Electronic supporting information

Development of synthetic equivalent of α,α-dicationic acetic acid leading to unnatural amino acid derivatives *via* tetrafunctionalized methanes

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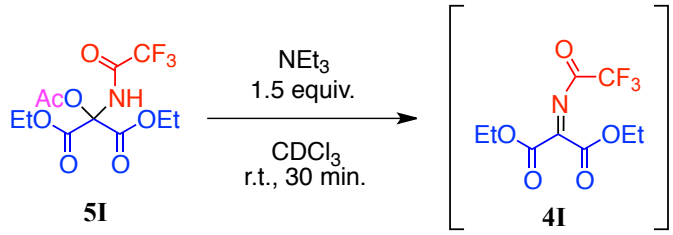
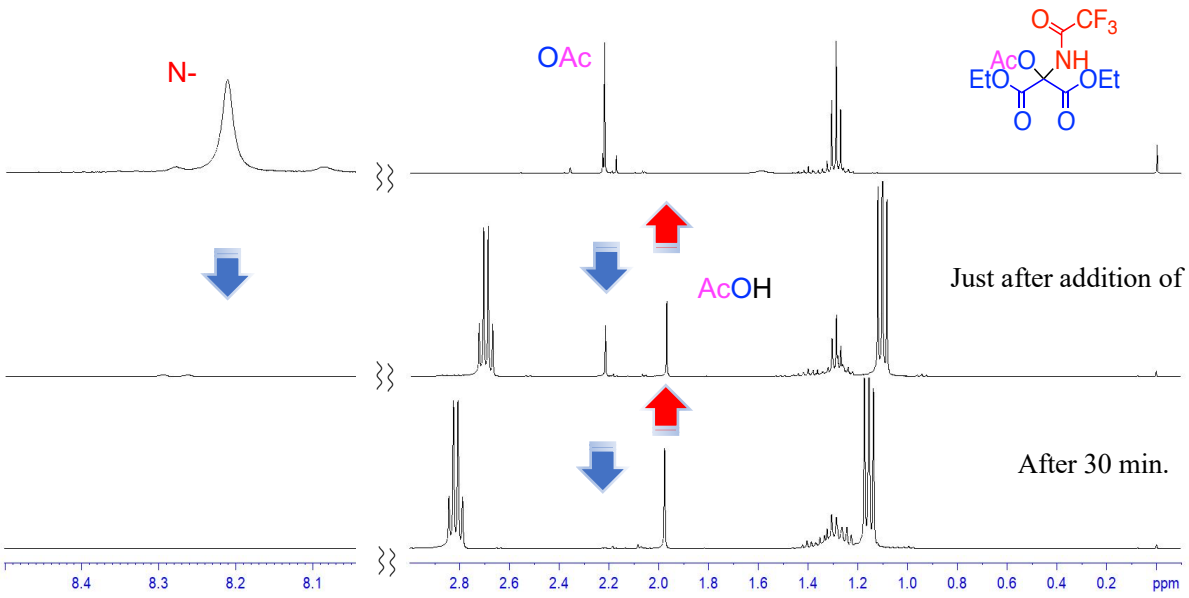
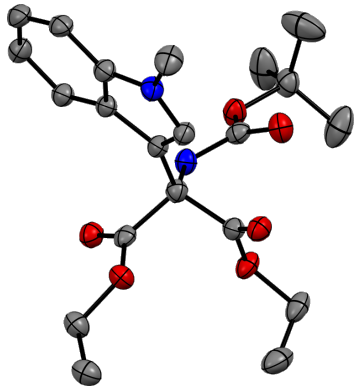
1. Monitoring the conversion of *N,O*-acetal 5i to *N*-acylimine 4i by ^{1}H NMR

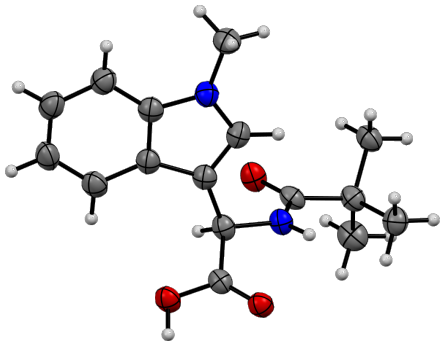




3. Single crystal X-ray diffraction data for compounds 11j and 16h



11j

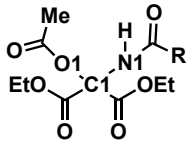


16h

Empirical formula	$C_{21}H_{28}N_2O_6$	$C_{16}H_{20}N_2O_3$
Formula weight	404.45	288.34
Temperature (K)	103(2)	103(2)
Crystal system	monoclinic	monoclinic
Space group	$P2_1$ (#4)	$P2_1/n$ (#14)
Unit cell Dimensions	a = 10.3357(3) Å, b = 7.9301(2) Å c = 13.6175(4) Å, β = 107.526(3)°	a = 11.4946(8) Å, b = 11.5682(6) Å c = 11.8250(7) Å, β = 104.642(7)°
Volume (Å)	1064.32(5)	1521.33(17)
Z	2	4
ρ_{calc} (g•cm^{-3})	1.259	1.259
Absorption coefficient (mm^{-1})	0.093	0.093
θ range (°)	2.08 to 29.37	2.18 to 29.37
Reflections collected	3961	2829
Independent reflections	3615	2041
Completeness to θ	100	100
Goodness-of-fit	1.046	1.065
Final R indices [$I > 2\sigma(I)$]	R_1 = 0.0443, wR_2 = 0.1137	R_1 = 0.0505, wR_2 = 0.1225
R indices (all data)	R_1 = 0.0486, wR_2 = 0.1163	R_1 = 0.0725, wR_2 = 0.1344
Largest diff. peak (e•Å)	0.157	0.195
Largest diff. hole (e•Å)	–0.187	–0.239
CCDC number	2130060	2130061

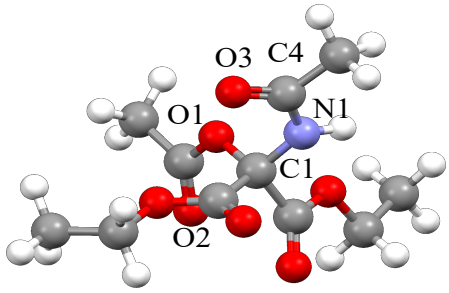
Single crystal was obtained from dichloromethane / hexane. Color labels: gray, carbon; white, hydrogen; blue, nitrogen; red, oxygen. The thermal ellipsoids are represented at 50% probability level. All hydrogen atoms of **6Jf** were omitted for clarity.

4. Computational study for compounds 5d, 5i and 5h



R	*n*-Bu	*t*-Bu	Me
C1–O1 (Å)	1.446	1.445	1.446
C1–N1 (Å)	1.432	1.433	1.432
N1–H (Å)	1.01	1.008	1.01

Cartesian coordinates [Å] of structure of compound 5d (optimized : B3LYP/6-31G(d,p))

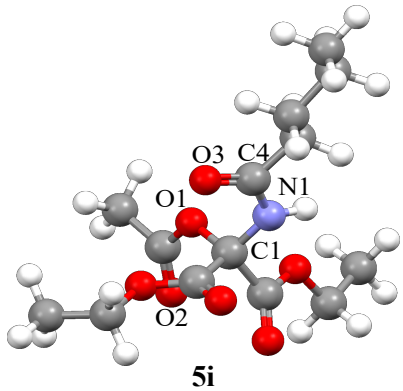


5d

R = Me	X	Y	Z
C	-1.2069	-0.3116	-0.9266
C	1.2414	0.2832	-0.8554
O	1.4419	0.935	-1.8493
O	-1.0511	-0.7708	-2.0272
O	2.0665	-0.6257	-0.3312
C	3.3237	-0.7973	-1.0336
H	3.8505	0.1613	-1.0295
H	3.1063	-1.0583	-2.0732
C	4.0988	-1.8843	-0.3168
H	5.0564	-2.0476	-0.8207
H	4.301	-1.6015	0.7203
H	3.543	-2.8261	-0.3195
C	0.4069	2.6808	0.5969
O	1.5782	2.4217	0.8121
O	-2.3858	-0.2087	-0.2809
C	-3.5115	-0.8486	-0.94
H	-3.2667	-1.9063	-1.07
H	-3.6325	-0.4058	-1.9328
C	-4.7304	-0.6434	-0.0639
H	-5.5999	-1.1198	-0.5267

H	-4.5812	-1.0869	0.9244
H	-4.9515	0.4205	0.0629
C	-0.0969	0.3673	-0.0711
O	0.0192	-0.213	1.248
C	0.2565	-1.9431	2.8228
H	0.0002	-2.989	2.9879
H	1.3306	-1.7978	2.9735
H	-0.265	-1.3024	3.5381
C	-0.0953	-1.5569	1.4095
O	-0.4341	-2.3179	0.5321
N	-0.4762	1.7371	0.1039
H	-1.4685	1.9203	0.1369
C	-0.187	4.0649	0.7817
H	-1.2318	4.0378	1.1055
H	0.4104	4.6062	1.5154
H	-0.1398	4.6047	-0.17

Cartesian coordinates [Å] of structure of compound 5i (optimized : B3LYP/6-31G(d,p))

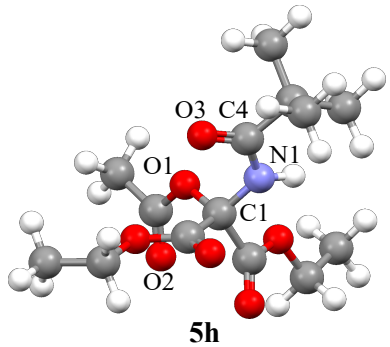


5i

R = *n*-Bu	X	Y	Z
C	-1.5793	1.079	-0.9078
C	-0.5924	-1.2412	-0.9289
O	-0.0699	-1.3513	-2.0093
O	-2.1542	0.8328	-1.935
O	-1.2635	-2.1952	-0.279
C	-1.3213	-3.4779	-0.9528
H	-0.2975	-3.8375	-1.0905
H	-1.7626	-3.3296	-1.9425
C	-2.1475	-4.4078	-0.0874
H	-2.2187	-5.3899	-0.565
H	-1.6882	-4.5376	0.8966
H	-3.1598	-4.017	0.049
C	1.8132	0.0011	0.1995

O	1.7828	-1.1987	0.4179
C	4.3512	0.0336	0.08
H	4.3285	-0.8464	0.7314
H	4.3453	-0.3508	-0.9477
O	-1.582	2.2696	-0.2753
C	-2.4788	3.2664	-0.8345
H	-3.4908	2.8524	-0.8207
H	-2.1999	3.4409	-1.8776
C	-2.3568	4.5167	0.0126
H	-3.0256	5.2906	-0.3761
H	-2.6325	4.3143	1.0512
H	-1.3353	4.908	-0.0053
C	-0.6187	0.1082	-0.1598
O	-0.9851	-0.0734	1.2274
C	-2.4198	-0.5601	3.026
H	-3.4617	-0.4793	3.3338
H	-2.0755	-1.5909	3.1541
H	-1.7857	0.0776	3.6469
C	-2.2944	-0.1798	1.5734
O	-3.2138	0.0093	0.8102
N	0.6833	0.7053	-0.1751
H	0.7064	1.7151	-0.1604
C	3.0753	0.8468	0.3176
H	3.0867	1.2701	1.3328
H	3.0208	1.699	-0.3713
C	5.63	0.8426	0.323
H	5.629	1.2232	1.3539
H	5.6339	1.7286	-0.3268
C	6.9039	0.0278	0.081
H	7.802	0.6262	0.2646
H	6.9447	-0.8465	0.74
H	6.9509	-0.3355	-0.9516

Cartesian coordinates [Å] of structure of compound 5h (optimized : B3LYP/6-31G(d,p))



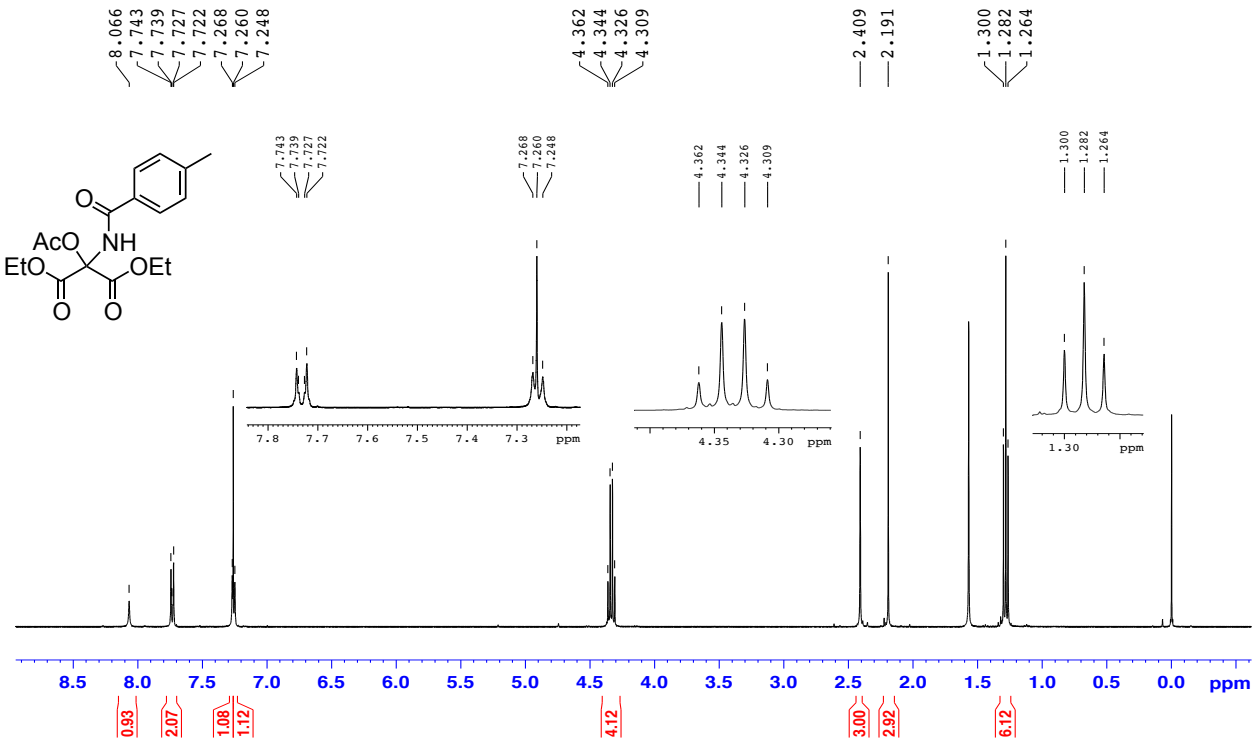
5h

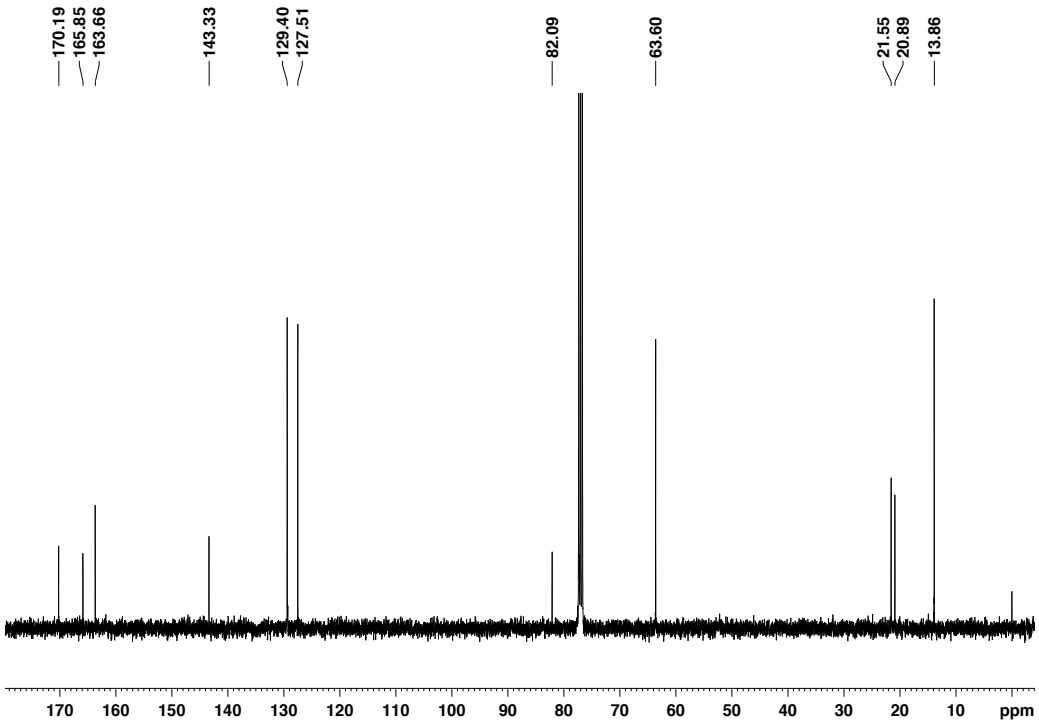
R = *t*-Bu	X	Y	Z
C	-3.4995	0.2834	0.2339
C	0.9645	-1.2781	-0.9242
C	0.6288	1.2196	-0.9202
O	0.1326	1.4777	-1.9883
O	1.5715	-1.1832	-1.9582
O	1.5493	1.948	-0.2845
C	1.9414	3.1717	-0.9563
H	1.0528	3.7997	-1.0679
H	2.3023	2.9172	-1.9569
C	3.0107	3.8314	-0.109
H	3.3379	4.7605	-0.5857
H	2.6271	4.0732	0.8863
H	3.8795	3.1765	0.0018
C	-2.0018	0.6581	0.2134
O	-1.6242	1.7917	0.4709
C	-4.0647	0.7355	1.5961
H	-3.6352	0.1527	2.4184
H	-3.8363	1.7886	1.771
H	-5.151	0.5999	1.6166
C	-4.1614	1.0971	-0.9016
H	-3.968	2.1636	-0.7671
H	-3.7708	0.8015	-1.8808
H	-5.244	0.9315	-0.8999
C	-3.776	-1.2163	0.0261
H	-3.3172	-1.8322	0.8089
H	-4.8541	-1.3994	0.0674
H	-3.4289	-1.5678	-0.9518
O	0.6578	-2.433	-0.3
C	1.252	-3.6265	-0.8772
H	2.3377	-3.4963	-0.8724
H	0.9269	-3.7101	-1.9182
C	0.8102	-4.808	-0.0378
H	1.2456	-5.7278	-0.44

