

Pharmacology of Valinate and *tert*-Leucinate Synthetic Cannabinoids 5F-AMBICA, 5F-AMB, 5F-ADB, AMB-FUBINACA, MDMB-FUBINACA, MDMB-CHMICA, and Their Analogues

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Contents:

Table S1: Names, CAS numbers, and references for selected compounds (pp. S2–S4).

Figures S1–S32: ^1H and ^{13}C NMR spectra for selected compounds (pp. S5–S36).

Figure S33: AUC for hypothermic and bradycardic effects of 5F-AMB and MDMB-FUBINACA (p. S37).

Figure S34: 24 Hour body temperature data for MDMB-FUBINACA (p. S38).

Figure S35: AUC for body temperature of 5F-AMB and MDMB-FUBINACA following pretreatment with CB₁ antagonist or CB₂ antagonist (p. S39).

Table S1. IUPAC names, CAS numbers, and selected references for valinate- and *tert*-leucinate-derived indole and indazole synthetic cannabinoids.

	IUPAC	CAS	Notified to EMCDDA	Refs
5F-AMB-PICA (10)	methyl (<i>S</i>)-2-(1-(5-fluoropentyl)-1 <i>H</i> -indole-3-carboxamido)-3-methylbutanoate	1616253-26-9 (racemate)	5 December 2014, Hungary	1-3
5F-MDMB-PICA (11)	methyl (<i>S</i>)-2-(1-(5-fluoropentyl)-1 <i>H</i> -indole-3-carboxamido)-3,3-dimethylbutanoate	-	-	4
5F-AMB-PINACA (12)	methyl (<i>S</i>)-2-(1-(5-fluoropentyl)-1 <i>H</i> -indazole-3-carboxamido)-3-methylbutanoate	1715016-74-2 (racemate) 1801552-03-3 (<i>S</i> -enantiomer)	18 June 2014, Hungary	2-9
5F-MDMB-PINACA (13)	methyl (<i>S</i>)-2-(1-(5-fluoropentyl)-1 <i>H</i> -indazole-3-carboxamido)-3,3-dimethylbutanoate	1715016-75-3 (racemate) 1838134-16-9 (<i>R</i> -enantiomer)	-	2, 4, 10
AMB-FUBICA (14)	methyl (<i>S</i>)-2-(1-(4-fluorobenzyl)-1 <i>H</i> -indole-3-carboxamido)-3-methylbutanoate	-	-	-
MDMB-FUBICA (15)	methyl (<i>S</i>)-2-(1-(4-fluorobenzyl)-1 <i>H</i> -indole-3-carboxamido)-3,3-dimethylbutanoate	-	-	-
AMB-FUBINACA (16)	methyl (<i>S</i>)-2-(1-(4-fluorobenzyl)-1 <i>H</i> -indazole-3-carboxamido)-3-methylbutanoate	1715016-76-4 (racemate)	-	2, 4
MDMB-FUBINACA (17)	methyl (<i>S</i>)-2-(1-(4-fluorobenzyl)-1 <i>H</i> -indazole-3-carboxamido)-3,3-dimethylbutanoate	1715016-77-5 (racemate)	October 2014, Russian Federation ^a	2-4
AMB-CHMICA (18)	methyl (<i>S</i>)-2-(1-(cyclohexylmethyl)-1 <i>H</i> -indole-3-carboxamido)-3-methylbutanoate	-	-	-
MDMB-CHMICA (19)	methyl (<i>S</i>)-2-(1-(cyclohexylmethyl)-1 <i>H</i> -indole-3-carboxamido)-3,3-dimethylbutanoate	1863065-84-2 (racemate)	12 September 2014, Hungary ^b	2-3, 7, 11
AMB-CHMINACA (20)	methyl (<i>S</i>)-2-(1-(cyclohexylmethyl)-1 <i>H</i> -indazole-3-carboxamido)-3-methylbutanoate	1863066-03-8 (racemate)	-	2
MDMB-CHMINACA (21)	methyl (<i>S</i>)-2-(1-(cyclohexylmethyl)-1 <i>H</i> -indazole-3-carboxamido)-3,3-dimethylbutanoate	1715016-78-6 (racemate)	-	2, 4

		1185888-32-7 (S-enantiomer)		
AMB-PICA (22)	methyl (S)-2-(1-(pentyl)-1H-indole-3-carboxamido)-3-methylbutanoate	-	-	-
MDMB-PICA (23)	methyl (S)-2-(1-(pentyl)-1H-indole-3-carboxamido)-3,3-dimethylbutanoate	-	-	-
AMB-PINACA (24)	methyl (S)-2-(1-(pentyl)-1H-indazole-3-carboxamido)-3-methylbutanoate	1863066-06-1 (racemate) 1890250-13-1 (S-enantiomer)	10 December 2014, Sweden	2-3, 9
MDMB-PINACA (25)	methyl (S)-2-(1-(pentyl)-1H-indazole-3-carboxamido)-3,3-dimethylbutanoate	-		-

^aAn alert was issued after the EMCDDA identified media reports of two outbreaks of serious adverse events associated with consumption of MDMB-FUBINACA.

^bTwo alerts were issued in December 2014 after the Austrian national focal point reported 7 non-fatal intoxications associated with use of a product called ‘Bonzai citrus’ and/or ‘Bonzai Winter Boost’ (which allegedly contained MDMB-CHMICA) and after the Swedish national focal point reported 4 deaths and 6 non-fatal intoxications associated with the use of MDMB-CHMICA that occurred between September and November 2014.

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Figure S1. ^1H NMR spectrum (300 MHz, CDCl_3 , 300 K) of 5F-AMB-PICA (**10**).

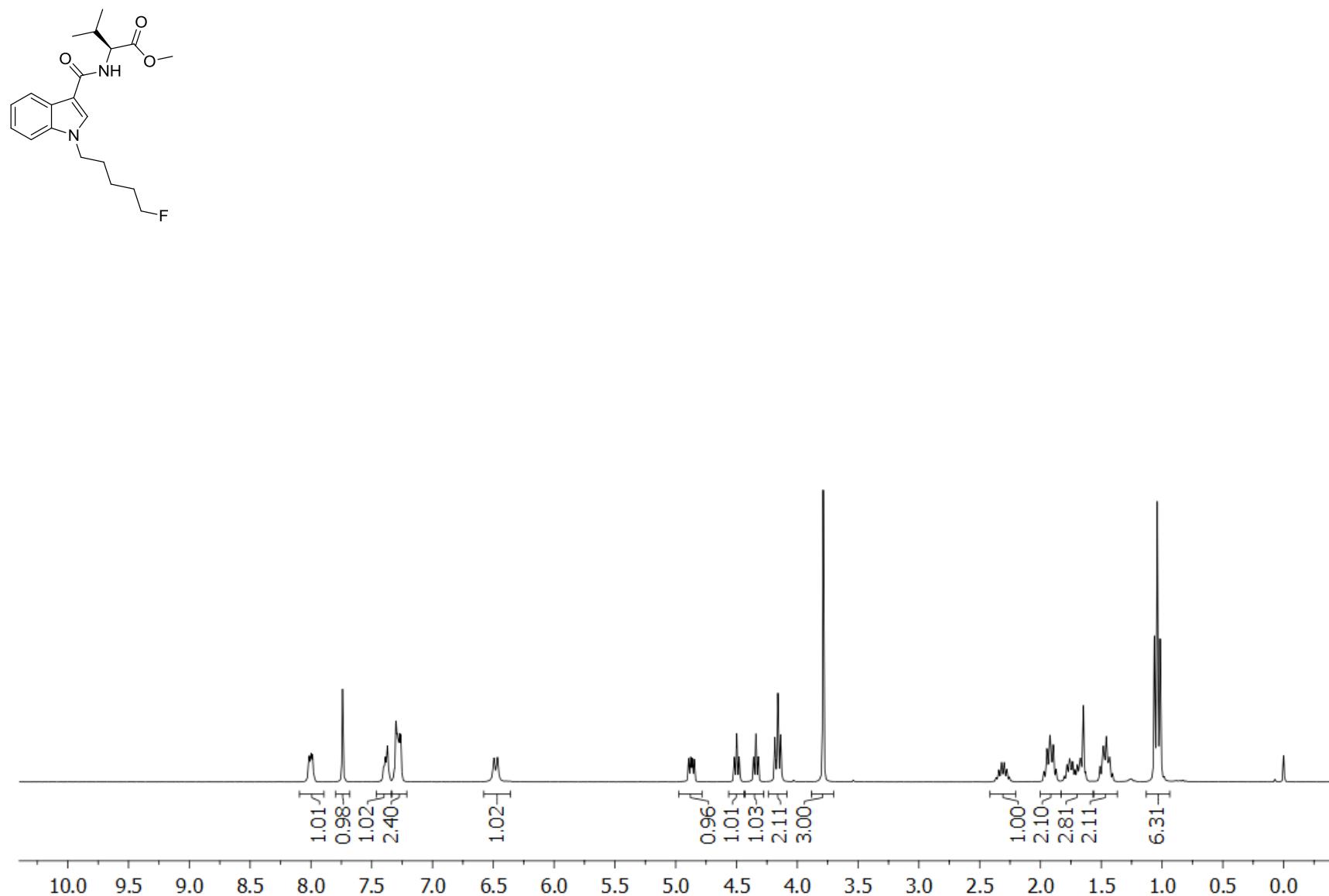


Figure S2. ^{13}C NMR spectrum (75 MHz, CDCl_3 , 300 K) of 5F-AMB-PICA (**10**).

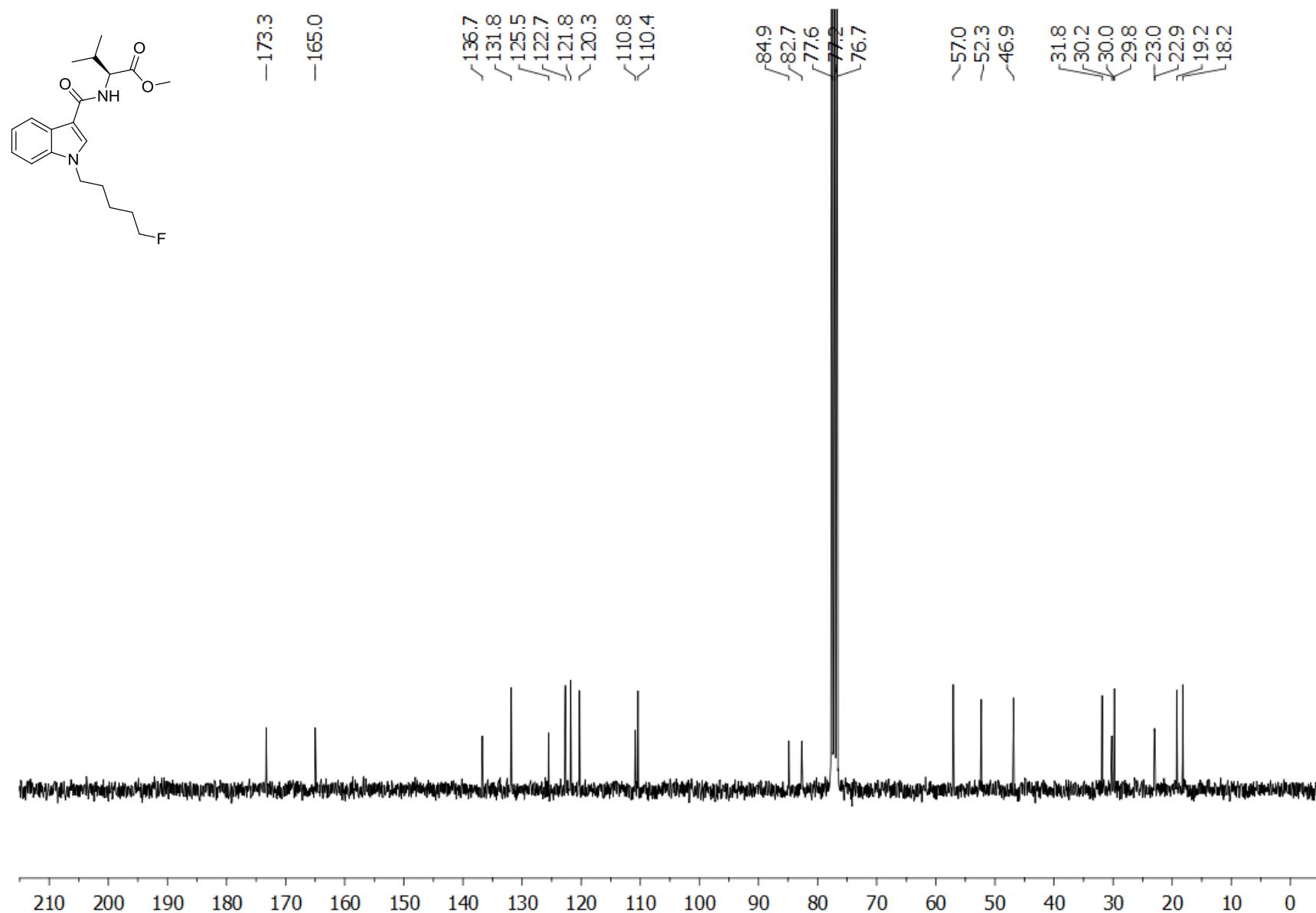


Figure S3. ^1H NMR spectrum (300 MHz, CDCl_3 , 300 K) of 5F-MDMB-PICA (**11**).

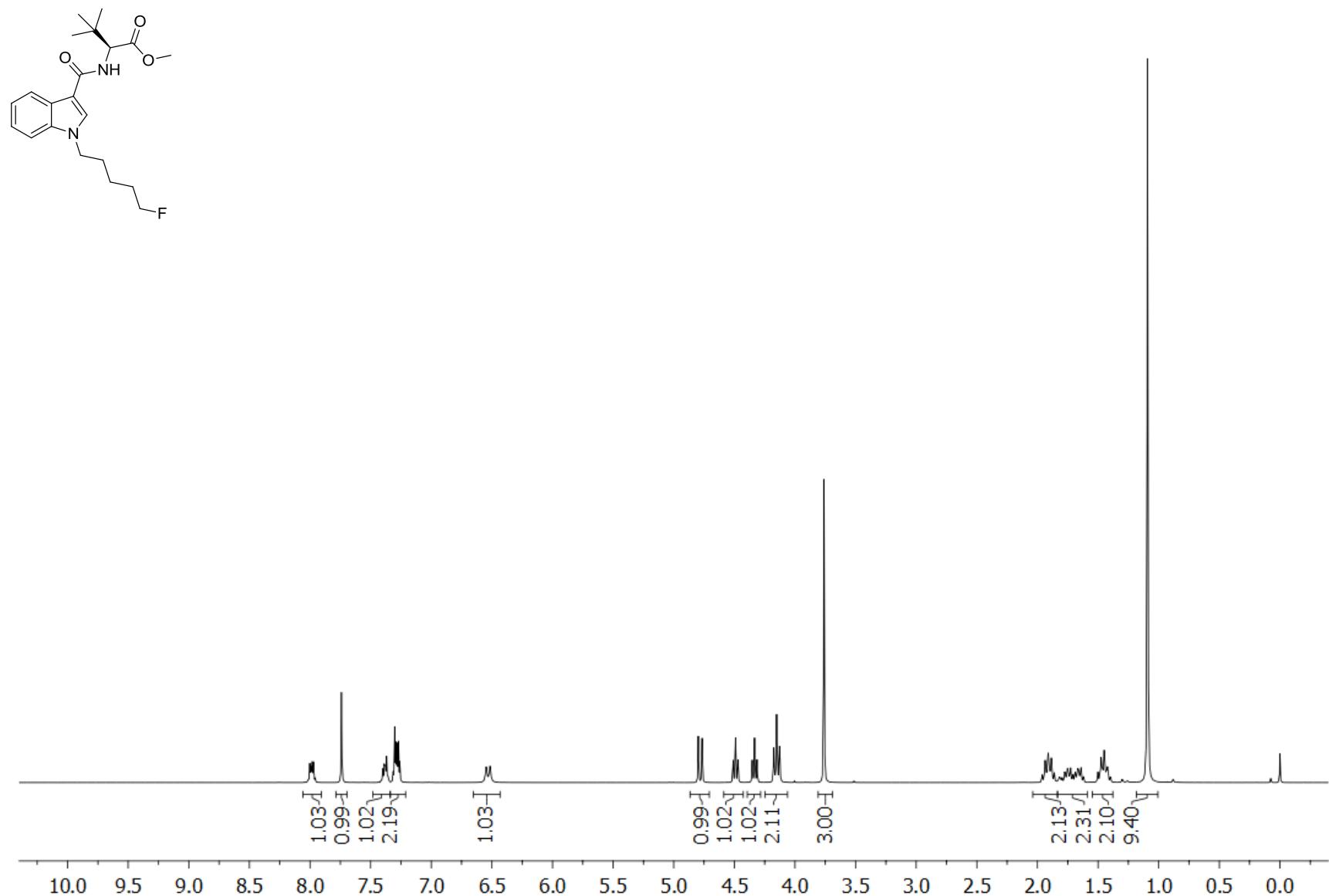


Figure S4. ^{13}C NMR spectrum (75 MHz, CDCl_3 , 300 K) of 5F-MDMB-PICA (**11**).

