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Generation and cascade reactions of *N*-[1,2-bis(methoxycarbonyl)vinyl]pyridinium species

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1. Experimental Section

1.1 Materials and characterization

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AVANCE II 300 spectrometer at 300 and 75 MHz, respectively, in $CDCl_3$ with tetramethylsilane as an internal reference standard or in DMSO-d_6. NMR signal assignment if present was based on COSY, HSQS and HMBS spectra. High-resolution mass spectra were obtained with a Bruker microTOF II instrument (ESI, positive or negative ion modes, capillary voltage 4500 V). The rectification was carried out using Fischer Spaltrohr-Kolonne HMS 500 AC. All reagents and solvents are commercially available and used without additional purification.

1.2 Synthesis

Dimethyl bromomaleate (*cis*-3)

Triethylamine (30 ml, 0.21 mol) was added to a vigorously stirred suspension of dimethyl *meso*-2,3-dibromosuccinate *meso*-**2** (62 g, 0.20 mol) in Et_2O (200 ml), and the mixture was stirred at room temperature for 2 h. The resulting mixture was sequentially washed with water, then with 0.1 M aqueous $NaHSO_4$, then with brine. The organic layer was dried over anhydrous $MgSO_4$, the solvent was removed *in vacuo* to give a mixture of dimethyl bromomaleate and dimethyl bromofumarate in a ratio of 7:1. The target product was obtained in pure form by rectification (m.p. 97°C, 15 mbar) in a yield of 94% (47 g). ^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] 6.46 (s, 1H), 3.84(s, 3H), 3.71 (s, 3H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ [ppm] 164.0, 163.3, 127.1, 126.4, 53.4, 52.3. The data correspond to those previously reported.[S1]

Dimethyl bromofumarate (*trans*-3)

Triethylamine (30 ml, 0.21 mol) was added to a vigorously stirred solution of dimethyl *dl*-2,3-dibromosuccinate *dl*-**2** (62 g, 0.20 mol) in Et_2O (200 ml), and the mixture was stirred at room temperature for 2 h. The resulting mixture was sequentially washed with water, then with 0.1 M aqueous $NaHSO_4$, then with brine. The organic layer was dried over anhydrous $MgSO_4$, the solvent was removed *in vacuo* to give a mixture of dimethyl bromofumarate and dimethyl bromomaleate in a ratio of 4:1. The target product was obtained in pure form by two successive crystallizations from the melt in a yield of 50% (25 g). ^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] 7.49 (s, 1H), 3.89(s, 3H), 3.82 (s, 3H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ [ppm] 164.0, 162.3, 130.7, 125.1, 54.1, 52.3. The data correspond to those previously reported.[S1]

1,1,2,3,4,5,6,7-Octa(methoxycarbonyl)cyclohepta-2,4-diene (4) and 1,1,2,3,4,5,6,7-octa(methoxycarbonyl)cyclohepta-3,5-diene (4')

A mixture of source of **1** (3.64 g for *meso*-**2** or *dl*-**2** or 2.67 g for *cis*-**3** and *trans*-**3**, 12 mmol, Table S1), dimethyl malonate (0.53 g, 4 mmol), pyridine (1.93 ml, 24 mmol for *meso*-**2** or *dl*-**2** or 0.97 ml, 12 mmol for *cis*-**3** and *trans*-**3**) and DMF (1.93 ml) was stirred at room temperature for the time indicated in Table S1. The resulting mixture was washed with water (20 ml) and ether (20 ml) simultaneously and the mixture was stirred until the powdery precipitate separated. The mixture was filtered and the residue was washed with water and ether to give the desired mixture of cycloheptadienes **4** and **4'**. Isomer **4** ^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] 5.15 (s, 1H), 4.71 (s, 1H), 3.85 (s, 3H), 3.80 (s, 3H), 3.79 (s, 3H), 3.74 (s, 3H), 3.73 (s, 6H), 3.72 (s, 3H), 3.70(s, 3H). Isomer **4'** ^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm] 5.08 (br.-s, 2H), 3.89 (s, 6H), 3.73 (s, 6H), 3.70 (s, 6H), 3.69 (s, 6H). The physical data correspond to those previously reported.[S2]

Table S1

Source	Time, days	Yield, %	Product, g
meso-**2**	5	58	1.29
dl-**2**	16	28	0.62
cis-**3**	5	63	1.40
trans-**3**	16	32	0.71

Pyridinium 5-dicyanomethylidene-2,3,4-tris(methoxycarbonyl)cyclopenta-1,3-dien-1-olate (5)

A source of **1** (3.64 g for *meso*-**2** or *dl*-**2** or 2.67 g for *cis*-**3** and *trans*-**3**, 12 mmol, Table S2), malononitrile (0.40 g, 6 mmol) DMF (2.42 ml) and pyridine (2.42 ml, 30 mmol for *meso*-**2** or *dl*-**2** or 1.45 ml, 18 mmol for *cis*-**3** and *trans*-**3**) was stirred at room temperature for the time indicated in Table S2. The resulting solution was poured into water and then filtered through a paper filter to form the desired product as dark-blue crystals in yields given in Table S2. ^{1}H NMR (300 MHz, DMSO-d_6) δ [ppm] 8.98 – 8.83 (m, 2H), 8.62 – 8.55(m, 1H), 8.06 (t, *J* = 6.8 Hz, 2H), 3.76 (s, 3H), 3.56 (s, 3H), 3.54 (s, 3H). The physical data correspond to those previously reported.[S3]

Table S2

Source	Time, days	Yield, %	Product, g
meso-**2**	21	62	1.48
dl-**2**	28	34	0.81
cis-**3**	21	17*	0.90**
trans-**3**	28	53	1.26

*NMR yield. ** Total weight

Heptamethyl cyclohepta-1,3,5-triene-1,2,3,4,5,6,7-heptacarboxylate (6)

A mixture of source of **1** (3.64 g for *meso*-**2** or *dl*-**2** or 2.67 g for *cis*-**3** and *trans*-**3**, 12 mmol, Table S3), 1-(methoxycarbonylmethyl)pyridinium bromide (0.63 g, 4 mmol) in DMF (2.24 ml) and pyridine (2.24 ml, 28 mmol for *meso*-**2** or *dl*-**2** or 1.12 ml, 14 mmol for *cis*-**3** and *trans*-**3**) was stirred at room temperature for the time indicated in Table S3. The resulting mixture was poured into water (25 ml), stirred for 30 min, the precipitate was filtered off and washed with water (20 ml) and ether (20 ml). The product was dried to give the desired product in yields in in Table S3. ^{1}H NMR (300 MHz, $CDCl_3$) δ [ppm], 5.16 (s, 1H), 3.77 (s, 6H), 3.75 (s, 6H), 3.74 (s, 6H), 3.52 (s, 3H). The physical data correspond to those previously reported.[S4]

Table S3

Source	Time, days	Yield, %	Product, g
meso-**2**	4	51	1.01
dl-**2**	12	27	0.54
cis-**3**	4	52	1.04
trans-**3**	12	29	0.58

(*E*)-1,1-Dicyano-6-methoxy-2,3,4-tris(methoxycarbonyl)-6-oxo-5-(pyridin-1-ium-1-yl)hex-2-en-1-ide (7)