H	1.1398	-4.6966	0.9988
H	-0.2786	-4.9135	-0.0464
C	0.305	-0.0941	-0.1576
O	0.7222	-0.0277	1.2245
C	2.2541	0.0403	3.0068
H	3.2393	-0.3197	3.3011
H	2.2006	1.1247	3.1442
H	1.4787	-0.4085	3.6325
C	2.0153	-0.2806	1.5541
O	2.8418	-0.7042	0.7786
N	-1.1094	-0.3259	-0.1586
H	-1.4004	-1.2912	-0.1729

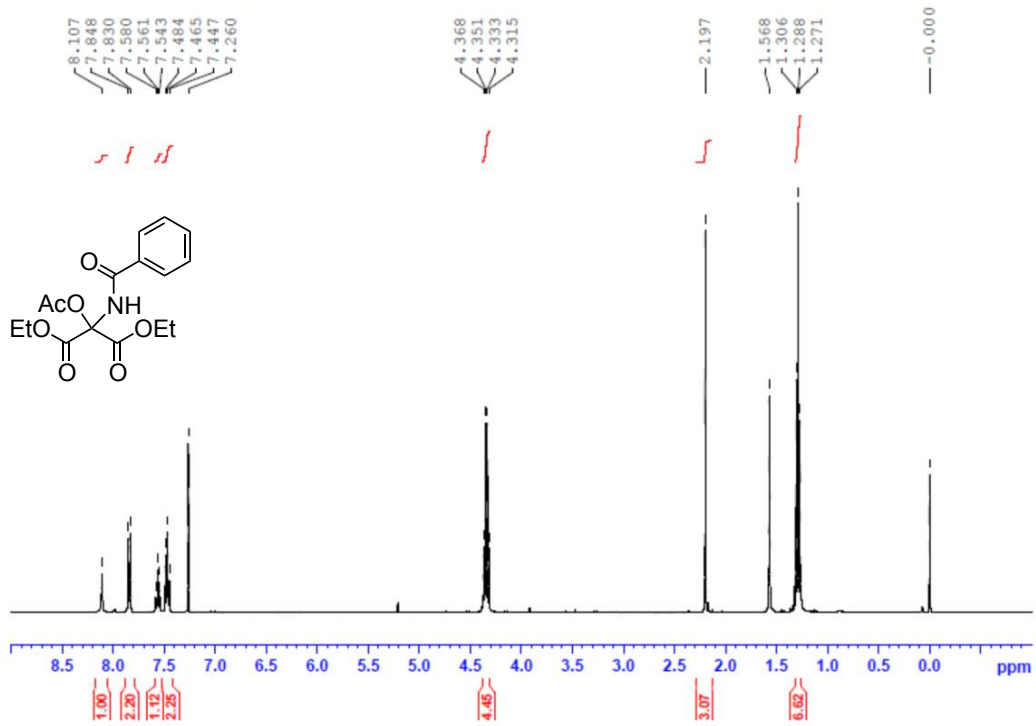
5. ^{1}H and ^{13}C NMR spectra of products 5-7

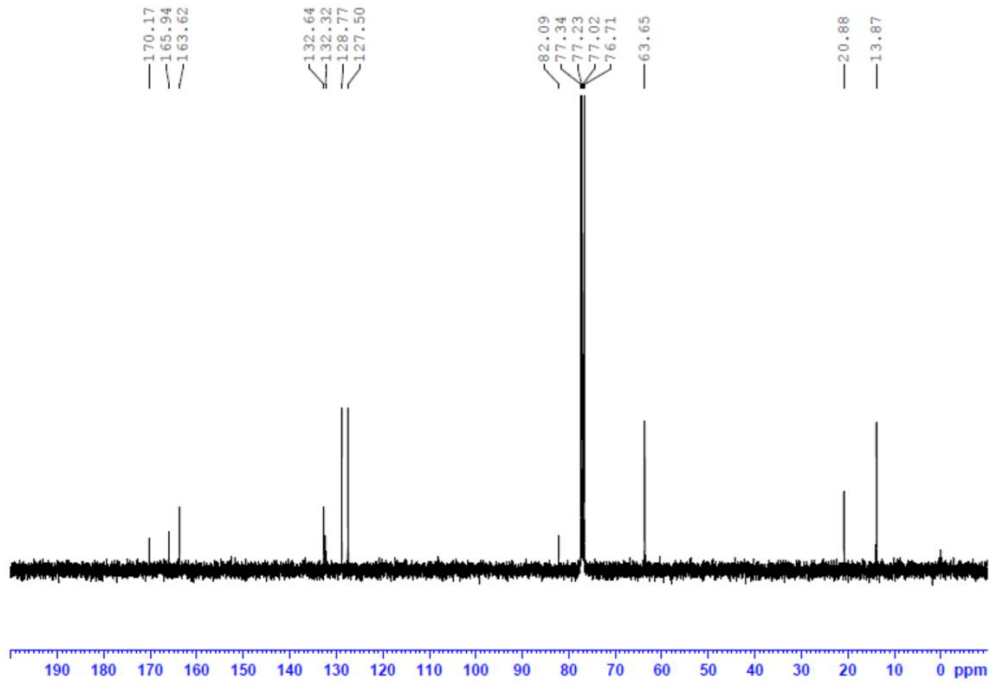
Diethyl α-acetoxy-α-[(4-methylbenzoyl)amino]malonate (5a) ($CDCl_3$)



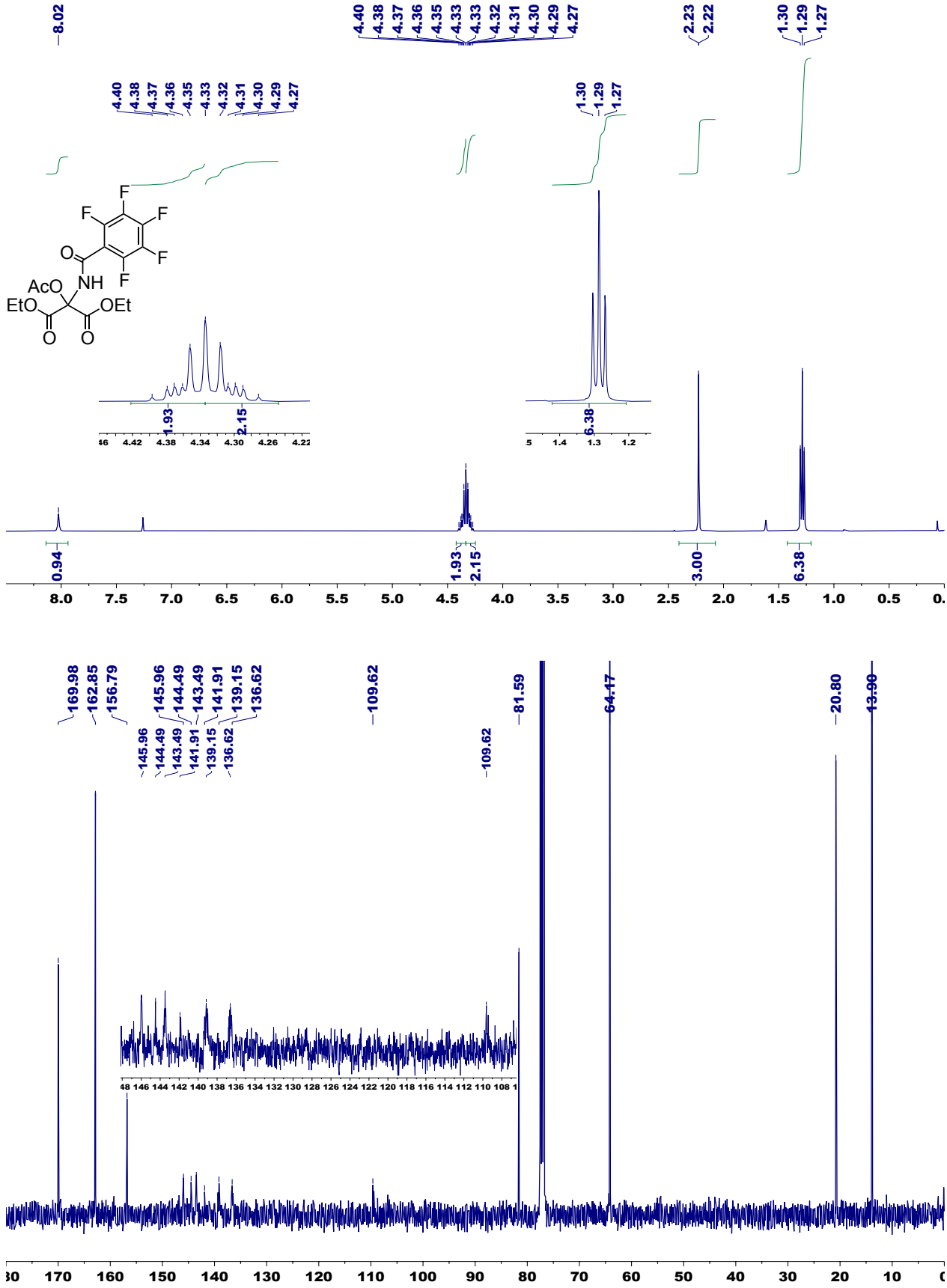


Diethyl α-acetoxy-α-(benzoylamino)malonate (5b) ($CDCl_3$)

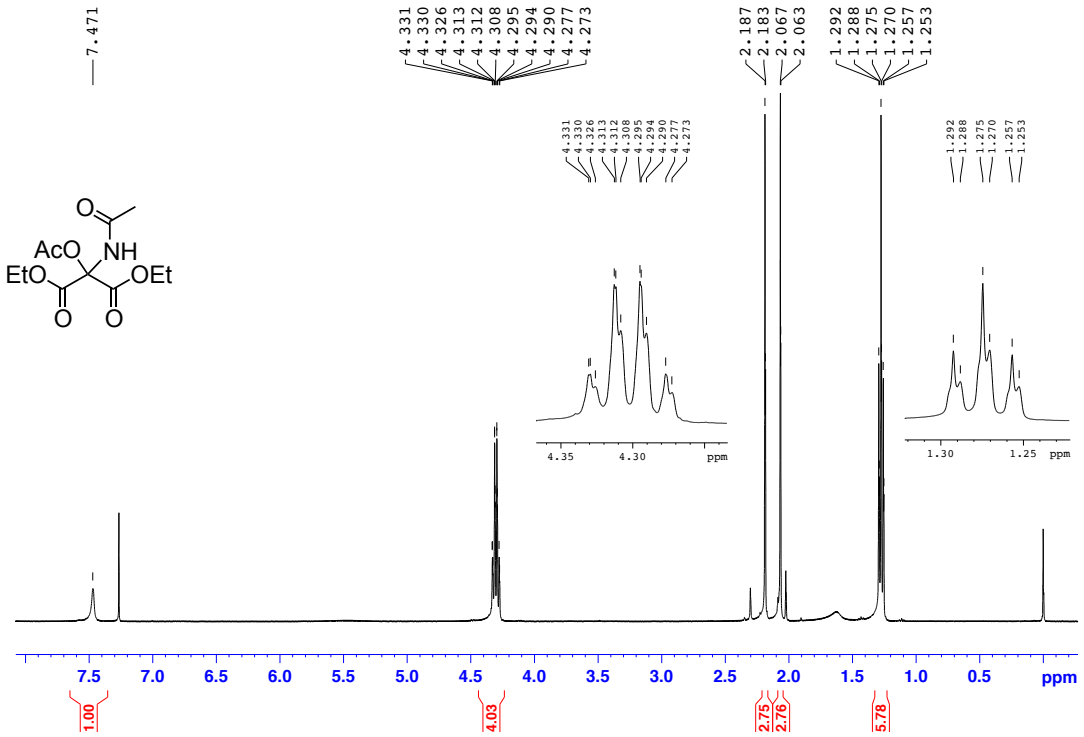


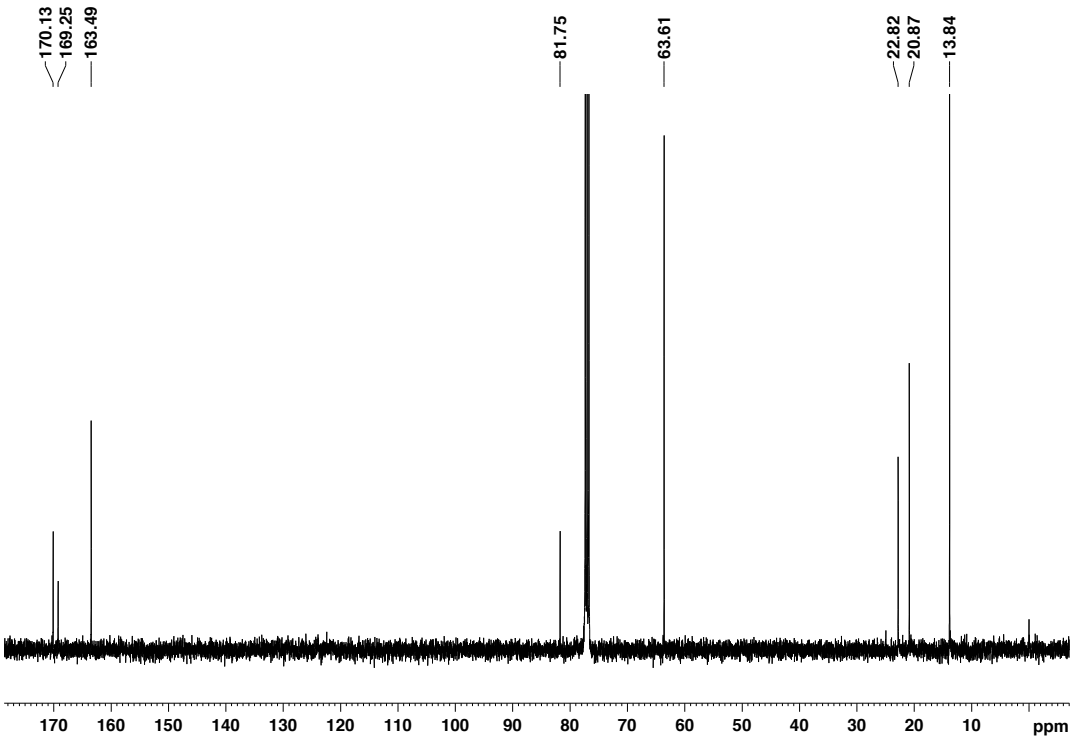


Diethyl α-acetoxy-α-(pentafluorobenzoylamino)malonate (5c) ($CDCl_3$)

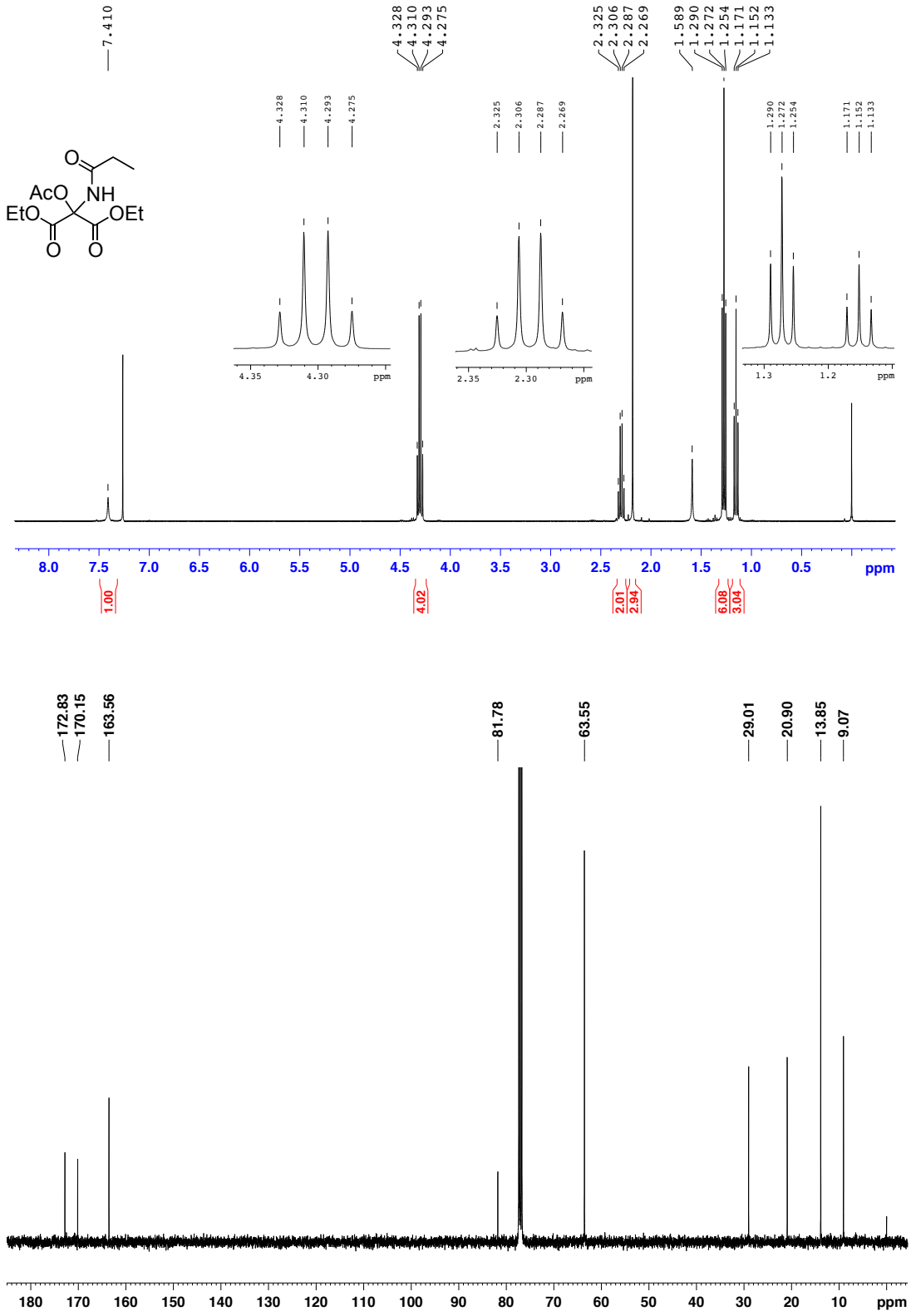


Diethyl α-acetoxy-α-(acetylamino)malonate (5d) ($CDCl_3$)