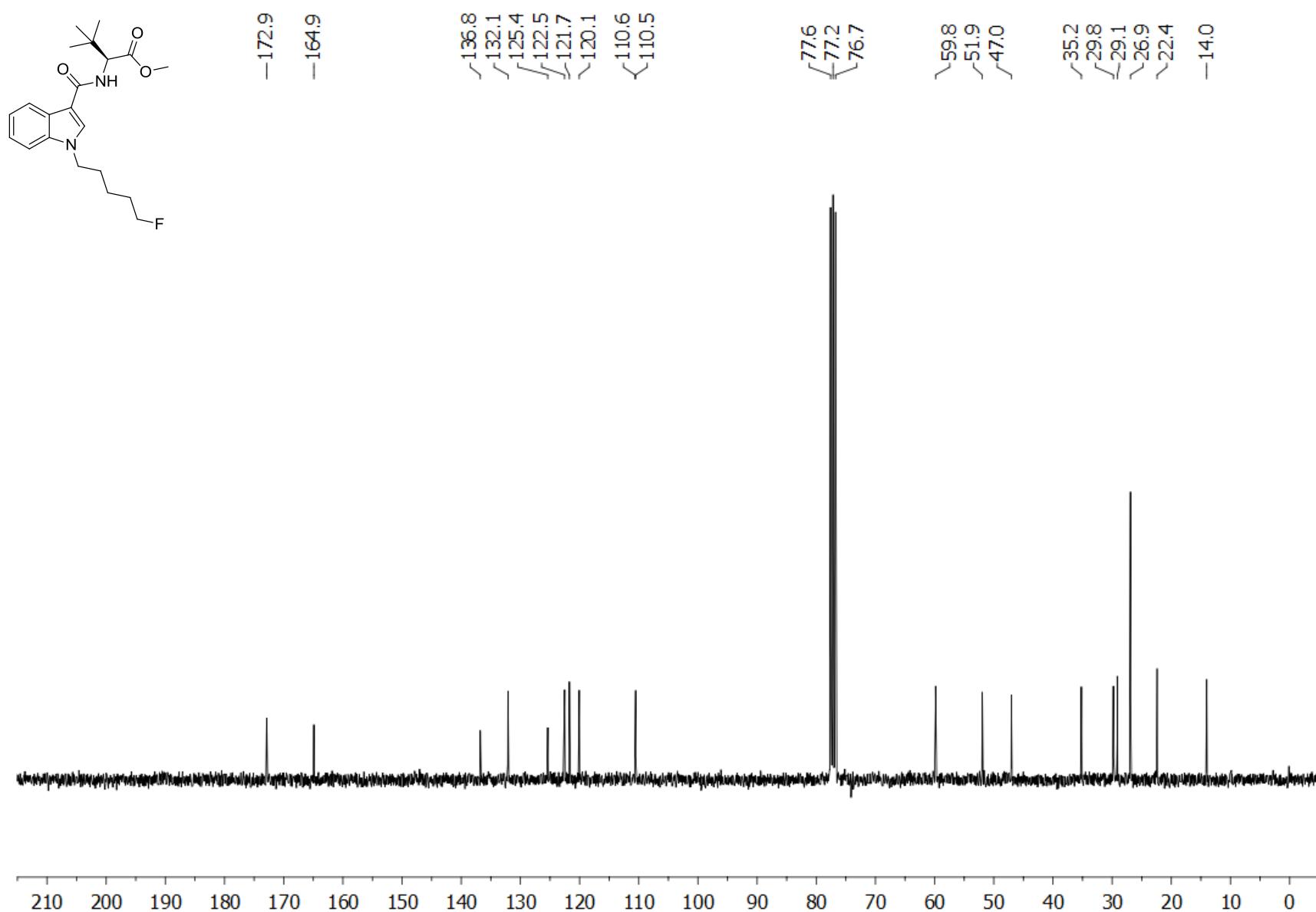


Figure S5. ^1H NMR spectrum (300 MHz, CDCl_3 , 300 K) of 5F-AMB-PINACA (**12**).

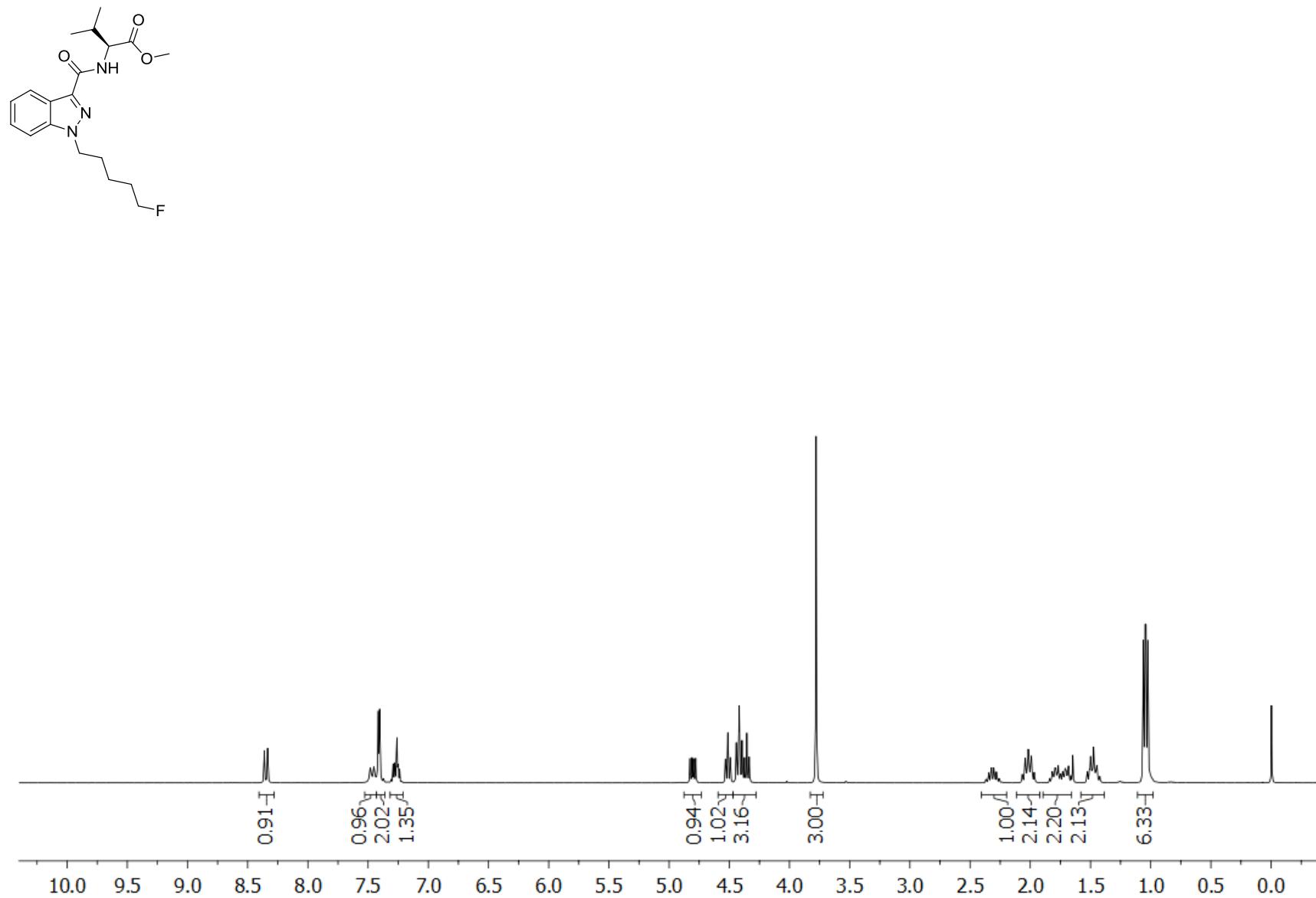


Figure S6. ^{13}C NMR spectrum (75 MHz, CDCl_3 , 300 K) of 5F-AMB-PINACA (**12**).

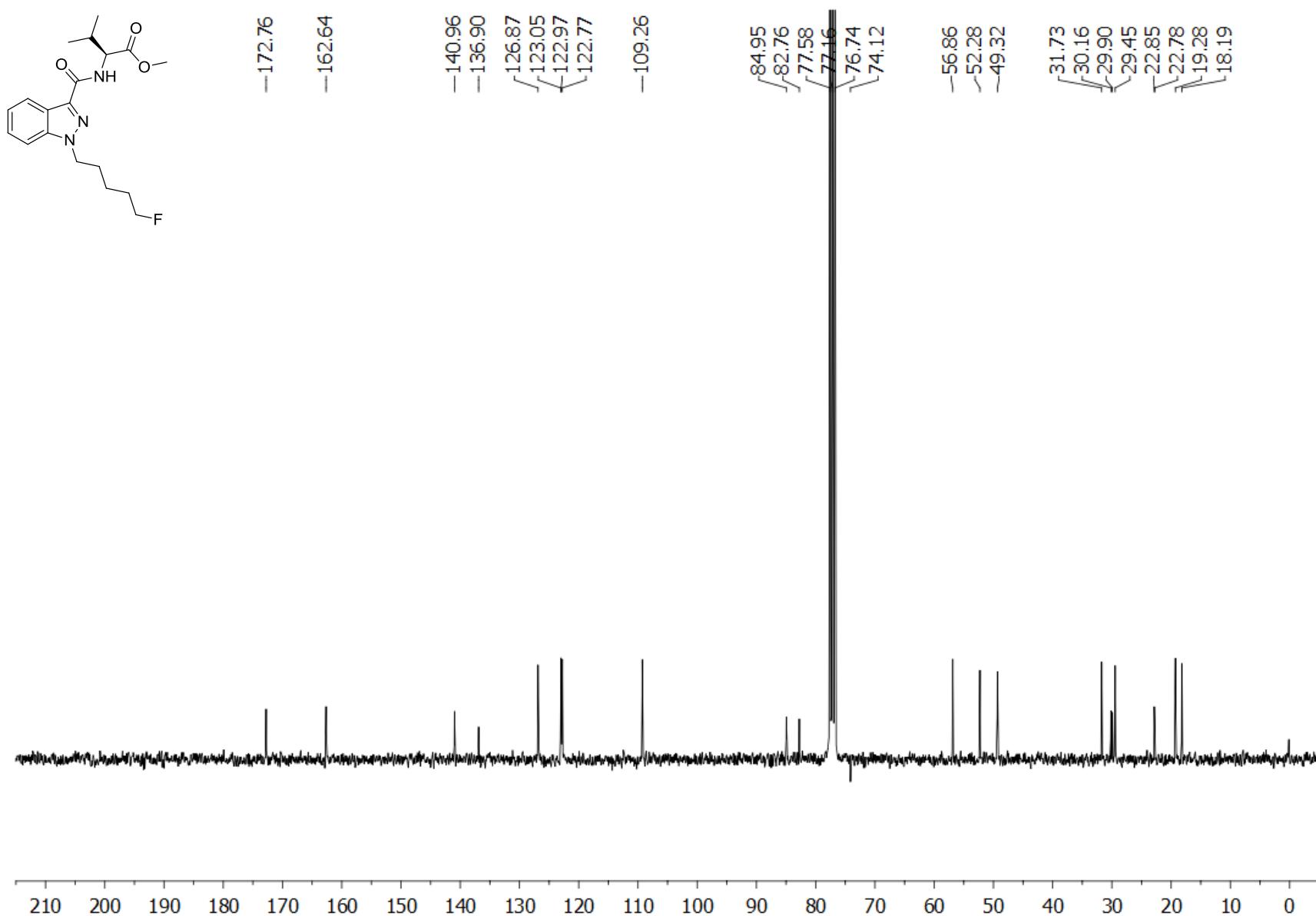


Figure S7. ^1H NMR spectrum (300 MHz, CDCl_3 , 300 K) of 5F-MDMB-PINACA (**13**).

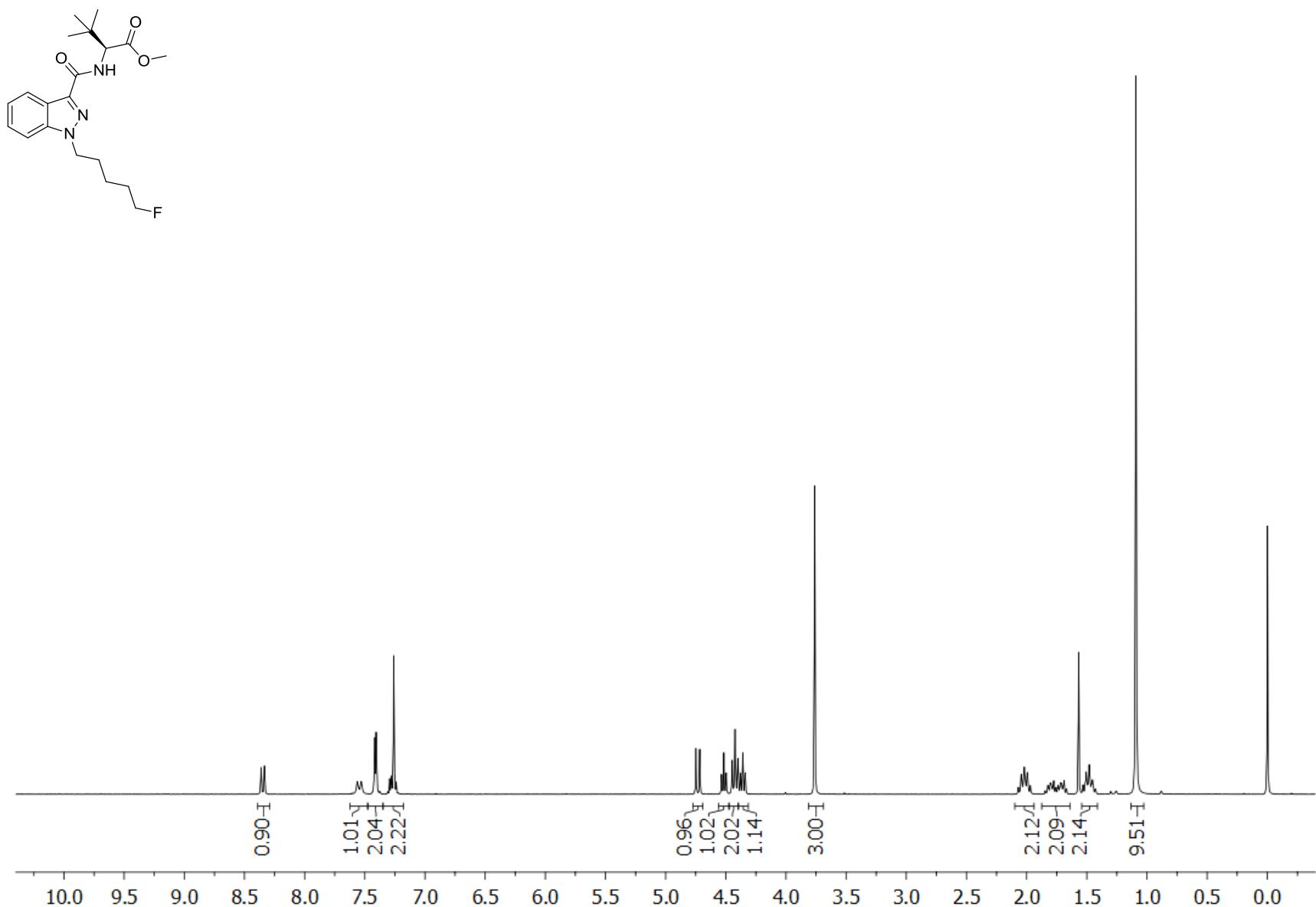


Figure S8. ^{13}C NMR spectrum (75 MHz, CDCl_3 , 300 K) of 5F-MDMB-PINACA (**13**).

