Supplementary Information for

Telescoped continuous flow synthesis of benzimidazoles from *o*-phenylenediamines and carboxylic acids

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1. Details of coupling reagents and bases/additives

Table S1. Details of coupling reagents and bases/additives.

Entry	Abbreviation	Specification	CAS No.	Matching additives /base
1	DPPCl	Diphenylphosphinic Chloride	1499-21-4	*N,N*-Diisopropylethylamine (DIPEA)
2	IBCF	Isobutyl chloroformate	543-27-1	*N*-methylmorpholine (NMM)
3	EDCI	*N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimide hydrochloride	25952-53-8	1-Hydroxybenzotriazole (HOBt)
4	DIC	*N,N*-Diisopropylcarbodiimide	693-13-0	1-Hydroxybenzotriazole (HOBt)
5	DCC	Dicyclohexylcarbodiimide	538-75-0	1-Hydroxybenzotriazole (HOBt)
6	CDI	1,1′-Carbonyldiimidazole	530-62-1	-
7	HATU	2-(7-azabenzotriazole)-*N,N,N′,N′*-tetramethylurea hexafluorophosphate	148893-10-1	Triethylamine (TEA)
8	HBTU	2-(1*H*-Benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate	94790-37-1	Triethylamine (TEA)
9	PivCl	Trimethylacetyl chloride	3282-30-2	Triethylamine (TEA)
10	PyBOP	1*H*-benzotriazol-1-yloxytripyrrolidinophosphonium hexafluorophosphate	128625-52-5	Triethylamine (TEA)
11	EEDQ	2-Ethoxy-1-ethoxycarbonyl-1,2-dihydroquinoline	16357-59-8	-
12	CDMT	2-Chloro-4,6-dimethoxy-1,3,5-triazine	3140-69-5	*N*-methylmorpholine (NMM)

All reagents were used without further purification. In order to deprotonate carboxylic acid, in general, 3 eq. additional bases or additives were added in the acylation reactions.

2. The effect of the flow rate of acetic acid for two-step cascaded synthesis of 5a in continuous flow reactor.

Table S2. Optimizations of the flow rate of acetic acid[a]

Entry	Flow rate of acetic acid (mL/min)	T_2 (°C)	t_2 (min)	Total yield **5a** (%)
1	0.088	110	5	65
2	0.175	110	5	88
3	**0.350**	**110**	**5**	**92**
4	0.525	110	5	92
5	0.700	110	5	81
6	0.875	110	5	63

[a]: The details of the two-step cascaded synthesis of **5a** are shown in Scheme 3.

Acetic acid is used to offer an acidic environment to promote cyclization, however, excessive acetic acid reduced the yield of **5a**, which may be due to a decrease in reaction concentration caused by excessive acetic acid, thus 0.350 mL/min was determined as the optimization condition.

3. Physical picture of reaction equipment

Fig. S1 show the photographic representation of reaction equipment of two-step continuous flow telescoped synthesis of benzimidazoles. The outer diameters (OD) of all stainless-steel capillaries (Beijing Xiongchuan Technology Co. Ltd.) are 1.590 mm, inner diameters (ID) are 0.668 mm. The two mixers, M1 and M2, have the same model (stainless-steel, SS-2UTF, Xiongchuan).

Fig. S1 Photographic representation of reaction equipment of two-step continuous flow telescoped synthesis of benzimidazoles.

General procedure for the continuous flow synthesis of benzimidazoles 5a

1a, **2a** and TEA mixed in DMF as solution A, HBTU mixed in DMF as solution B. The two solutions were delivered respectively stainless-steel coil reactor (0.668 mm inner diameter, 1.590 mm outer diameter, Xiongchuan) using two syringe pumps (LSP02-2A, repeat precision ≤ ±1 %, Longer), and mixed in a cross-flow T-junction micromixer I (1.2 mm bore, 316L, Xiongchuan). The flow rates of solution A and solution B were controlled at 0.175 mL/min. The stainless-steel microtube reactors R1 (0.668 mm inner diameter, 1.590 mm outer diameter) attached to the micromixer I were used to conduct the monoacylation

reaction. The length of microtube reactors R1 is 15 meters, the total internal volume is 5.25 mL, the corresponding residence time of monoacylation (t_1) is 15 min. The microtube reactors R1 was placed in an external water bath temperature controller, and the temperature of monoacylation (T_1) was controlled at 50 °C. CH_3COOH was pumped into the micromixer II (same type as micromixer I) by a syringe pump (LSP02-2A, repeat precision ≤ ±1 %, Longer) with the flow rate of 0.350 mL. The microtube reactors R2 (same type as R1) attached to the micromixer II were used to conduct the cyclization reaction. The length of microtube reactors R2 is 10 meters, the total internal volume is 3.5 mL, the corresponding residence time of cyclization (t_2) is 5 min. The microtube reactors R2 was placed in an external oil bath temperature controller, and the temperature of monoacylation (T_2) was controlled at 110 °C. After a steady state has been reached (40 min), the product solution was collected for 30 min. The reaction mixture (21 mL) was poured into water (21 mL), extracted with Et_2O (3 x 21 mL). The organic phase was washed with aqueous $NaHCO_3$ (3 × 21 mL), then subjected to vacuum distillation. A 0.80 g white refined solid was obtained with 99.8% HPLC purity after recrystallization in 50% EtOH, vacuum distillation and drying.

4. Scaling up

Fig. S2 and Fig. S3. respectively show the schematic diagram and photographic representation of scale up for the synthesis of **5g** (**5h**) in continuous flow. To reduce the pressure drop in the scaling up experiment, we employed tubing with a larger internal diameter. The outer diameters (OD) of all stainless-steel capillaries (Beijing Xiongchuan Technology Co. Ltd.) are 3.175 mm, inner diameters (ID) are 2.175 mm. The internal volume of the two-stage reaction tubes, as well as the reaction temperature and residence times, are labeled in Fig S2. The two mixers, M1 and M2, have the same model (stainless-steel, SS-2UTF, Xiongchuan).

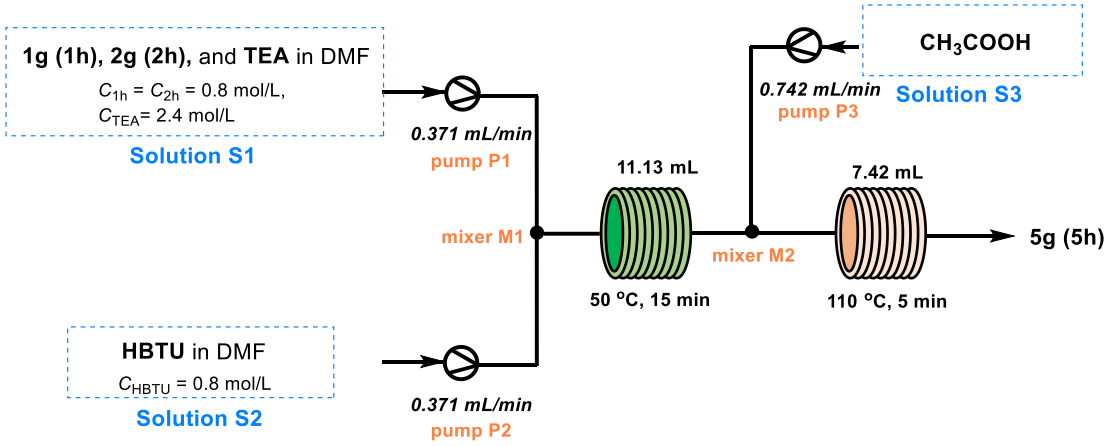


Fig. S2. Schematic diagram of scaling up for the synthesis of **5h** in continuous flow.

Fig. S3. Photographic representation of scaling up for the synthesis of **5g**/**5h** in

continuous flow.

Preparation of Reaction Solutions (As exemplified by compound 5h):

Solution S1: 15.0 g 4-Bromo-1,2-diaminobenzene (**1h**), 19.3 g (1R,3S,4S)-N-Boc-2-azabicyclo[2.2.1]heptane-3-carboxylic acid and (**2h**), and 24.24 g triethylamine (TEA) were dissolved in DMF, transferred to 100 mL volumetric bottle and replenished to the graduation line.

(initial concentration in **Solution S1: C_{1h} = C_{2h} = 0.8 mol/L, C_{TEA}= 2.4 mol/L**)

The solution S1 was pumped into continuous flow reactor by pump P1 (JJRZ-02004F, Hangzhou Jingjin, repeat precision ≤ ±1%), the flow rate was 0.371 mL/min.

Solution S2: 30.3 g HBTU was dissolved in DMF, transferred to 100 mL volumetric bottle and replenished to the graduation line.

(initial concentration in **Solution S2: C_{HBTU} = 0.8 mol/L**)

The solution S2 was pumped into continuous flow reactor by pump P2 (JJRZ-02004F, Hangzhou Jingjin), the flow rate was 0.371 mL/min.

Solution S3: neat CH_3COOH, was pumped into continuous flow reactor by pump P2 (JJRZ-02004F, Hangzhou Jingjin), the flow rate was 0.742 mL/min.

After a steady state has been reached (40 min), the product solution was collected for 100 min. The reaction mixture (148 mL) was poured into water (148 mL), extracted with Et2O (3 x 148 mL). The organic phase was washed with aqueous $NaHCO_3$ (3 × 148 mL), then subjected to vacuum distillation. A 10.5 g white refined solid **5h** was obtained with 99.5% HPLC purity after recrystallization in 50% EtOH, vacuum distillation and drying.

5. HPLC chromatograms

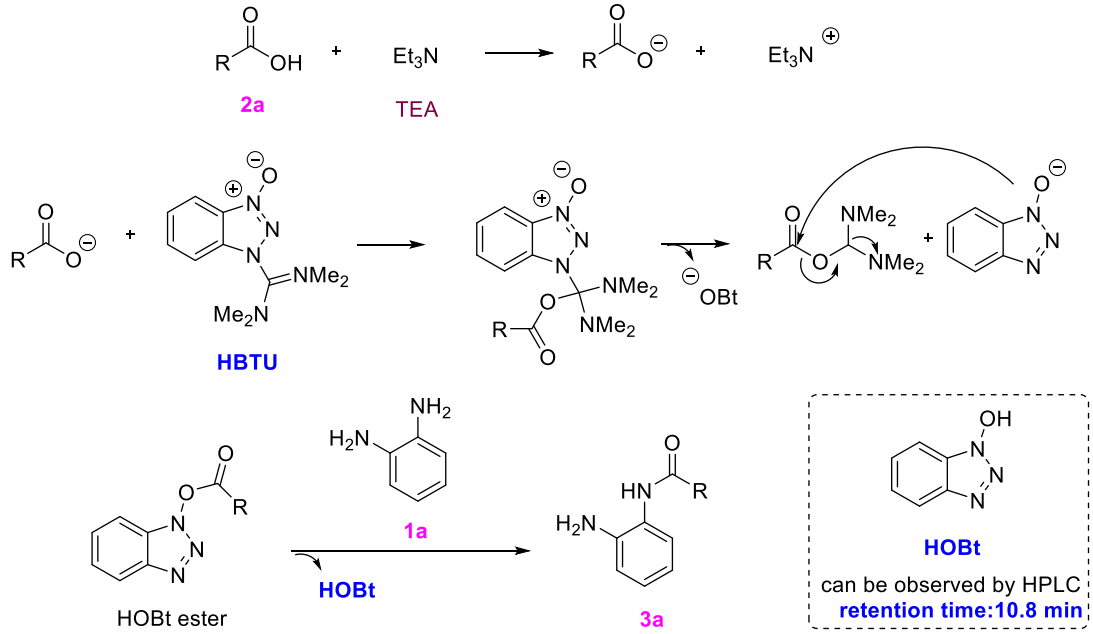
Conversion of substrates to products of the two-step continuous reactions reported in Scheme 4 were determined by HPLC as described above. The HPLC chromatograms of the products in Scheme 4 are shown here, labelled with the benzimidazoles product. HPLC instrument is Shimadzu Essentia LC-16, and the HPLC testing conditions is shown in Table S3.

Table S3. HPLC testing conditions.

chromatographic column	C18 (5 μm, 4.6 × 250 mm, XB-C18, Wlech)		
mobile phase	A: 0.1 wt% aqueous formic acid solution, B: MeOH		
	min.	A%	B%
	0	90	10
	0-15.00	0	100
	15.01-20.00	0	100
	20.01	90	10
	20.01-25.00	90	10
column temperature	30 ºC		
detection wavelength	275 nm		
flow rate	1 mL/min		
injection volume	10 μL		

According to the reported literature [1, 2], the possible mechanism and reaction path of HBTU-mediated amidation are shown in Scheme S1, Due to the completion of the monoacylation reaction mediated by HBTU, HBTU will decompose into HOBt after the reaction, in all reaction mixture chromatograms, the peak at 10.8 min is HOBt.

The possible reaction mechanism of HBTU-mediated amidation:



Scheme S1. The reaction mechanism of HBTU-mediated the synthesis of **3a** from **1a** and **2a**

Model reaction: **3a** and **5a**

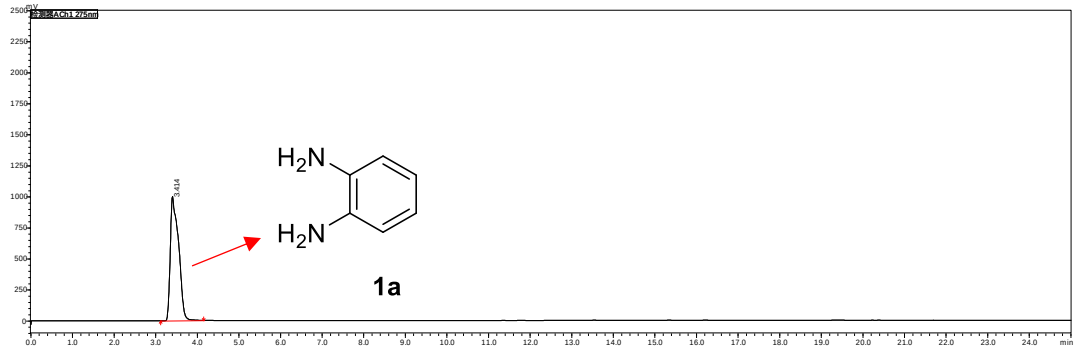


Fig. S4. HPLC chromatogram of **1a**

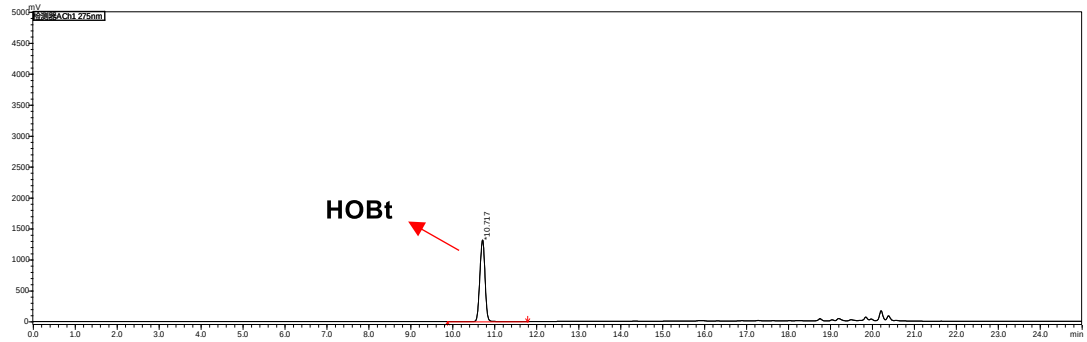


Fig. S5. HPLC chromatogram of HOBt

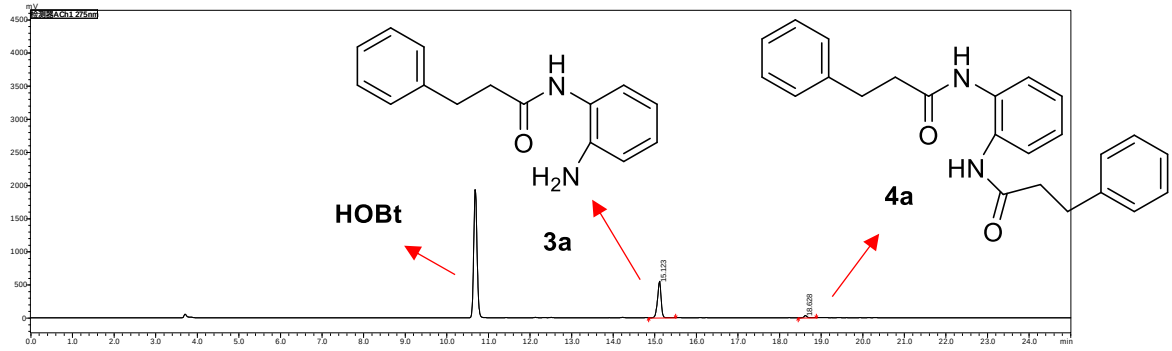


Fig. S6. HPLC chromatogram of monoacylation reaction mixture for the synthesis of **3a** in continuous-flow. Conditions: molar flow ratio (**1a**: **2a**: HBTU: TEA) = 1: 1: 1 :3, T_1= 50 ºC, t_1= 15 min.

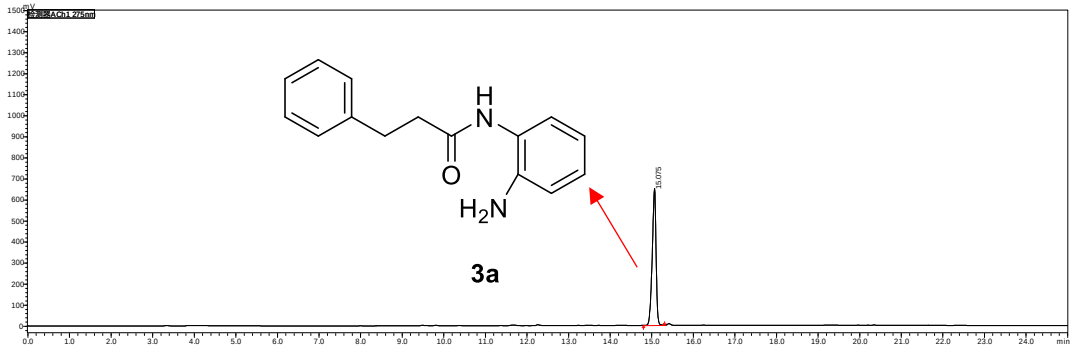


Fig. S7. HPLC chromatogram of purified **3a** (monoacylation target product)

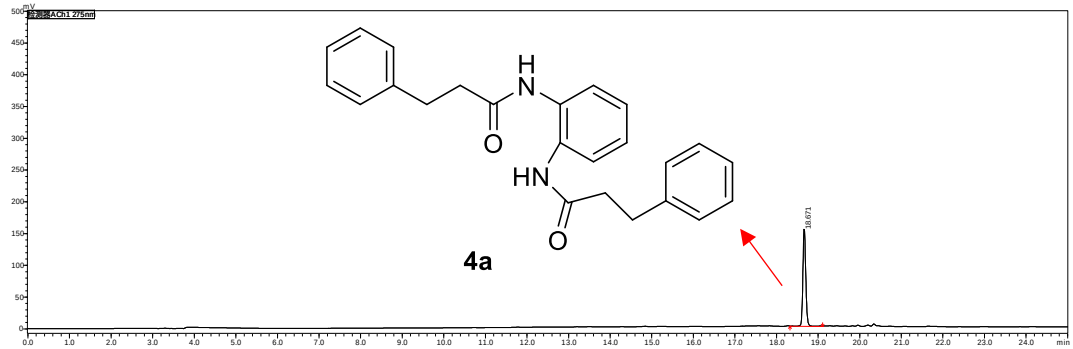


Fig. S8. HPLC chromatogram of purified **4a** (monoacylation by-product)

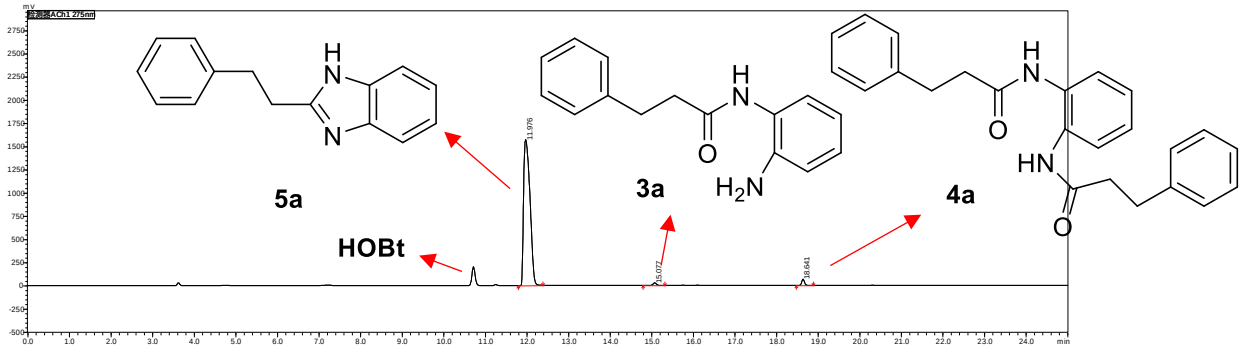


Fig. S9. HPLC chromatogram of monoacylation-cyclization cascaded reaction mixture for the synthesis of **5a** in continuous-flow. Conditions: molar flow ratio (**1a**: **2a**: HBTU: TEA) = 1: 1: 1 :3, T_1= 50 ºC, t_1= 15 min. T_2= 110 ºC, t_2= 5 min.

