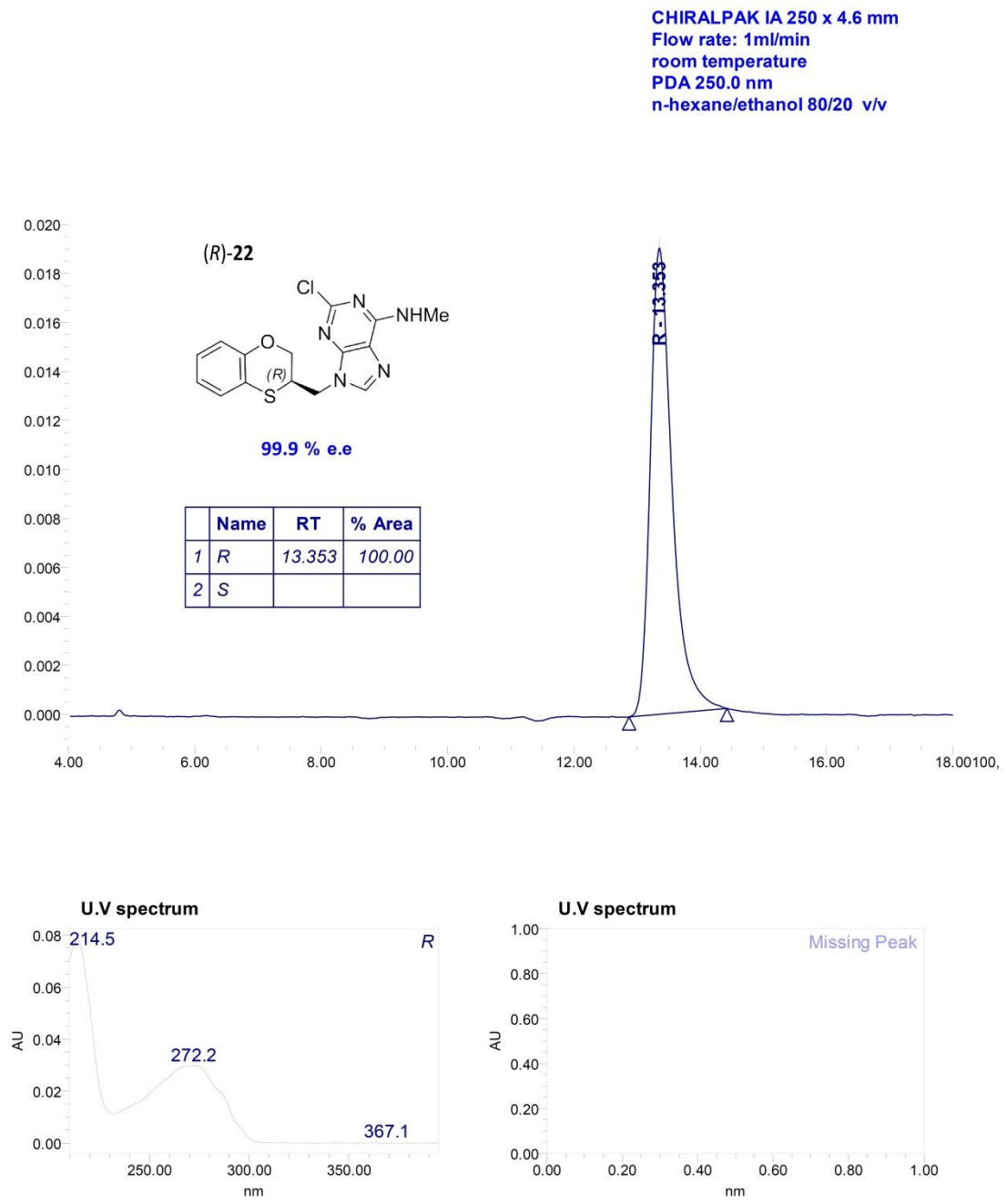

U.V spectrum
214.5
R
279.3
323.2
369.5
U.V spectrum
214.5
S
279.3
323.2
369.5
AU
nm

Figure S14



	Name	RT	% Area
1	R	13.364	48.74
2	S	14.592	51.26

Figure S15



	Name	RT	% Area
1	R	13.353	100.00
2	S		

Figure S16

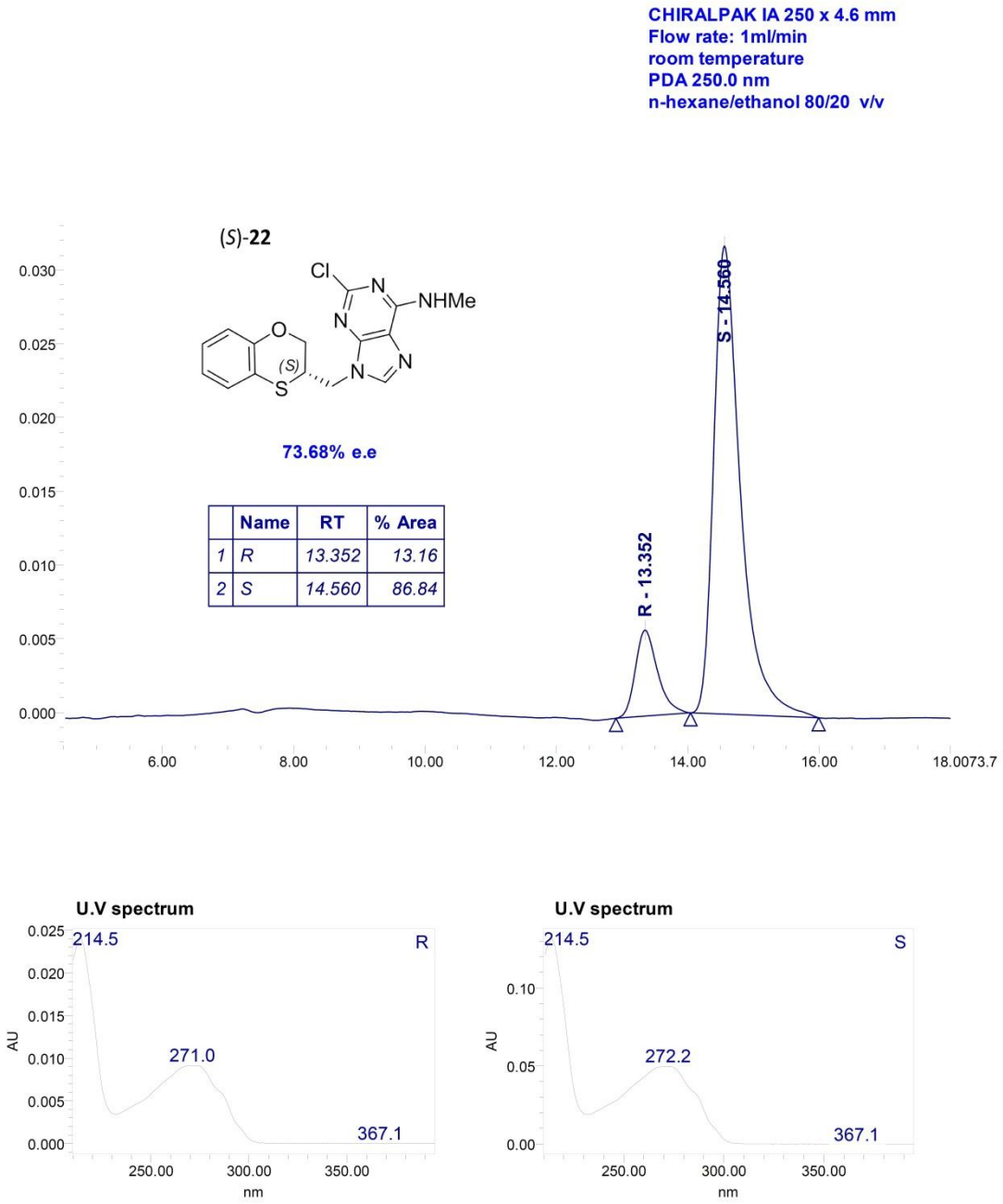

CHIRALPAK IA 250 x 4.6 mm
Flow rate: 1ml/min
room temperature
PDA 250.0 nm
n-hexane/ethanol 80/20 v/v
(S)-22
73.68% e.e
Name RT % Area
1 R 13.352 13.16
2 S 14.560 86.84
R - 13.352
S - 14.560
U.V spectrum
214.5
271.0
367.1
R
U.V spectrum
214.5
272.2
367.1
S
AU
nm

Figure S17

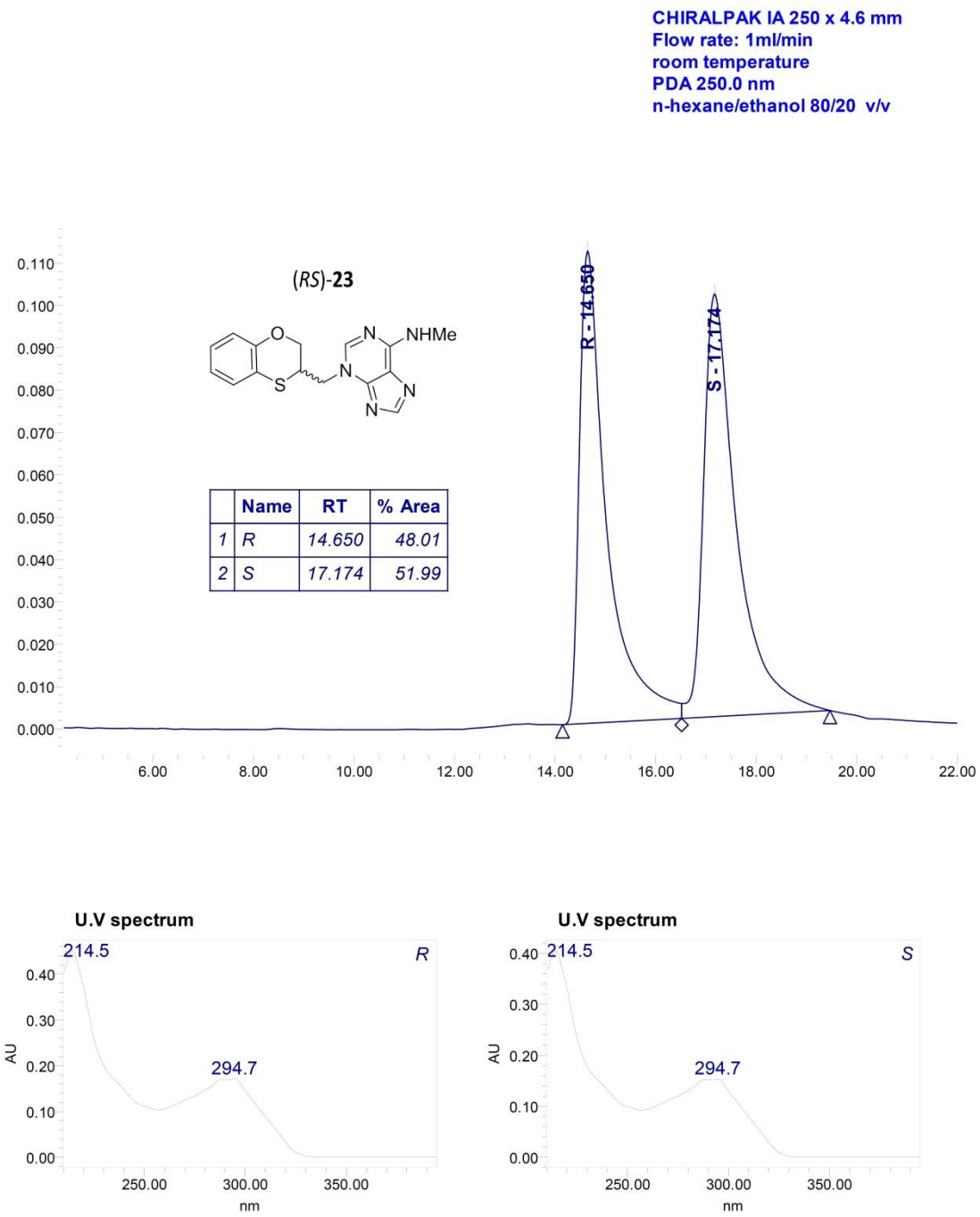

CHIRALPAK IA 250 x 4.6 mm
Flow rate: 1ml/min
room temperature
PDA 250.0 nm
n-hexane/ethanol 80/20 v/v
(RS)-23
NHMe
R - 14.650
S - 17.174
Name RT % Area
1 R 14.650 48.01
2 S 17.174 51.99
U.V spectrum
214.5
294.7
R
U.V spectrum
214.5
294.7
S
AU
nm

Figure S18

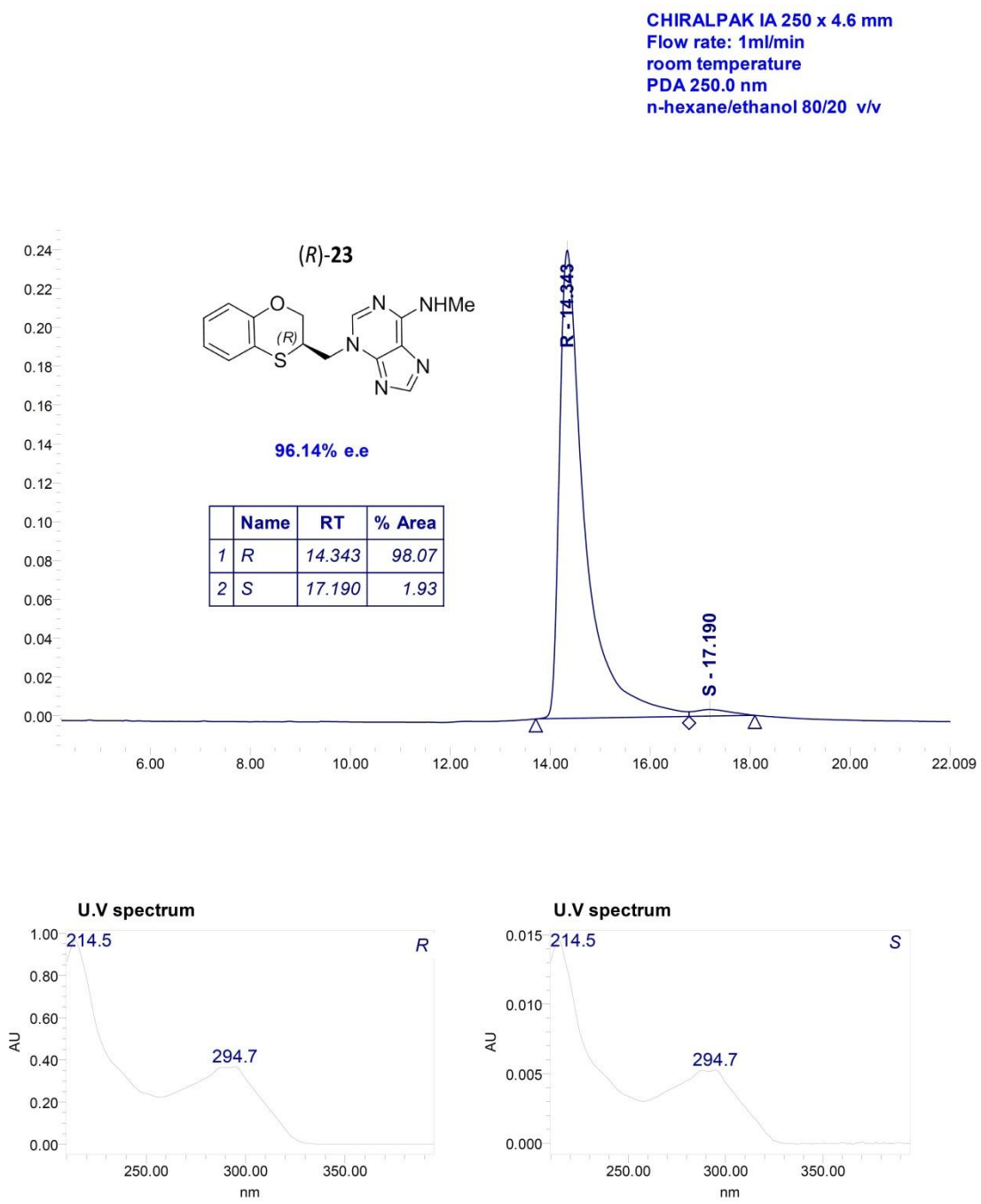

CHIRALPAK IA 250 x 4.6 mm
Flow rate: 1ml/min
room temperature
PDA 250.0 nm
n-hexane/ethanol 80/20 v/v
(R)-23
NHMe
96.14% e.e
Name RT % Area
1 R 14.343 98.07
2 S 17.190 1.93
R - 14.343
S - 17.190
U.V spectrum
214.5
294.7
R
U.V spectrum
214.5
294.7
S
AU
nm