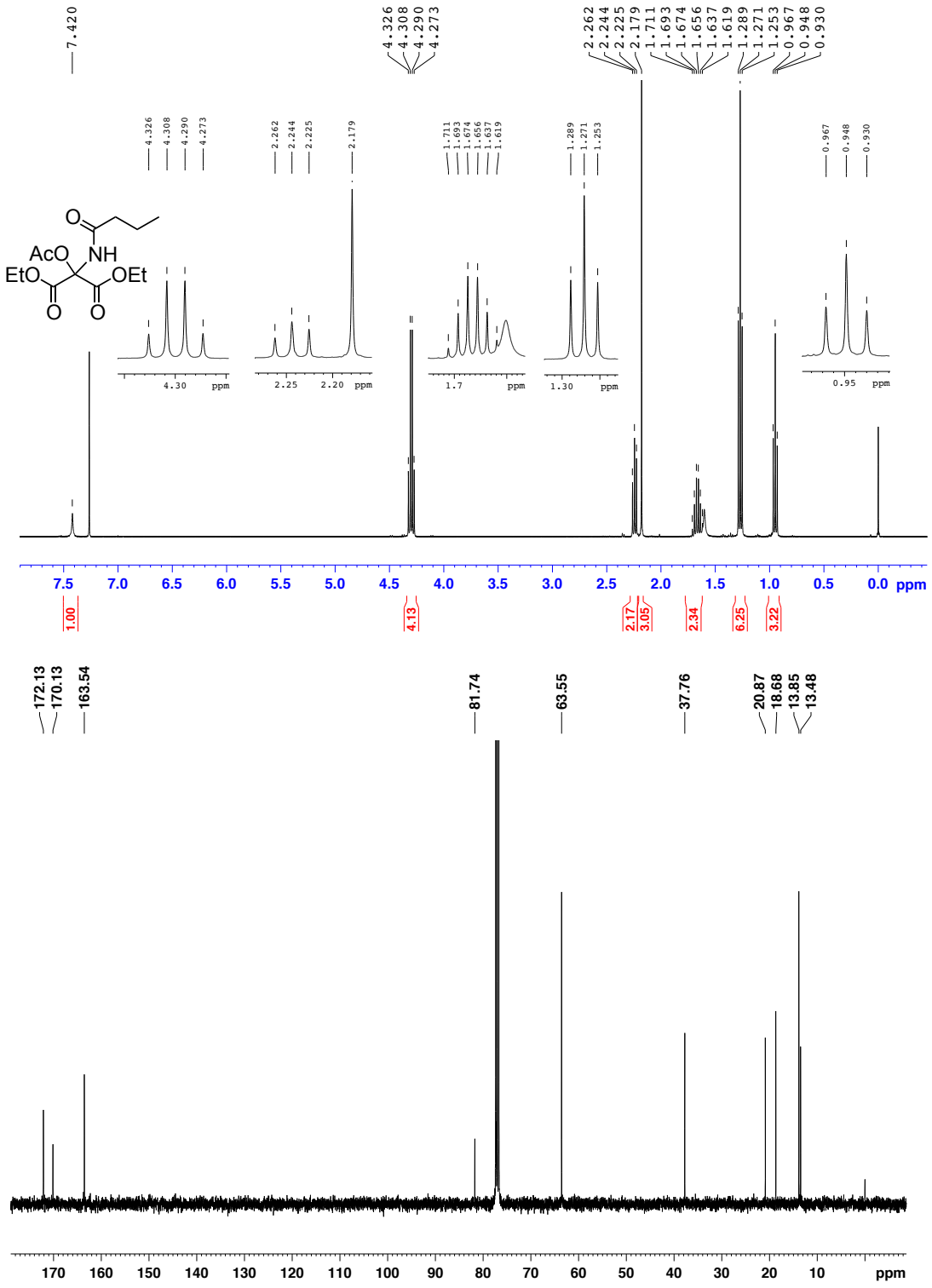




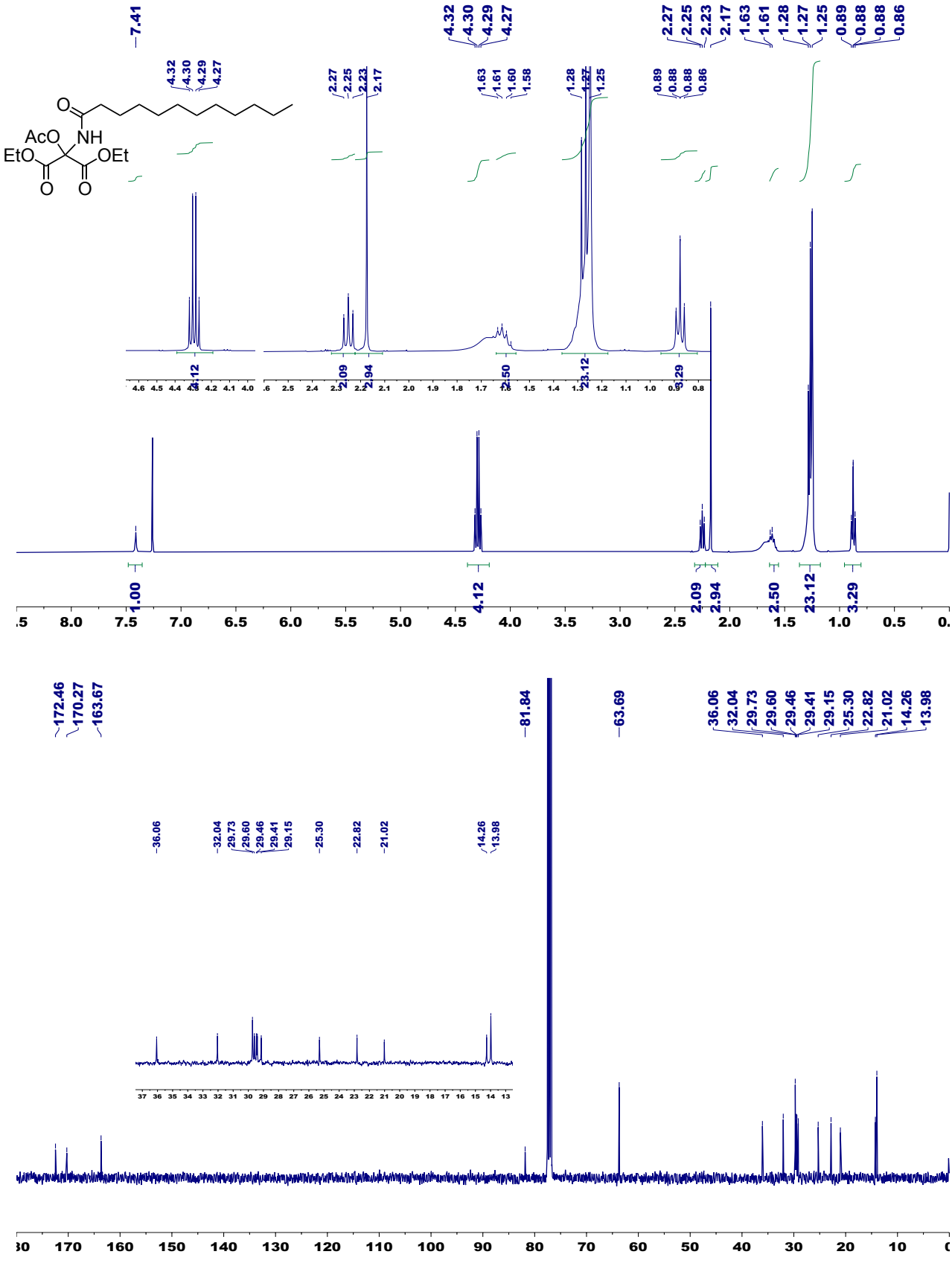
Diethyl α-acetoxy-α-(propanoylamino)malonate (5e) ($CDCl_3$)



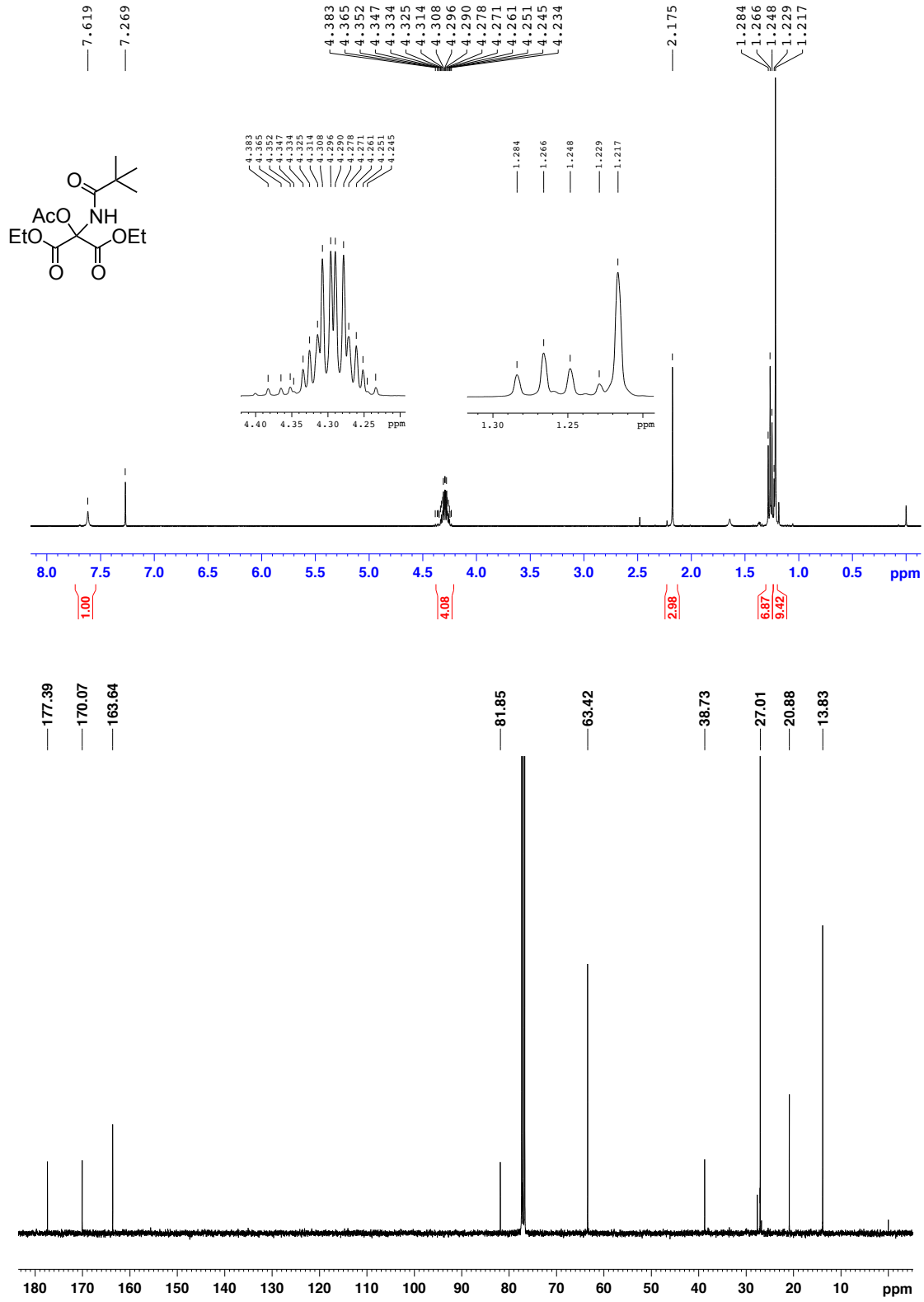
Diethyl α-acetoxy-α-(butanoylamino)malonate (5f) ($CDCl_3$)



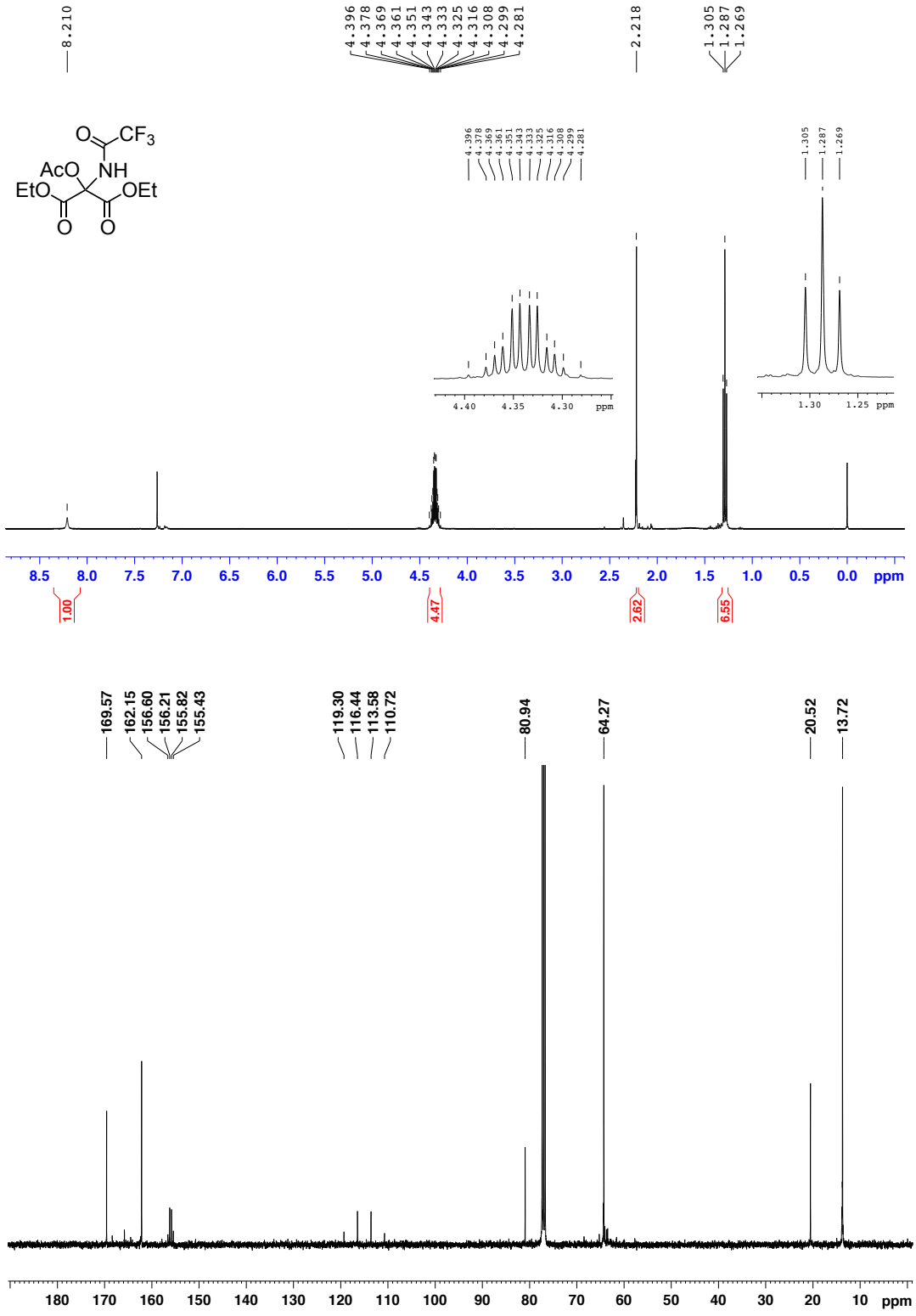
Diethyl α-acetoxy-α-(dodecanoylamino)malonate (5g) ($CDCl_3$)



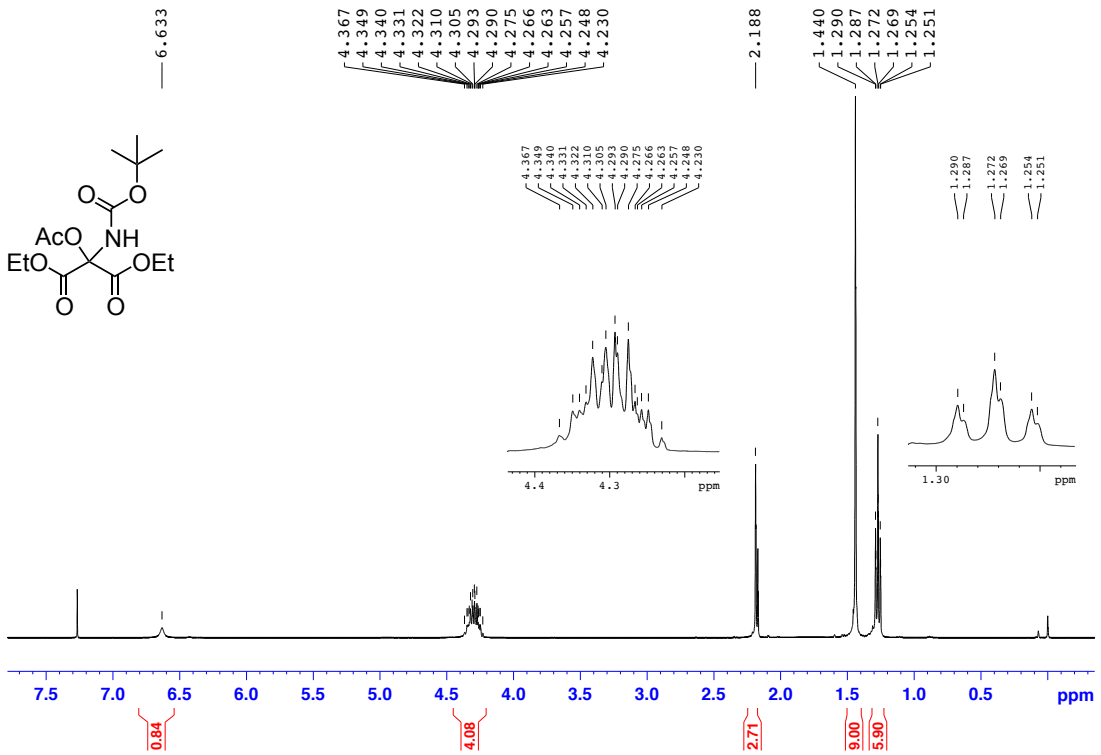
Diethyl α-acetoxy-α-(pivaloylamino)malonate (5h) ($CDCl_3$)

