Supporting Information for

Structure-activity relationships of valine-, *tert*-leucine-, and phenylalanine amino acid-derived synthetic cannabinoid receptor agonists related to ADB-BUTINACA, APP-BUTINACA, and ADB-P7AICA

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Table S1. Reported compounds and selected identifiers.

Ms#	CAS	Synonym	SMILES
9	-	AB-BUTICA	O=C(N[C@@H](C(C)C)C(N)=O)C1=CN(CCCC)C2=CC=CC=C21
10	-	ADB-BUTICA	O=C(N[C@@H](C(C)(C)C)C(N)=O)C1=CN(CCCC)C2=CC=CC=C21
11	-	APP-BUTICA	O=C(N[C@@H](CC1=CC=CC=C1)C(N)=O)C2=CN(CCCC)C3=CC=CC=C32
12	-	AB-BUTINACA	O=C(N[C@@H](C(C)C)C(N)=O)C1=NN(CCCC)C2=CC=CC=C21
13	-	ADB-BUTINACA	O=C(N[C@@H](C(C)(C)C)C(N)=O)C1=NN(CCCC)C2=CC=CC=C21
14	-	APP-BUTINACA	O=C(N[C@@H](CC1=CC=CC=C1)C(N)=O)C2=NN(CCCC)C3=CC=CC=C32
15	-	AB-BUT7AICA	O=C(N[C@@H](C(C)C)C(N)=O)C1=CN(CCCC)C2=NC=CC=C21
16	-	ADB-BUT7AICA	O=C(N[C@@H](C(C)(C)C)C(N)=O)C1=CN(CCCC)C2=NC=CC=C21
17	-	APP-BUT7AICA	O=C(N[C@@H](CC1=CC=CC=C1)C(N)=O)C2=CN(CCCC)C3=NC=CC=C32
18	2366271-73-8	AB-P7AICA	O=C(N[C@@H](C(C)C)C(N)=O)C1=CN(CCCCC)C2=NC=CC=C21
19	2366273-07-4	ADB-P7AICA	O=C(N[C@@H](C(C)(C)C)C(N)=O)C1=CN(CCCCC)C2=NC=CC=C21
20	-	APP-P7AICA	O=C(N[C@@H](CC1=CC=CC=C1)C(N)=O)C2=CN(CCCCC)C3=NC=CC=C32
22	154287-01-1	-	O=C(C1=CN(CCCC)C2=C1C=CC=C2)O
24	173600-01-6	-	O=C(C1=NN(CCCC)C2=C1C=CC=C2)OC
27	-	-	O=C(C1=CN(CCCC)C2=NC=CC=C21)OC
28	-	-	O=C(C1=CN(CCCCC)C2=NC=CC=C21)OC
25	173600-11-8	-	O=C(C1=NN(CCCC)C2=C1C=CC=C2)O
29	1237067-22-9	-	O=C(C1=CN(CCCC)C2=NC=CC=C21)O
30	2366268-53-1	-	O=C(C1=CN(CCCCC)C2=NC=CC=C21)O

Figure S1. Concentration-displacement curves at the hCB1 receptor derived from the [^{3}H]CP-55,940 mediated in vitro receptor affinity assay upon the concentration-dependent stimulation with the 12 test compounds. Substances are clustered in their respective indole, indazole and butyl-7-azaindole or pentyl-7-azaindole group. Data are given as mean receptor affinity ± SEM (n = 3).

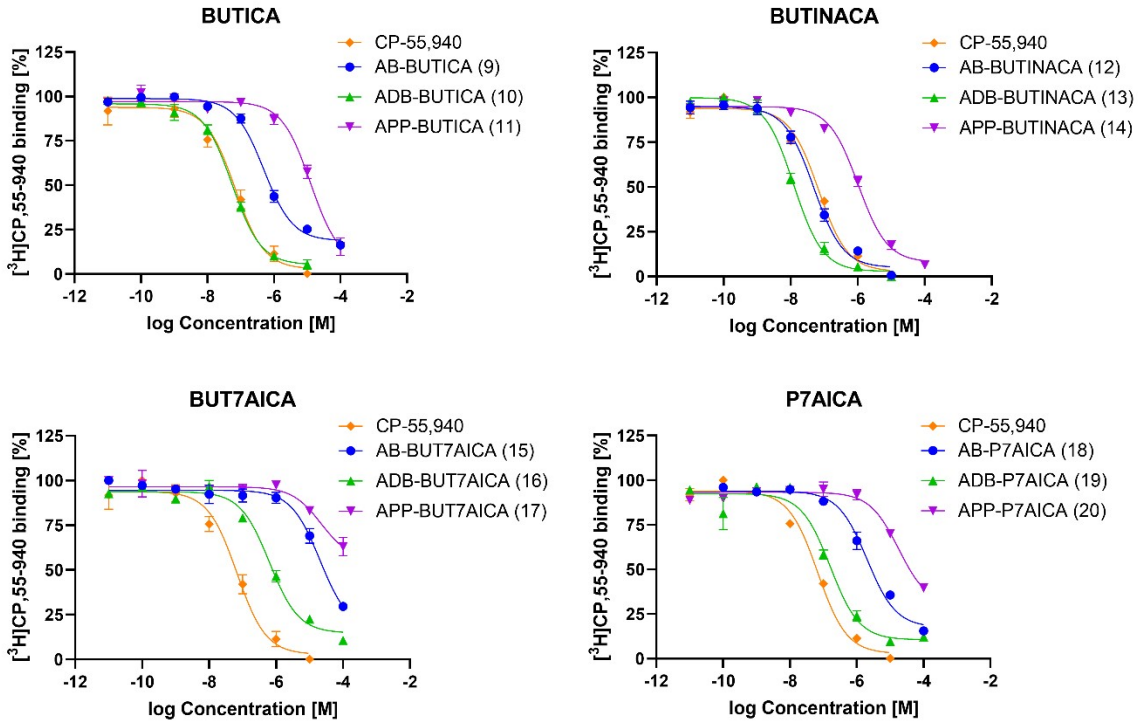

Figure S2. Electrostatic potential (ESP) map of CB1 (PDB: 6N4B) with ADB-BUT7AICA (**16**, yellow) in the binding site.

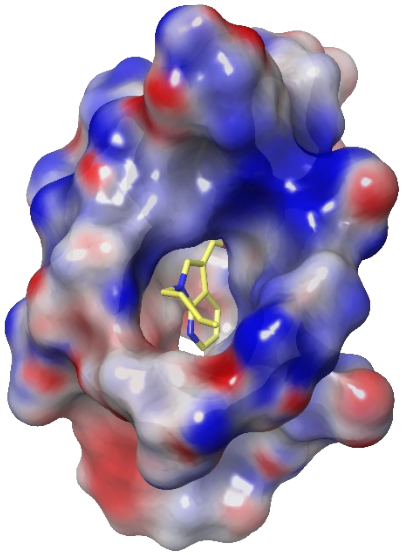

Figure S3. Electrostatic potential map of ADB-BUTICA (**10**).

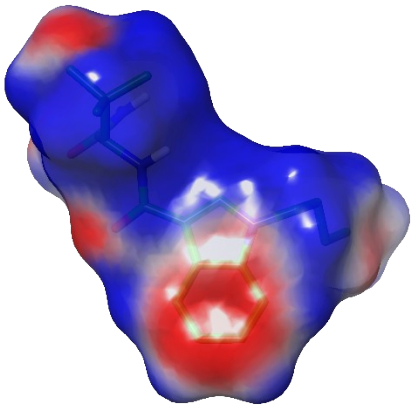

Figure S4. Electrostatic potential map of ADB-BUTINACA (**13**).

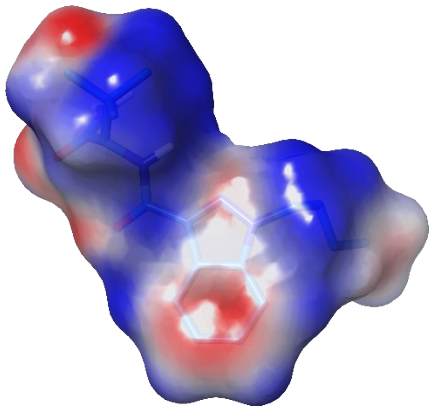

Figure S5. Electrostatic potential map of ADB-BUT7AICA (**16**).

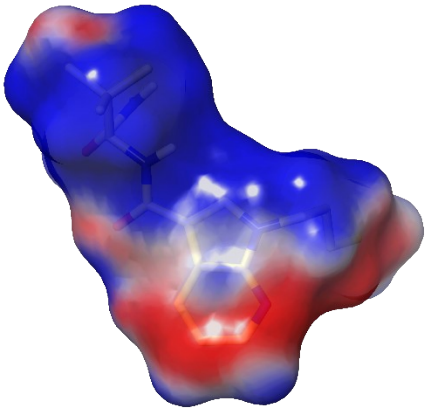

Figure S6. Electrostatic potential map of ADB-P7AICA (**19**).

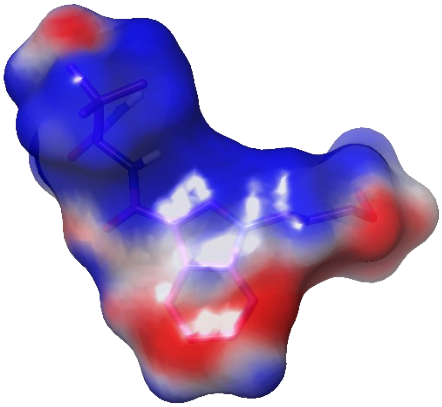

Figure S7. ^{1}H (400 MHz, DMSO-d_6) and ^{13}C (100 MHz, DMSO-d_6) NMR spectra for (*S*)-*N*-(1-amino-3-methyl-1-oxobutan-2-yl)-1-butyl-1*H*-indole-3-carboxamide (AB-BUTICA, **9**).