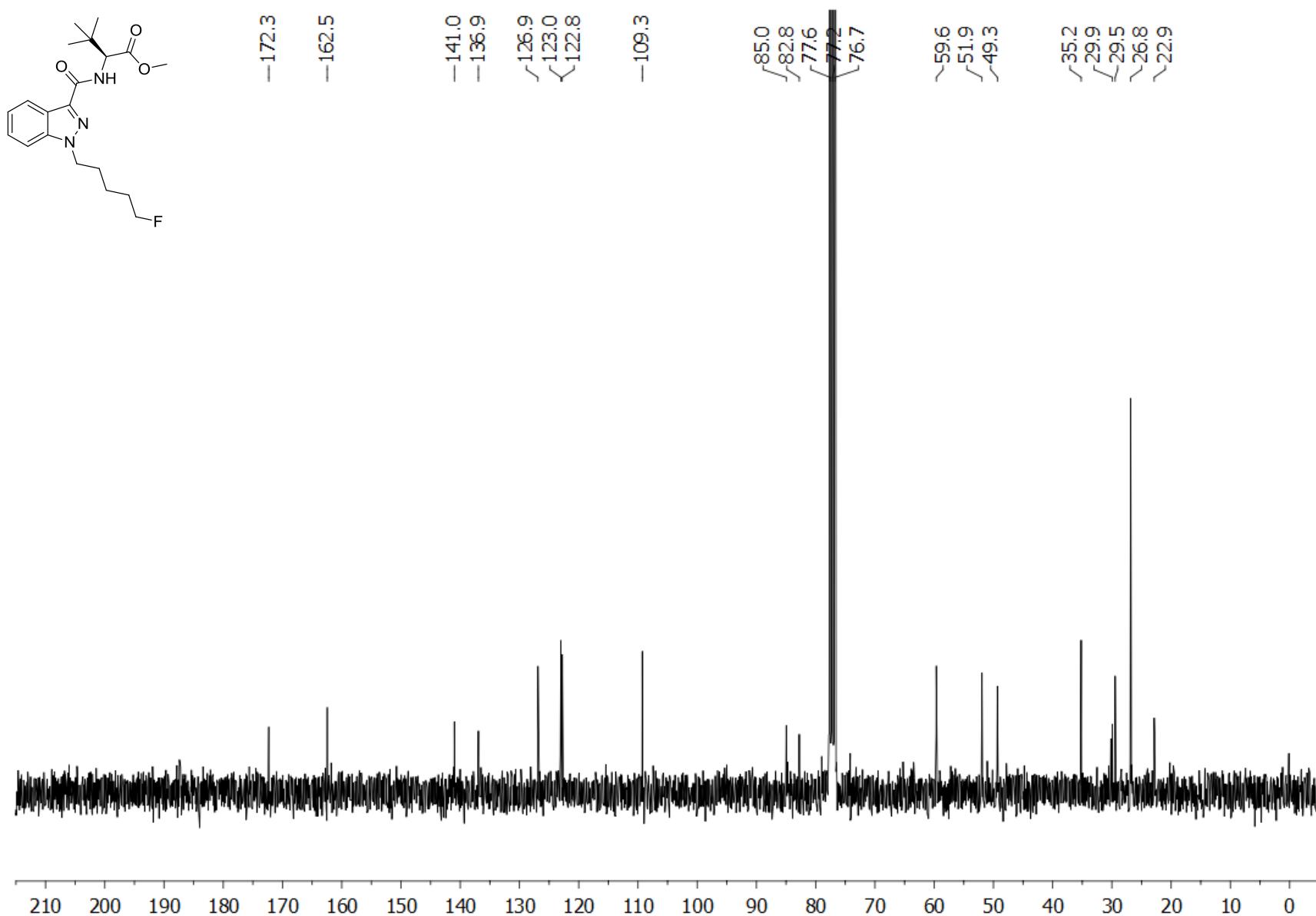


Figure S9. ^1H NMR spectrum (300 MHz, CDCl_3 , 300 K) of AMB-FUBICA (**14**).

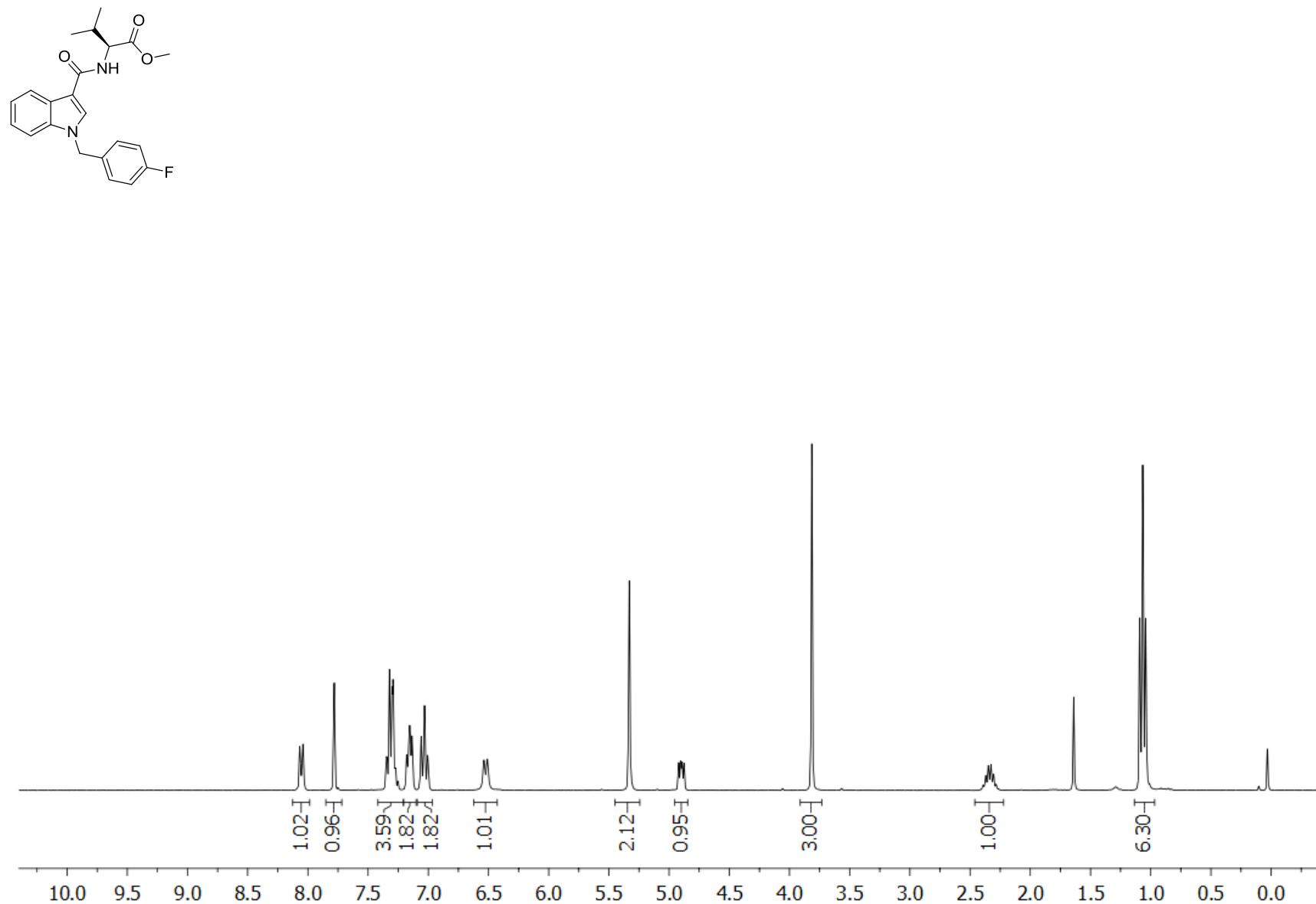


Figure S10. ^{13}C NMR spectrum (75 MHz, CDCl_3 , 300 K) of AMB-FUBICA (**14**).

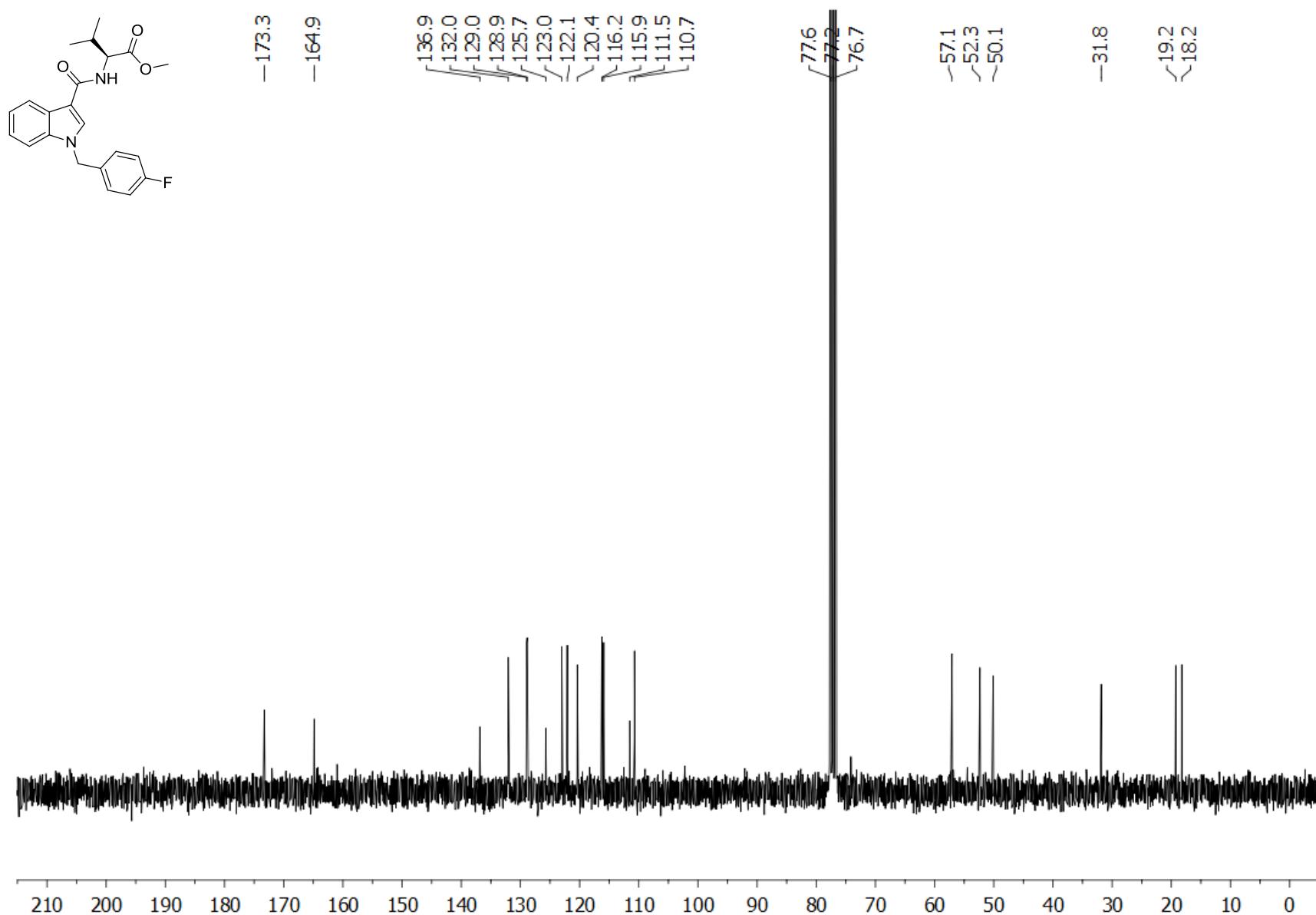


Figure S11. ^1H NMR spectrum (300 MHz, CDCl_3 , 300 K) of MDMB-FUBICA (**15**).

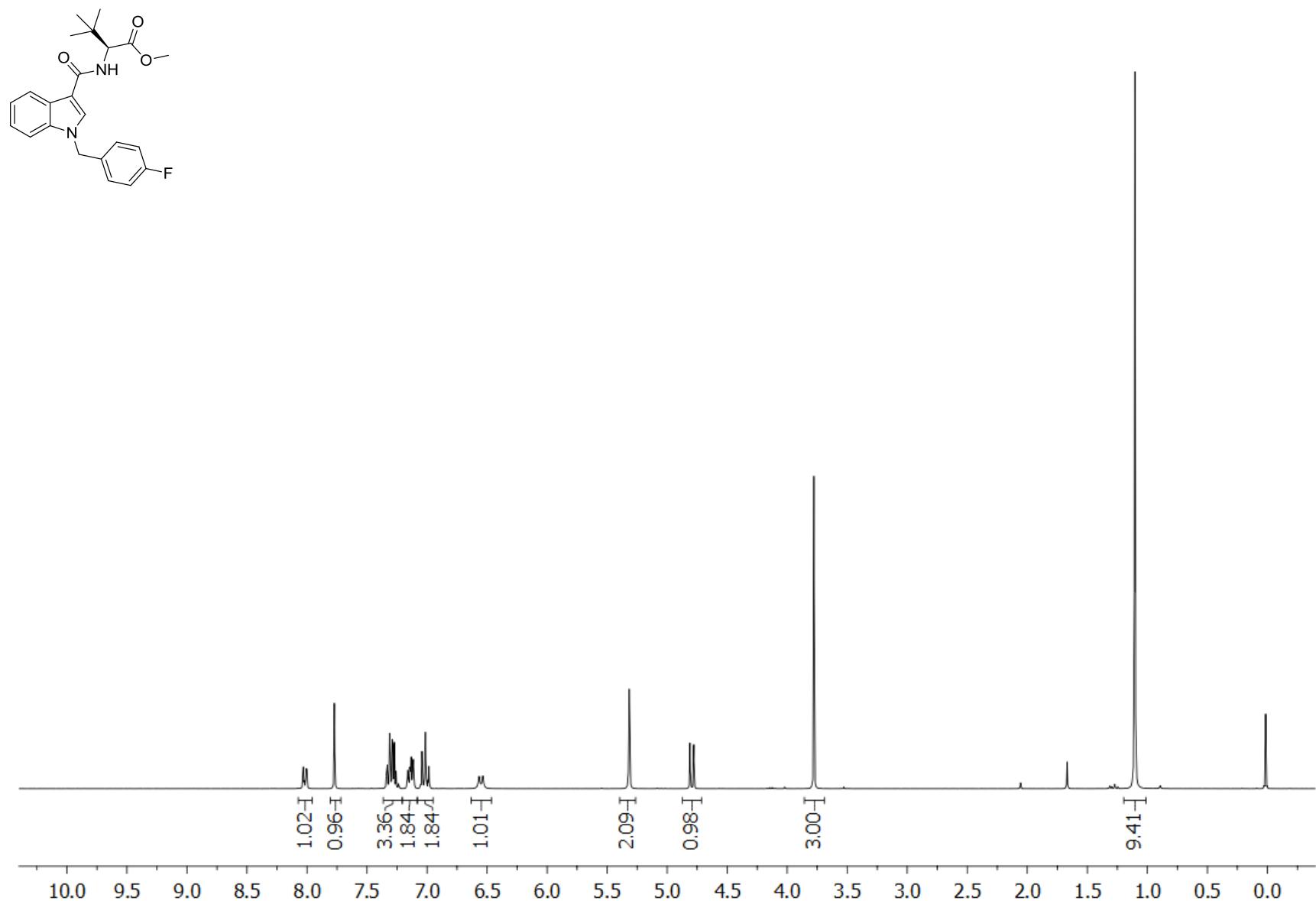


Figure S12. ^{13}C NMR spectrum (75 MHz, CDCl_3 , 300 K) of MDMB-FUBICA (**15**).

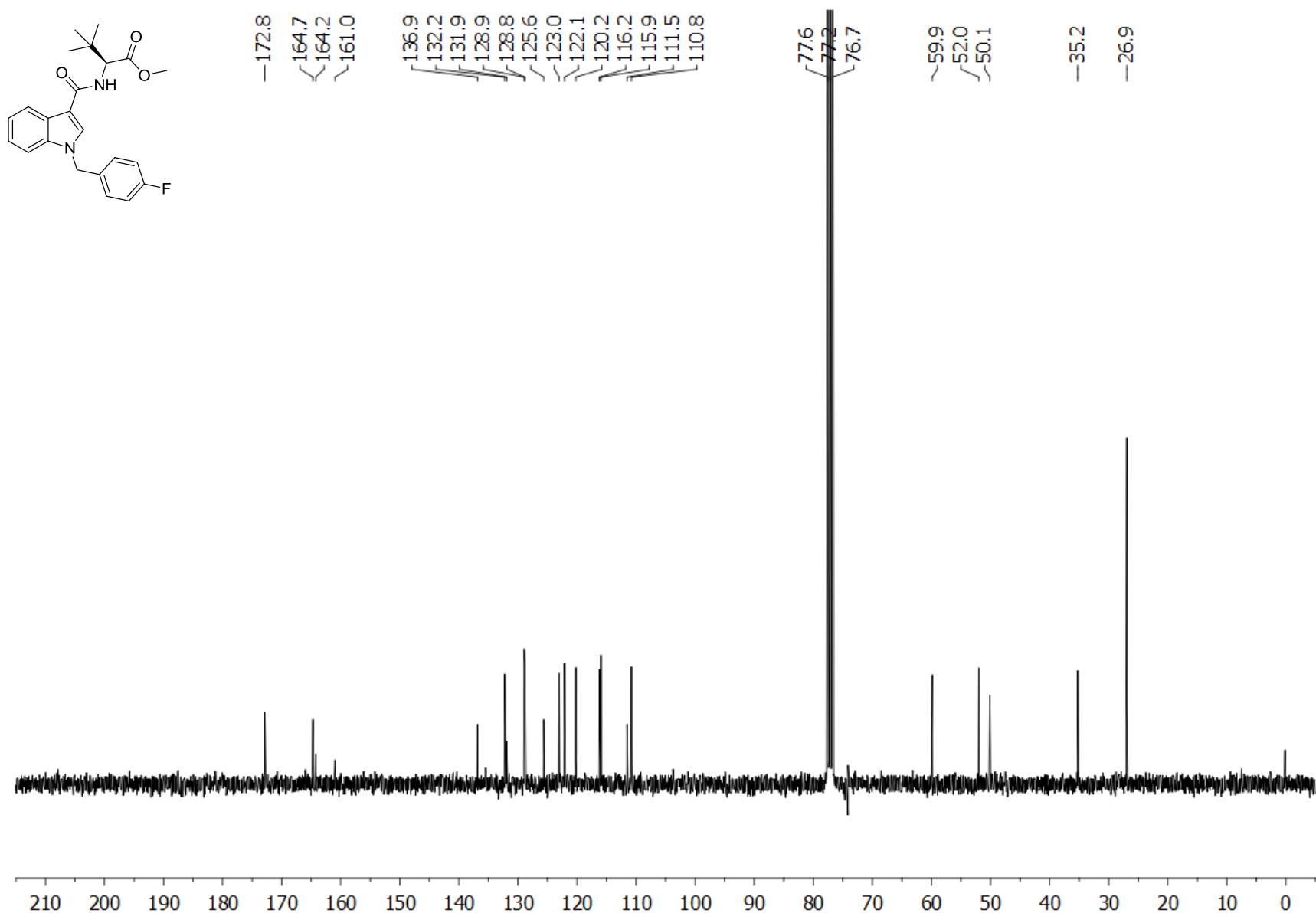


Figure S13. ^1H NMR spectrum (300 MHz, CDCl_3 , 300 K) of AMB-FUBINACA (**16**).