A solution of malononitrile (0.20 g, 3,03 mmol), dimethyl acetylenedicarboxylate (0.78 ml, 6.36 mmol) in methanol (5 ml) was cooled to 0 °C. A mixture of pyridine (0.25 ml, 3.03 mmol), AcOH (0.17 ml, 3.03 mmol) and methanol (2 ml) was added dropwise in 15 min and the mixture was allowed to warm to room temperature and vigorously stirred for 2 h. The yellow precipitate was filtered and washed with methanol to give **7** (1.06 g, 82%) as yellow powder. HRMS: calcd for $C_{20}H_{19}N_3O_8$ M + Na 452.1064, found: *m/z* 452.1056; IR (KBr) 3148, 3086, 3062, 2975, 2956, 2194, 2169, 1760, 1733, 1680, 1635, 1514, 1440 cm^{-1}. *threo*-**7:** ^1H NMR (300 MHz, DMSO-d_6): δ [ppm] 9.08 (d, *J* = 6 Hz, 2H), 8.67 (m, 2H), 8.18 (t, *J* = 8.4 Hz, 1H), 6.07 (d, *J* = 7.4 Hz, 1H), 5.30 (d, *J* = 7.4 Hz, 1H), 3.77 (s, 3H), 3.65 (s, 3H), 3.56 (s, 3H), 3.16 (s, 3H).^{13}C NMR (75.5 MHz, DMSO-d_6): δ [ppm] 170.6, 167.4, 165.9, 164.3, 150.9, 146.8, 146.2, 126.4, 120.3, 93.6, 69.4, 52.9, 52.0, 51.7, 52.1, 44.5. *erythro*-**7:** ^1H NMR (300 MHz, (DMSO-d_6): δ [ppm] 8.87 (d, *J* = 6 Hz, 2H), 8.72 (m, 2H), 8.21 (t, *J* = 7.7 Hz, 1H), 6.17 (d, *J* = 8.8 Hz, 1H), 5.30 (d, *J* = 8.8 Hz, 1H), 3.81 (s, 3H), 3.65 (s, 3H), 3.50 (s, 3H), 3.39 (s, 3H). ^{13}C NMR (75.5 MHz, (DMSO-d_6): δ [ppm] 170.2, 167.1, 166.3, 164.2, 152.5, 146.9, 144.5, 127.5, 119.9, 93.6, 69.8, 53.3, 52.2, 51.5, 50.5, 44.0.

Investigation of elimination of HBr from *meso*-2 or *dl*-2.

To a solution of dimethyl 2,3-dibromosuccinate *meso*-**2** or *dl*-**2** (3.3 mmol, 1.0 g) in DMF (0.53 ml) was added triethylamine (3.3 mmol, 0.46 ml) or pyridine (6.6 mmol, 0.530 ml or 3.3 mmol, 0.265 ml) and the mixture stirred for 2.5 h at room temperature. The sample was dissolved in DMSO-d_6 and analyzed by ^1H NMR spectroscopy.

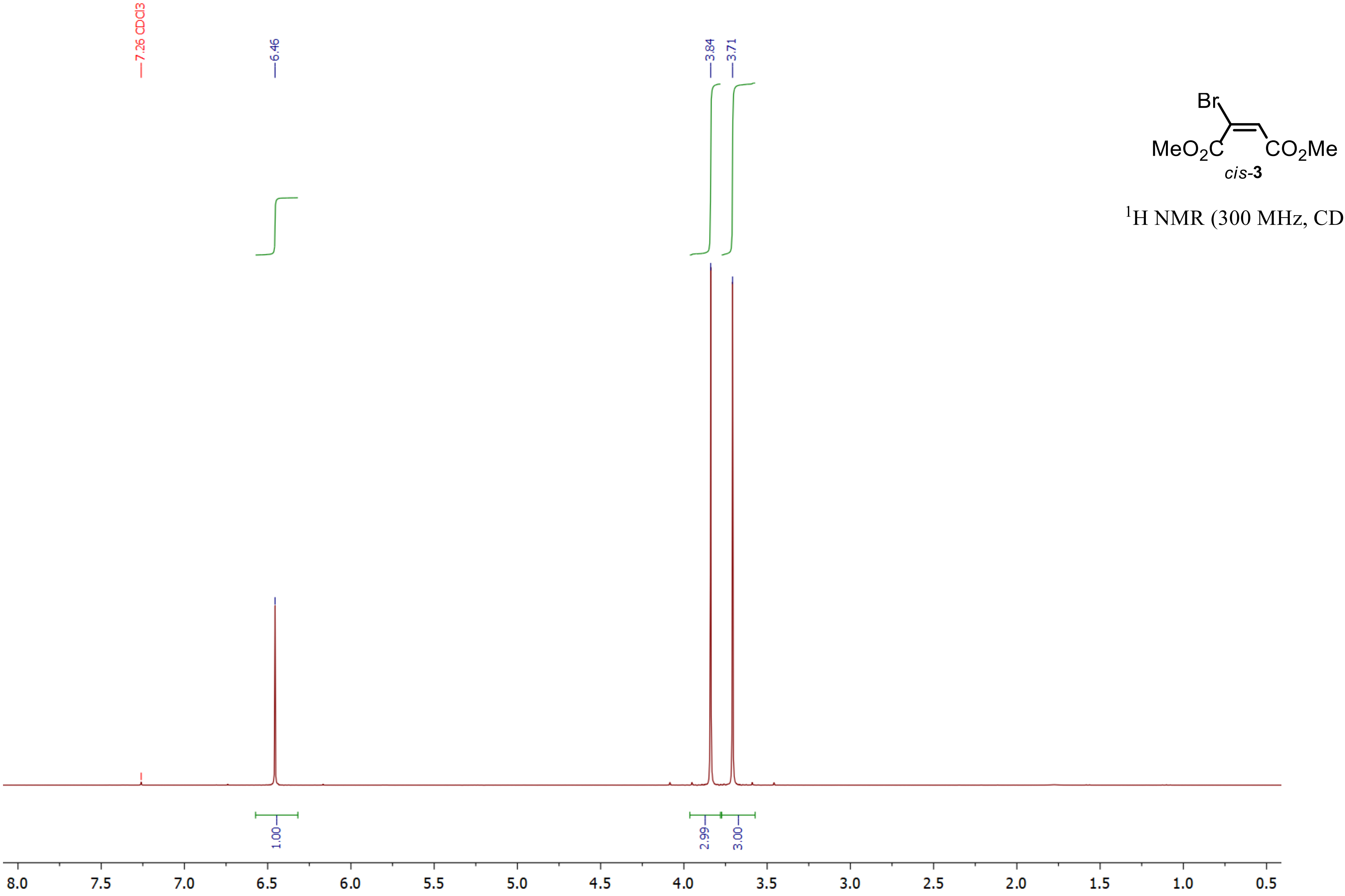
Investigation of formation of *N*-[1,2-bis(methoxycarbonyl)vinyl]pyridinium salt from *cis*-3 and *trans*-3

A mixture *cis*-**3** (lines *1* and *2*, see Figure 1 in the main text) or *trans*-**3** (*3* and *4*), (2.23 g,10 mmol) in DMF (3.2 ml) and pyridine (1.61 ml, 20 mmol) with the addition of trifluoroacetic acid (0.75 ml, 10 mmol) (*1* and *3* only) was allowed to stay at room temperature. The reaction mixture was monitored every 20-50 h by means of ^1H NMR spectroscopy by dissolving an aliquot in DMSO-d_6.