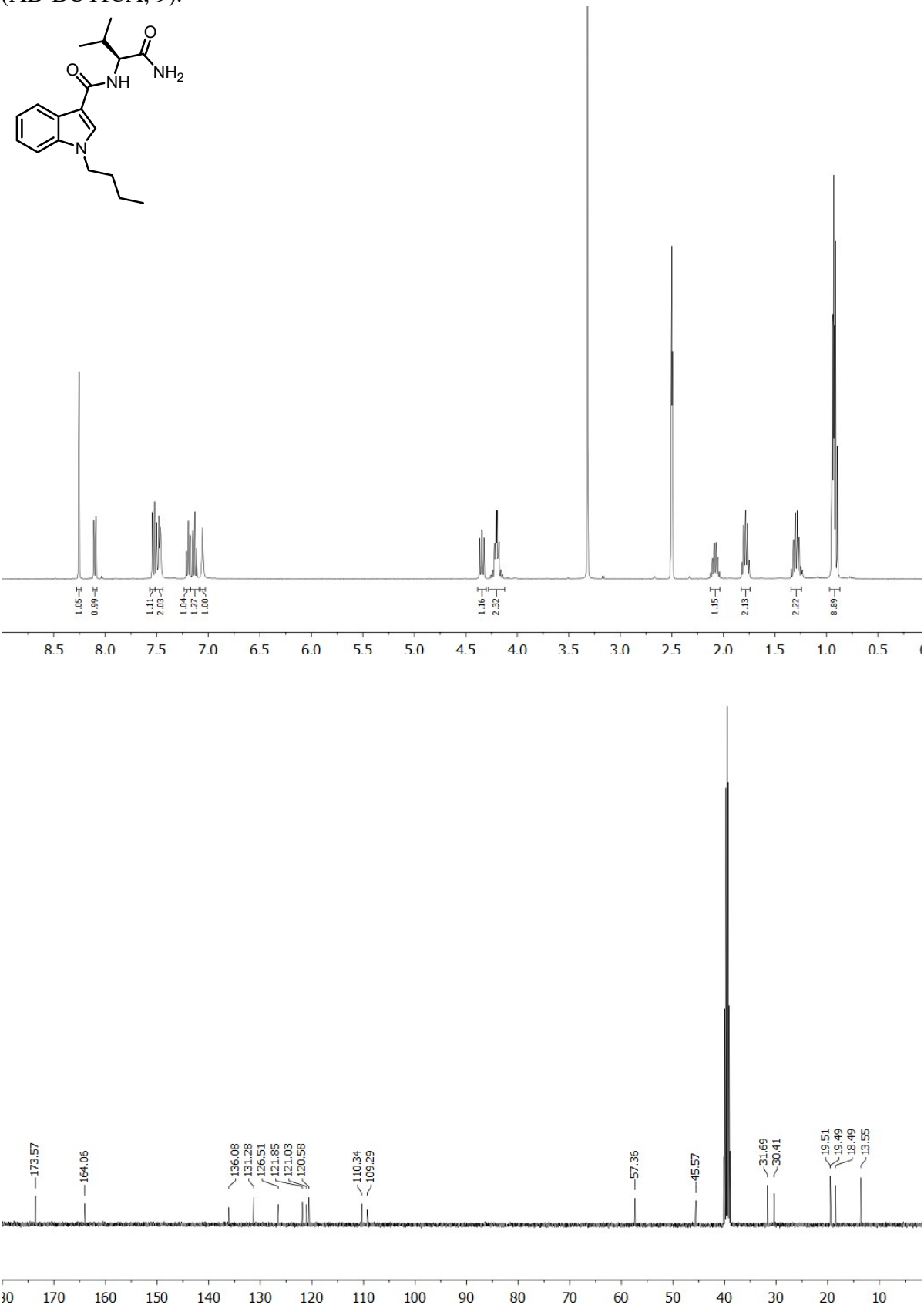

Figure S8. ^{1}H (400 MHz, DMSO-d_6) and ^{13}C (100 MHz, DMSO-d_6) NMR spectra for (*S*)-*N*-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-butyl-1*H*-indole-3-carboxamide (ADB-BUTICA, **10**).

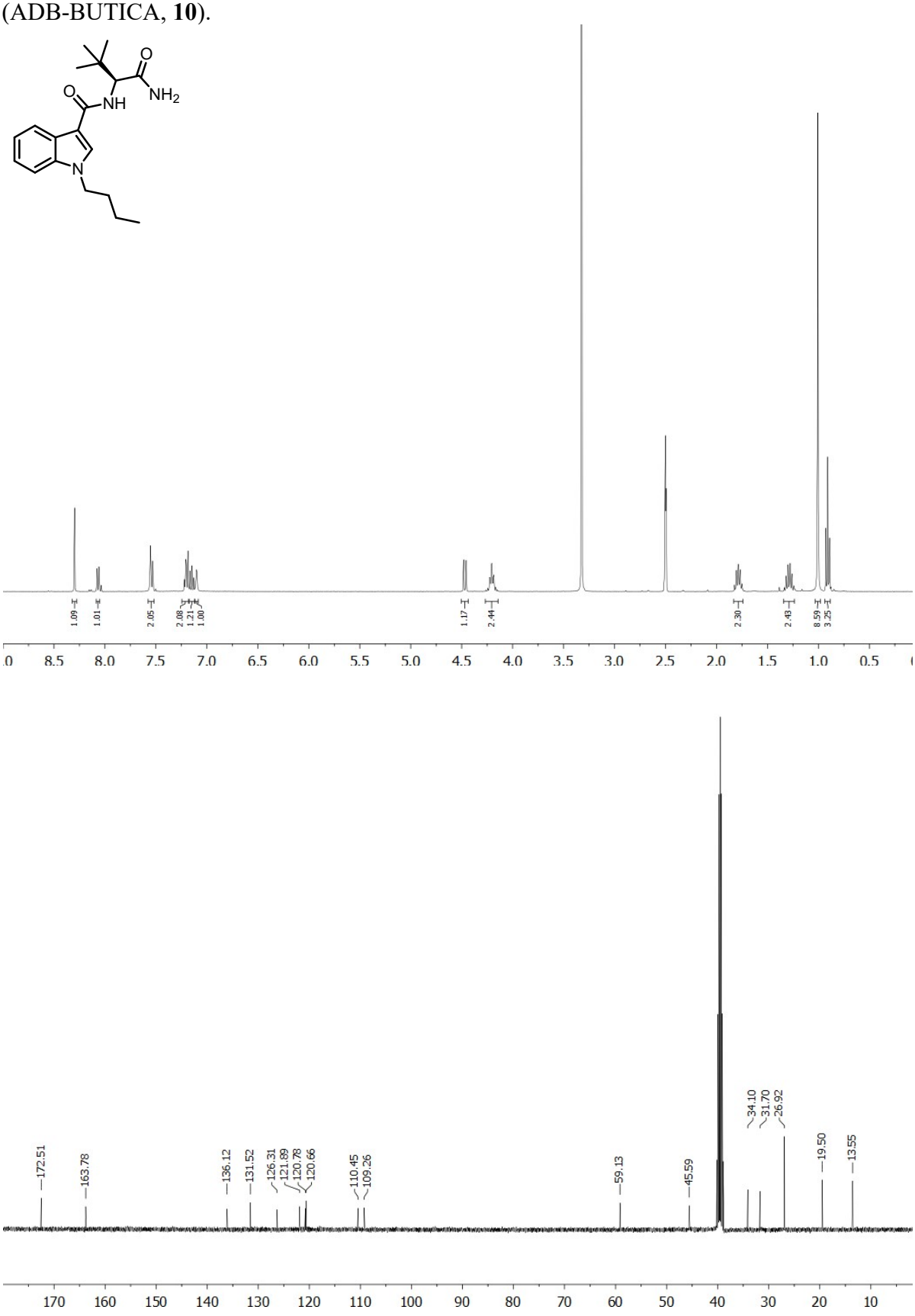

Figure S9. ^{1}H (400 MHz, DMSO-d_6) and ^{13}C (100 MHz, DMSO-d_6) NMR spectra for (*S*)-*N*-(1-amino-1-oxo-3-phenylpropan-2-yl)-1-butyl-1*H*-indole-3-carboxamide (APP-BUTICA, **11**).

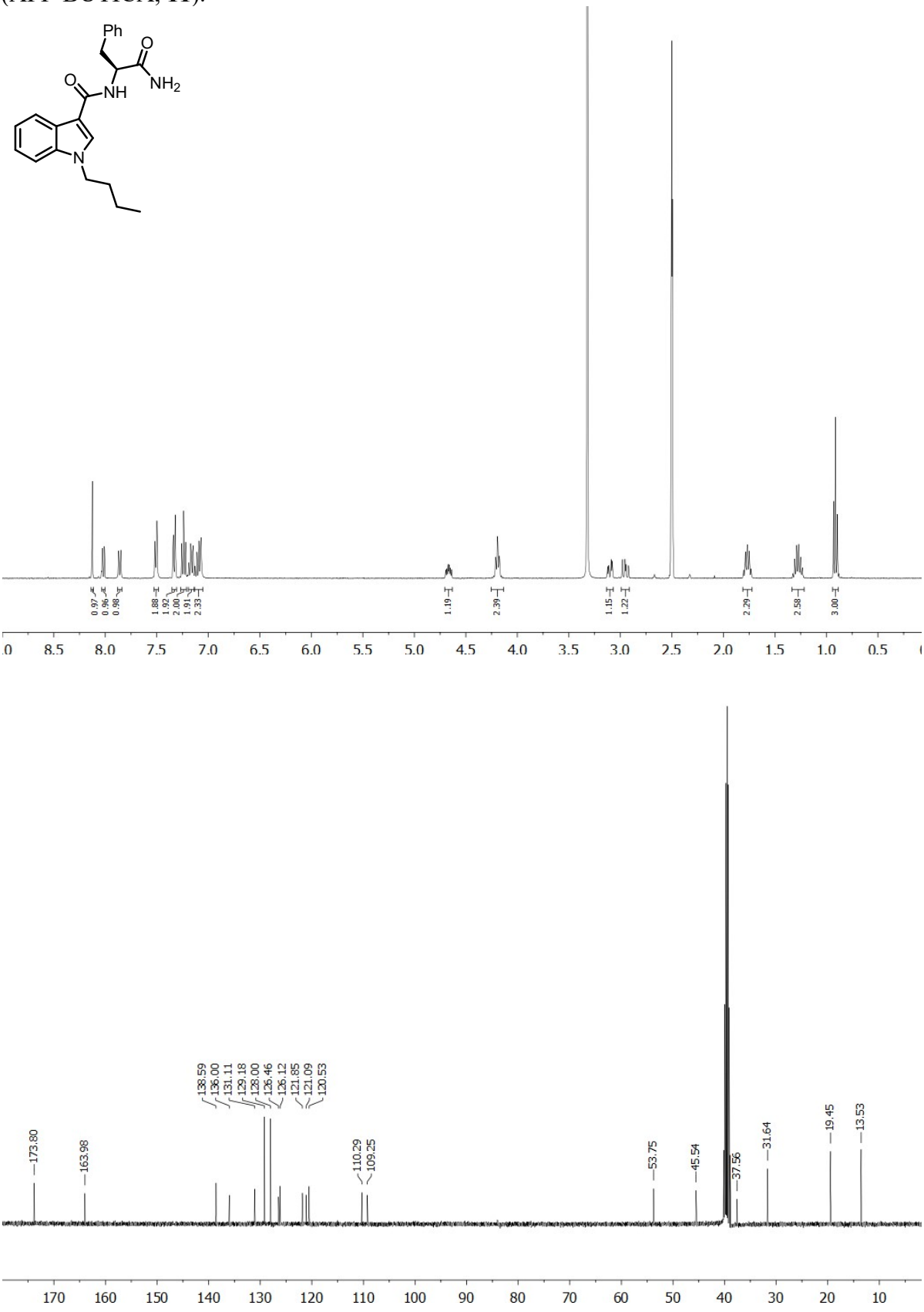

Figure S10. ^{1}H (400 MHz, DMSO-d_6) and ^{13}C (100 MHz, DMSO-d_6) NMR spectra for (*S*)-*N*-(1-amino-3-methyl-1-oxobutan-2-yl)-1-butyl-1*H*-indazole-3-carboxamide (AB-BUTINACA, **12**).