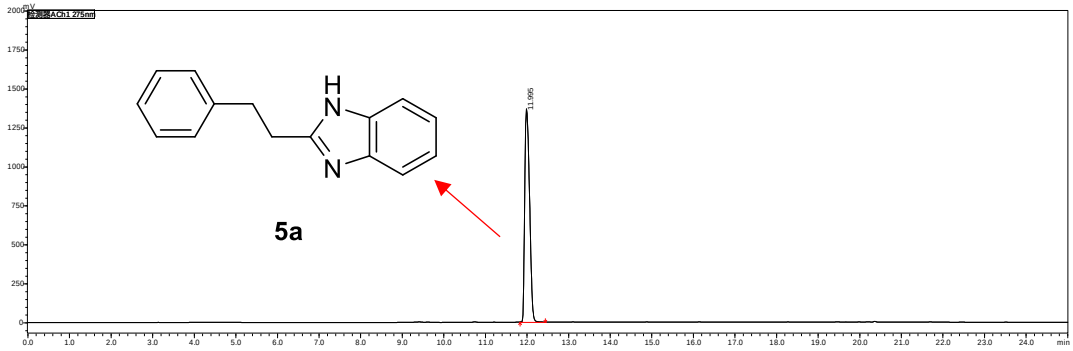


Fig. S10. HPLC chromatogram of **5a**

substrate scope: **5ab**

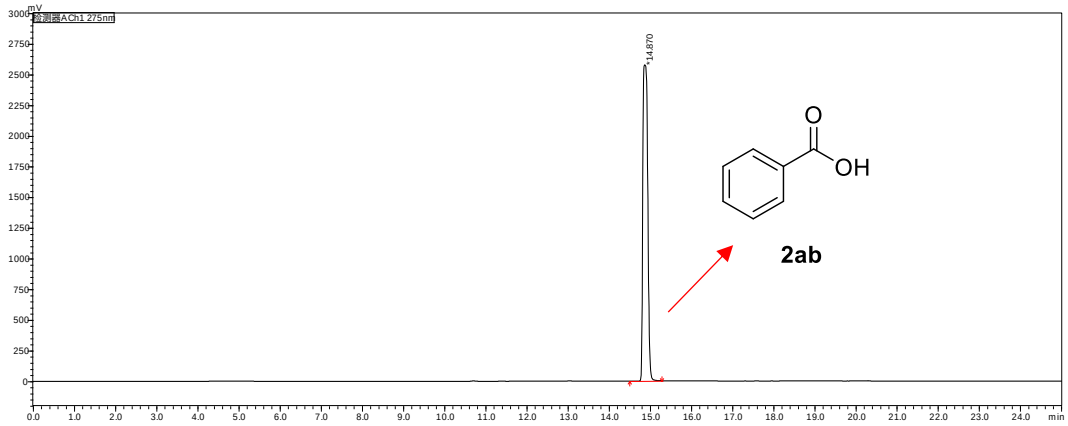


Fig. S11. HPLC chromatogram of **2ab**

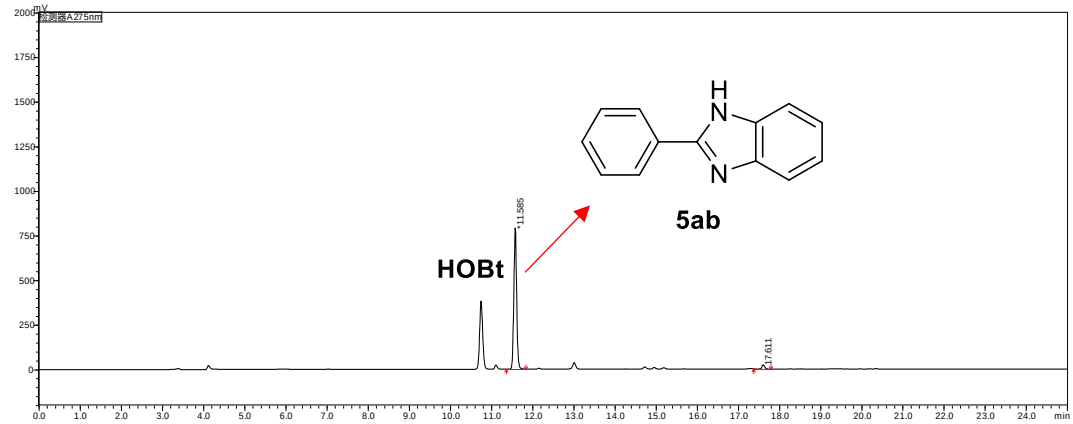


Fig. S12. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5ab**

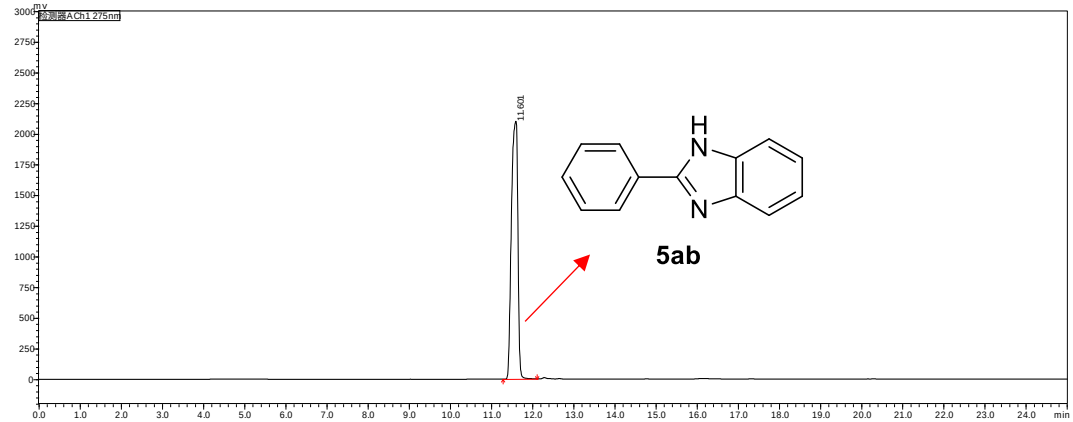


Fig. S13. HPLC chromatogram of purified **5ab**

substrate scope: **5ac**

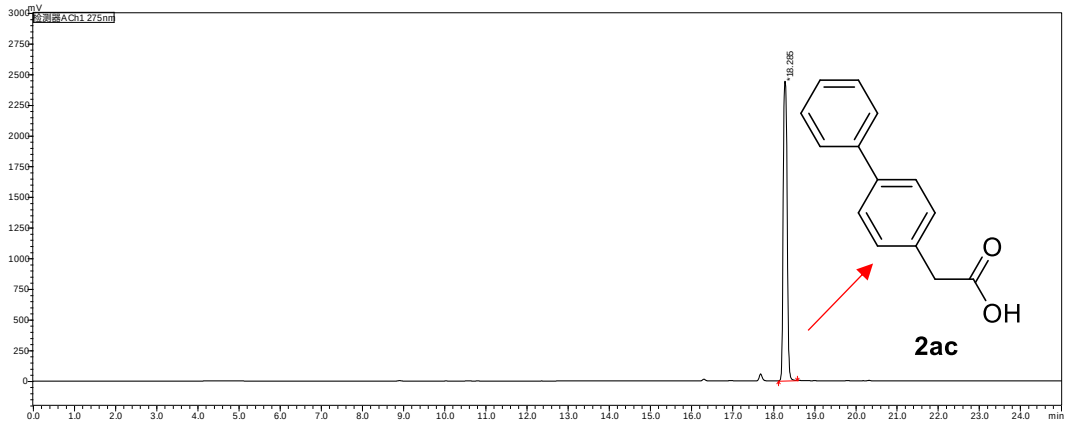


Fig. S14. HPLC chromatogram of **2ac**

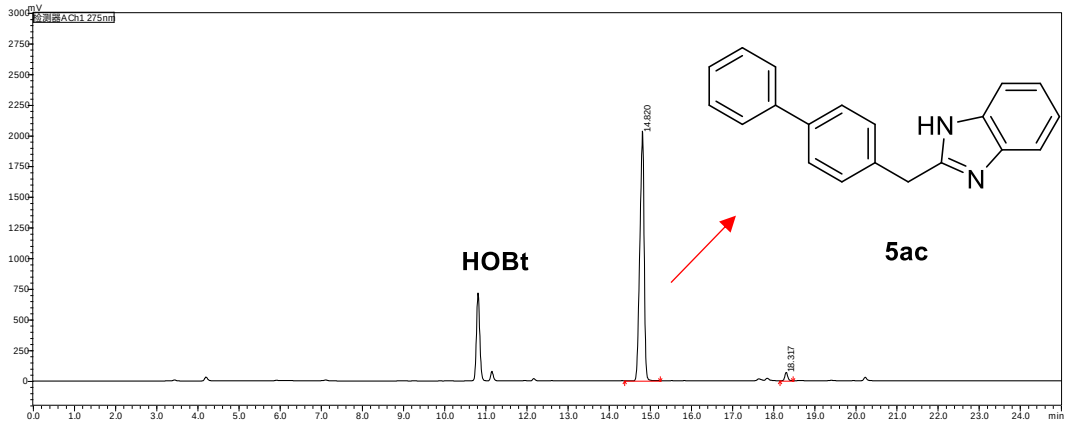


Fig. S15. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5ac**

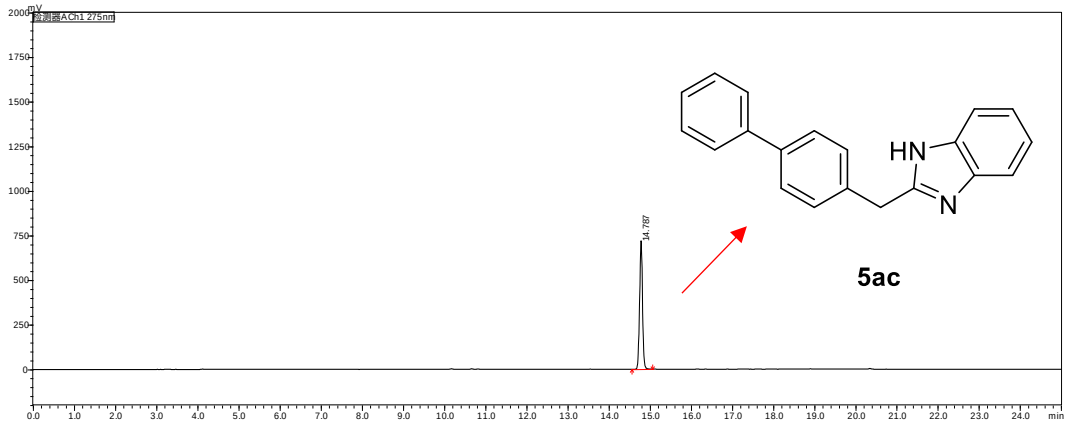


Fig. S16. HPLC chromatogram of purified **5ac**

substrate scope: **5ad**

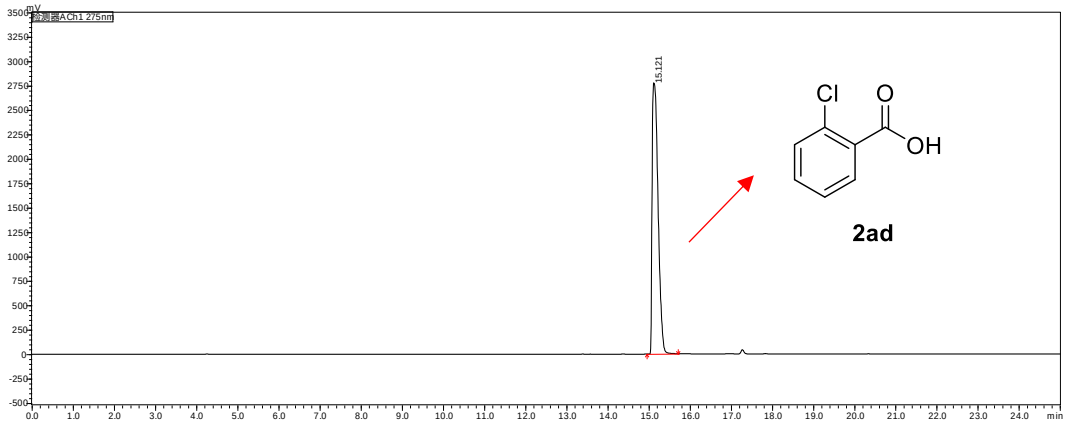


Fig. S17. HPLC chromatogram of **2ad**

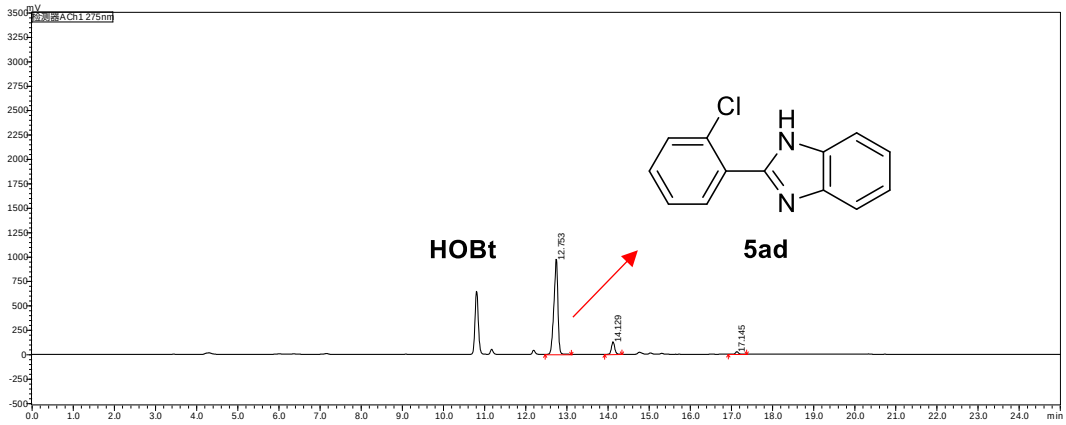


Fig. S18. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5ad**

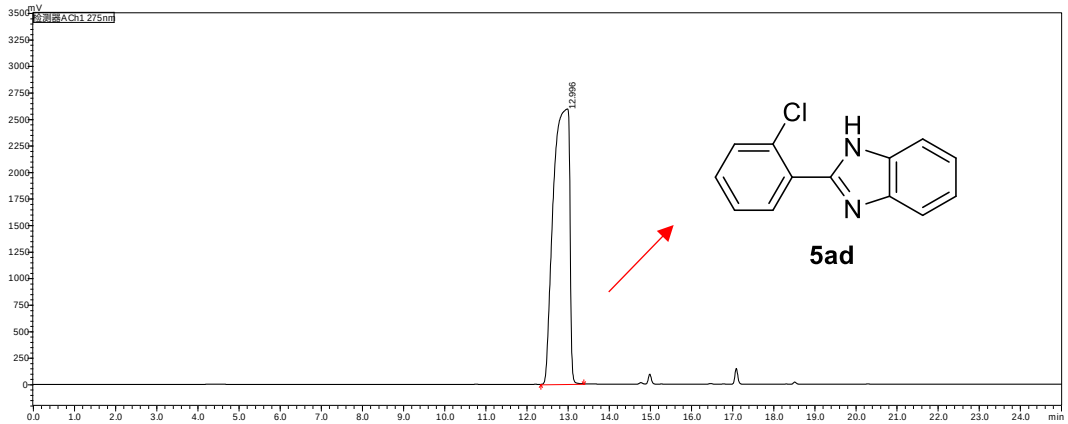


Fig. S19. HPLC chromatogram of purified **5ad**

substrate scope: **5ae**

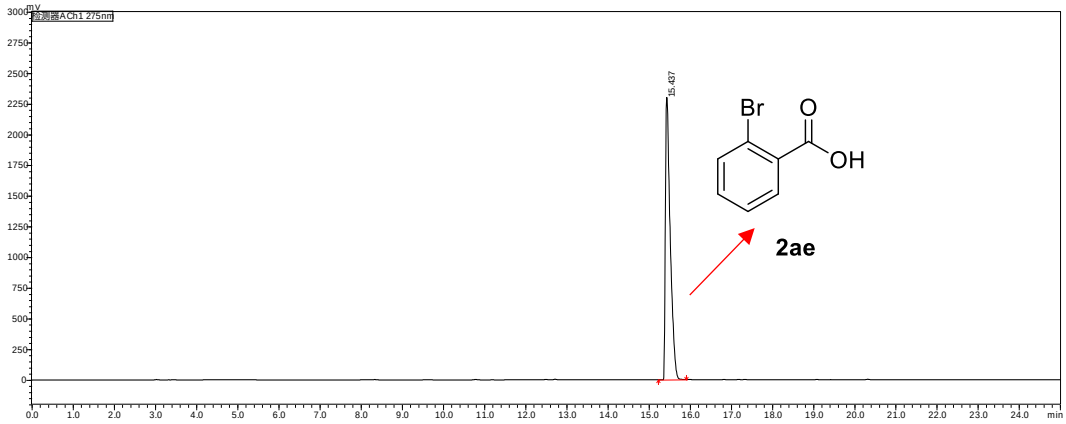


Fig. S20. HPLC chromatogram of **2ae**

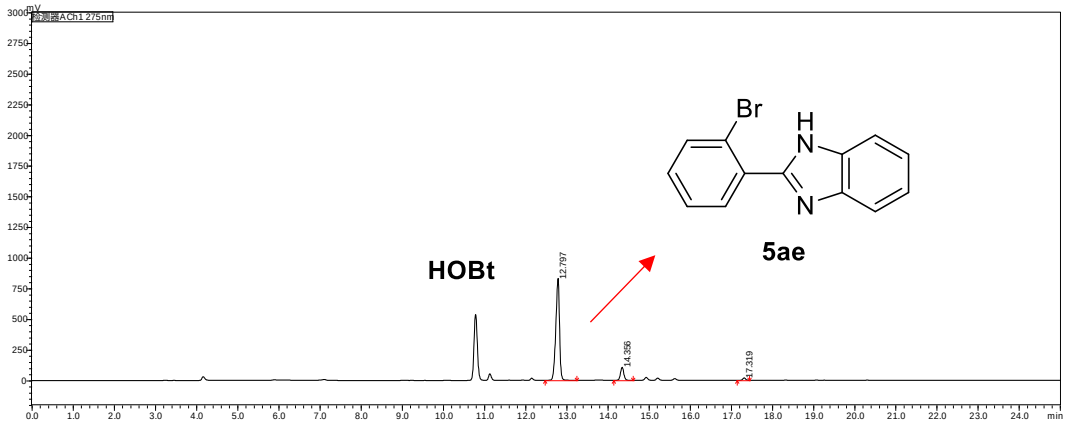


Fig. S21. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5ae**

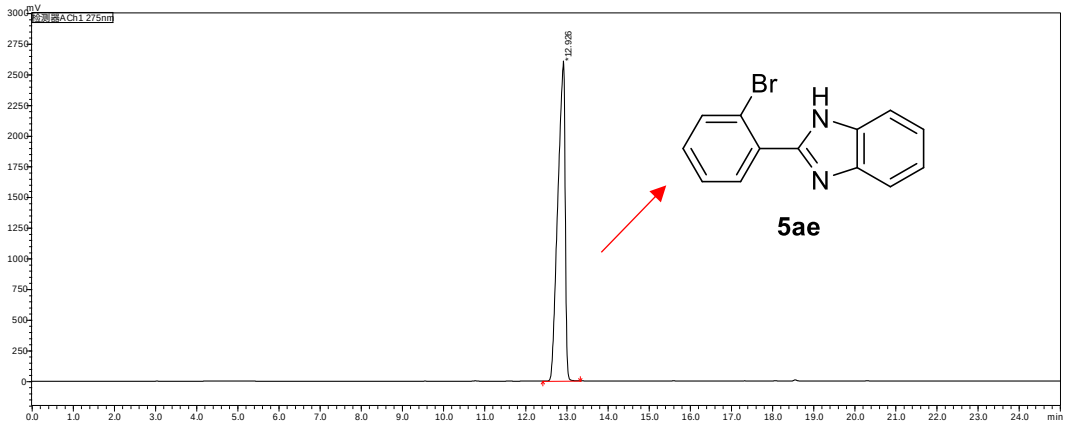


Fig. S22. HPLC chromatogram of purified **5ae**

substrate scope: **5af**

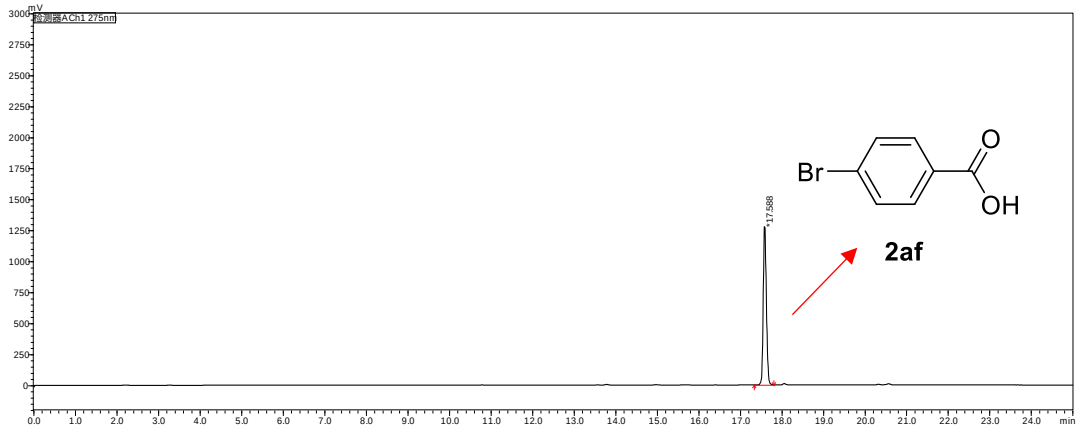


Fig. S23. HPLC chromatogram of **2af**

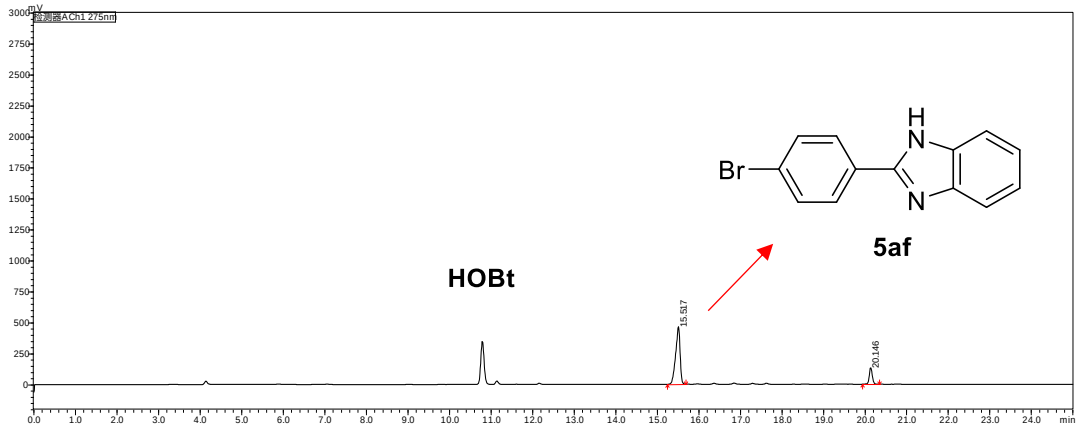


Fig. S24. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5af**

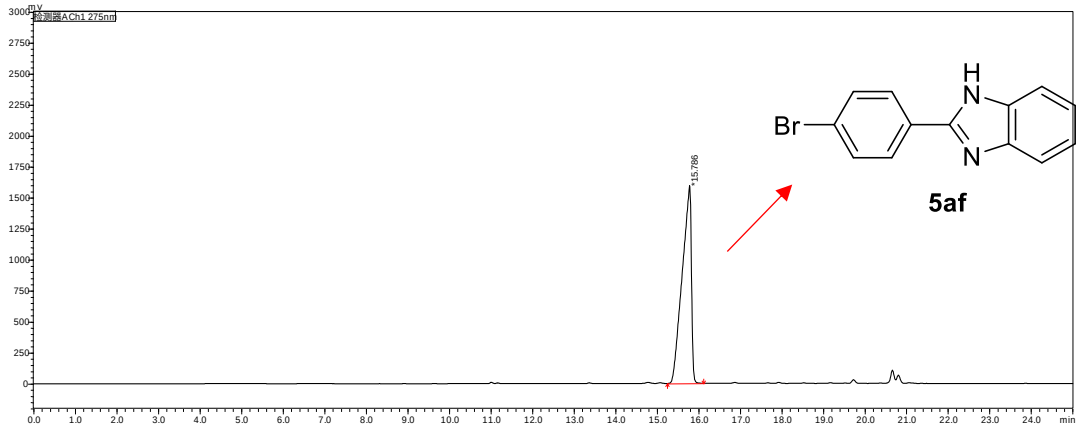


Fig. S25. HPLC chromatogram of purified **5af**

substrate scope: **5ag**

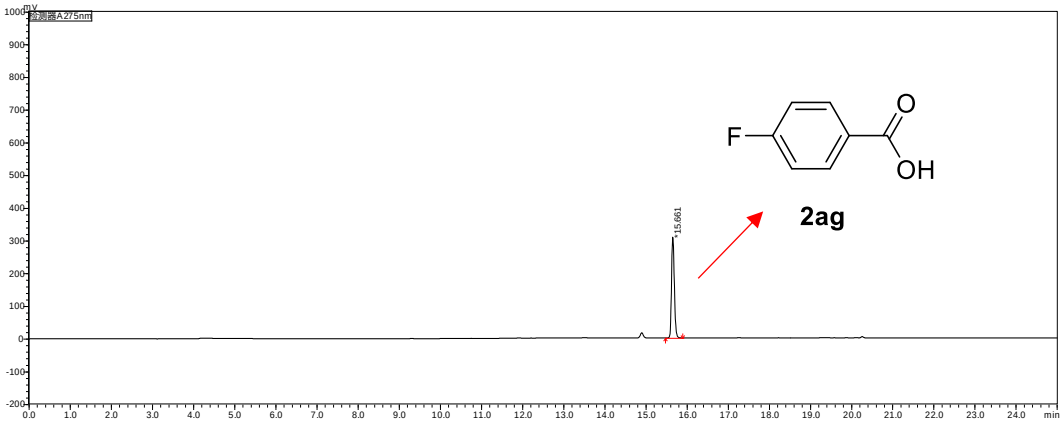


Fig. S26. HPLC chromatogram of **2ag**

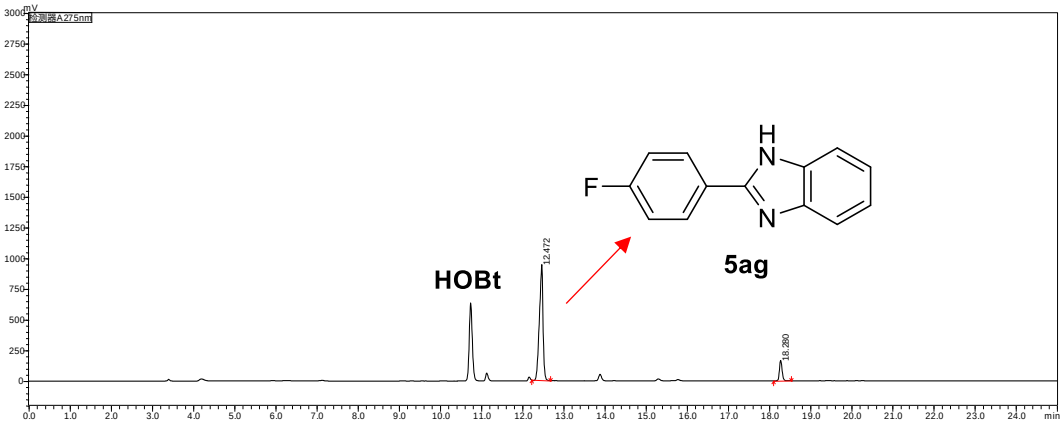


Fig. S27. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5ag**

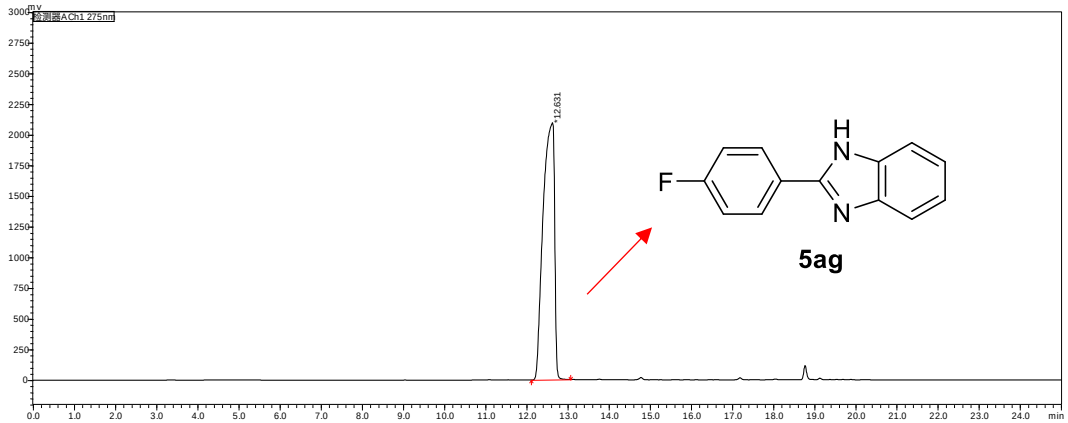


Fig. S28. HPLC chromatogram of purified **5ag**

substrate scope: **5ah**

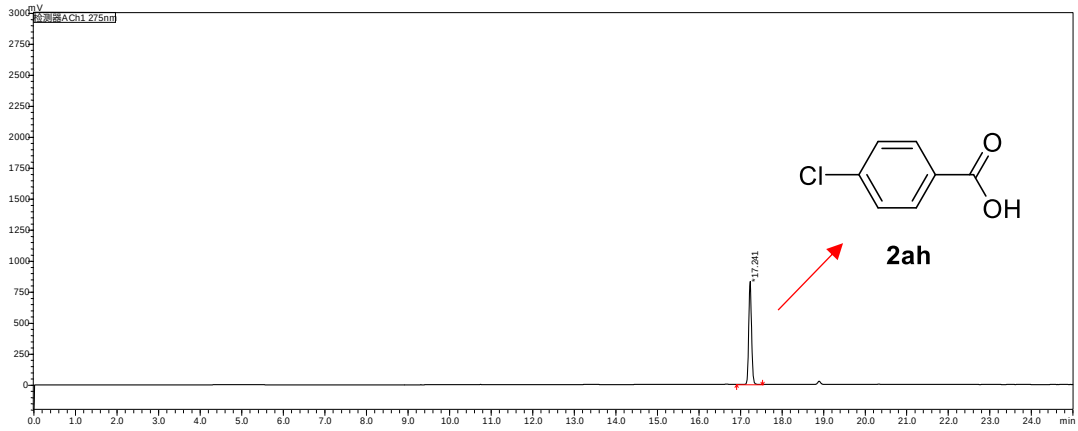


Fig. S29. HPLC chromatogram of **2ah**

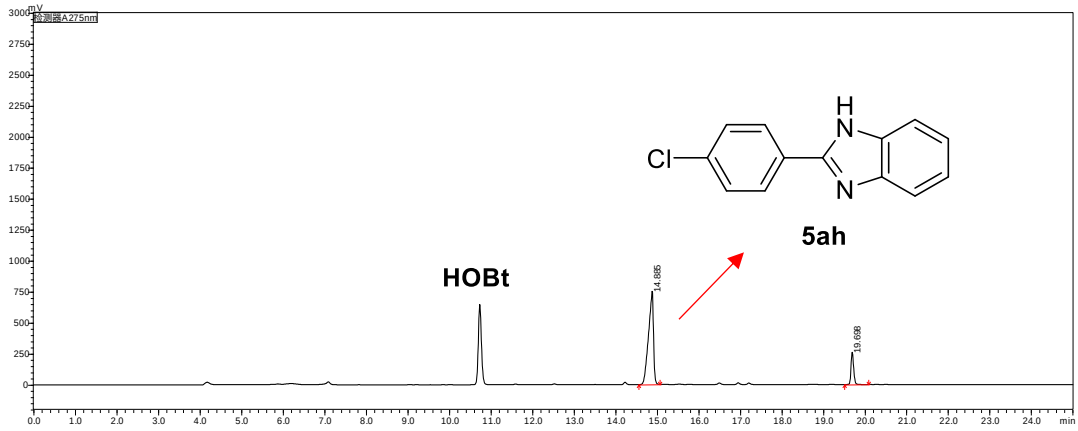


Fig. S30. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5ah**

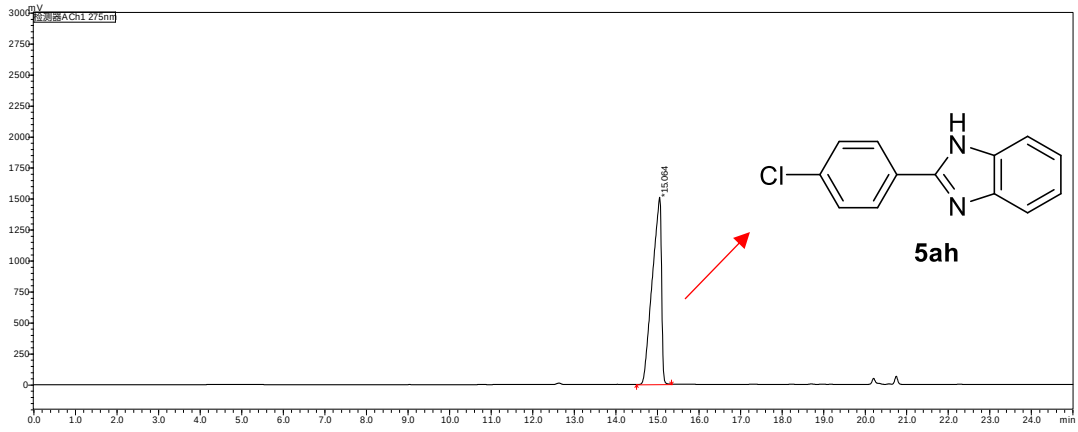


Fig. S31. HPLC chromatogram of purified **5ah**

substrate scope: **5ai**

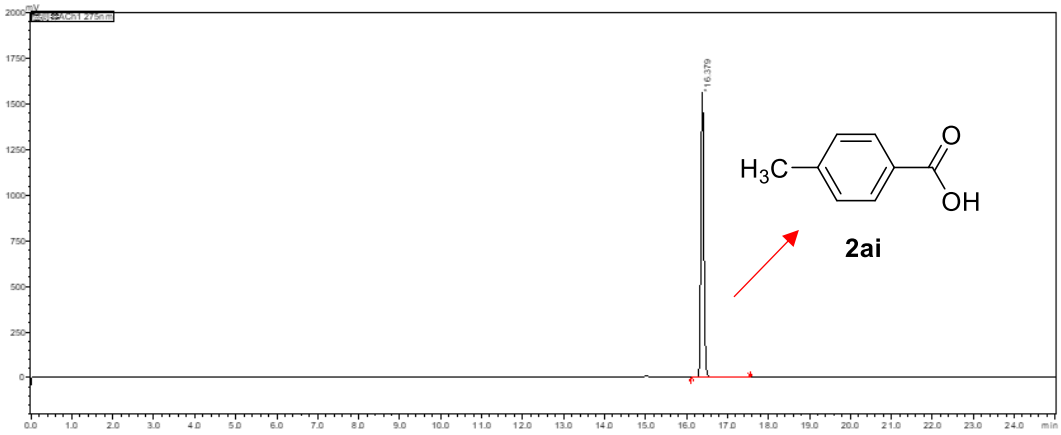


Fig. S32. HPLC chromatogram of **2ai**

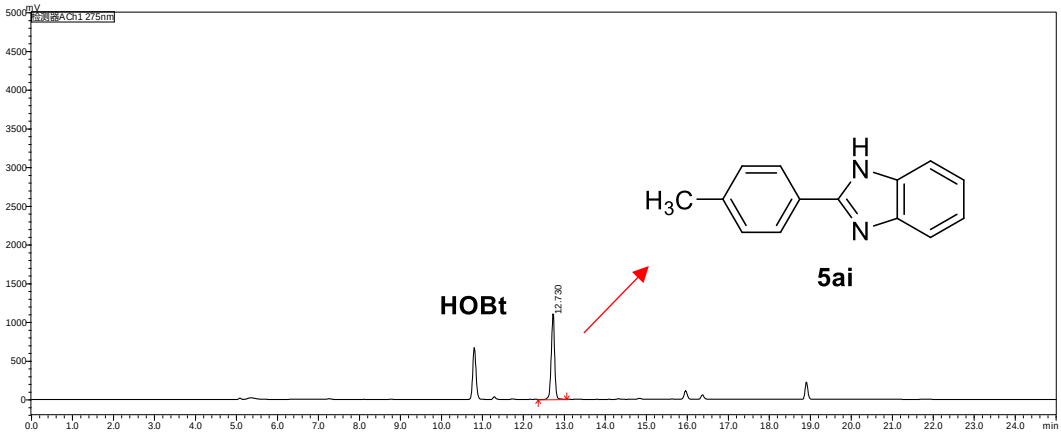


Fig. S33. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5ai**

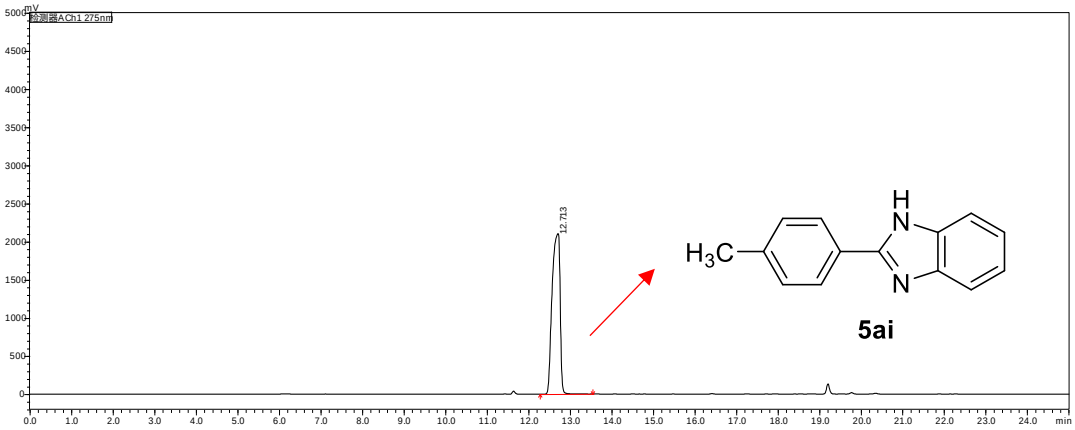


Fig. S34. HPLC chromatogram of purified **5ai**

substrate scope: **5aj**

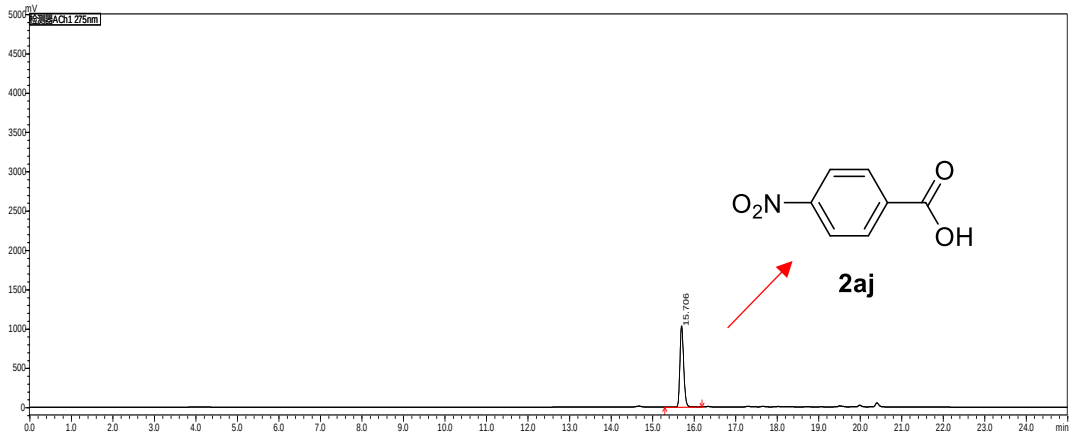


Fig. S35. HPLC chromatogram of **2aj**