2. References

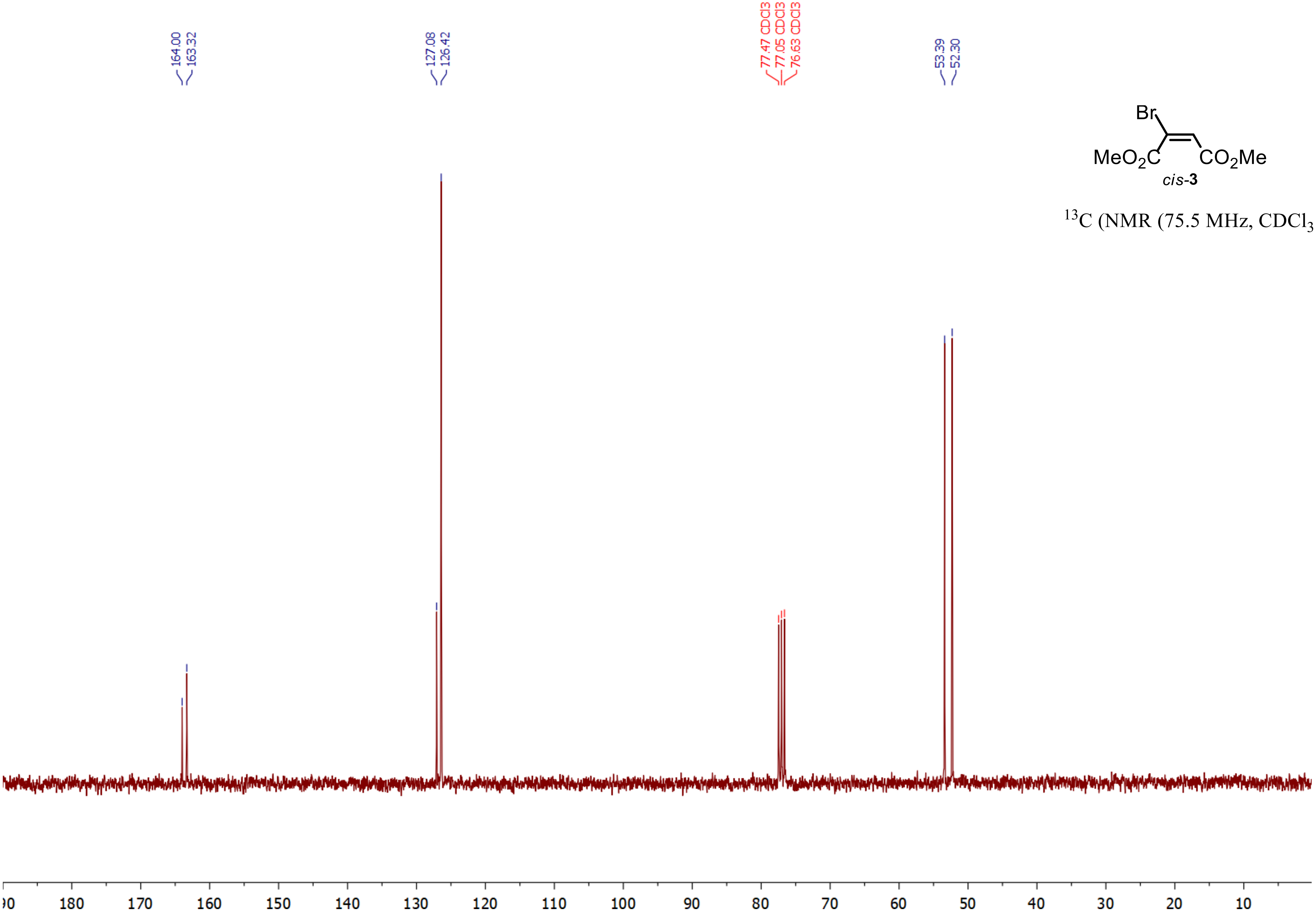
S1 B. L. Booth and R. G. Hargreaves, *J. Organomet. Chem.*, 1971, **33**, 365.
S2 A. S. Kelch, P. G. Jones, I. Dix and H. Hopf, *Beilstein J. Org. Chem.*, 2013, **9**, 1705.
S3 E. Le Goff and R. B. LaCount, *J. Org. Chem.*, 1964, **29**, 423.
S4 A. Y. Belyy, D. N. Platonov, R. F. Salikov, A. A. Levina and Y. V. Tomilov, *Synlett*, 2018, **29**, 1157.

3. NMR spectra



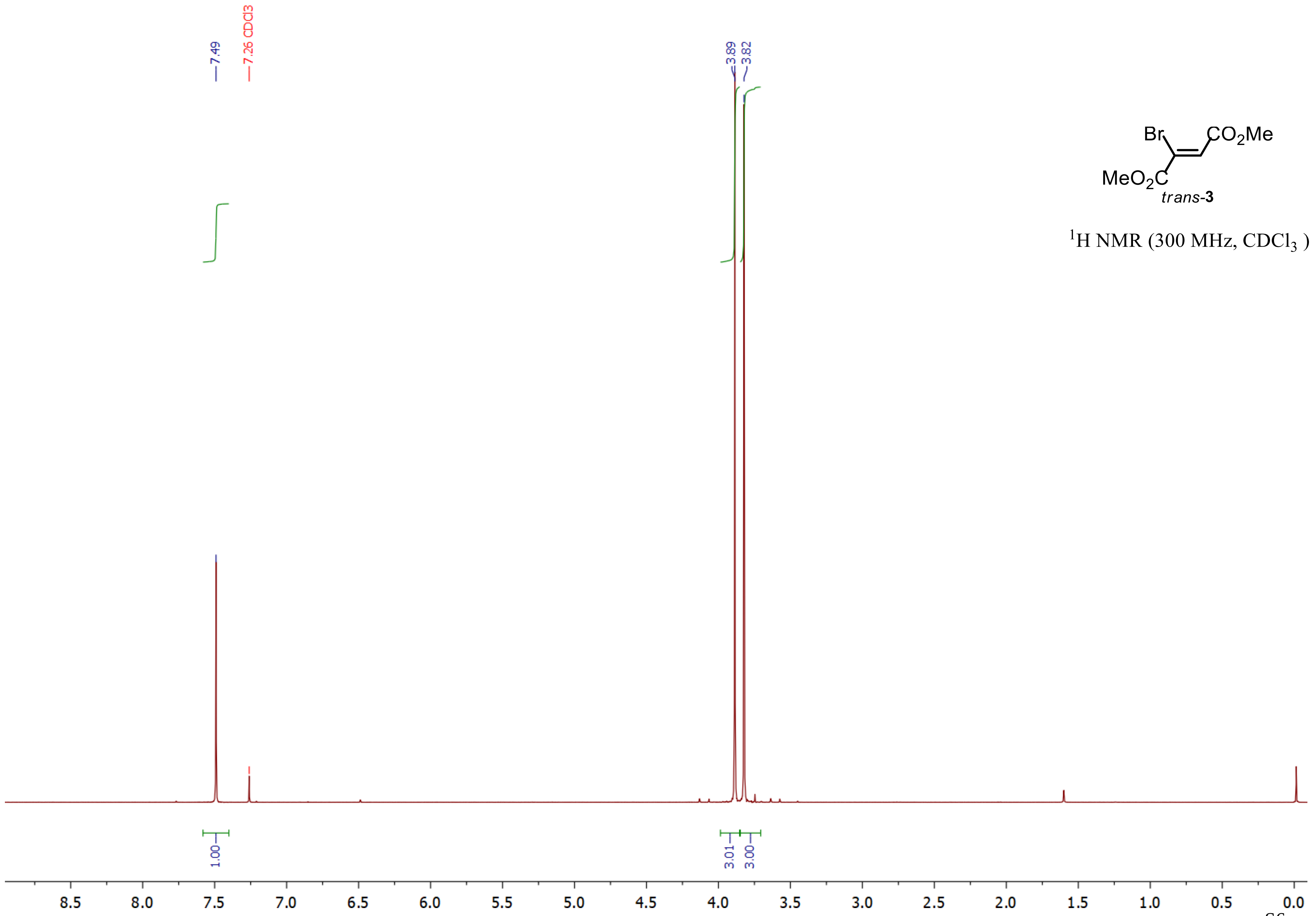
cis-**3**

^{1}H NMR (300 MHz, $CDCl_3$)