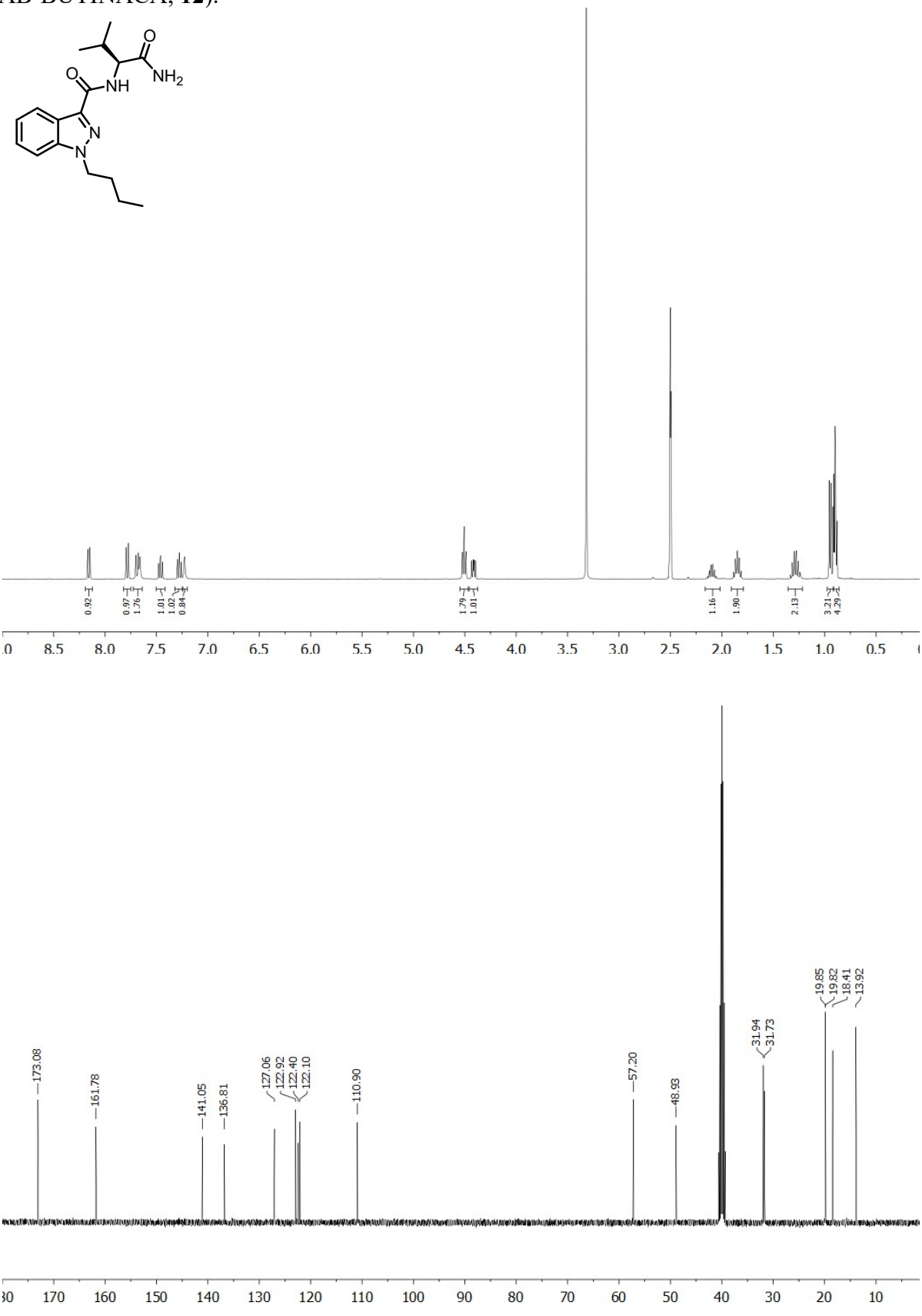

Figure S11. ^{1}H (400 MHz, DMSO-d_6) and ^{13}C (100 MHz, DMSO-d_6) NMR spectra for (*S*)-*N*-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-butyl-1*H*-indazole-3-carboxamide (ADB-BUTINACA, **13**).

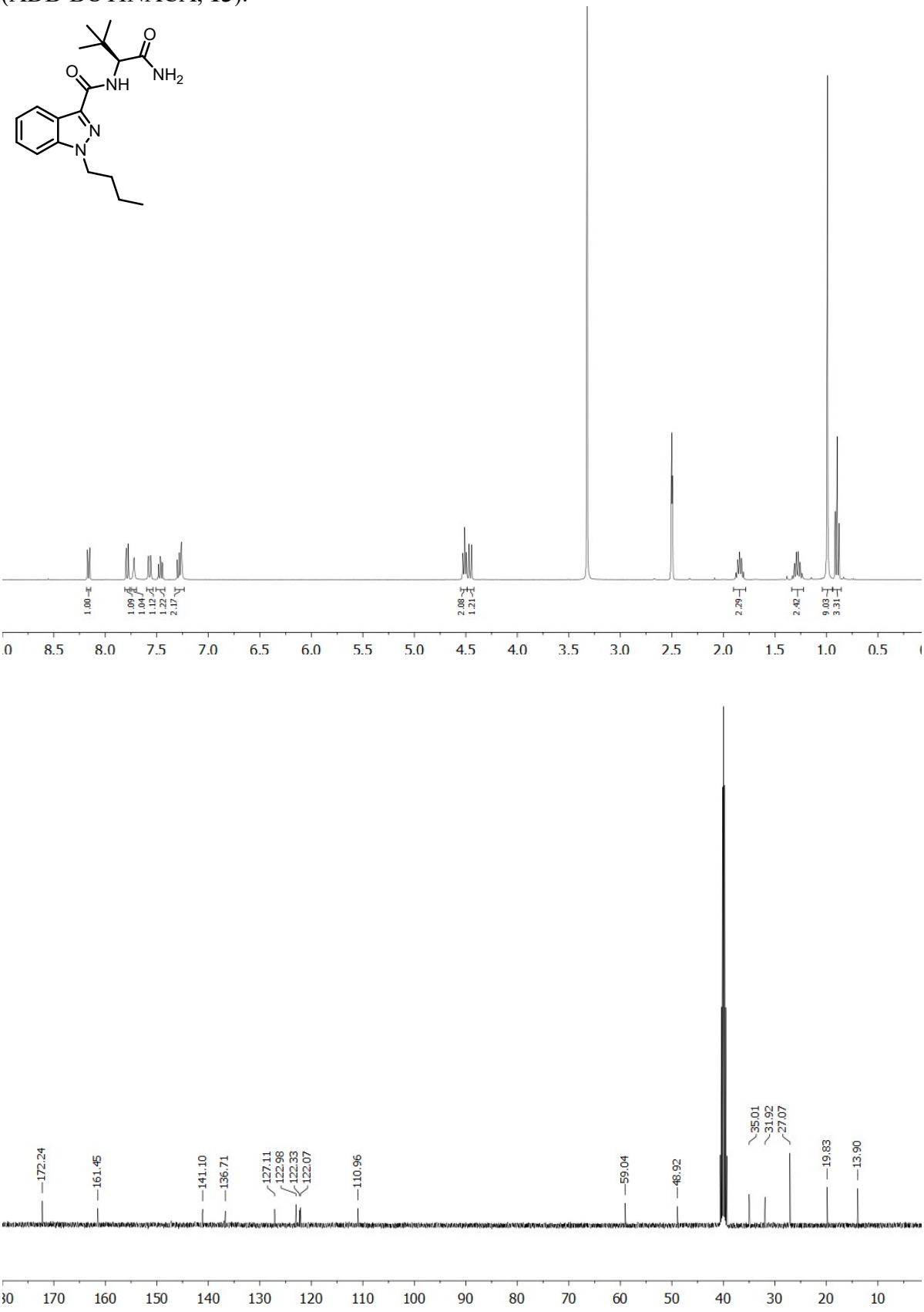

Figure S12. ^{1}H (400 MHz, $CDCl_3$) and ^{13}C (100 MHz, DMSO-d_6) NMR spectra for (*S*)-*N*-(1-amino-1-oxo-3-phenylpropan-2-yl)-1-butyl-1*H*-indazole-3-carboxamide (APP-BUTINACA, **14**).