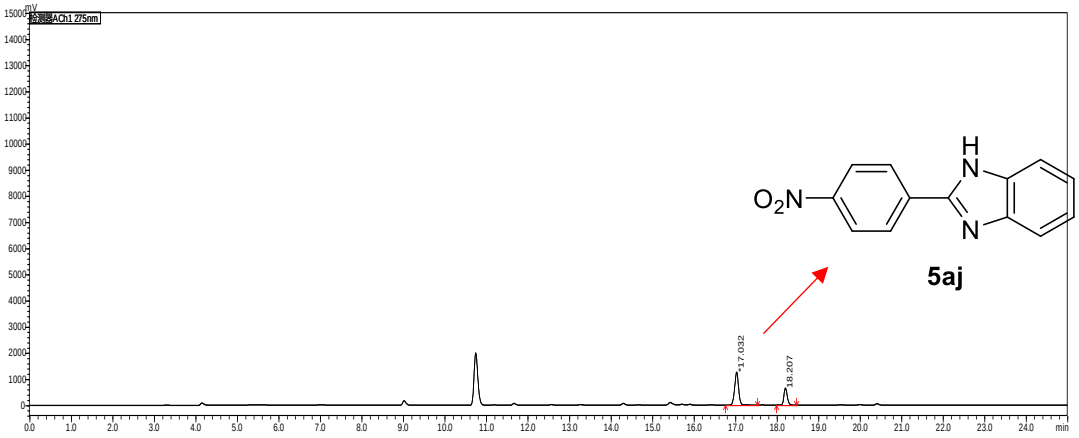


Fig. S36. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5aj**

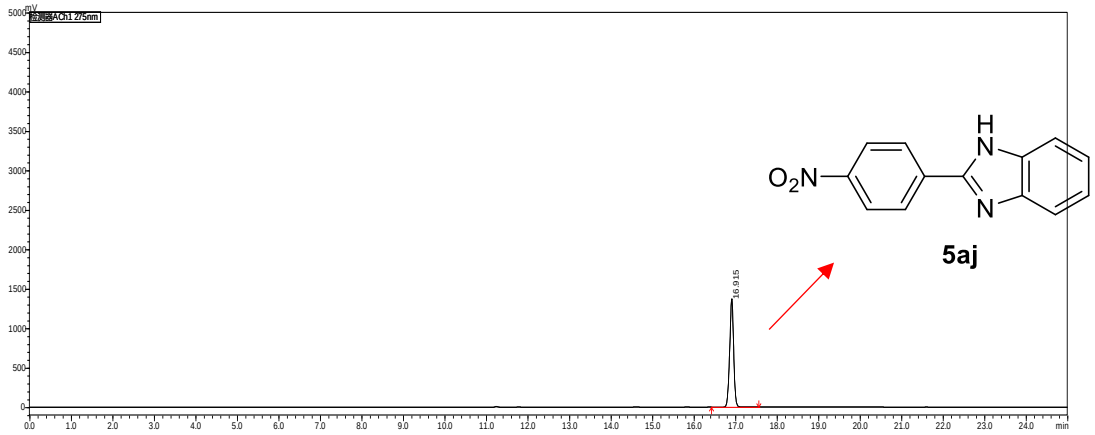


Fig. S37. HPLC chromatogram of purified **5aj**

substrate scope: **5ak**

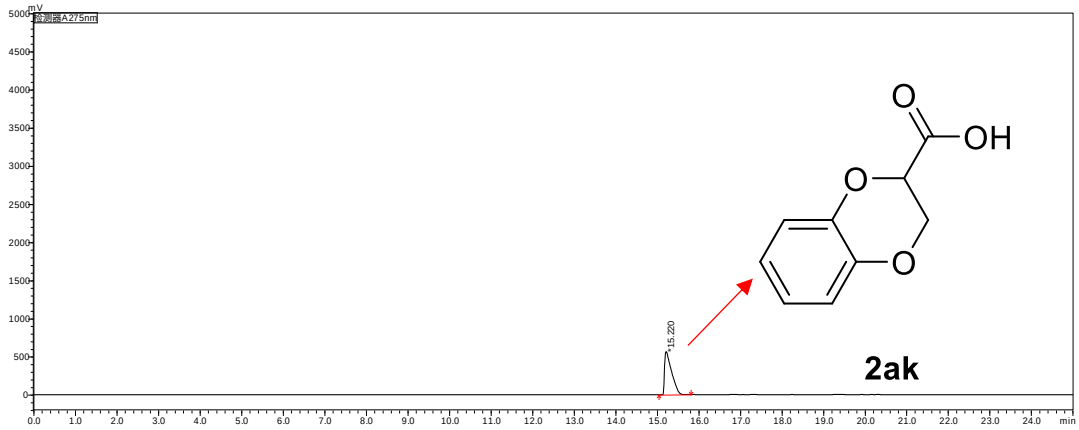


Fig. S38. HPLC chromatogram of **2ak**

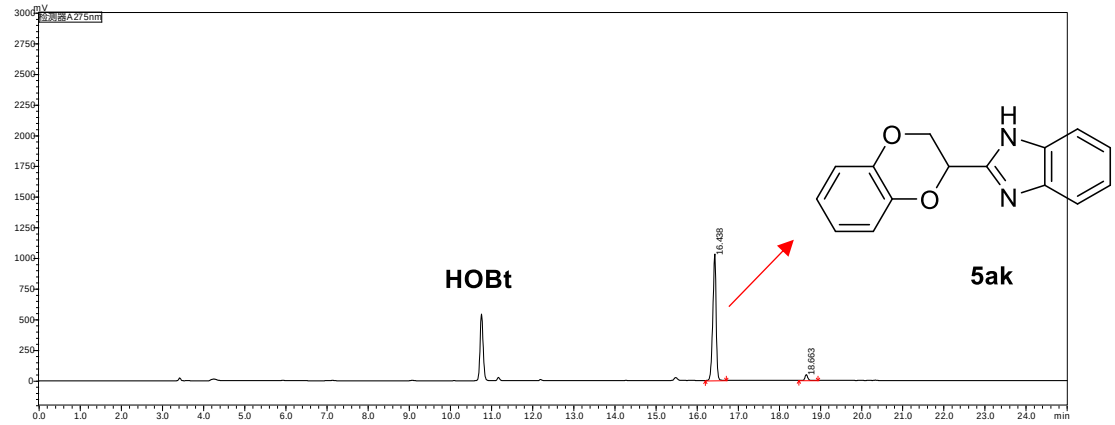


Fig. S39. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5ak**

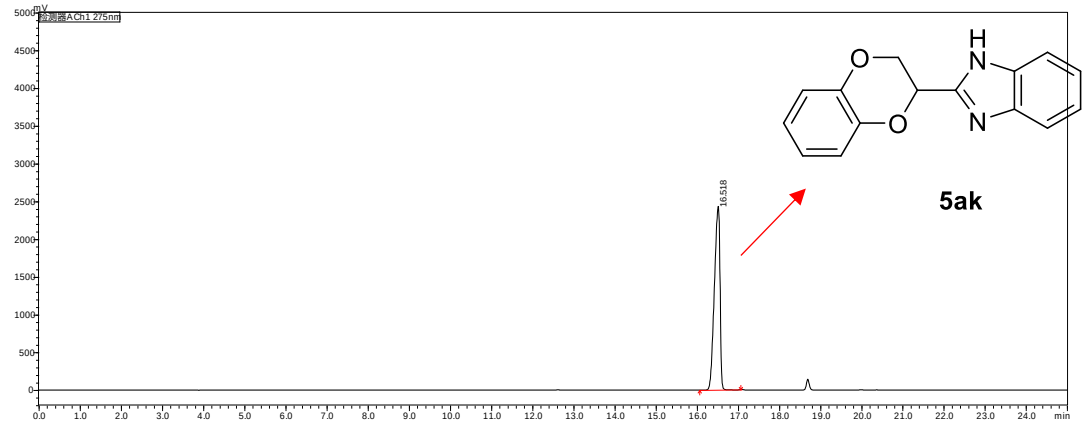


Fig. S40. HPLC chromatogram of purified **5ak**

substrate scope: **5al**

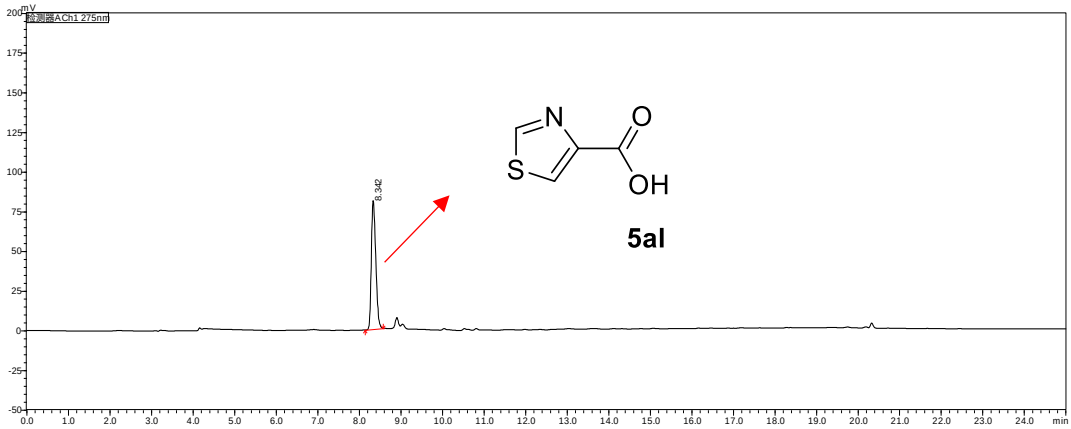


Fig. S41. HPLC chromatogram of **2al**

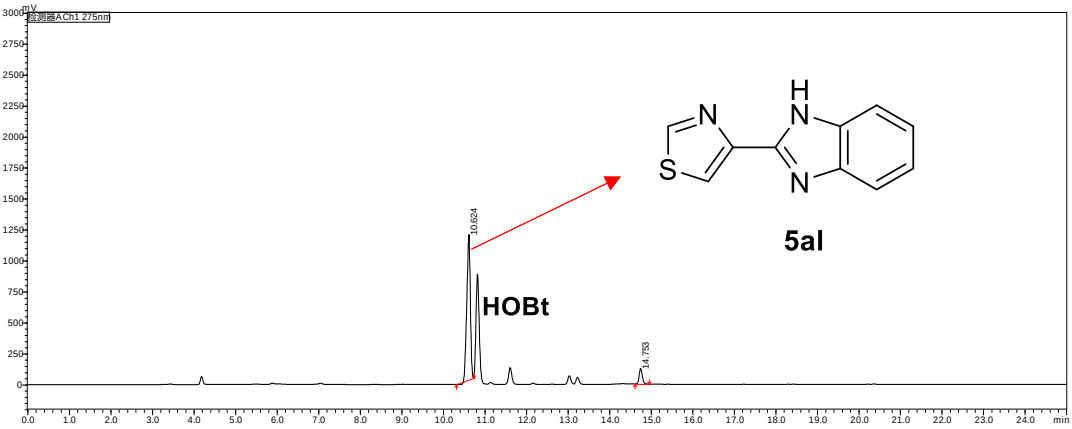


Fig. S42. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5al**

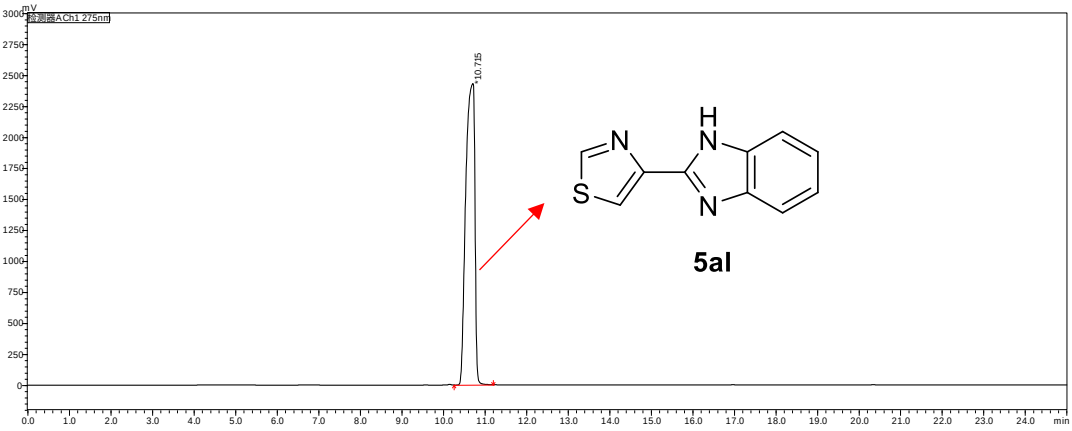


Fig. S43. HPLC chromatogram of purified **5al**

substrate scope: **5am**

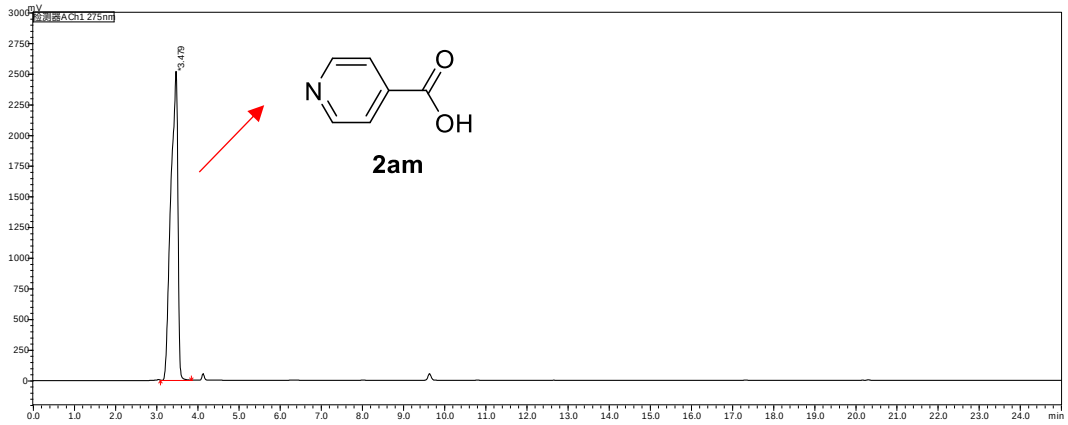


Fig. S44. HPLC chromatogram of **2am**

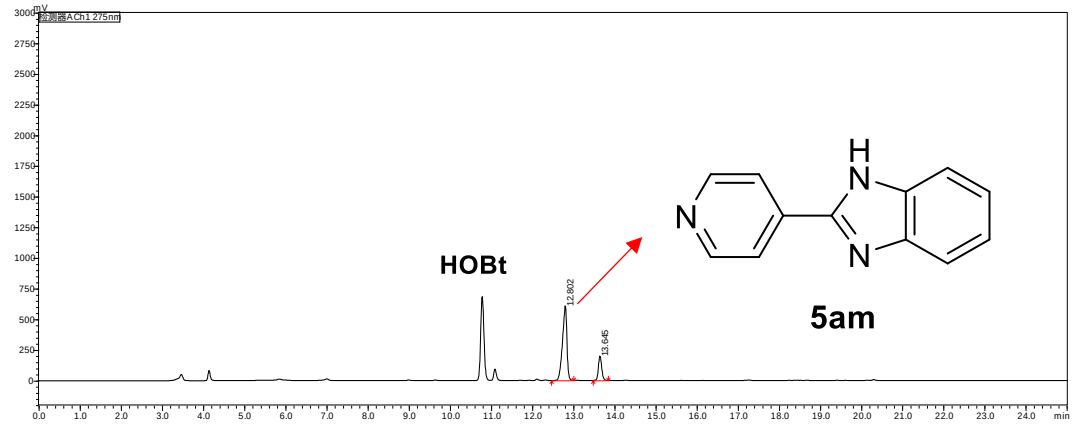


Fig. S45. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5am**

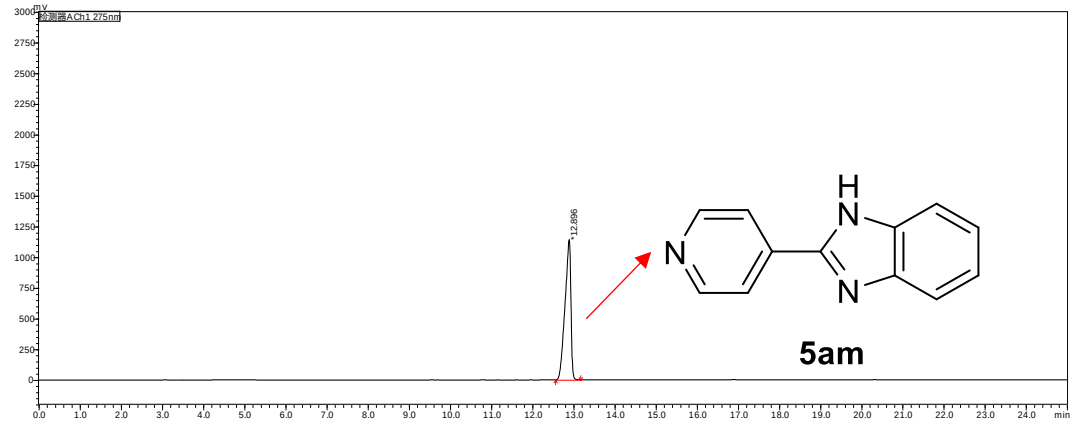


Fig. S46. HPLC chromatogram of purified **5am**

substrate scope: **5an**

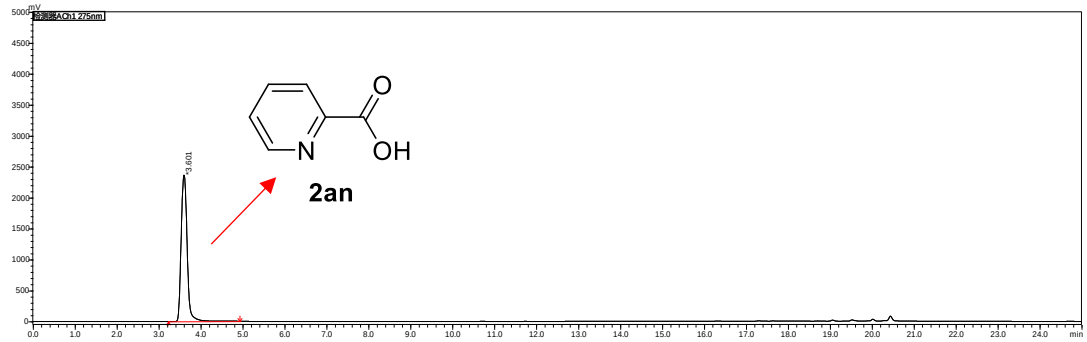


Fig. S47. HPLC chromatogram of **2an**

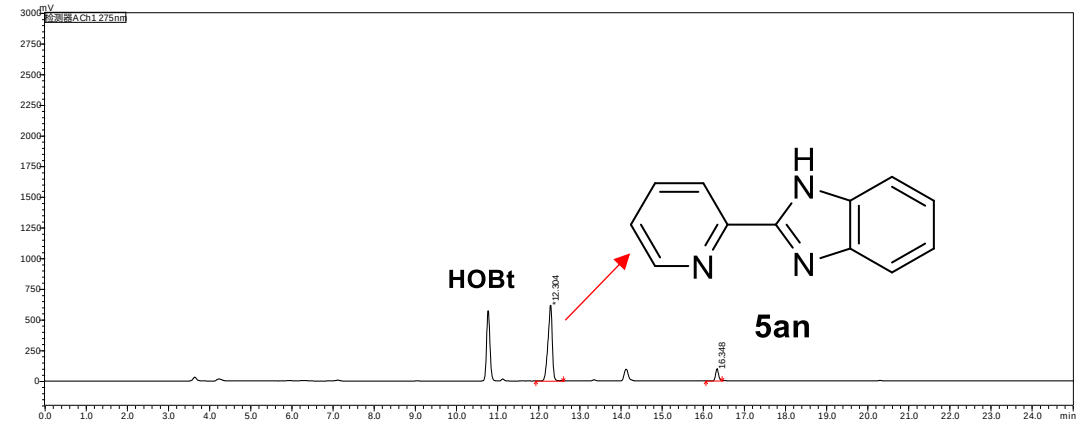


Fig. S48. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5an**

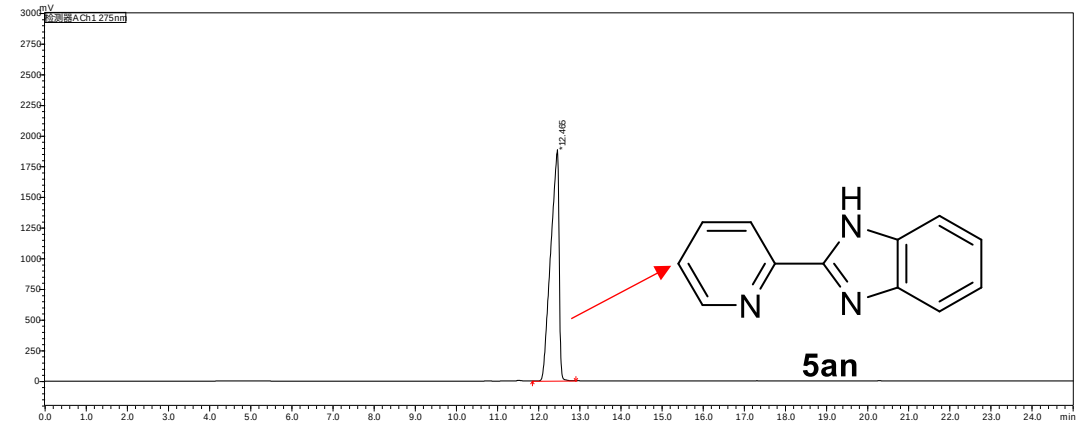


Fig. S49. HPLC chromatogram of purified **5an**

substrate scope: **5ao**

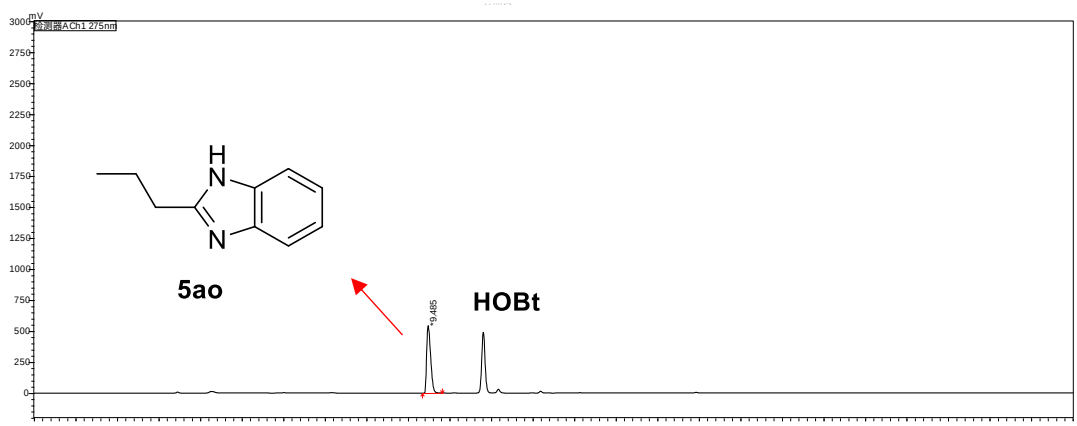


Fig. S50. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5ao**

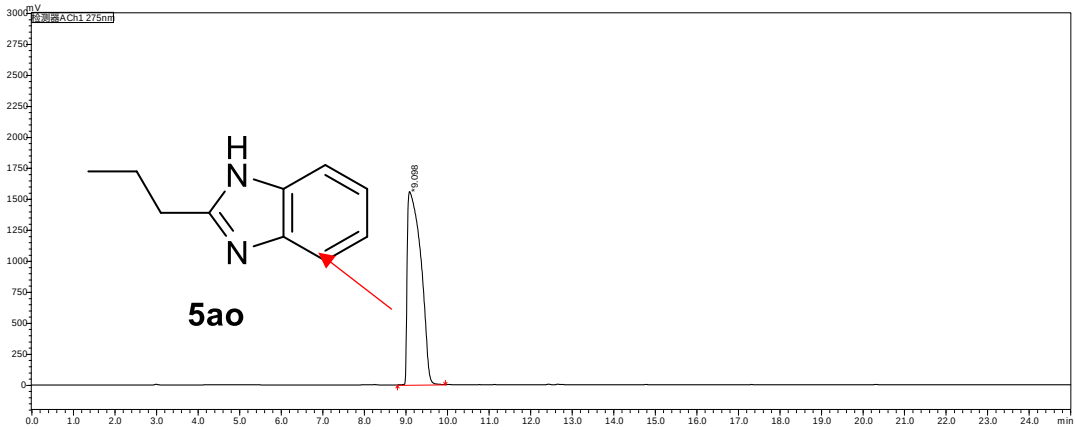


Fig. S51. HPLC chromatogram of purified **5ao**

substrate scope: **5ap**

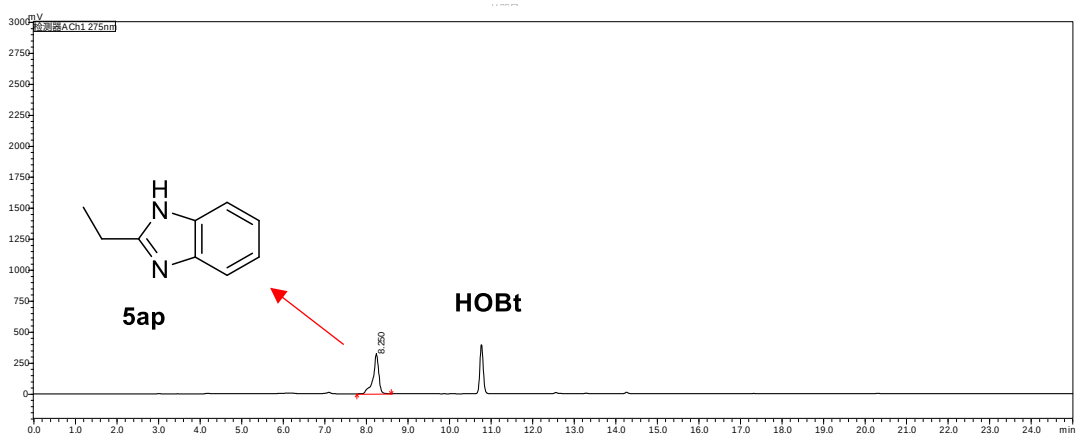


Fig. S52. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5ap**

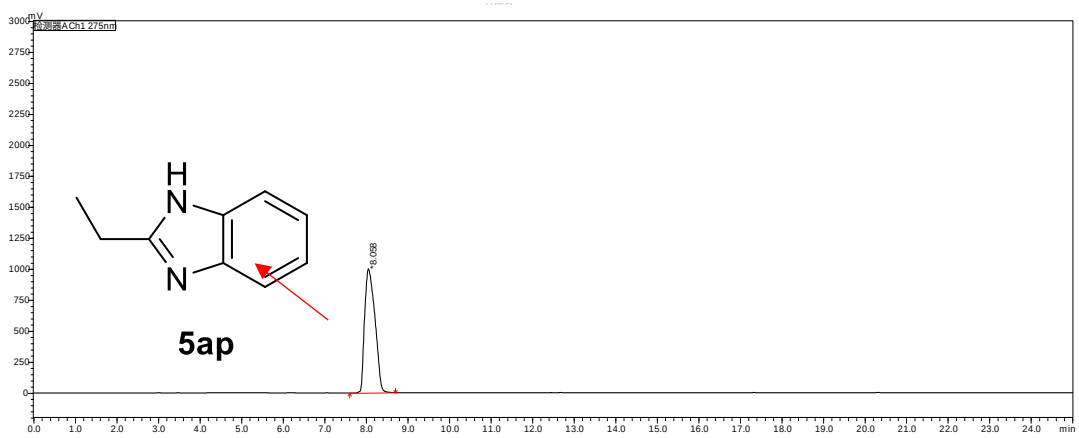


Fig. S53. HPLC chromatogram of purified **5ap**

substrate scope: **5aq**

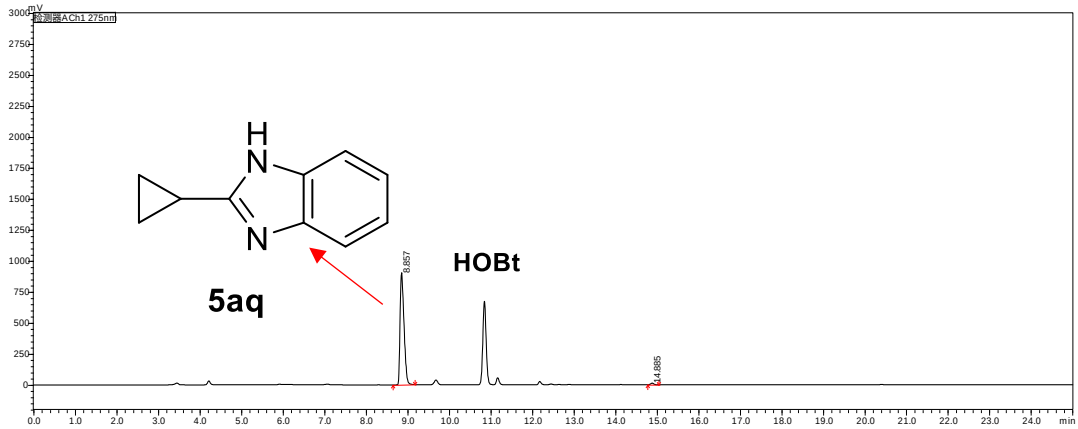


Fig. S54. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5aq**

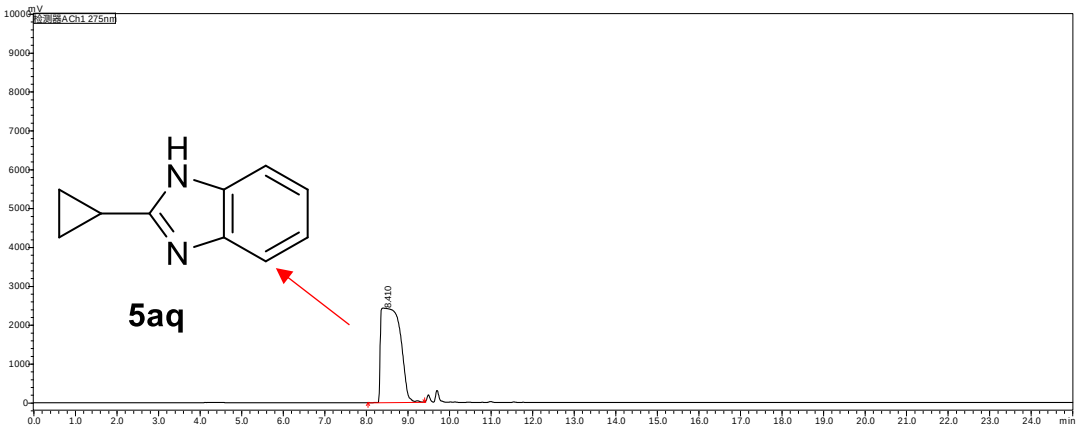


Fig. S55. HPLC chromatogram of purified **5aq**

substrate scope: **5ar**

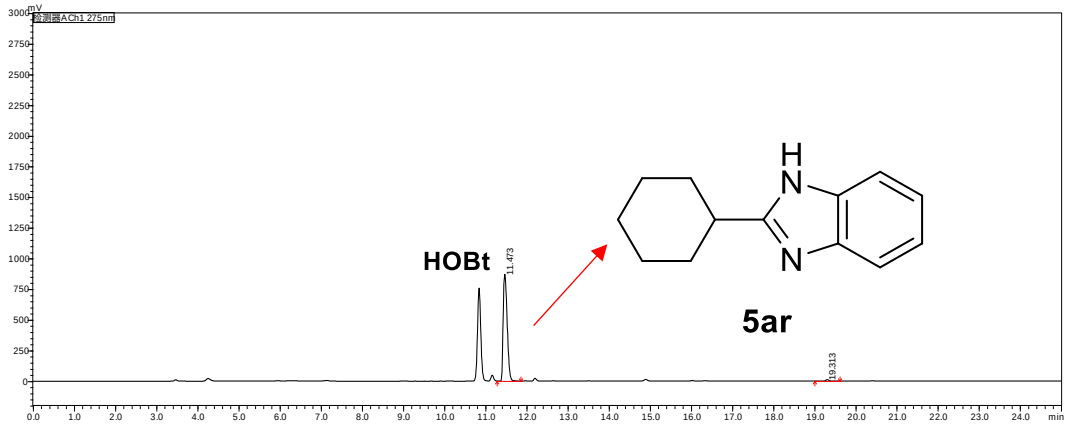


Fig. S56. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5ar**

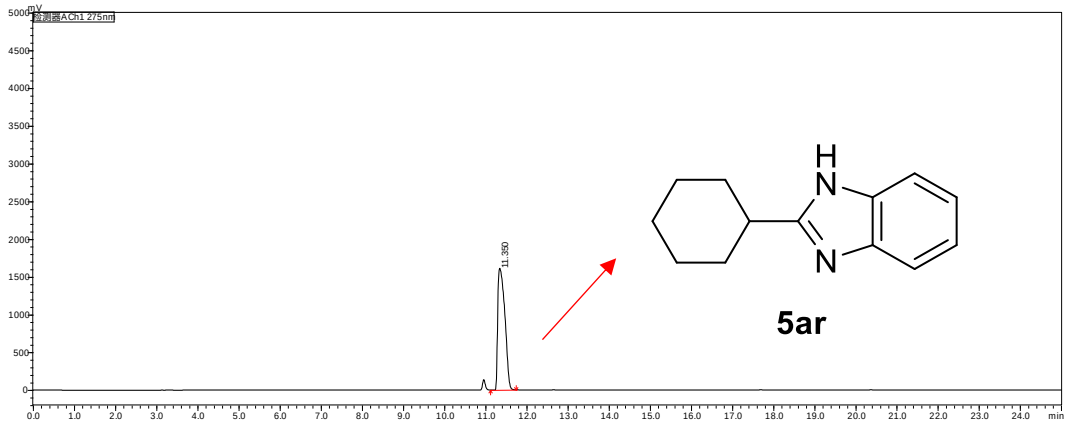


Fig. S57. HPLC chromatogram of purified **5ar**

substrate scope: **5ba**

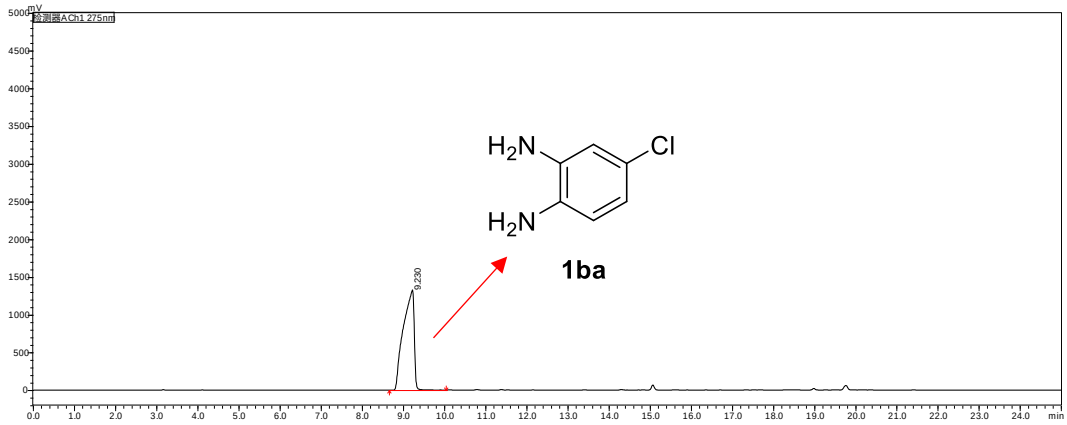


Fig. S58. HPLC chromatogram of **1ba**

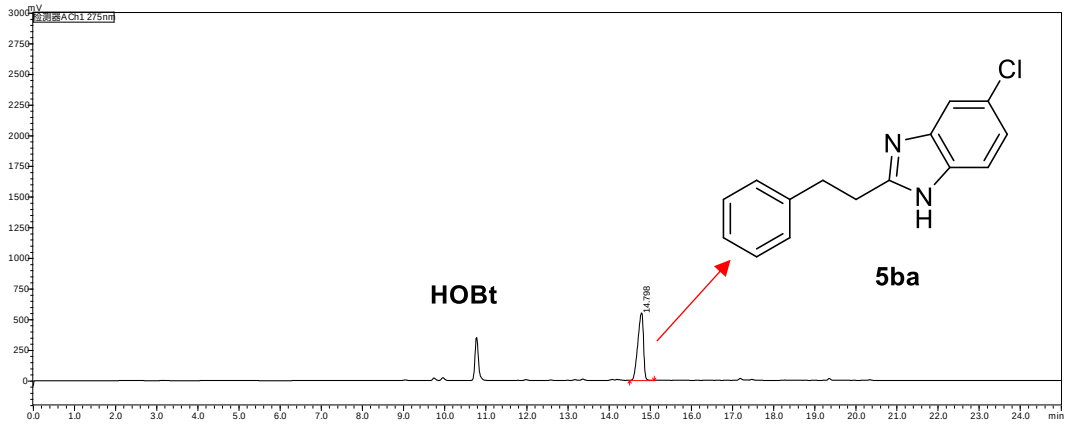


Fig. S59. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5ba**

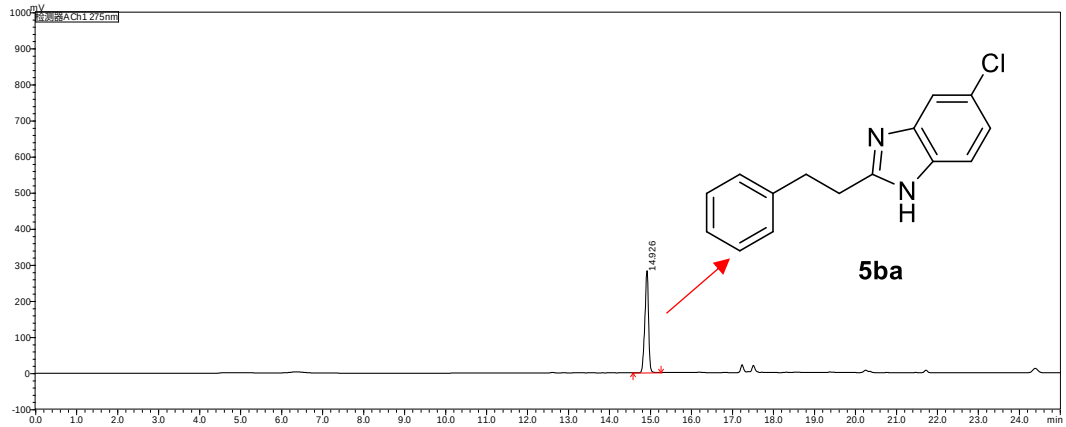


Fig. S60. HPLC chromatogram of purified **5ba**

substrate scope: **5ca**