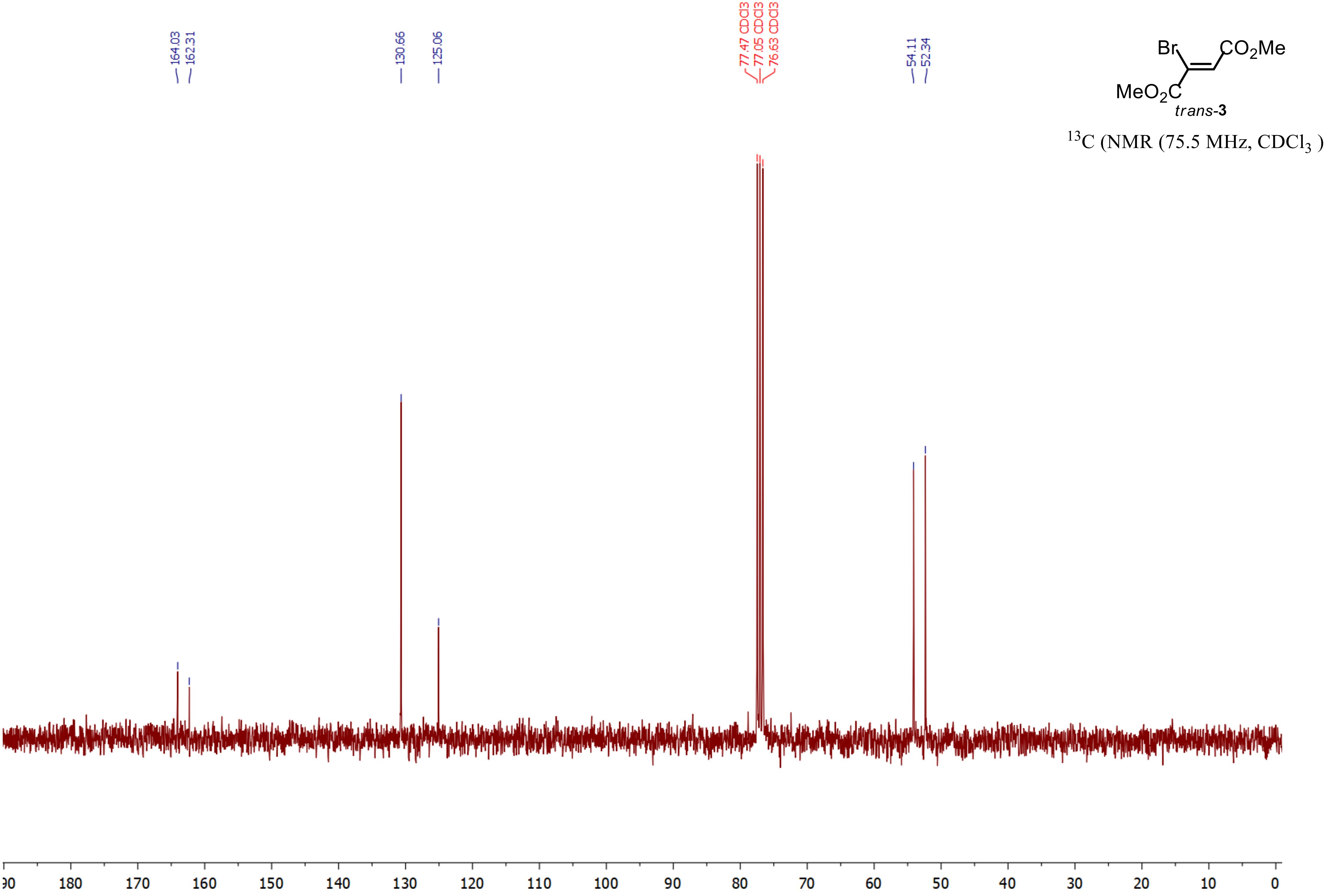
cis-**3**

^{13}C (NMR (75.5 MHz, $CDCl_3$)



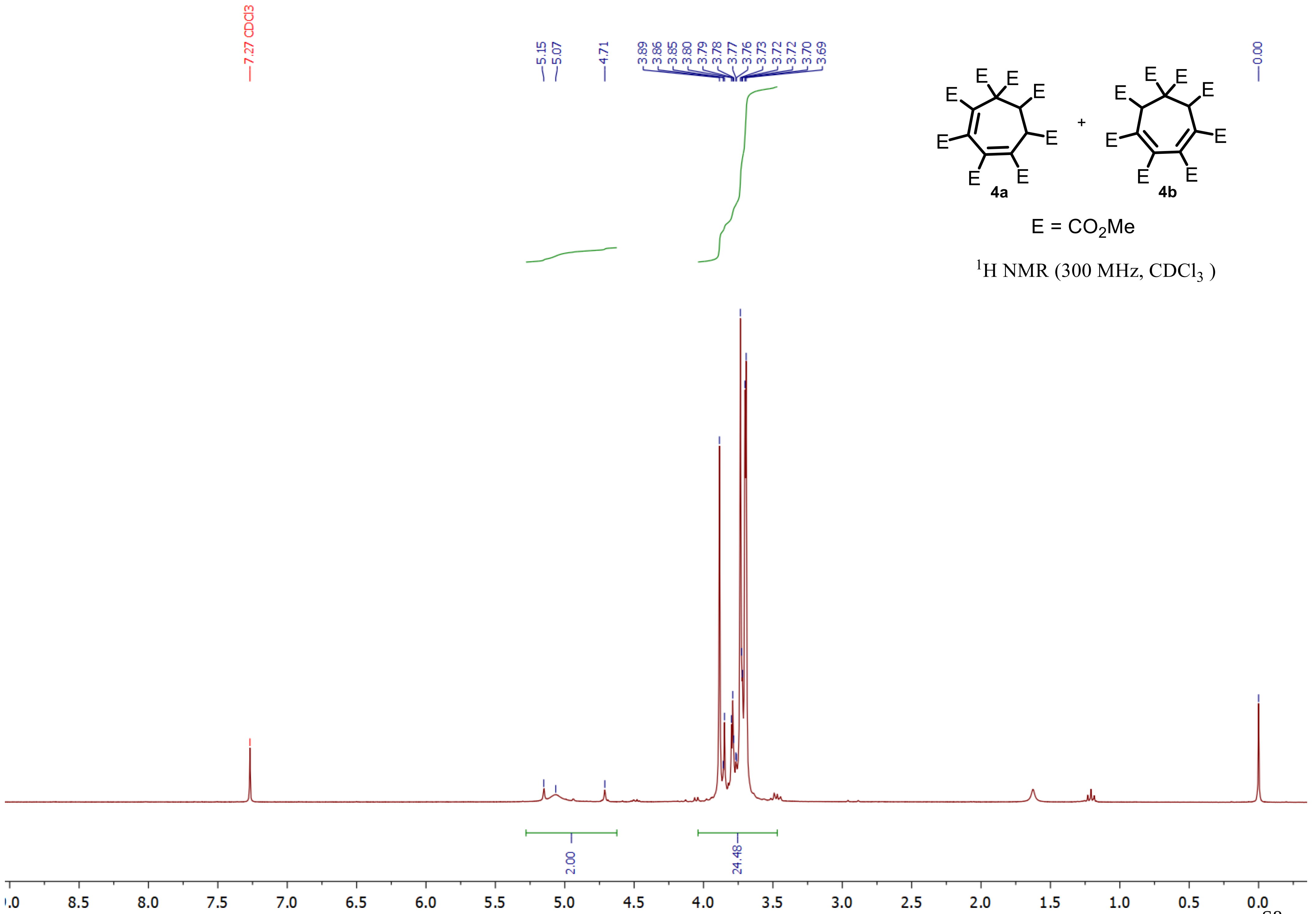
trans-**3**

^{1}H NMR (300 MHz, $CDCl_3$)