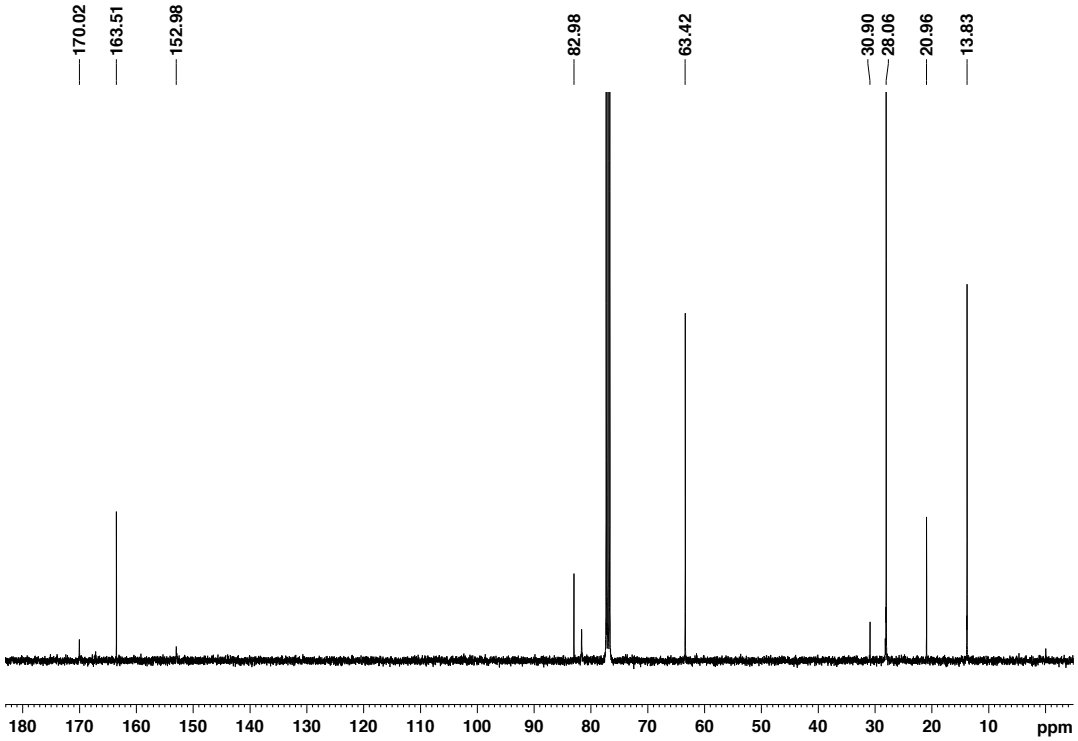


Diethyl α-acetoxy-α-[(trifluoroacetyl)amino]malonate (5i) ($CDCl_3$)

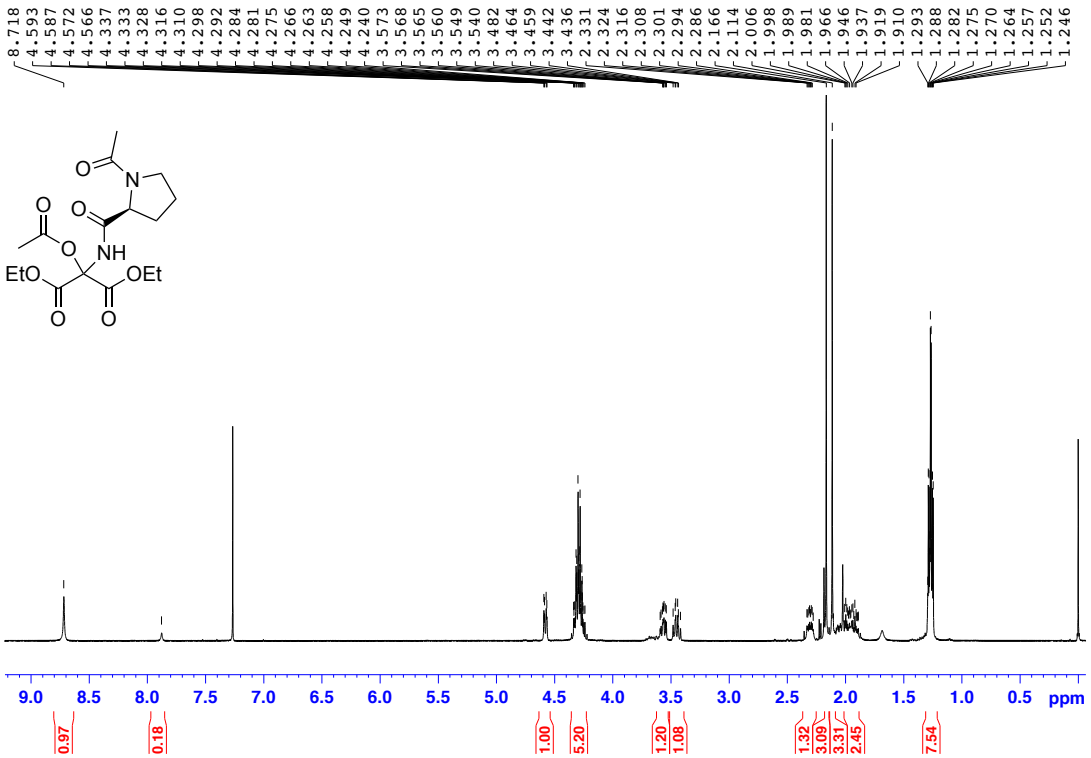


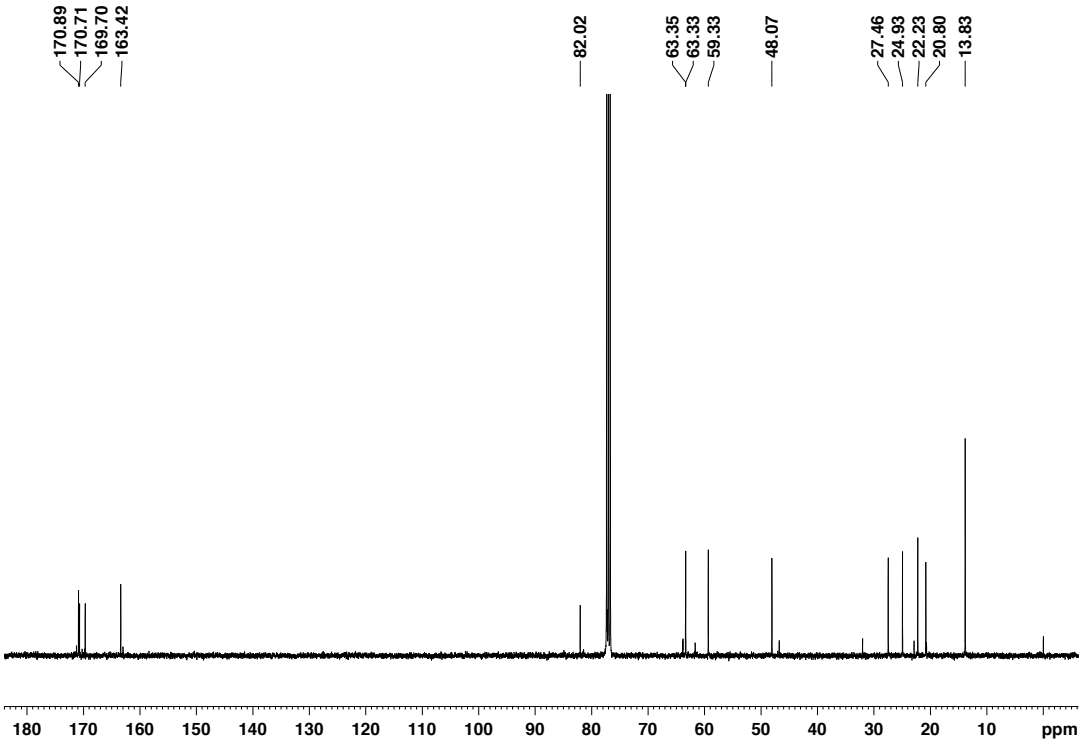
Diethyl α-acetoxy-α-[(*tert*-butoxycarbonyl)amino]malonate (5j) ($CDCl_3$)



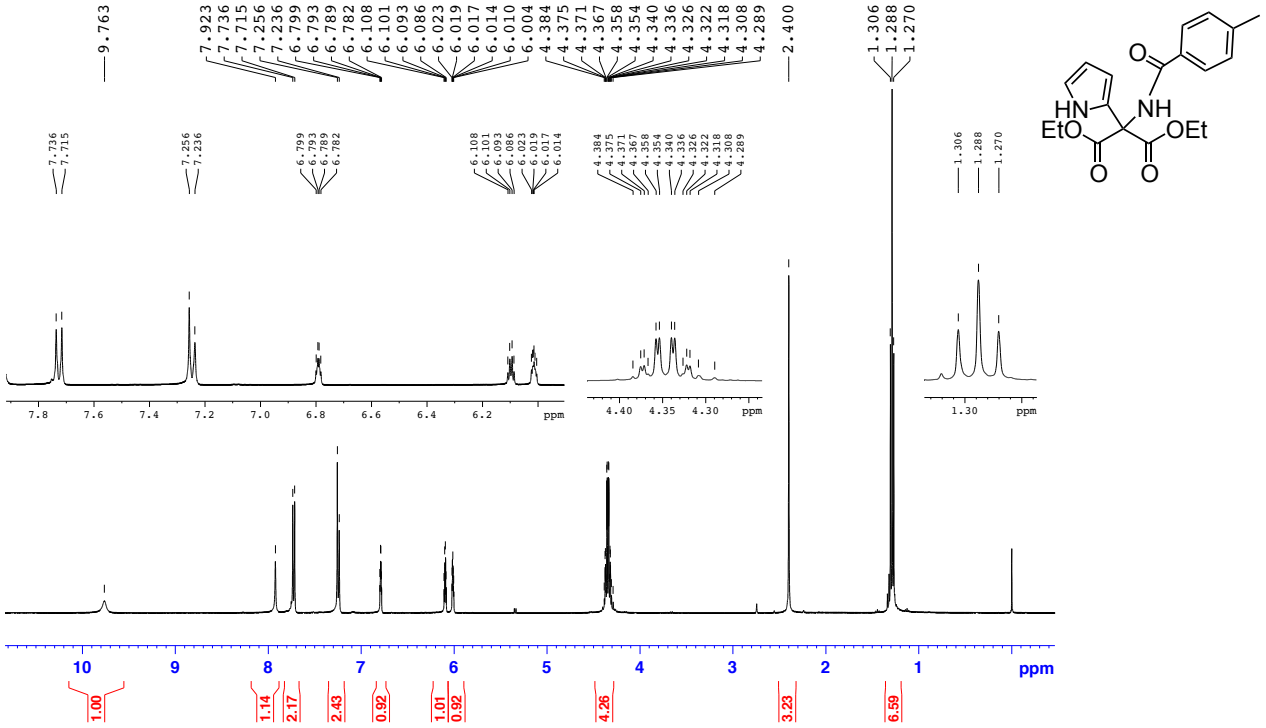


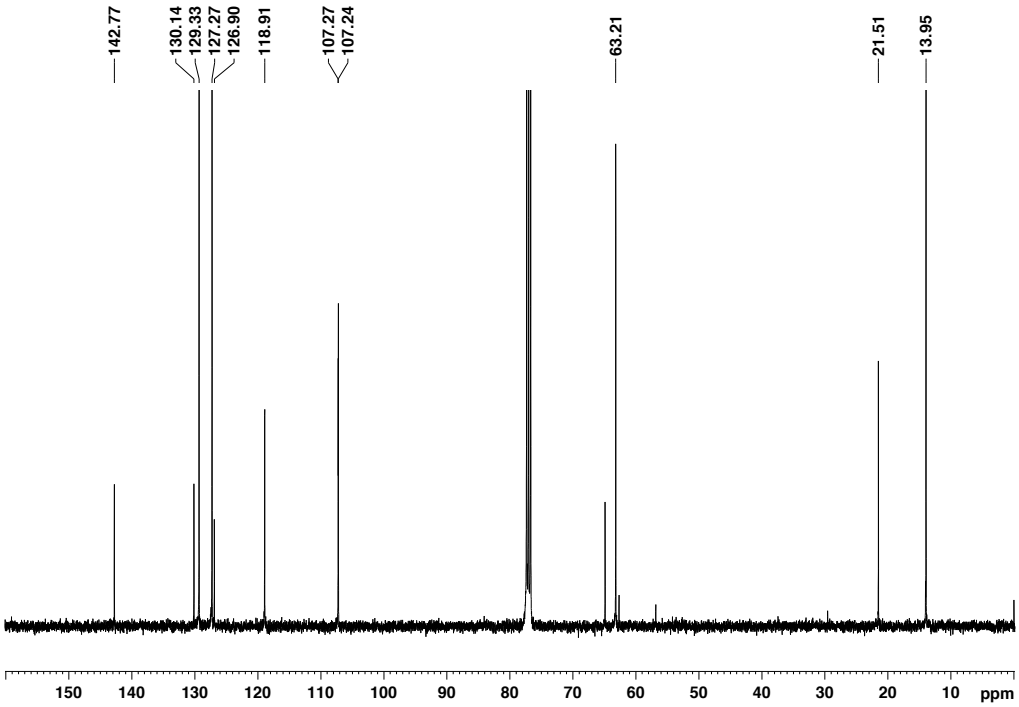
Diethyl α-acetoxy-α-(1-acetylproline-2-carboxamino)malonate (5l) ($CDCl_3$)



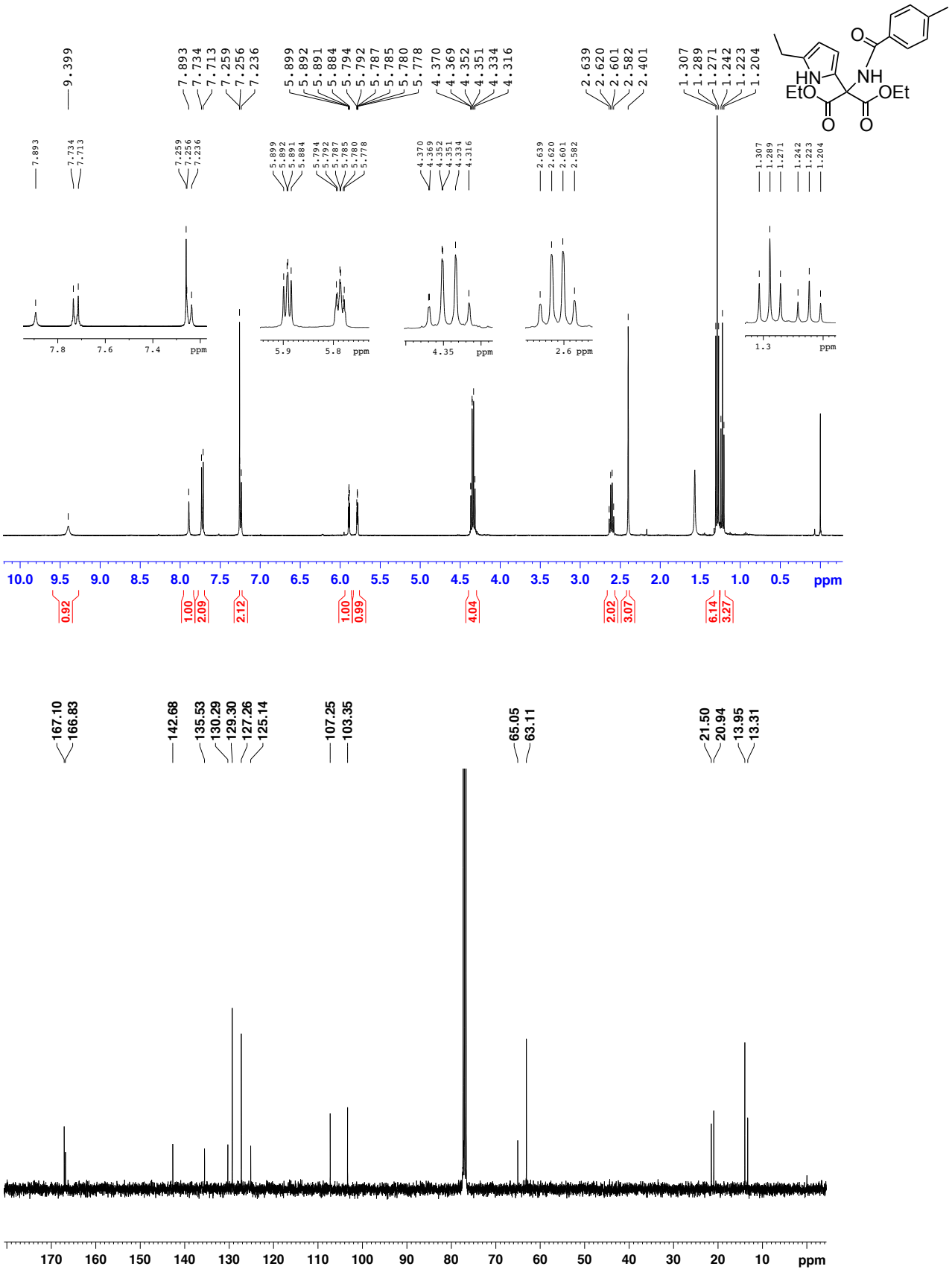


Diethyl α-[(4-methylbenzoyl)amino]-α-(1*H*-pyrrol-2-yl)malonate (6a) ($CDCl_3$)