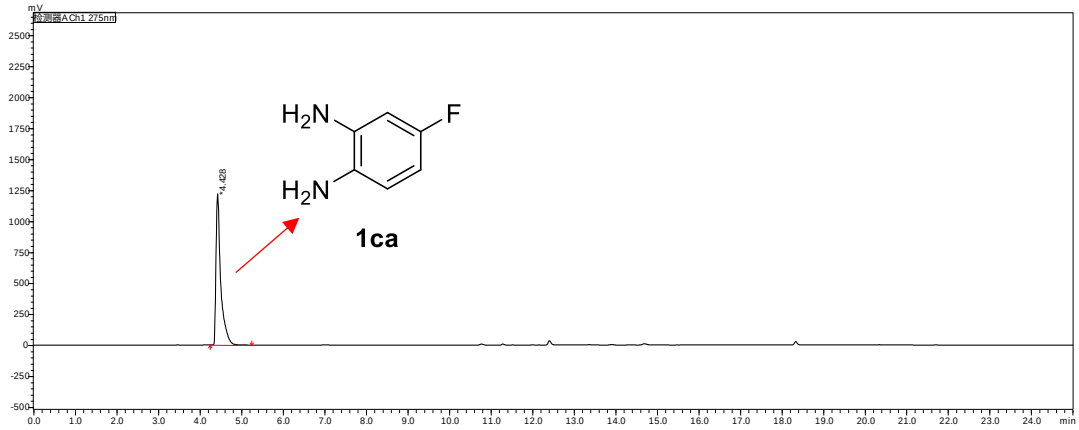


Fig. S61. HPLC chromatogram of **1ca**

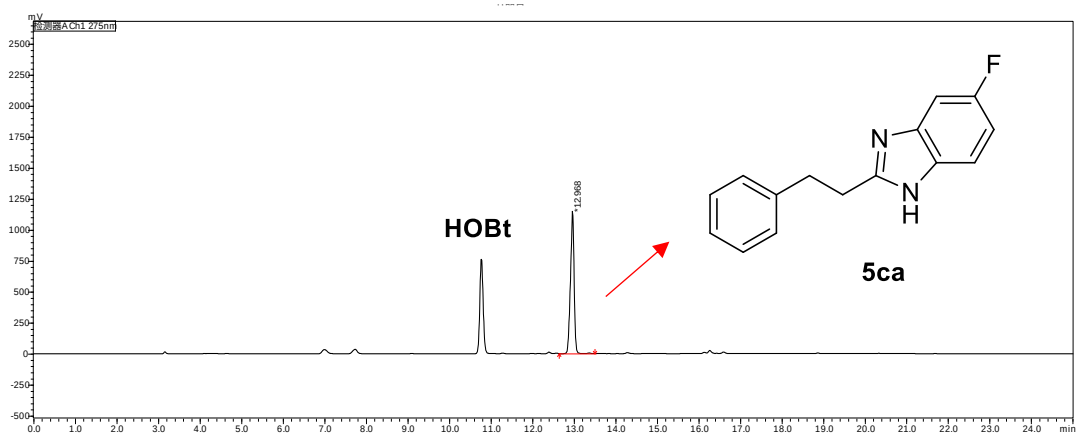


Fig. S62. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5ca**

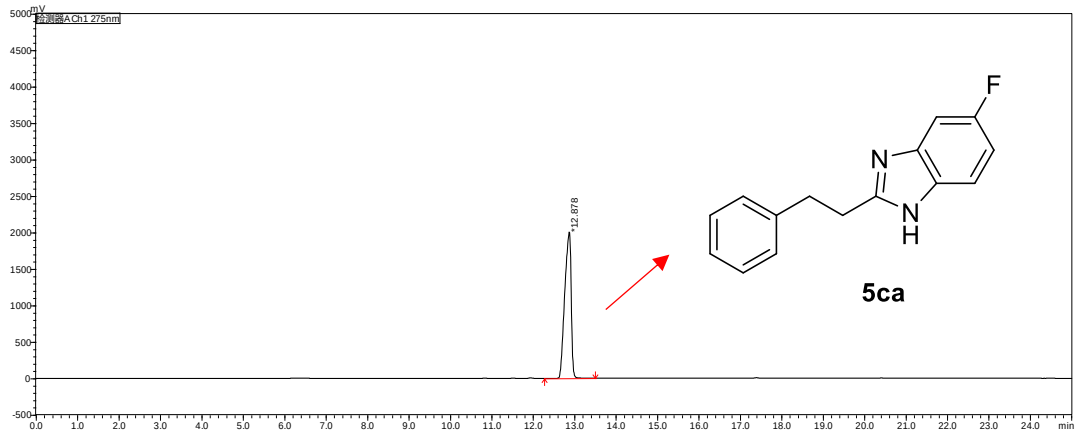


Fig. S63. HPLC chromatogram of purified **5ca**

substrate scope: **5da**

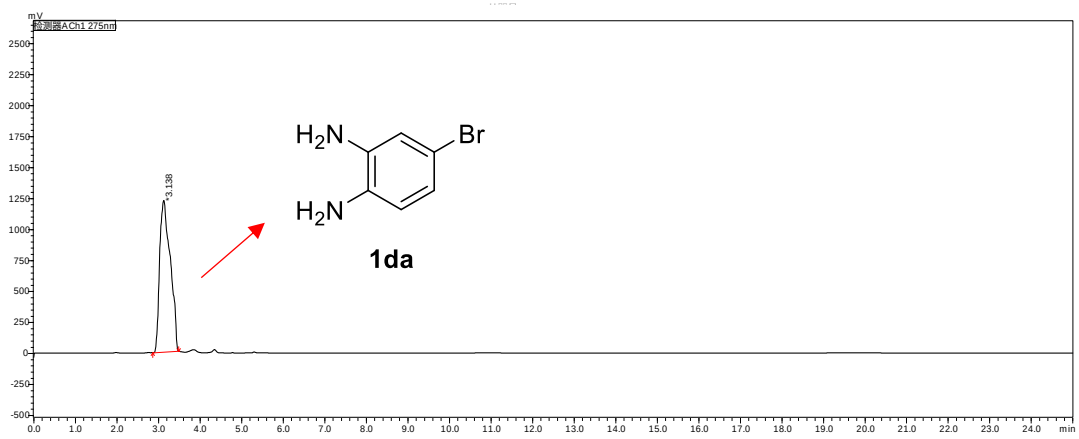


Fig. S64. HPLC chromatogram of **1da**

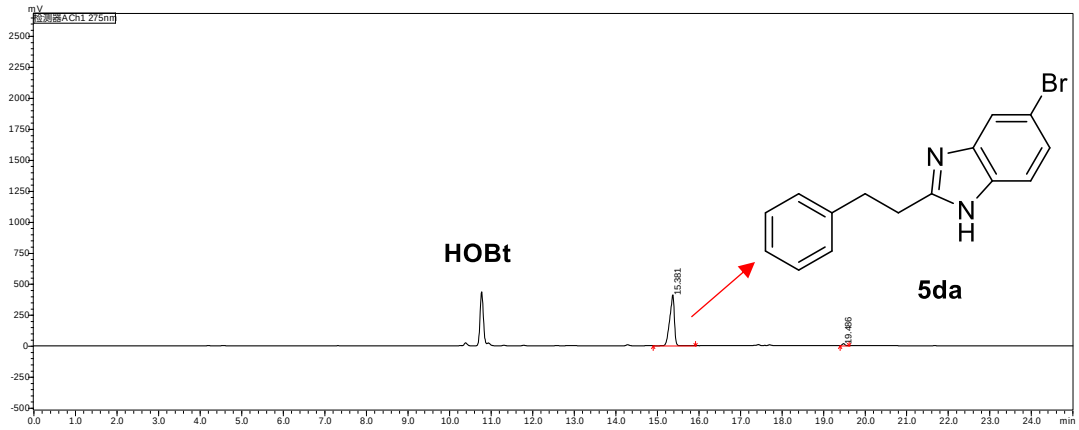


Fig. S65. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5da**

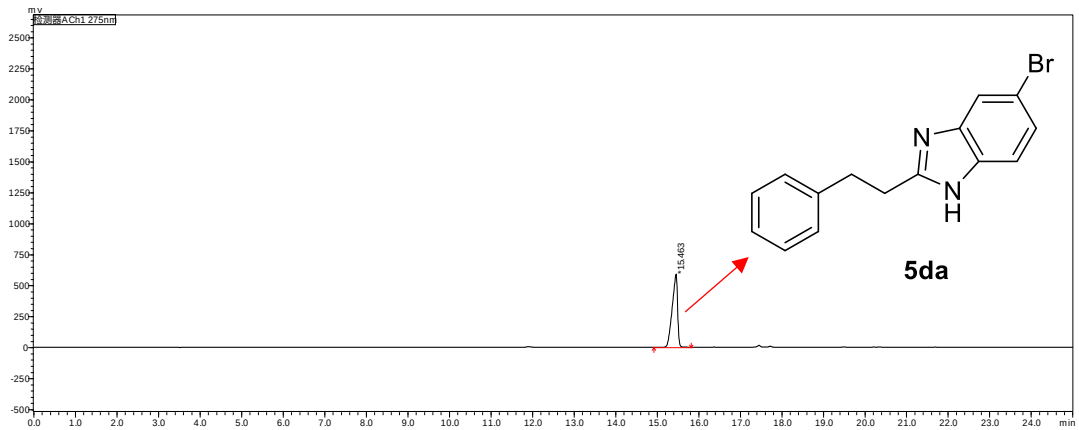


Fig. S66. HPLC chromatogram of purified **5da**

substrate scope: **5ea**

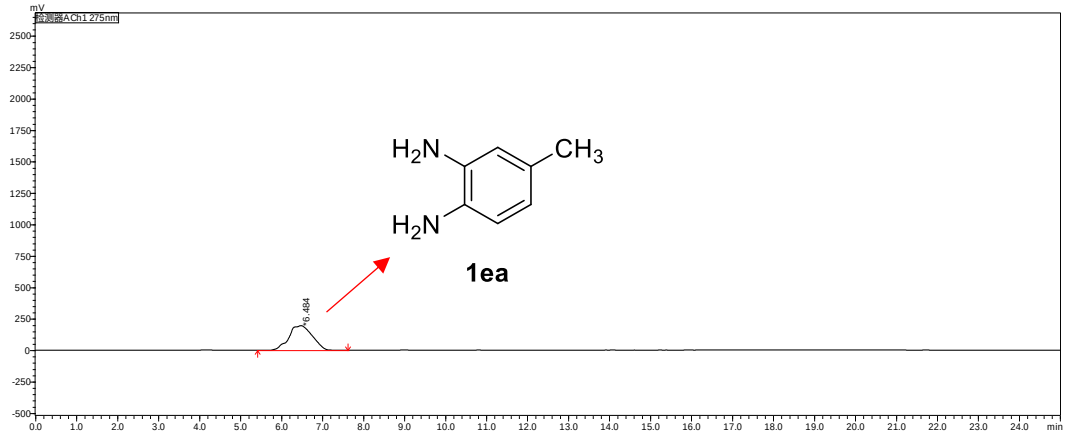


Fig. S67. HPLC chromatogram of **1ea**

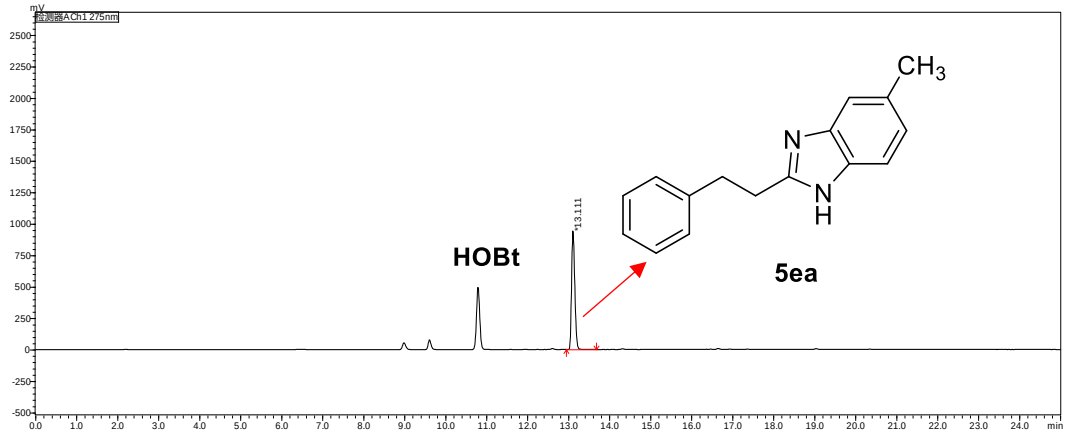


Fig. S68. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5ea**

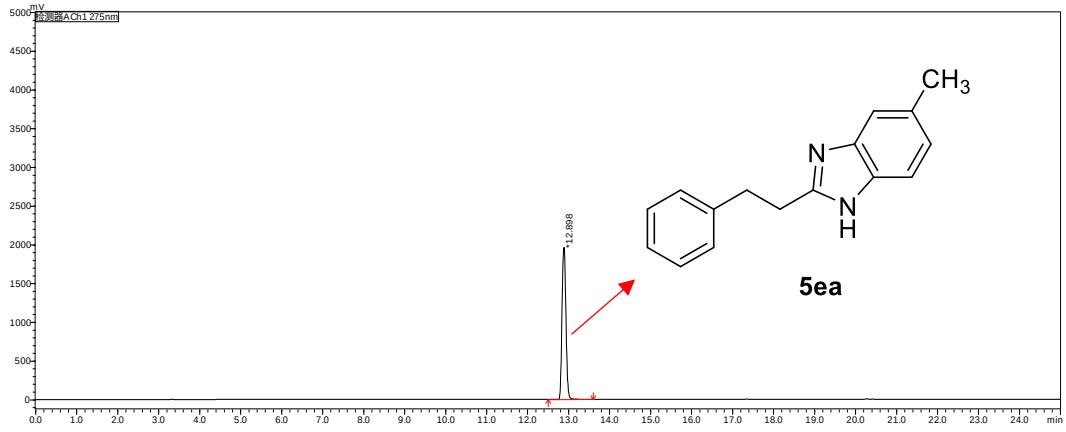


Fig. S69. HPLC chromatogram of purified **5ea**

substrate scope: **5fa**

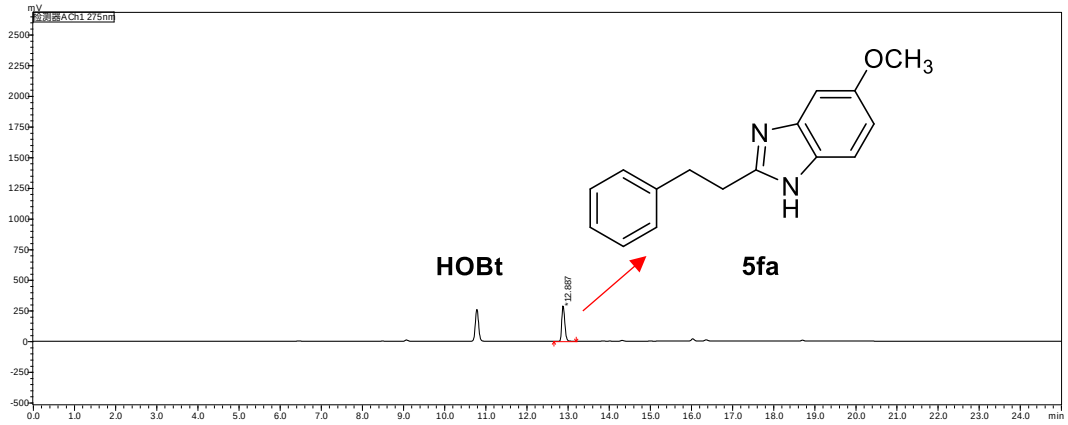


Fig. S70. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5fa**

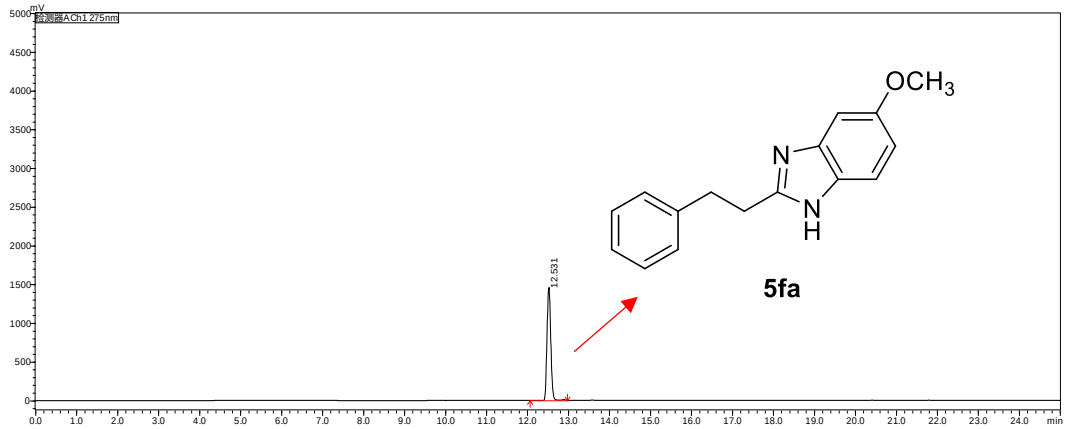


Fig. S71. HPLC chromatogram of purified **5fa**

substrate scope: **5ga**

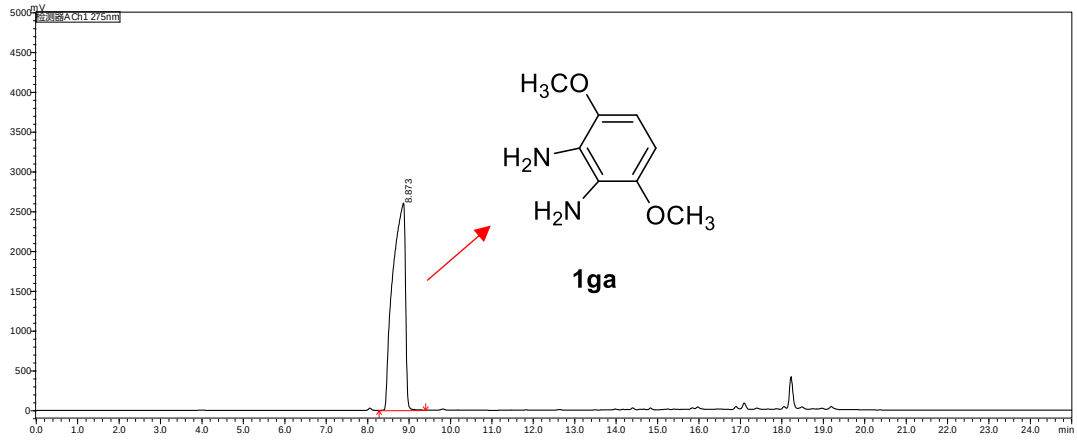


Fig. S72. HPLC chromatogram of **1ga**

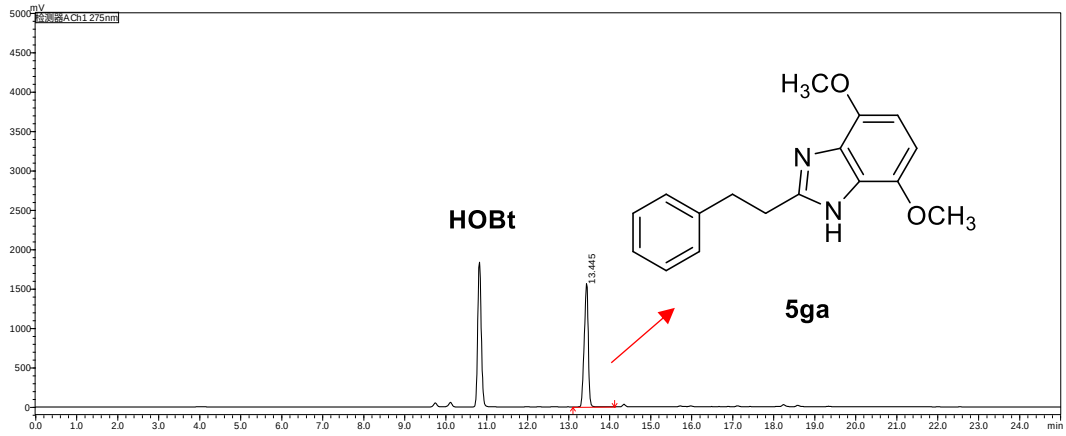


Fig. S73. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5ga**

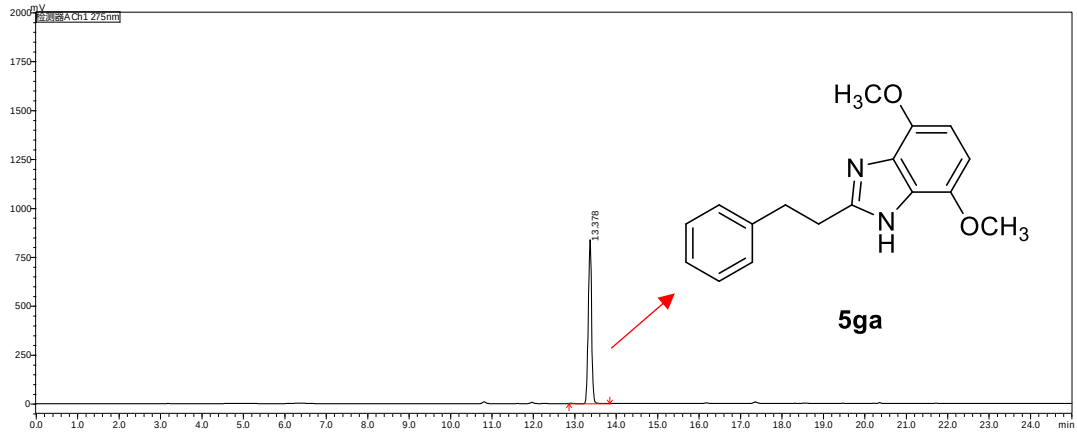


Fig. S74. HPLC chromatogram of purified **5ga**

substrate scope: **5ha**

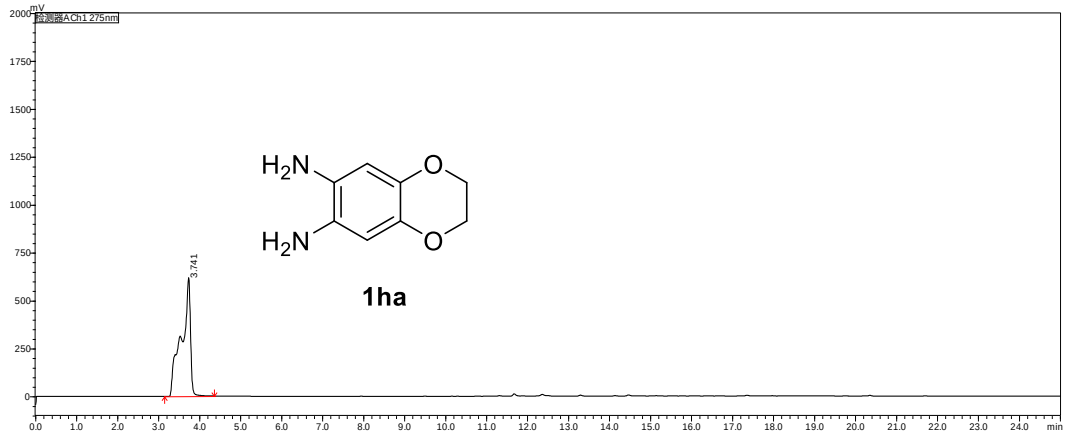


Fig. S75. HPLC chromatogram of **1ha**

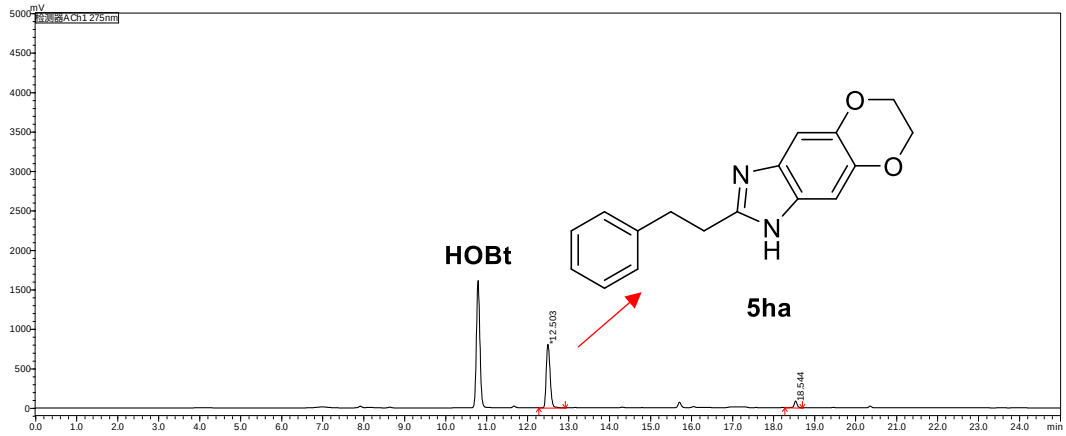


Fig. S76. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5ha**

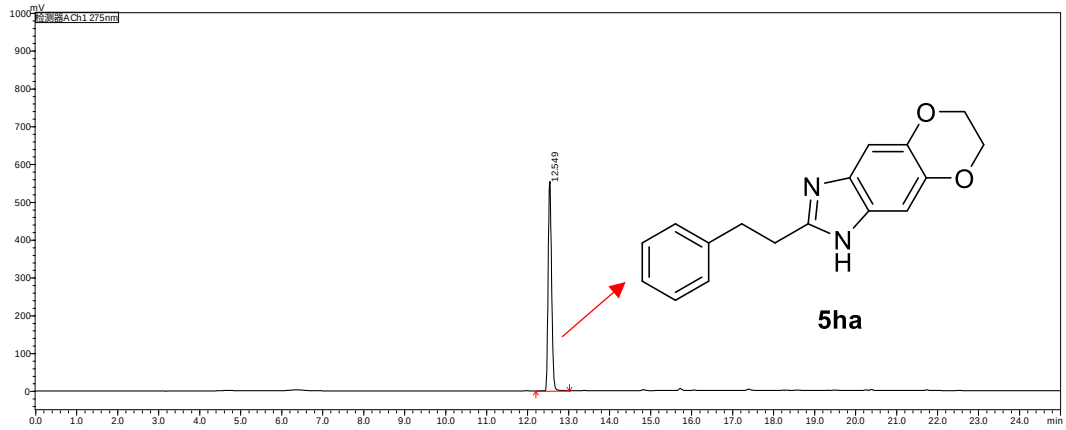


Fig. S77. HPLC chromatogram of purified **5ha**

substrate scope: **5ia**

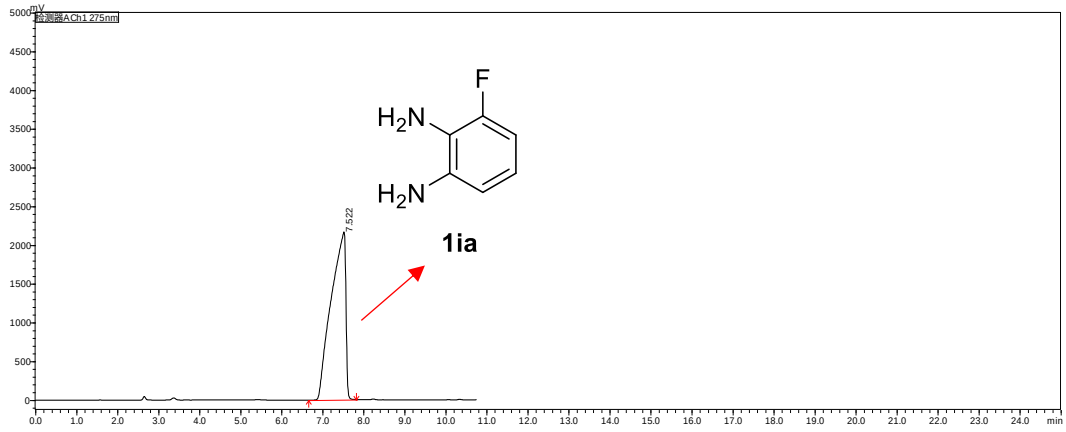


Fig. S78. HPLC chromatogram of **1ia**

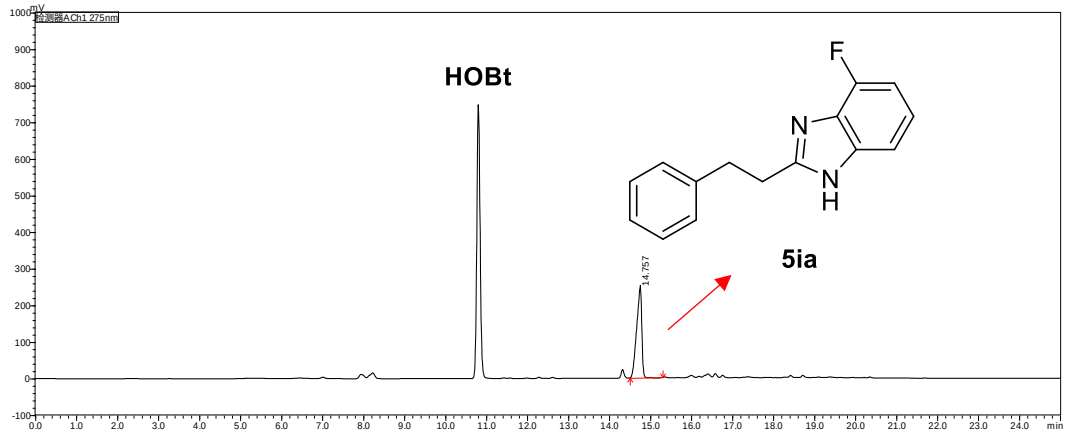


Fig. S79. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5ia**

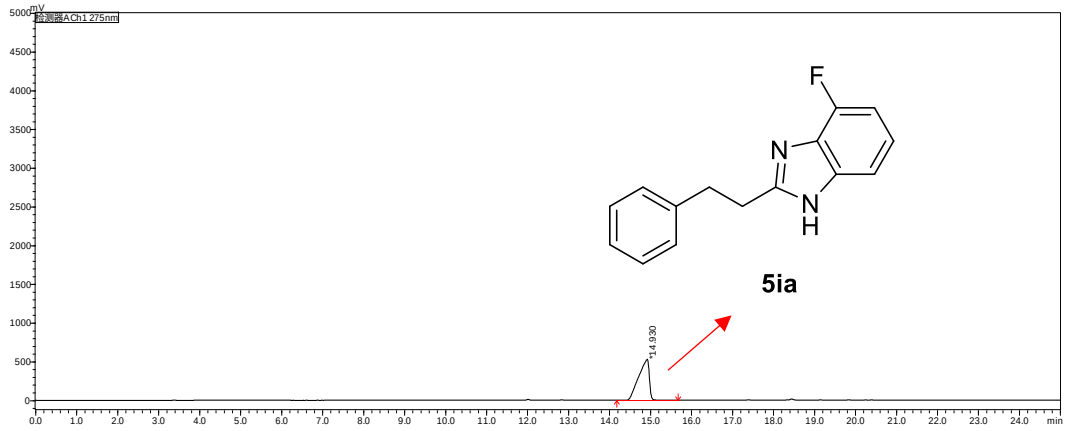


Fig. S80. HPLC chromatogram of purified **5ia**

substrate scope: **5ja**

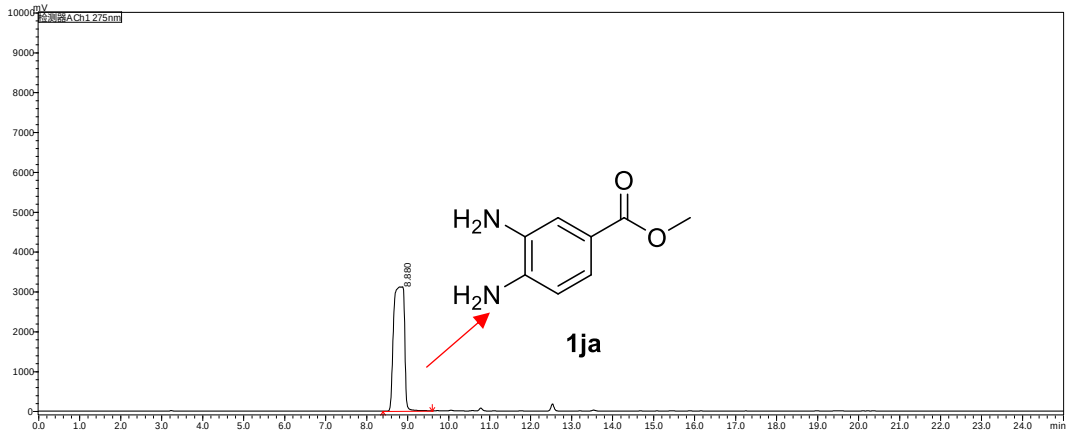


Fig. S81. HPLC chromatogram of **1ja**

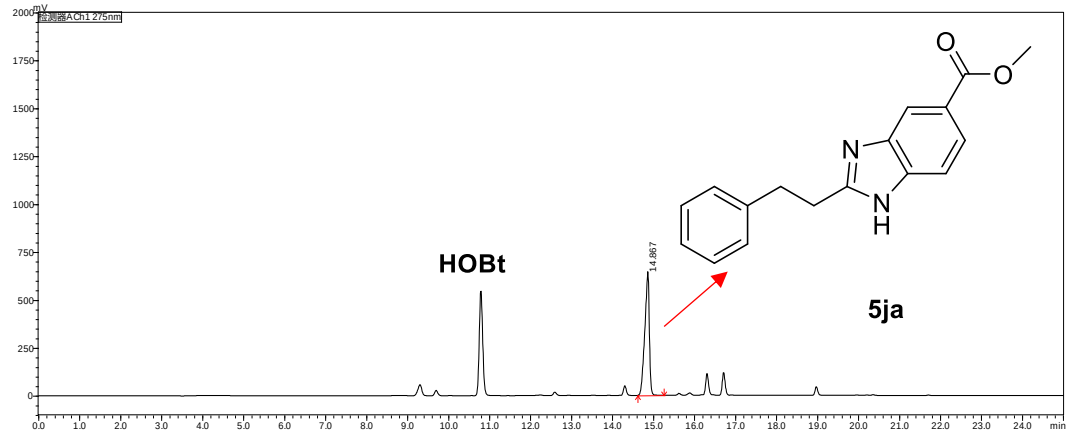


Fig. S82. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5ja**

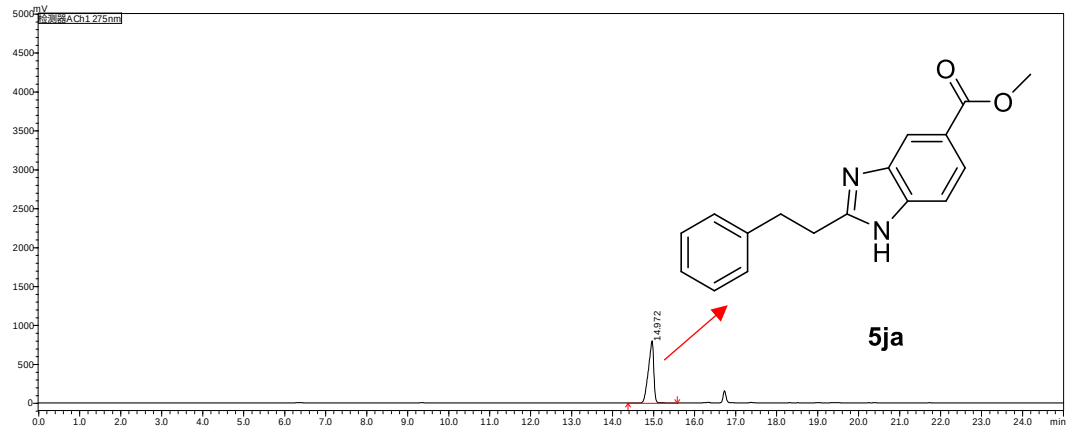


Fig. S83. HPLC chromatogram of purified **5ja**

substrate scope: **5ka**

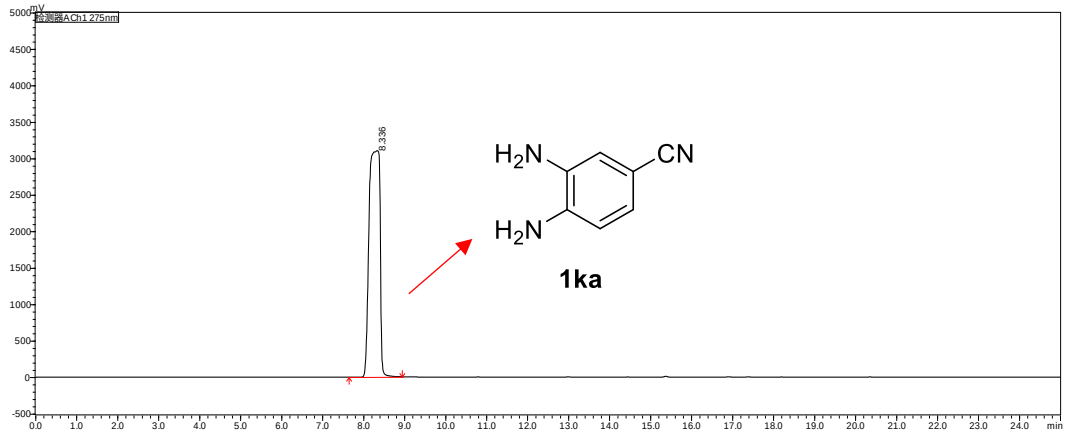


Fig. S84. HPLC chromatogram of **1ka**

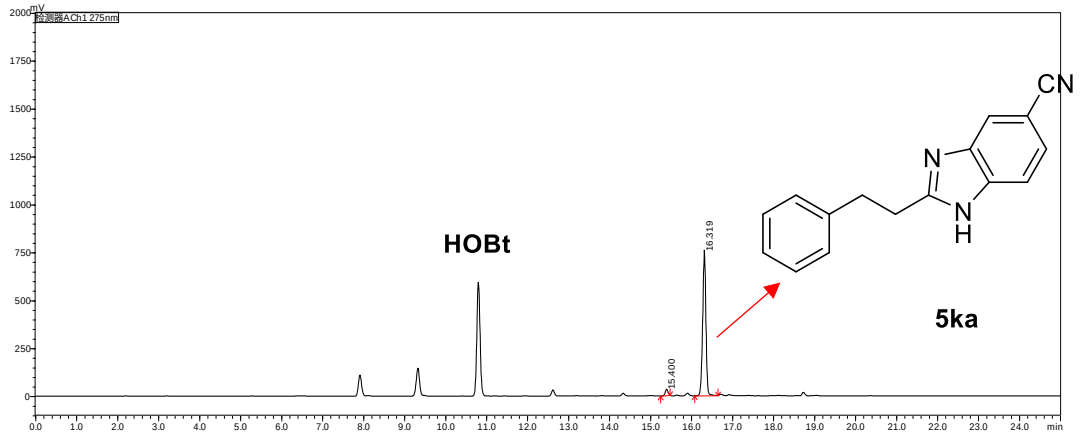


Fig. S85. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5ka**

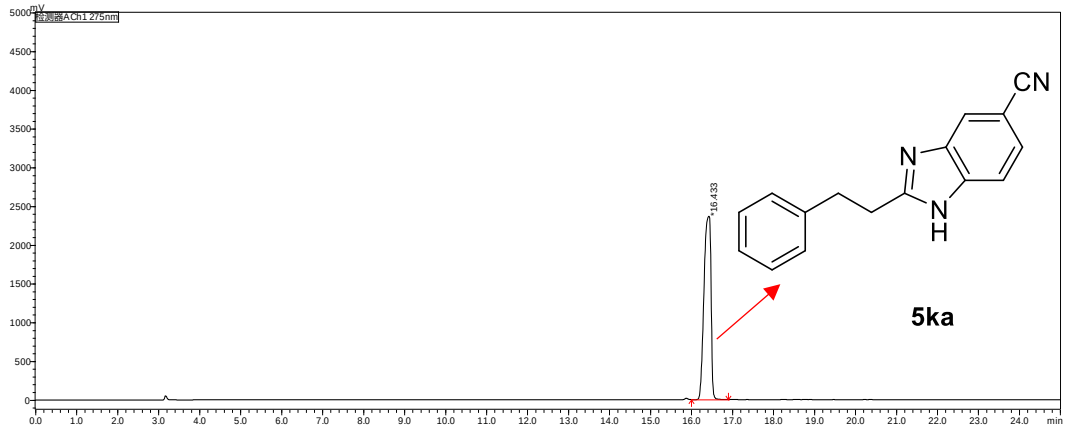


Fig. S86. HPLC chromatogram of purified **5ka**

substrate scope: **5la**