trans-**3**

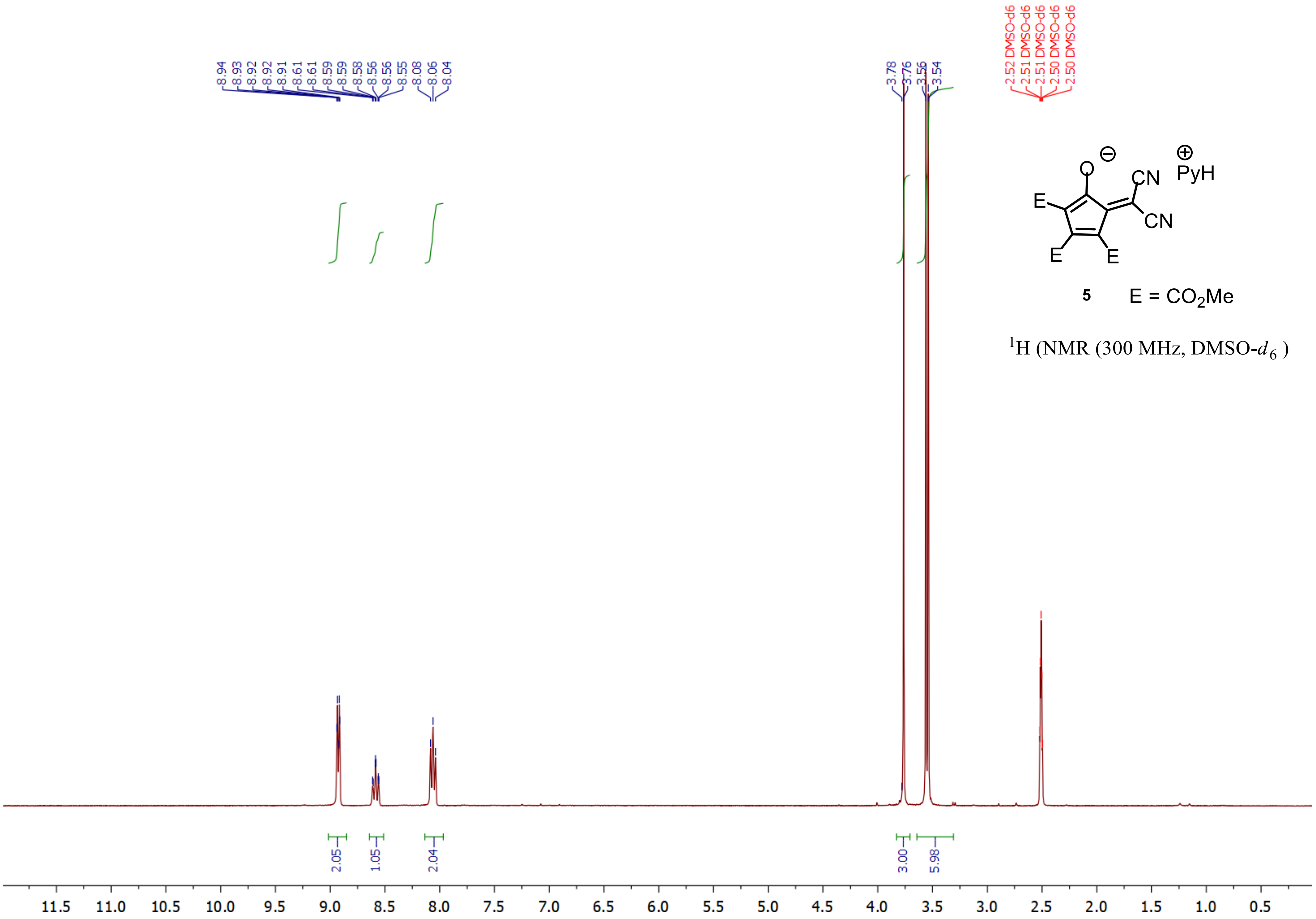
^{13}C (NMR (75.5 MHz, CDCl$_3$)