Figure S19

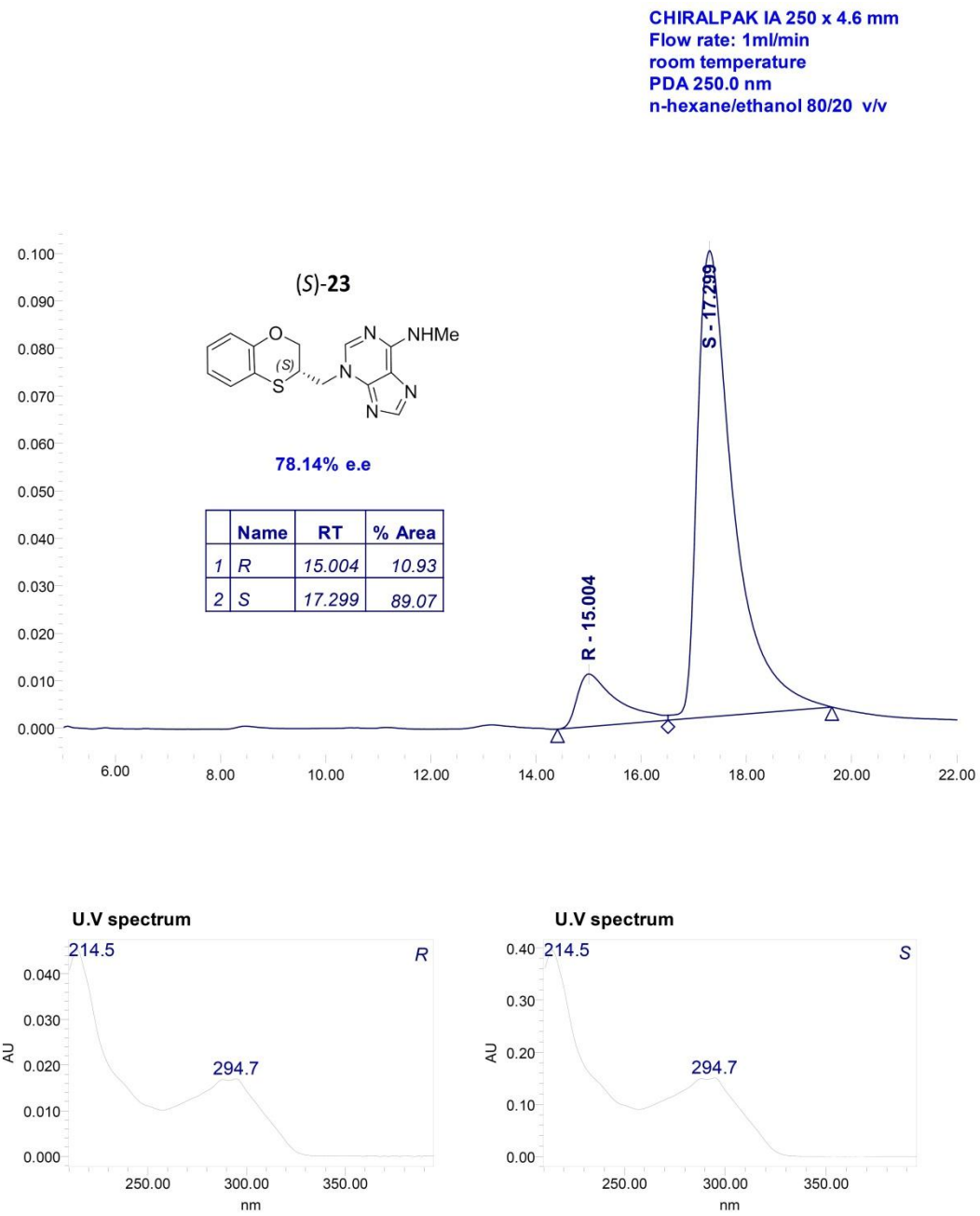
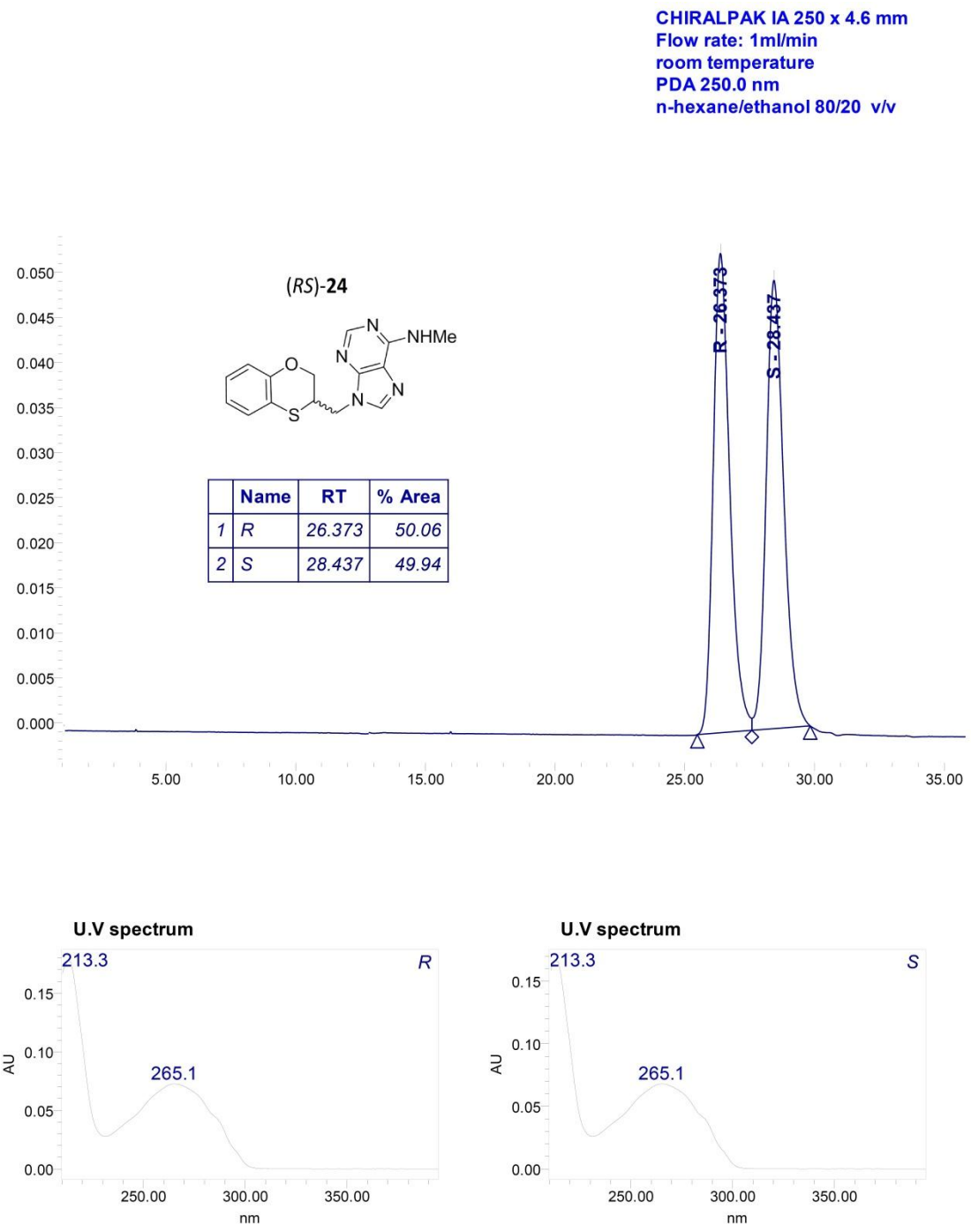

CHIRALPAK IA 250 x 4.6 mm
Flow rate: 1ml/min
room temperature
PDA 250.0 nm
n-hexane/ethanol 80/20 v/v
(S)-23
78.14% e.e
Name RT % Area
1 R 15.004 10.93
2 S 17.299 89.07
R - 15.004
S - 17.299
U.V spectrum
214.5
294.7
R
U.V spectrum
214.5
294.7
S
AU
nm

Figure S20



	Name	RT	% Area
1	R	26.373	50.06
2	S	28.437	49.94

Figure S21

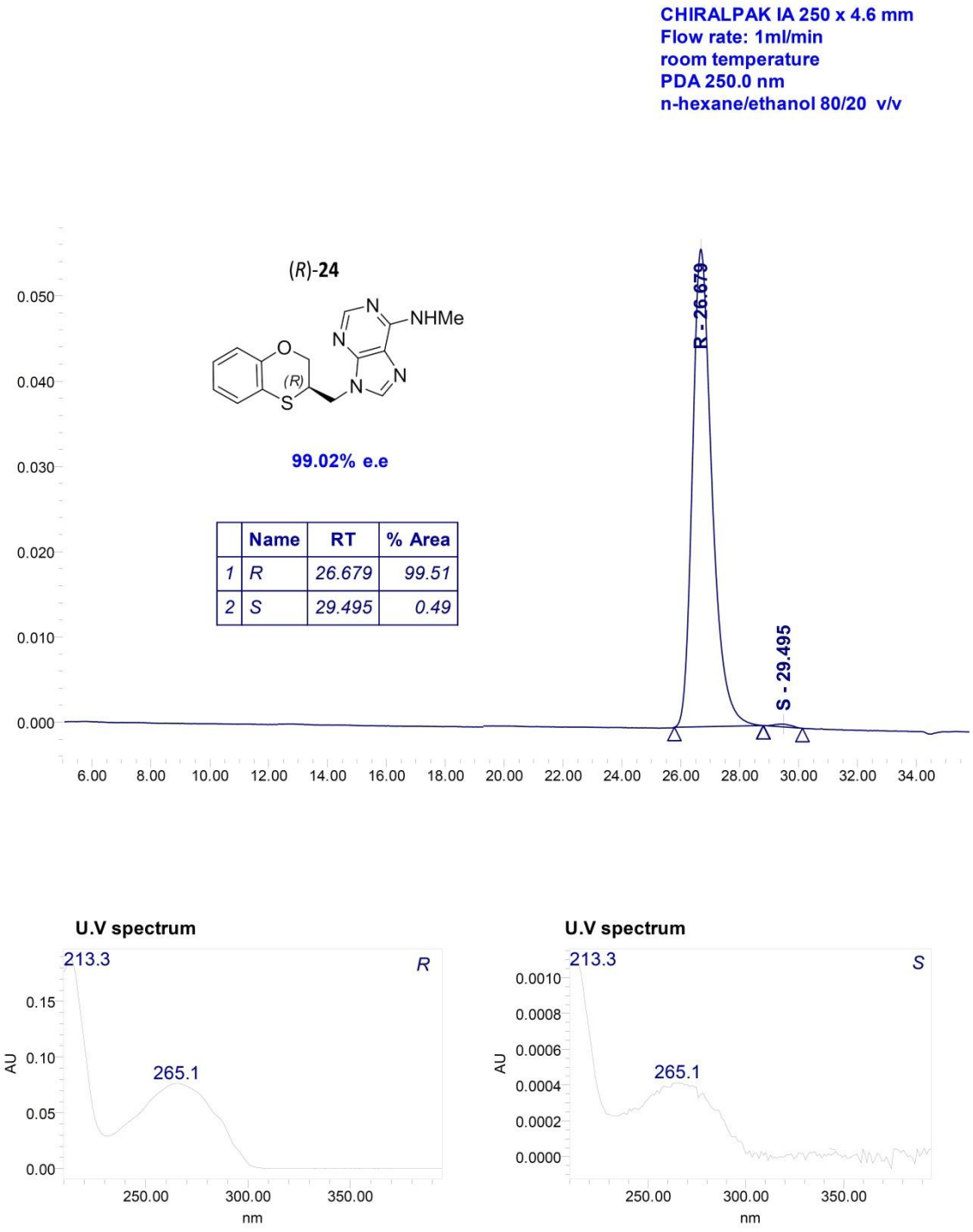

CHIRALPAK IA 250 x 4.6 mm
Flow rate: 1ml/min
room temperature
PDA 250.0 nm
n-hexane/ethanol 80/20 v/v
(R)-24
NHMe
99.02% e.e
Name RT % Area
1 R 26.679 99.51
2 S 29.495 0.49
R - 26.679
S - 29.495
U.V spectrum
213.3
265.1
AU
nm
U.V spectrum
213.3
265.1
AU
nm

Figure S22

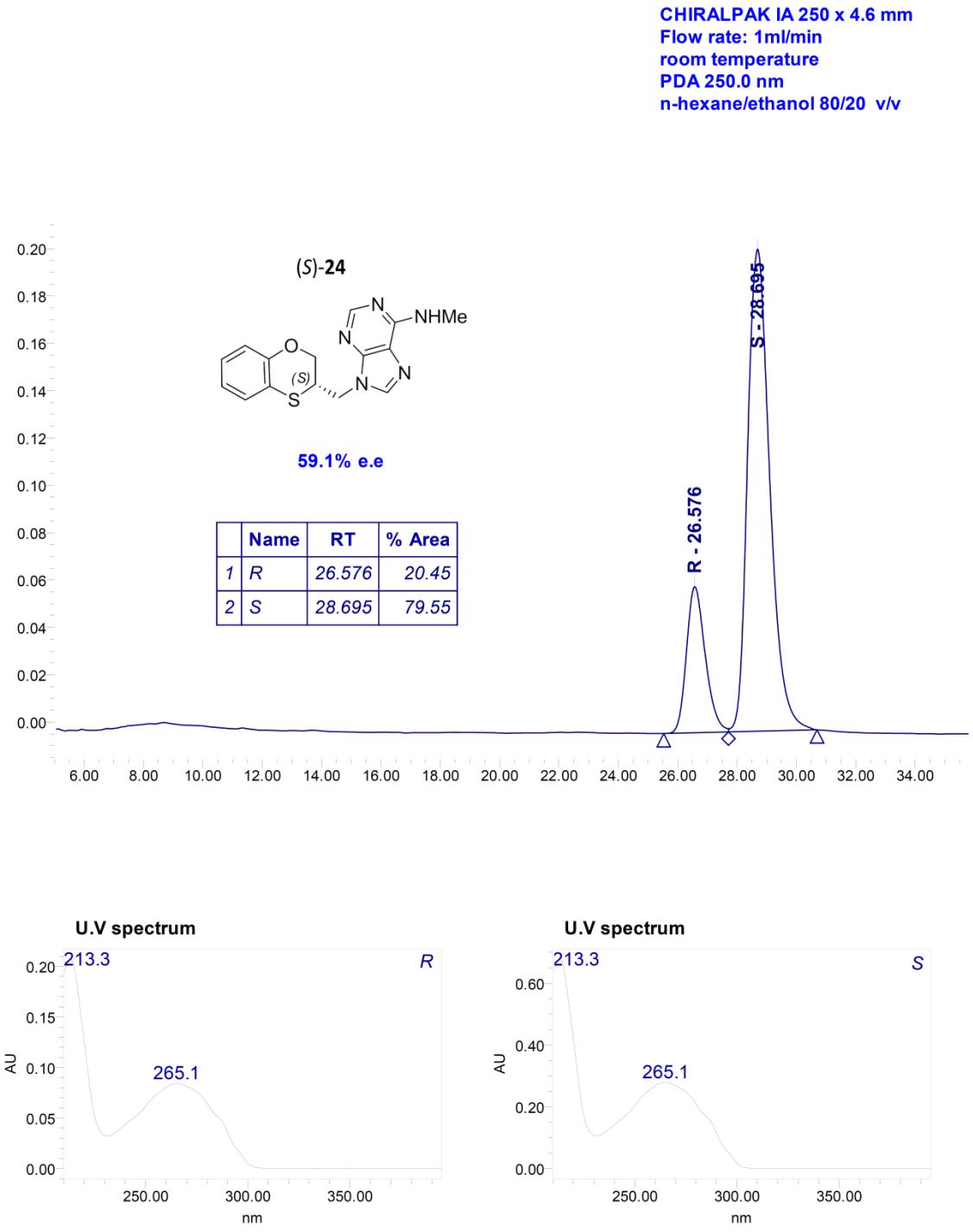
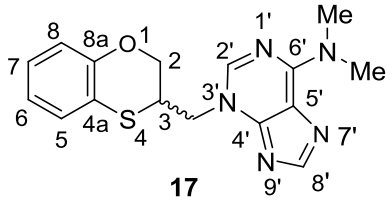
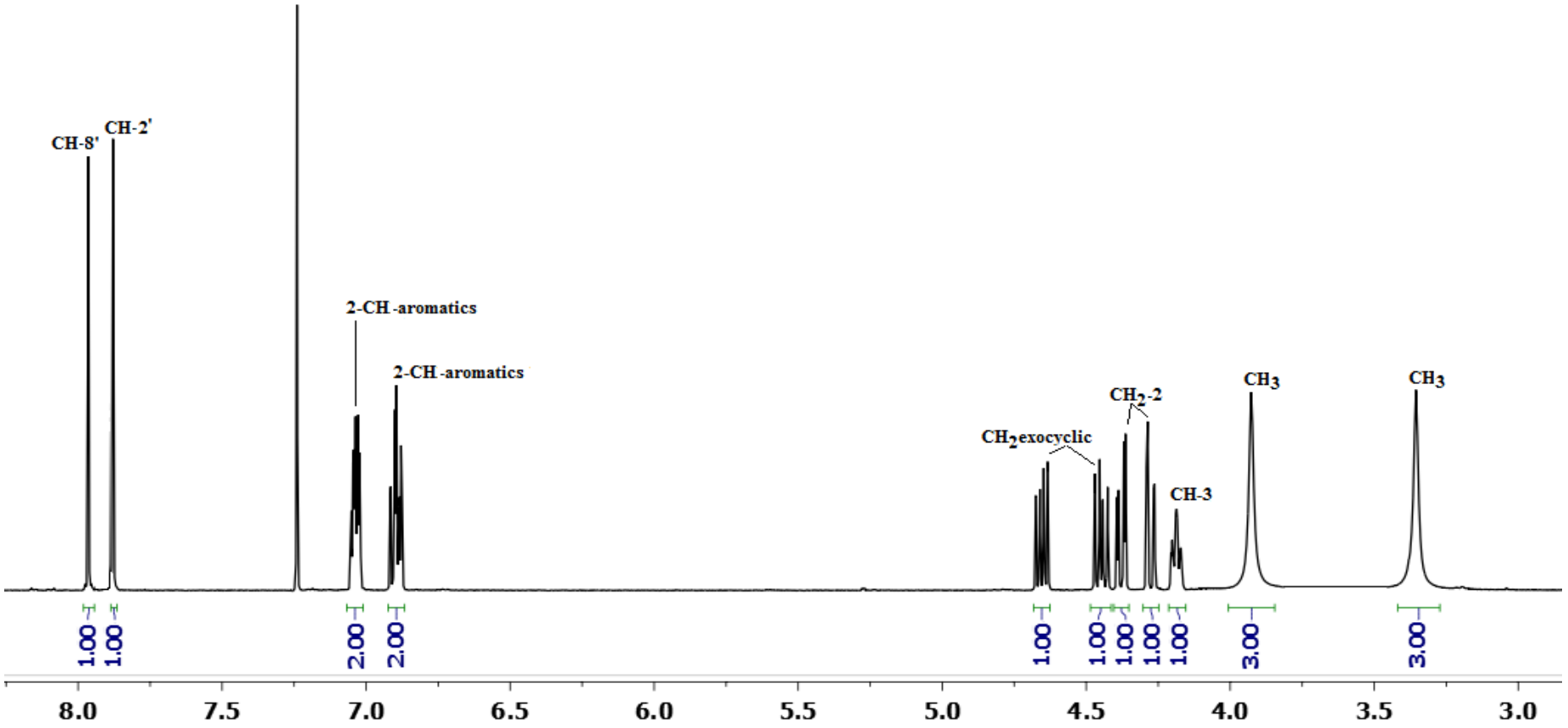