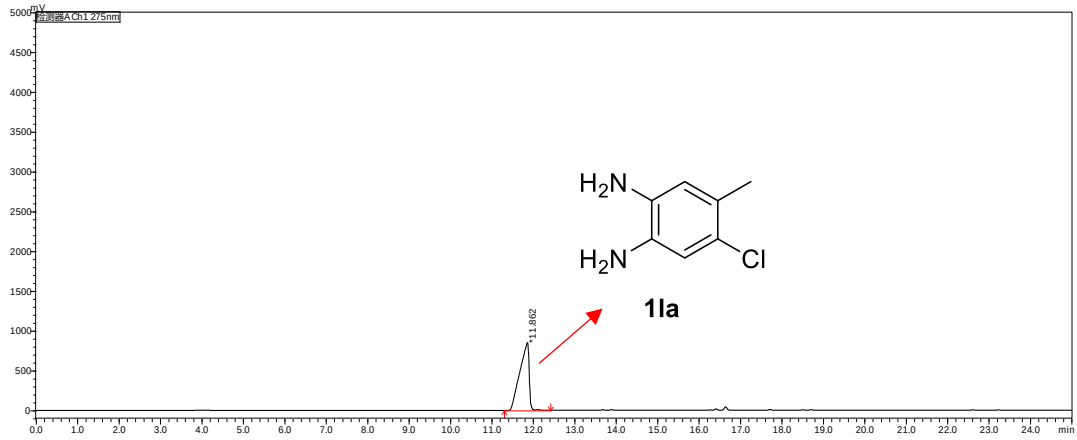


Fig. S87. HPLC chromatogram of **1la**

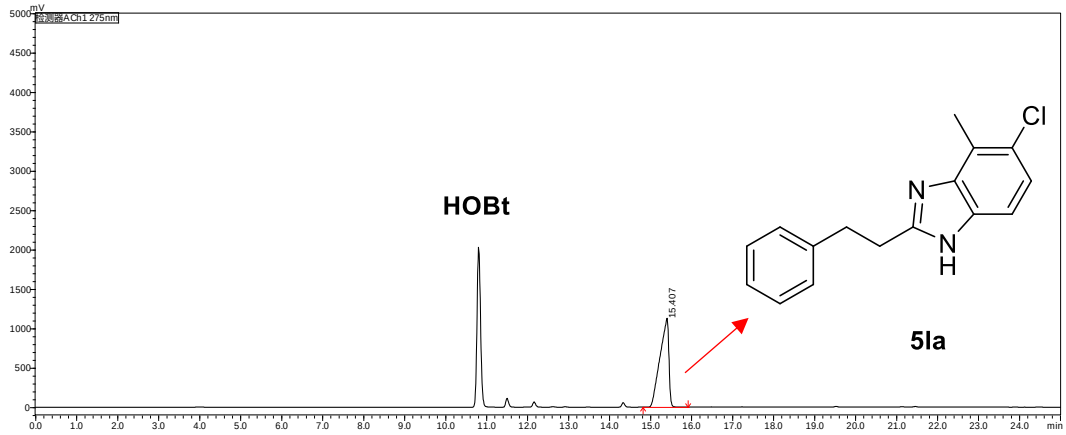


Fig. S88. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5la**

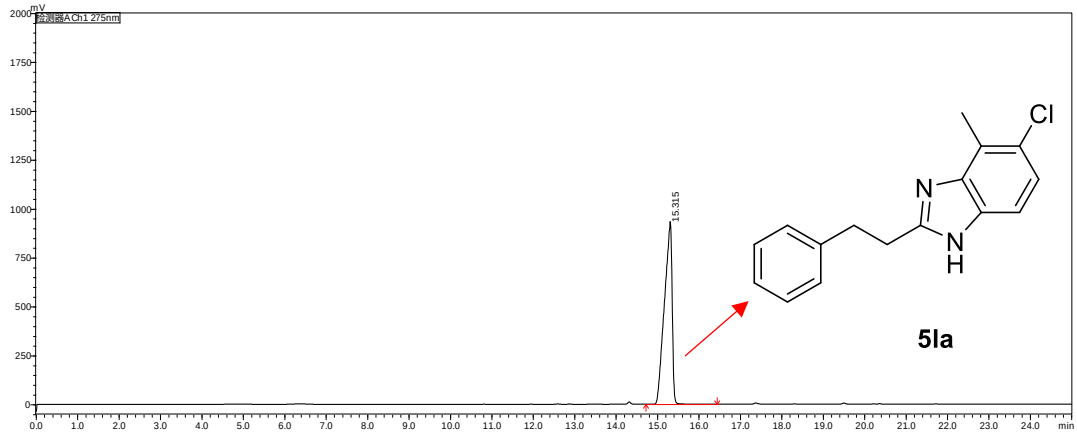


Fig. S89. HPLC chromatogram of purified **5la**

substrate scope: **5c**

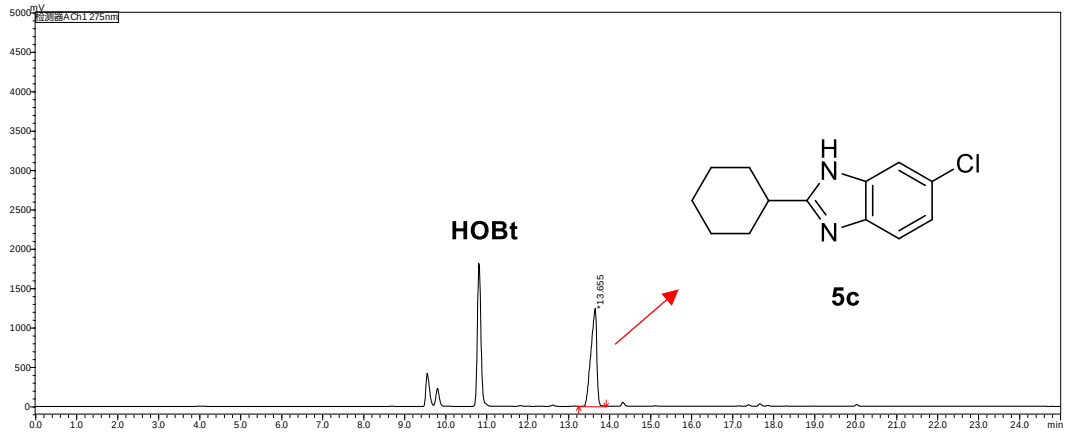


Fig. S90. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5c**

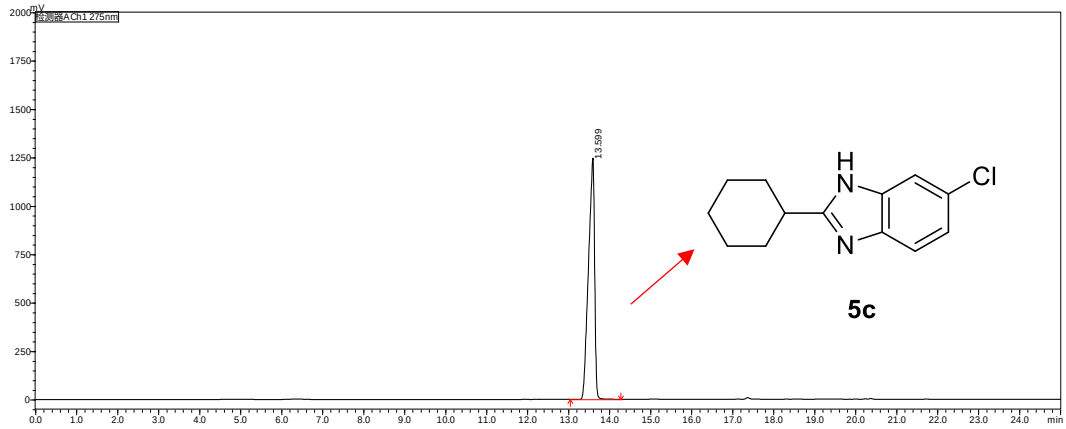


Fig. S91. HPLC chromatogram of purified **5c**

substrate scope: **5d**

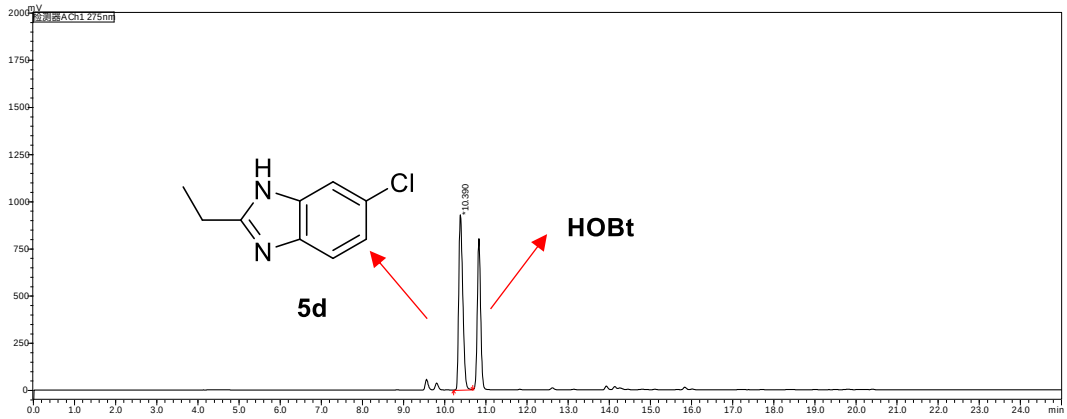


Fig. S92. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5d**

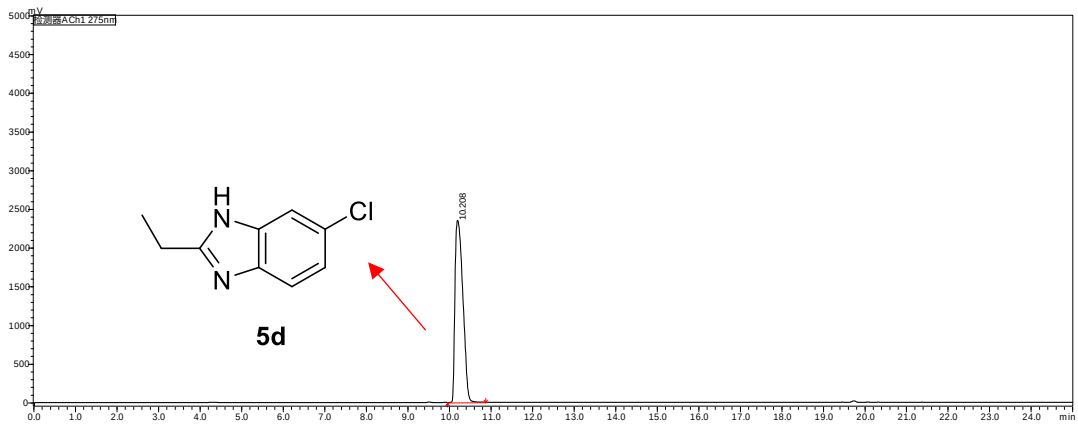


Fig. S93. HPLC chromatogram of purified **5d**

substrate scope: **5e**

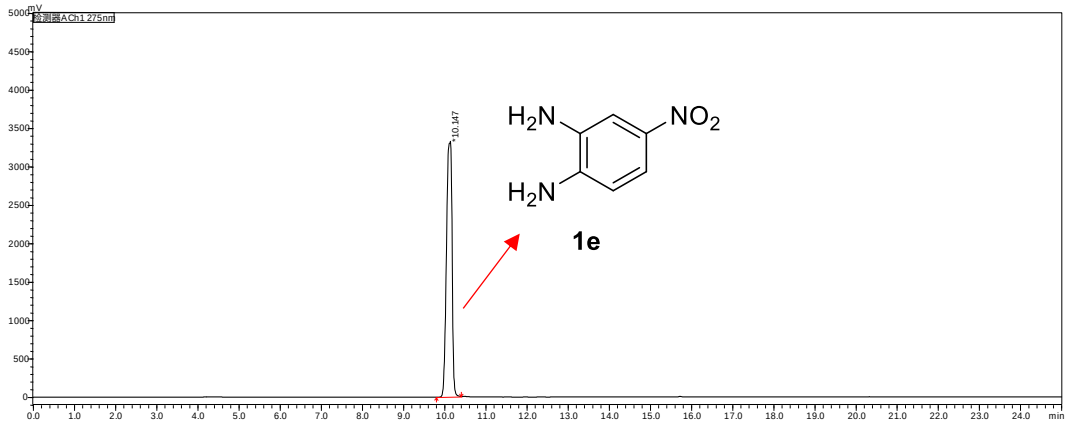


Fig. S94. HPLC chromatogram of **1e**

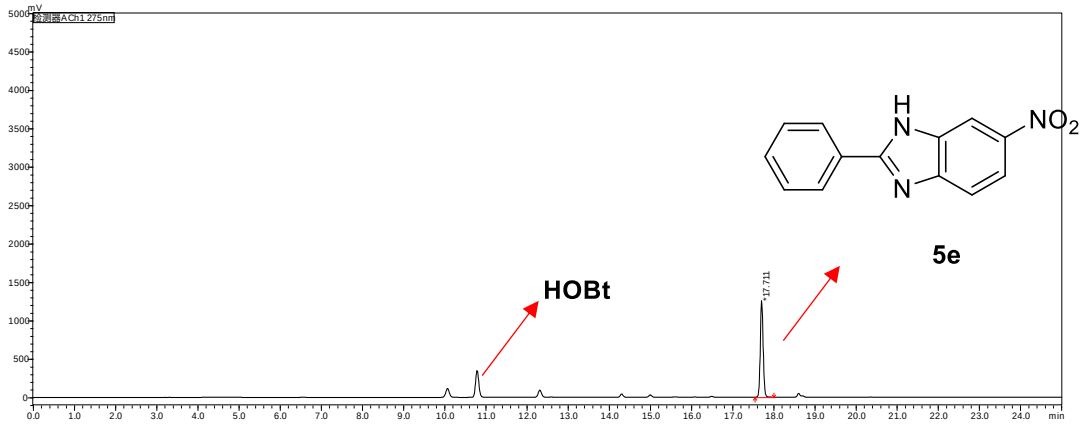


Fig. S95. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5e**

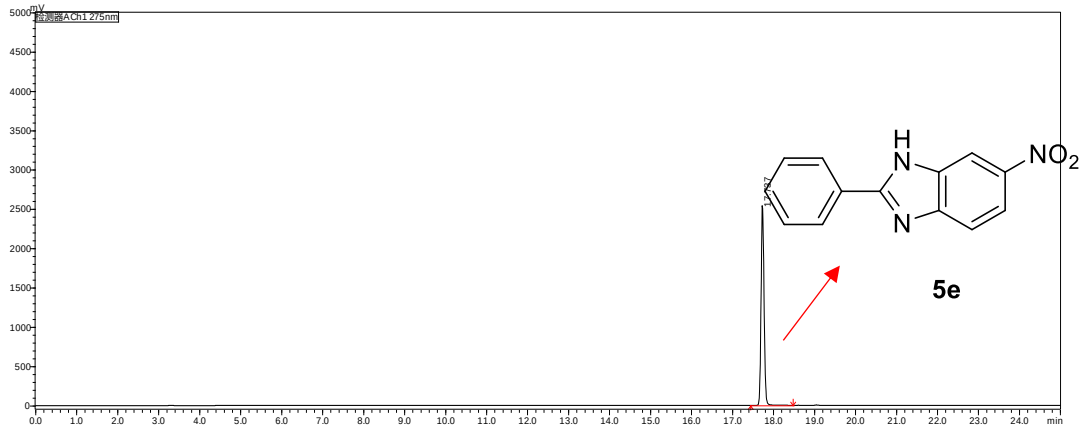


Fig. S96. HPLC chromatogram of purified **5e**

substrate scope: **5f**

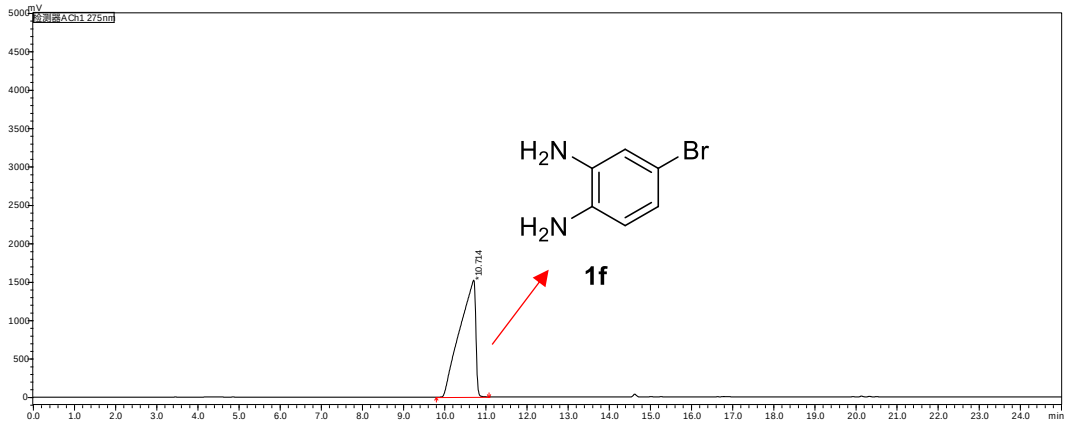


Fig. S97. HPLC chromatogram of **1f**

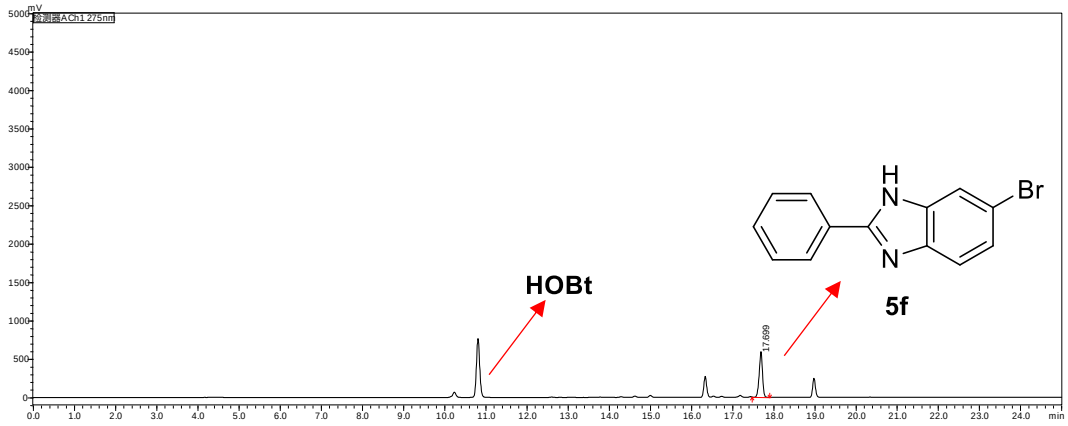


Fig. S98. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5f**

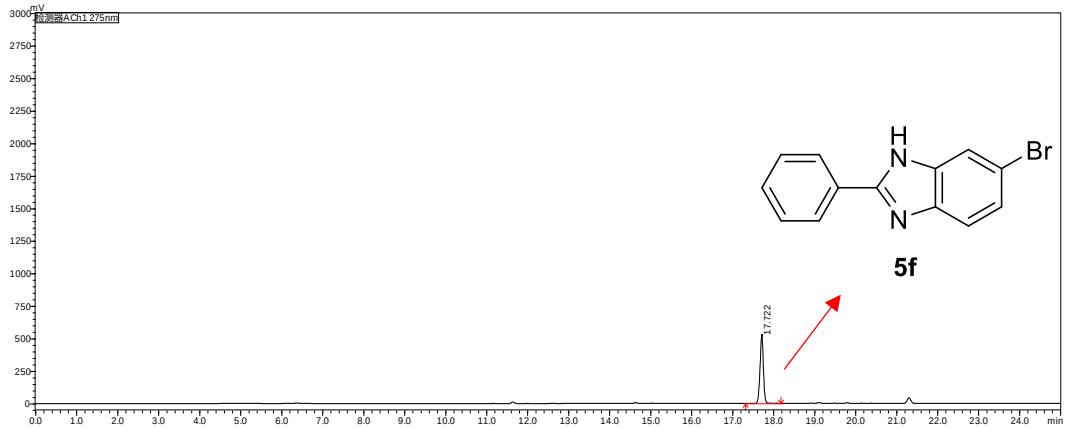


Fig. S99. HPLC chromatogram of purified **5f**

substrate scope: **5g**

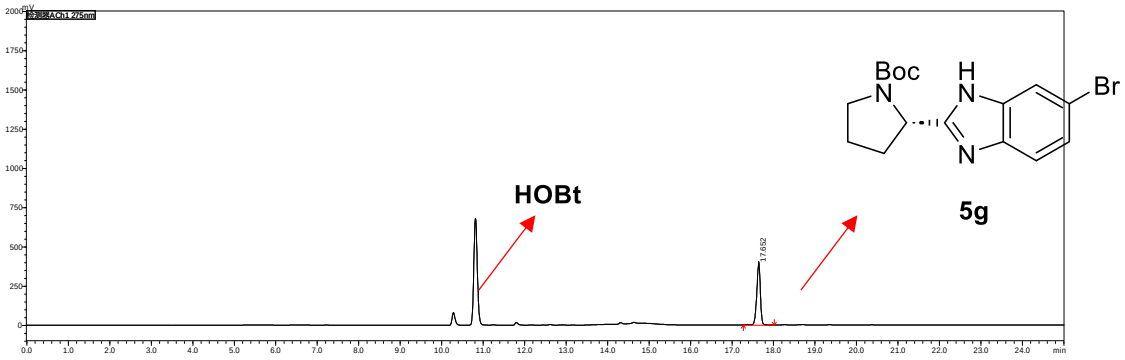


Fig. S100. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5g**

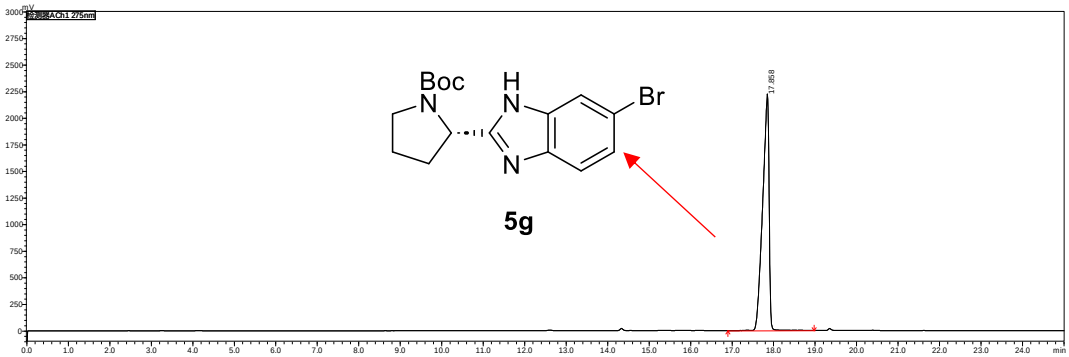


Fig. S101. HPLC chromatogram of purified **5g**

substrate scope: **5h**

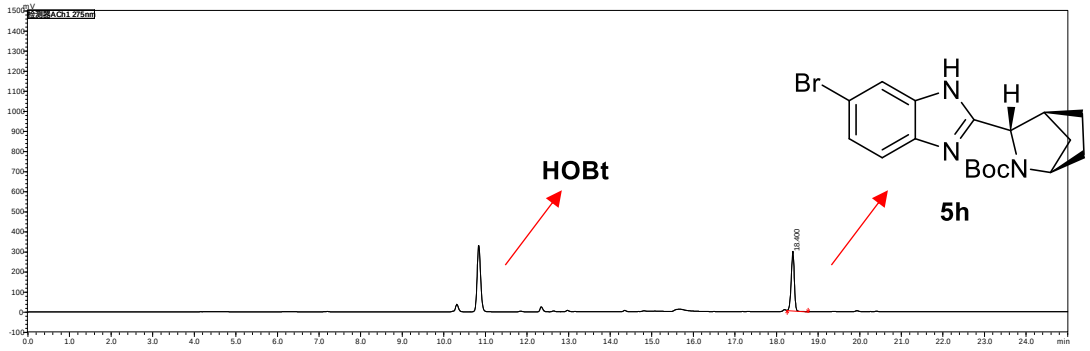


Fig. S102. HPLC chromatogram of two-step cascaded reaction mixture for the synthesis of **5h**

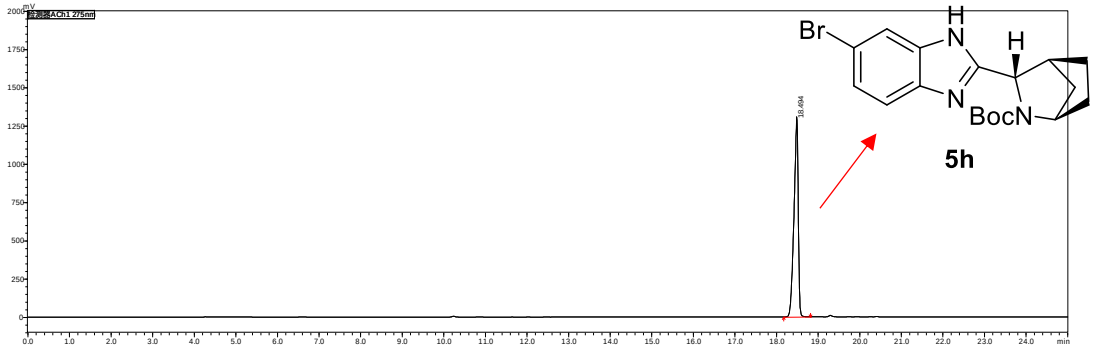


Fig. S103. HPLC chromatogram of purified **5h**

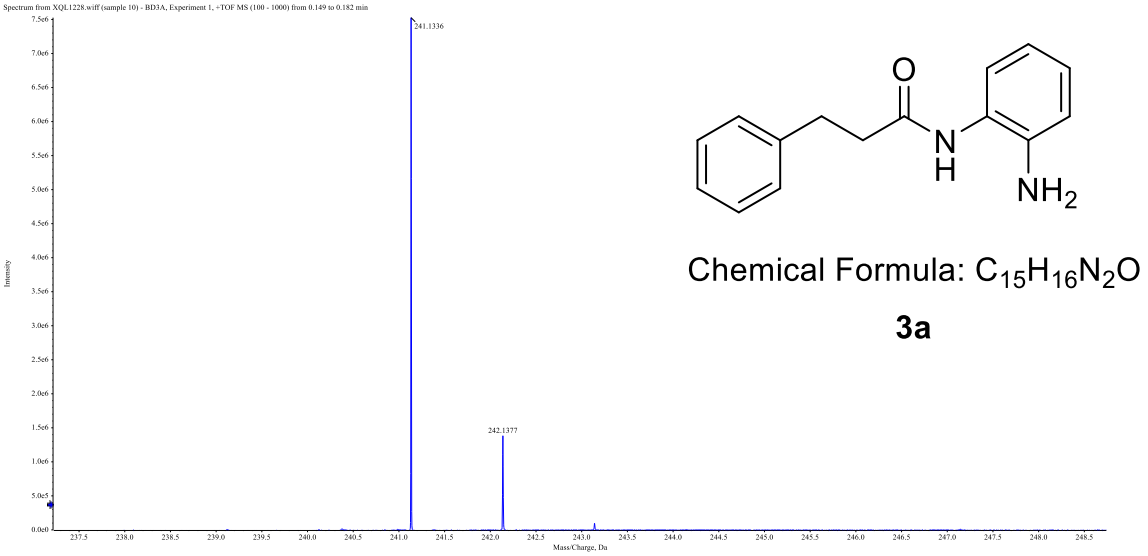
6. Product identification by HRMS

HRMS testing conditions:

Instrument: AB Sciex X500r QTOF

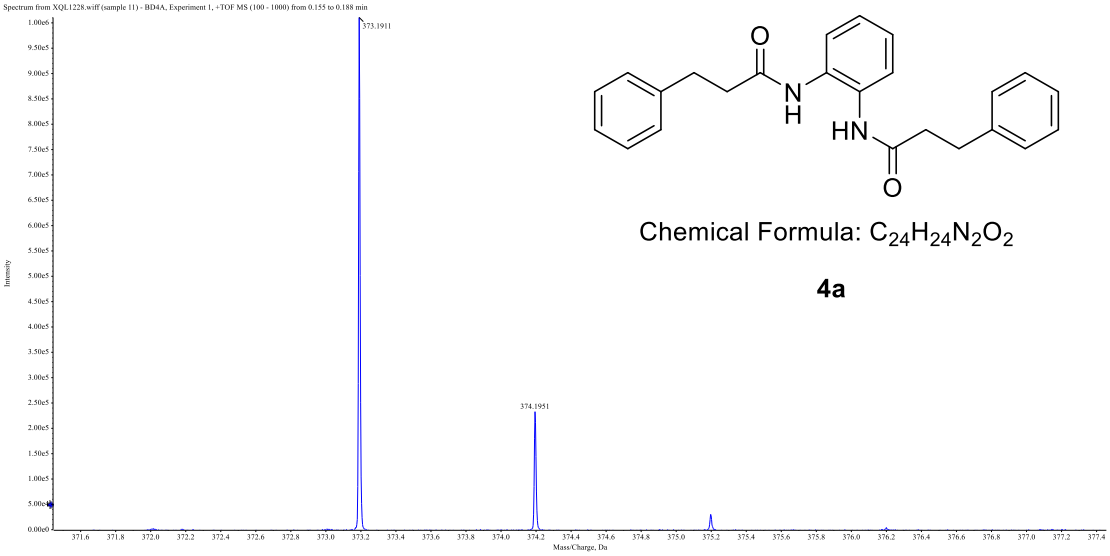
Positive mode: voltage: 5500V, Ion source temperature: 500 ℃, Nitrogen flow rate: 50 psi, Collection mass number range: 50-1000, Collision voltage: 10V.

HRMS for **3a**



Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C15H16N2O	241.1335	9.0	0.2	1			NA/NA

HRMS for **4a**

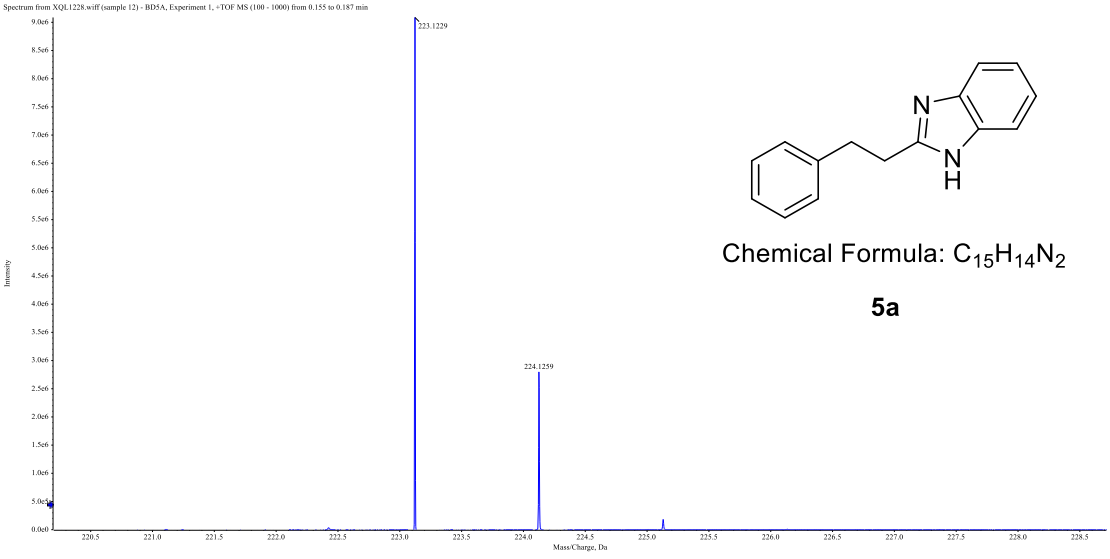


Chemical Formula: $C_{24}H_{24}N_2O_2$

4a

Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C24H24N2O2	373.1911	14.0	0.1	1			NA/NA

HRMS for **5a**

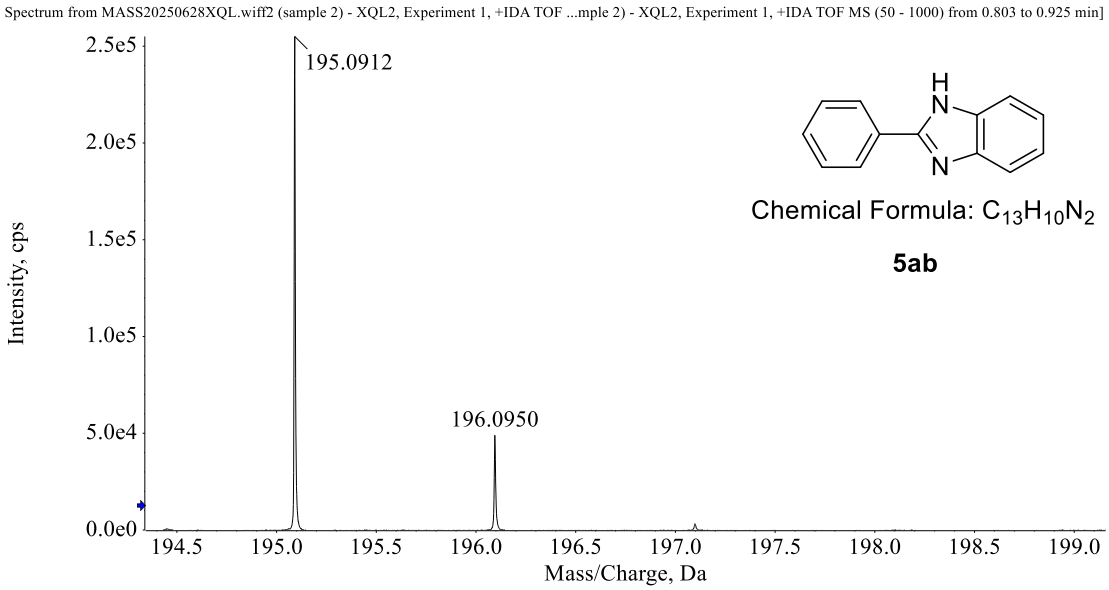


Chemical Formula: $C_{15}H_{14}N_2$

5a

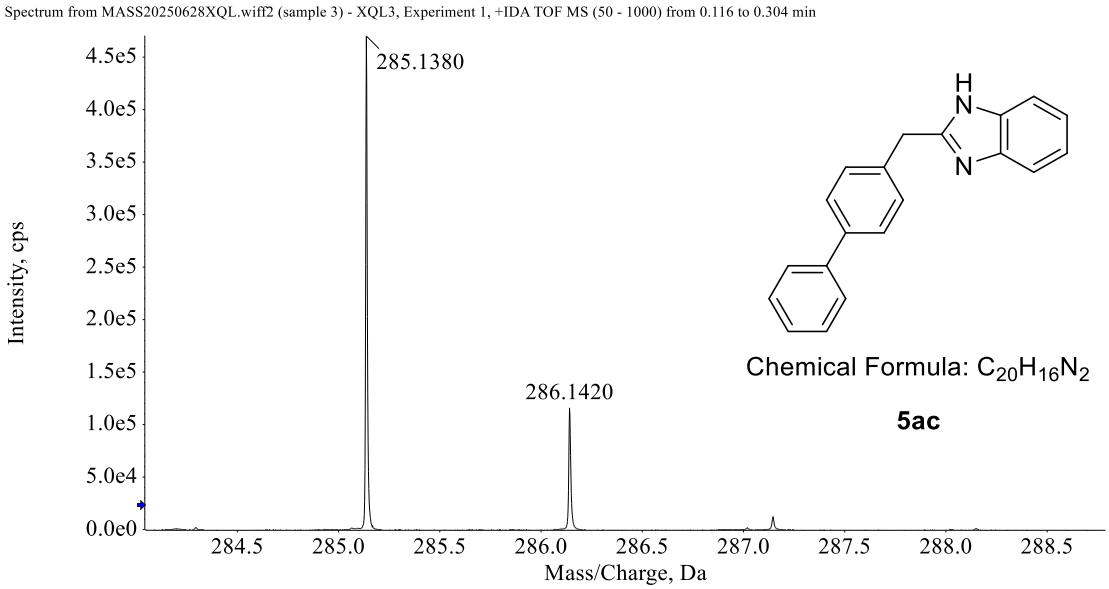
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C15H14N2	223.1230	10.0	-0.3	1			NA/NA