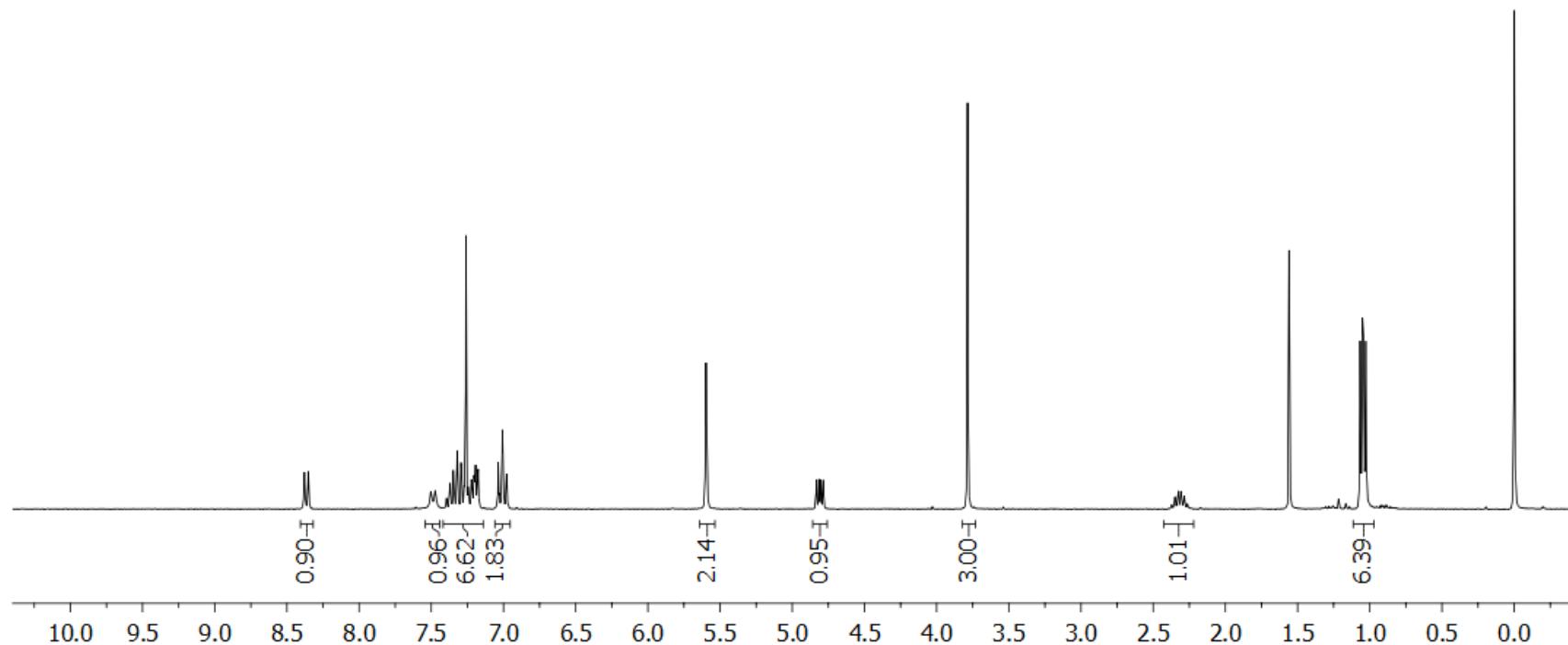
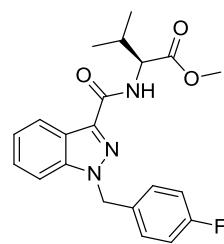


Figure S14. ^{13}C NMR spectrum (75 MHz, CDCl_3 , 300 K) of AMB-FUBINACA (**16**).

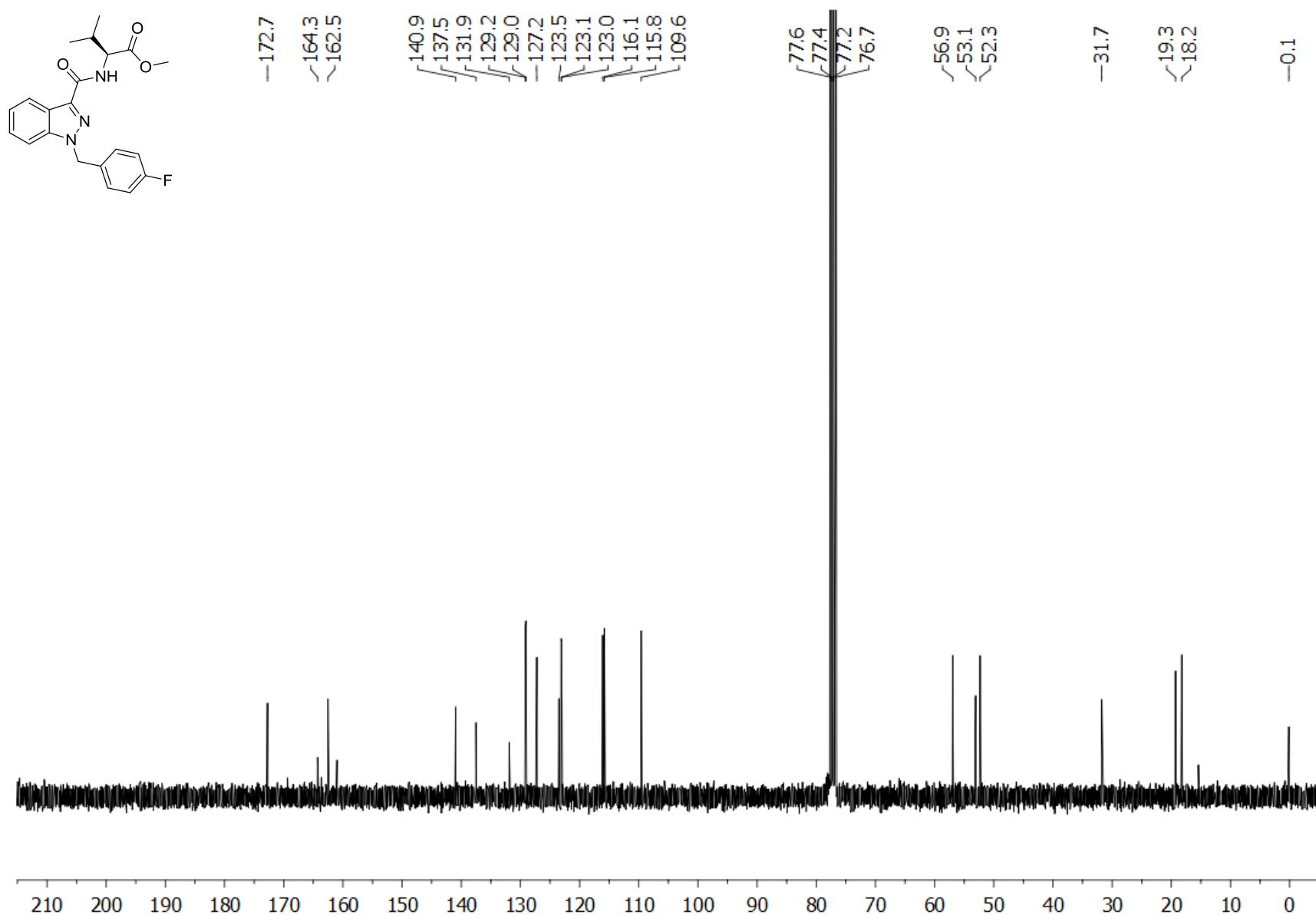


Figure S15. ^1H NMR spectrum (300 MHz, CDCl_3 , 300 K) of MDMB-FUBINACA (**17**).

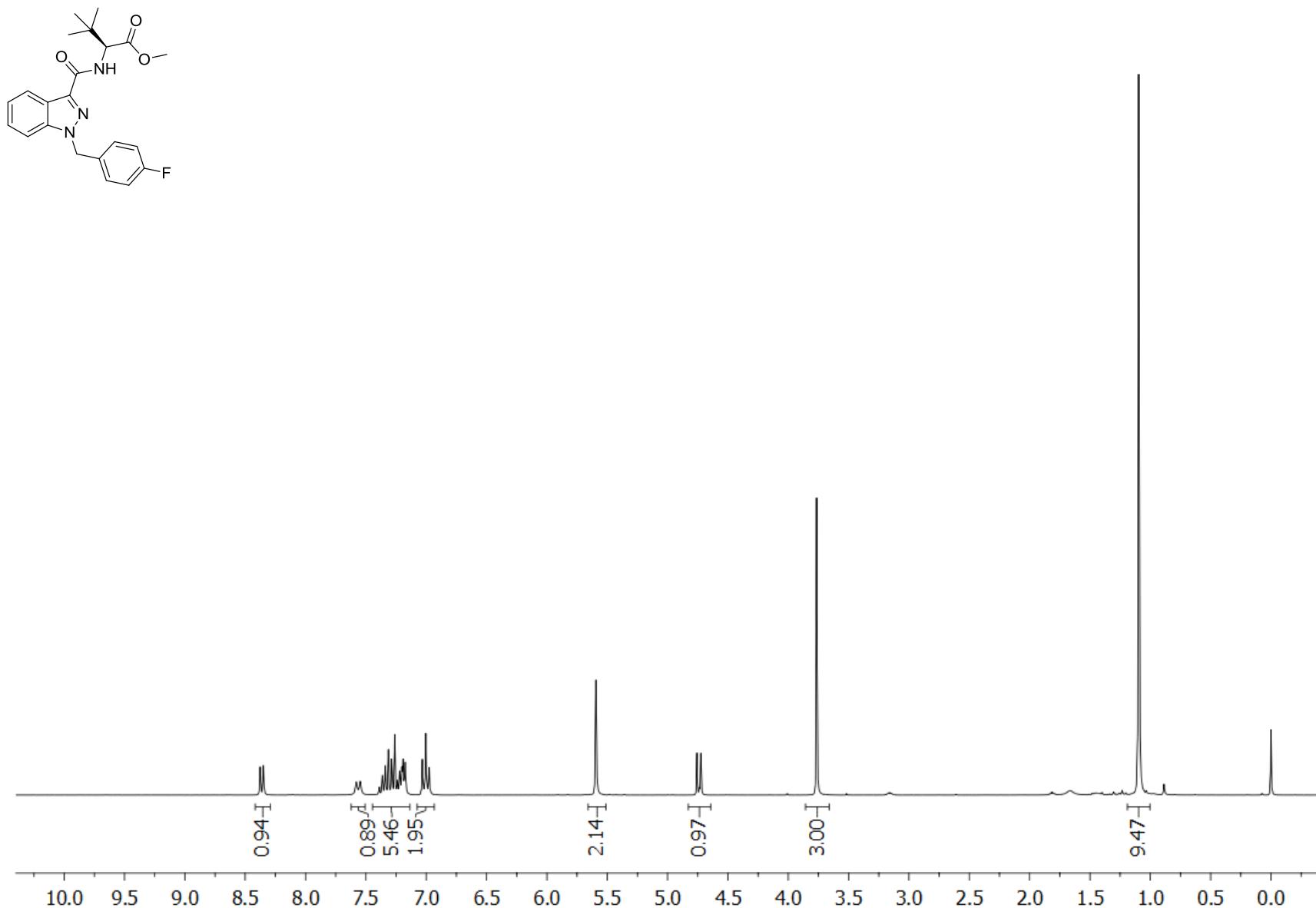


Figure S16. ^{13}C NMR spectrum (75 MHz, CDCl_3 , 300 K) of MDMB-FUBINACA (**17**).

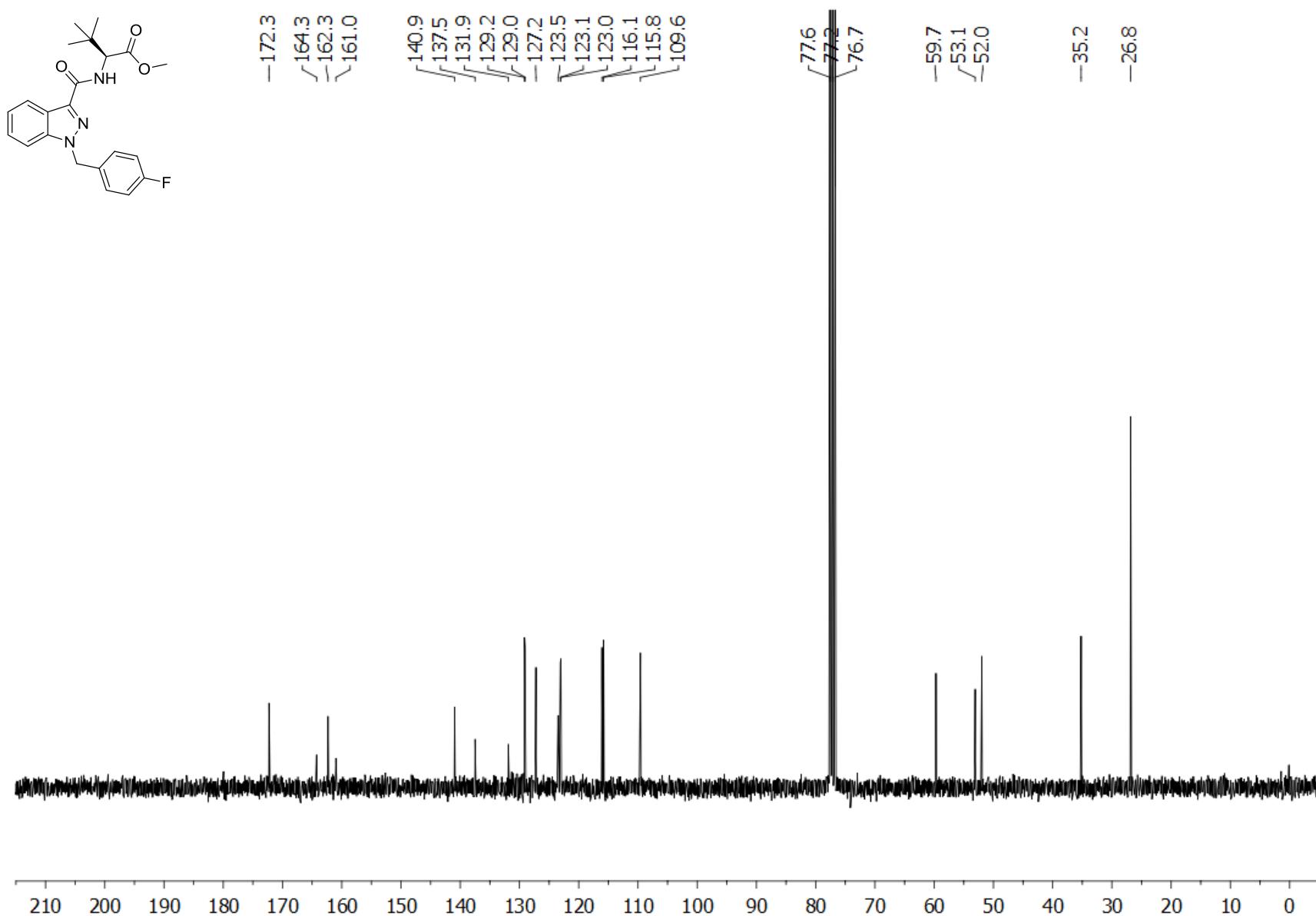


Figure S17. ^1H NMR spectrum (300 MHz, CDCl_3 , 300 K) of AMB-CHMICA (**18**).