CHIRALPAK IA 250 x 4.6 mm
Flow rate: 1ml/min
room temperature
PDA 250.0 nm
n-hexane/ethanol 80/20 v/v
(S)-24
NHMe
59.1% e.e
Name RT % Area
1 R 26.576 20.45
2 S 28.695 79.55
R - 26.576
S - 28.695
AU
nm
U.V spectrum
213.3
265.1
R
S

Figure S23

500 MHz, $CDCl_3$

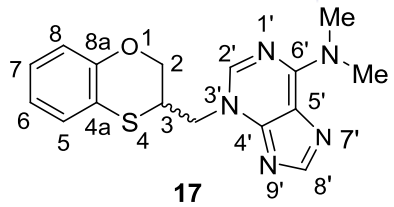


17

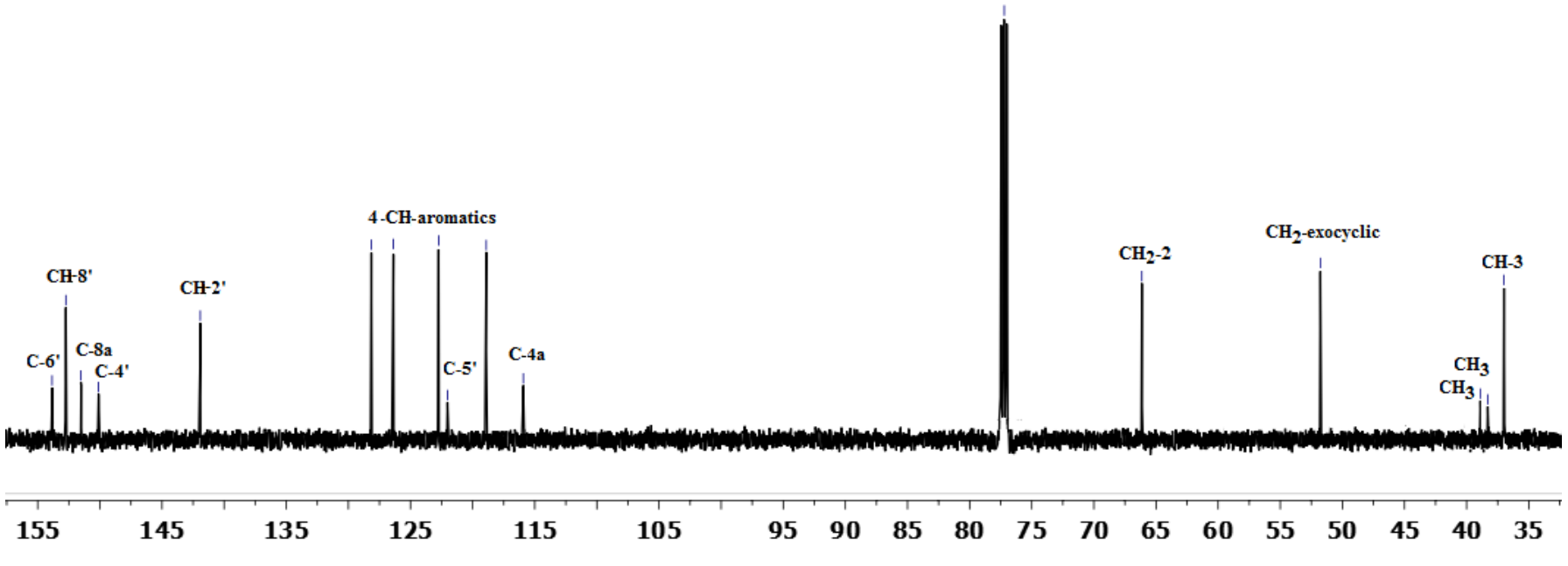


500 MHz, $CDCl_3$

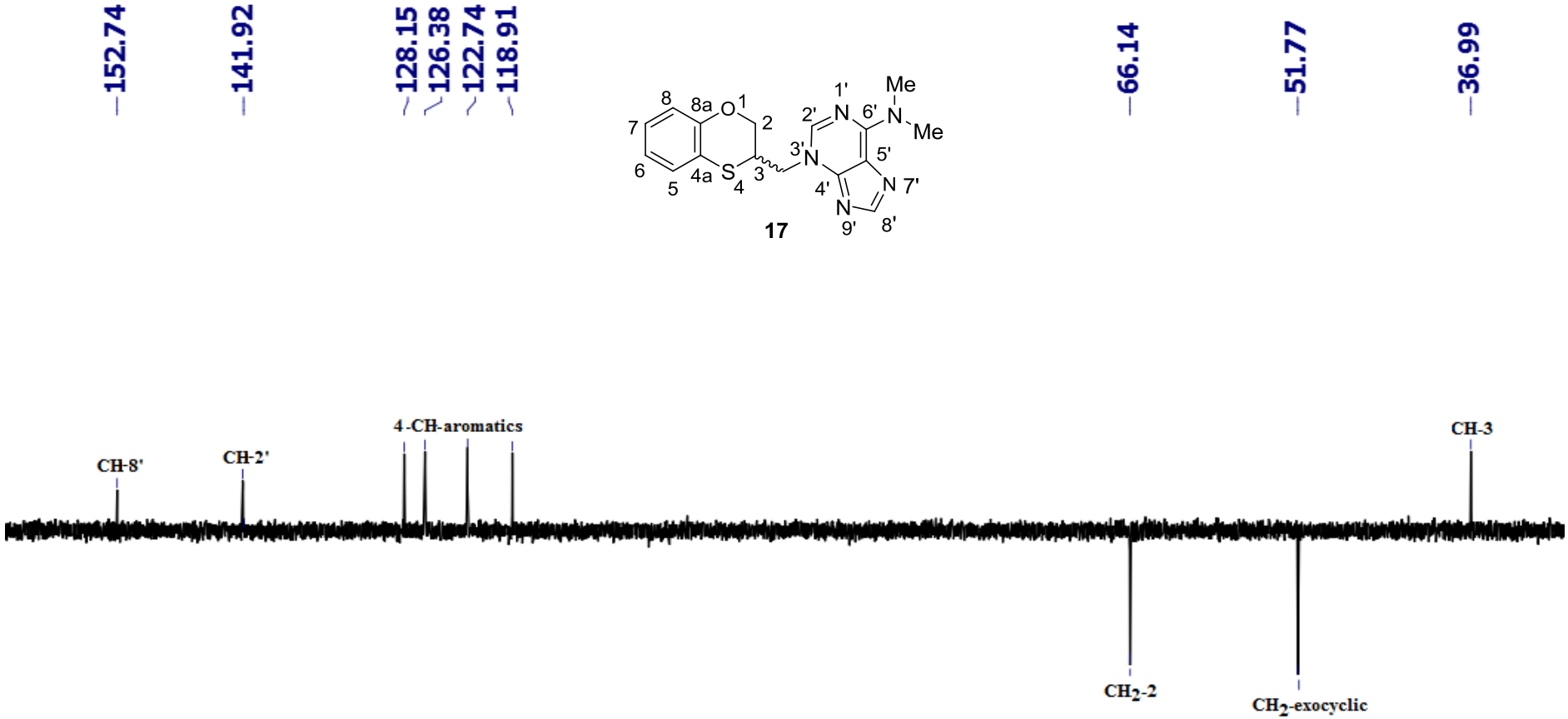
153.85
152.74
151.27
150.11
141.92
128.15
126.38
122.74
122.02
118.91
115.92
66.14
51.77
39.95
38.23
36.99