HRMS for **5ab**



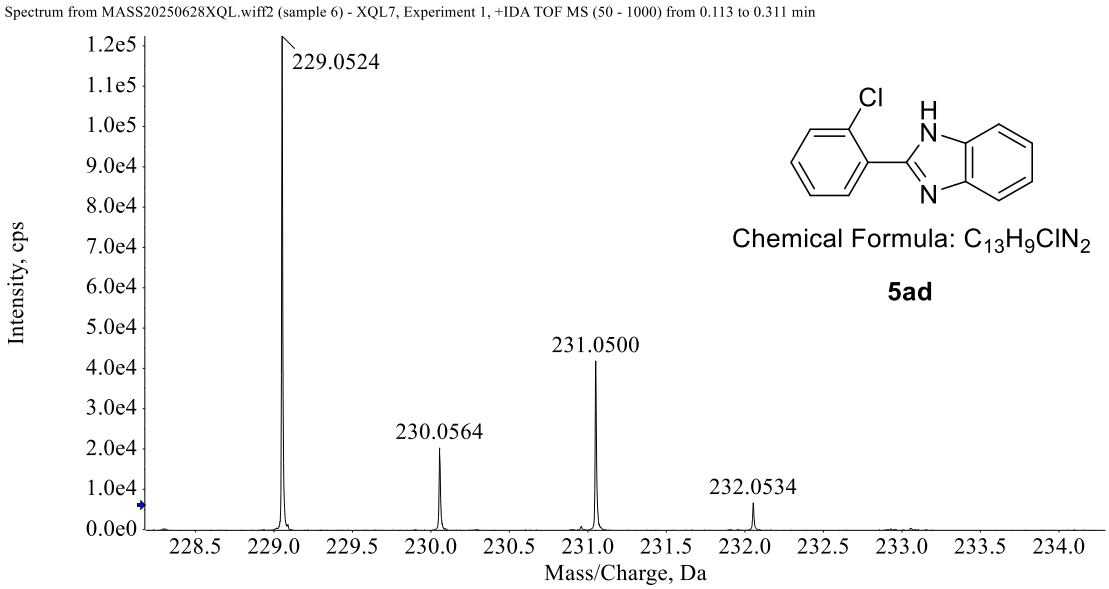
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C13H10N2	195.0917	10.0	-2.4	1			NA/NA

HRMS for **5ac**



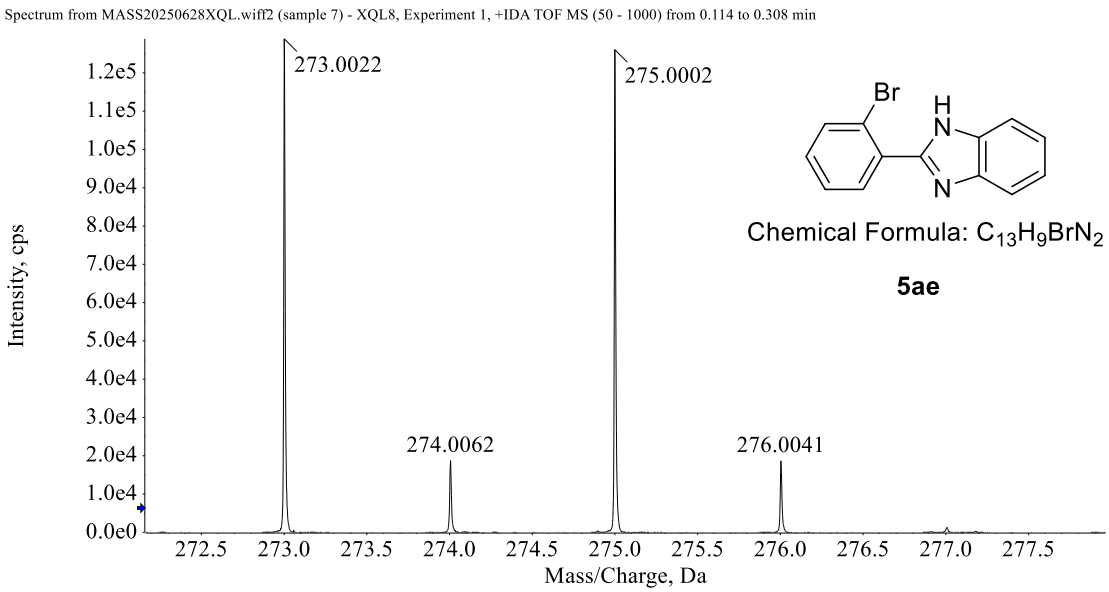
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C20H16N2	285.1386	14.0	-2.2	1			NA/NA

HRMS for **5ad**



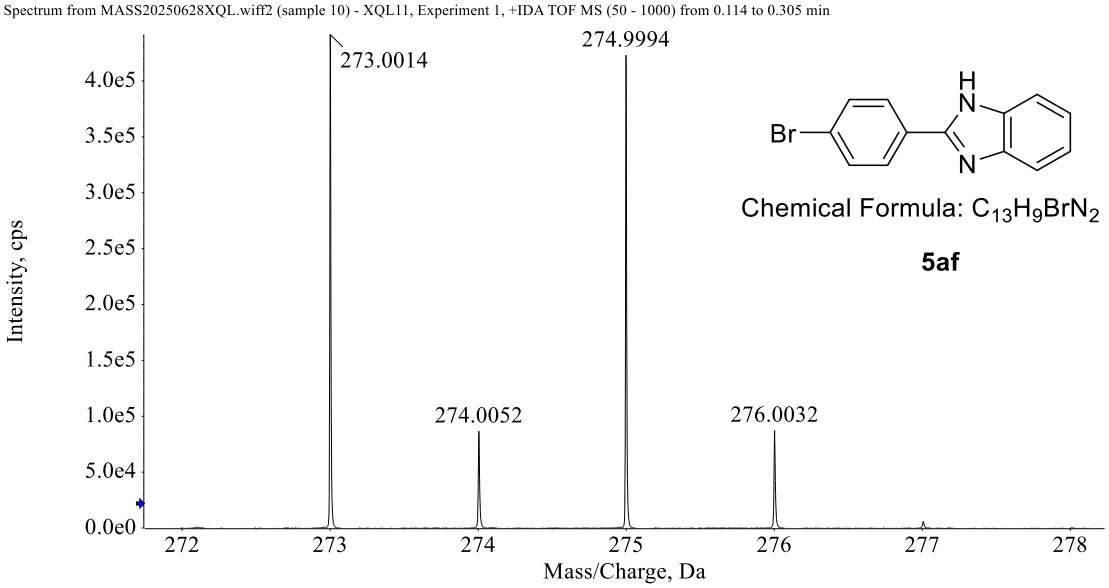
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C13H9ClN2	229.0527	10.0	-1.3	1			NA/NA

HRMS for **5ae**



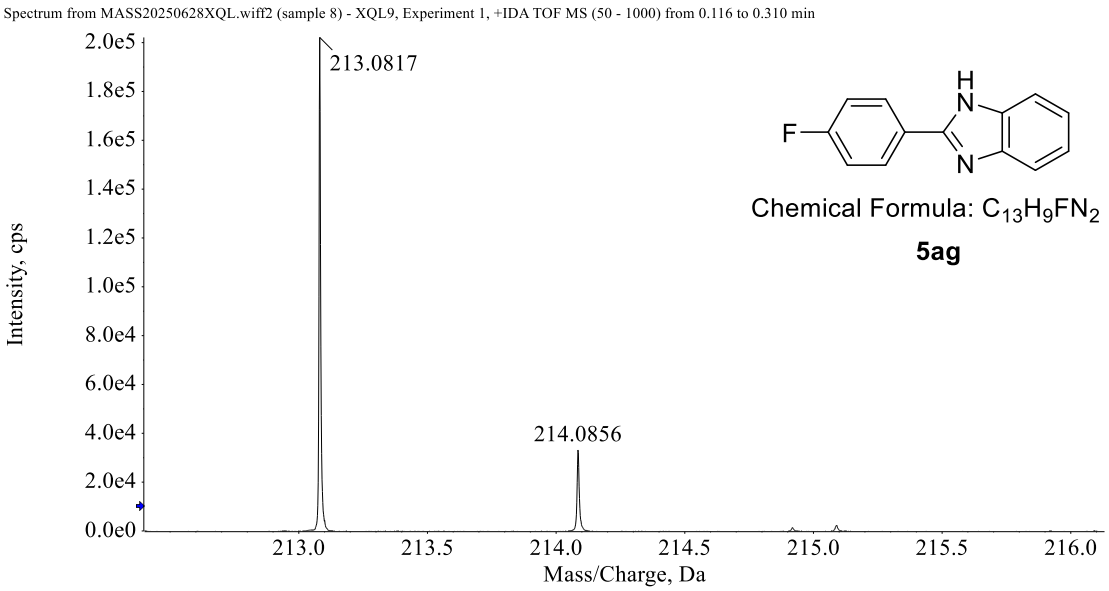
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C13H9BrN2	273.0022	10.0	0.0	1			NA/NA

HRMS for **5af**



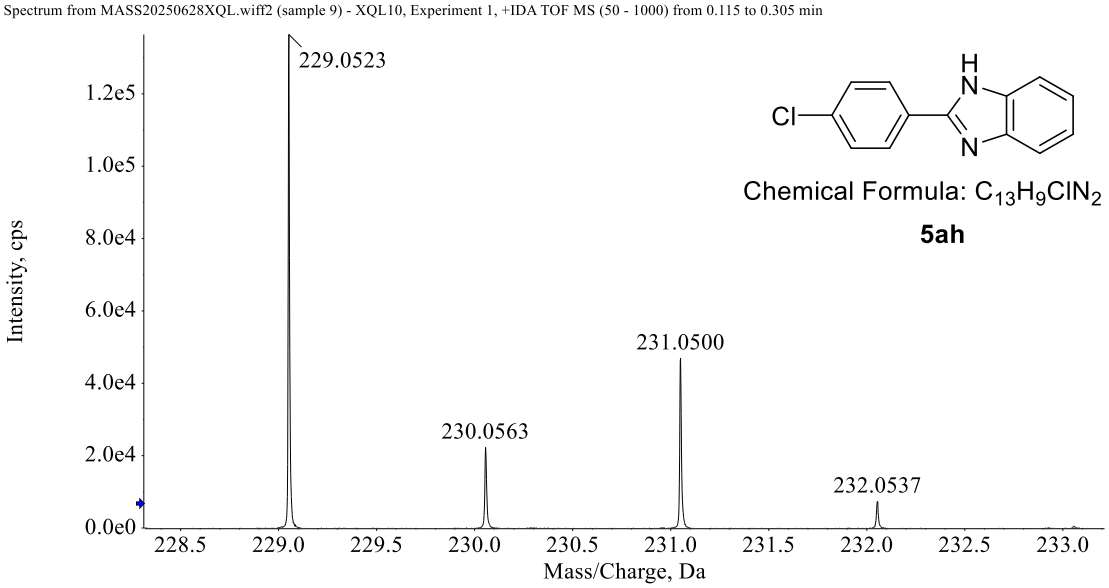
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C13H9BrN2	273.0022	10.0	-2.9	1			NA/NA

HRMS for **5ag**



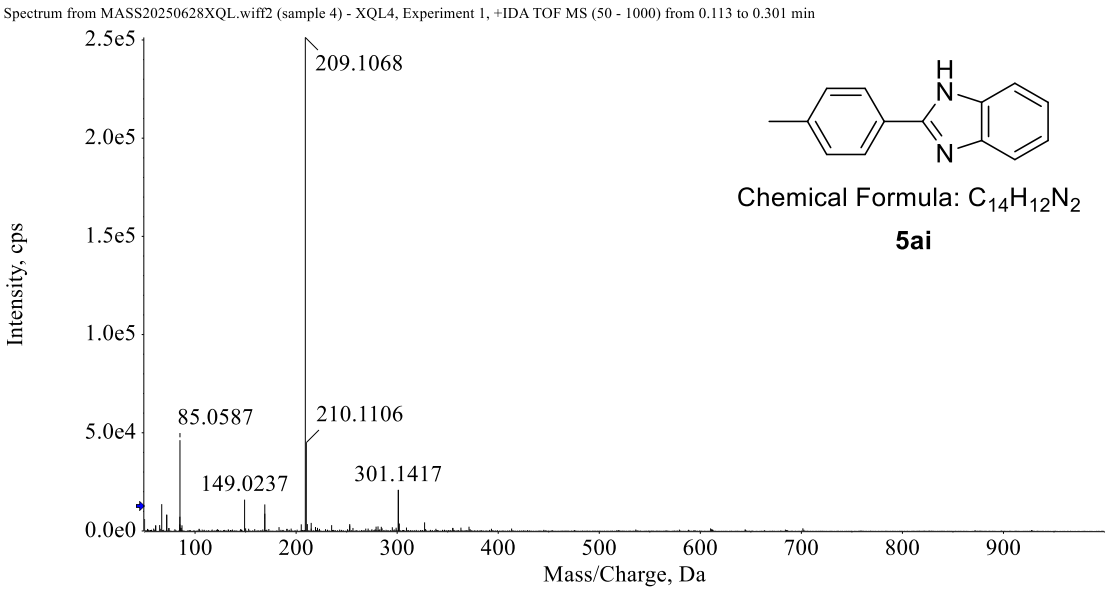
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C13H9FN2	213.0823	10.0	-2.6	1			NA/NA

HRMS for **5ah**



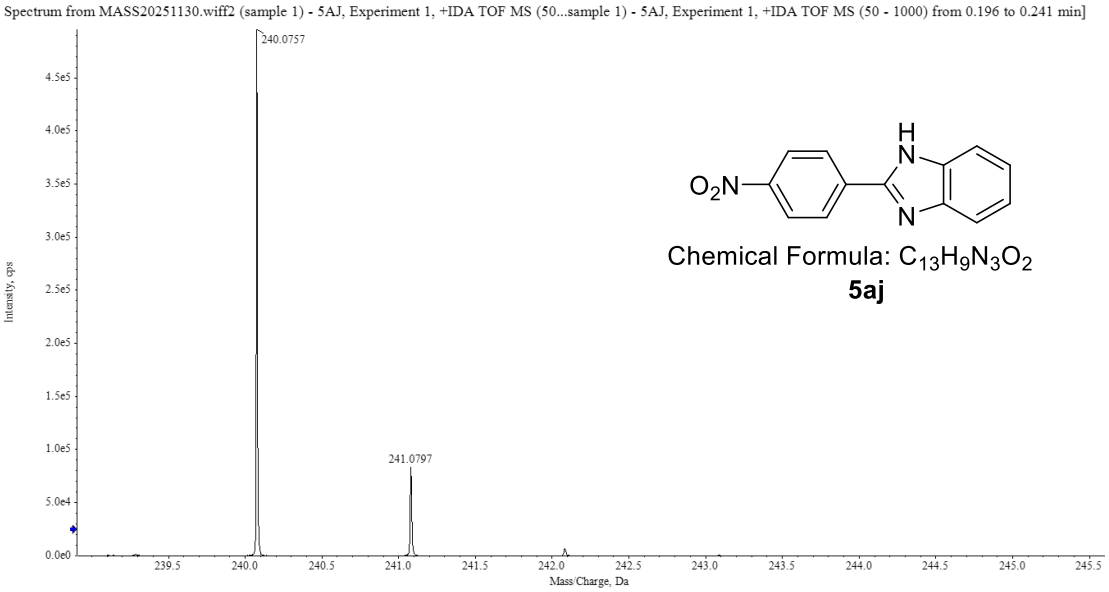
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C13H9ClN2	229.0527	10.0	-1.8	1			NA/NA

HRMS for **5ai**



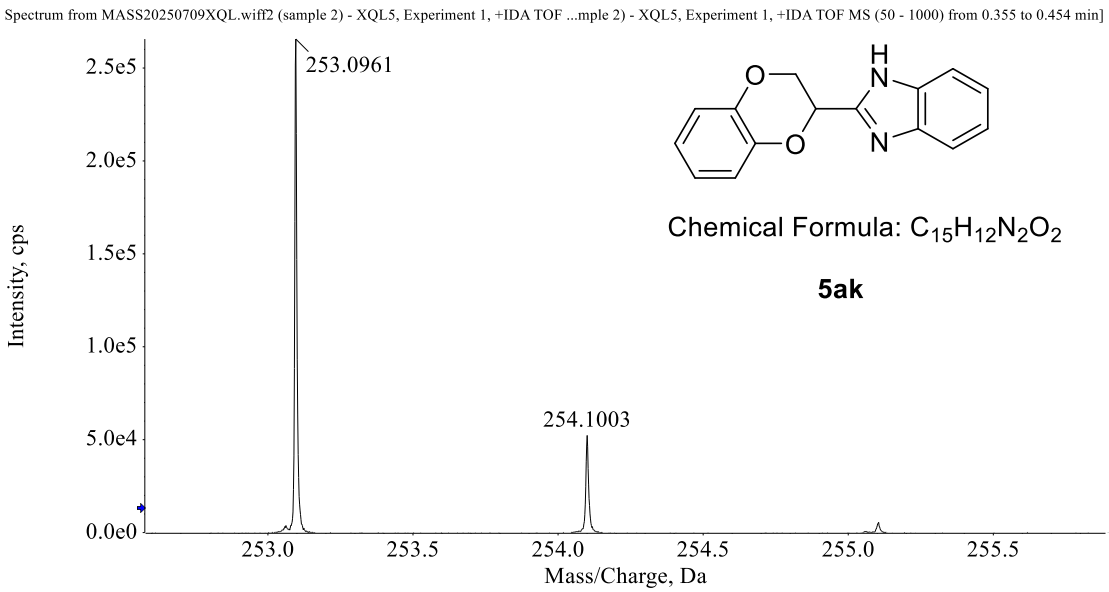
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C14H12N2	209.1073	10.0	-2.5	1			NA/NA

HRMS for **5aj**



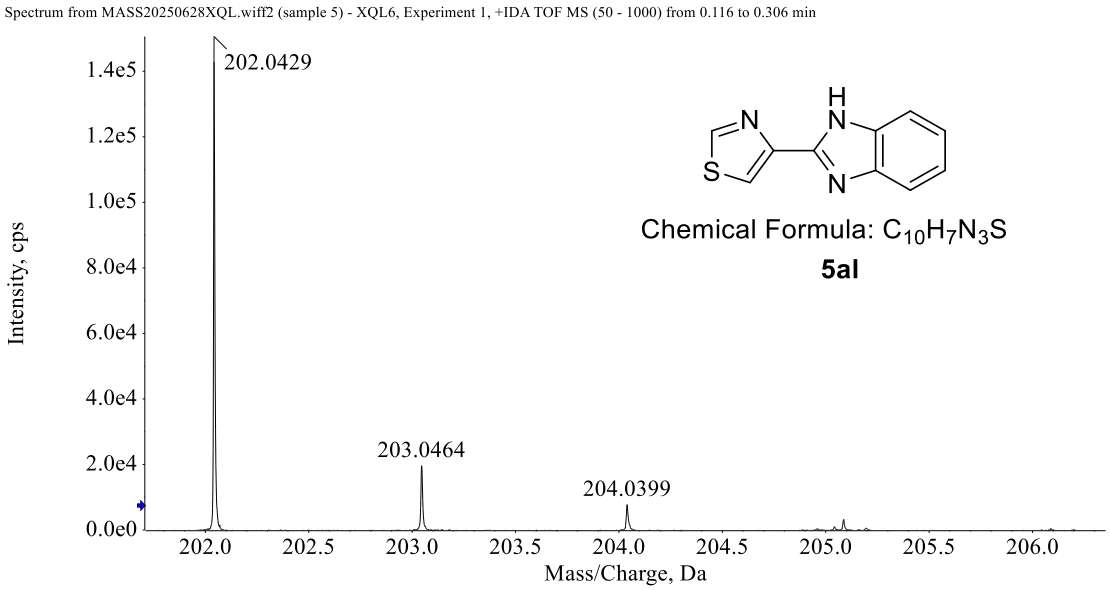
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C13H9N3O2	240.0768	11.0	-4.4	1			NA/NA

HRMS for **5ak**



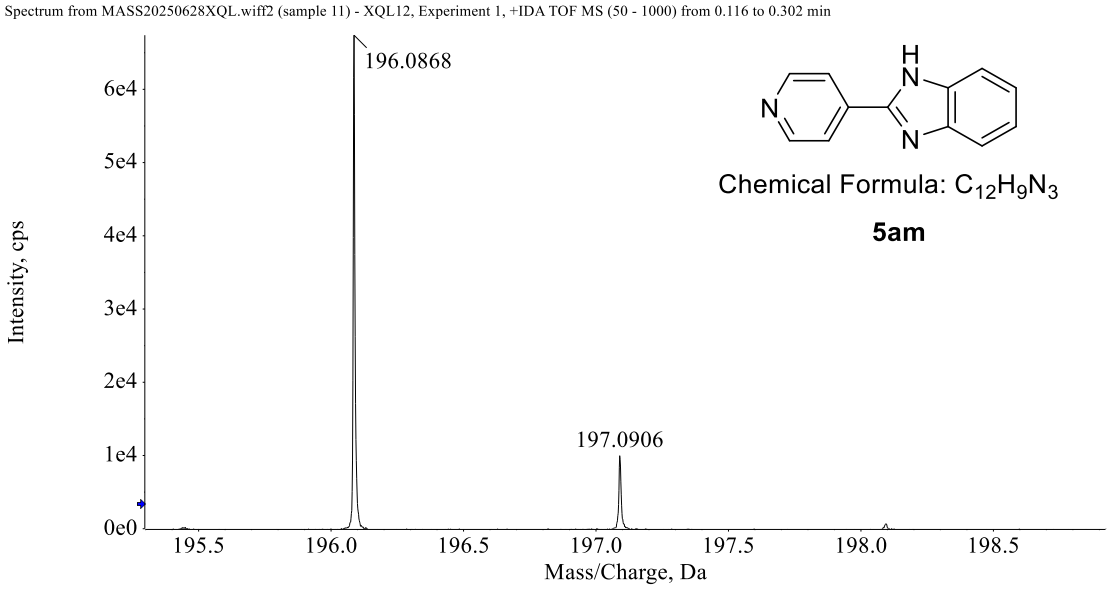
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C15H12N2O2	253.0972	11.0	-4.2	1			NA/NA

HRMS for **5al**



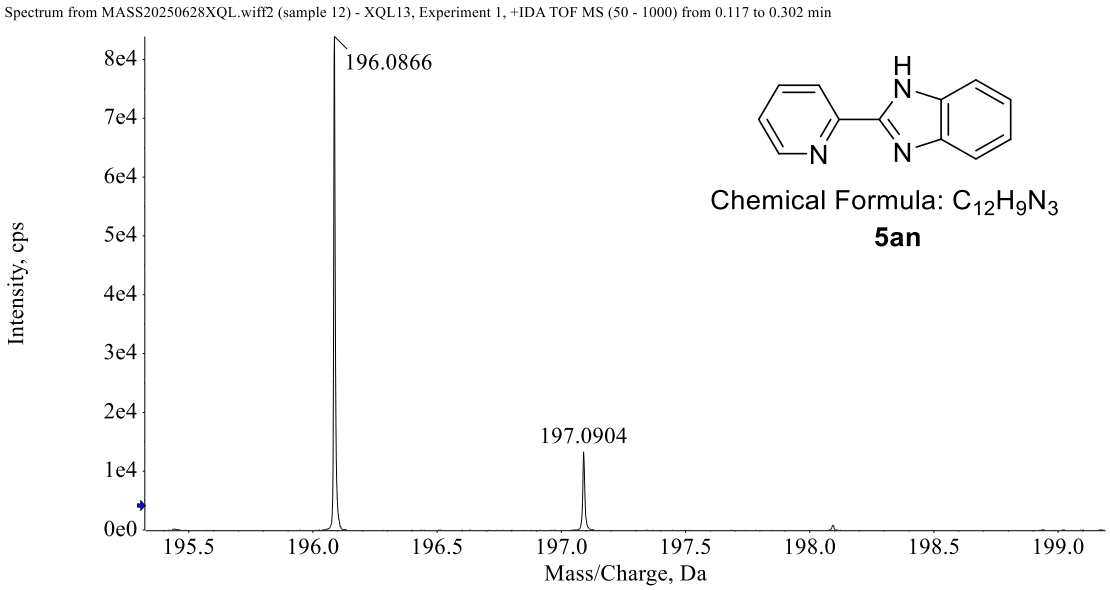
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C10H7N3S	202.0433	9.0	-2.2	1			NA/NA

HRMS for **5am**



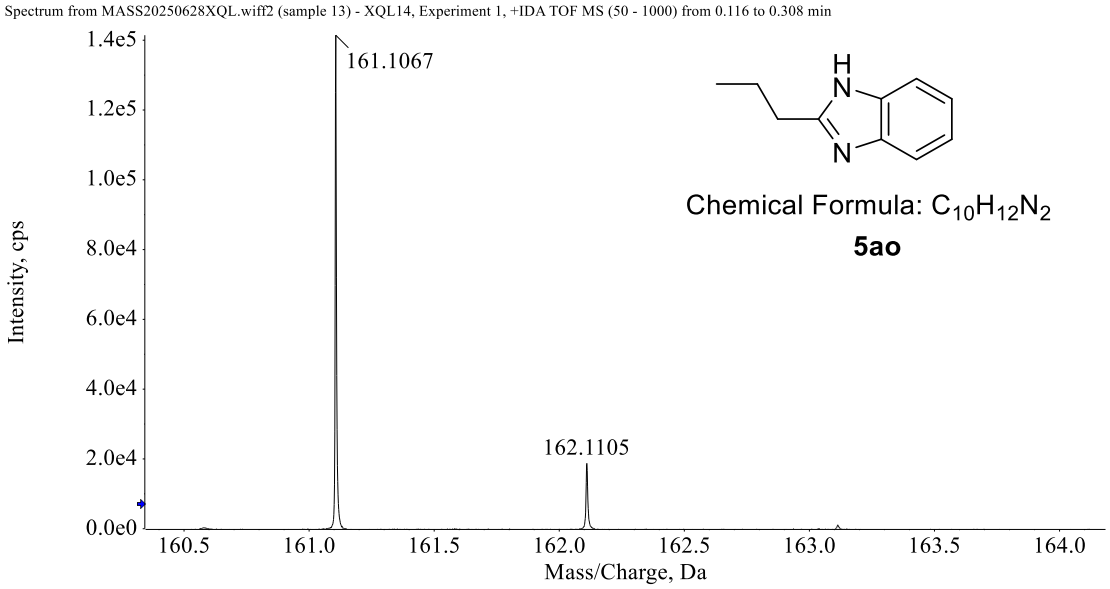
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C12H9N3	196.0869	10.0	-0.6	1			NA/NA

HRMS for **5an**



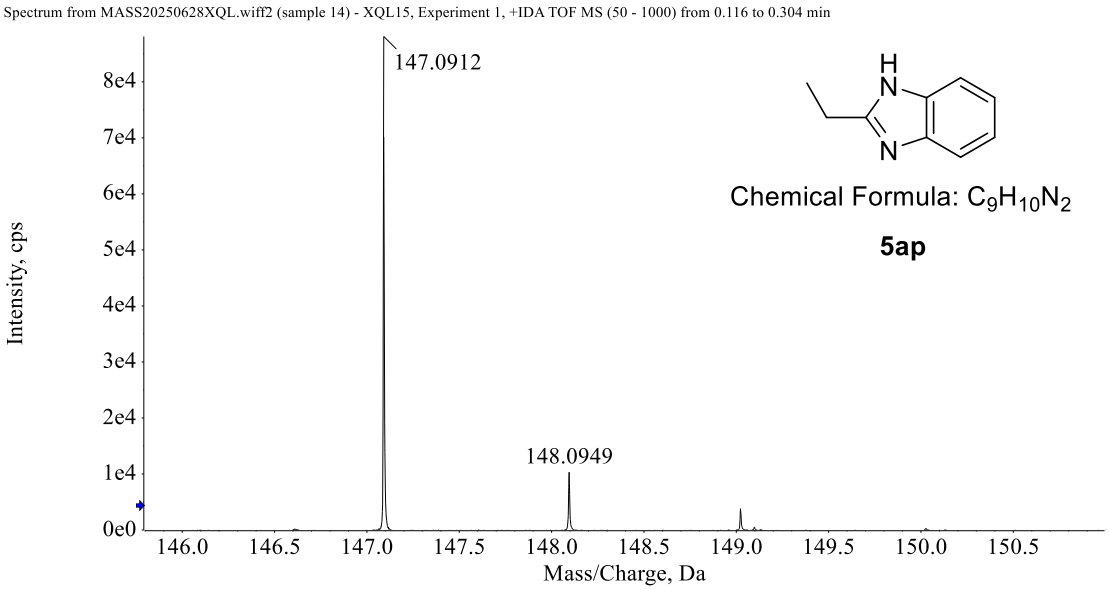
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C12H9N3	196.0869	10.0	-1.7	1			NA/NA

HRMS for **5ao**



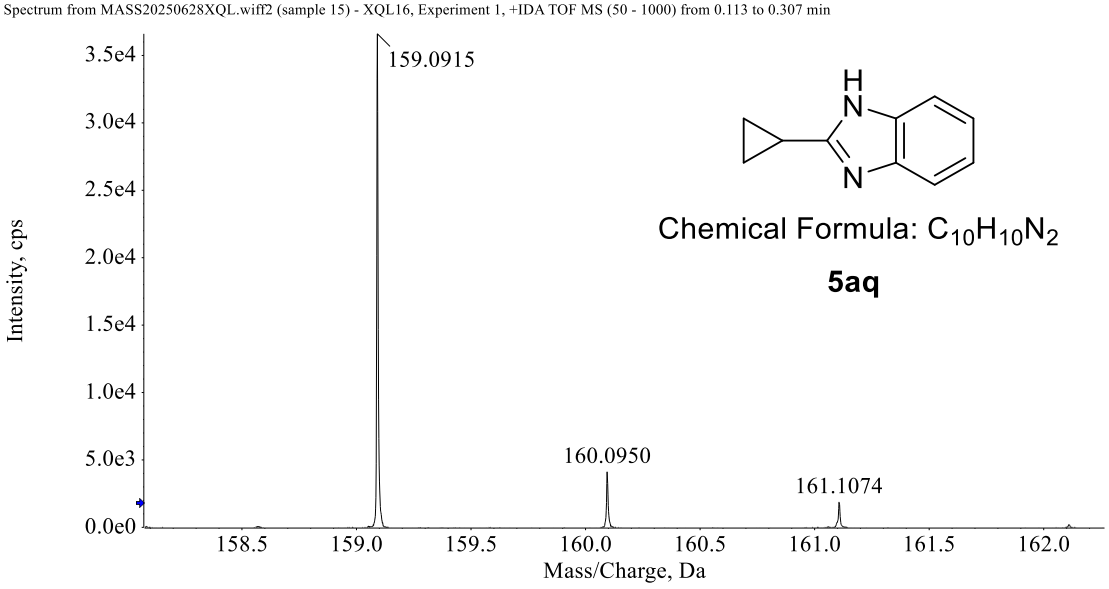
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C10H12N2	161.1073	6.0	-3.9	1			NA/NA

HRMS for **5ap**



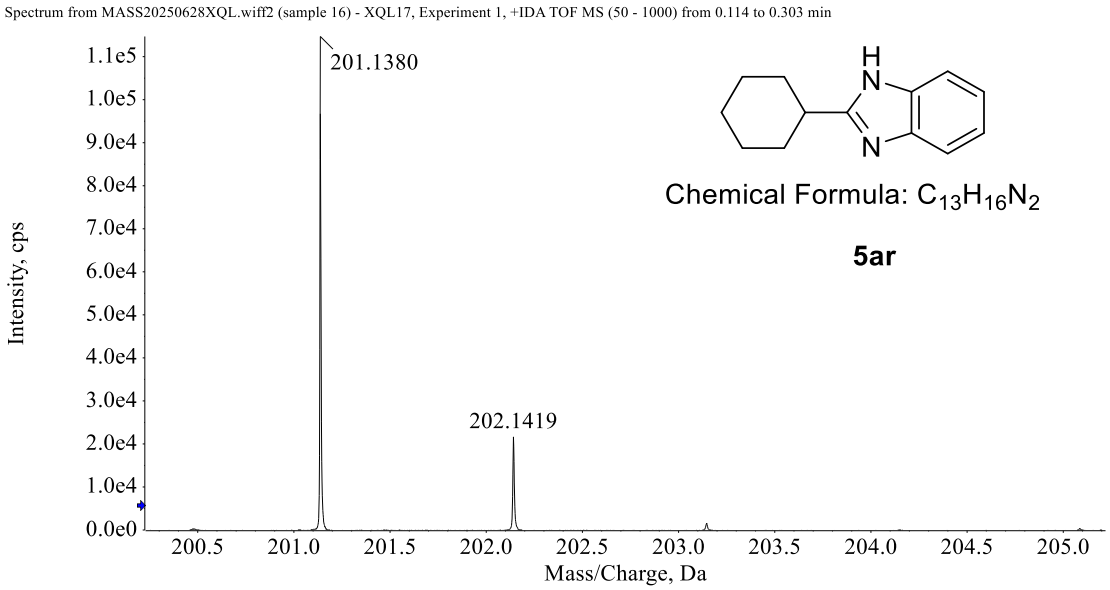
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C9H10N2	147.0917	6.0	-3.2	1			NA/NA

HRMS for **5aq**



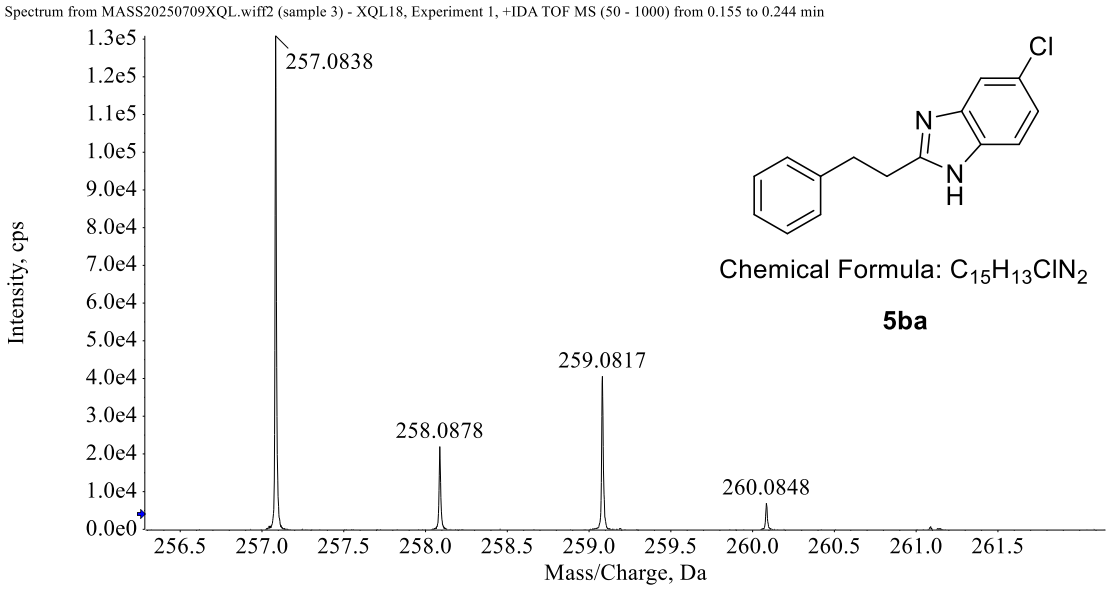
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C10H10N2	159.0917	7.0	-1.1	1			NA/NA