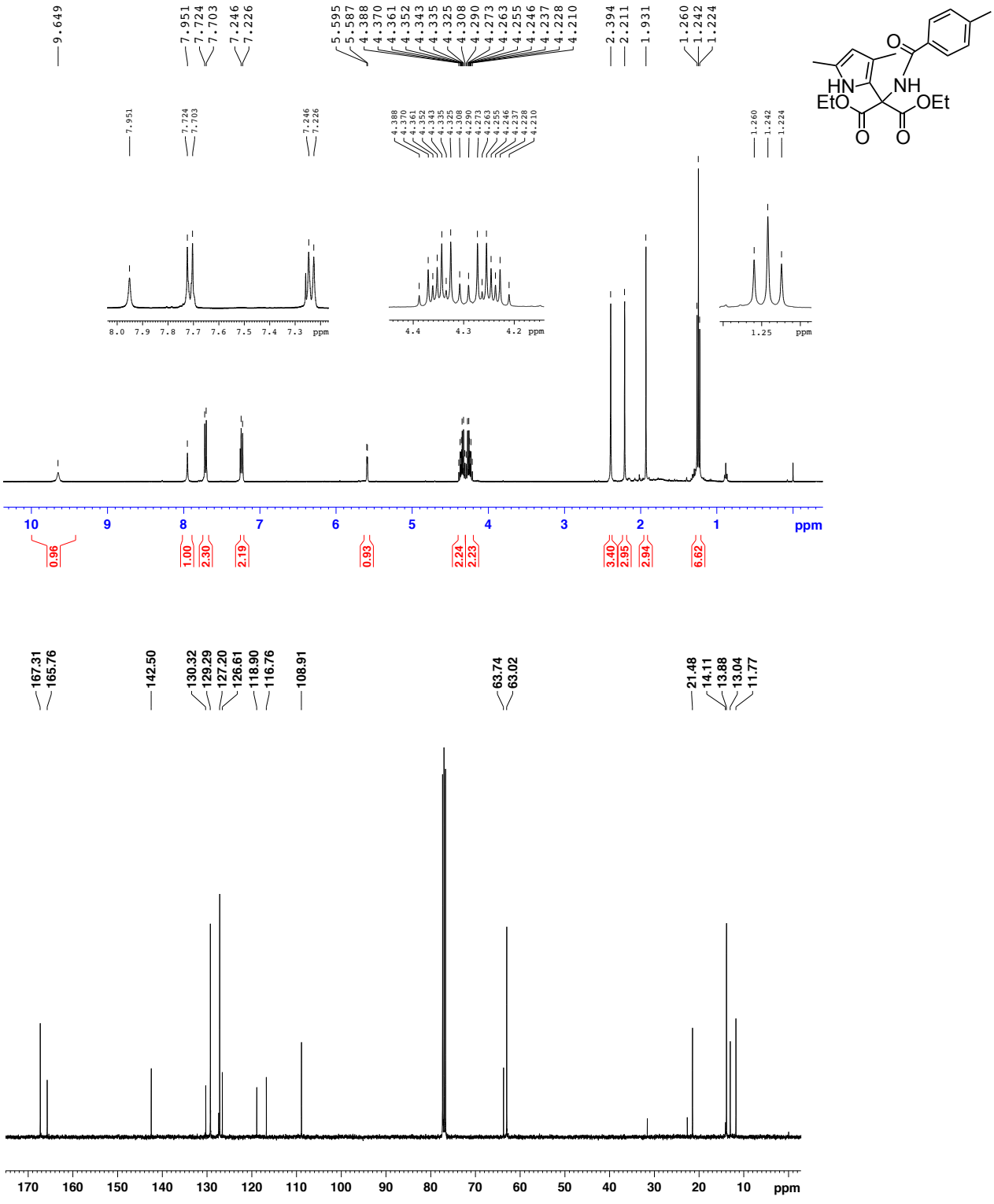




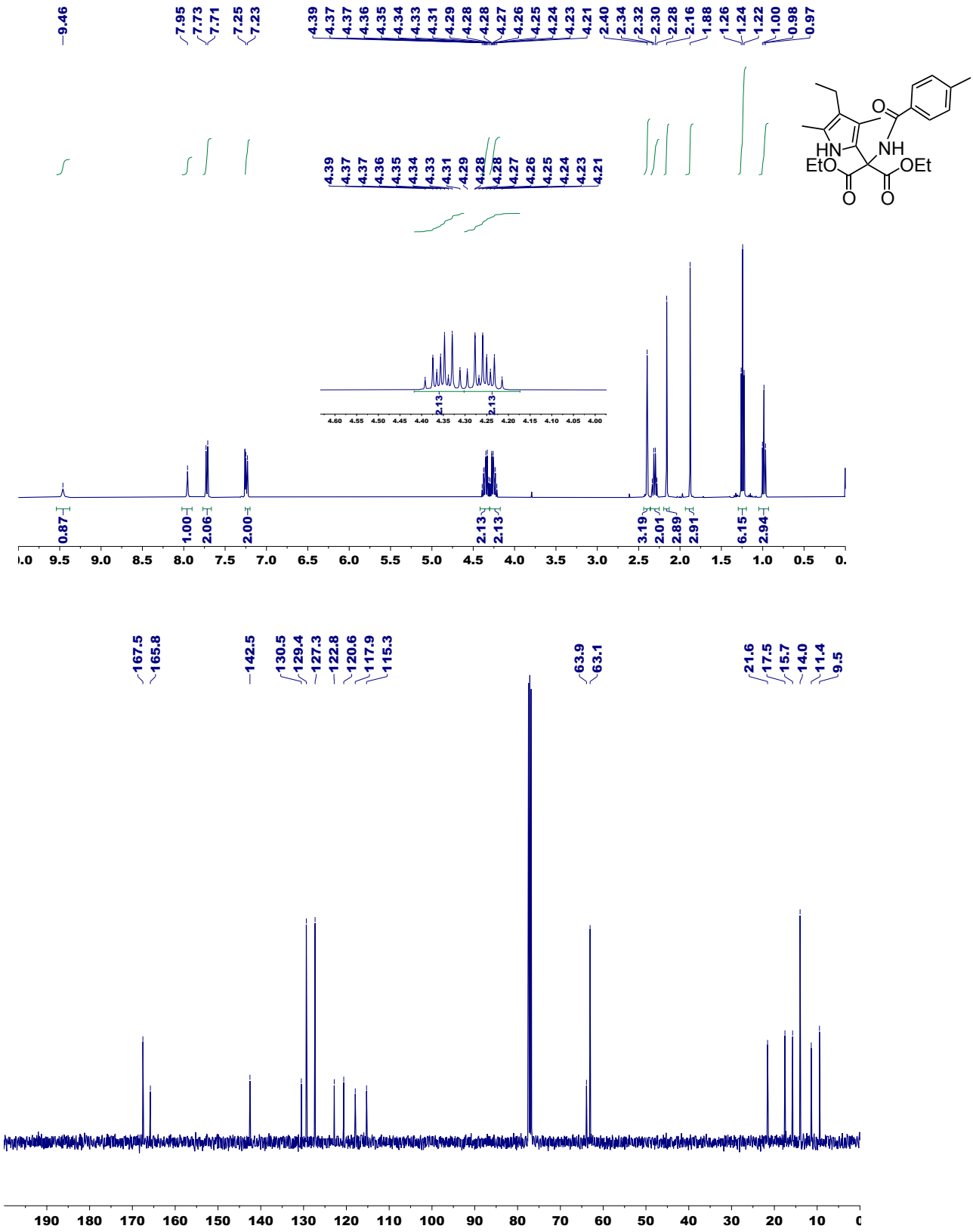
Diethyl α-(5-ethyl-1*H*-pyrrol-2-yl)-α-[(4-methylbenzoyl)amino]malonate (7a) ($CDCl_3$)



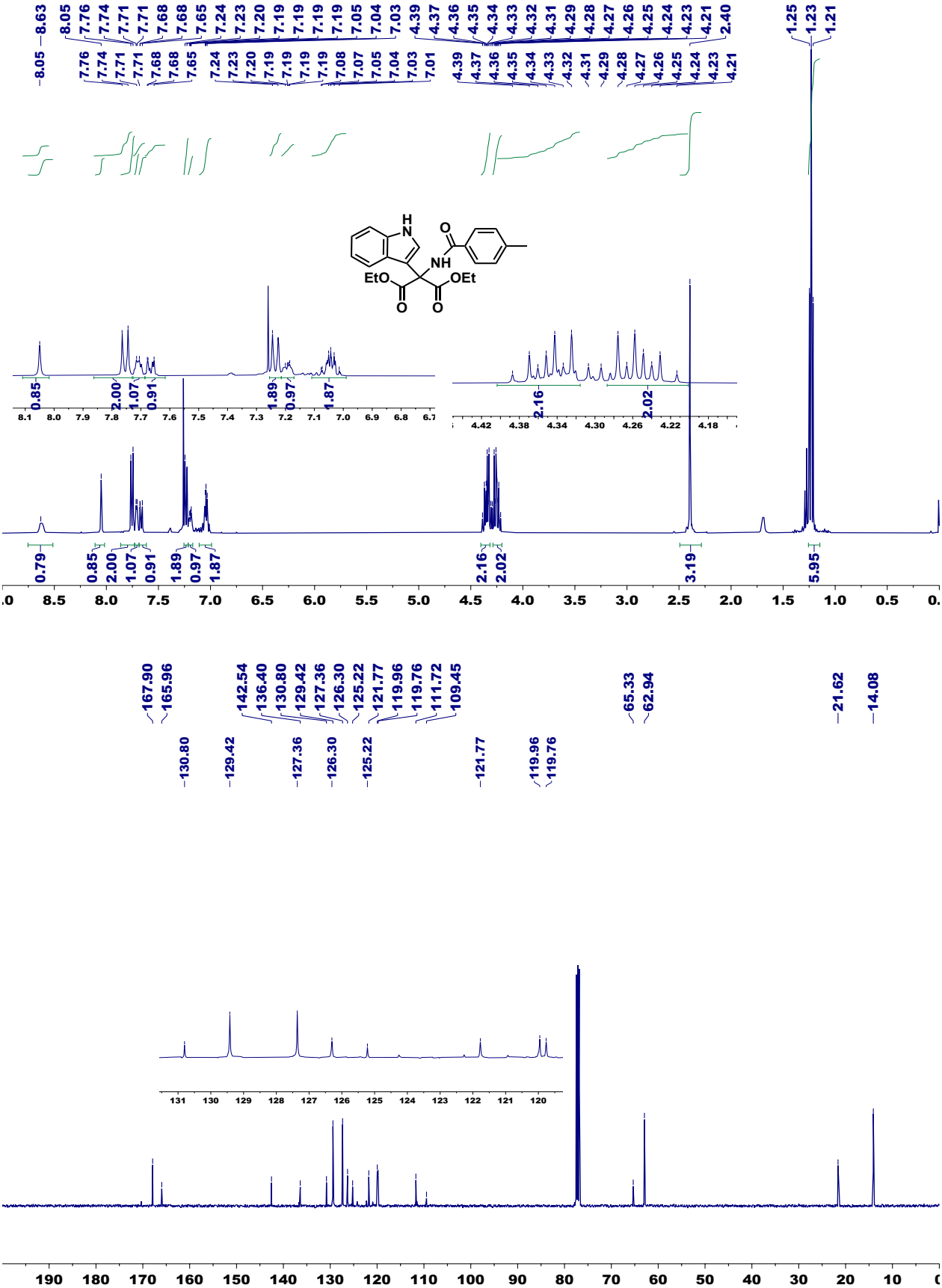
Diethyl α-[(4-methylbenzoyl)amino]-α-(3,5-dimethyl-1*H*-pyrrol-2-yl)malonate (8a) ($CDCl_3$)



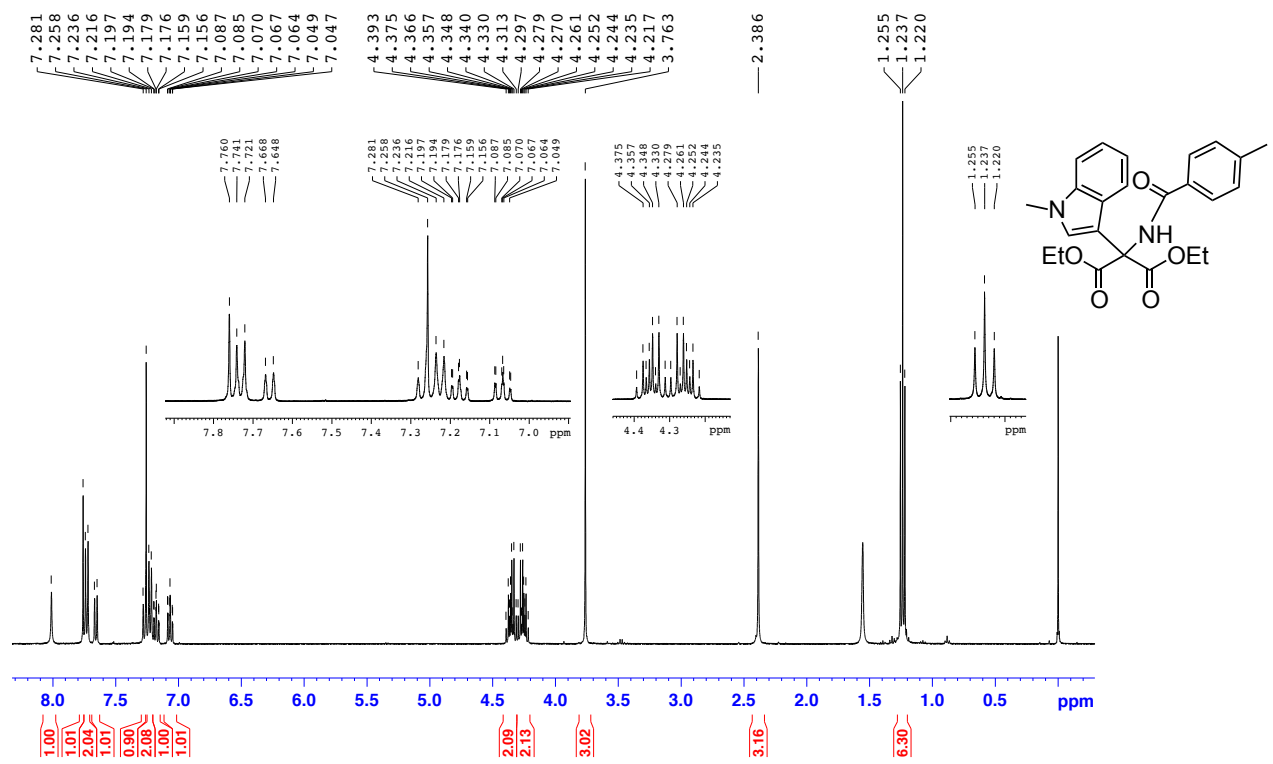
Diethyl α-(4-ethyl-3,5-dimethyl-1*H*-pyrrol-2-yl)-α-[(4-methylbenzoyl)amino]malonate (9a) ($CDCl_3$)

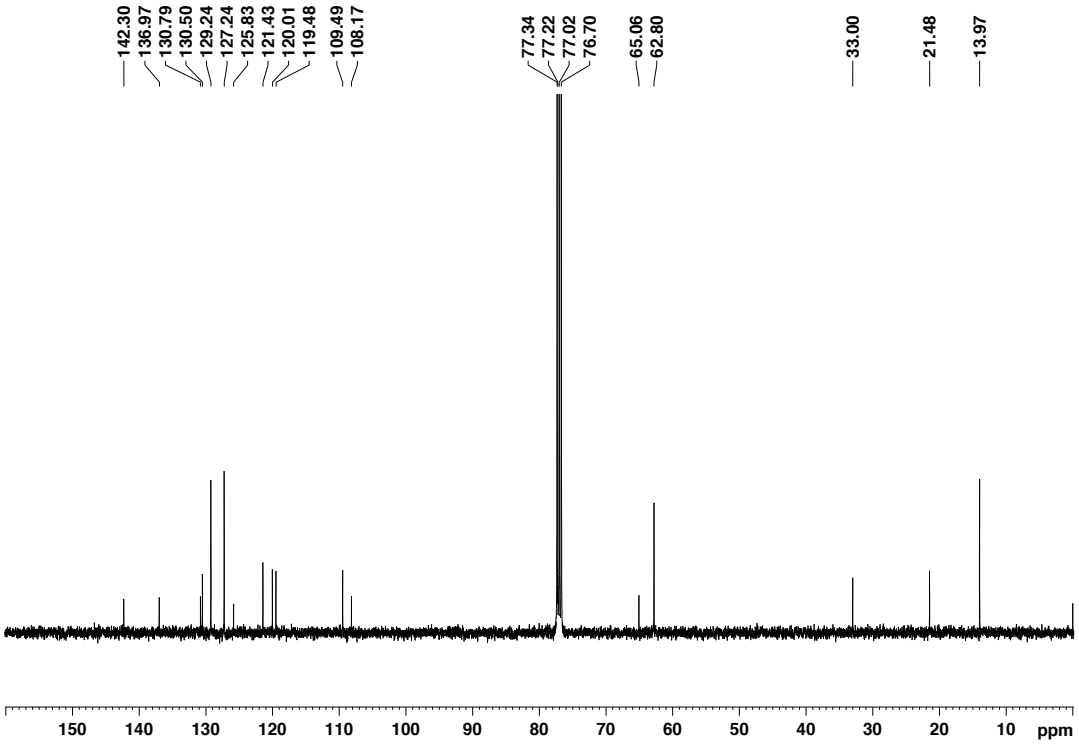


Diethyl α-(1*H*-indole-3-yl)-α-[(4-methylbenzoyl)amino]malonate (10a) ($CDCl_3$)

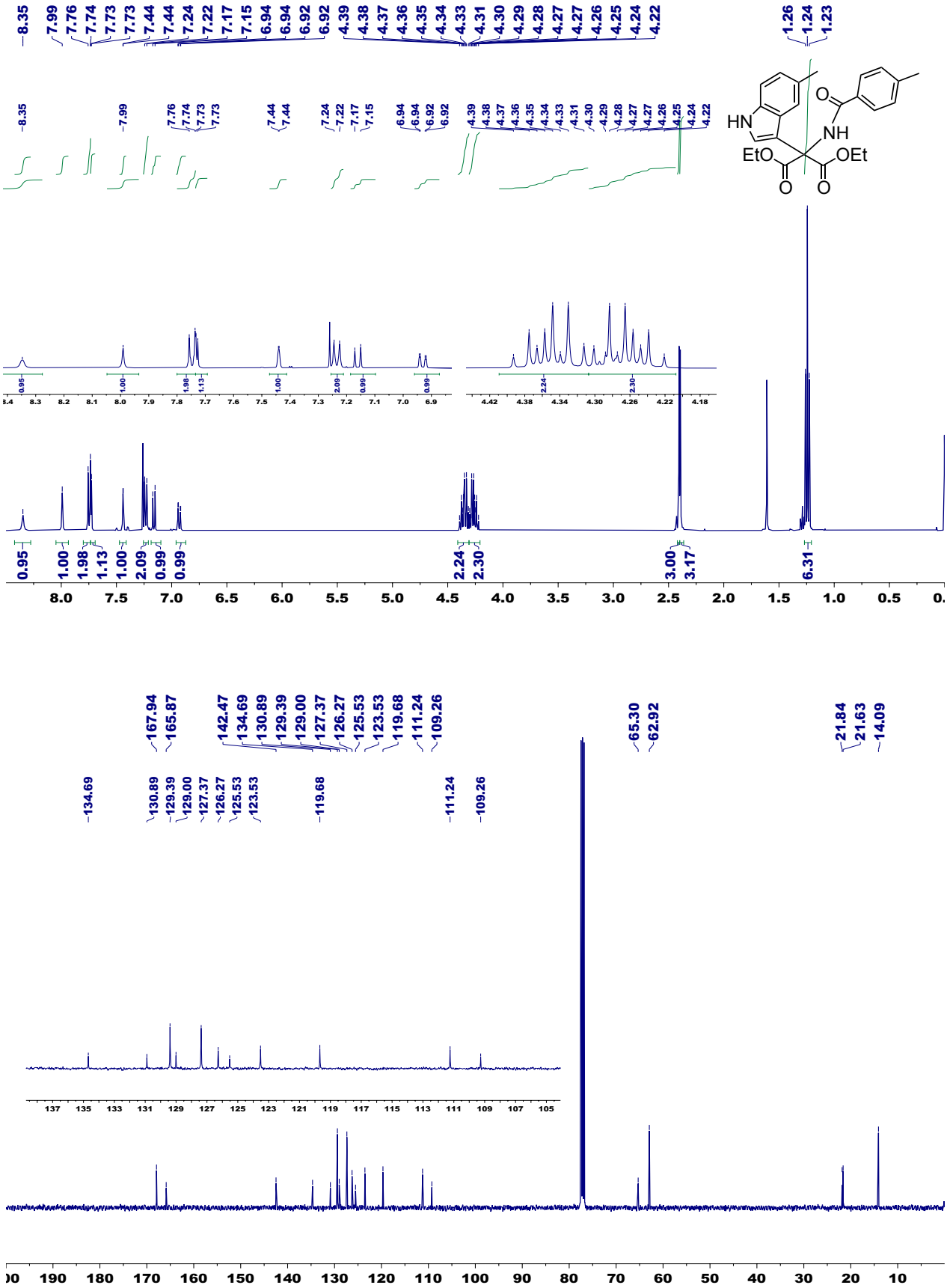


Diethyl α-[(4-methylbenzoyl)amino]-α-(1-methylindol-3-yl)malonate (11a) ($CDCl_3$)