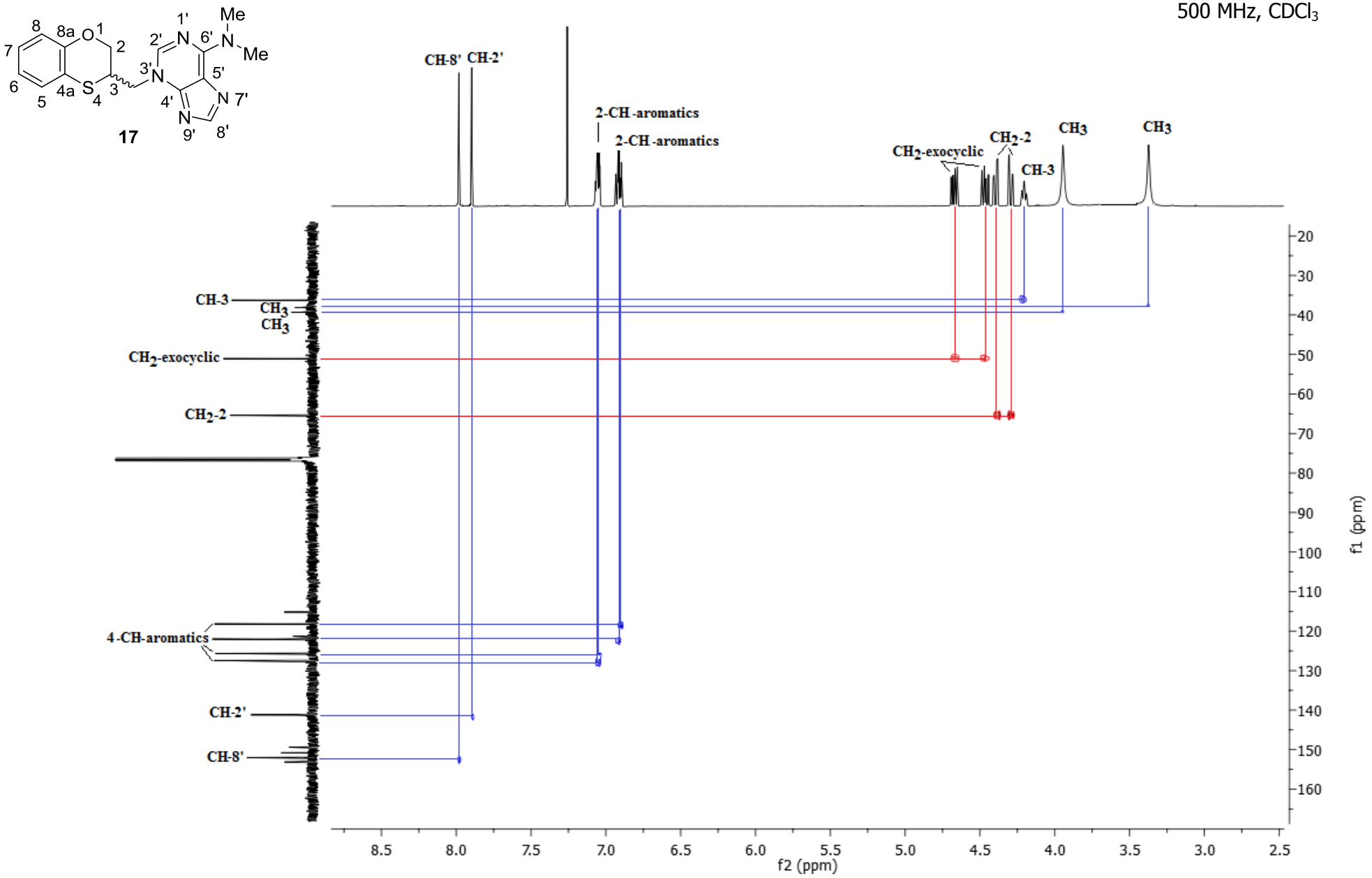
17

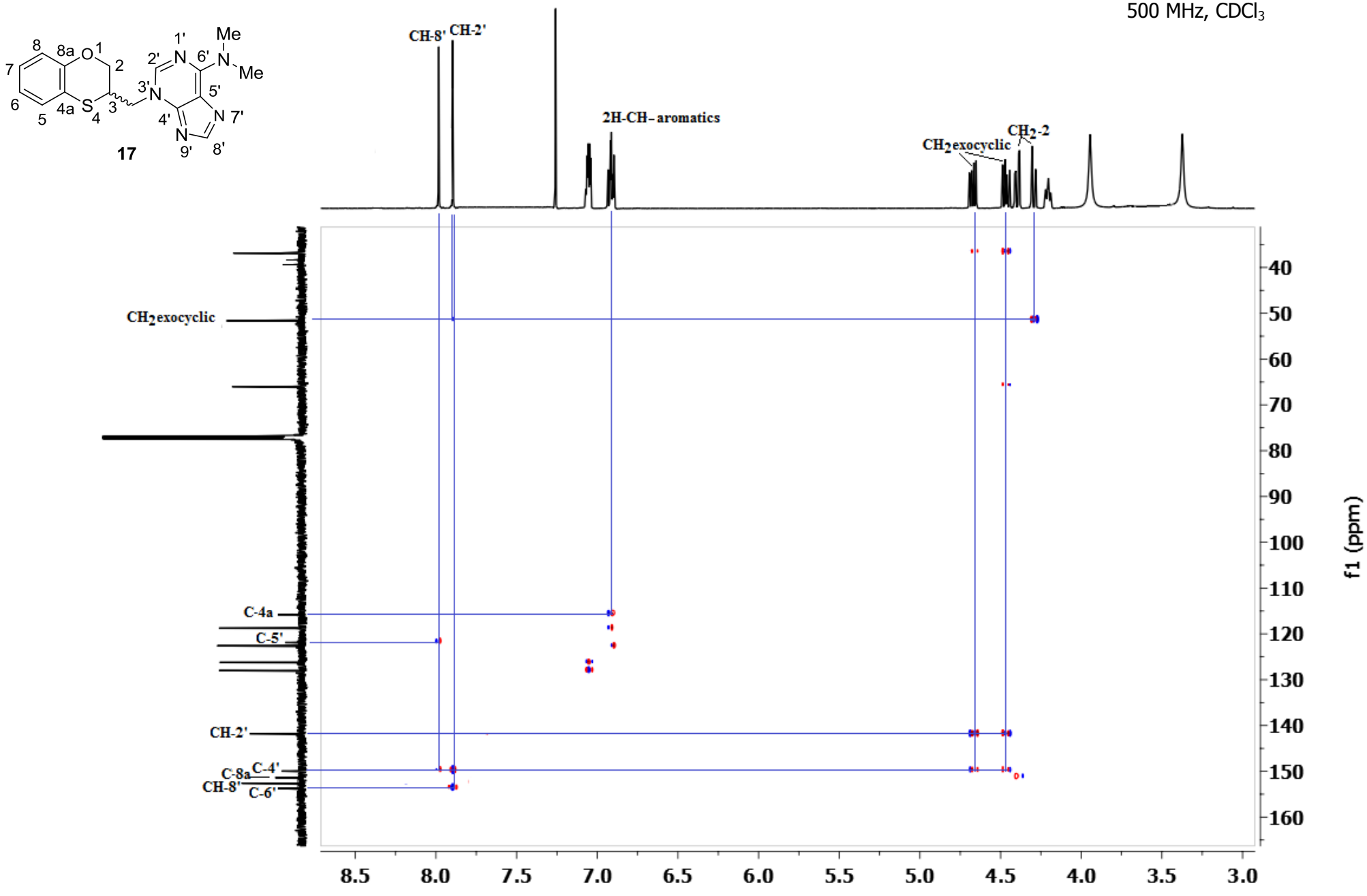


500 MHz, $CDCl_3$



17


500 MHz, CDCl3
17
CH-8' CH-2'
2-CH-aromatics
2-CH-aromatics
CH2-exocyclic
CH2-2
CH-3
CH3
CH3
CH-3
CH3
CH3
CH2-exocyclic
CH2-2
4-CH-aromatics
CH-2'
CH-8'
f2 (ppm)
f1 (ppm)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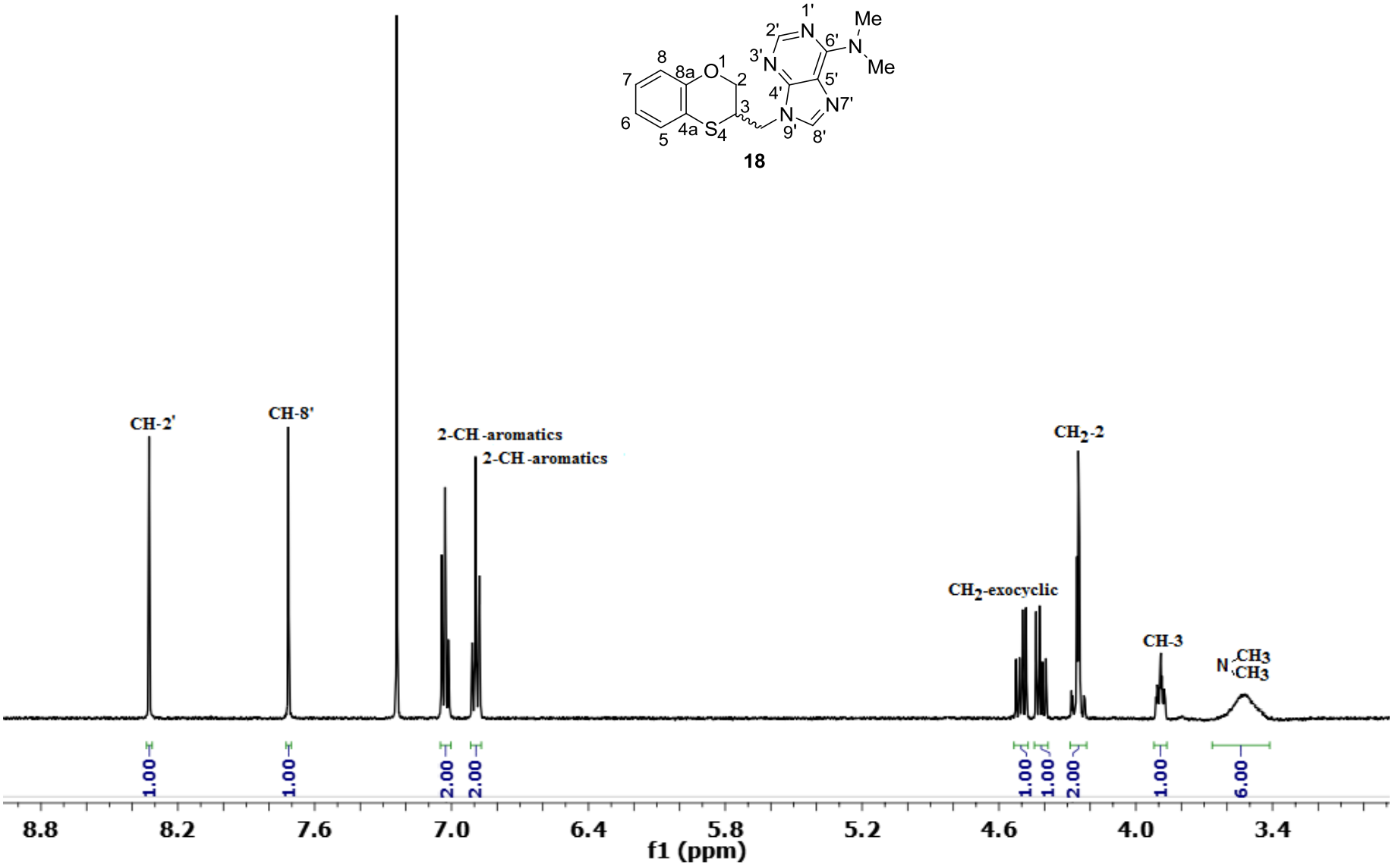
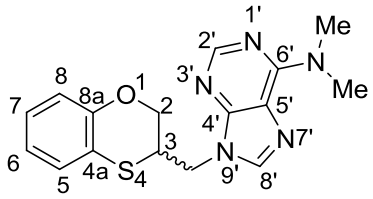
CH-2'
2H-CH-aromatics
CH2exocyclic
CH2-2
CH2exocyclic
C-4a
C-5'
CH-2'
C-8a
C-4'
CH-8'
C-6'
f1 (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
40
50
60
70
80
90
100
110
120
130
140
150
160
17

500 MHz, $CDCl_3$

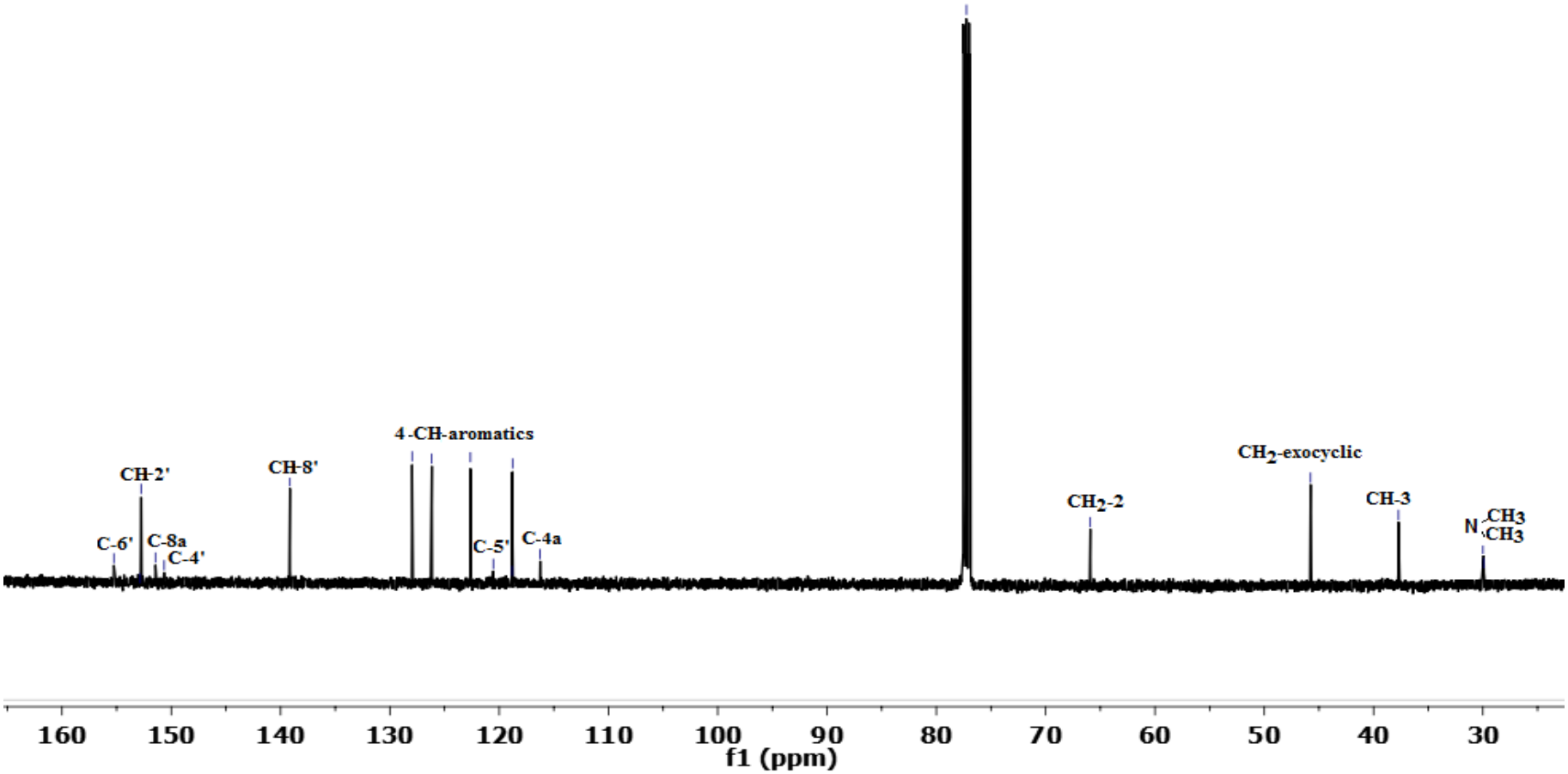


500 MHz, $CDCl_3$

155.25
152.84
151.45
150.65
139.15
127.96
126.17
122.63
120.54
118.82
116.25
65.91
45.76
37.72
29.93



18



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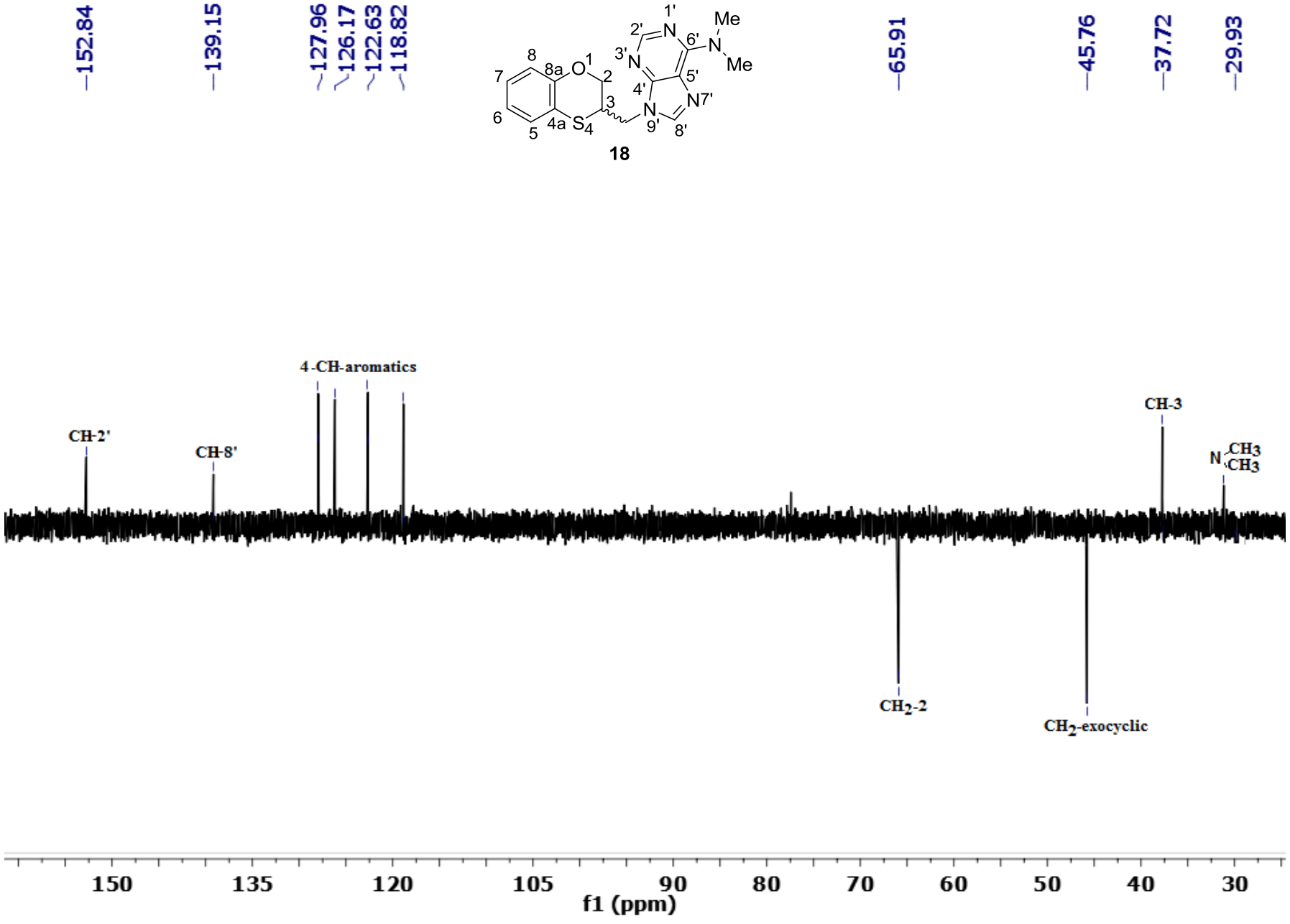

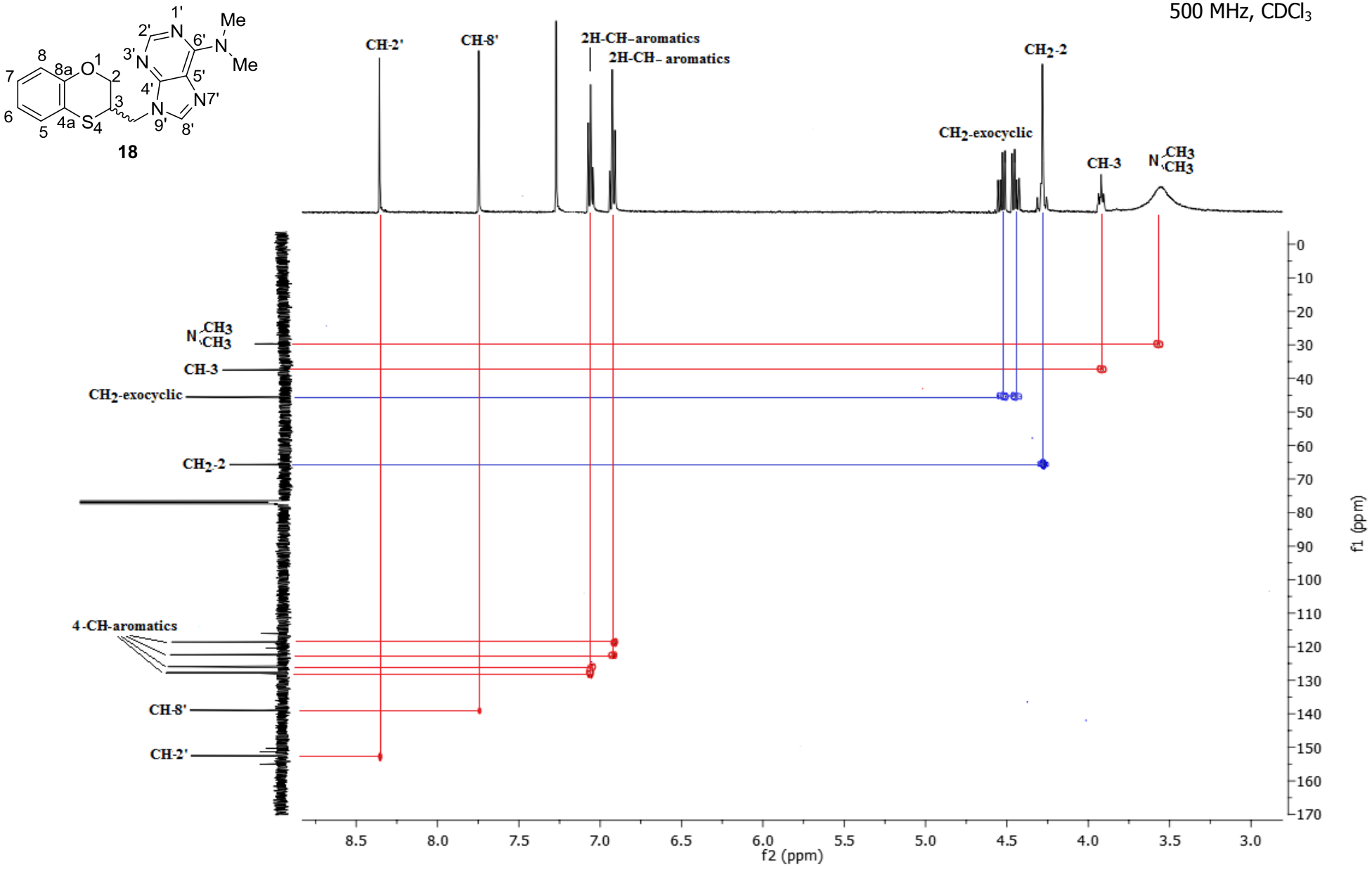
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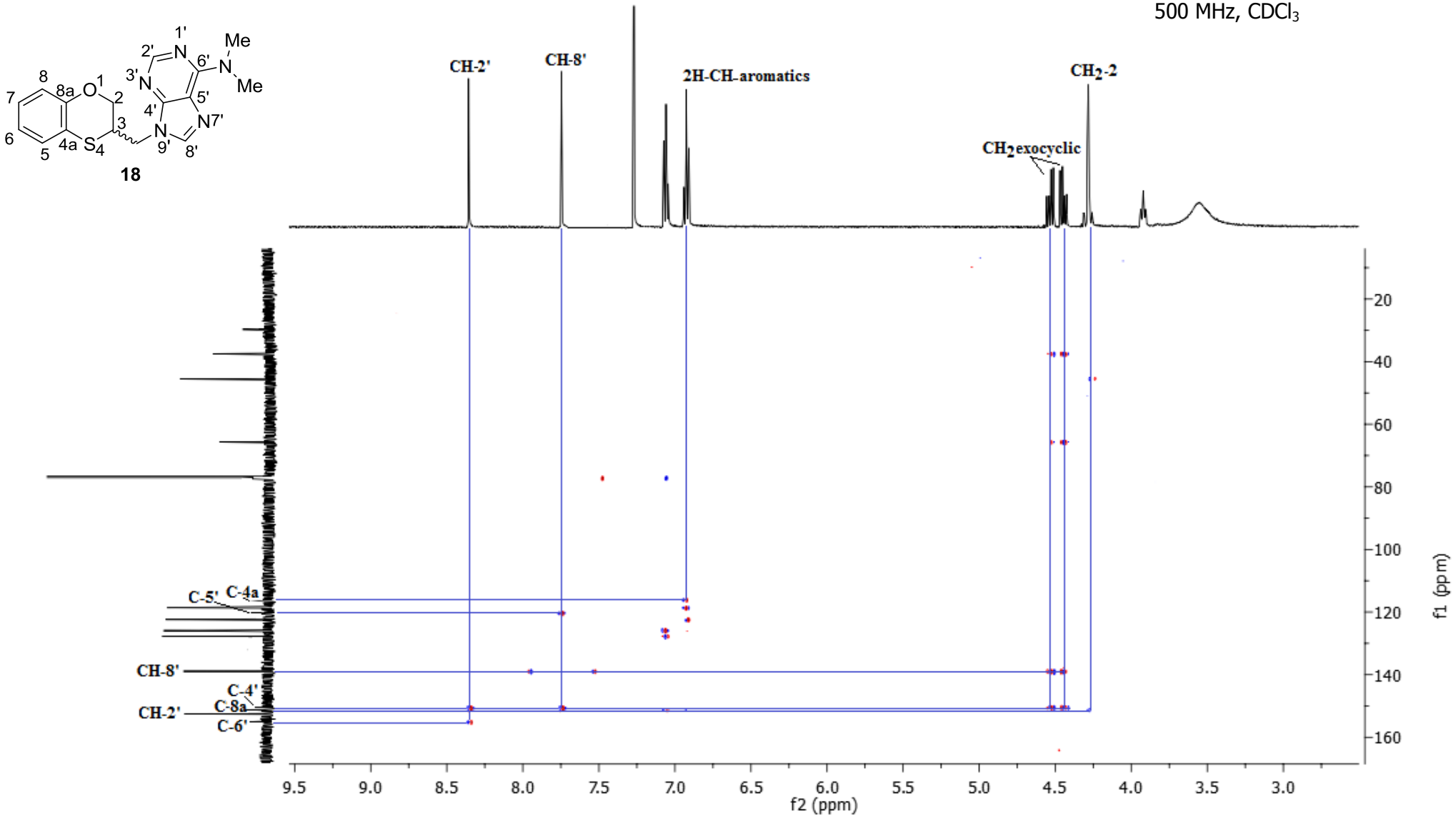
CH-8'
2H-CH-aromatics
2H-CH- aromatics
CH2-2
CH2-exocyclic
CH-3
N(CH3)2
4-CH-aromatics
f2 (ppm)
f1 (ppm)