4a + **4b**

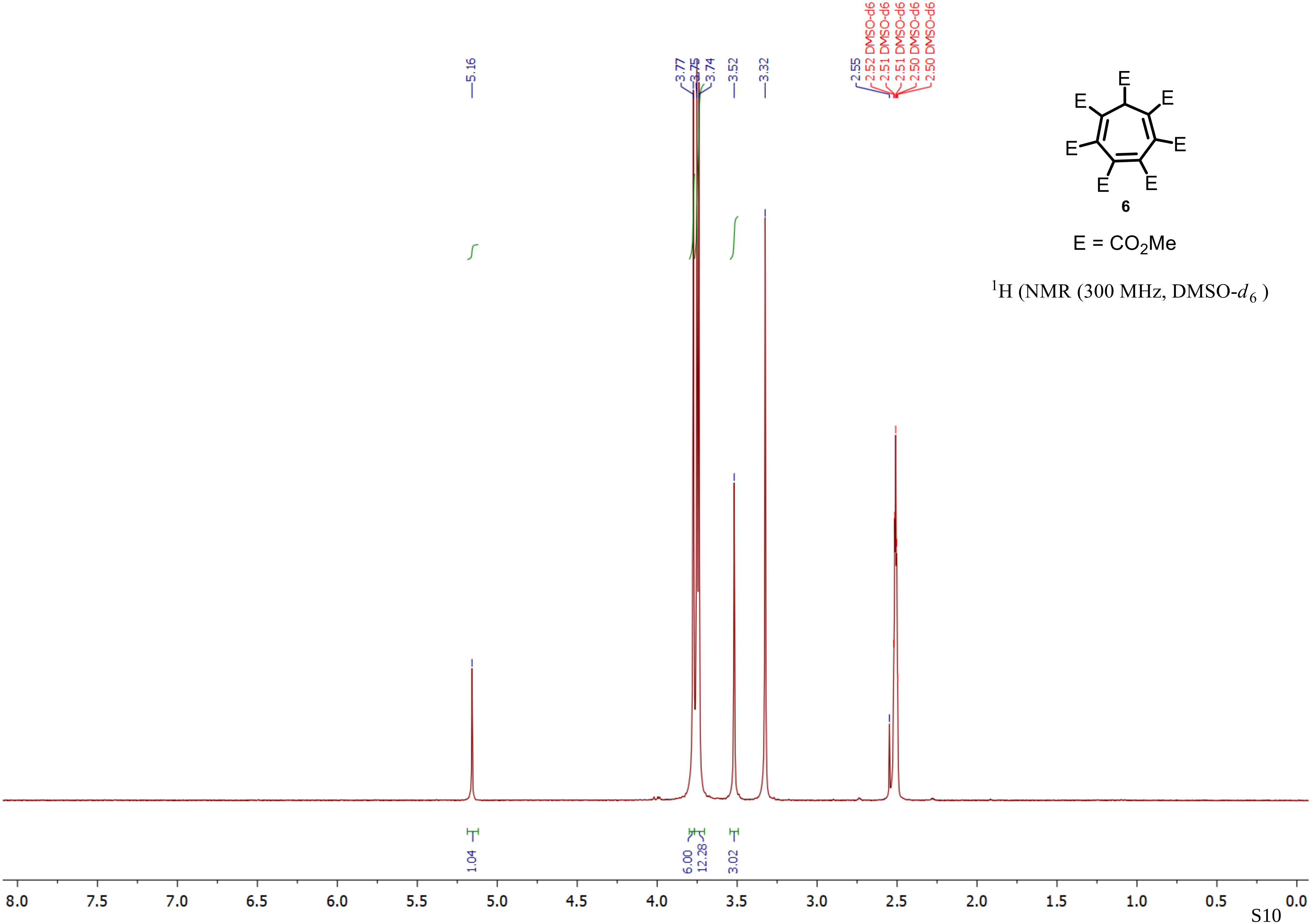
E = CO_2Me

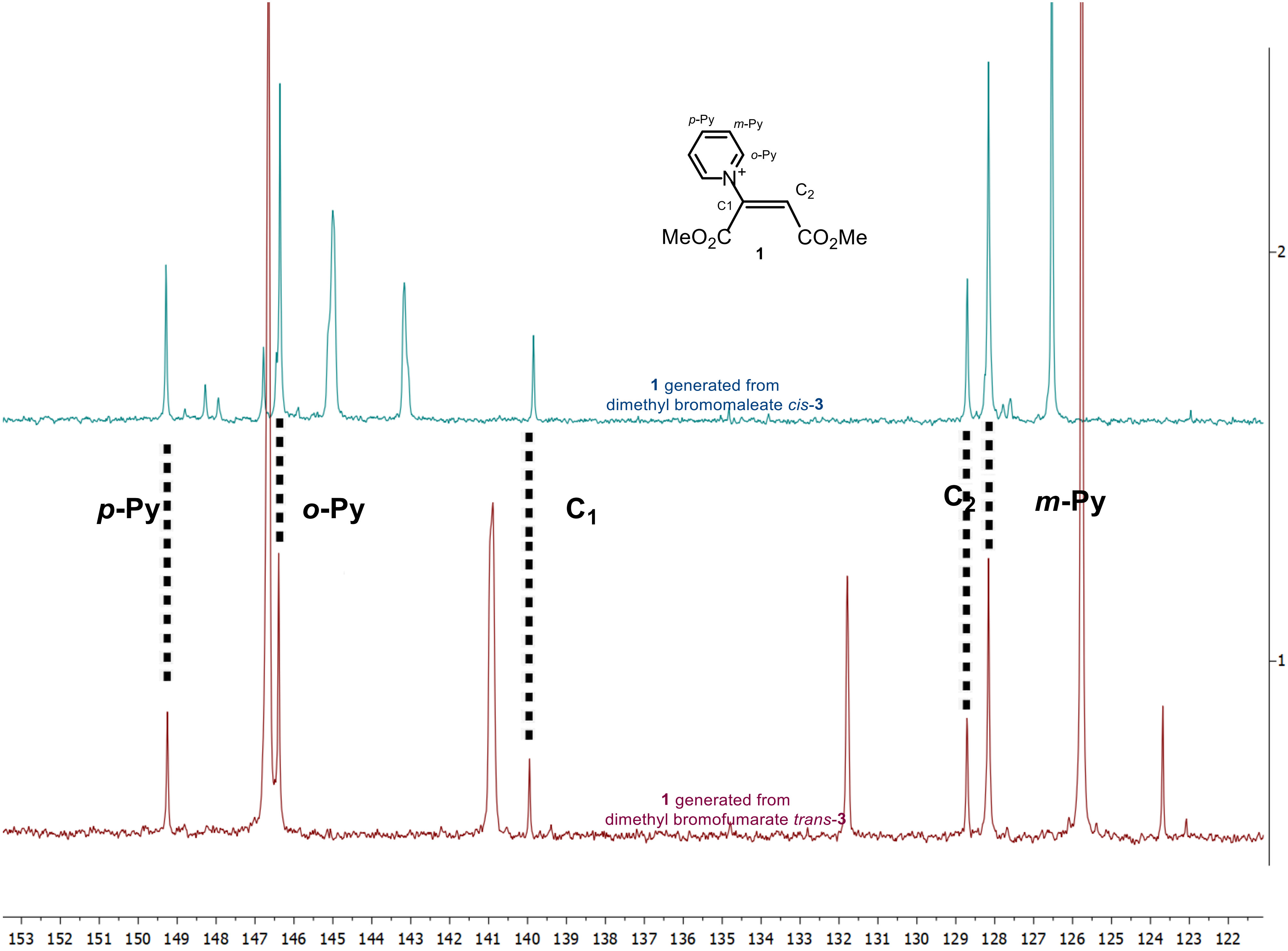
^1H NMR (300 MHz, $CDCl_3$)



5 E = CO_2Me

^1H (NMR (300 MHz, DMSO-d_6)


5.16
3.77
3.75
3.74
3.52
3.32
2.55
2.52 DMSO-d6
2.51 DMSO-d6
2.51 DMSO-d6
2.50 DMSO-d6
2.50 DMSO-d6
E
6
E = CO2Me
1H (NMR (300 MHz, DMSO-d6)
1.04
6.00
12.28
3.02
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