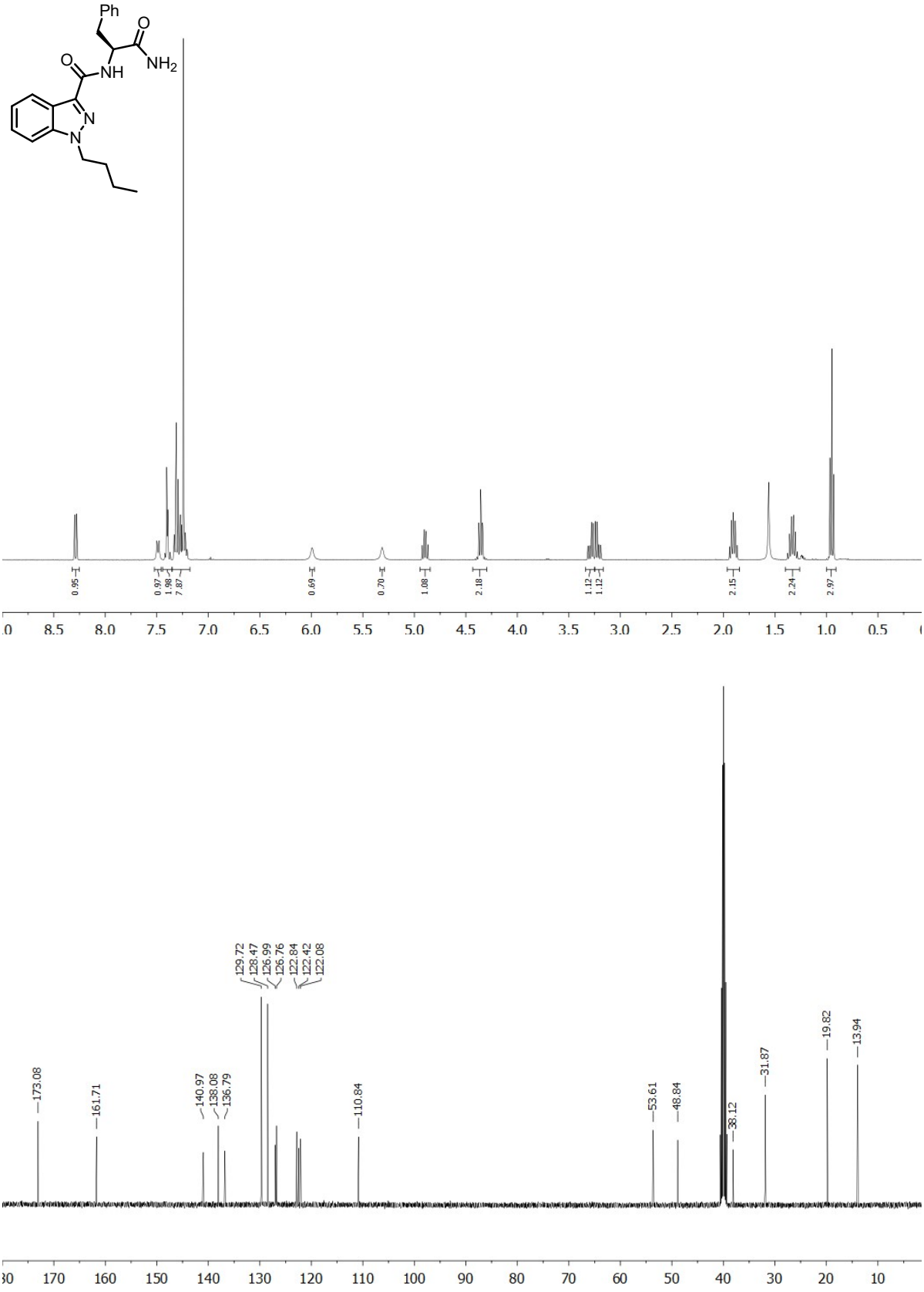

Figure S13. ^{1}H (400 MHz, DMSO-d_6) and ^{13}C (100 MHz, DMSO-d_6) NMR spectra for (*S*)-*N*-(1-amino-3-methyl-1-oxobutan-2-yl)-1-butyl-1*H*-pyrrolo[2,3-*b*]pyridine-3-carboxamide (AB-BUT7AICA, **15**).

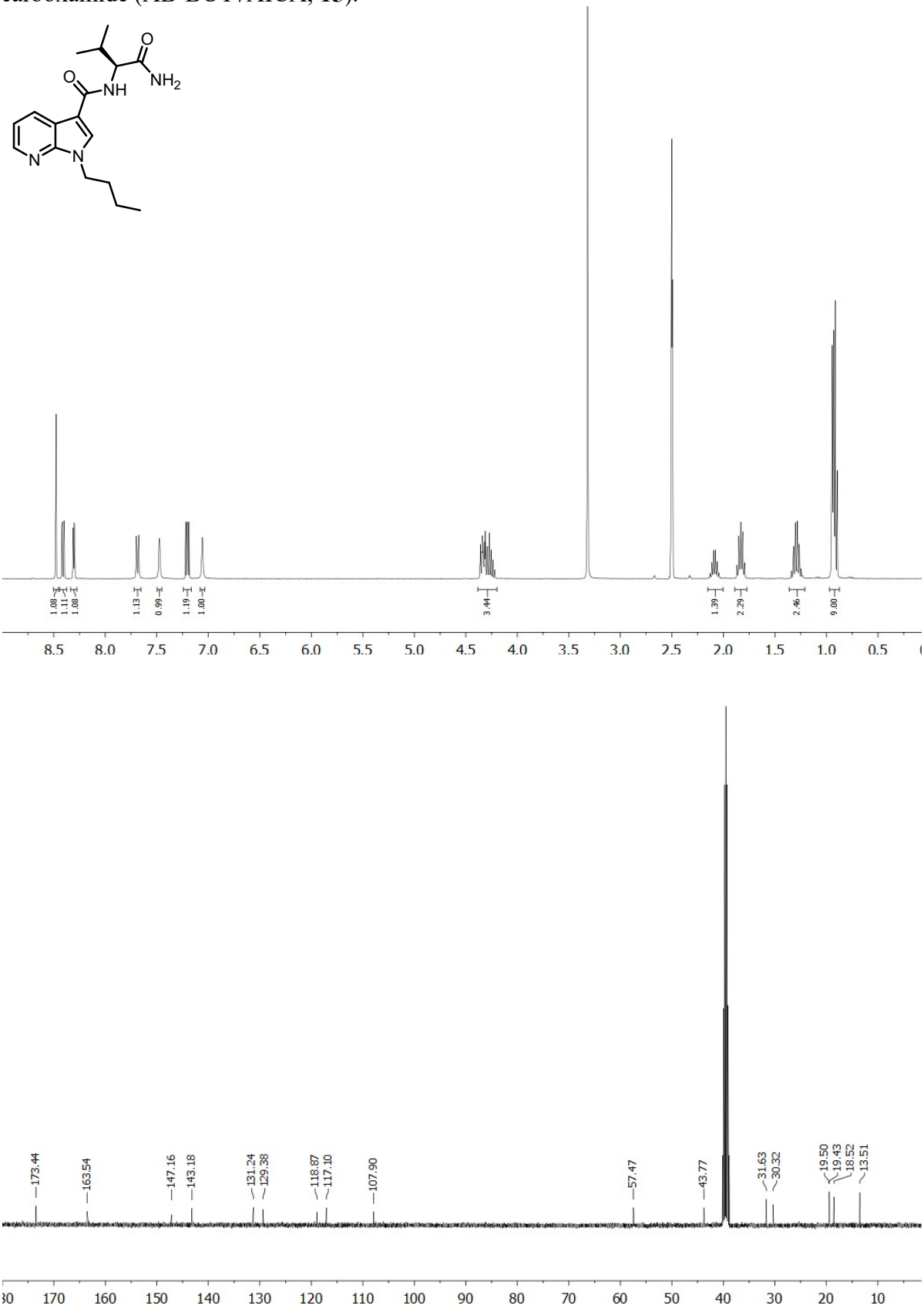

Figure S14. ^{1}H (400 MHz, DMSO-d_6) and ^{13}C (100 MHz, $CDCl_3$) NMR spectra for (*S*)-*N*-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-butyl-1*H*-pyrrolo[2,3-*b*]pyridine-3-carboxamide (ADB-BUT7AICA, **16**).

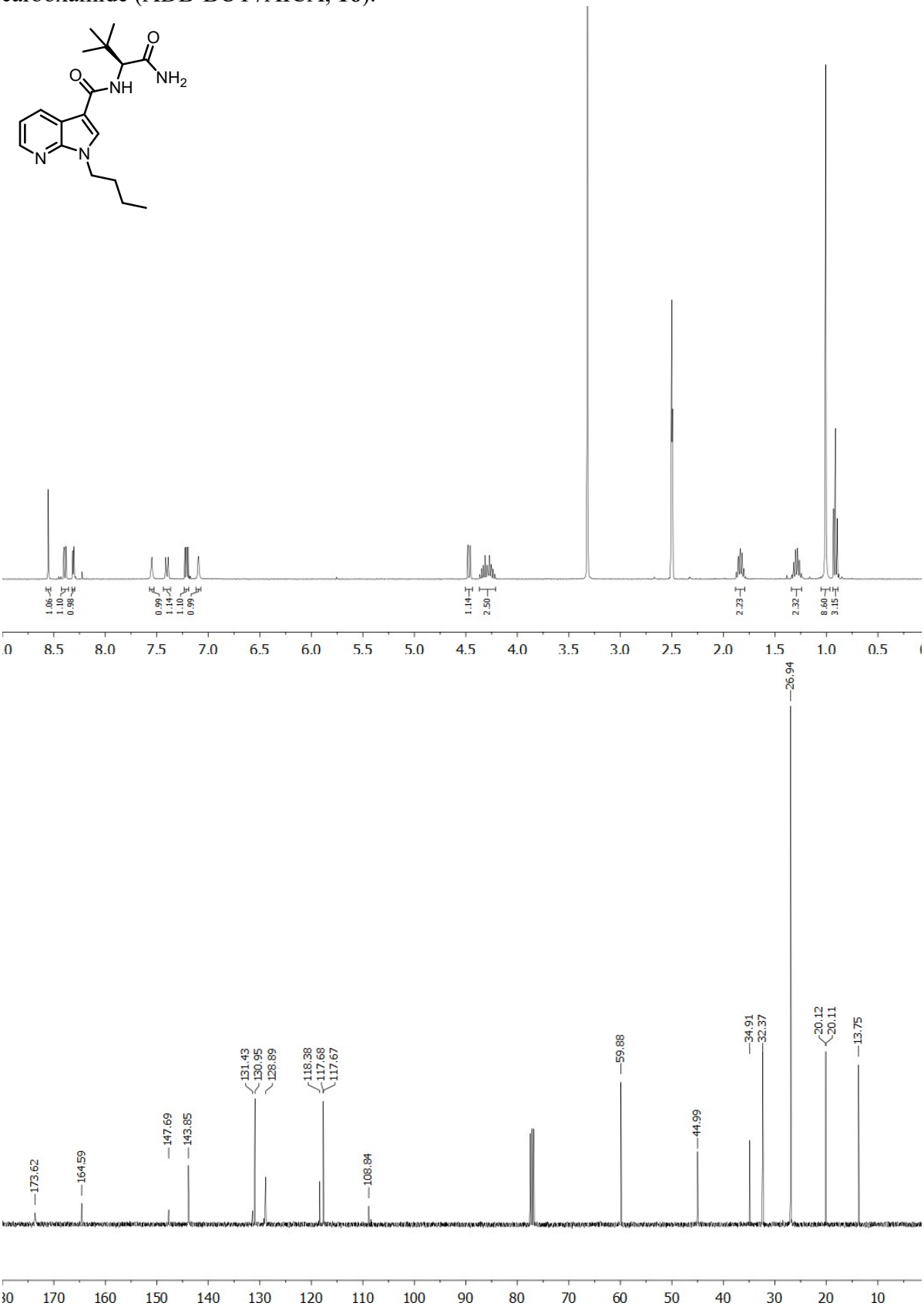

Figure S15. ^{1}H (400 MHz, $CDCl_3$) and ^{13}C (100 MHz, DMSO-d_6) NMR spectra for (*S*)-*N*-(1-amino-1-oxo-3-phenylpropan-2-yl)-1-butyl-1*H*-pyrrolo[2,3-*b*]pyridine-3-carboxamide (APP-BUT7AICA, **17**).