18


500 MHz, CDCl3
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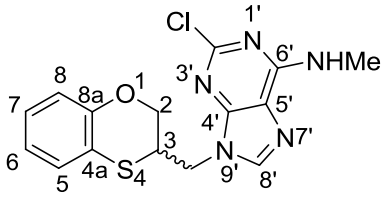
CH-8'
2H-CH-aromatics
CH2-2
CH2exocyclic
C-5'
C-4a
CH-8'
C-4'
C-8a
CH-2'
C-6'
f2 (ppm)
f1 (ppm)

18

500 MHz, $CDCl_3$



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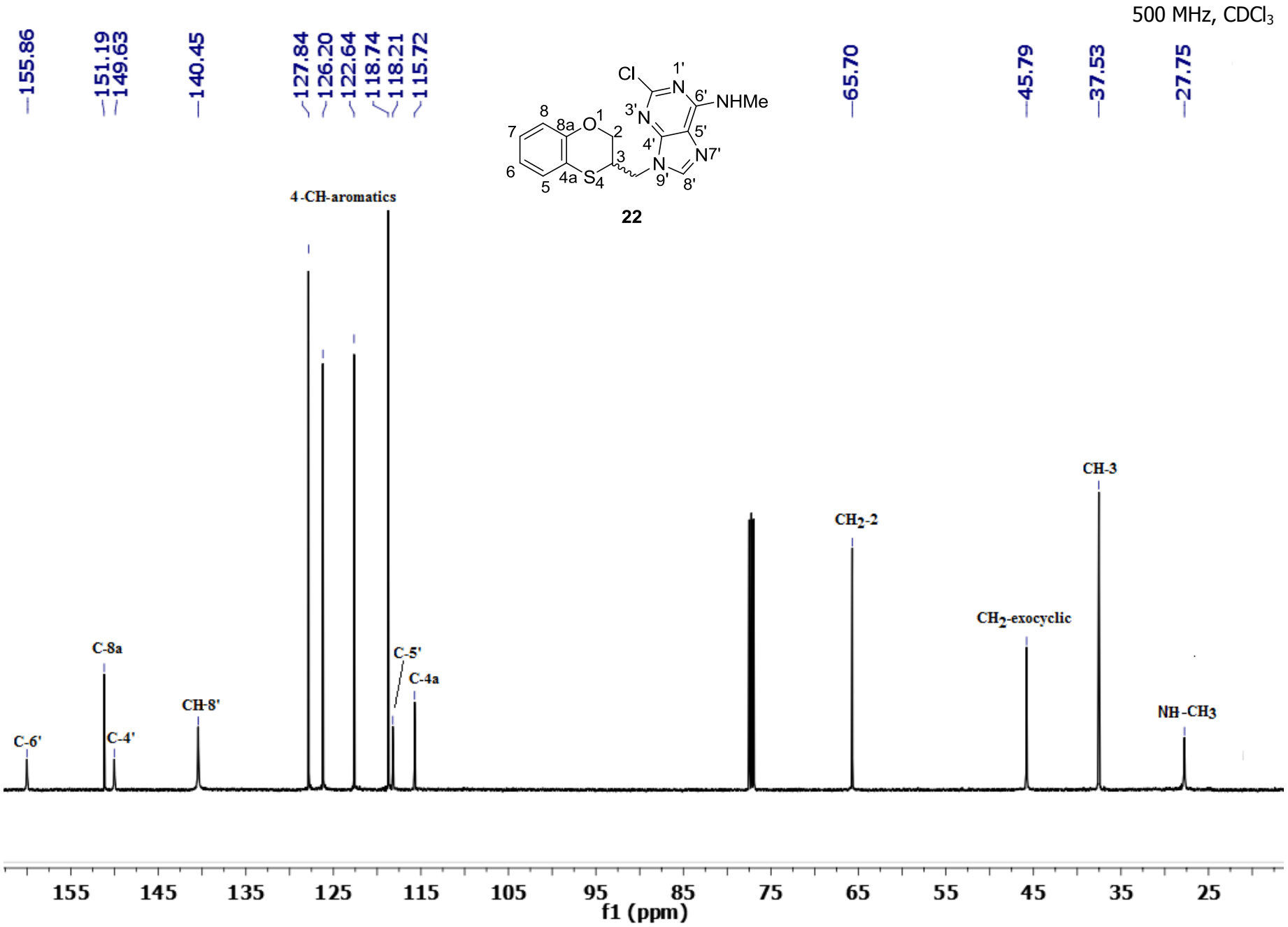
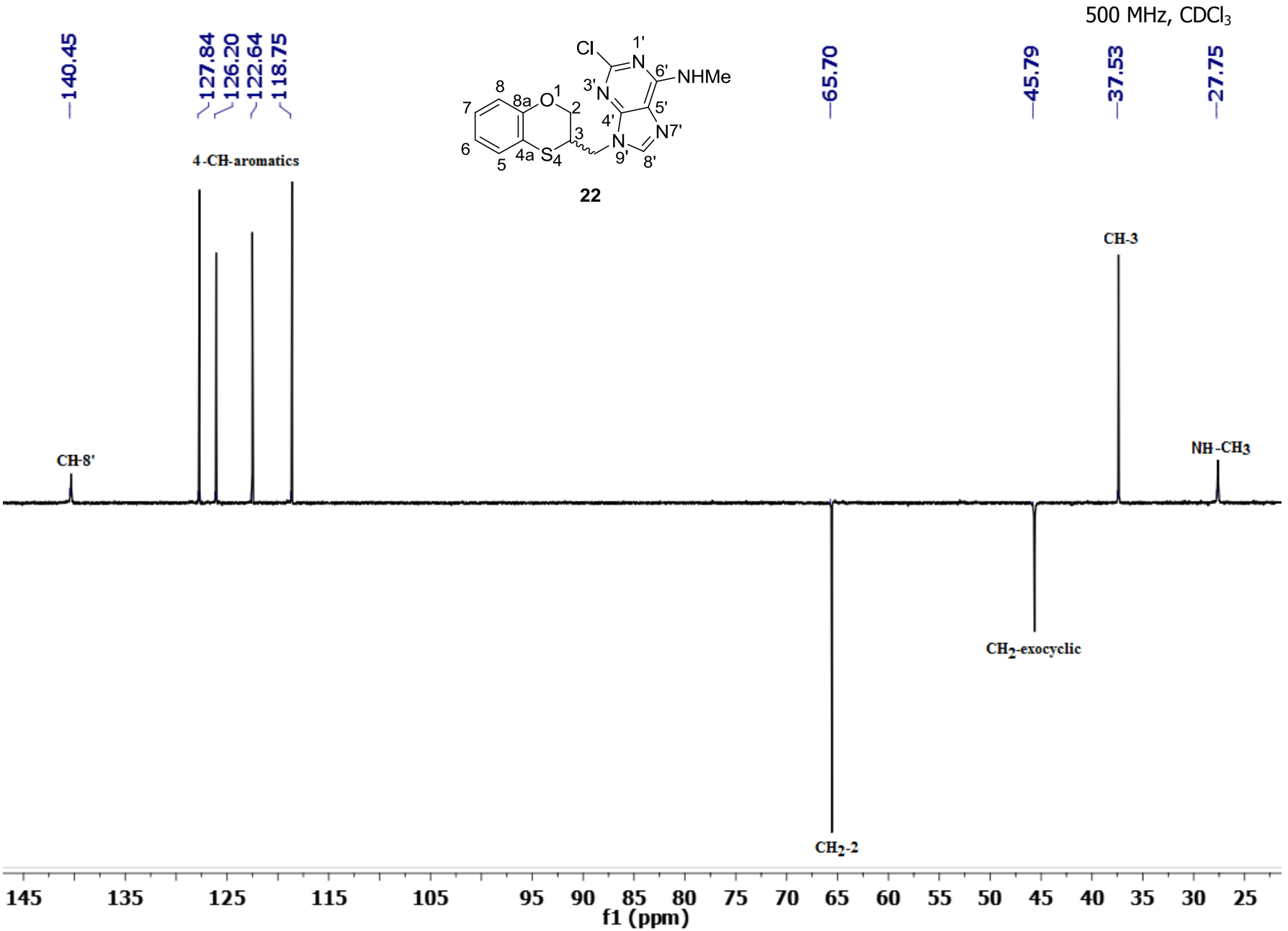
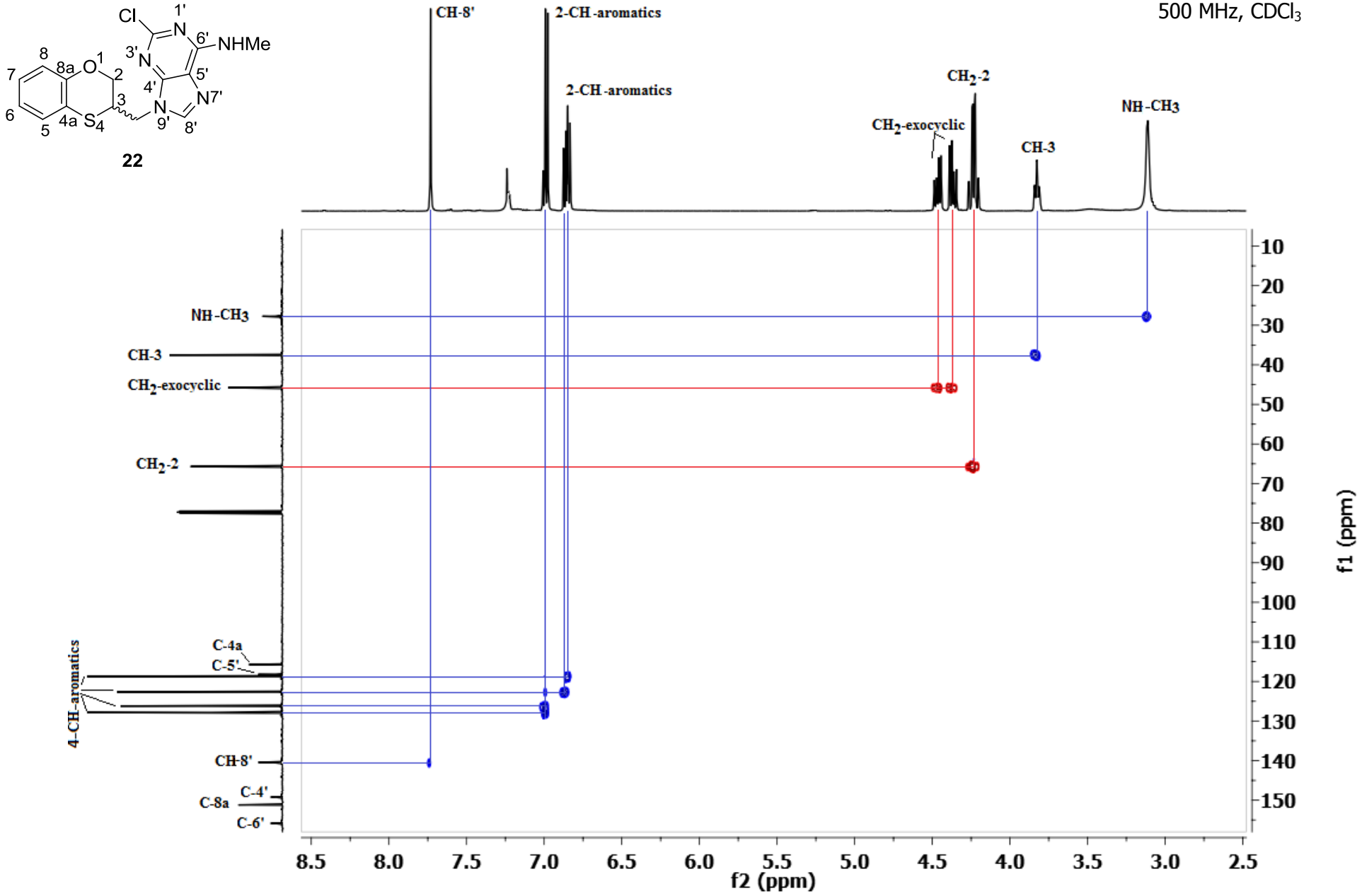

500 MHz, CDCl3
155.86
151.19
149.63
140.45
127.84
126.20
122.64
118.74
118.21
115.72
65.70
45.79
37.53
27.75
Cl
1'
N
6'
NHMe
3'
N
5'
4'
N7'
N
9'
8'
8
8a
O
1
2
7
3
6
4a
S4
5
22
4-CH-aromatics
CH3
CH2-2
CH2-exocyclic
C-8a
C-5'
C-4a
CH-8'
NH-CH3
C-6'
C-4'
155
145
135
125
115
105
95
85
75
65
55
45
35
25
f1 (ppm)


500 MHz, CDCl3
140.45
127.84
126.20
122.64
118.75
65.70
45.79
37.53
27.75
4-CH-aromatics
CH-8'
CH-3
NH-CH3
CH2-exocyclic
CH2-2
f1 (ppm)

22


500 MHz, CDCl3
CH-8'
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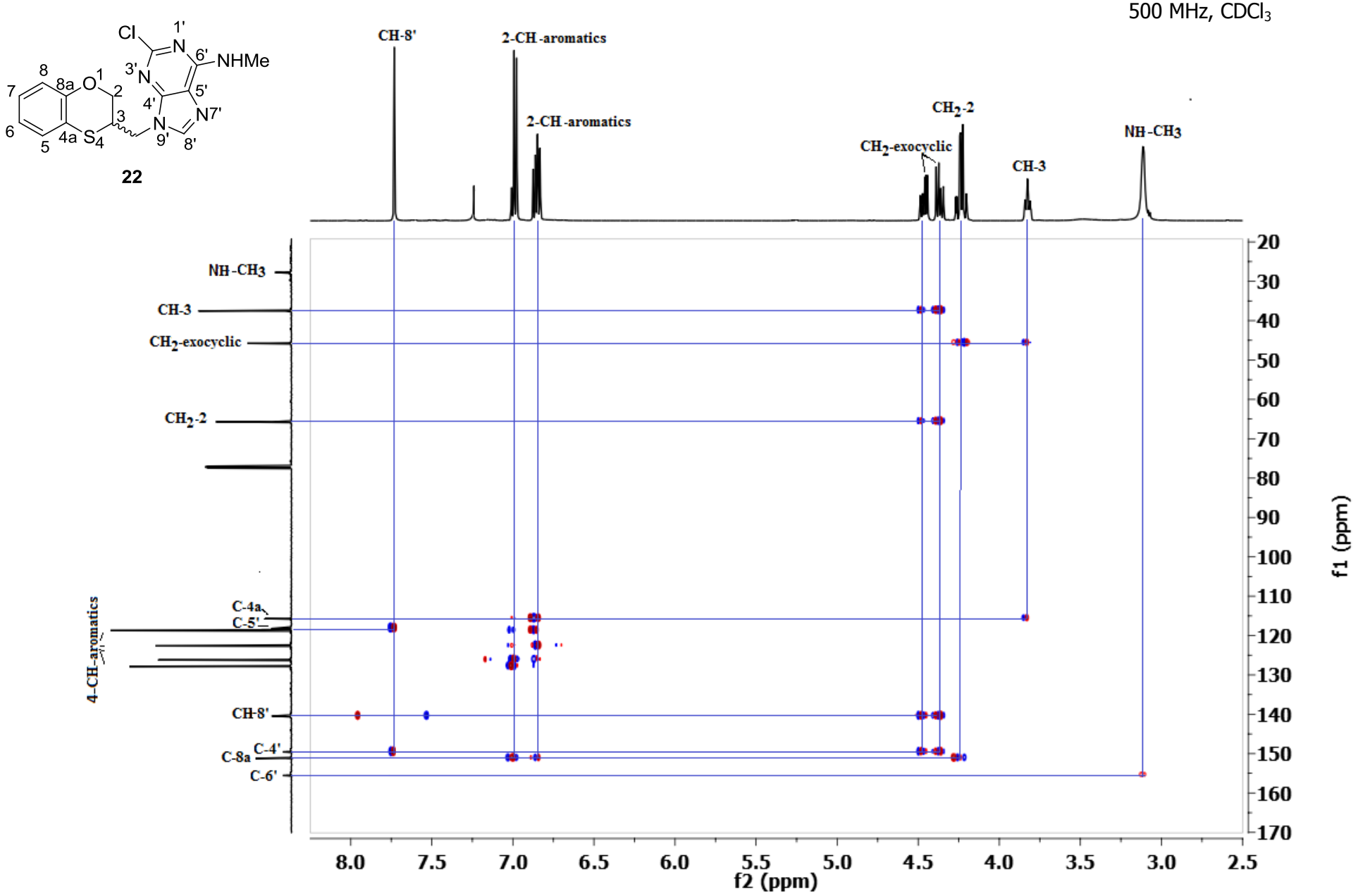
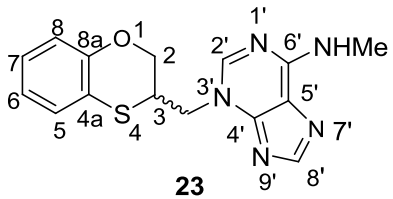
2-CH-aromatics
CH2-2
CH2-exocyclic
CH-3
NH-CH3
NH-CH3
CH-3
CH2-exocyclic
CH2-2
4-CH-aromatics
C-4a
C-5'
CH-8'
C-8a
C-4'
C-6'
f2 (ppm)
f1 (ppm)