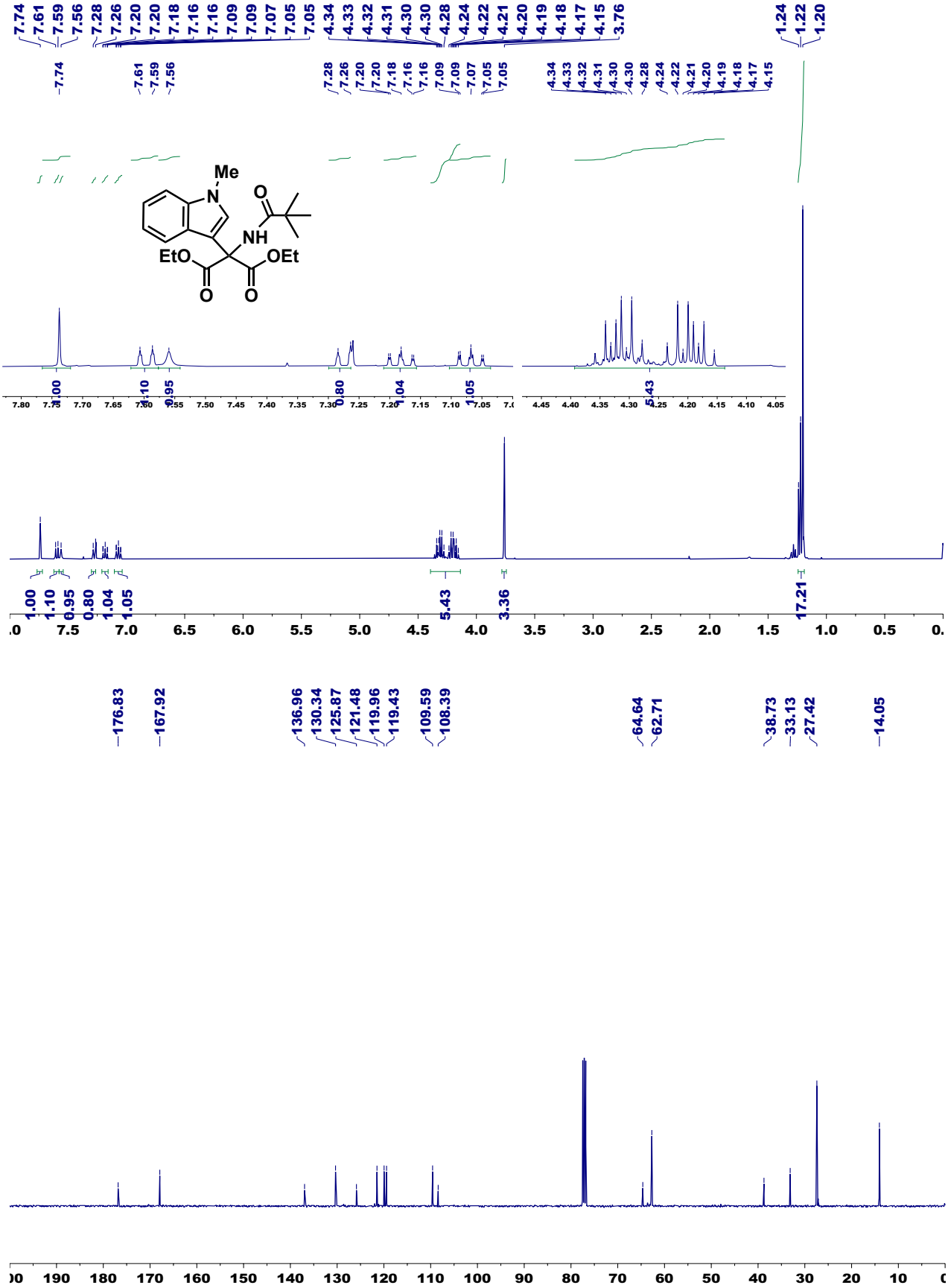




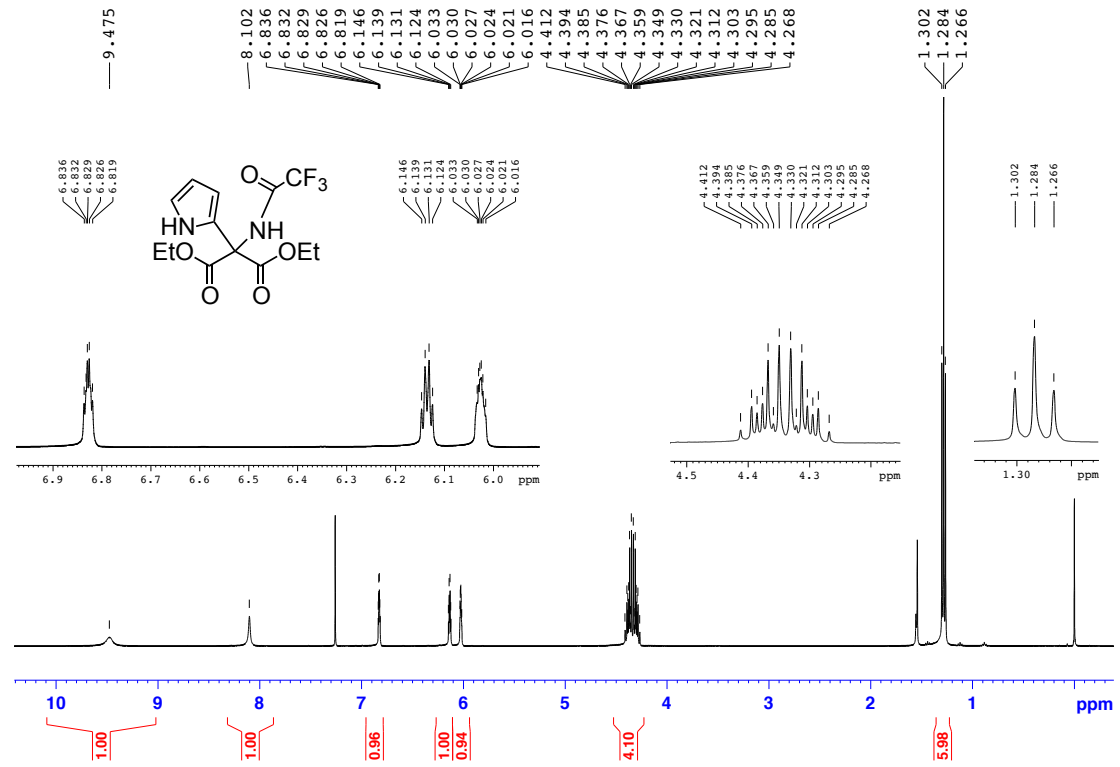
Diethyl α-[(4-methylbenzoyl)amino]-α-(1*H*-5-methylindol-3-yl)malonate (12a) ($CDCl_3$)

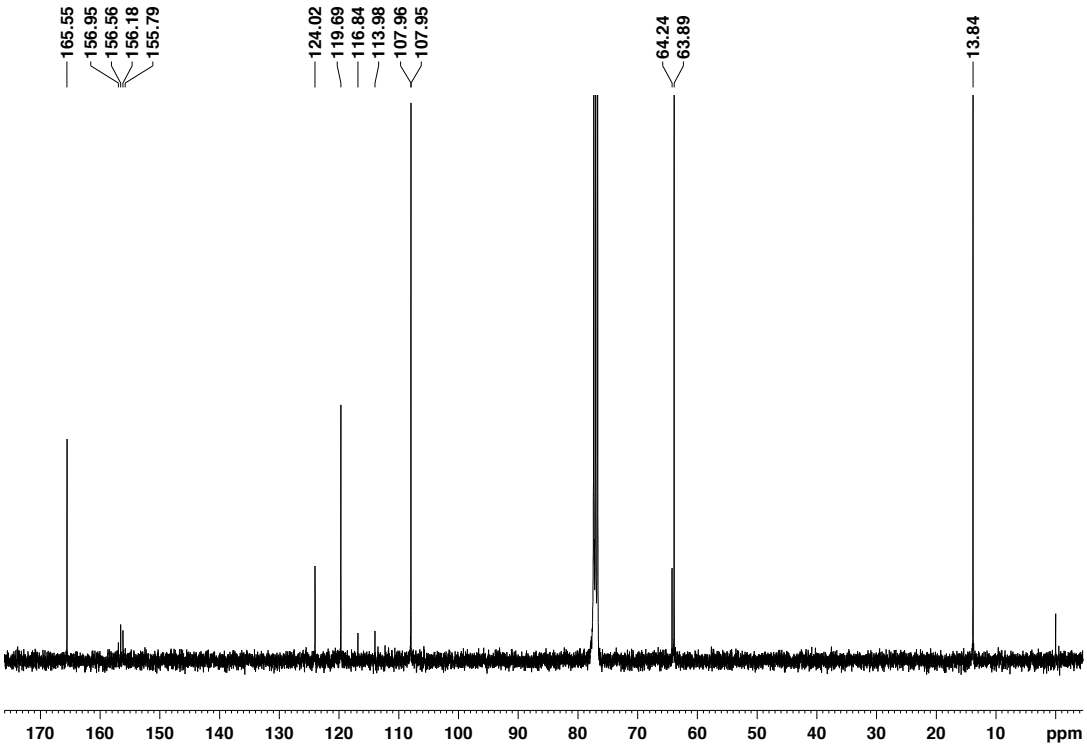


Diethyl α-(1-methylindol-3-yl)-α-(pivaloylamino)malonate (11h) ($CDCl_3$)

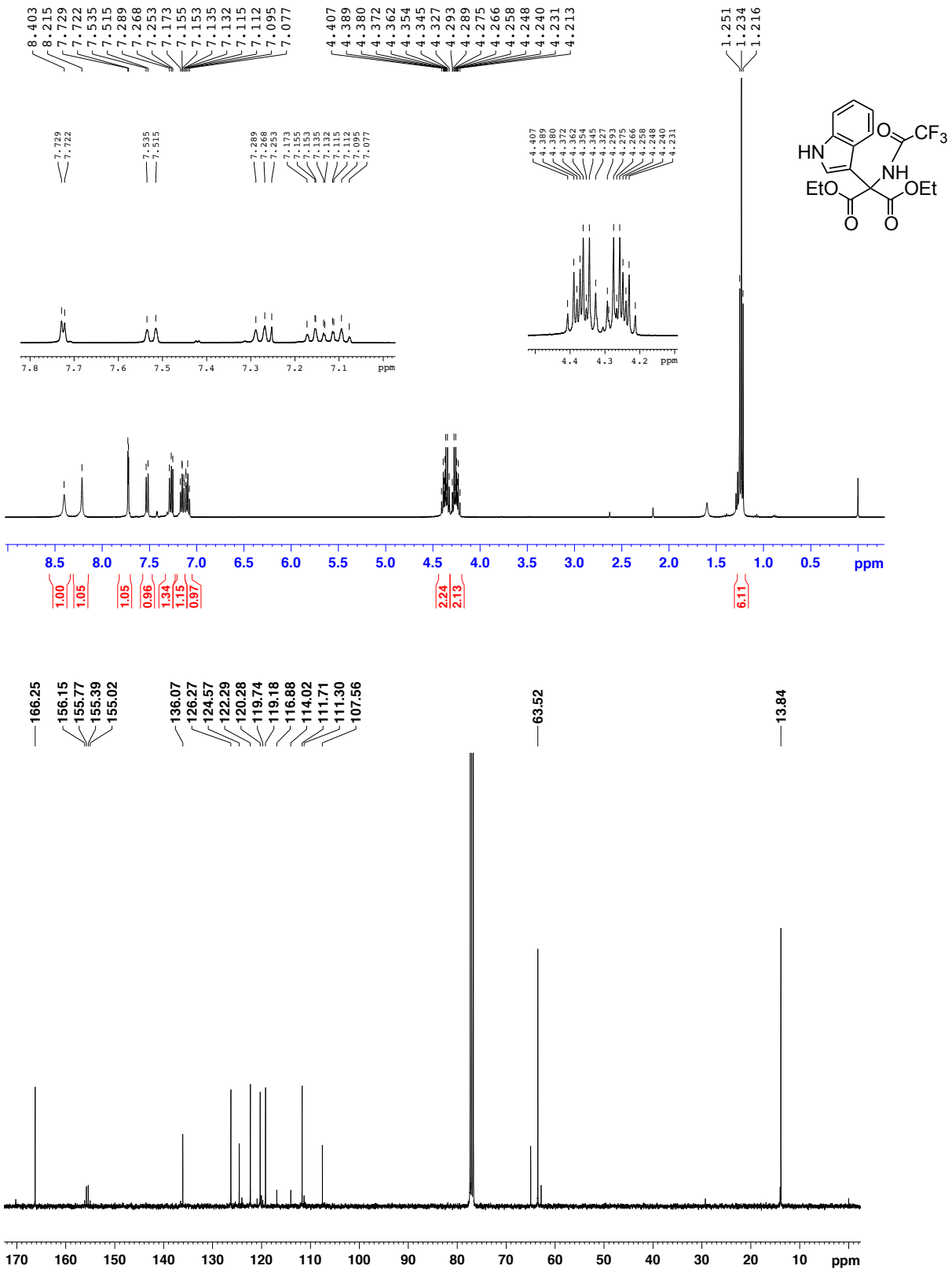


Diethyl α-[(trifluoroacetyl)amino]-α-(1*H*-pyrrol-2-yl)malonate (6i) ($CDCl_3$)

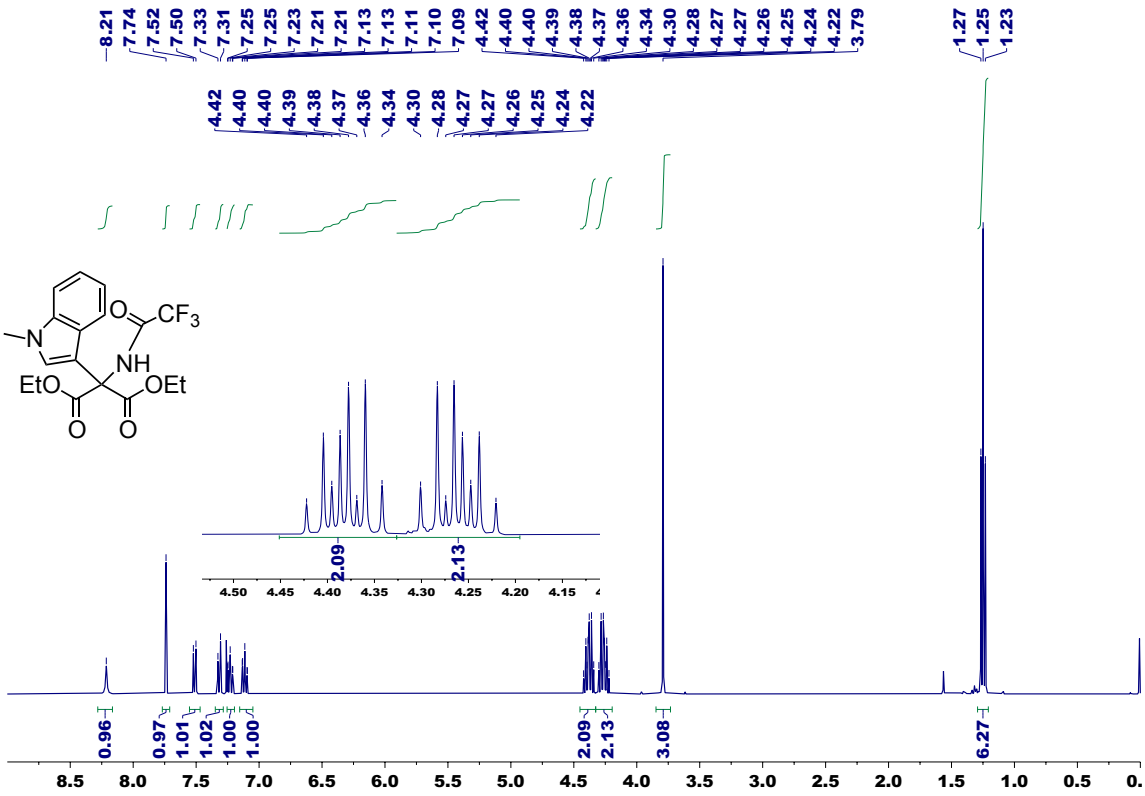


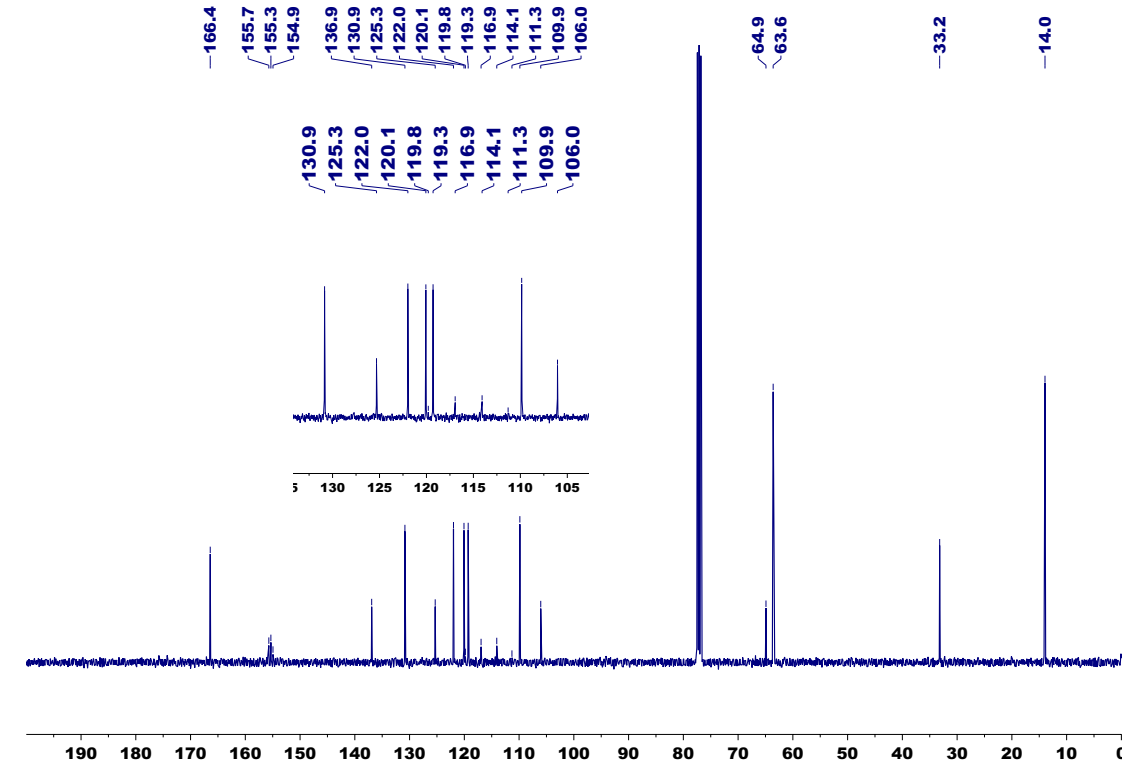


Diethyl α-[(trifluoroacetyl)amino]-α-(1*H*-indole-3-yl)malonate (10i) ($CDCl_3$)