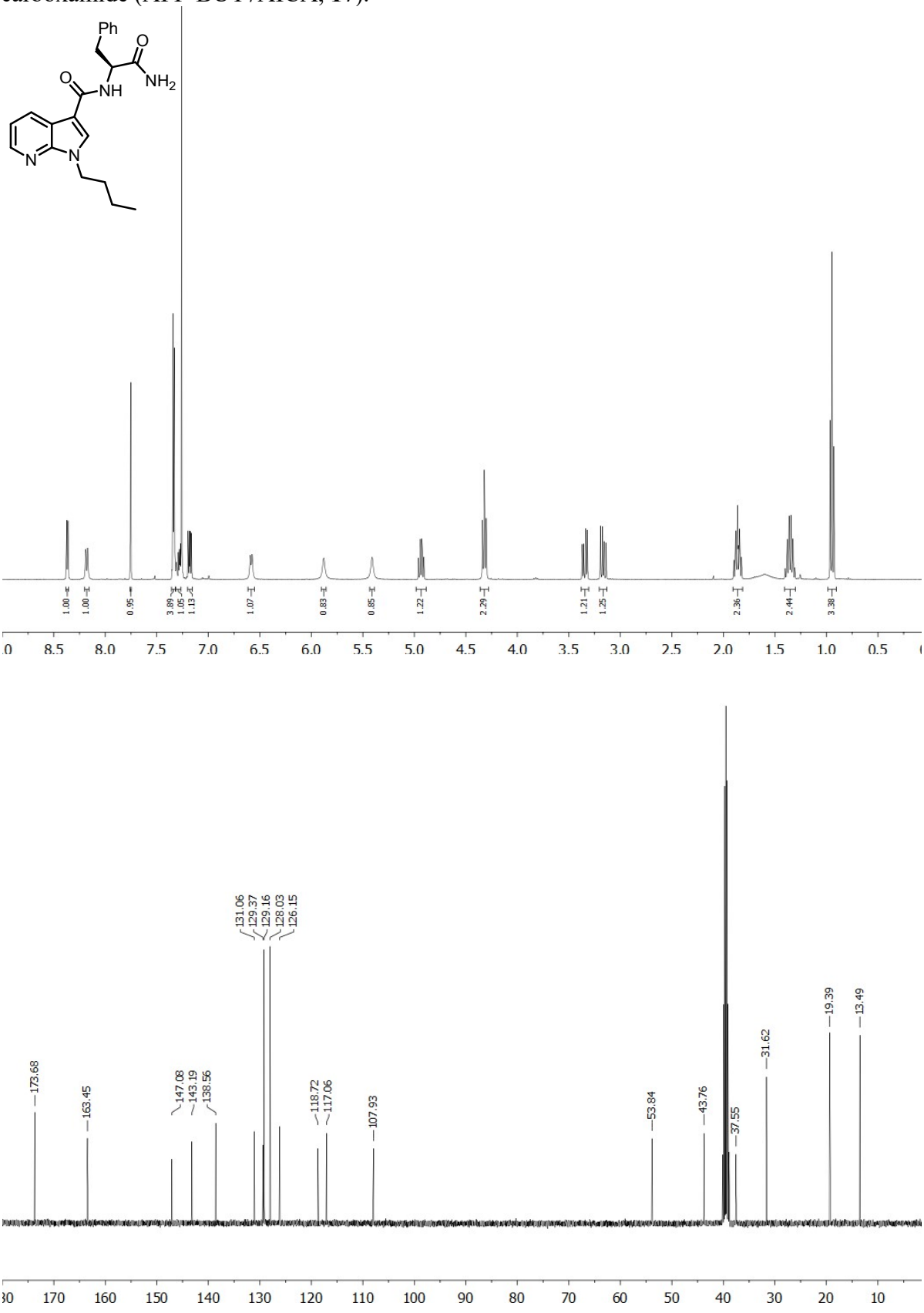

Figure S16. ^{1}H (400 MHz, DMSO-d_6) and ^{13}C (100 MHz, DMSO-d_6) NMR spectra for |(*S*)-*N*-(1-amino-3-methyl-1-oxobutan-2-yl)-1-pentyl-1*H*-pyrrolo[2,3-*b*]pyridine-3-carboxamide (AB-P7AICA, **18**).

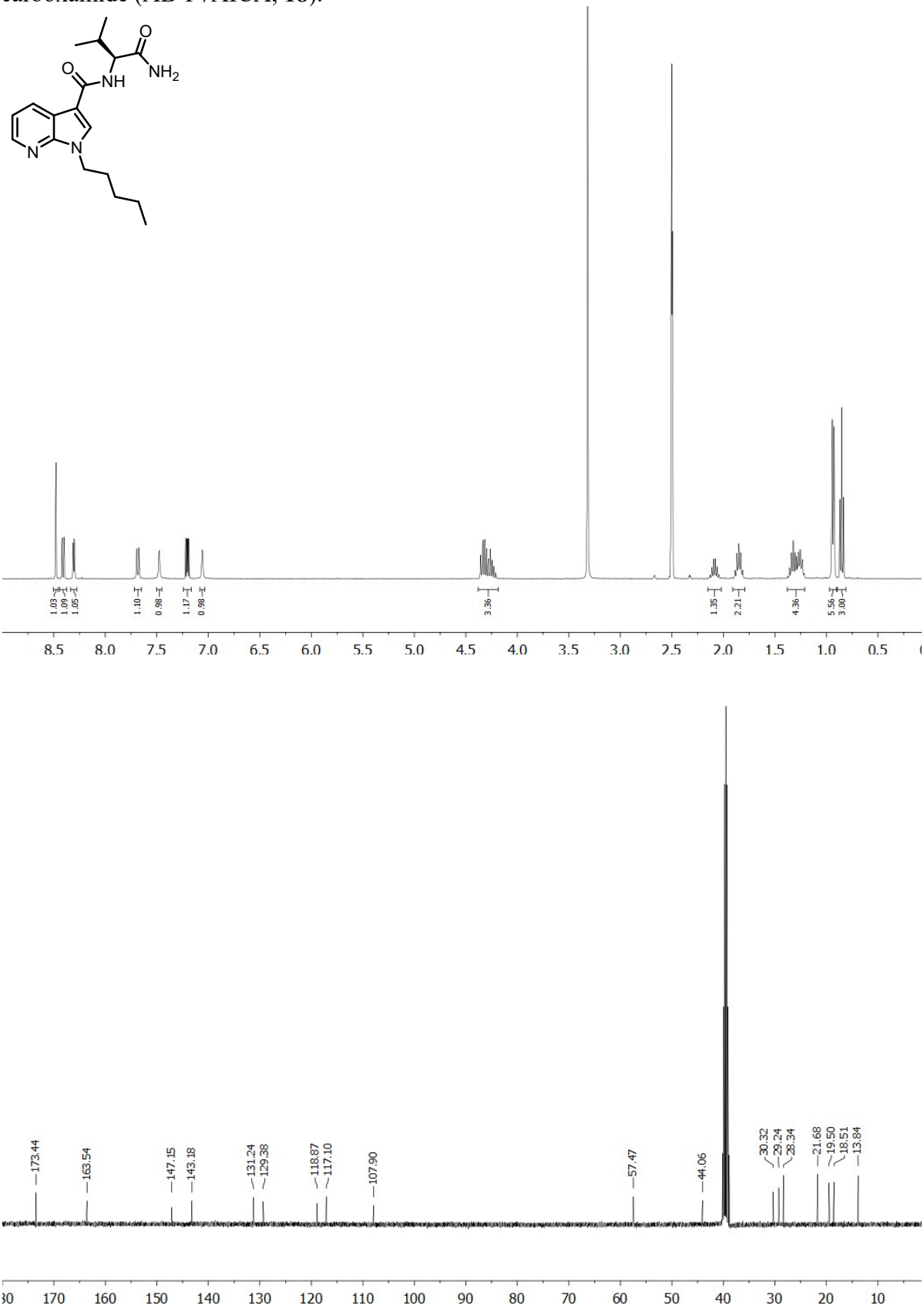

Figure S17. ^{1}H (400 MHz, $CDCl_3$) and ^{13}C (100 MHz, DMSO-d_6) NMR spectra for (*S*)-*N*-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-pentyl-1*H*-pyrrolo[2,3-*b*]pyridine-3-carboxamide (ADB-P7AICA, **19**).

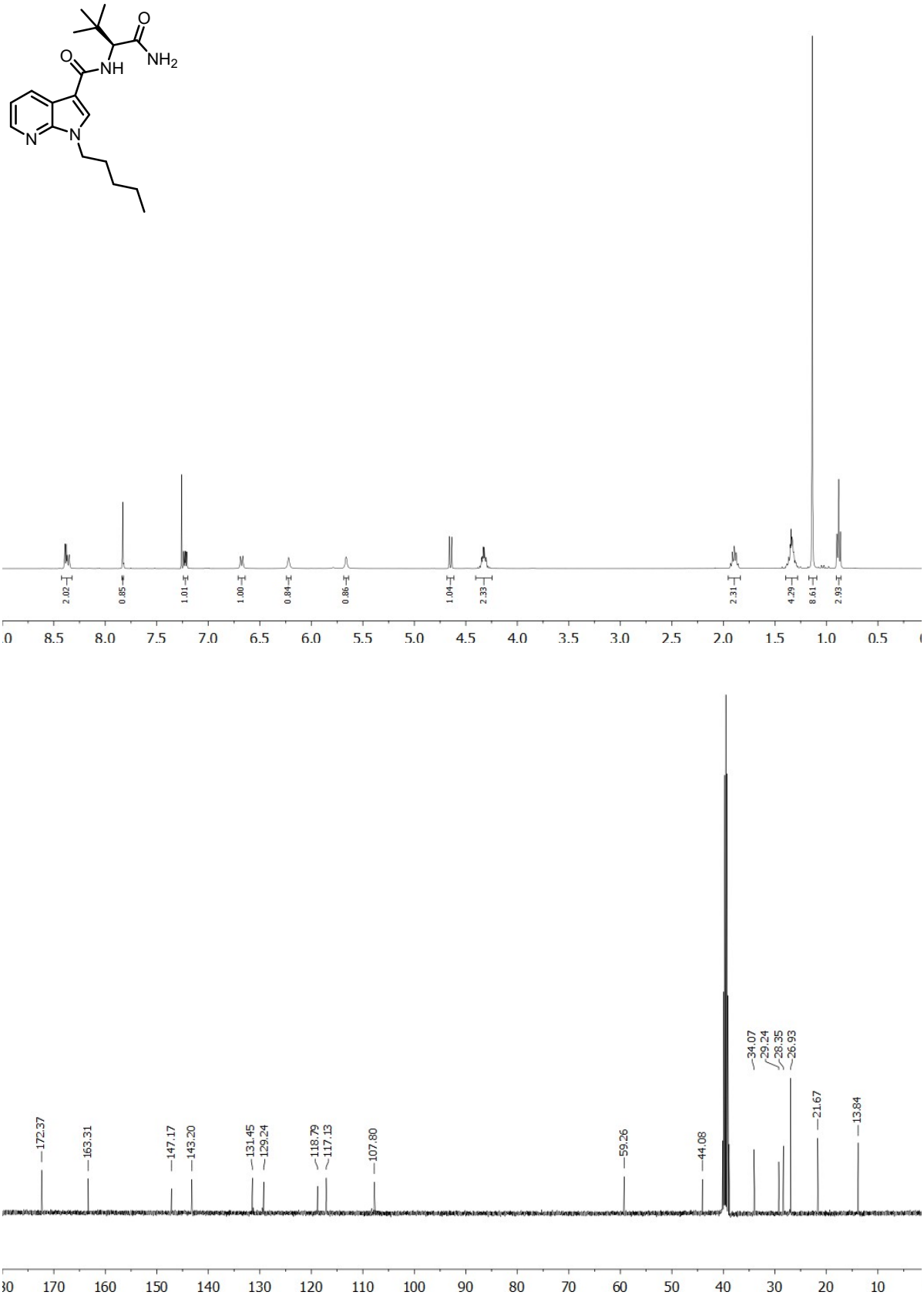

Figure S18. ^{1}H (400 MHz, $CDCl_3$) and ^{13}C (100 MHz, DMSO-d_6) NMR spectra for (*S*)-*N*-(1-amino-1-oxo-3-phenylpropan-2-yl)-1-pentyl-1*H*-pyrrolo[2,3-*b*]pyridine-3-carboxamide (APP-P7AICA, **20**).