22


500 MHz, CDCl3
22
CH-8'
2-CH-aromatics
2-CH-aromatics
CH2-2
CH2-exocyclic
CH-3
NH-CH3
NH-CH3
CH-3
CH2-exocyclic
CH2-2
4-CH-aromatics
C-4a
C-5'
CH-8'
C-8a
C-4'
C-6'
f2 (ppm)
f1 (ppm)

500 MHz, $CDCl_3$



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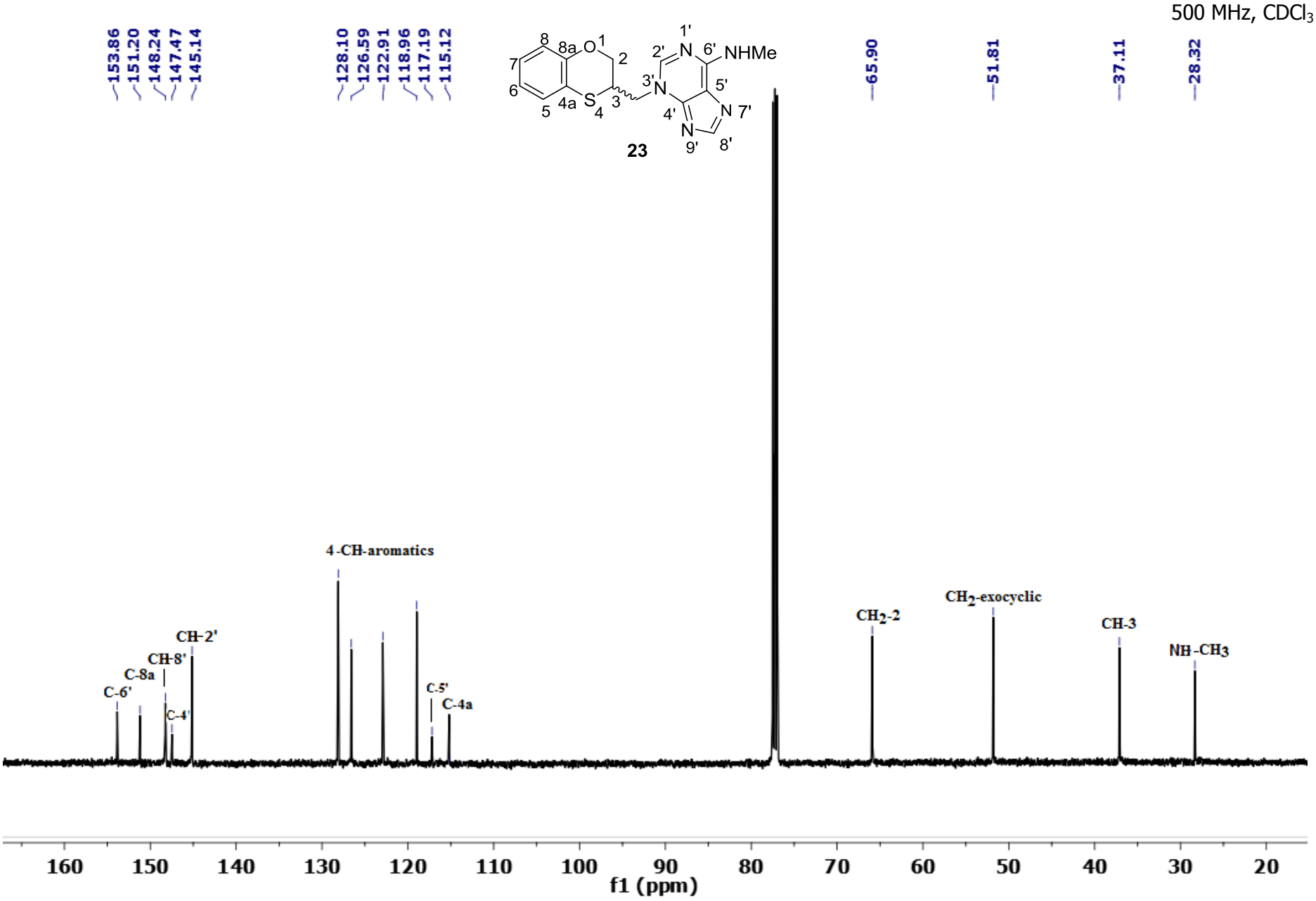
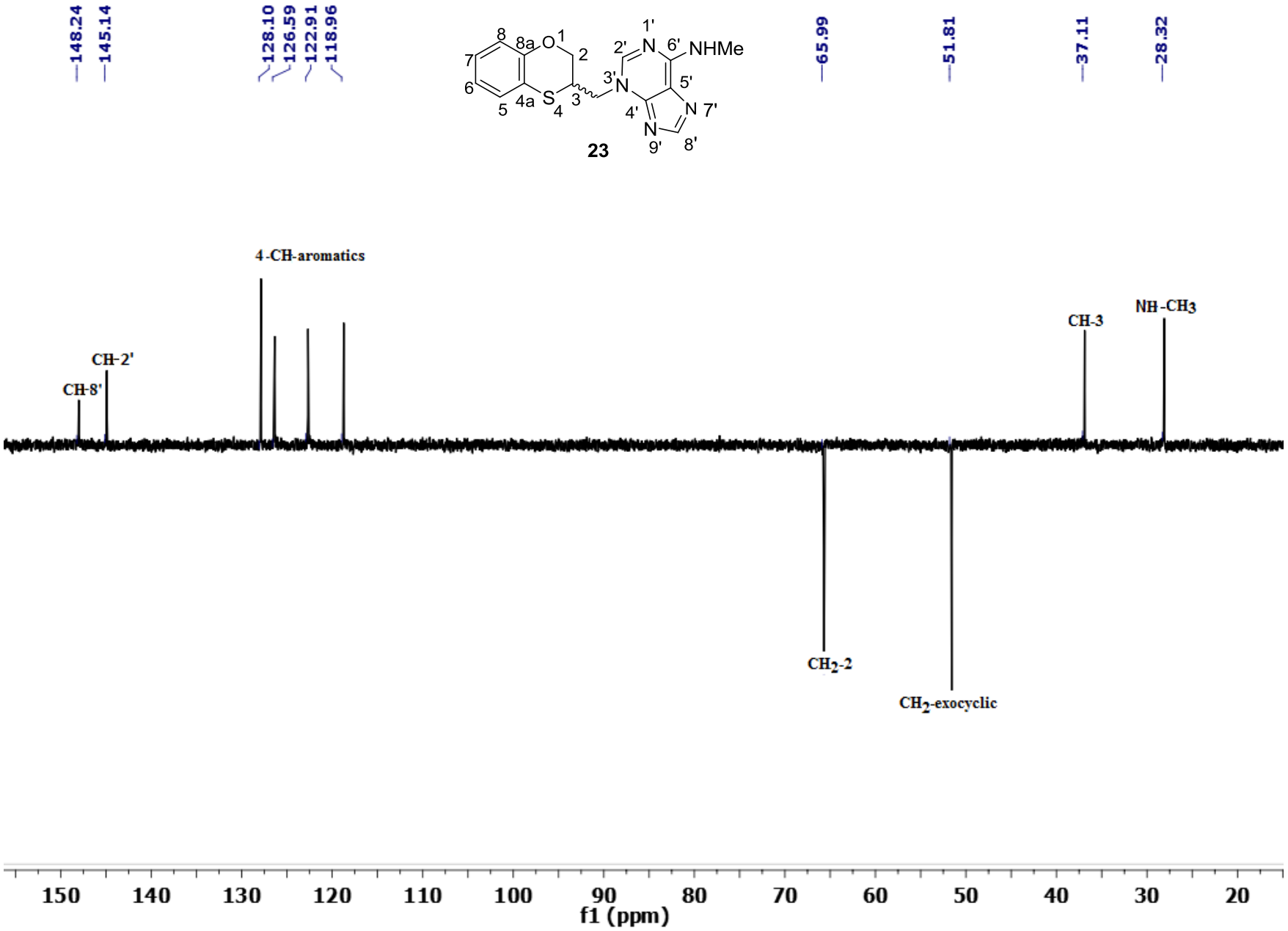
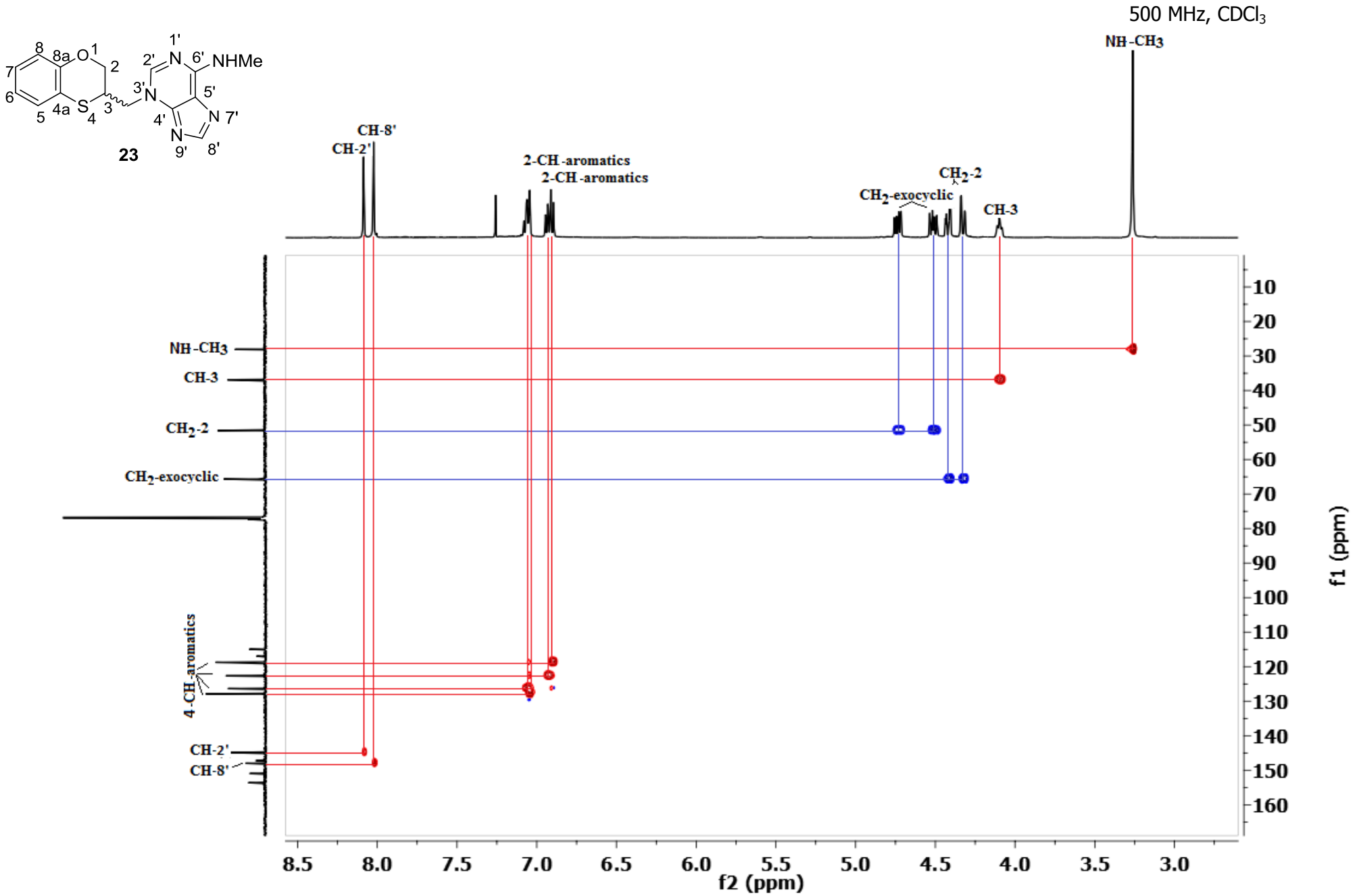
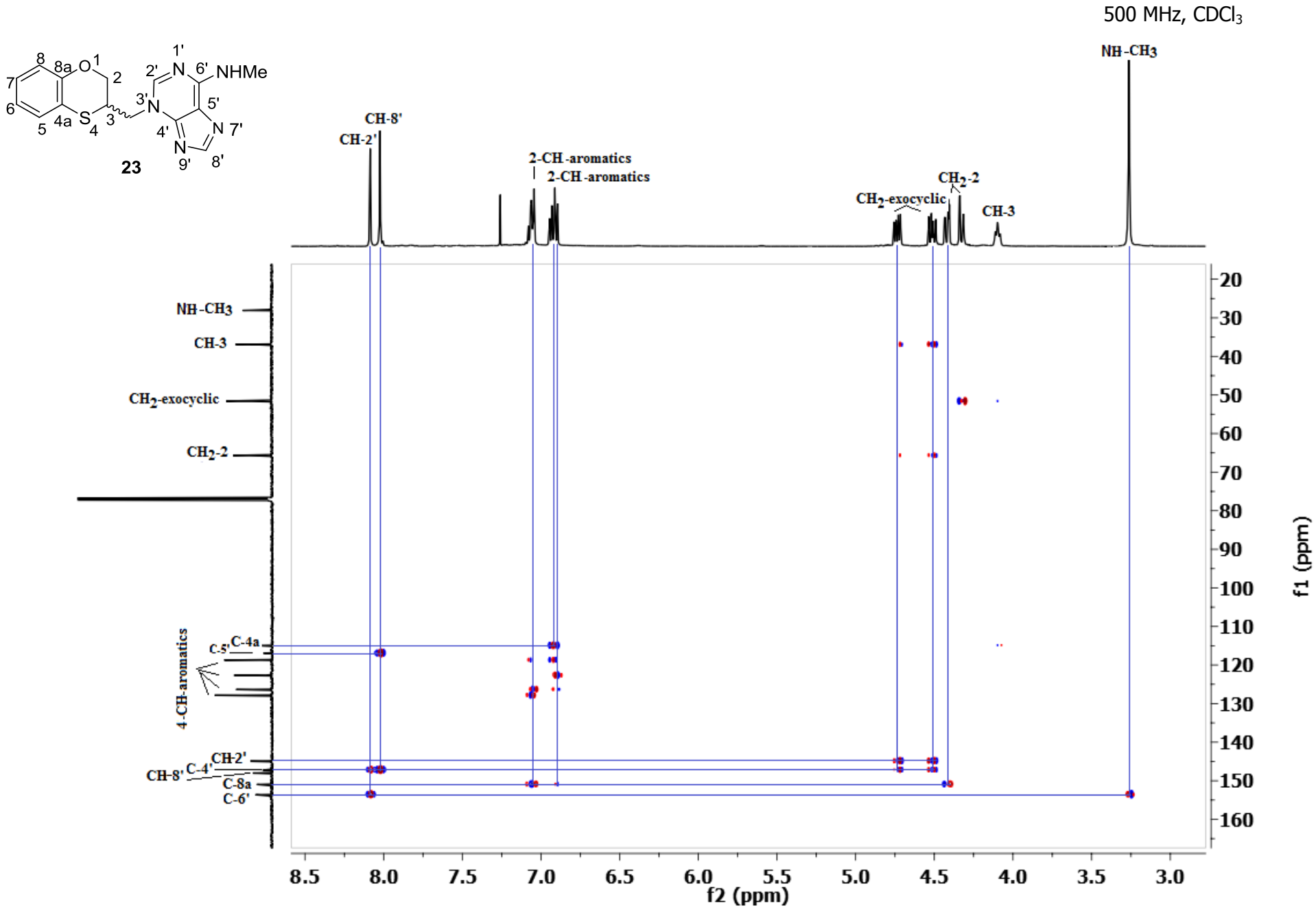

500 MHz, CDCl3
153.86
151.20
148.24
147.47
145.14
128.10
126.59
122.91
118.96
117.19
115.12
65.90
51.81
37.11
28.32
NHMe
23
4-CH-aromatics
CH-2'
CH-8'
C-8a
C-6'
C-4'
C-5'
C-4a
CH2-2
CH2-exocyclic
CH-3
NH-CH3
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