p-Py
m-Py
o-Py
C1
C2
MeO2C
CO2Me
1
1 generated from
dimethyl bromomaleate cis-3
p-Py
o-Py
C1
C2
m-Py
1 generated from
dimethyl bromofumarate trans-3
2
1
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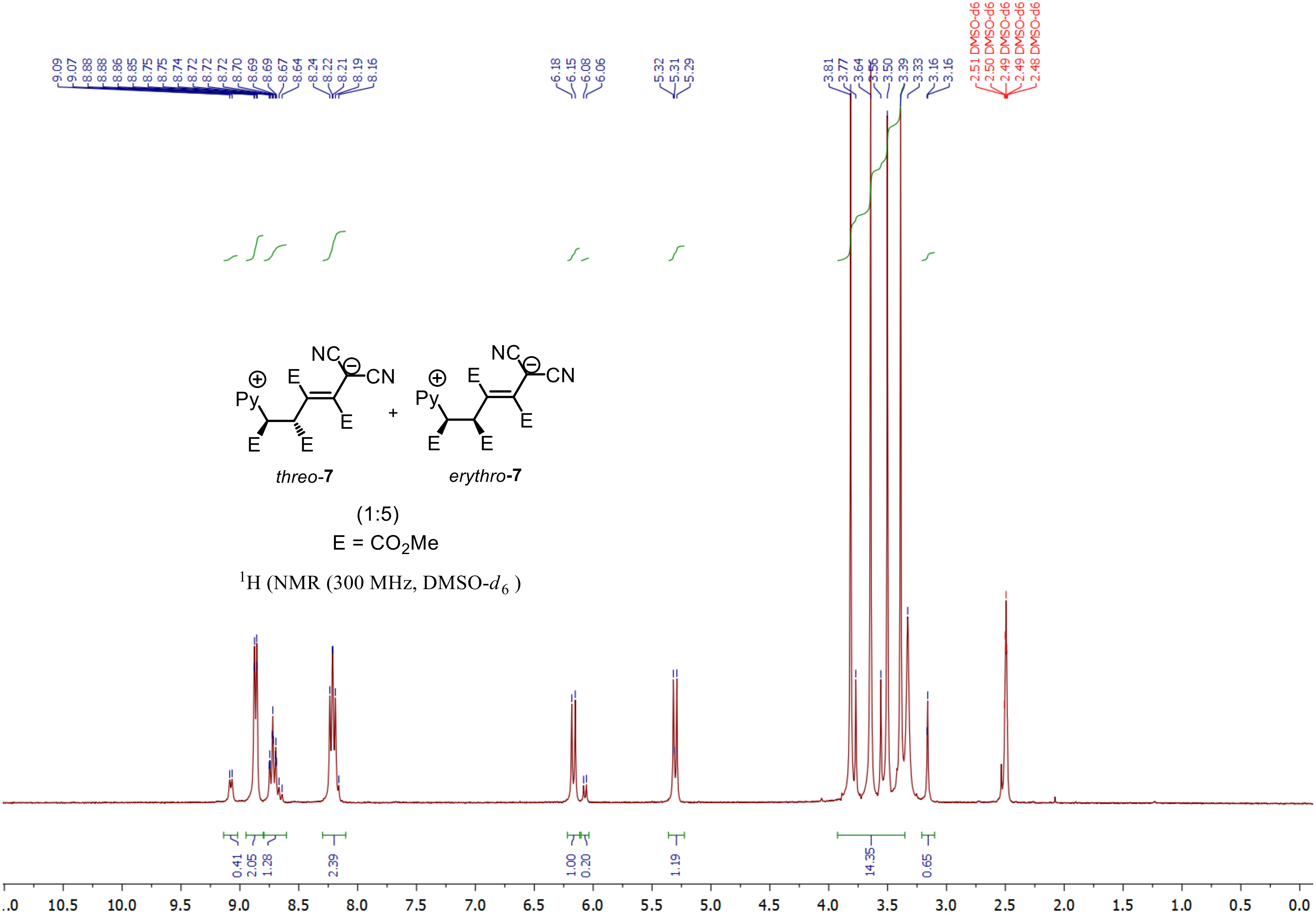
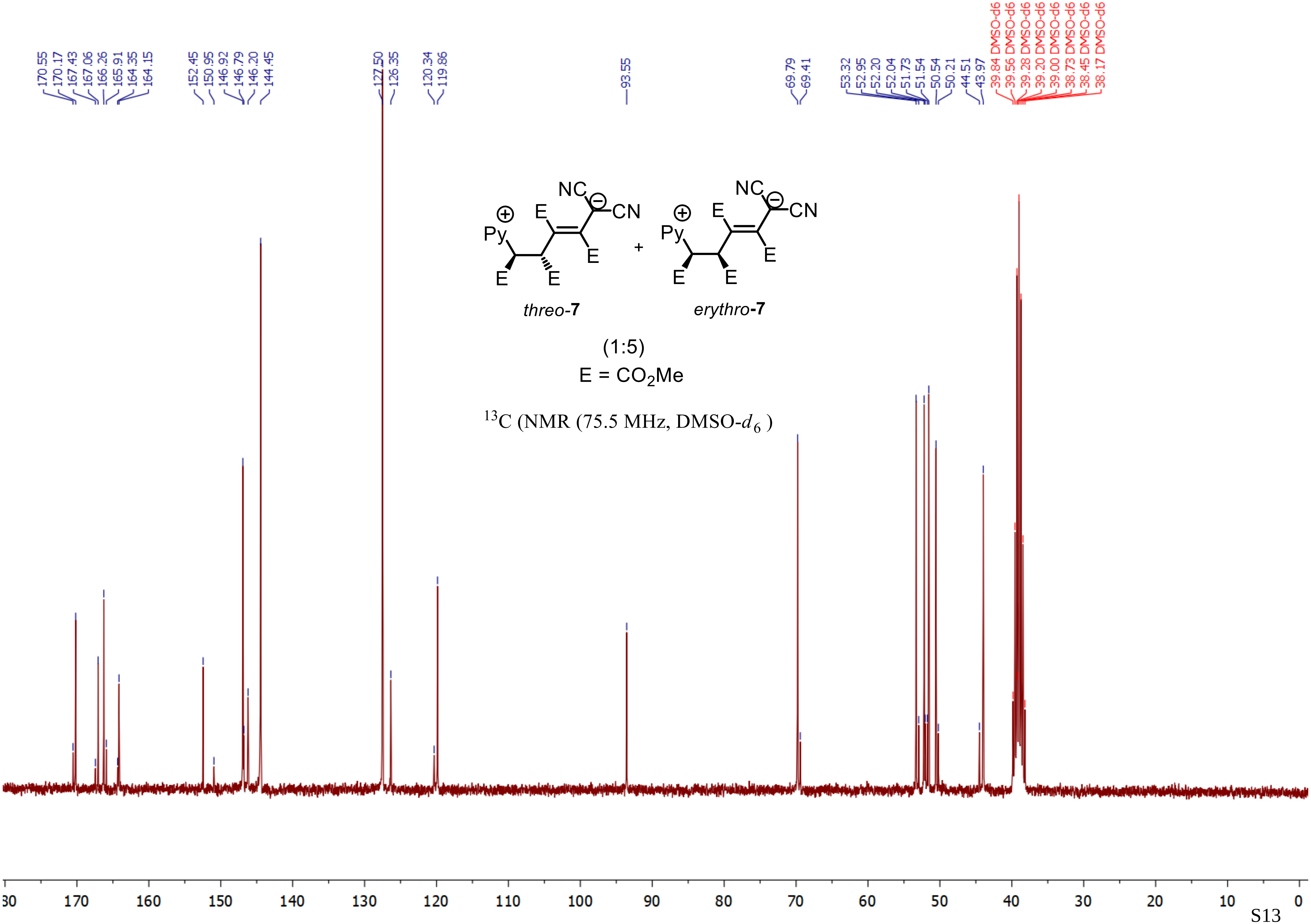


(1:5)