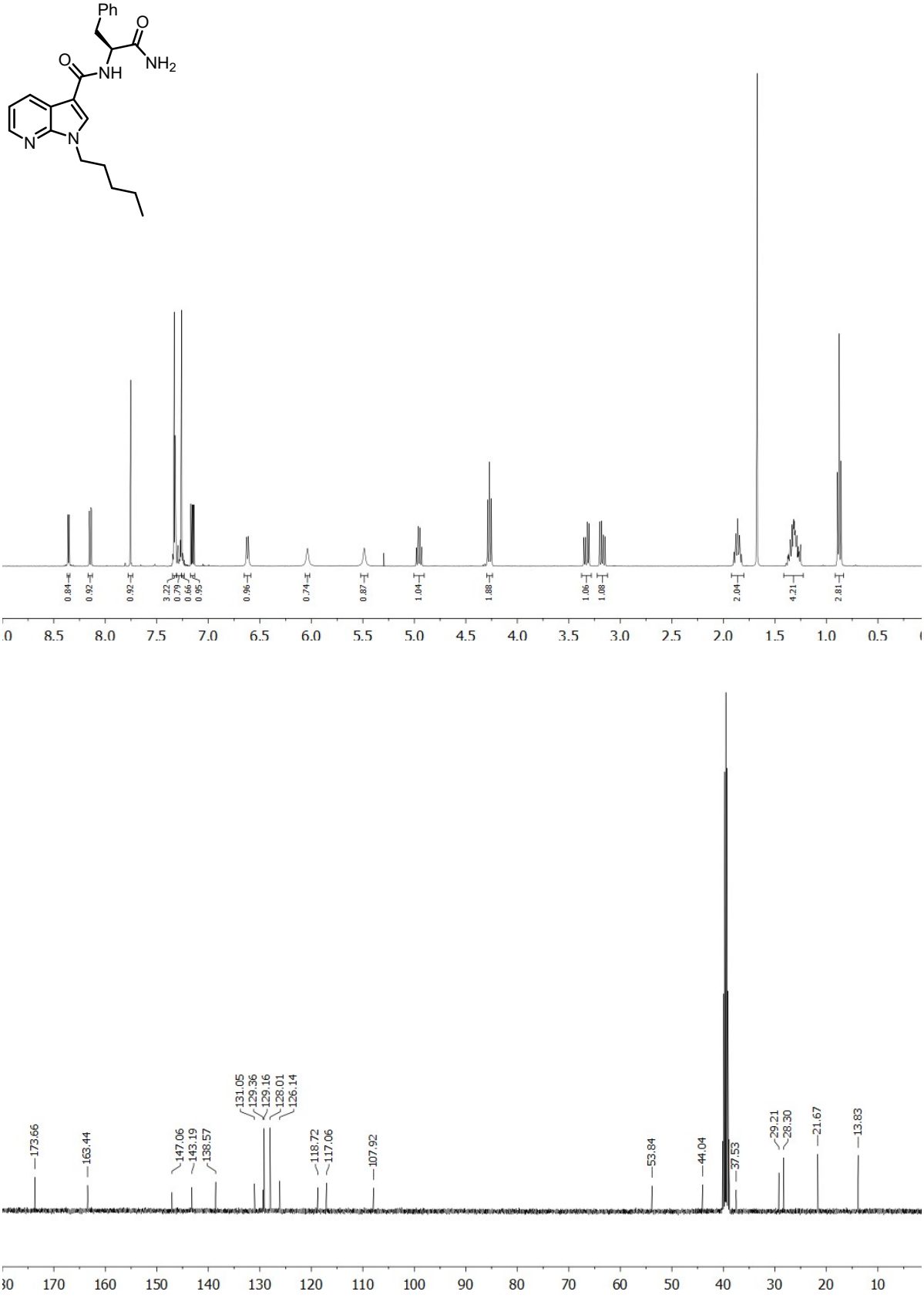

Figure S19. FTIR spectrum for (*S*)-*N*-(1-amino-3-methyl-1-oxobutan-2-yl)-1-butyl-1*H*-indole-3-carboxamide (AB-BUTICA, **9**).

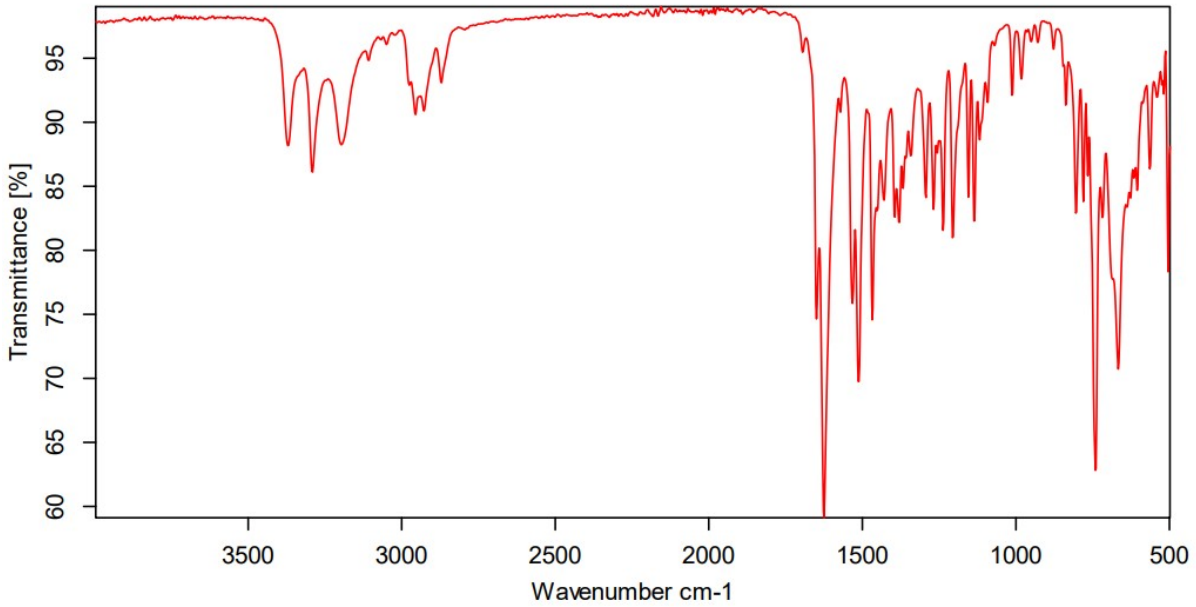

Figure S20. FTIR spectrum for (*S*)-*N*-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-butyl-1*H*-indole-3-carboxamide (ADB-BUTICA, **10**).

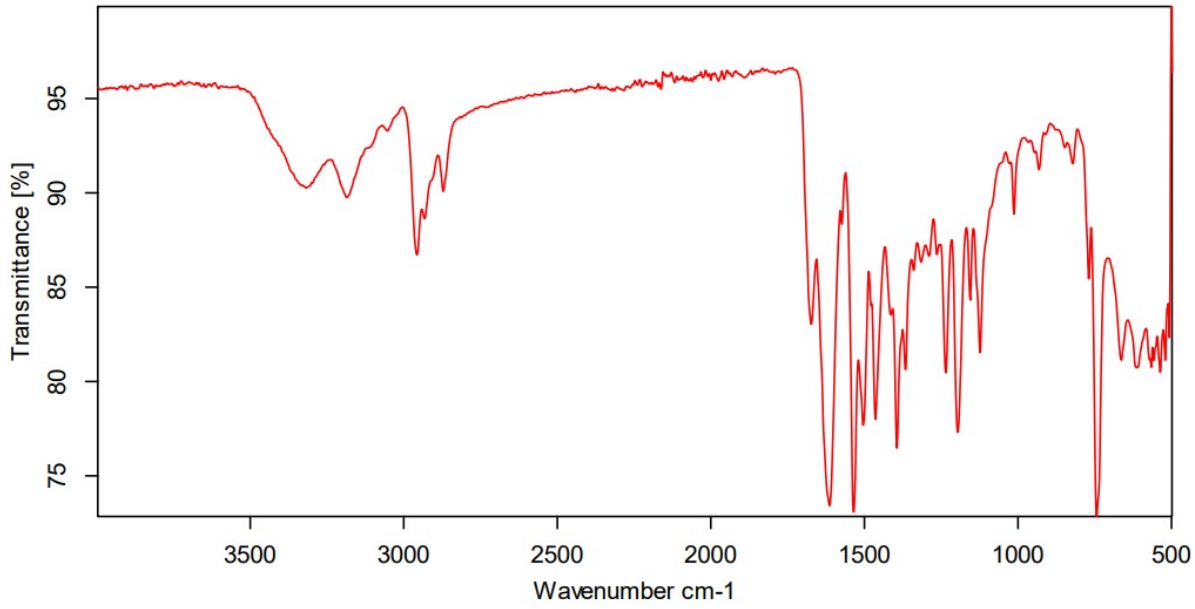

Figure S21. FTIR spectrum for (*S*)-*N*-(1-amino-1-oxo-3-phenylpropan-2-yl)-1-butyl-1*H*-indole-3-carboxamide (APP-BUTICA, **11**).