HRMS for **5ar**



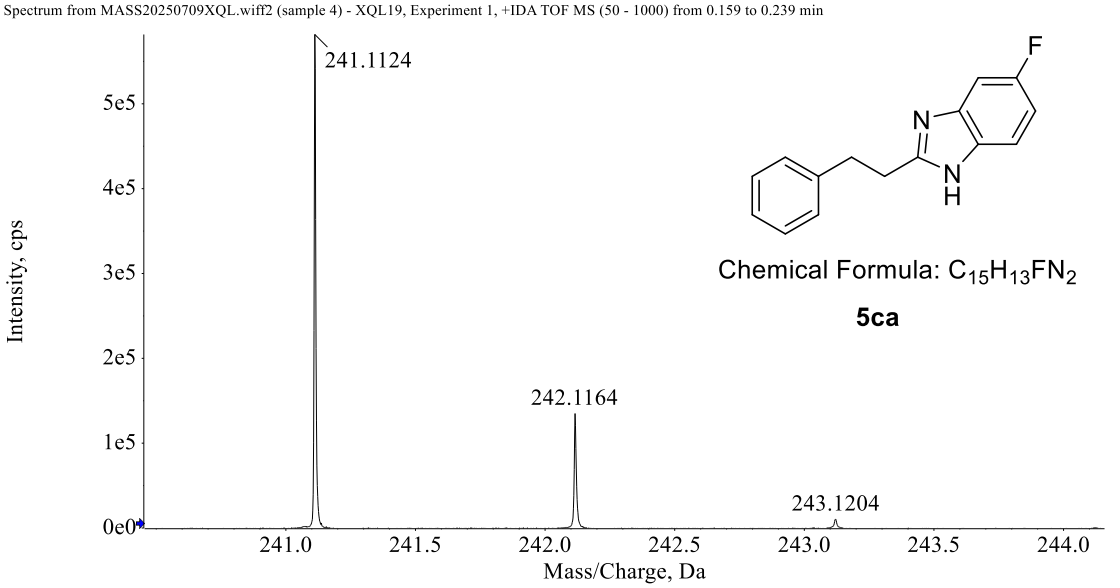
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C13H16N2	201.1386	7.0	-3.1	1			NA/NA

HRMS for **5ba**



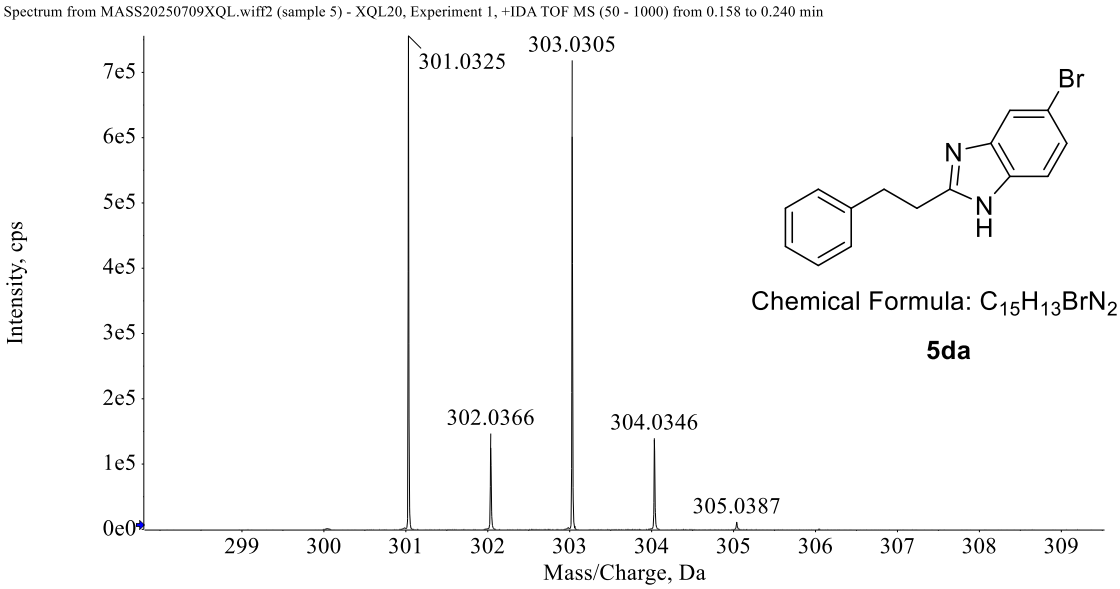
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C15H13ClN2	257.0840	10.0	-0.8	1			NA/NA

HRMS for **5ca**



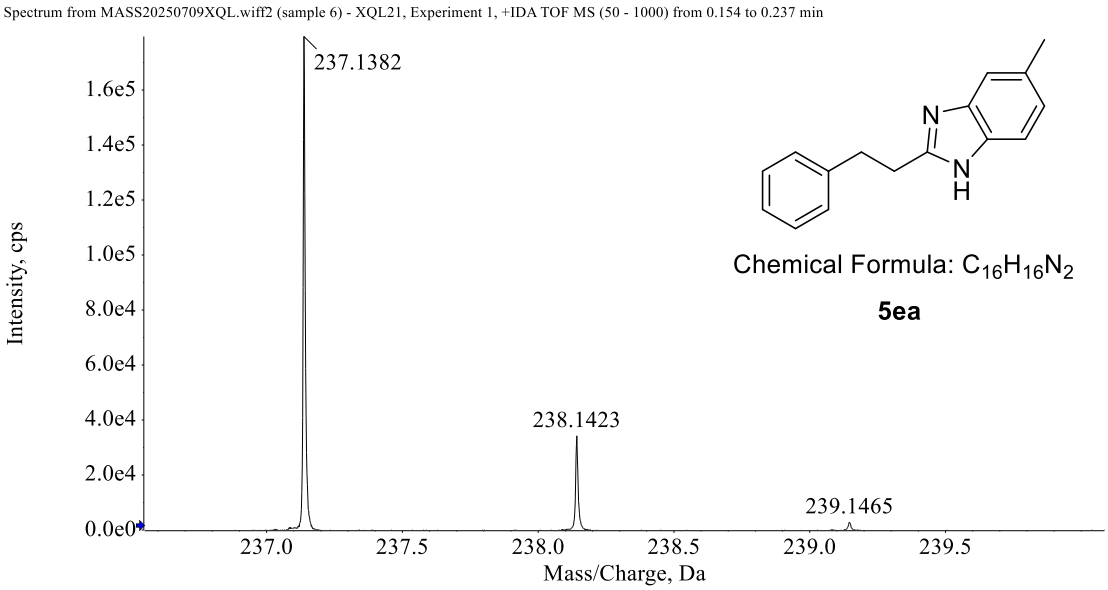
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C15H13FN2	241.1136	10.0	-4.8	1			NA/NA

HRMS for **5da**



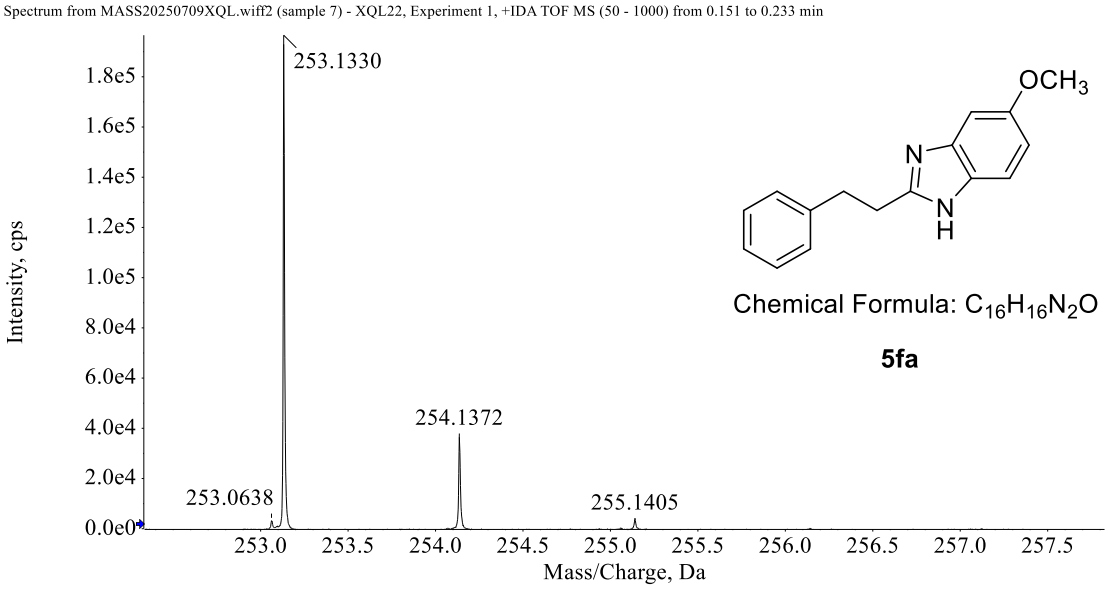
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C15H13BrN2	301.0335	10.0	-3.3	1			NA/NA

HRMS for **5ea**



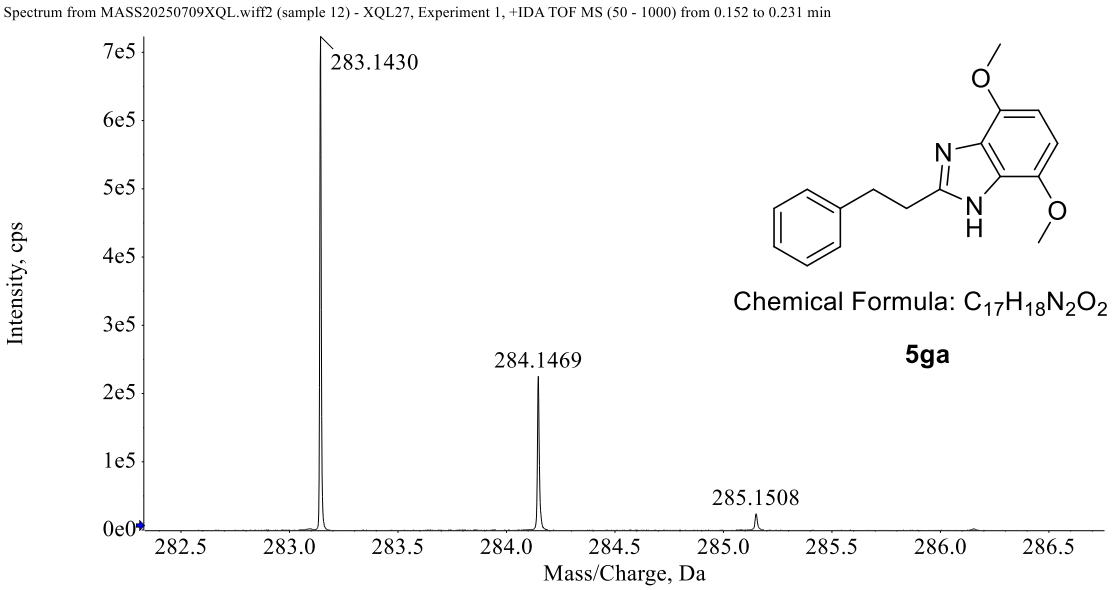
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C16H16N2	237.1386	10.0	-1.8	1			NA/NA

HRMS for **5fa**



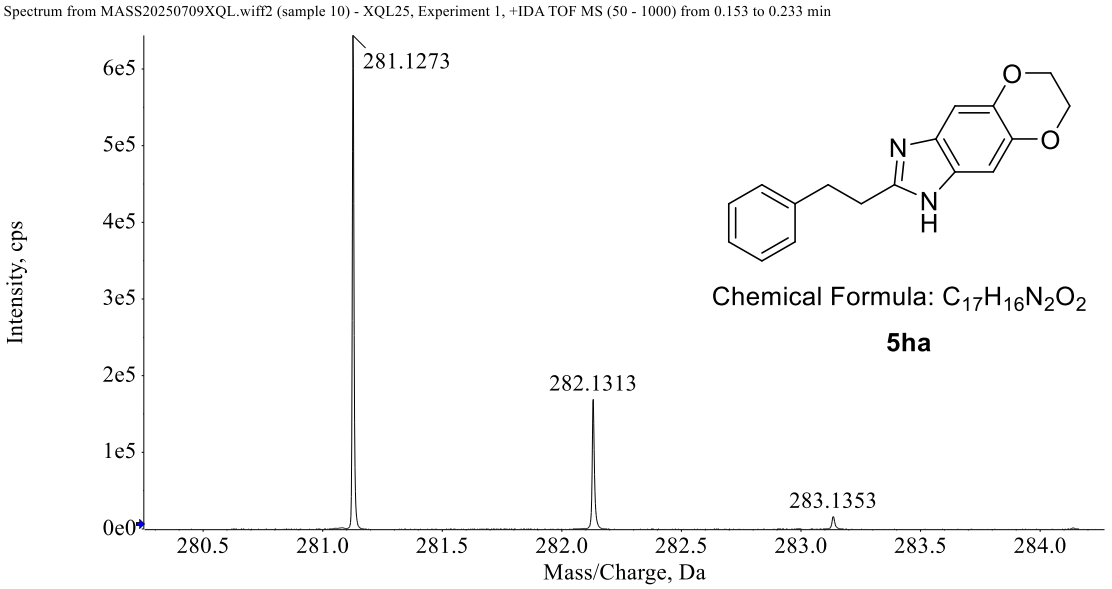
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C16H16N2O	253.1335	10.0	-2.1	1			NA/NA

HRMS for **5ga**



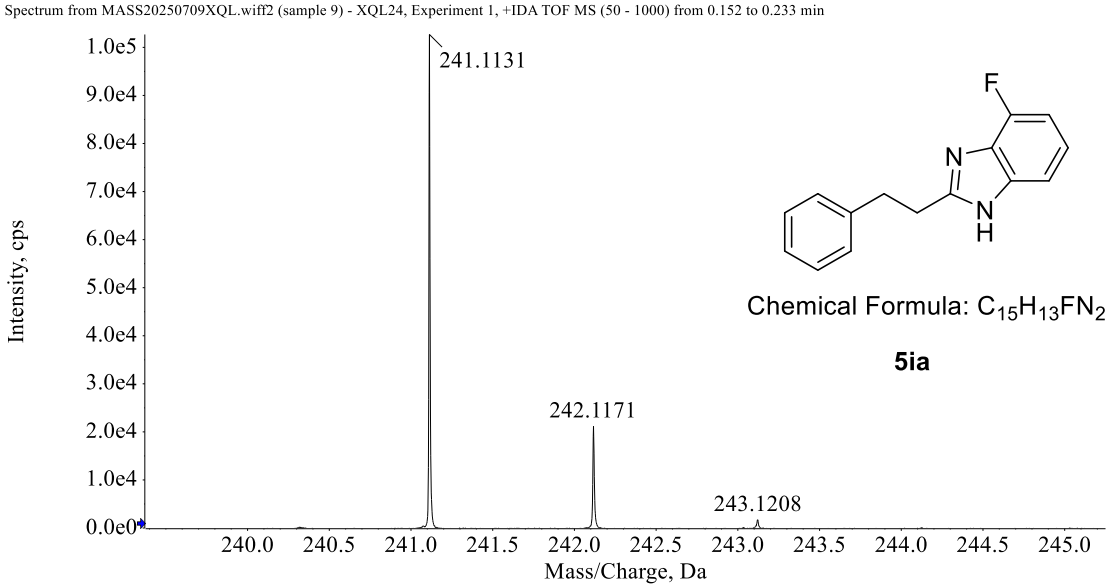
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C17H18N2O2	283.1441	10.0	-3.9	1			NA/NA

HRMS for **5ha**



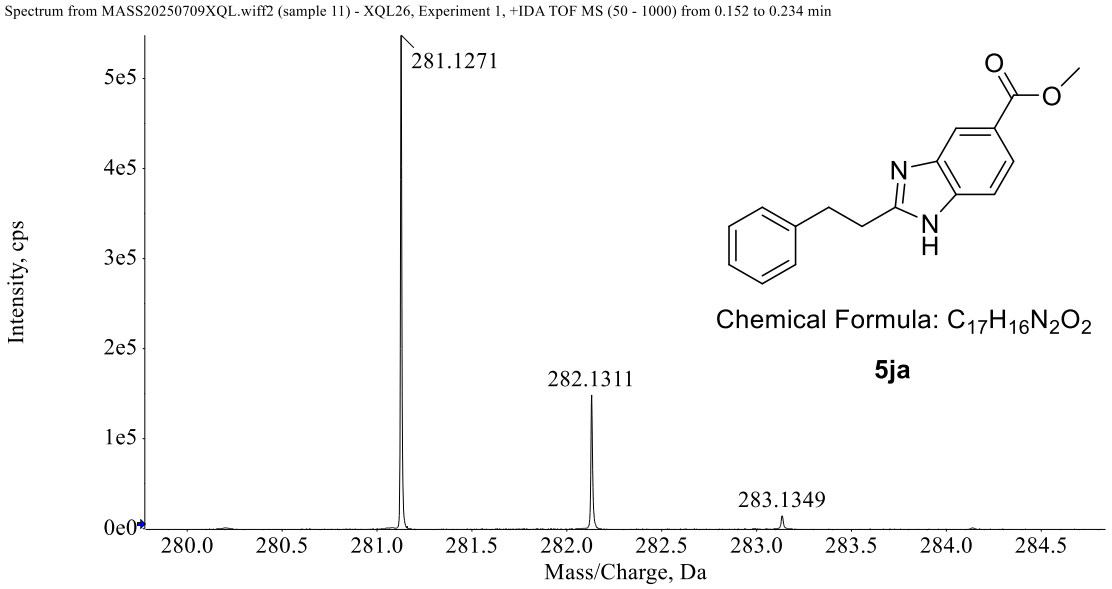
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C17H16N2O2	281.1285	11.0	-4.1	1			NA/NA

HRMS for **5ia**



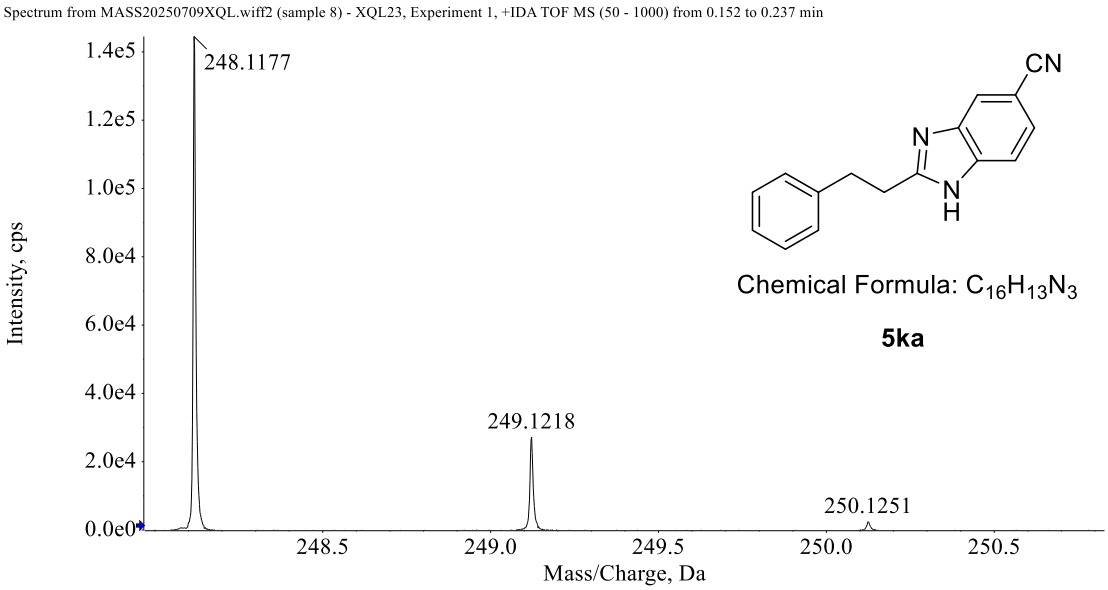
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C15H13FN2	241.1136	10.0	-1.9	1			NA/NA

HRMS for **5ja**



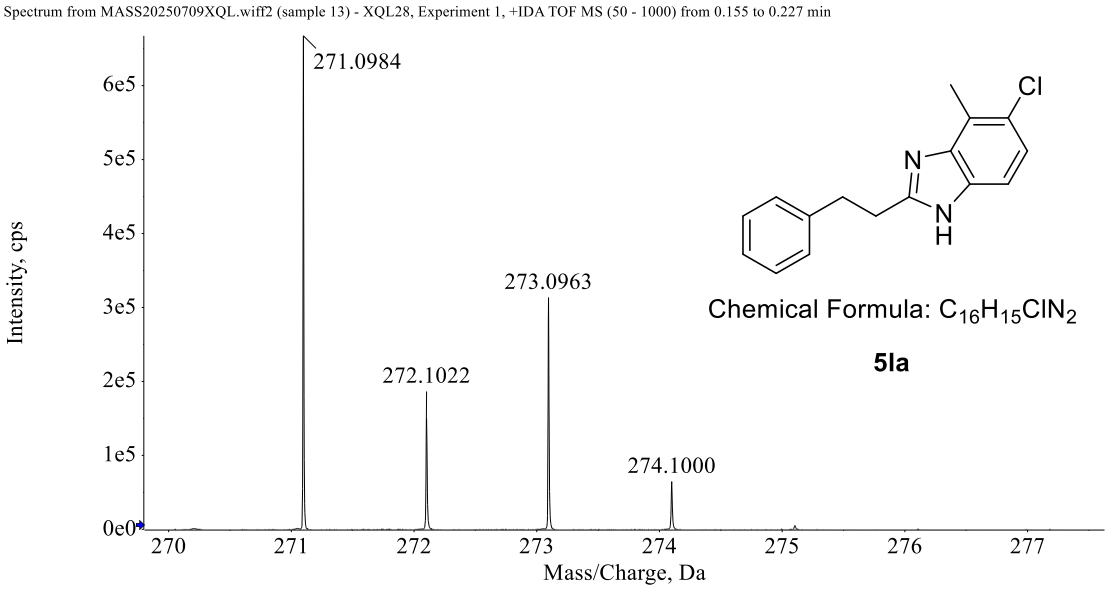
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C17H16N2O2	281.1285	11.0	-4.8	1			NA/NA

HRMS for **5ka**



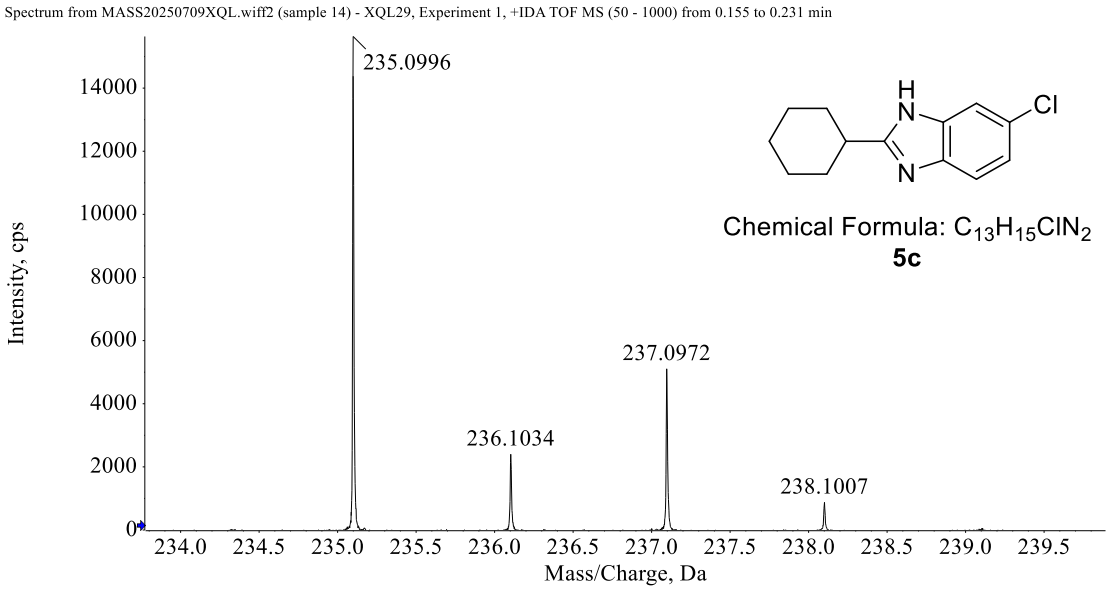
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C16H13N3	248.1182	12.0	-2.1	1			NA/NA

HRMS for **5la**



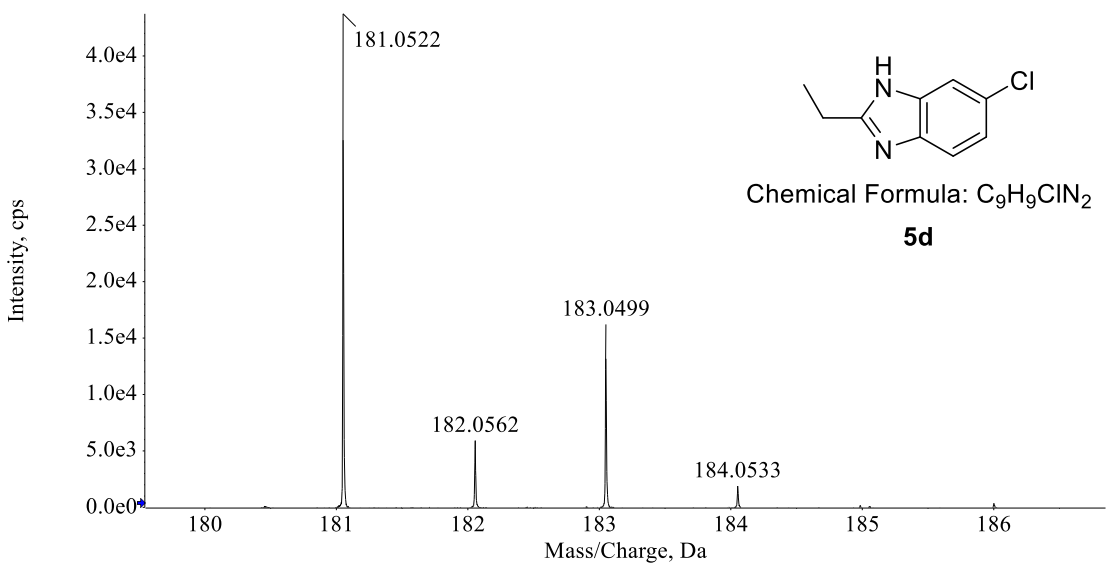
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C16H15ClN2	271.0997	10.0	-4.6	1			NA/NA

HRMS for **5c**



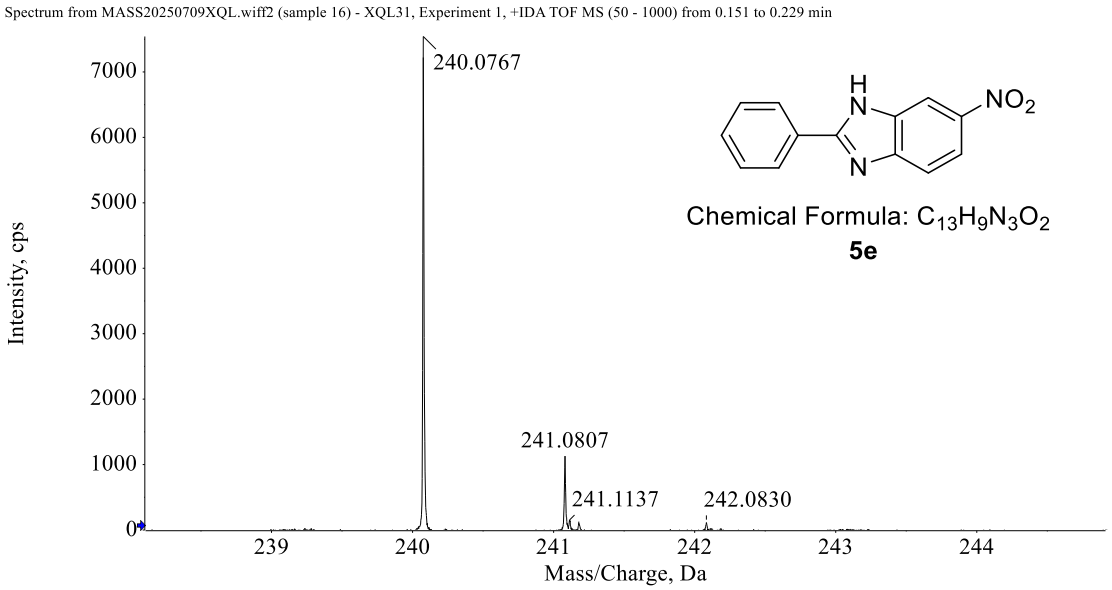
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C13H15ClN2	235.0997	7.0	-0.2	1			NA/NA

HRMS for **5d**



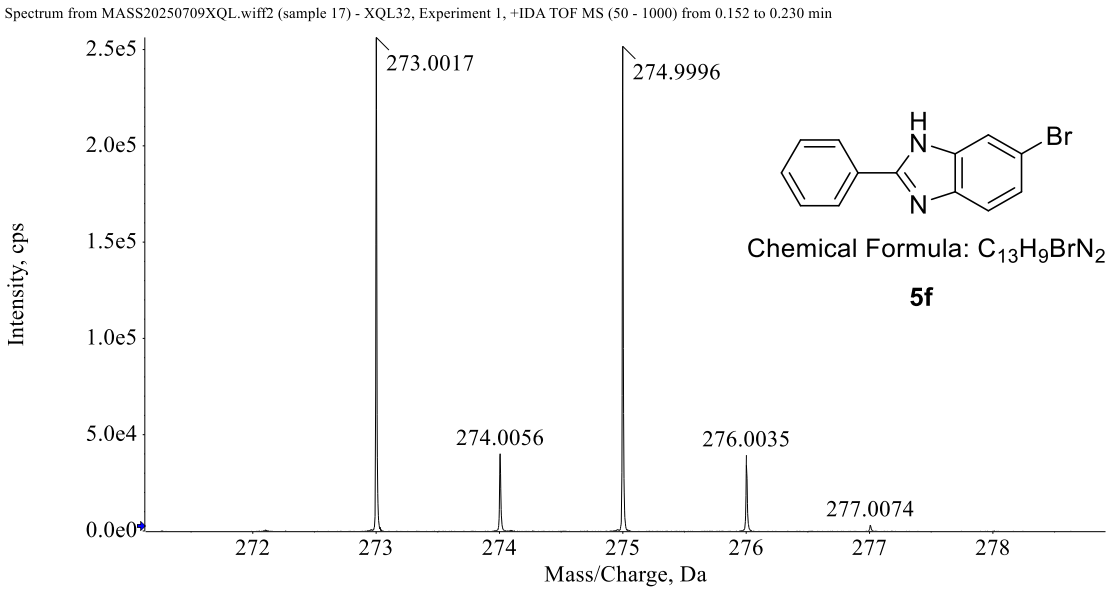
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C9H9ClN2	181.0527	6.0	-2.8	1			NA/NA

HRMS for **5e**



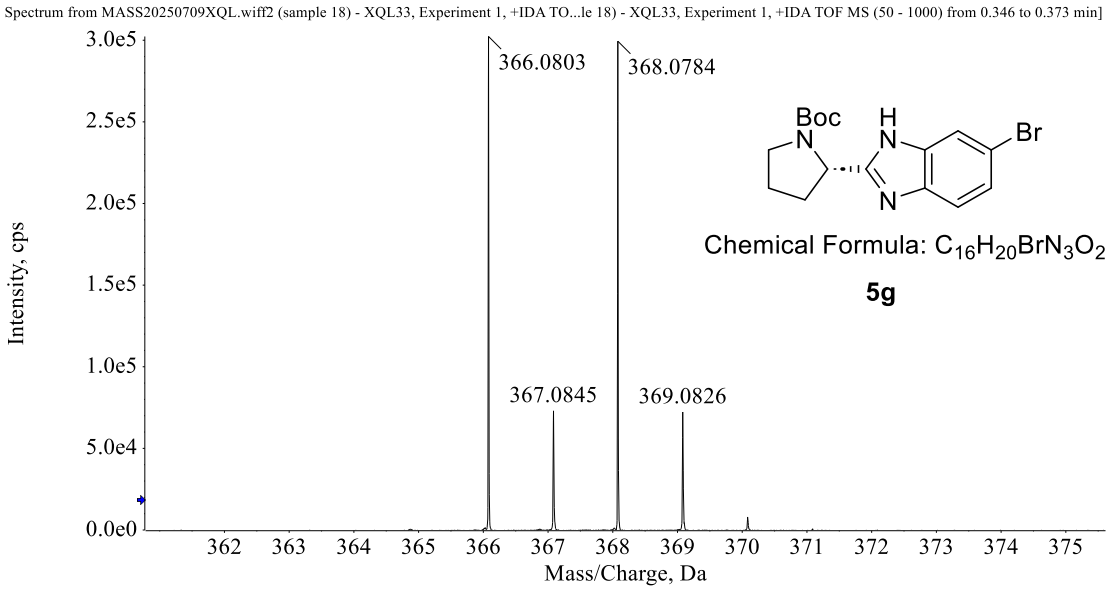
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C13H9N3O2	240.0768	11.0	-0.2	1			NA/NA

HRMS for **5f**



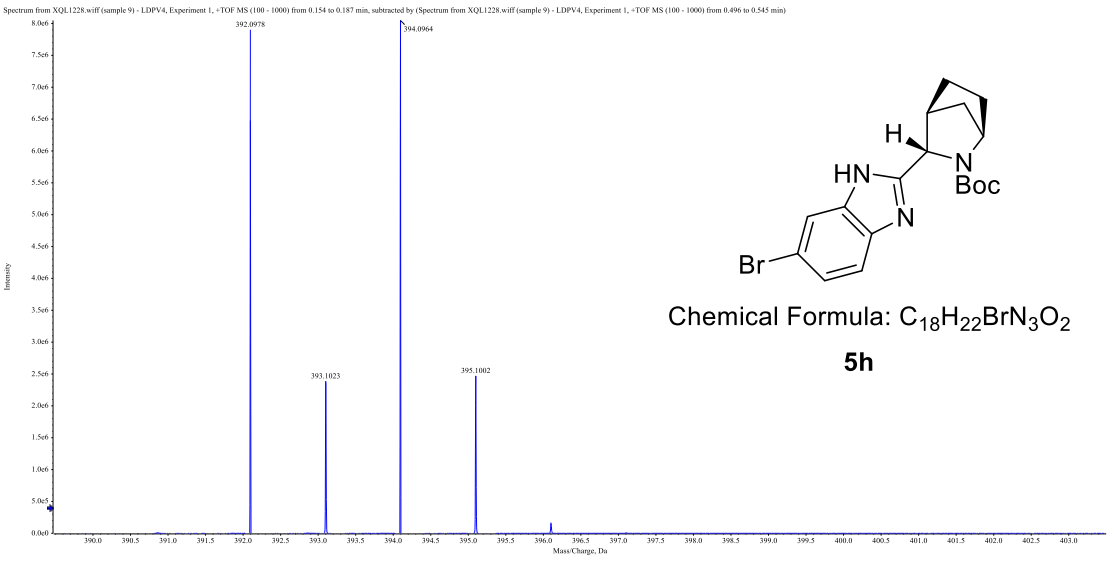
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C13H9BrN2	273.0022	10.0	-1.8	1			NA/NA

HRMS for **5g**



Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C16H20BrN3O2	366.0812	8.0	-2.4	1			NA/NA

HRMS for **5h**

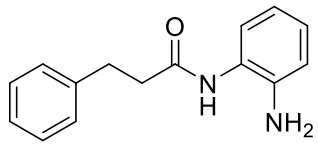


Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C18H22N3O2Br	392.0968	9.0	2.5	1			NA/NA

7. NMR characterization data

^{1}H NMR and ^{13}C NMR experiments were performed on Bruker avance 600 MHz and Bruker avance III 500M NMR spectrometer, using DMSO-*d6* as the solvent with tetramethylsilane (TMS) as an internal standard at room temperature. NMR spectra data are reported as chemical shift (in ppm) (multiplicity, integration, coupling constants (in Hz). Multiplicity is reported as follows: s = singlet, d = doublet, t = triplet, m = multiplets, dd = doublet of doublet.