E = CO_2Me

^{1}H (NMR (300 MHz, DMSO-d_6)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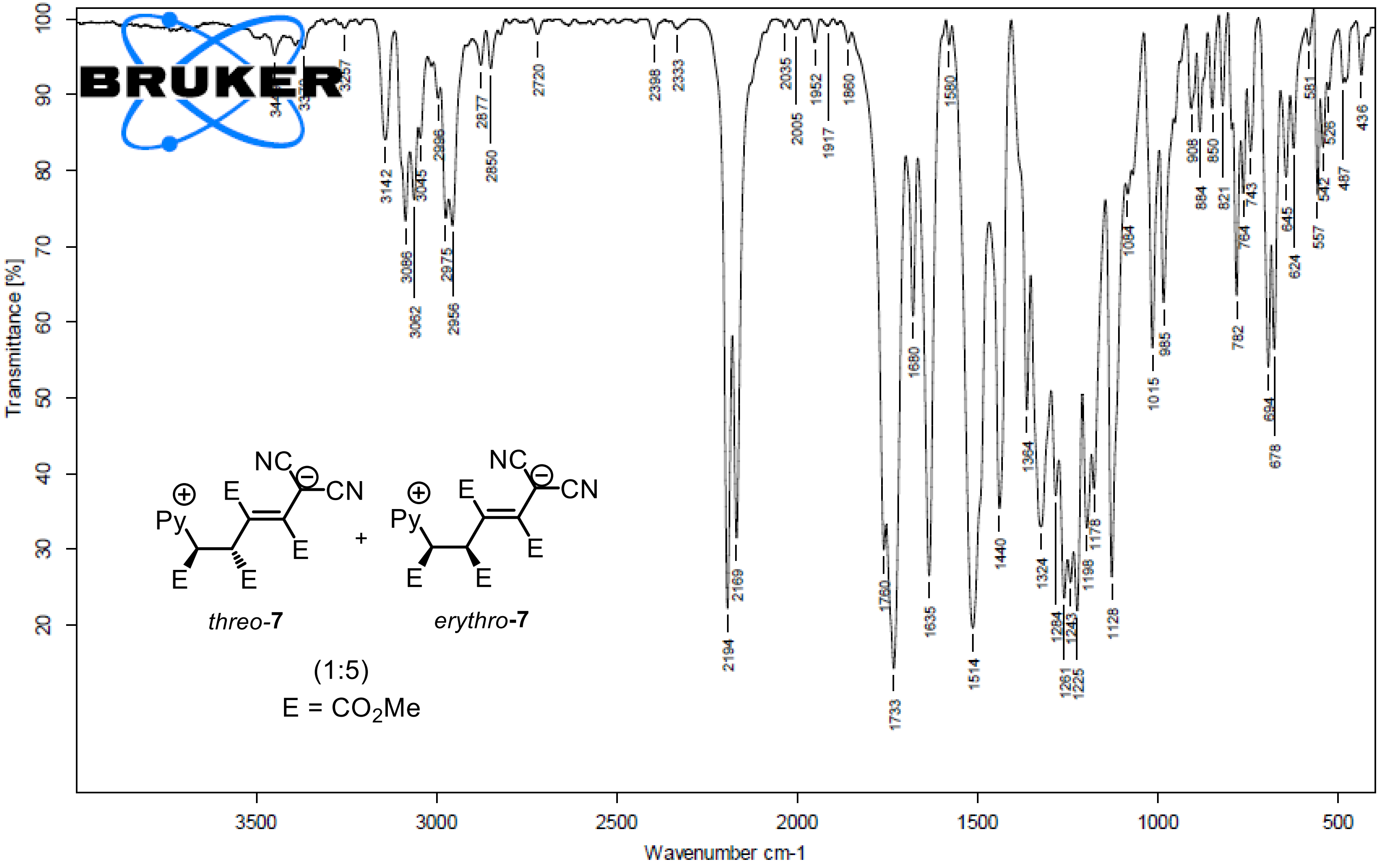
146.20
144.45
127.50
126.35
120.34
119.86
93.55
69.79
69.41
53.32
52.95
52.20
52.04
51.73
51.54
50.54
50.21
44.51
43.97
39.84 DMSO-d6
39.56 DMSO-d6
39.28 DMSO-d6
39.20 DMSO-d6
39.00 DMSO-d6
38.73 DMSO-d6
38.45 DMSO-d6
38.17 DMSO-d6
NC
CN
Py
E
+
threo-7
erythro-7
(1:5)
E = CO2Me
13C (NMR (75.5 MHz, DMSO-d6)
30
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


Transmittance [%]
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80
70
60
50
40
30
20
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1
3257
3142
3086
3062
3045
2996
2975
2956
2877
2850
2720
2398
2333
2194
2169
2035
2005
1952
1917
1860
1760
1733
1680
1635
1580
1514
1440
1364
1324
1284
1261
1243
1225
1198
1178
1128
1084
1015
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908
884
850
821
782
764
743
694
678
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624
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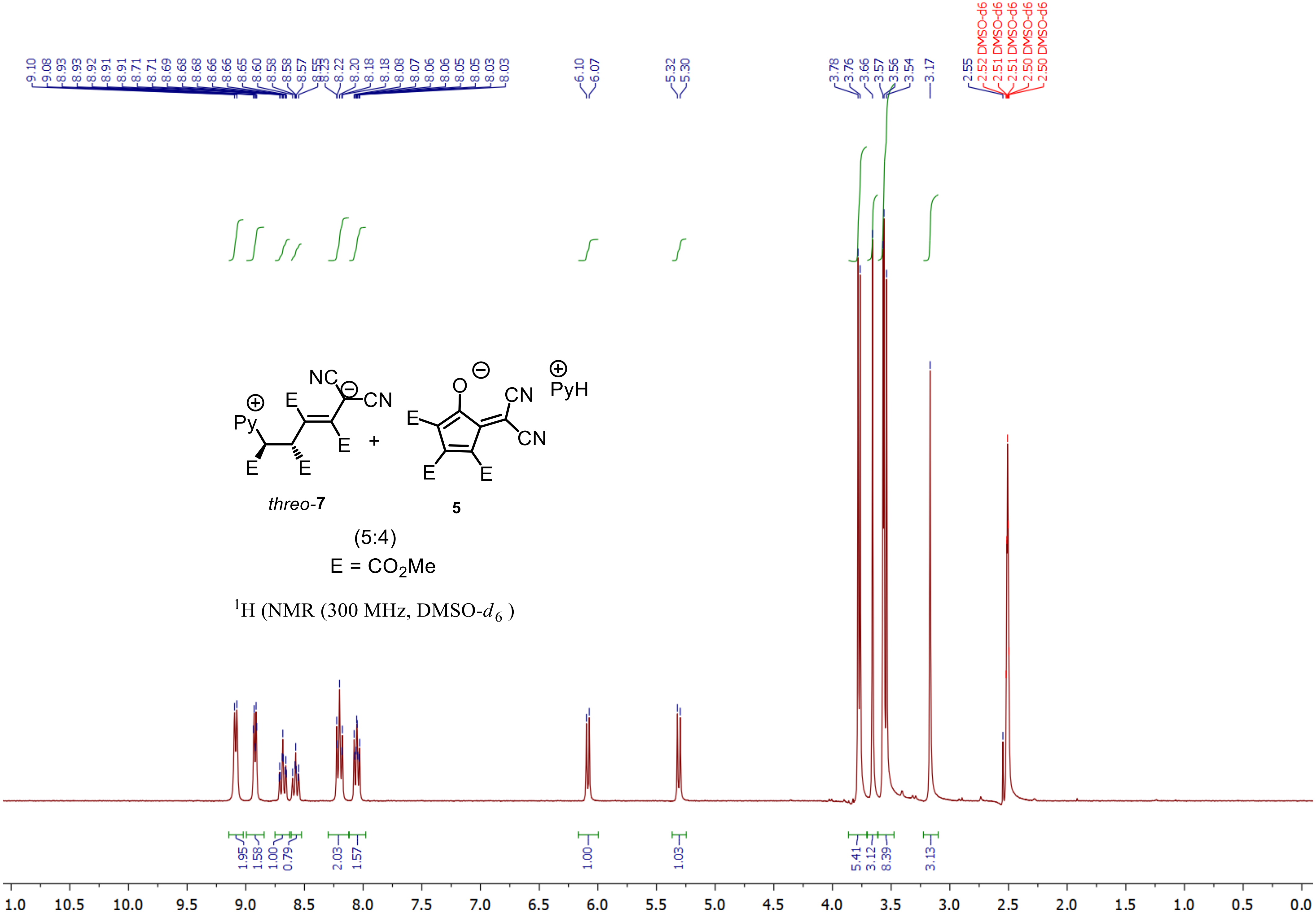
+
threo-7
erythro-7
(1:5)
E = CO$_2$Me



(5:4)
E = CO_2Me

^{1}H (NMR (300 MHz, DMSO-d_6)