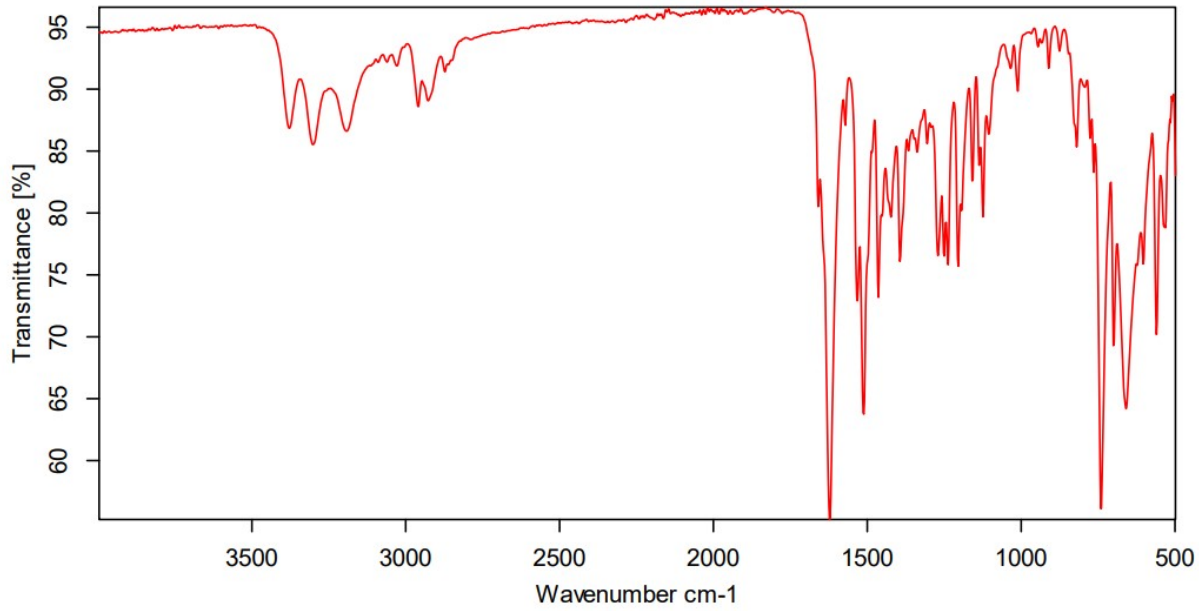

Figure S22. FTIR spectrum for (*S*)-*N*-(1-amino-3-methyl-1-oxobutan-2-yl)-1-butyl-1*H*-indazole-3-carboxamide (AB-BUTINACA, **12**).

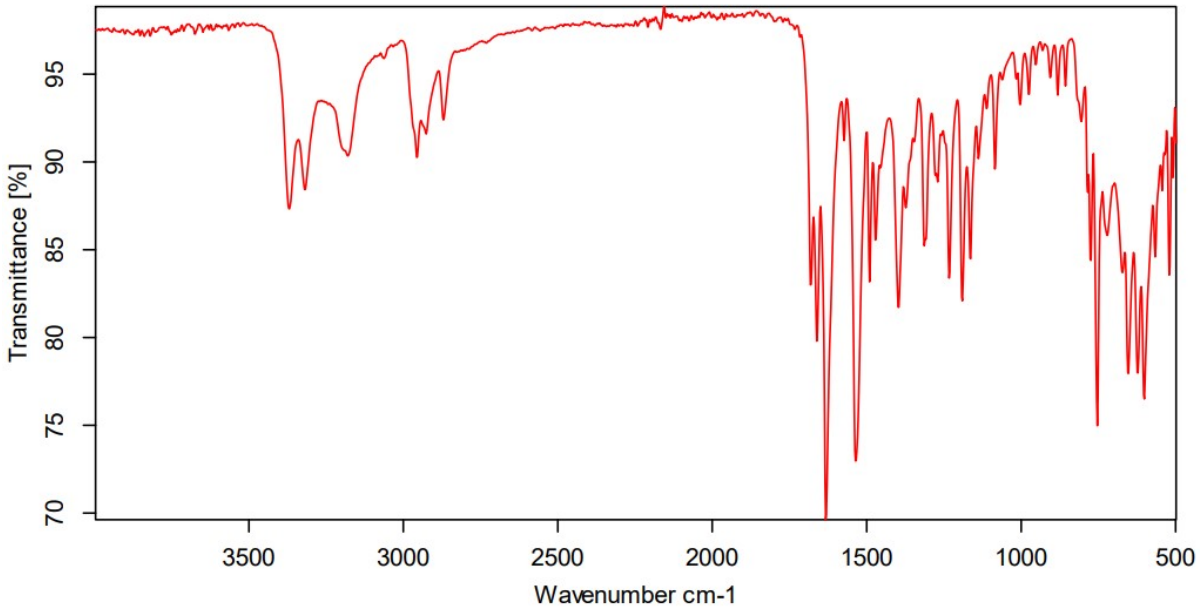

Figure S23. FTIR spectrum for (*S*)-*N*-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-butyl-1*H*-indazole-3-carboxamide (ADB-BUTINACA, **13**).

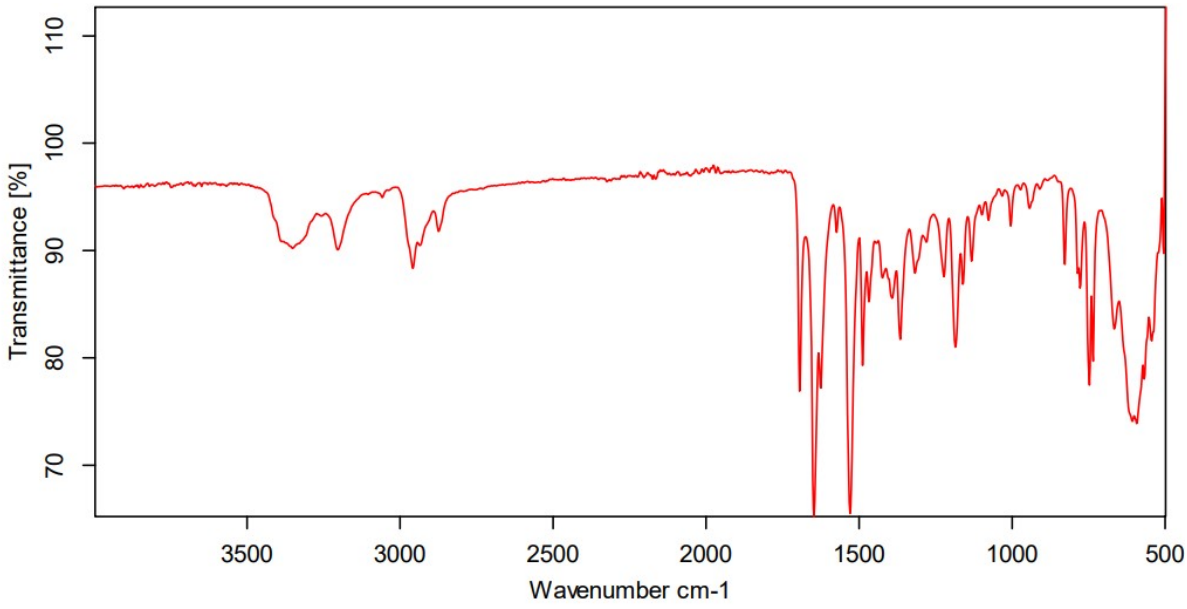

Figure S24. FTIR spectrum for (*S*)-*N*-(1-amino-1-oxo-3-phenylpropan-2-yl)-1-butyl-1*H*-indazole-3-carboxamide (APP-BUTINACA, **14**).

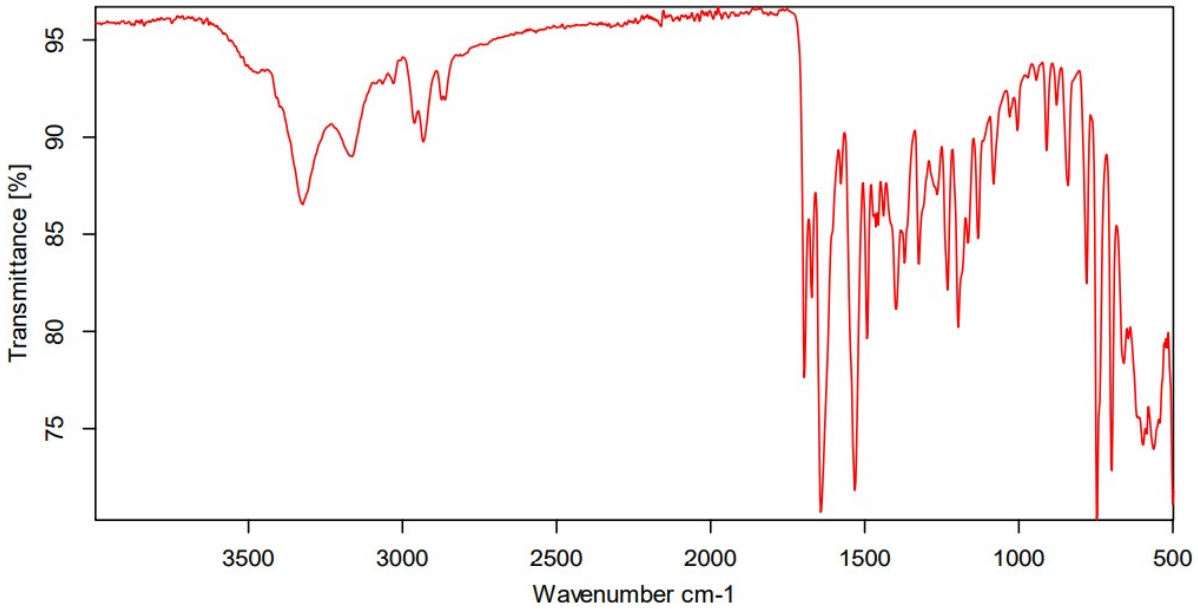

Figure S25. FTIR spectrum for (*S*)-*N*-(1-amino-3-methyl-1-oxobutan-2-yl)-1-butyl-1*H*-pyrrolo[2,3-*b*]pyridine-3-carboxamide (AB-BUT7AICA, **15**).

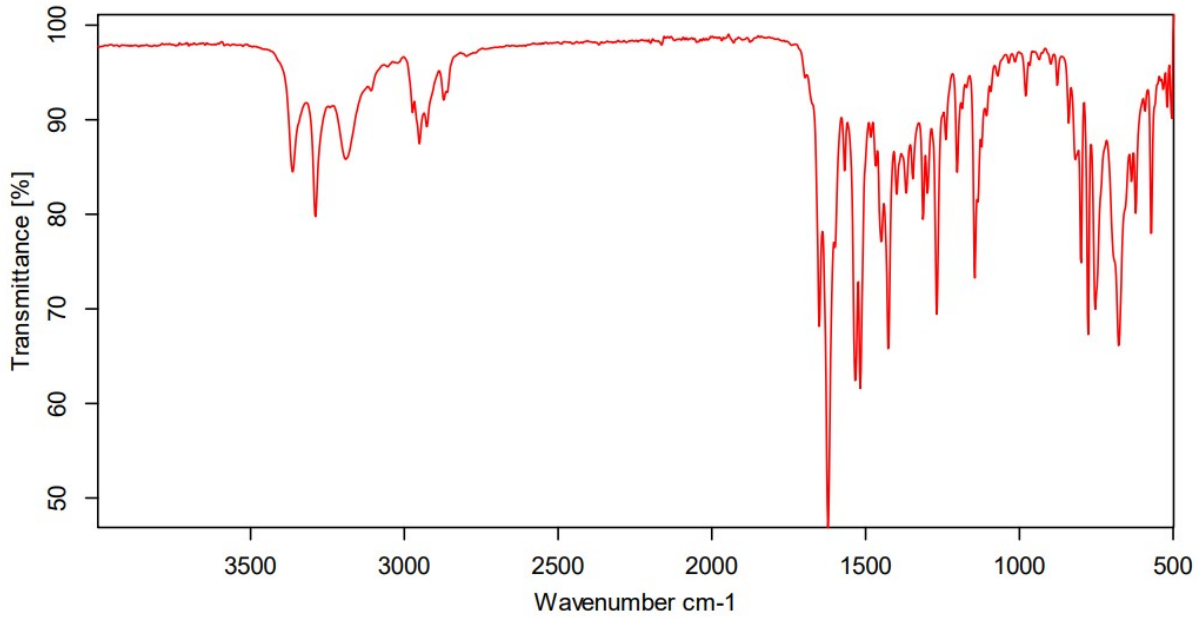

Figure S26. FTIR spectrum for (*S*)-*N*-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-butyl-1*H*-pyrrolo[2,3-*b*]pyridine-3-carboxamide (ADB- BUT7AICA, **16**).