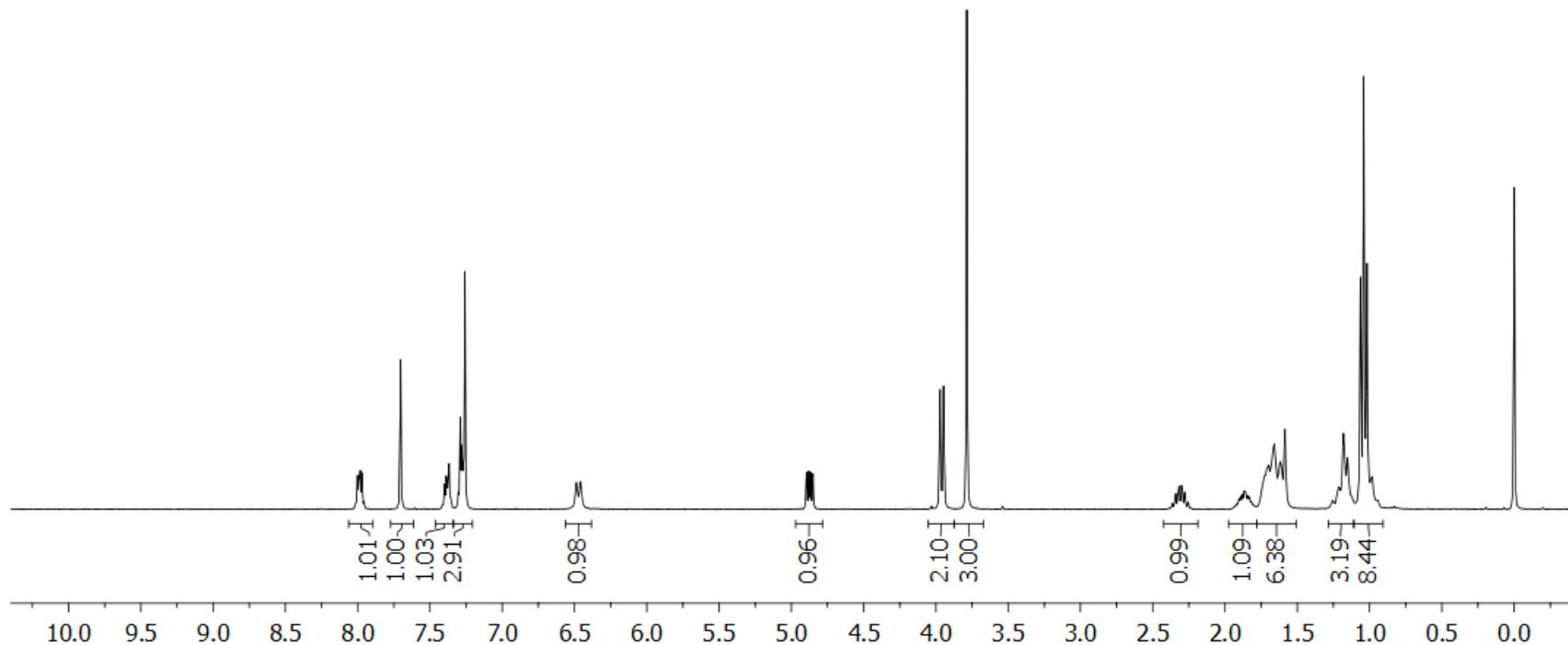
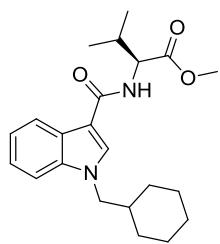


Figure S18. ^{13}C NMR spectrum (75 MHz, CDCl_3 , 300 K) of AMB-CHMICA (**18**).

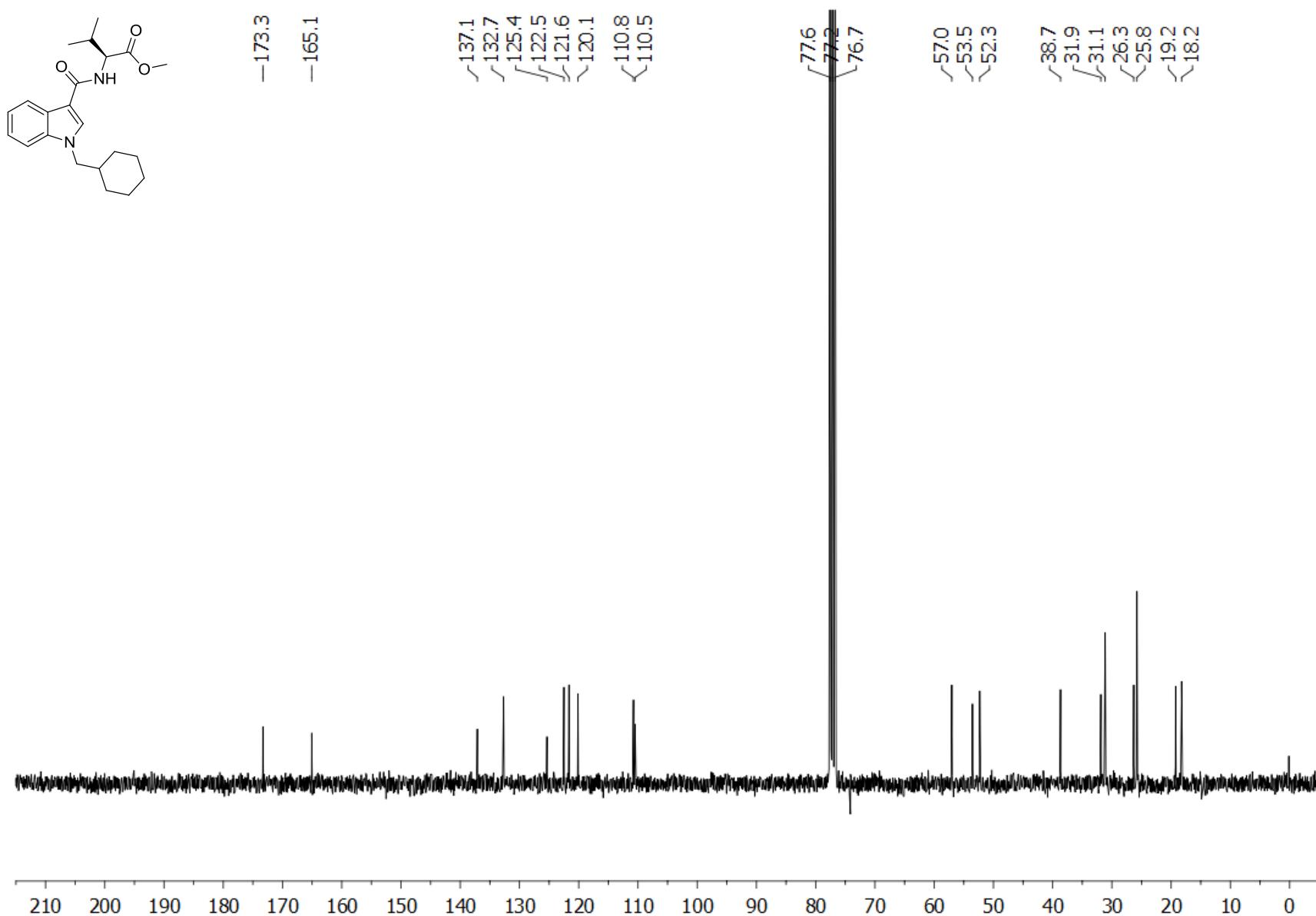


Figure S19. ^1H NMR spectrum (300 MHz, CDCl_3 , 300 K) of MDMB-CHMICA (**19**).

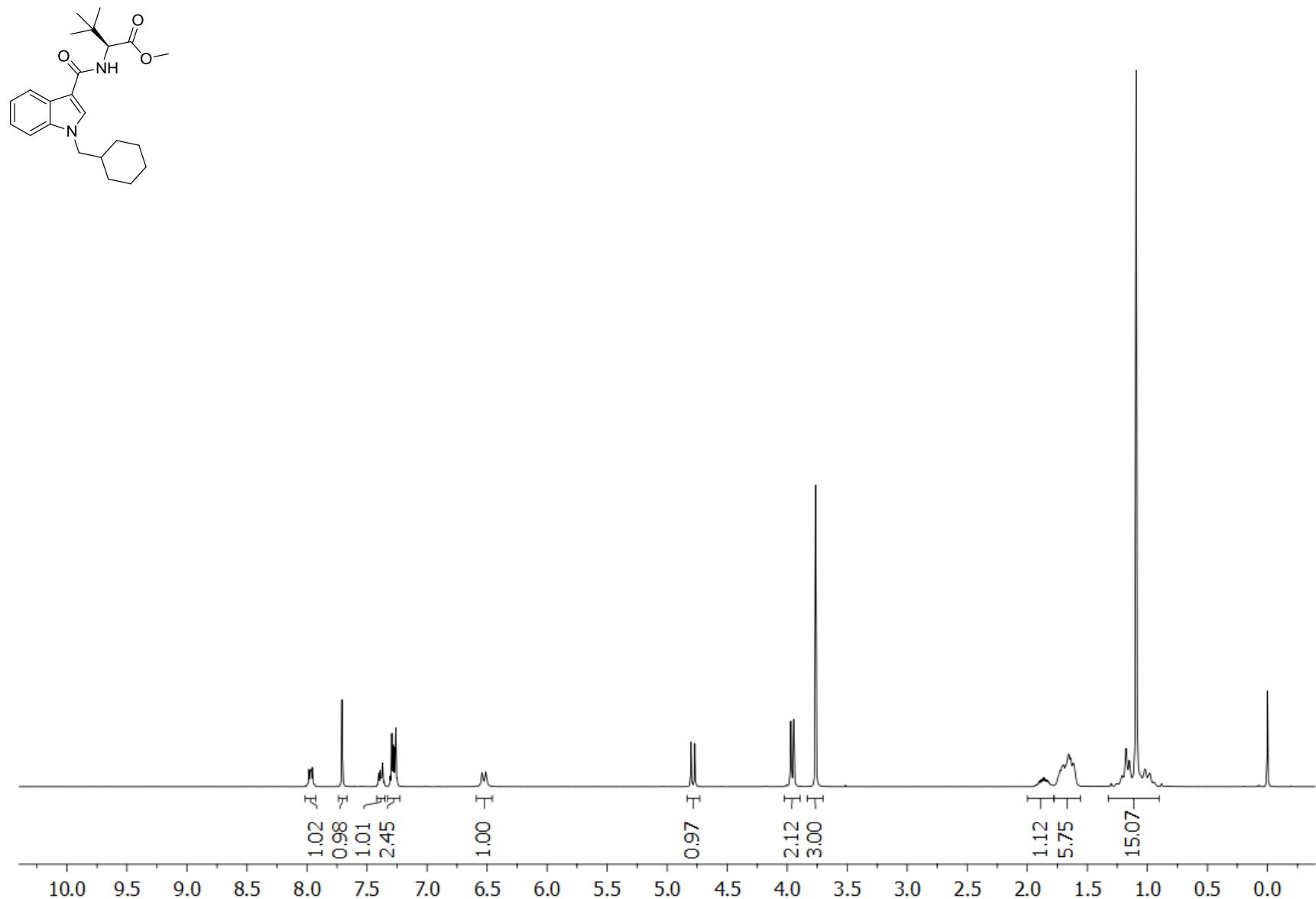


Figure S20. ^{13}C NMR spectrum (75 MHz, CDCl_3 , 300 K) of MDMB-CHMICA (**19**).

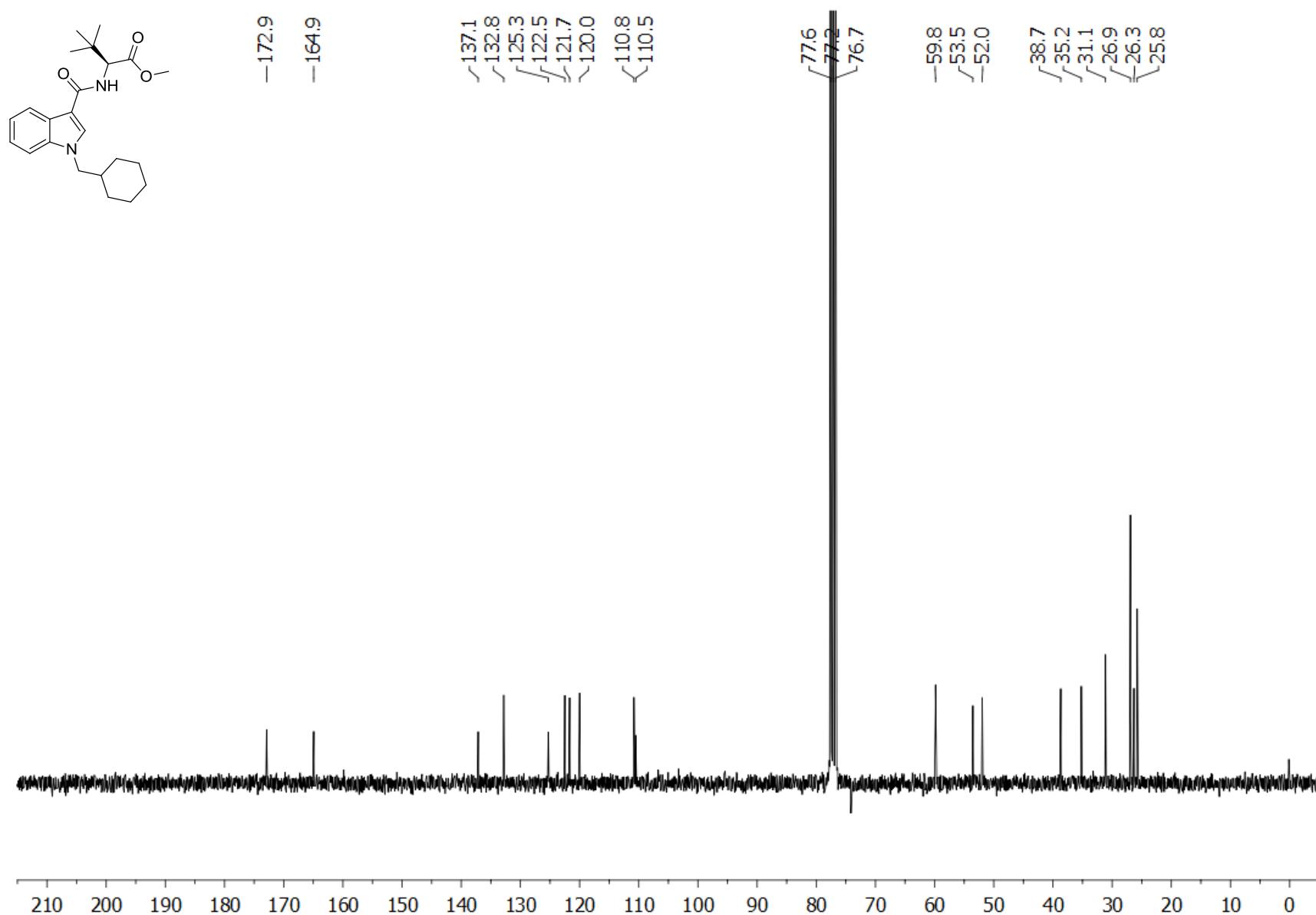


Figure S21. ^1H NMR spectrum (300 MHz, CDCl_3 , 300 K) of AMB-CHMINACA (**20**).

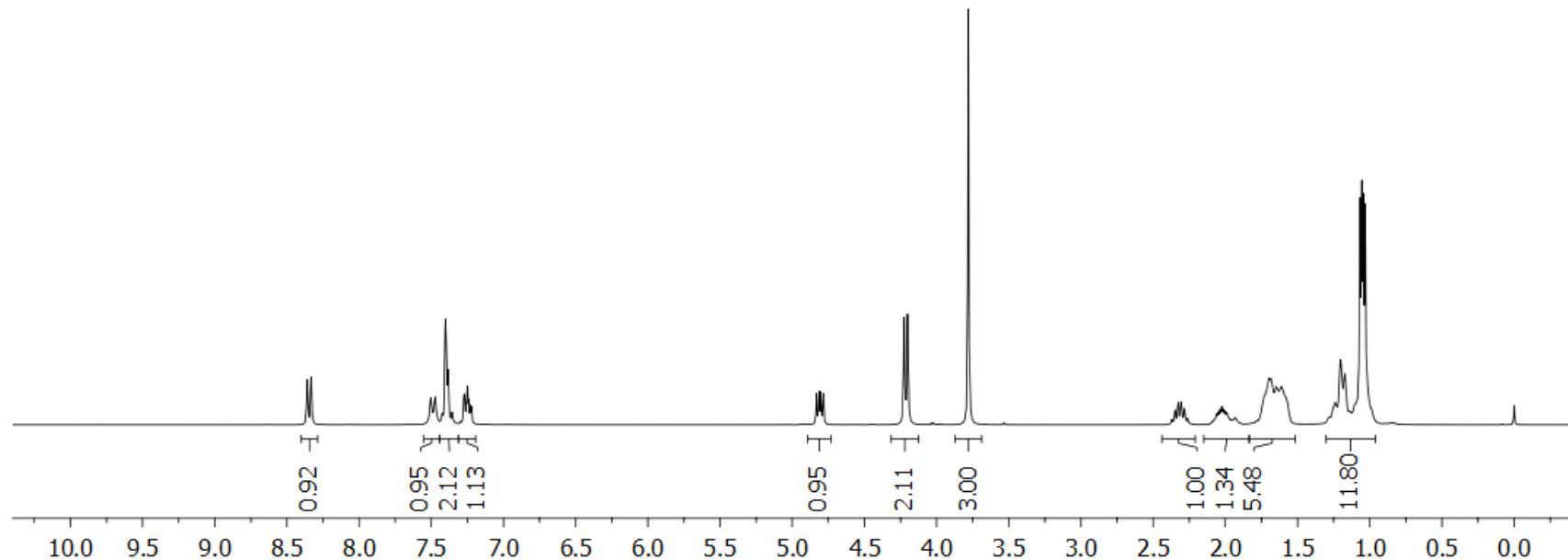
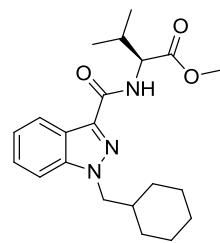


Figure S22. ^{13}C NMR spectrum (75 MHz, CDCl_3 , 300 K) of AMB-CHMINACA (**20**).