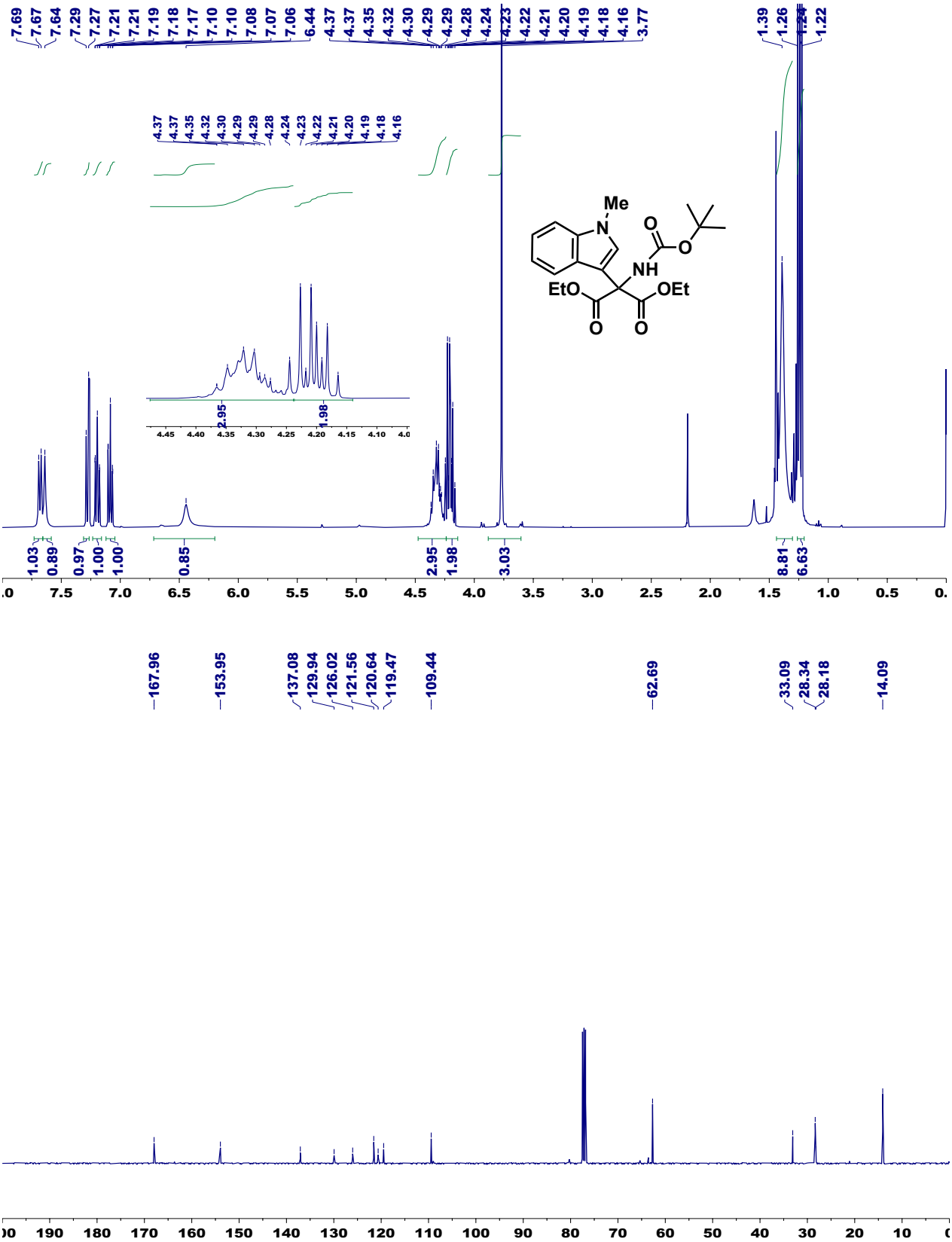


Diethyl α-[(trifluoroacetyl)amino]-α-(1-methylindol-3-yl)malonate (11i) ($CDCl_3$)

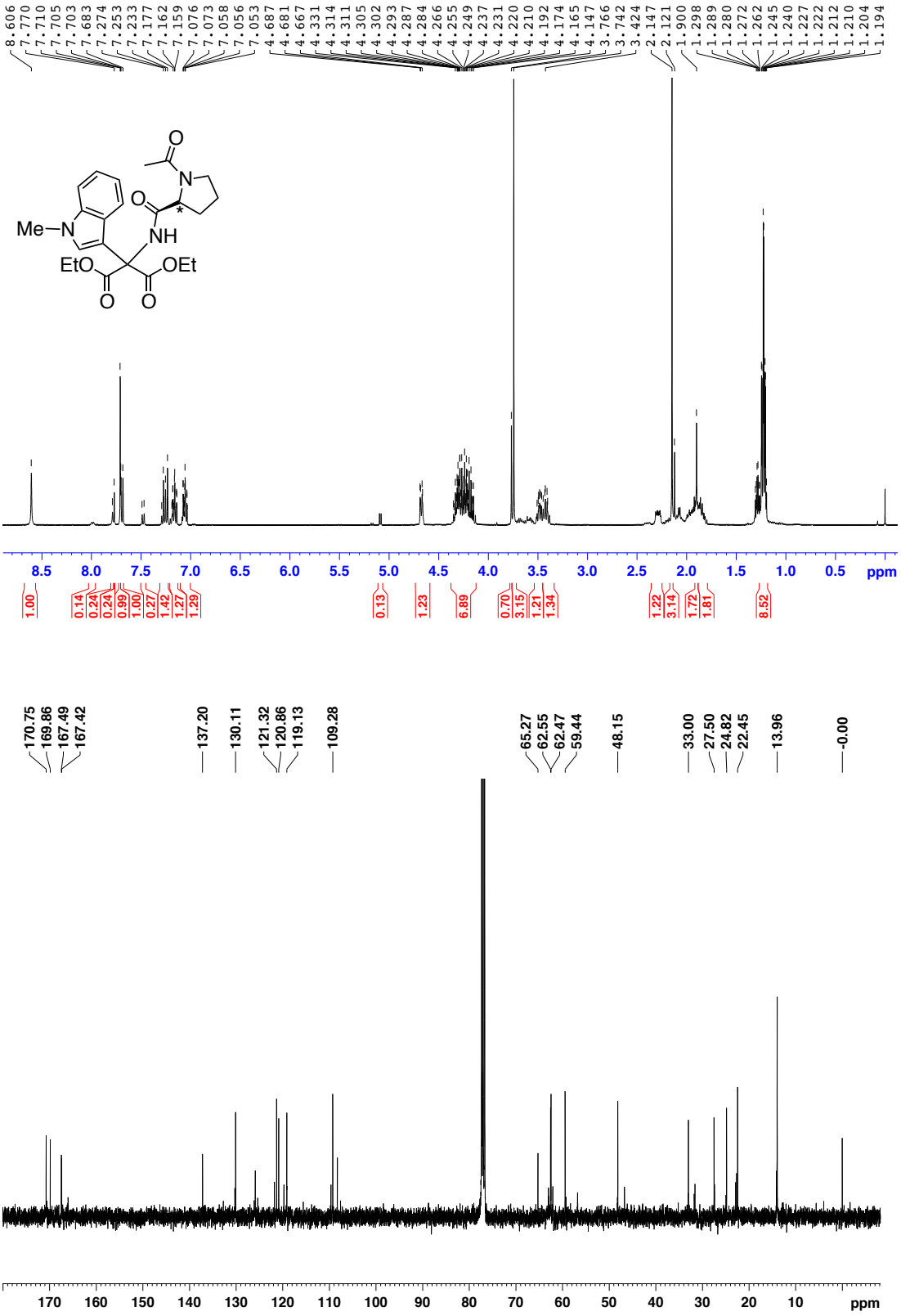




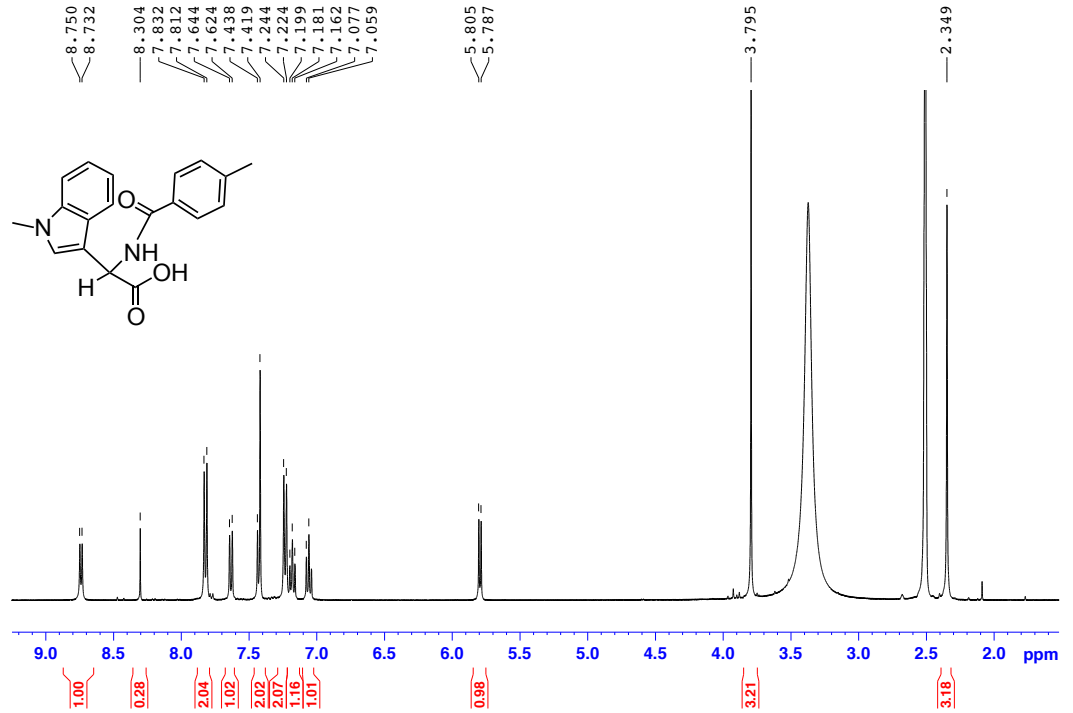
Diethyl α-[(*tert*-butoxycarbonyl)amino]-α-(1-methylindol-3-yl)malonate (11j) ($CDCl_3$)

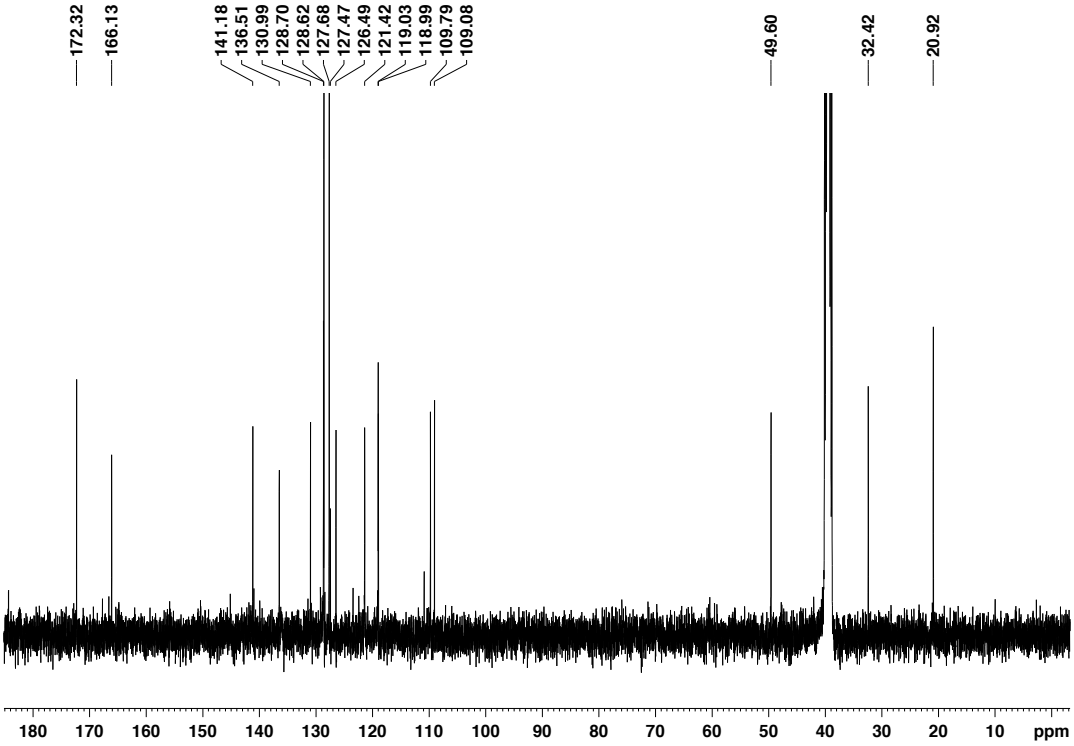


Diethyl α-(1-acetylproline-2-carboxamino)-α-(1-methylindol-3-yl)malonate (11l) ($CDCl_3$)

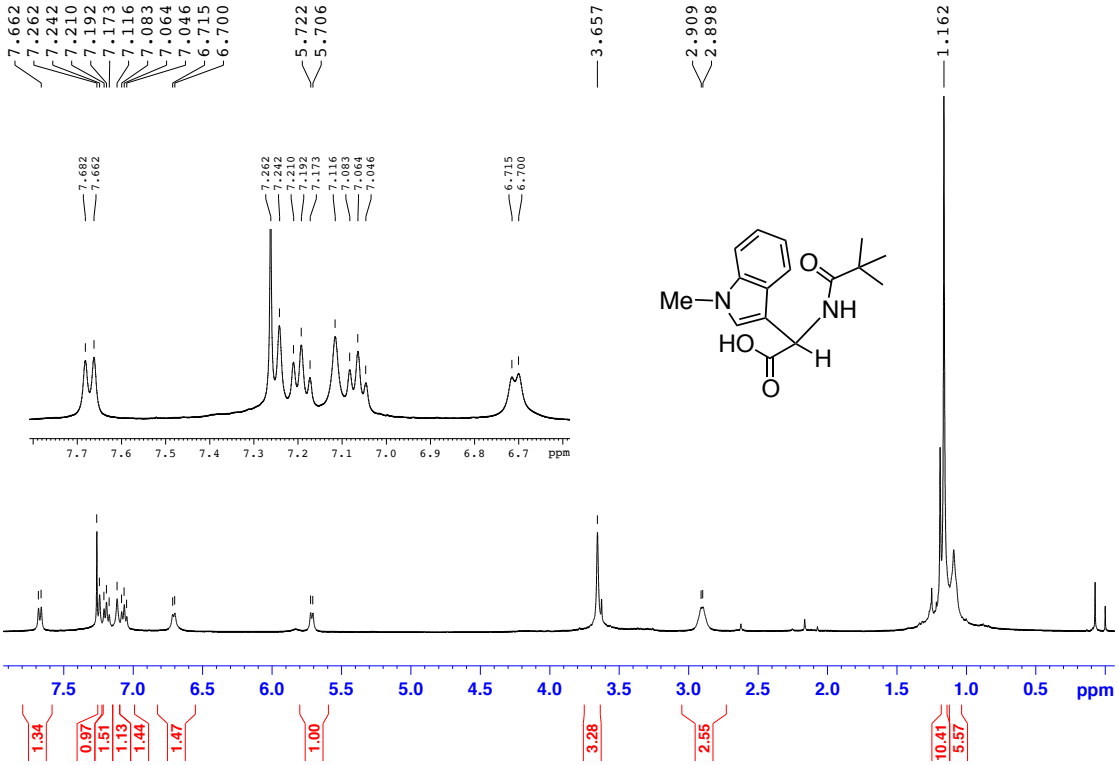


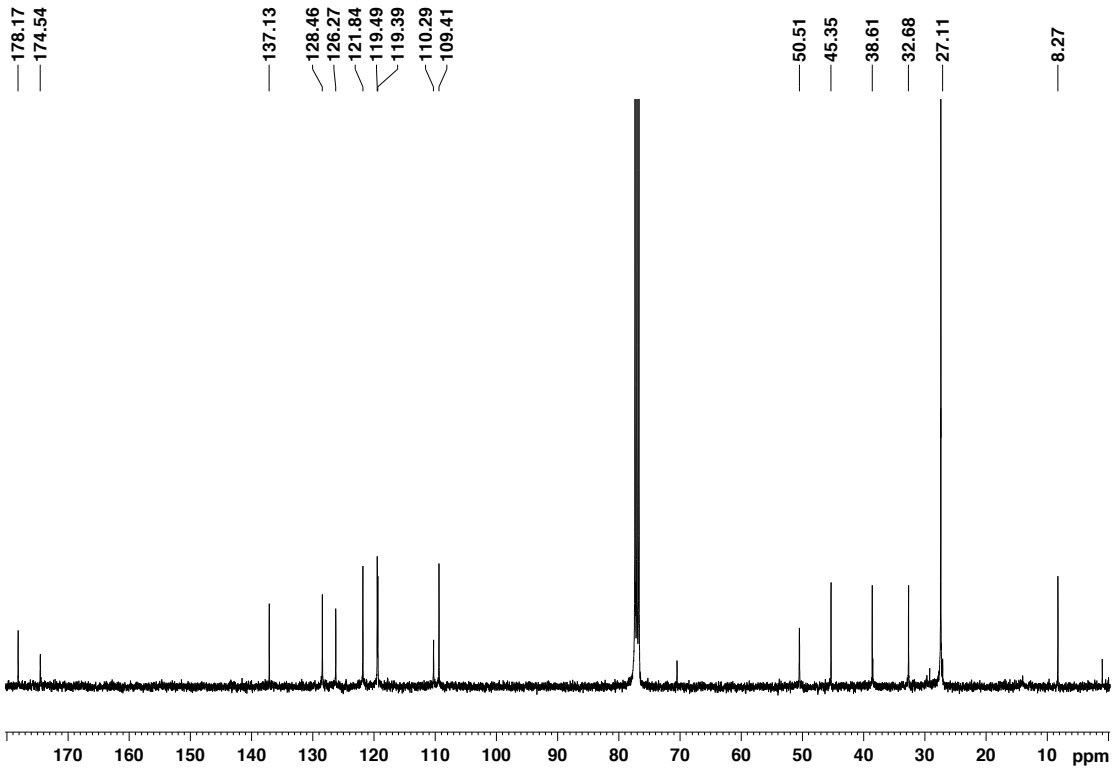
2-[(4-Methylbenzoyl)amino]-2-(1-methylindol-3-yl)ethanoic acid (16a) (DMSO-d_6)