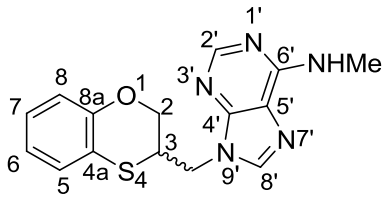
500 MHz, $CDCl_3$




500 MHz, CDCl3
NH-CH3
CH-8'
CH-2'
2-CH-aromatics
2-CH-aromatics
CH2-2
CH2-exocyclic
CH-3
NH-CH3
CH-3
CH2-2
CH2-exocyclic
4-CH-aromatics
CH-2'
CH-8'
f2 (ppm)
f1 (ppm)
23


500 MHz, CDCl3
NH-CH3
CH-8'
CH-2'
2-CH-aromatics
2-CH-aromatics
CH2-2
CH2-exocyclic
CH-3
NH-CH3
CH-3
CH2-exocyclic
CH2-2
4-CH-aromatics
C-5'
C-4a
CH-2'
CH-8'
C-4'
C-8a
C-6'
f2 (ppm)
f1 (ppm)
23

600 MHz, $CDCl_3$



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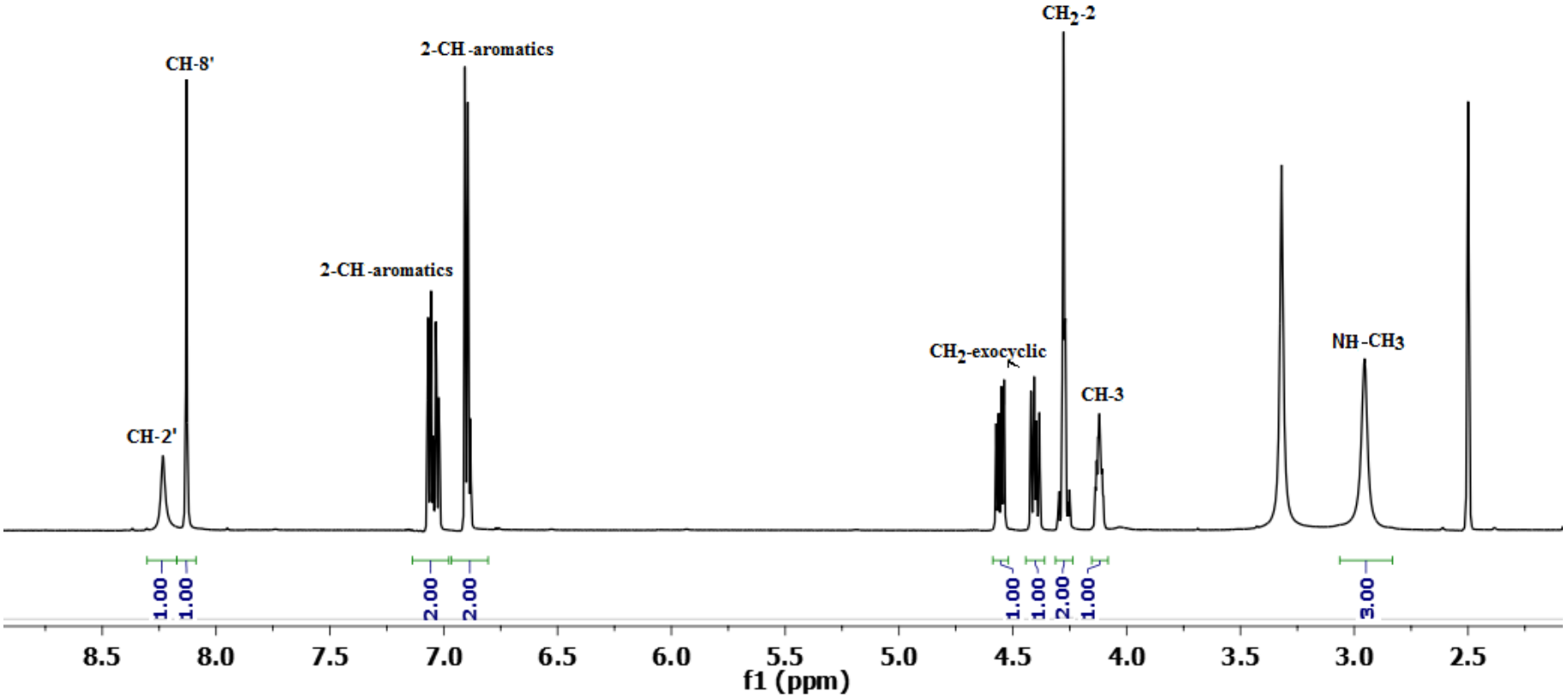
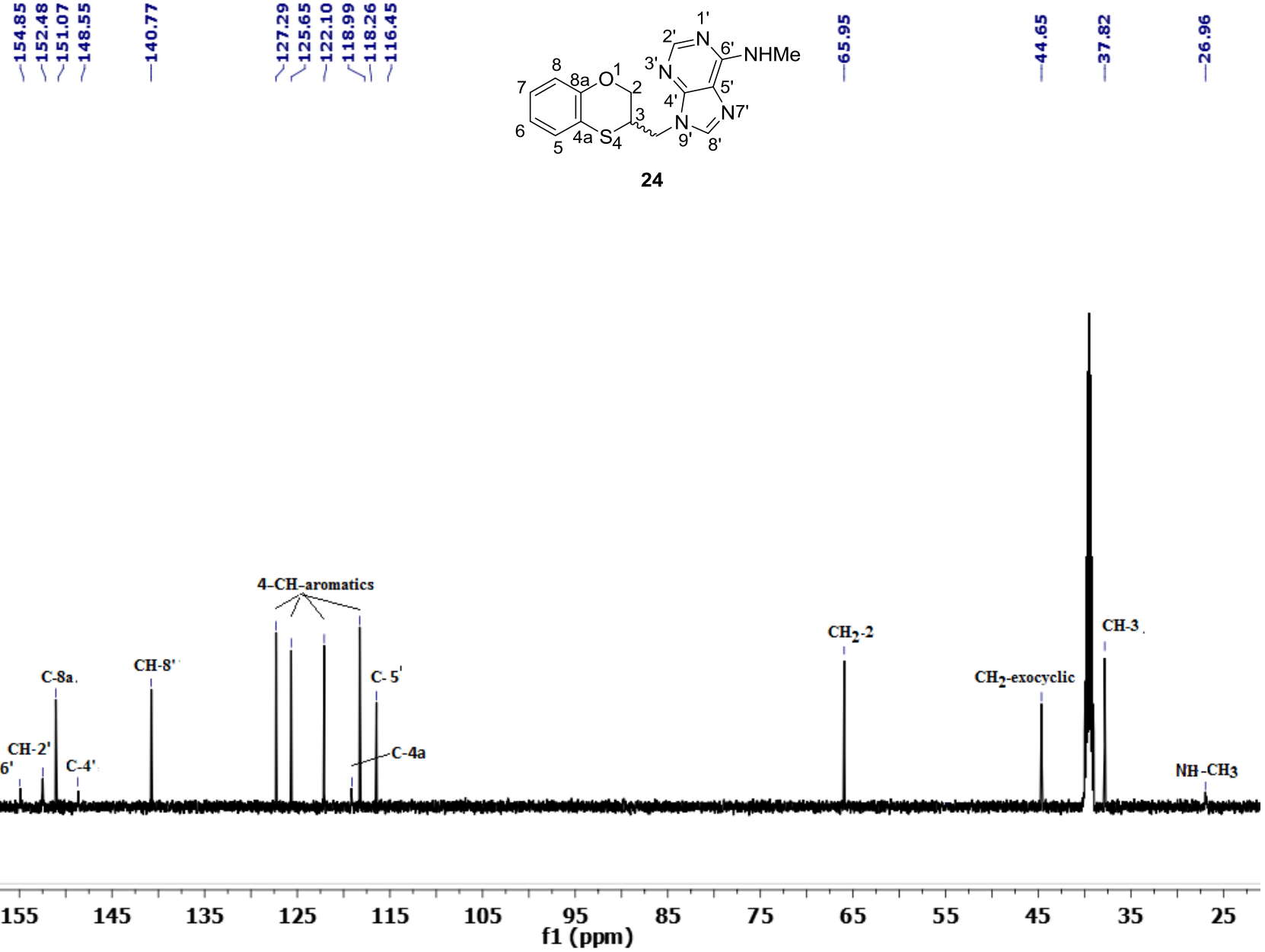
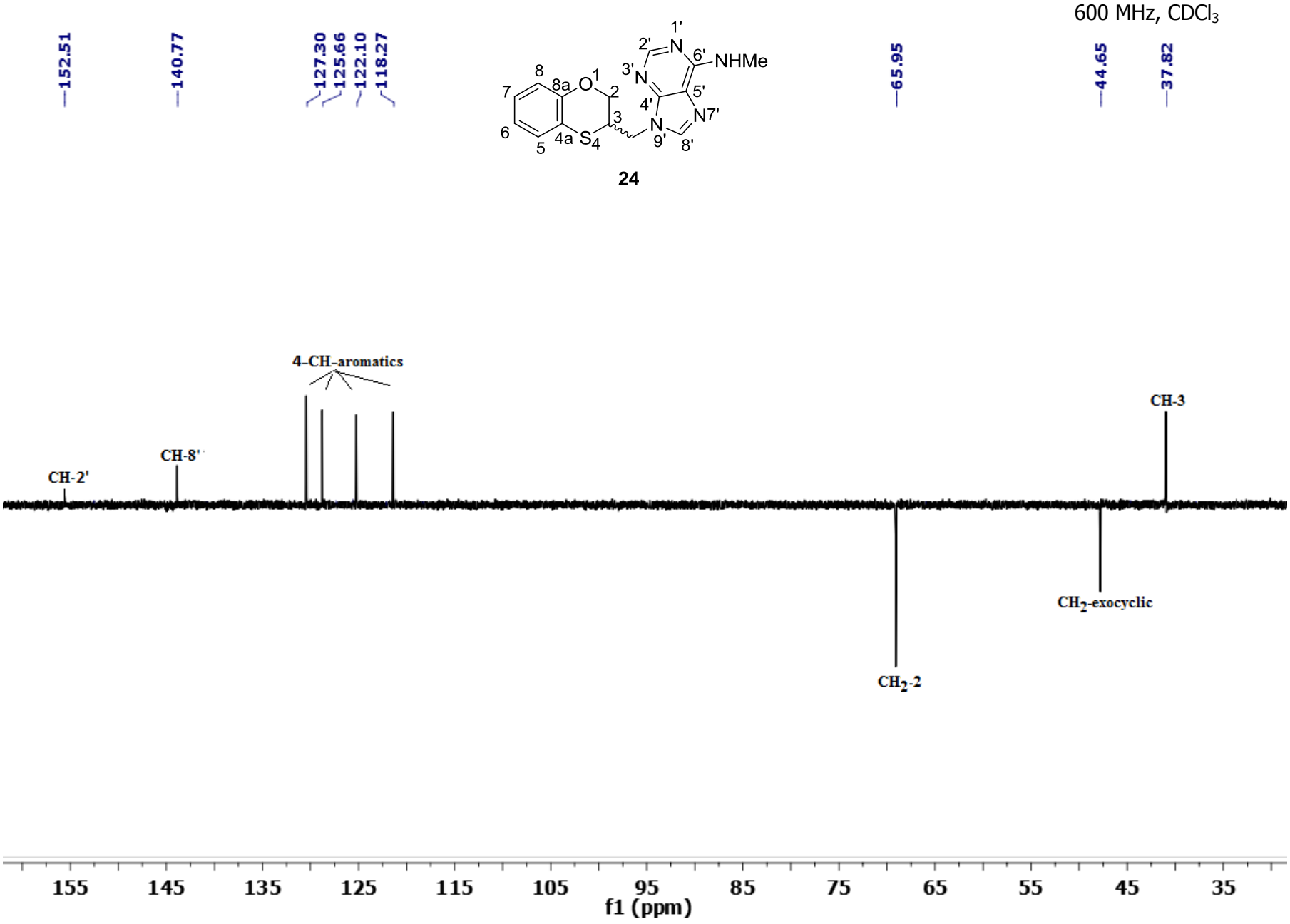
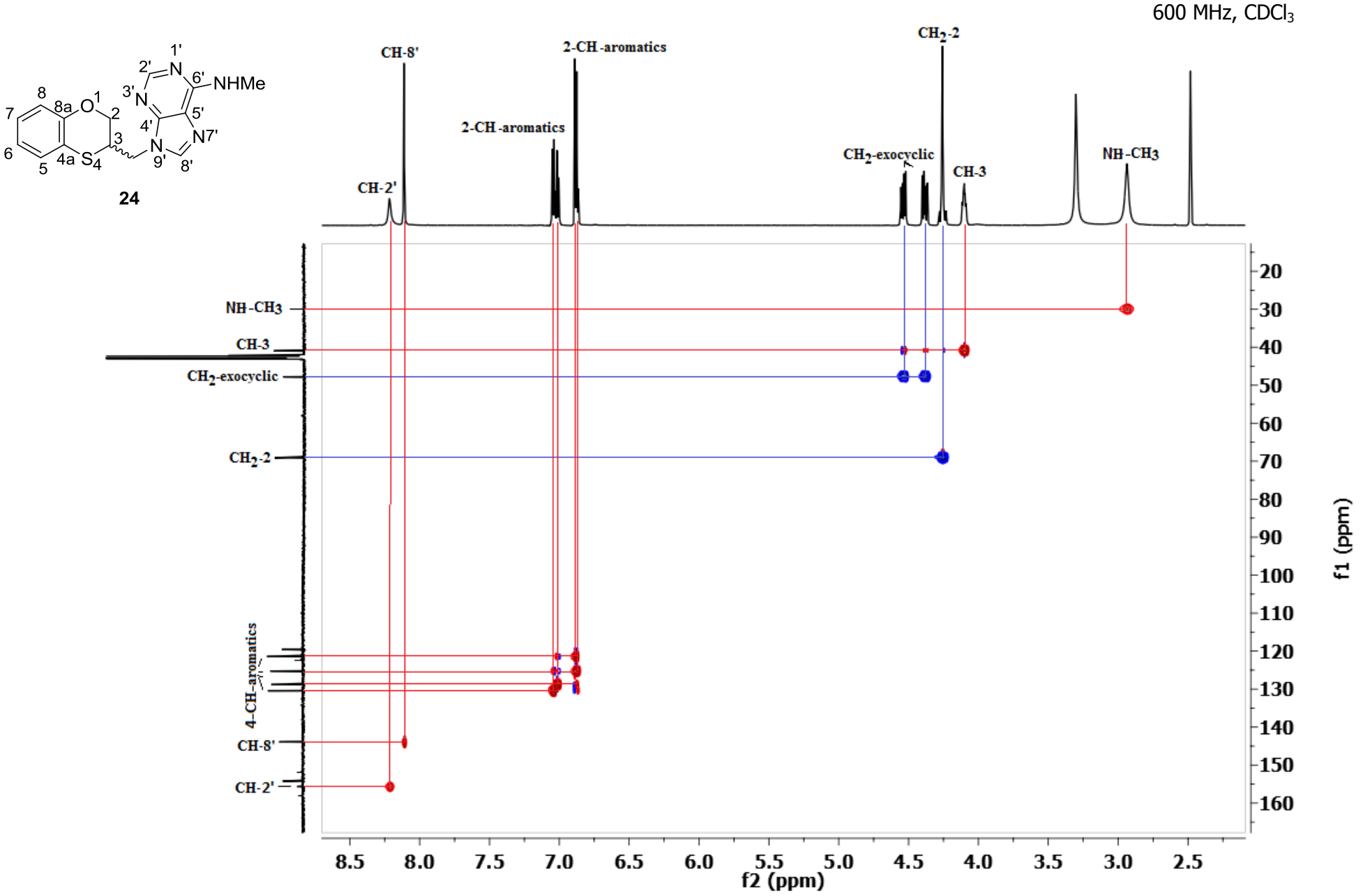
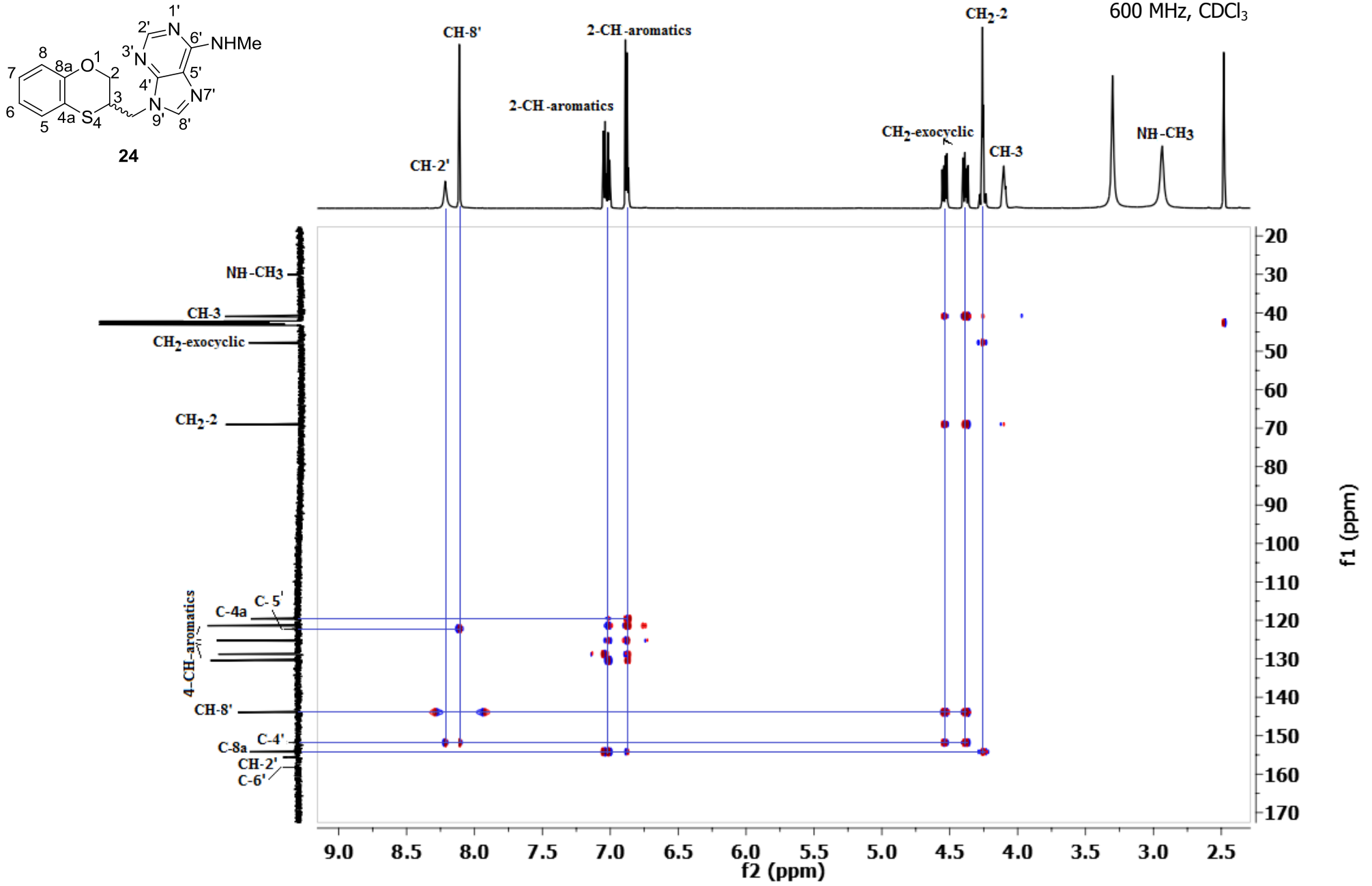