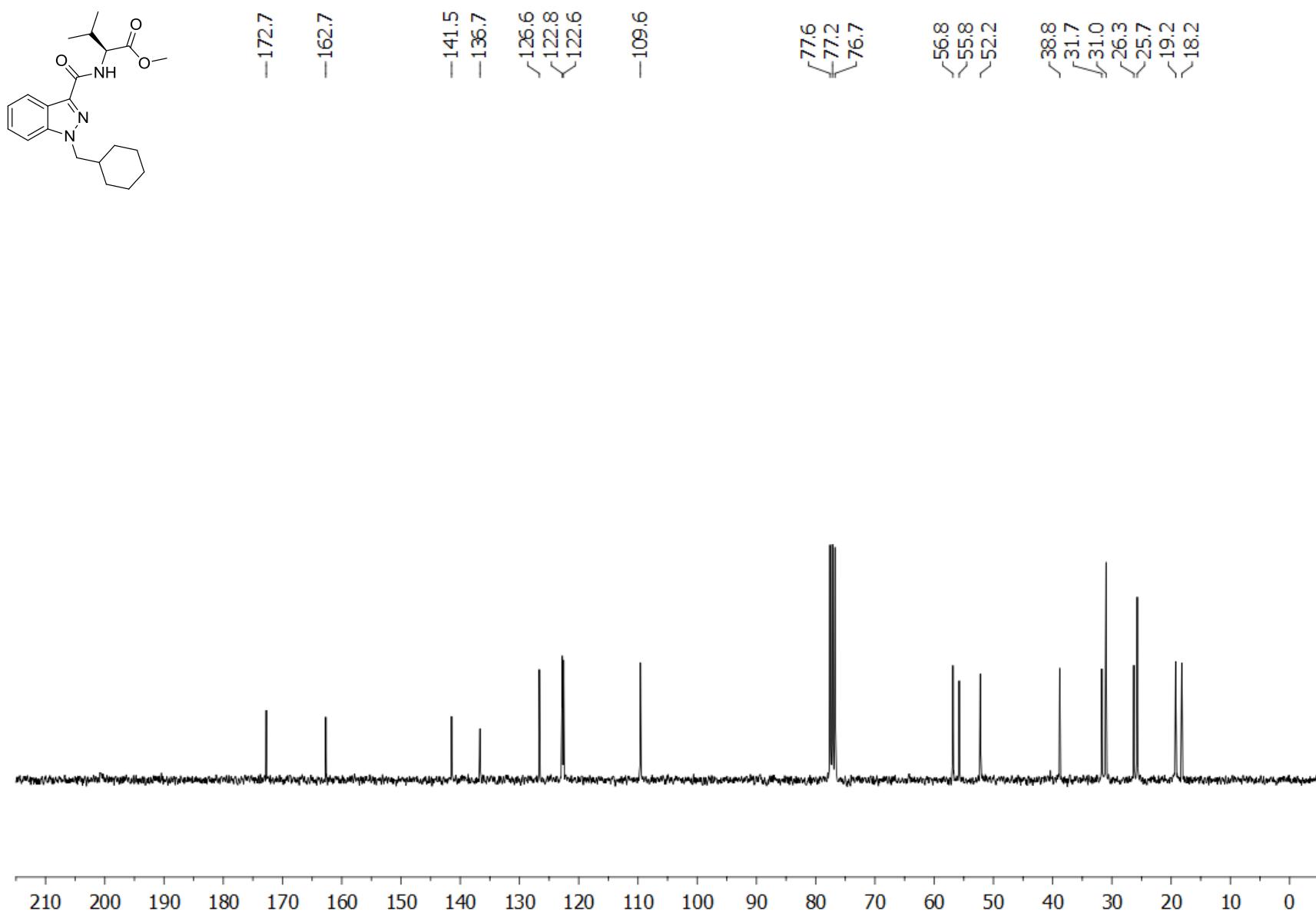


Figure S23. ^1H NMR spectrum (300 MHz, CDCl_3 , 300 K) of MDMB-CHMINACA (**21**).

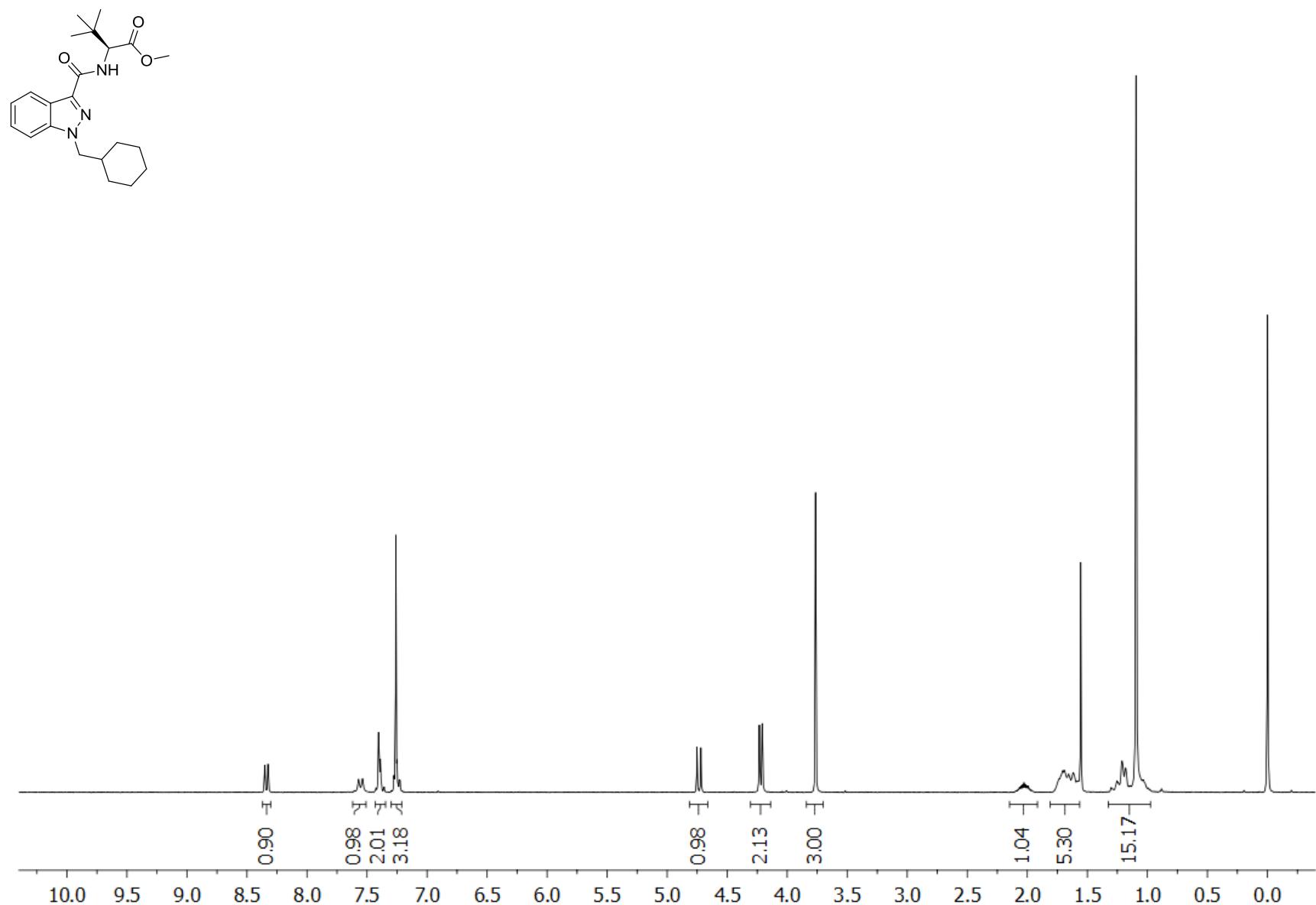


Figure S24. ^{13}C NMR spectrum (75 MHz, CDCl_3 , 300 K) of MDMB-CHMINACA (**21**).

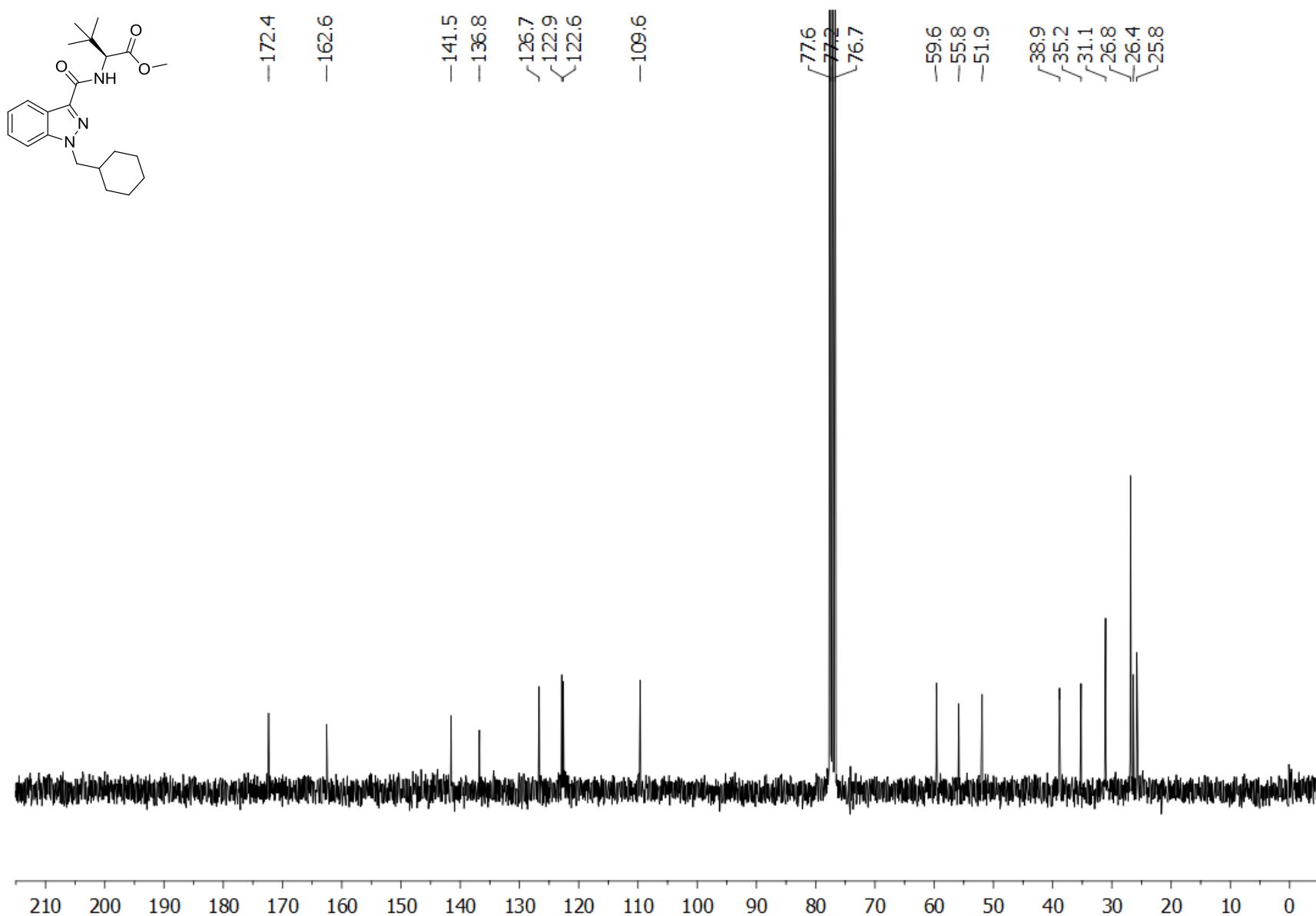


Figure S25. ^1H NMR spectrum (300 MHz, CDCl_3 , 300 K) of AMB-PICA (**22**).

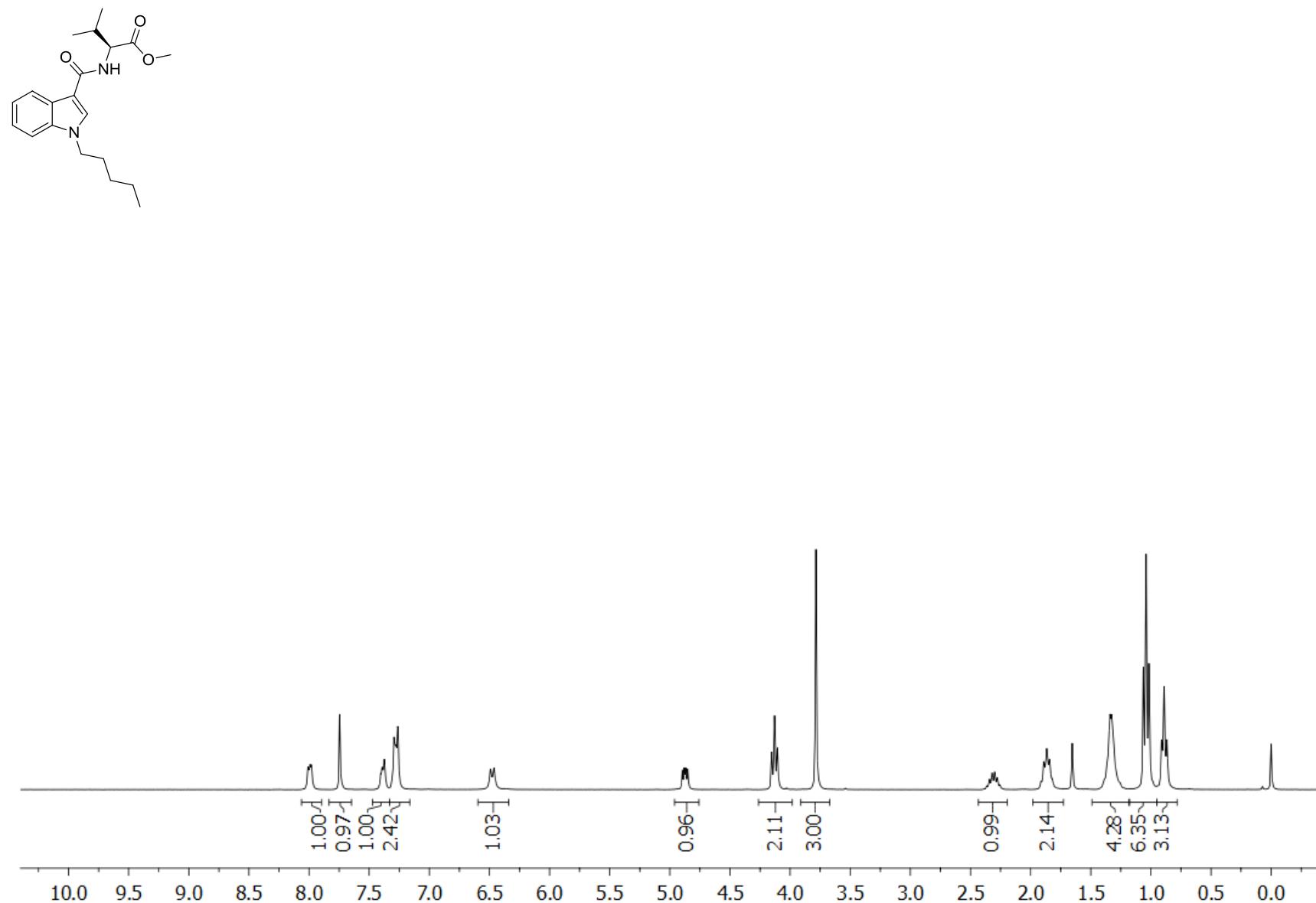


Figure S26. ^{13}C NMR spectrum (75 MHz, CDCl_3 , 300 K) of AMB-PICA (**22**).