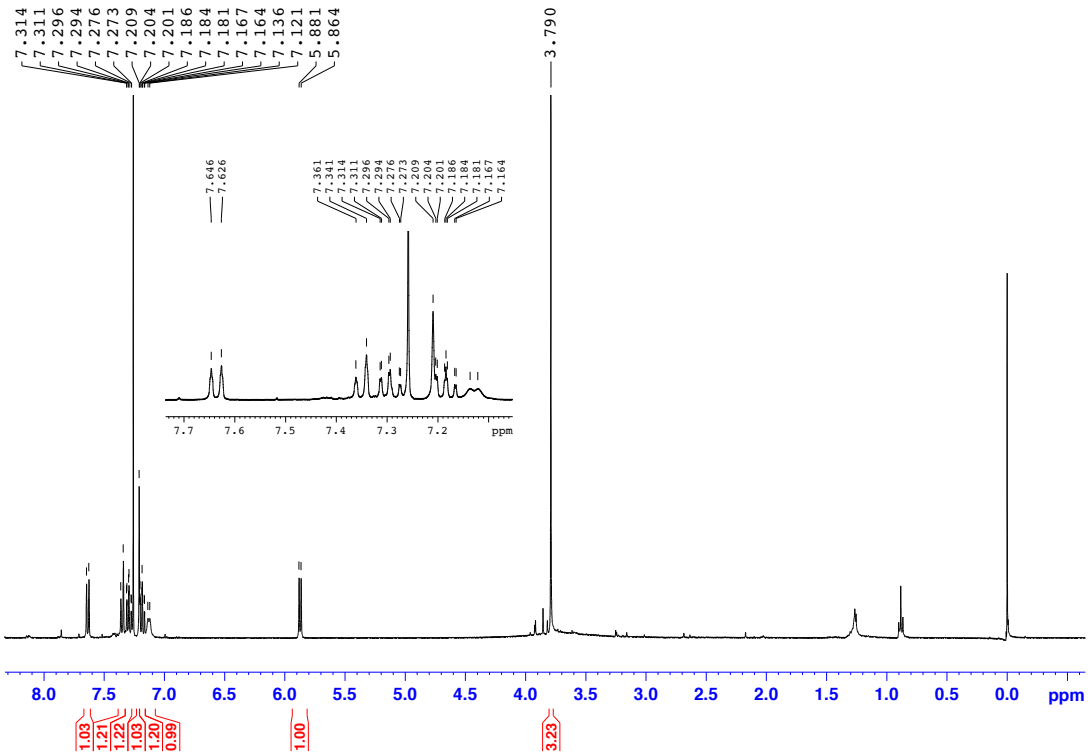


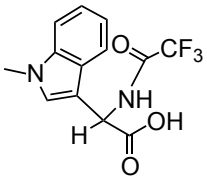
2-(1-Methylindol-3-yl)-2-[(pivaloyl)amino]ethanoic acid (16h) ($CDCl_3$)



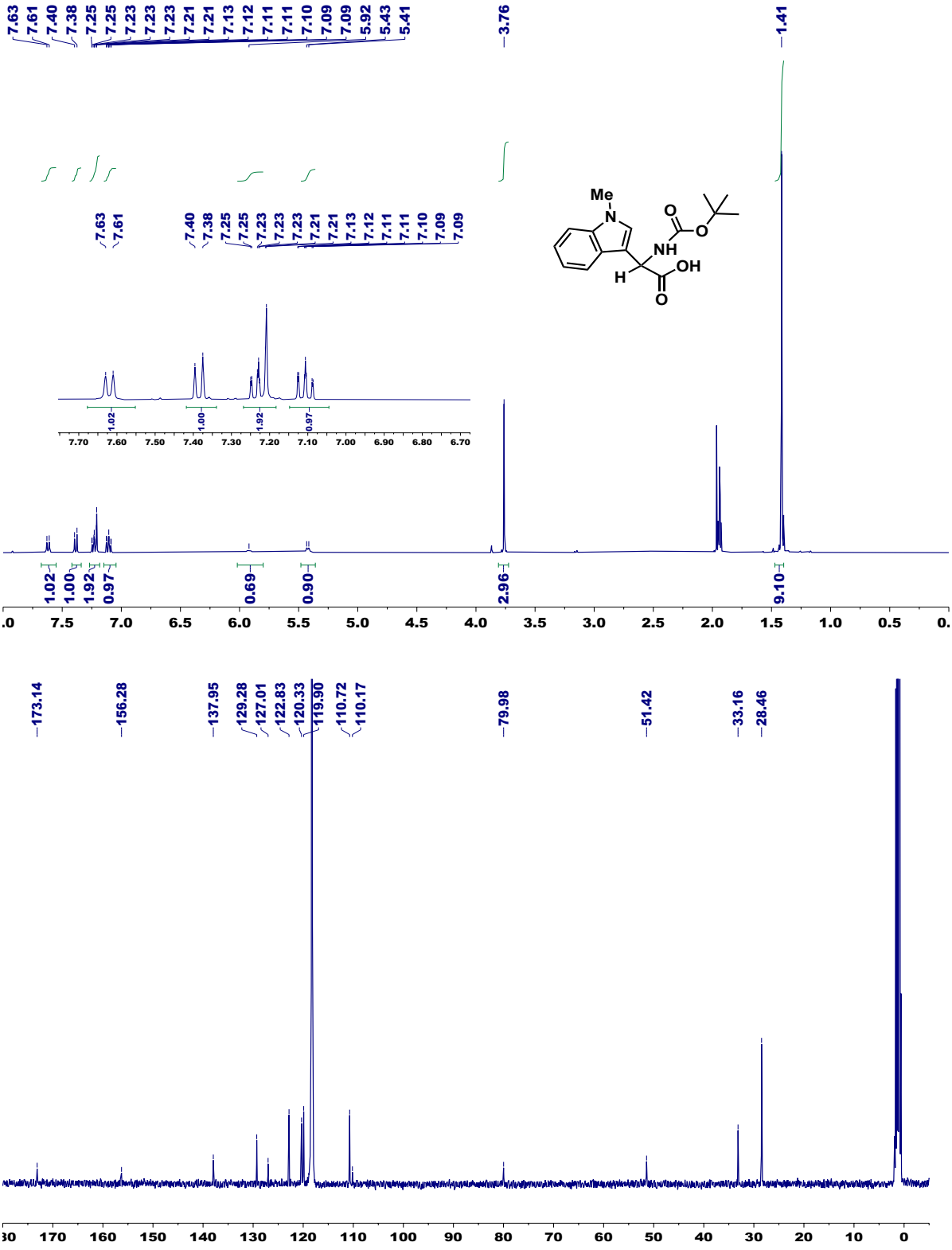


2-(1-Methylindol-3-yl)-2-[(trifluoreacetyl)amino]ethanoic acid (16i) ($CDCl_3$)

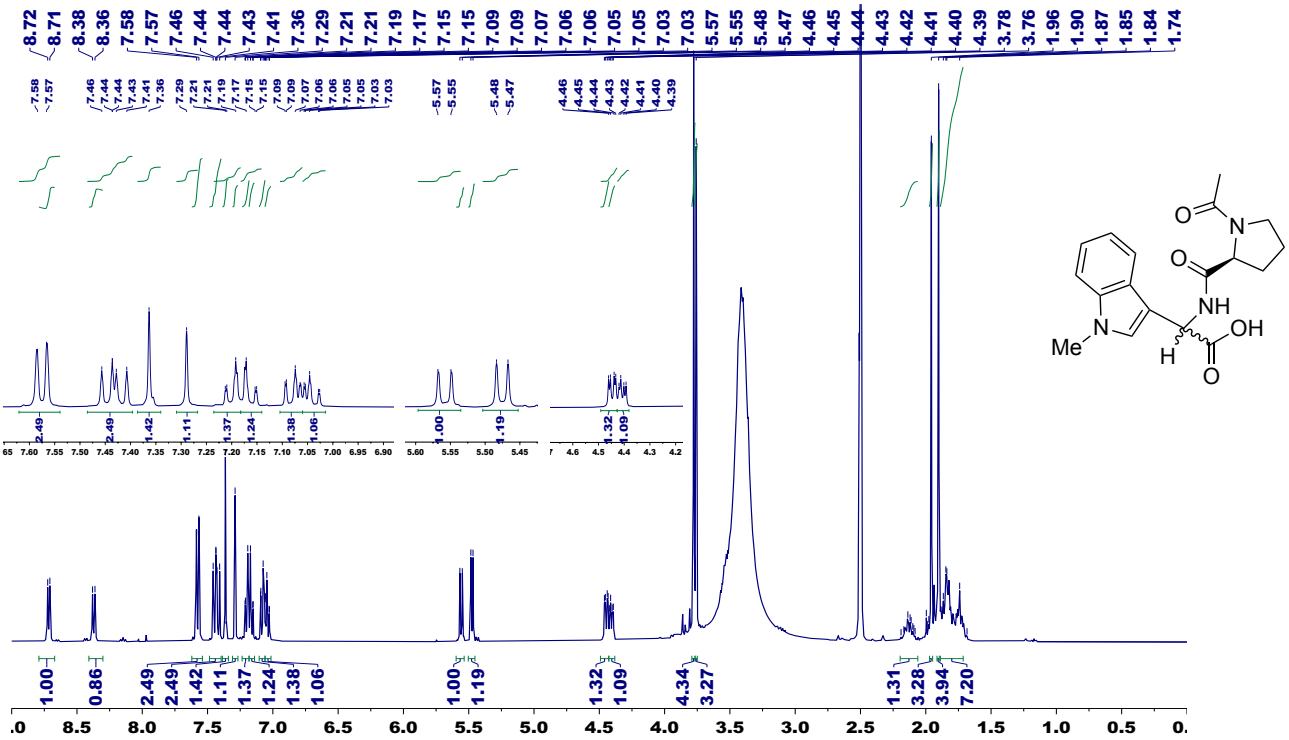


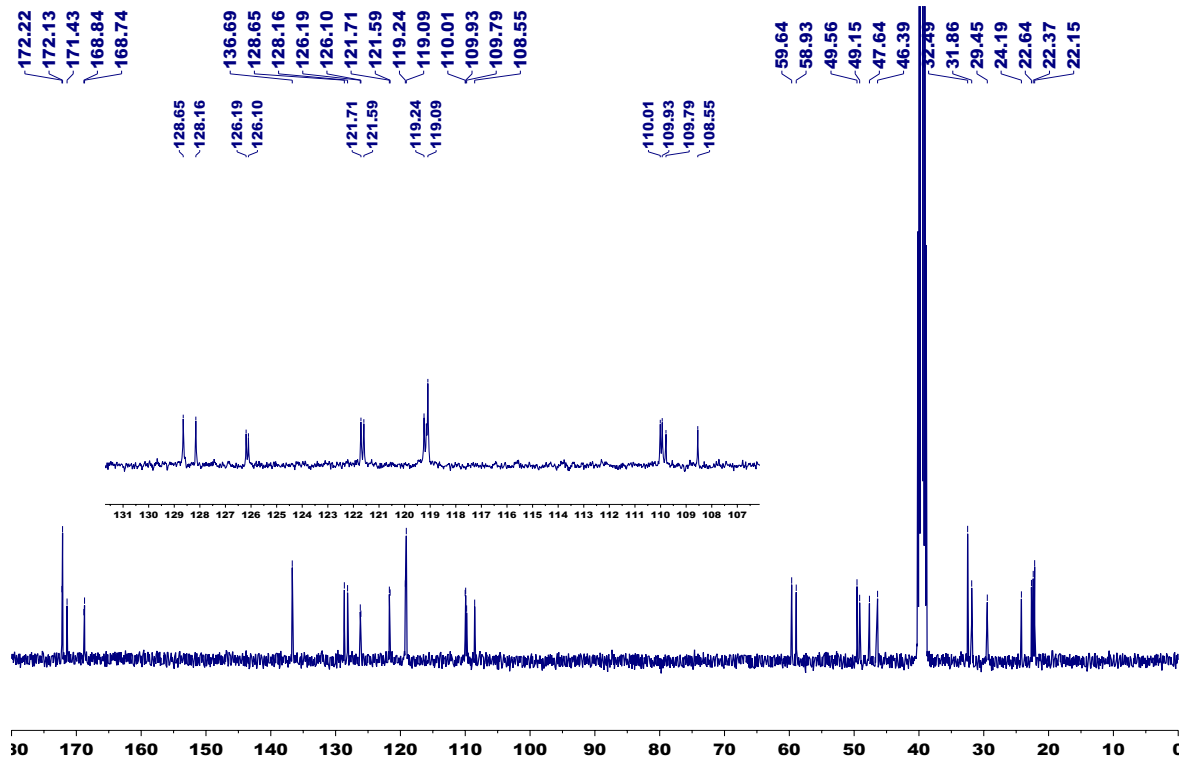


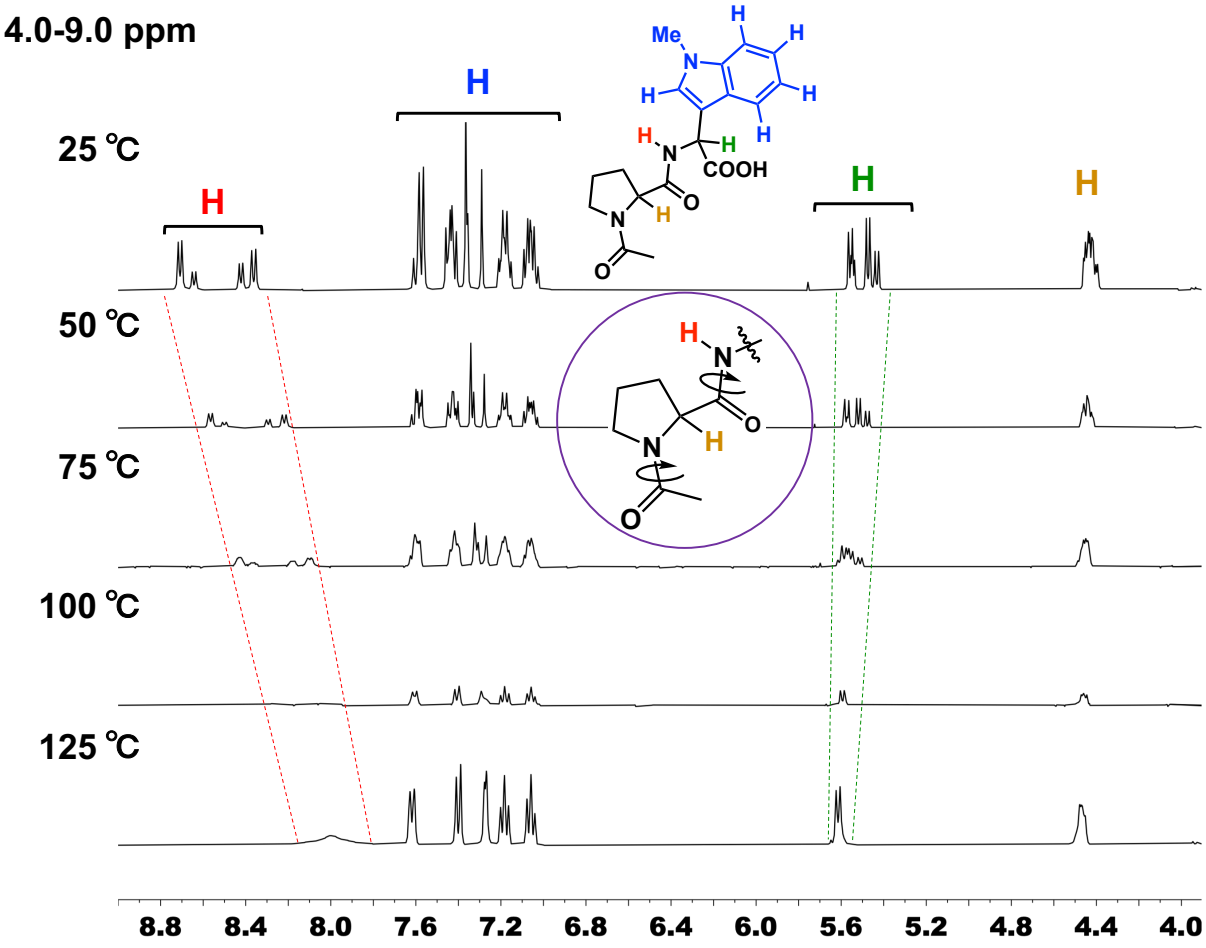
2-(*tert*-butoxycarbonylamino)-2-(1-methylindol-3-yl)ethanoic acid (16j) (CD_3CN)



2-(1-Acetylproline-2-carboxamino)-2-(1-methylindol-3-yl)ethanoic acid (16l) (DMSO-d_6)






4.0-9.0 ppm
25 ℃
50 ℃
75 ℃
100 ℃
125 ℃
H
H
H
H
Me
N
COOH
O
8.8
8.4
8.0
7.6
7.2
6.8
6.4
6.0
5.6
5.2
4.8
4.4
4.0