600 MHz, $CDCl_3$




600 MHz, CDCl3
152.51
140.77
127.30
125.66
122.10
118.27
65.95
44.65
37.82
NHMe
24
4-CH-aromatics
CH-8'
CH-2'
CH-3
CH2-exocyclic
CH2-2
155
145
135
125
115
105
95
85
75
65
55
45
35
f1 (ppm)


600 MHz, CDCl3
CH-8'
2-CH-aromatics
CH2-2
2-CH-aromatics
CH2-exocyclic
CH-3
NH-CH3
CH-2'
NH-CH3
CH-3
CH2-exocyclic
CH2-2
4-CH-aromatics
CH-8'
CH-2'
f2 (ppm)
f1 (ppm)
NHMe
24


24
600 MHz, CDCl3
CH-8'
2-CH-aromatics
2-CH-aromatics
CH2-2
CH2-exocyclic
CH-3
NH-CH3
CH-2'
NH-CH3
CH-3
CH2-exocyclic
CH2-2
4-CH-aromatics
C-4a
C-5'
CH-8'
C-8a
C-4'
CH-2'
C-6'
f2 (ppm)
f1 (ppm)

Structure of (*RS*)-17

Figures S24 and S25 display the X-ray diffraction of (*RS*)-**17**. The crystal packing in (*RS*)-**17** reveals that pairs of molecules form a dimeric structure by two symmetry-related –C-H···π interactions involving the –C10-H10A and the five-membered ring of the purine moiety of (*RS*)-**17** (C-H···centroid distance: 2.90Å and C-H···centroid angle: 151.0º). In addition, there are additional C-H···π interactions connecting dimers involving the -C22-H22B bond and the six-membered aromatic ring of the 2,3-dihydro-1,4-benzoxathiin moiety (C-H···centroid distance: 2.64 Å and C-H···centroid angle: 166.0º). Therefore these C-H···π interactions build infinite chains. The cooperative effect of non-classical H-bond interactions (C22-H22A···N1, 3.459 Å and 149.0º) generates the 3D supramolecular architecture in the crystal.

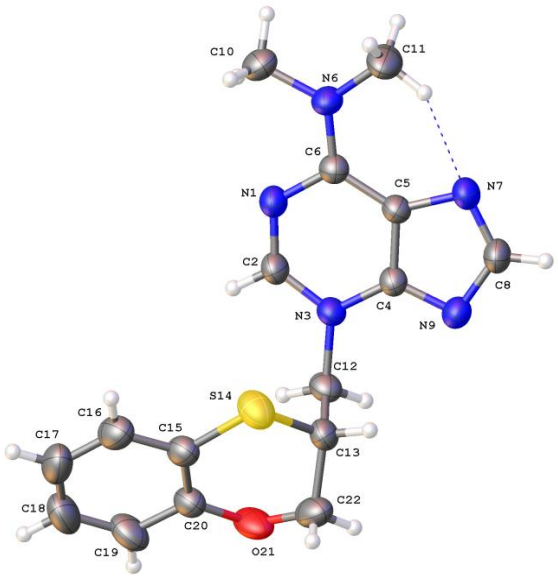


Figure S24. Molecular structure of (*RS*)-**17**. Hydrogen atoms are drawn as spheres of arbitrary radius. Ellipsoids of the non-hydrogen atoms are drawn at the 50% probability level.

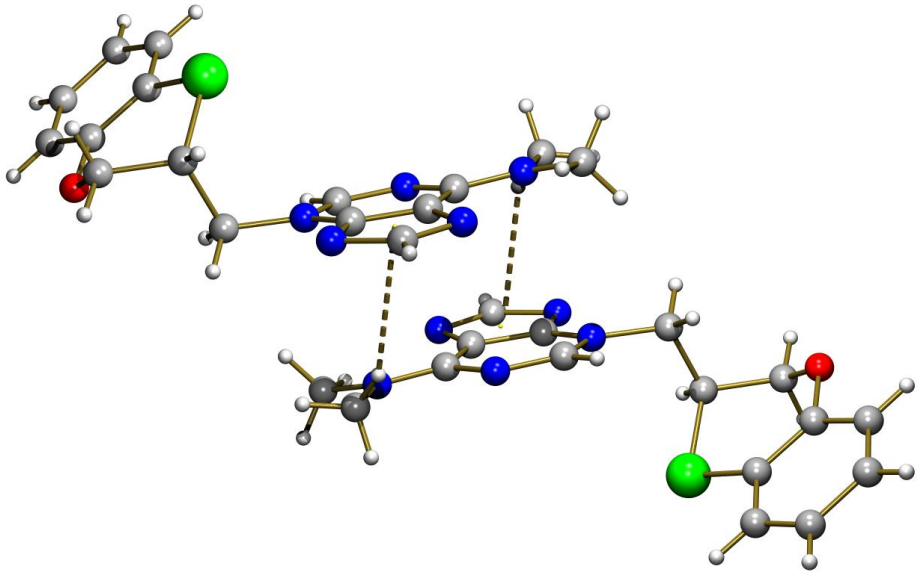


Figure S25. Detail of the dimeric structure of (*RS*)-**17** built by base pairing through --C-H···π interactions.

Structure of (*R*)-22

Figures S26 and S27 show the X-ray structure of (*R*)-**22**. The crystal of (*R*)-**22** builds ribbons running along the *a* axis by intermolecular H-bonding interactions between adjacent (*R*)-**22** molecules by –N-H···O(2,3-dihydro-1,4-benzoxathiin moiety) interactions (2.985(5)Å, 139.64º). These ribbons are stabilized by –C-H···π, involving the –C21-H21A bond and the six membered aromatic ring of the 2,3-dihydro-1,4-benzoxathiin moiety (C-H···centroid distance: 2.62 Å and C-H···centroid angle: 168.0º) and non-classical –C-H···N hydrogen interactions (C8-H8···N7, 3.311(6) Å, 153º). These ribbons are associated by –C-H···Cl interactions (3.559 Å, 125.11º) to build the 3D network.

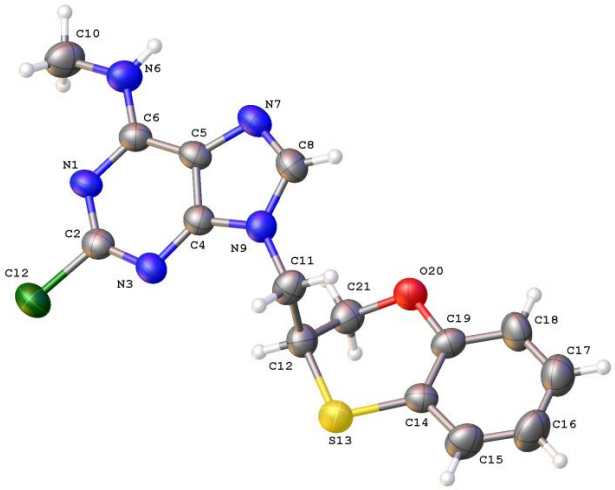


Figure S26. Molecular structure of (*R*)-**22**. Hydrogen atoms are drawn as spheres of arbitrary radius. Ellipsoids of the non-hydrogen atoms are drawn at the 50% probability level.

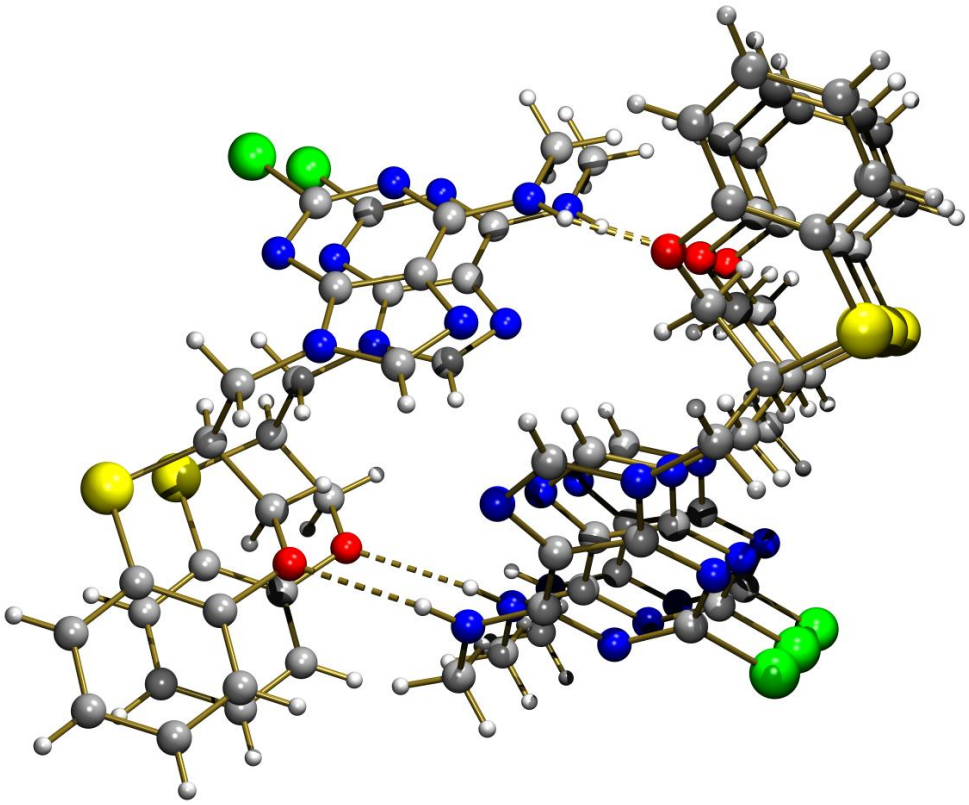


Figure S27. Fragment of a ribbon built by base pairing through -N–H···O interactions

X-ray structure of (*RS*)-24

Figures S28 and S29 display the X-ray diffraction of (*RS*)-**24**. In the crystal of (*RS*)-**24**, pairs of adjacent (*RS*)-**24** molecules are H-bonded by intermolecular symmetric interactions -N–H···N(imidazole) (3.07 Å, 149.0º). π,π-stacking interactions are observed between five- and six-membered rings (purine moiety) of anti-parallel neighbouring (*RS*)-**24** molecules (centroid-centroid distances: 3.786 and 3.527 Å) connecting pairs and generating a ribbon structure running along the a axis. Ribbons are associated by C-H···π interactions (C-H··· six-membered aromatic ring of the 2,3-dihydro-1,4-benzoxathiin moiety: C-H···centroid distance: 2.74 and 2.67Å and C-H···centroid angle: 161.0 and 173º) giving rise to two-dimensional frameworks parallel to the *ab* plane. Finally, additional C-H···π interactions involving the –C47-H47 bond and the six membered aromatic ring of the purine moiety (C-H···centroid distance: 2.74 Å and C-H···centroid angle: 173.0º) cooperate to reach the 3D structure.

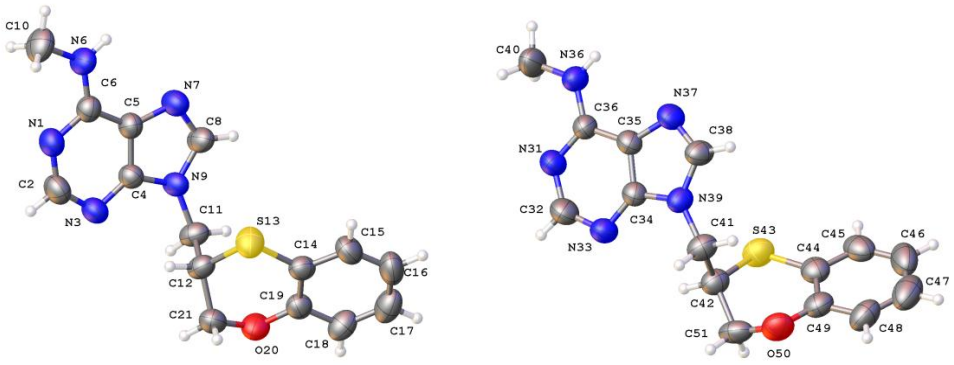


Figure S28. Molecular structure of (*RS*)-**24**. Hydrogen atoms are drawn as spheres of arbitrary radius. Ellipsoids of the non-hydrogen atoms are drawn at the 50% probability level.

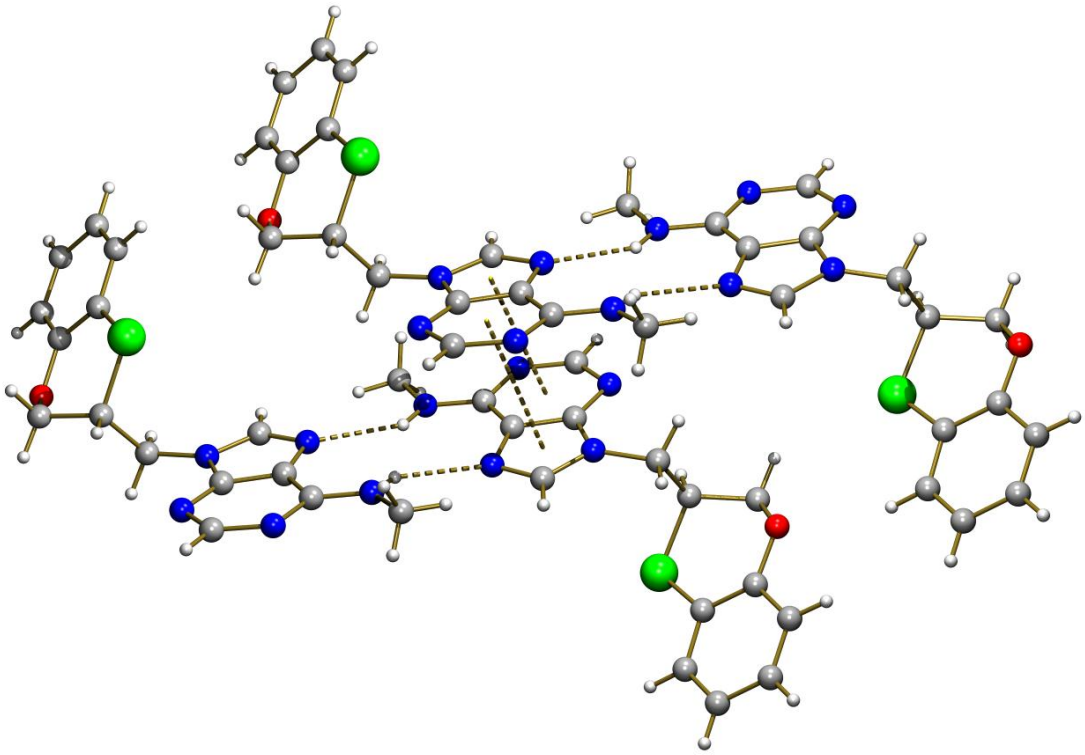


Figure S29. Fragment of a ribbon structure built by base pairing through symmetric N–H···N interactions and π,π-stacking interactions involving aromatic rings of the purine moiety of (*RS*)-**24**.

REFERENCES

[1] BRUKER, APEX2 Software, Bruker AXS Inc, Madison, Wisconsin, USA, **2010**.

[2] Sheldrick, G.M. A short history of SHELX. *ActaCryst.*, **2008**, *A64*, 112–122.