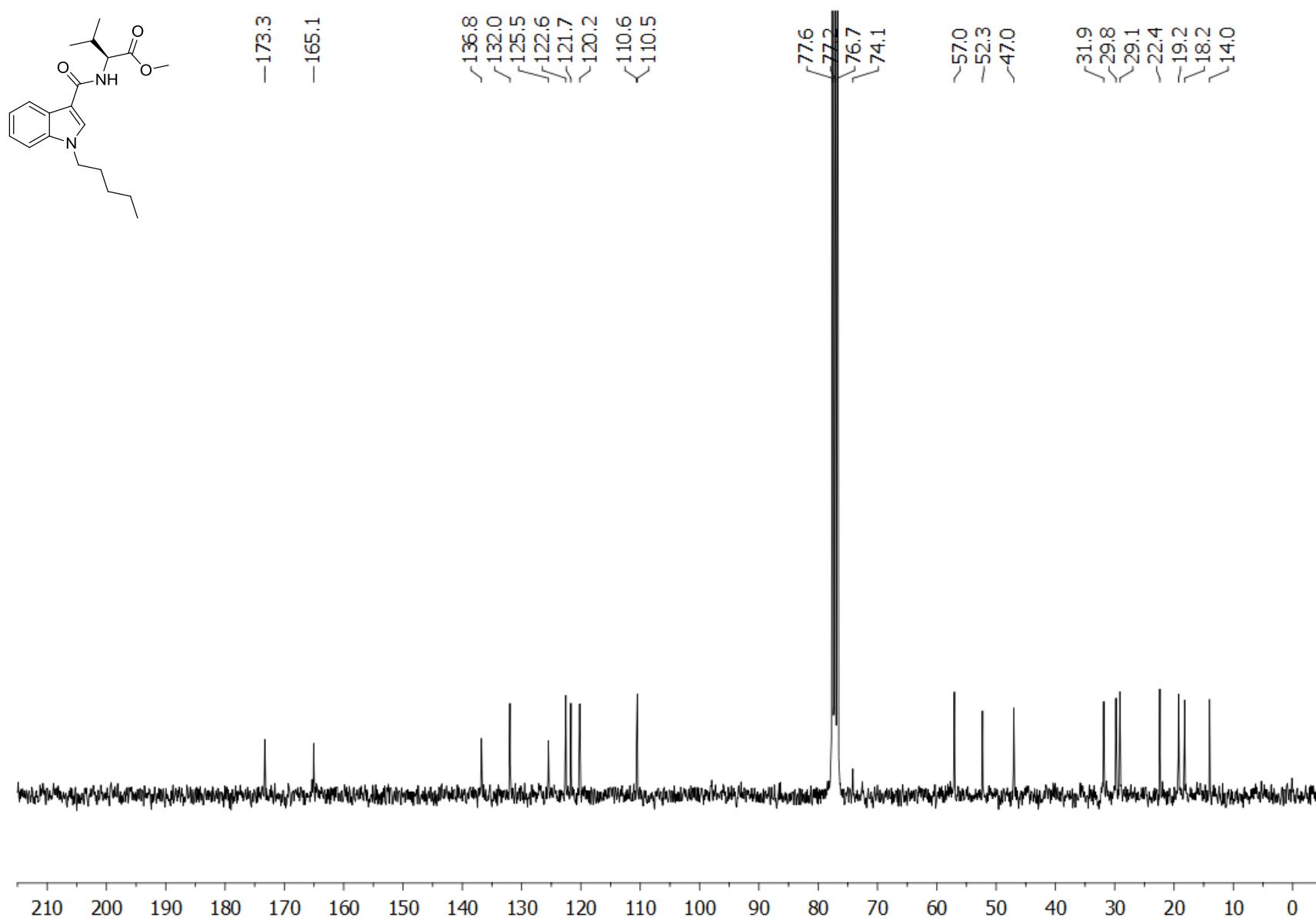


Figure S27. ^1H NMR spectrum (300 MHz, CDCl_3 , 300 K) of MDMB-PICA (**23**).

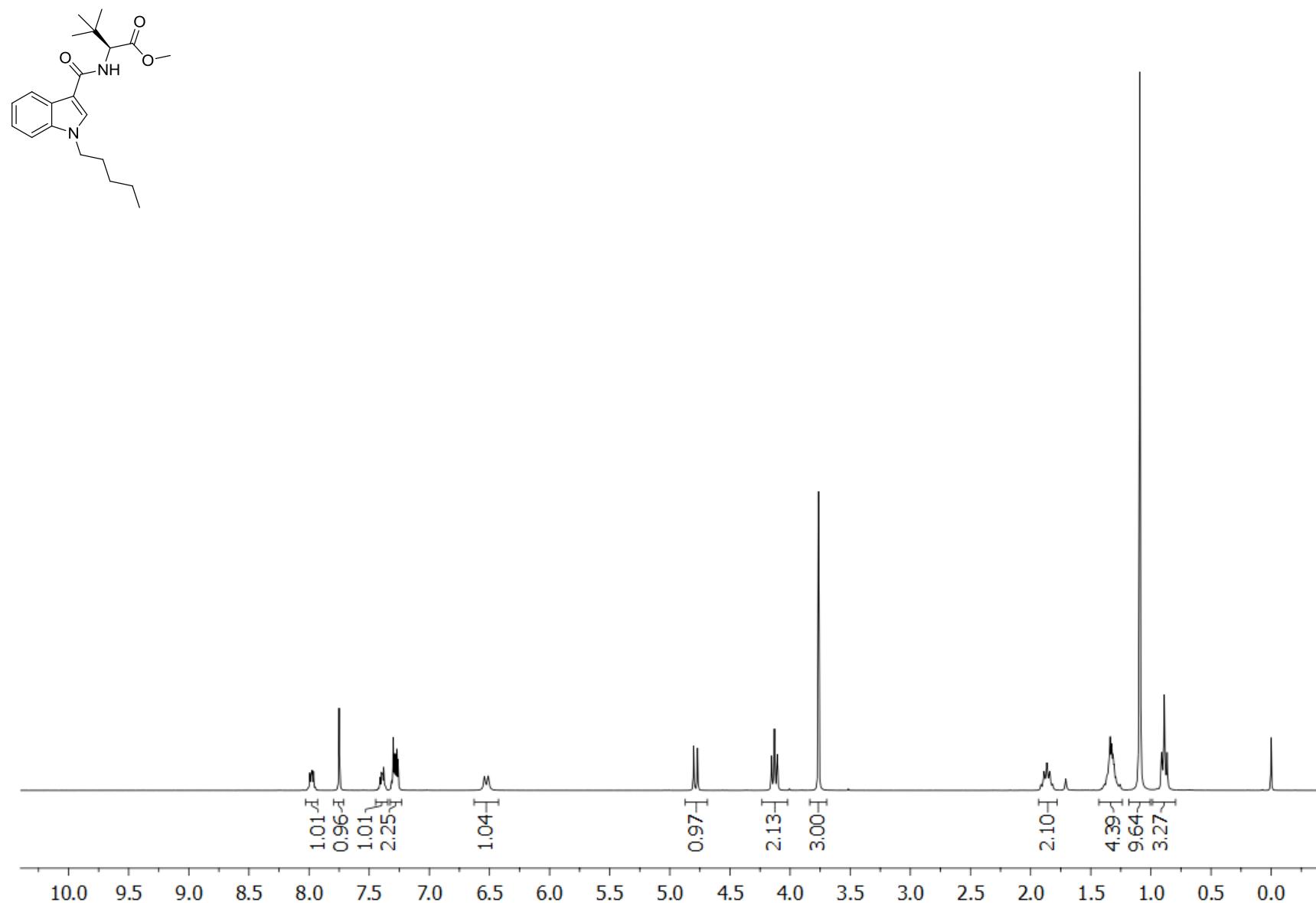


Figure S28. ^{13}C NMR spectrum (75 MHz, CDCl_3 , 300 K) of MDMB-PICA (**23**).

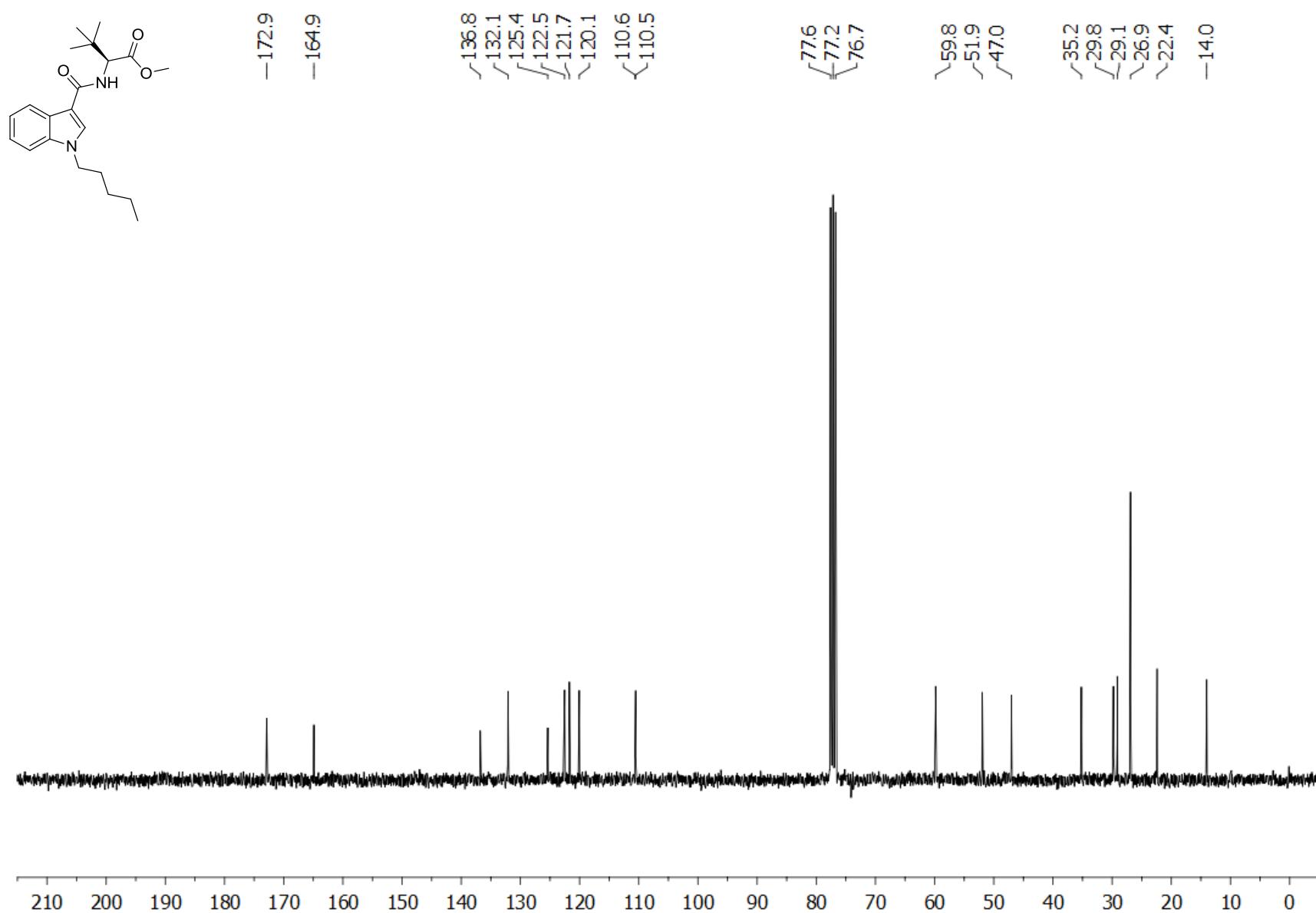


Figure S29. ^1H NMR spectrum (300 MHz, CDCl_3 , 300 K) of AMB-PINACA (**24**).

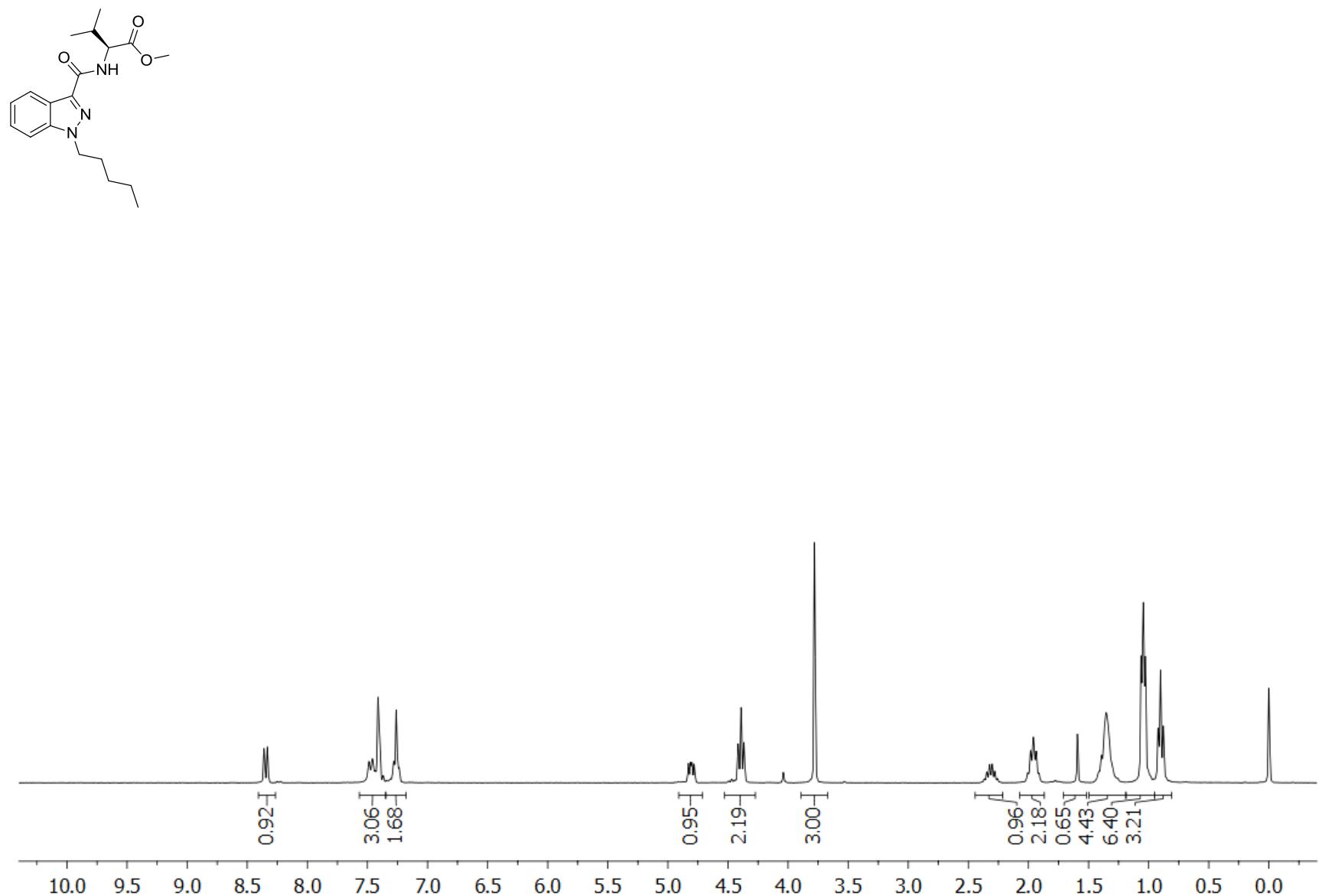


Figure S30. ^{13}C NMR spectrum (75 MHz, CDCl_3 , 300 K) of AMB-PINACA (**24**).

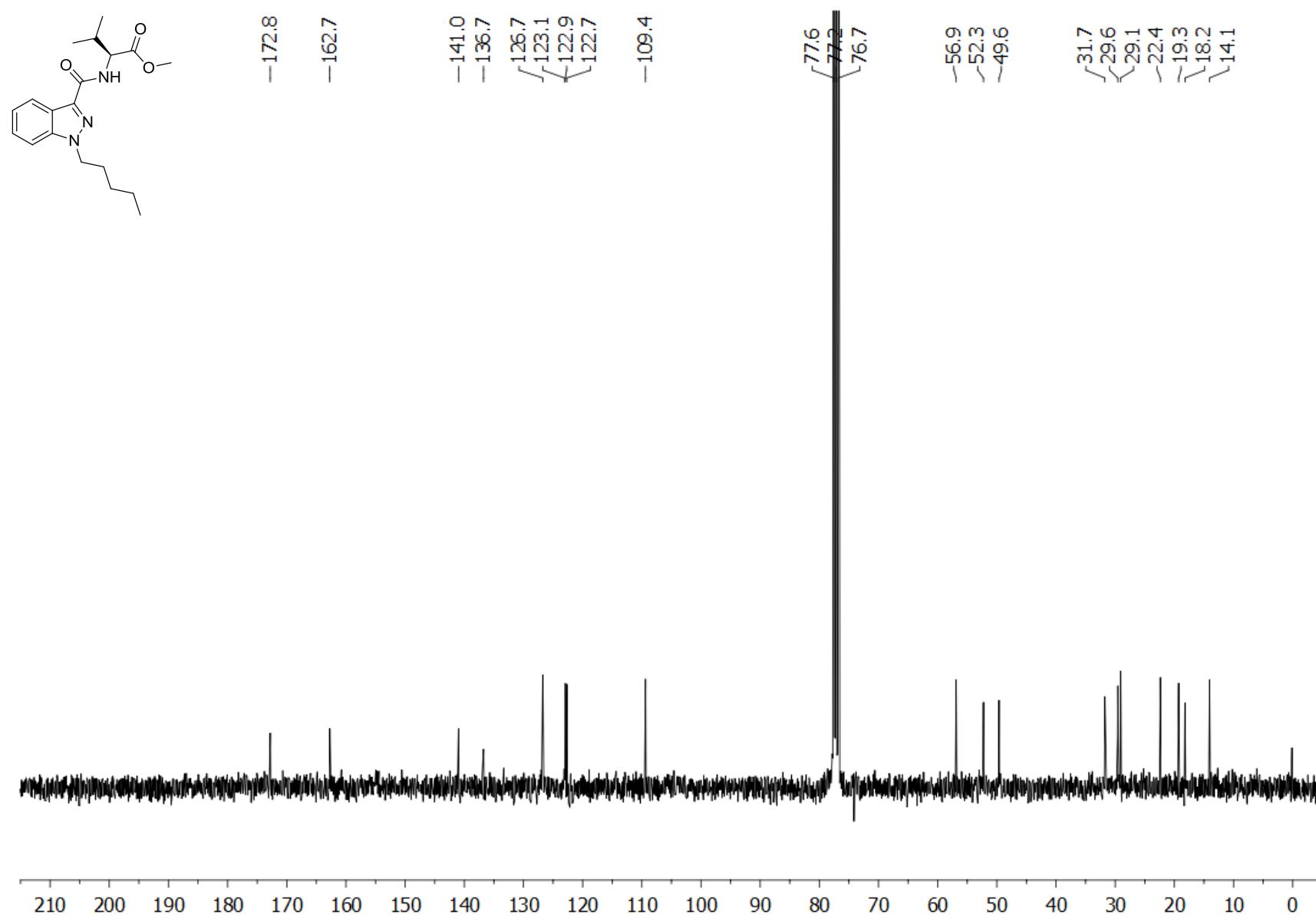


Figure S31. ^1H NMR spectrum (300 MHz, CDCl_3 , 300 K) of MDMB-PINACA (**25**).