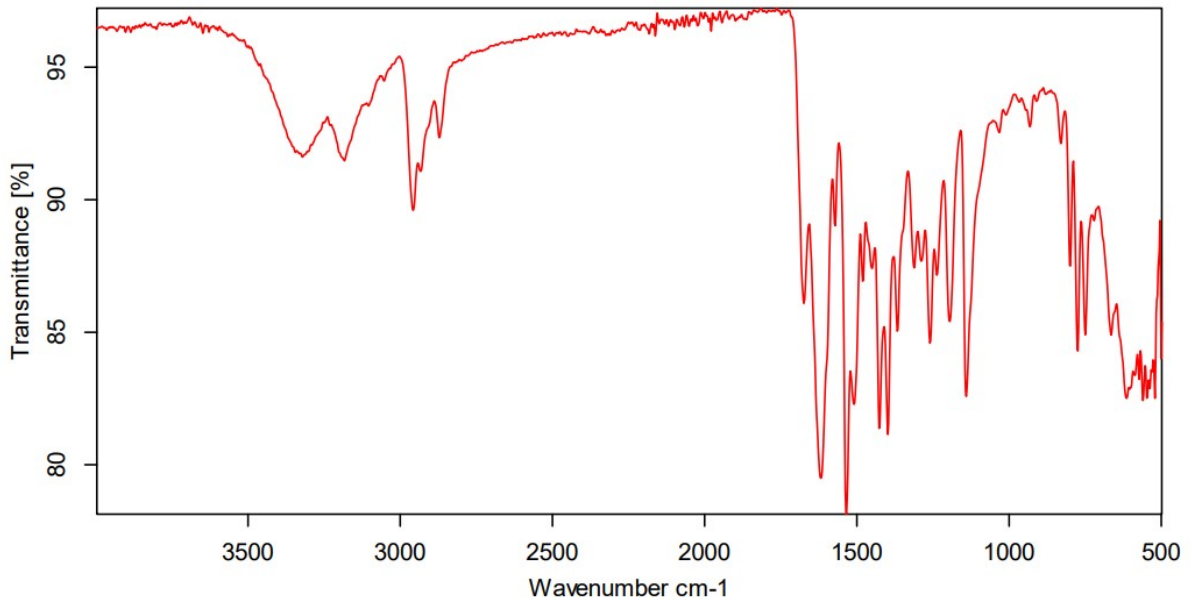

Figure S27. FTIR spectrum for (*S*)-*N*-(1-amino-1-oxo-3-phenylpropan-2-yl)-1-butyl-1*H*-pyrrolo[2,3-*b*]pyridine-3-carboxamide (APP-BUT7AICA, **17**).

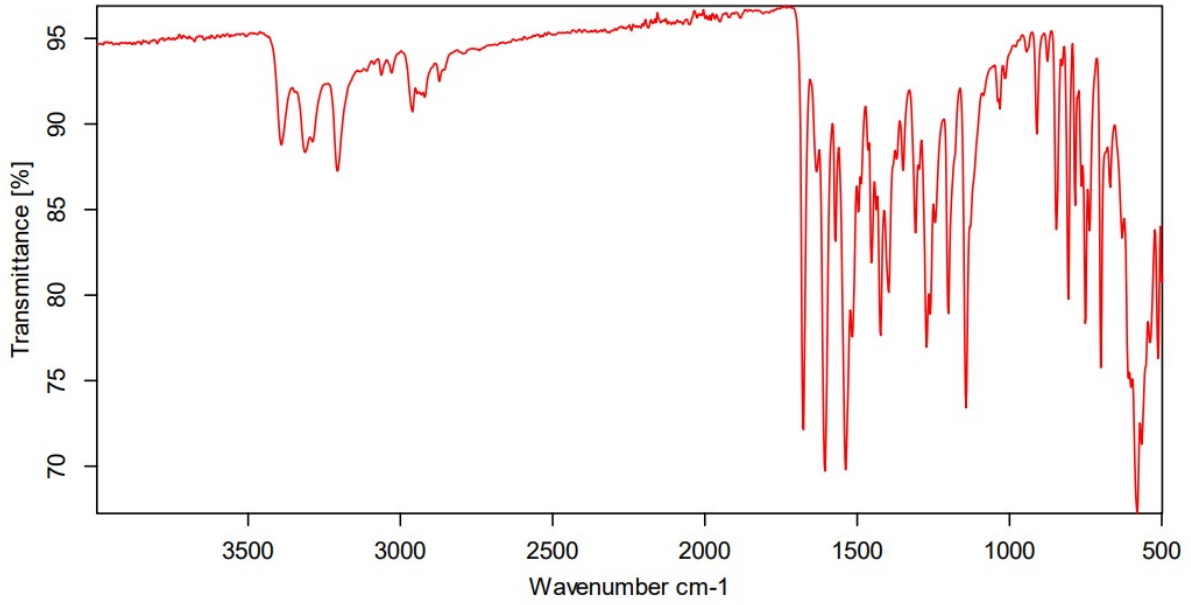

Figure S28. FTIR spectrum for (*S*)-*N*-(1-amino-3-methyl-1-oxobutan-2-yl)-1-pentyl-1*H*-pyrrolo[2,3-*b*]pyridine-3-carboxamide (AB-P7AICA, **18**).

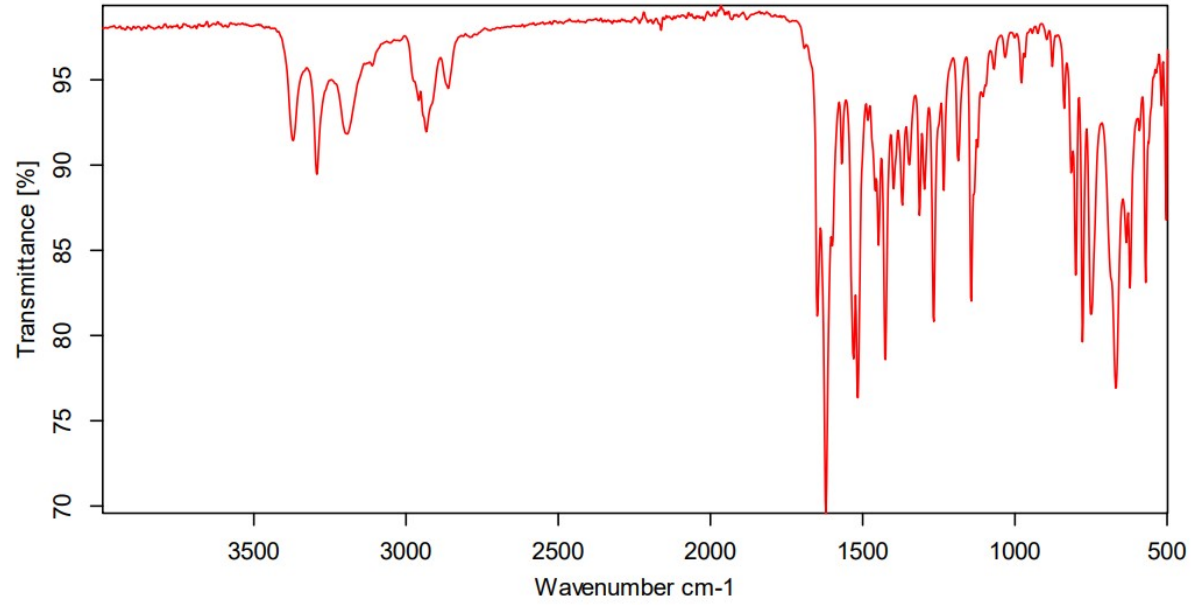

Figure S29. FTIR spectrum for (*S*)-*N*-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-pentyl-1*H*-pyrrolo[2,3-*b*]pyridine-3-carboxamide (ADB-P7AICA, **19**).

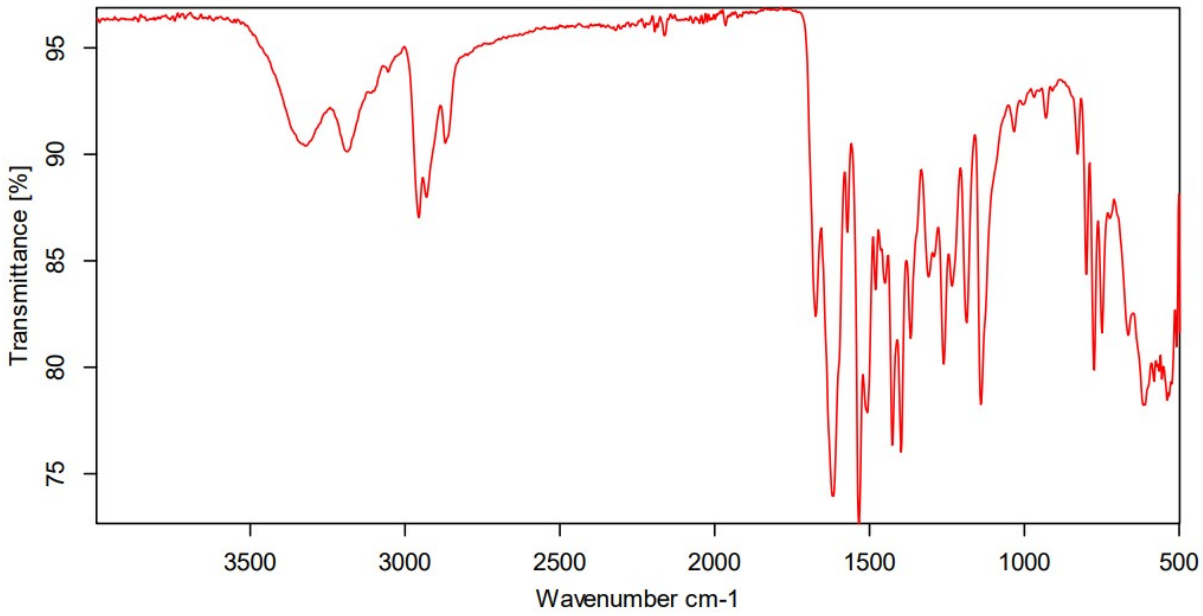

Figure S30. FTIR spectrum for (*S*)-*N*-(1-amino-1-oxo-3-phenylpropan-2-yl)-1-pentyl-1*H*-pyrrolo[2,3-*b*]pyridine-3-carboxamide (APP-P7AICA, **20**).