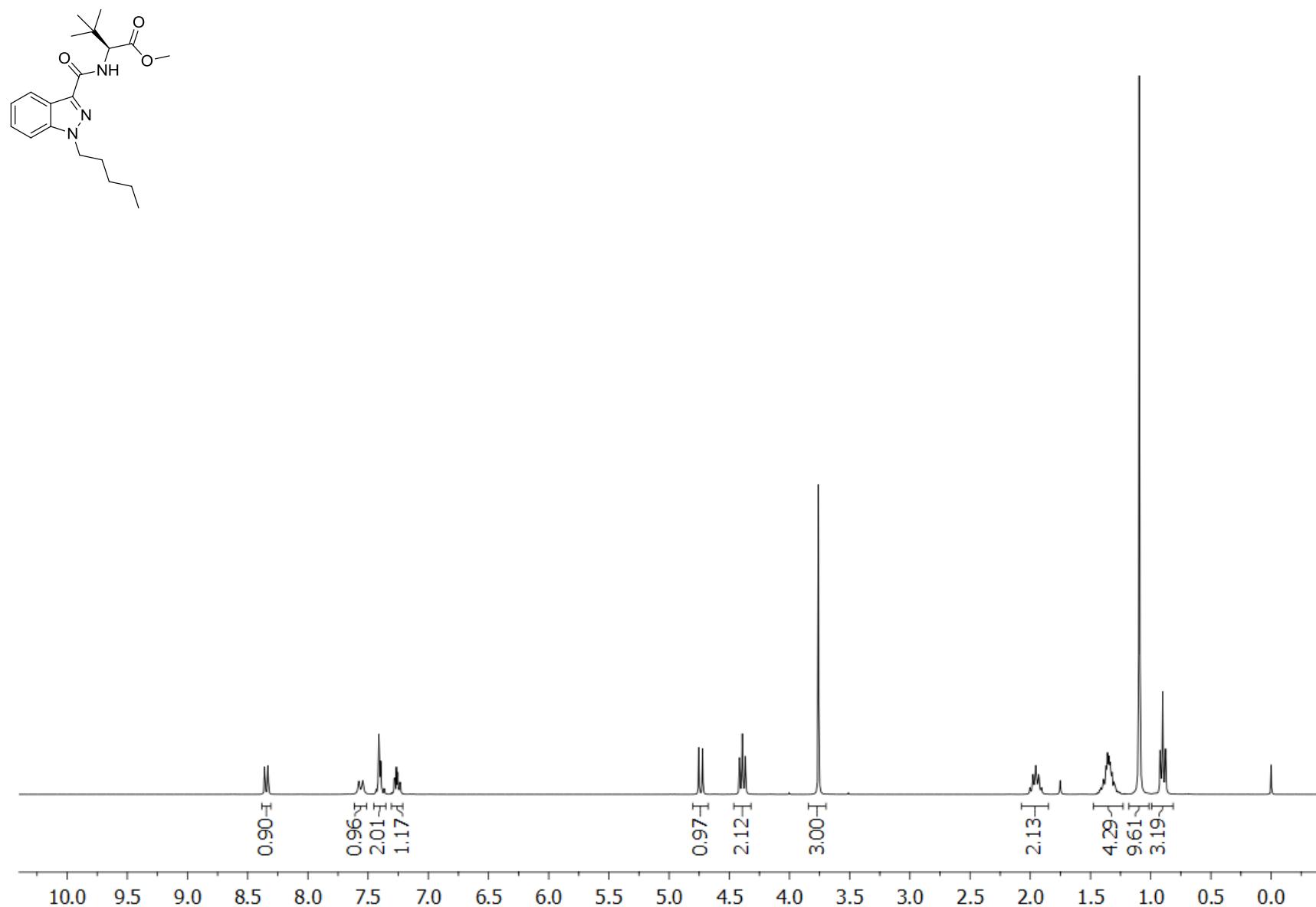


Figure S32. ^{13}C NMR spectrum (75 MHz, CDCl_3 , 300 K) of MDMB-PINACA (**25**).

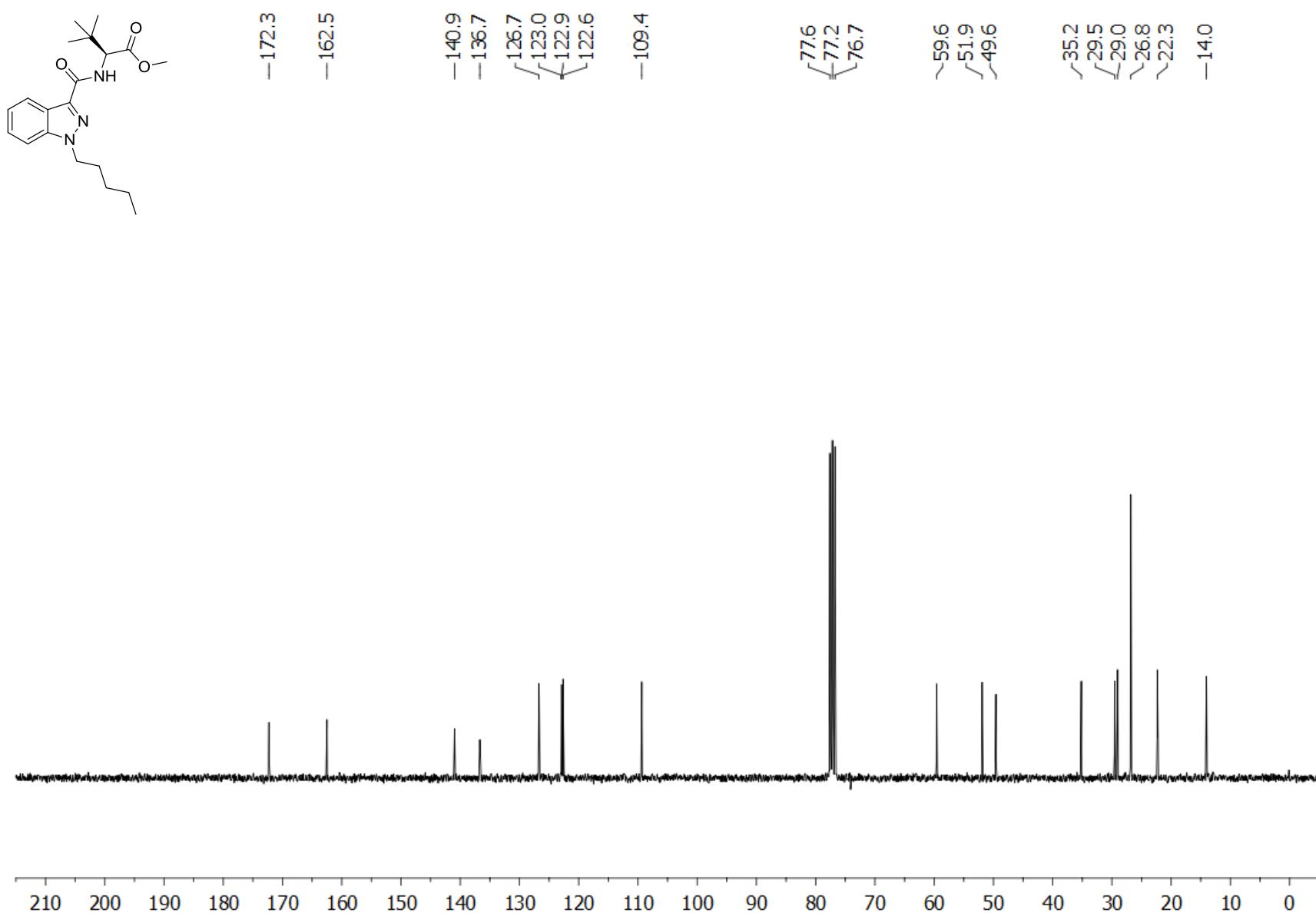


Figure S33. Mean normalized area under the vehicle baseline curve (AUC \pm SEM) for (a) body temperature and (b) heart rate over the 6 hours immediately following doses of 0.1, 0.3, and 1 mg/kg MDMB-FUBINACA and 5F-AMB. MDMB-FUBINACA produced a larger hypothermic response compared to 5F-AMB at 0.3 and 1 mg/kg. * $P < .05$.

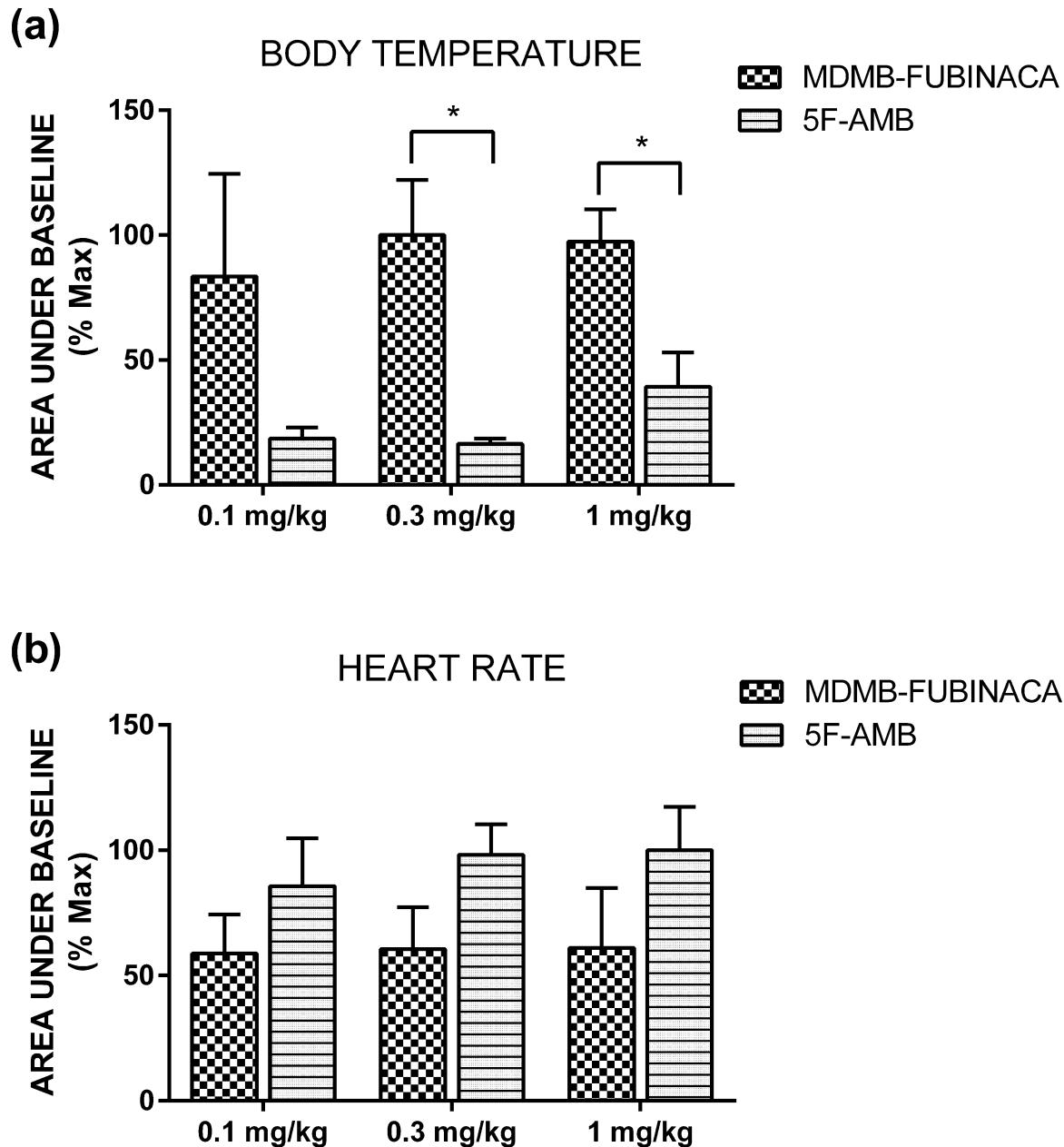


Figure S34. Body temperature data 24 hr following injection with 0.1 mg/kg MDMB-FUBINACA. Body temperature returned to baseline after 8 hr. Dashed line denotes time of intraperitoneal injection. Body temperature returned to baseline after 8 hr. Each point represents the mean \pm SEM for four animals.

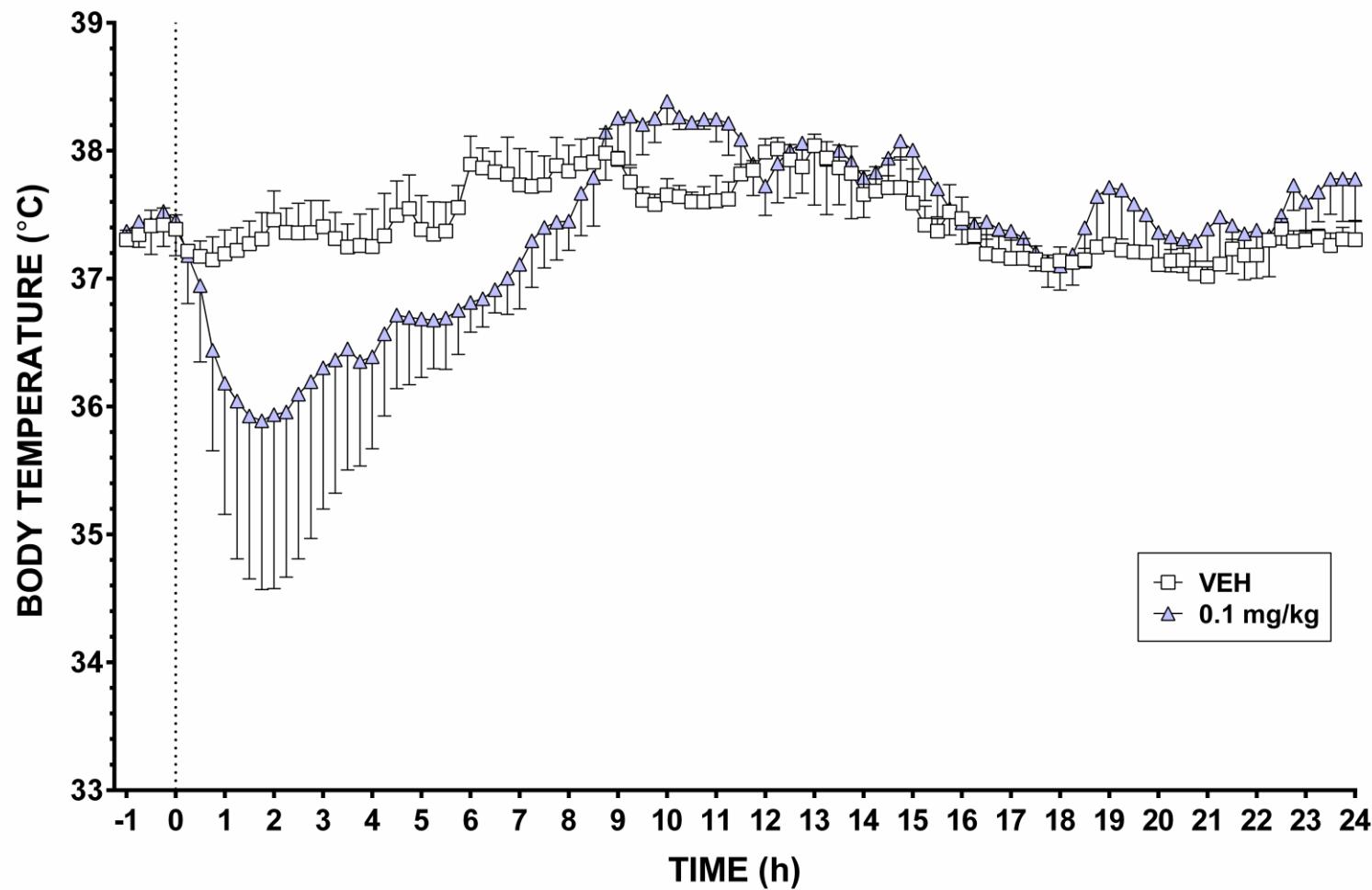


Figure S35. Mean area under the vehicle-vehicle baseline curve (AUC \pm SEM) for body temperature for (a) 5F-AMB (3 mg/kg) and (b) MDMB-FUBINACA (1 mg/kg), following pretreatment with vehicle, rimonabant (CB₁ antagonist, 3 mg/kg), or SR144528 (CB₂ antagonist, 3 mg/kg). The area was significantly reduced for both 5F-AMB and MDMB-FUBINACA by rimonabant but not SR144528. * p < .05 compared to vehicle.