3a



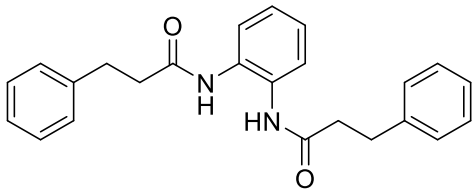
Chemical Formula: $C_{15}H_{16}N_2O$

3a

^{1}H NMR (600 MHz, DMSO) δ 9.09 (s, 1H), 7.33 – 7.23 (m, 4H), 7.19 (t, *J* = 7.1 Hz, 1H), 7.11 (d, *J* = 9.0 Hz, 1H), 6.88 (t, *J* = 8.3 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 1H), 6.52 (t, *J* = 8.2 Hz, 1H), 4.75 (s, 2H), 2.91 (t, *J* = 7.7 Hz, 2H), 2.70 – 2.57 (m, 2H).

^{13}C NMR (151 MHz, DMSO) δ 170.8, 142.4, 141.7, 128.7, 126.4, 126.2, 125.8, 123.7, 116.5, 116.2, 37.8, 31.5.

4a



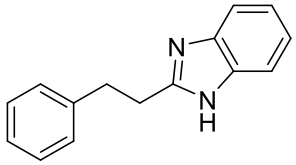
Chemical Formula: $C_{24}H_{24}N_2O_2$

4a

^{1}H NMR (600 MHz, DMSO) δ 9.29 (s, 2H), 7.53 – 7.41 (m, 2H), 7.31 – 7.21 (m, 8H), 7.17 (t, J = 7.0 Hz, 2H), 7.12 (dd, J = 5.9, 3.6 Hz, 2H), 2.90 (t, J = 7.7 Hz, 4H), 2.62 (t, J = 7.7 Hz, 4H).

^{13}C NMR (151 MHz, DMSO) δ 171.1, 141.5, 130.8, 128.7, 128.7, 38.0, 31.2.

5a



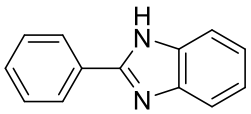
Chemical Formula: $C_{15}H_{14}N_2$

5a

^{1}H NMR (600 MHz, DMSO) δ 12.22 (s, 1H), 7.52 (d, *J* = 7.3 Hz, 1H), 7.41 (d, *J* = 7.2 Hz, 1H), 7.31 – 7.24 (m, 4H), 7.21 – 7.16 (m, 1H), 7.11 (dd, *J* = 8.5, 6.7 Hz, 2H), 3.11 (s, 4H).

^{13}C NMR (151 MHz, DMSO) δ 154.7, 141.5, 126.5, 121.8, 121.2, 118.5, 111.1, 33.7, 30.8.

5ab



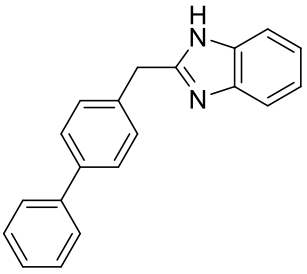
Chemical Formula: $C_{13}H_{10}N_2$

5ab

^{1}H NMR (600 MHz, DMSO) δ 8.23 (d, *J* = 8.5 Hz, 2H), 7.70 – 7.60 (m, 2H), 7.56 (t, *J* = 7.6 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.23 (dd, *J* = 6.0, 3.1 Hz, 2H).

^{13}C NMR (151 MHz, DMSO) δ 151.7, 130.6, 130.3, 129.4, 126.9, 122.6.

5ac



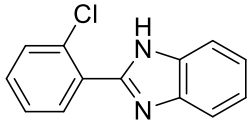
Chemical Formula: $C_{20}H_{16}N_2$

5ac

^{1}H NMR (600 MHz, DMSO) δ 7.66 – 7.59 (m, 4H), 7.49 (dd, *J* = 5.9, 3.2 Hz, 2H), 7.44 (dd, *J* = 17.0, 7.9 Hz, 4H), 7.35 (t, *J* = 7.4 Hz, 1H), 7.13 (dd, *J* = 6.0, 3.1 Hz, 2H), 4.22 (s, 2H).

^{13}C NMR (151 MHz, DMSO) δ 154.0, 140.4, 139.4, 138.9, 137.4, 129.8, 129.4, 127.8, 127.2, 127.0, 121.7, 115.0, 35.0.

5ad



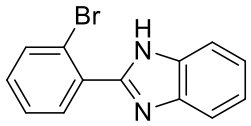
Chemical Formula: $C_{13}H_9ClN_2$

5ad

^{1}H NMR (600 MHz, DMSO) δ 7.92 (dd, *J* = 7.4, 1.9 Hz, 1H), 7.66 (td, *J* = 5.7, 2.2 Hz, 3H), 7.54 (dtd, *J* = 16.4, 7.4, 1.5 Hz, 2H), 7.30 – 7.20 (m, 2H).

^{13}C NMR (151 MHz, DMSO) δ 149.5, 139.1, 132.5, 132.1, 131.7, 130.8, 130.2, 127.9, 122.8, 115.8.

5ae



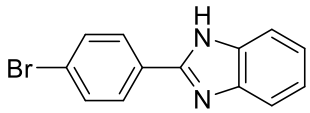
Chemical Formula: $C_{13}H_9BrN_2$

5ae

^{1}H NMR (600 MHz, DMSO) δ 12.76 (s, 1H), 7.83 (d, *J* = 7.5 Hz, 1H), 7.77 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.73 – 7.52 (m, 3H), 7.47 (t, *J* = 6.9 Hz, 1H), 7.31 – 7.19 (m, 2H).

^{13}C NMR (151 MHz, DMSO) δ 150.9, 133.8, 132.8, 132.7, 131.8, 128.2, 123.0, 122.0, 119.6, 112.1.

5af



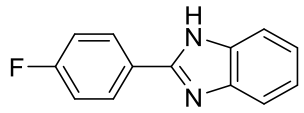
Chemical Formula: $C_{13}H_9BrN_2$

5af

^{1}H NMR (600 MHz, DMSO) δ 13.06 (s, 1H), 8.14 (d, *J* = 8.5 Hz, 2H), 7.83 – 7.43 (m, 4H), 7.22 (s, 2H).

^{13}C NMR (151 MHz, DMSO) δ 150.7, 144.1, 135.4, 132.35 (d, *J* = 28.7 Hz), 129.8, 128.8, 123.7, 123.2, 122.2, 119.4, 111.9.

5ag



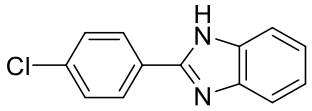
Chemical Formula: $C_{13}H_9FN_2$

5ag

^{1}H NMR (600 MHz, DMSO) δ 12.99 (s, 1H), 8.26 (dd, *J* = 8.7, 5.5 Hz, 2H), 7.62 (dd, *J* = 20.7, 12.1 Hz, 2H), 7.39 (t, *J* = 8.8 Hz, 2H), 7.21 (d, *J* = 3.1 Hz, 2H).

^{13}C NMR (151 MHz, DMSO) δ 164.3, 162.7, 150.9, 144.2, 135.5, 129.2, 127.2, 122.9, 122.2, 119.3, 116.5, 116.3, 111.8.

5ah



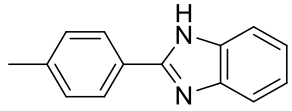
Chemical Formula: $C_{13}H_9ClN_2$

5ah

^{1}H NMR (600 MHz, DMSO) δ 13.03 (s, 1H), 8.23 (d, *J* = 8.5 Hz, 2H), 7.64 (d, *J* = 8.4 Hz, 4H), 7.25 (s, 2H).

^{13}C NMR (151 MHz, DMSO) δ 150.6, 144.2, 135.5, 134.9, 129.3, 128.6, 123.3, 122.3, 119.4, 111.8.

5ai



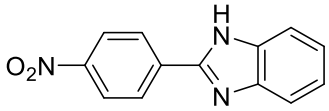
Chemical Formula: $C_{14}H_{12}N_2$

5ai

^{1}H NMR (600 MHz, DMSO) δ 12.87 (s, 1H), 8.10 (d, *J* = 8.1 Hz, 2H), 7.66 (s, 1H), 7.54 (s, 1H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.20 (s, 2H), 2.37 (s, 3H).

^{13}C NMR (151 MHz, DMSO) δ 151.9, 144.3, 140.0, 135.4, 129.9, 127.9, 126.8, 122.8, 122.0, 119.1, 111.6, 21.4.

5aj



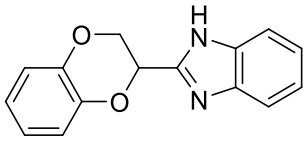
Chemical Formula: $C_{13}H_9N_3O_2$

5aj

^{1}H NMR (500 MHz, DMSO) δ 13.24 (s, 1H), 8.55 – 8.20 (m, 4H), 7.65 (s, 2H), 7.41 – 7.05 (m, 2H).

^{13}C NMR (126 MHz, DMSO) δ 148.9, 147.6, 135.9, 127.2, 124.1, 122.8, 111.8.

5ak



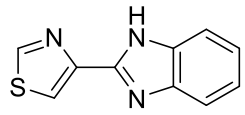
Chemical Formula: $C_{15}H_{12}N_2O_2$

5ak

^{1}H NMR (500 MHz, DMSO) δ 12.76 (s, 1H), 7.59 (s, 2H), 7.22 (dd, *J* = 6.0, 3.2 Hz, 2H), 7.07 – 6.99 (m, 1H), 6.94 (dt, *J* = 6.6, 3.0 Hz, 1H), 6.92 – 6.85 (m, 2H), 5.61 (dd, *J* = 7.3, 2.6 Hz, 1H), 4.68 (dd, *J* = 11.6, 2.6 Hz, 1H), 4.50 (dd, *J* = 11.6, 7.3 Hz, 1H).

^{13}C NMR (126 MHz, DMSO) δ 149.2, 142.8, 142.5, 122.1, 121.7, 121.6, 117.3, 117.1, 69.5, 65.66.

5al



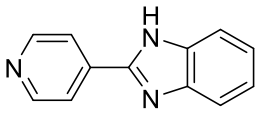
Chemical Formula: $C_{10}H_7N_3S$

5al

^{1}H NMR (600 MHz, DMSO) δ 12.99 (s, 1H), 9.33 (d, *J* = 1.6 Hz, 1H), 8.46 (d, *J* = 1.6 Hz, 1H), 7.67 (d, *J* = 6.8 Hz, 1H), 7.53 (d, *J* = 6.7 Hz, 1H), 7.21 (s, 2H).

^{13}C NMR (151 MHz, DMSO) δ 156.0, 147.5, 147.5, 144.2, 134.8, 123.1, 122.2, 119.9, 119.2, 112.2.

5am



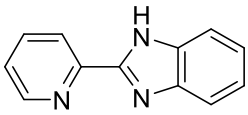
Chemical Formula: $C_{12}H_9N_3$

5am

^{1}H NMR (600 MHz, DMSO) δ 13.28 (s, 1H), 8.76 (dd, *J* = 4.6, 1.5 Hz, 2H), 8.11 (dd, *J* = 4.6, 1.5 Hz, 2H), 7.68 (s, 2H), 7.27 (s, 2H).

^{13}C NMR (151 MHz, DMSO) δ 150.9, 149.2, 146.57 – 141.32 (m), 137.6, 123.4, 120.8, 120.0, 112.3.

5an



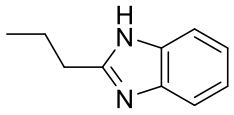
Chemical Formula: $C_{12}H_9N_3$

5an

^{1}H NMR (600 MHz, DMSO) δ 13.18 (s, 1H), 8.81 – 8.71 (m, 1H), 8.40 (d, *J* = 7.9 Hz, 1H), 8.03 (td, *J* = 7.7, 1.7 Hz, 1H), 7.77 (d, *J* = 7.9 Hz, 1H), 7.61 (d, *J* = 7.8 Hz, 1H), 7.54 (ddd, *J* = 7.5, 4.8, 1.1 Hz, 1H), 7.28 (dt, *J* = 15.1, 6.8 Hz, 2H).

^{13}C NMR (151 MHz, DMSO) δ 151.2, 149.8, 149.0, 144.3, 137.9, 135.4, 125.1, 123.6, 122.3, 121.9, 119.7, 112.5.

5ao



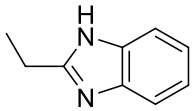
Chemical Formula: $C_{10}H_{12}N_2$

5ao

^{1}H NMR (600 MHz, DMSO) δ 7.46 (dd, *J* = 5.7, 3.2 Hz, 2H), 7.11 (dd, *J* = 5.9, 3.1 Hz, 2H), 2.79 (t, *J* = 7.5 Hz, 2H), 1.79 (dd, *J* = 14.8, 7.4 Hz, 2H), 0.95 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, DMSO) δ 155.4, 138.7, 121.4, 114.8, 30.9, 21.4, 14.1.

5ap



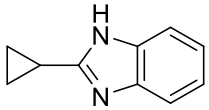
Chemical Formula: $C_9H_{10}N_2$

5ap

^{1}H NMR (600 MHz, DMSO) δ 7.47 (s, 1H), 7.11 (s, 1H), 2.85 (q, *J* = 7.5 Hz, 1H), 1.33 (t, *J* = 7.6 Hz, 2H).

^{13}C NMR (151 MHz, DMSO) δ 156.6, 139.8, 121.4, 114.8, 22.4, 12.6.

5aq



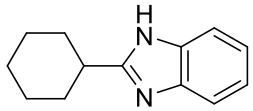
Chemical Formula: $C_{10}H_{10}N_2$

5aq

^{1}H NMR (600 MHz, DMSO) δ 12.20 (s, 1H), 7.41 (dd, *J* = 5.8, 3.2 Hz, 2H), 7.16 – 6.89 (m, 2H), 2.17 – 2.01 (m, 1H), 1.17 – 0.79 (m, 4H).

^{13}C NMR (151 MHz, DMSO) δ 157.4, 121.4, 9.8, 9.1.

5ar



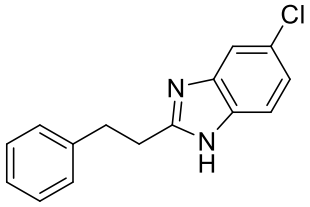
Chemical Formula: $C_{13}H_{16}N_2$

5ar

^{1}H NMR (600 MHz, DMSO) δ 12.10 (s, 1H), 7.52 (d, *J* = 7.4 Hz, 1H), 7.40 (d, *J* = 7.4 Hz, 1H), 7.10 (p, *J* = 6.2 Hz, 2H), 2.90 – 2.77 (m, 1H), 2.02 (dd, *J* = 13.0, 2.7 Hz, 2H), 1.83 – 1.76 (m, 2H), 1.73 – 1.66 (m, 1H), 1.61 (dd, *J* = 12.2, 3.0 Hz, 2H), 1.44 – 1.34 (m, 2H), 1.31 – 1.22 (m, 1H).

^{13}C NMR (151 MHz, DMSO) δ 159.3, 143.5, 134.6, 121.7, 121.1, 118.6, 111.1, 38.1, 31.7, 26.0, 25.9.

5ba



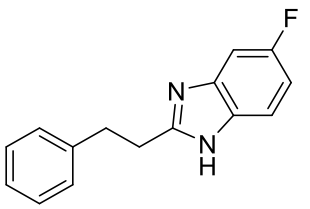
Chemical Formula: $C_{15}H_{13}ClN_2$

5ba

^{1}H NMR (600 MHz, DMSO) δ 12.45 (s, 1H), 7.55 (s, 1H), 7.49 (d, J = 6.9 Hz, 1H), 7.33 – 7.22 (m, 4H), 7.21 – 7.16 (m, 1H), 7.15 (dd, J = 8.5, 1.8 Hz, 1H), 3.12 (s, 4H).

^{13}C NMR (151 MHz, DMSO) δ 156.4, 141.3, 128.8, 128.6, 126.5, 121.8, 33.6, 30.8.

5ca



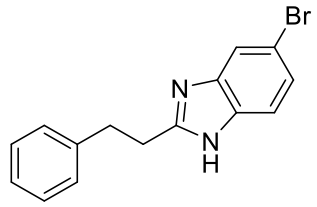
Chemical Formula: $C_{15}H_{13}FN_2$

5ca

^{1}H NMR (500 MHz, DMSO) δ 12.37 (s, 1H), 7.46 (s, 1H), 7.27 (d, *J* = 7.2 Hz, 5H), 7.18 (s, 1H), 6.97 (t, *J* = 8.0 Hz, 1H), 3.11 (s, 4H).

^{13}C NMR (126 MHz, DMSO) δ 159.0, 157.2, 155.9, 140.9, 128.3, 128.2, 126.0, 109.0, 108.8, 33.1, 30.3.

5da



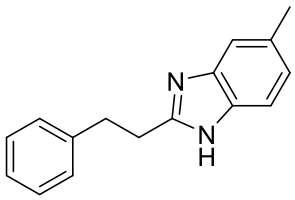
Chemical Formula: $C_{15}H_{13}BrN_2$

5da

^{1}H NMR (500 MHz, DMSO) δ 12.49 (s, 1H), 7.67 (s, 1H), 7.44 (d, *J* = 8.5 Hz, 1H), 7.33 – 7.22 (m, 5H), 7.21 – 7.14 (m, 1H), 3.11 (s, 4H).

^{13}C NMR (126 MHz, DMSO) δ 155.8, 140.8, 128.3, 128.2, 126.0, 123.9, 113.3, 33.1, 30.2.

5ea



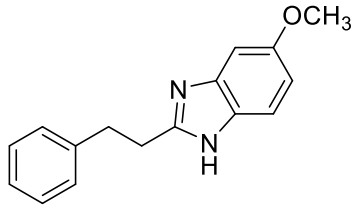
Chemical Formula: $C_{16}H_{16}N_2$

5ea

^{1}H NMR (500 MHz, DMSO) δ 12.07 (s, 1H), 7.45 – 7.13 (m, 7H), 6.93 (s, 1H), 3.17 – 2.97 (m, 4H), 2.38 (s, 3H).

^{13}C NMR (126 MHz, DMSO) δ 153.7, 141.3, 141.0, 130.5, 128.3, 128.2, 125.9, 122.7, 122.2, 117.9, 117.6, 110.5, 110.2, 33.3, 30.3, 21.2.

5fa



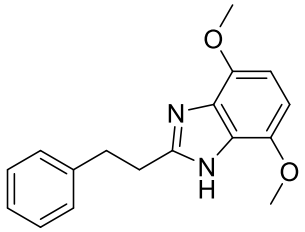
Chemical Formula: $C_{16}H_{16}N_2O$

5fa

^{1}H NMR (500 MHz, DMSO) δ 12.05 (s, 1H), 7.44 – 7.22 (m, 5H), 7.21 – 7.15 (m, 1H), 7.12 – 6.87 (m, 1H), 6.74 (t, *J* = 9.6 Hz, 1H), 3.76 (s, 3H), 3.08 (s, 4H).

^{13}C NMR (126 MHz, DMSO) δ 155.3, 154.7, 153.2, 144.1, 141.0, 137.6, 134.7, 128.3, 128.2, 125.9, 118.4, 110.8, 110.6, 109.8, 101.1, 94.3, 55.4, 33.3, 30.3.

5ga



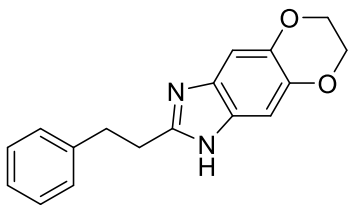
Chemical Formula: $C_{17}H_{18}N_2O_2$

5ga

^{1}H NMR (500 MHz, DMSO) δ 12.44 (s, 1H), 7.31 – 7.21 (m, 4H), 7.21 – 7.13 (m, 1H), 6.54 (s, 2H), 3.86 (s, 6H), 3.20 – 2.99 (m, 4H).

^{13}C NMR (126 MHz, DMSO) δ 152.6, 145.0, 141.1, 140.0, 134.5, 128.3, 128.2, 102.1, 55.6, 33.5, 30.2.

5ha



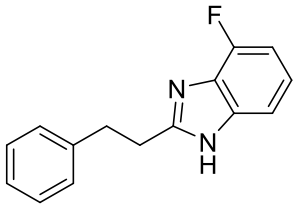
Chemical Formula: $C_{17}H_{16}N_2O_2$

5ha

^{1}H NMR (500 MHz, DMSO) δ 7.25 (dt, *J* = 14.7, 7.3 Hz, 4H), 7.17 (t, *J* = 7.0 Hz, 1H), 6.91 (s, 2H), 4.21 (s, 4H), 3.05 (dd, *J* = 10.5, 4.7 Hz, 4H).

^{13}C NMR (126 MHz, DMSO) δ 153.9, 141.0, 139.6, 128.3, 128.1, 125.9, 101.0, 63.8, 33.2, 30.3.

5ia



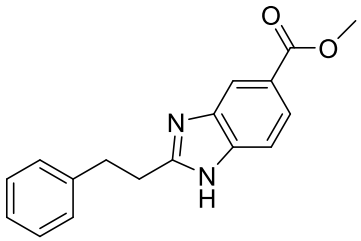
Chemical Formula: $C_{15}H_{13}FN_2$

5ia

^{1}H NMR (500 MHz, DMSO) δ 12.58 (s, 1H), 7.40 – 7.24 (m, 5H), 7.19 (t, *J* = 6.3 Hz, 1H), 7.11 (td, *J* = 7.9, 5.2 Hz, 1H), 7.01 – 6.87 (m, 1H), 3.14 (s, 4H).

^{13}C NMR (126 MHz, DMSO) δ 155.0, 140.8, 137.4, 128.3, 128.2, 121.8, 107.3, 106.4, 33.2, 30.2.

5ja



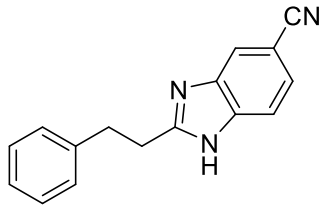
Chemical Formula: $C_{17}H_{16}N_2O_2$

5ja

^{1}H NMR (500 MHz, DMSO) δ 12.63 (s, 1H), 8.12 (s, 1H), 7.80 (dd, *J* = 8.4, 1.0 Hz, 1H), 7.58 (d, *J* = 7.8 Hz, 1H), 7.34 – 7.24 (m, 4H), 7.23 – 7.15 (m, 1H), 3.86 (s, 3H), 3.27 – 2.98 (m, 4H).

^{13}C NMR (126 MHz, DMSO) δ 166.8, 140.8, 128.34 (d, *J* = 4.4 Hz), 128.2, 126.02 (d, *J* = 12.0 Hz), 122.6, 51.8, 33.1, 30.4.

5ka



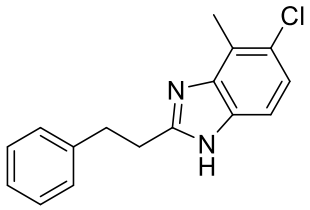
Chemical Formula: $C_{16}H_{13}N_3$

5ka

^{1}H NMR (500 MHz, DMSO) δ 12.81 (s, 1H), 8.21 – 7.87 (m, 1H), 7.76 – 7.57 (m, 1H), 7.53 (d, *J* = 7.6 Hz, 1H), 7.32 – 7.23 (m, 4H), 7.22 – 7.14 (m, 1H), 3.23 – 3.05 (m, 4H).

^{13}C NMR (126 MHz, DMSO) δ 157.5, 140.7, 128.3, 128.2, 126.1, 122.9, 120.1, 119.1, 115.7, 112.2, 103.1, 32.9, 30.2.

5la



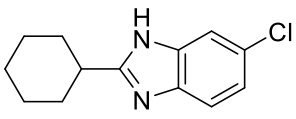
Chemical Formula: $C_{16}H_{15}ClN_2$

5la

^{1}H NMR (500 MHz, DMSO) δ 12.38 (s, 1H), 7.39 – 7.23 (m, 5H), 7.23 – 7.16 (m, 1H), 7.14 (d, *J* = 8.5 Hz, 1H), 3.13 (s, 4H), 2.52 (d, *J* = 9.4 Hz, 3H).

^{13}C NMR (126 MHz, DMSO) δ 155.1, 140.9, 128.3, 128.2, 126.0, 121.7, 33.3, 30.4, 14.2.

5c



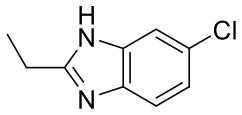
Chemical Formula: $C_{13}H_{15}ClN_2$

5c

^{1}H NMR (500 MHz, DMSO) δ 12.32 (s, 1H), 7.88 – 7.32 (m, 2H), 7.13 (s, 1H), 2.93 – 2.74 (m, 1H), 2.02 (dd, *J* = 13.0, 2.6 Hz, 2H), 1.85 – 1.74 (m, 2H), 1.74 – 1.66 (m, 1H), 1.65 – 1.54 (m, 2H), 1.46 – 1.33 (m, 2H), 1.32 – 1.19 (m, 1H).

^{13}C NMR (126 MHz, DMSO) δ 160.6, 160.1, 144.1, 141.9, 134.9, 132.9, 125.6, 125.1, 121.3, 121.0, 119.3, 117.6, 111.9, 110.5, 37.6, 31.0, 25.4, 25.4.

5d



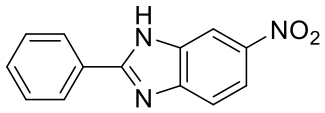
Chemical Formula: $C_9H_9ClN_2$

5d

^{1}H NMR (500 MHz, DMSO) δ 7.53 (s, 1H), 7.48 (d, *J* = 7.7 Hz, 1H), 7.14 (d, *J* = 7.1 Hz, 1H), 2.85 (d, *J* = 6.8 Hz, 2H), 1.32 (s, 3H).

^{13}C NMR (126 MHz, DMSO) δ 157.7, 140.0, 137.1, 125.4, 121.2, 115.2, 114.3, 21.9, 11.9.

5e



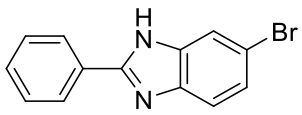
Chemical Formula: $C_{13}H_9N_3O_2$

5e

^{1}H NMR (500 MHz, DMSO) δ 13.64 (s, 1H), 8.48 (s, 1H), 8.30 – 8.19 (m, 2H), 8.13 (dd, *J* = 8.8, 2.1 Hz, 1H), 7.77 (d, *J* = 8.8 Hz, 1H), 7.69 – 7.49 (m, 3H).

^{13}C NMR (126 MHz, DMSO) δ 155.7, 142.6, 130.9, 129.0, 129.0, 126.9, 118.0.

5f



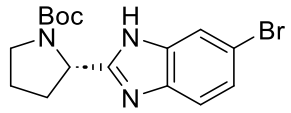
Chemical Formula: $C_{13}H_9BrN_2$

5f

^{1}H NMR (500 MHz, DMSO) δ 13.16 (s, 1H), 8.20 (d, *J* = 7.3 Hz, 2H), 7.82 (s, 1H), 7.55 (dt, *J* = 24.2, 7.0 Hz, 4H), 7.36 (d, *J* = 7.5 Hz, 1H).

^{13}C NMR (126 MHz, DMSO) δ 152.4, 130.2, 129.6, 129.2, 128.9, 128.5, 126.5, 124.9, 114.2.

5g



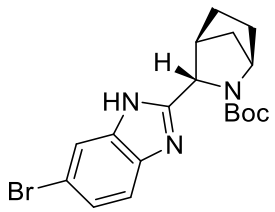
Chemical Formula: $C_{16}H_{20}BrN_3O_2$

5g

^{1}H NMR (500 MHz, DMSO) δ 12.74 – 12.15 (m, 1H), 7.87 – 7.57 (m, 1H), 7.56 – 7.37 (m, 1H), 7.28 (d, *J* = 6.6 Hz, 1H), 5.05 – 4.75 (m, 1H), 3.68 – 3.51 (m, 1H), 3.50 – 3.40 (m, 1H), 2.45 – 2.20 (m, 1H), 2.16 – 1.76 (m, 3H), 1.40 (s, 4H), 1.08 (s, 5H).

^{13}C NMR (126 MHz, DMSO) δ 158.6, 158.2, 158.0, 153.7, 153.1, 144.7, 142.3, 135.2, 133.0, 124.2, 123.9, 120.7, 120.0, 113.6, 113.1, 112.7, 78.8, 78.3, 55.6, 55.1, 46.7, 46.4, 33.2, 31.8, 28.1, 27.7, 23.8, 23.1.

5h



Chemical Formula: $C_{18}H_{22}BrN_3O_2$

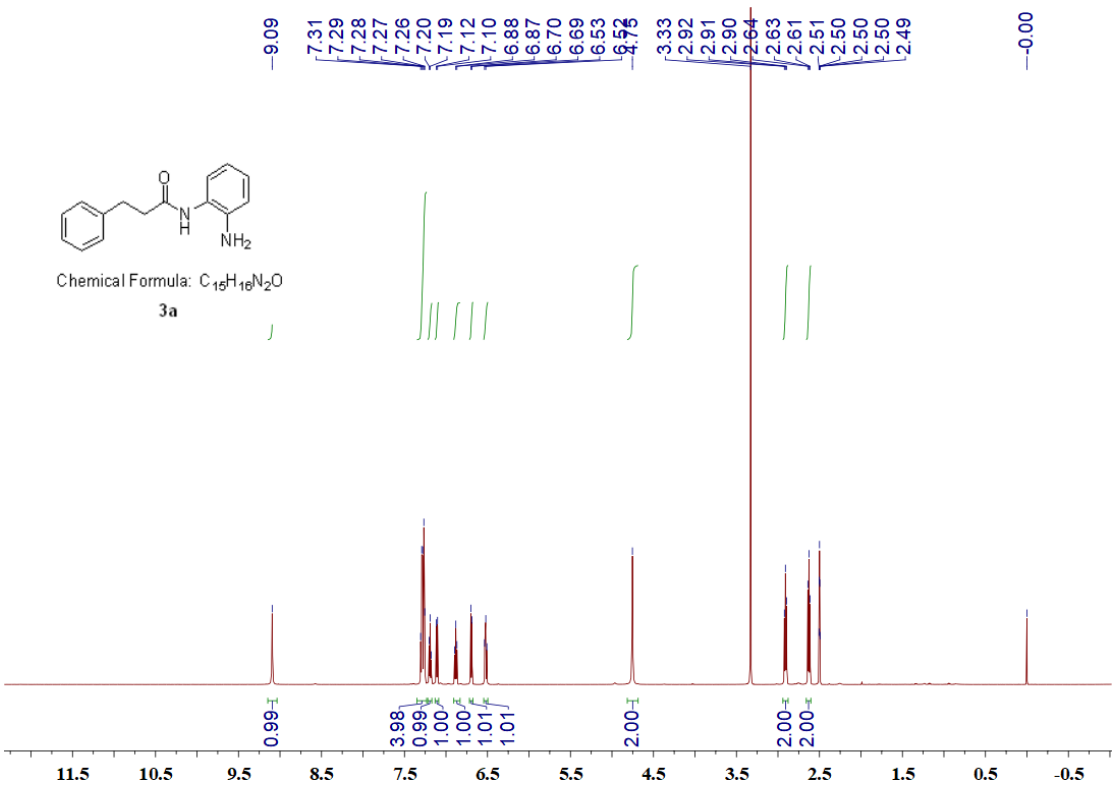
5h

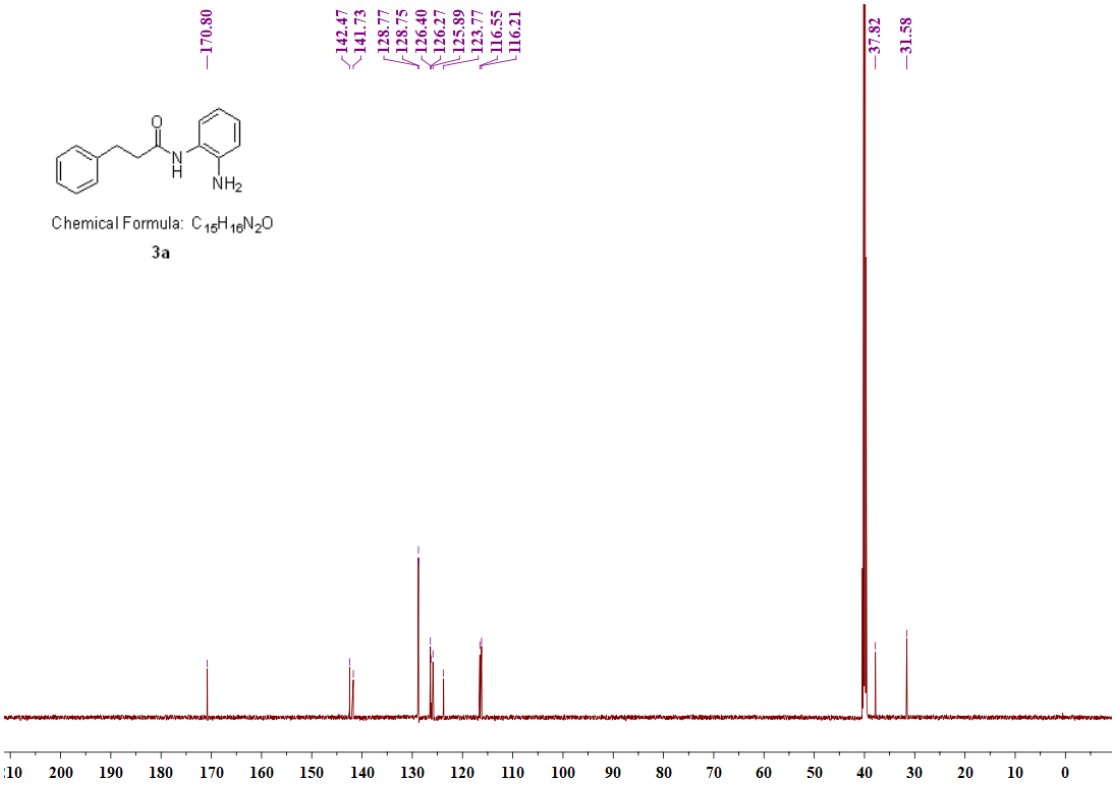
^{1}H NMR (600 MHz, DMSO) δ 12.38 (dd, *J* = 74.7, 42.8 Hz, 1H), 7.79 – 7.36 (m, 2H), 7.33 – 7.16 (m, 1H), 4.50 – 4.40 (m, 1H), 4.32 – 4.08 (m, 1H), 2.69 – 2.57 (m, 1H), 1.97 (dd, *J* = 5.9, 1.8 Hz, 1H), 1.83 – 1.54 (m, 4H), 1.42 (s, 5H), 1.36 – 1.27 (m, 1H), 1.11 (d, *J* = 2.6 Hz, 4H).

^{13}C NMR (151 MHz, DMSO) δ 157.3, 156.9, 156.4, 154.8, 153.4, 145.3, 142.9, 135.62, 133.4, 125.2, 121.3, 120.6, 114.8, 80.1, 62.4, 57.8, 56.4, 44.5, 43.6, 35.37, 34.4, 30.4, 30.0, 28.6, 28.3, 27.6, 27.4.

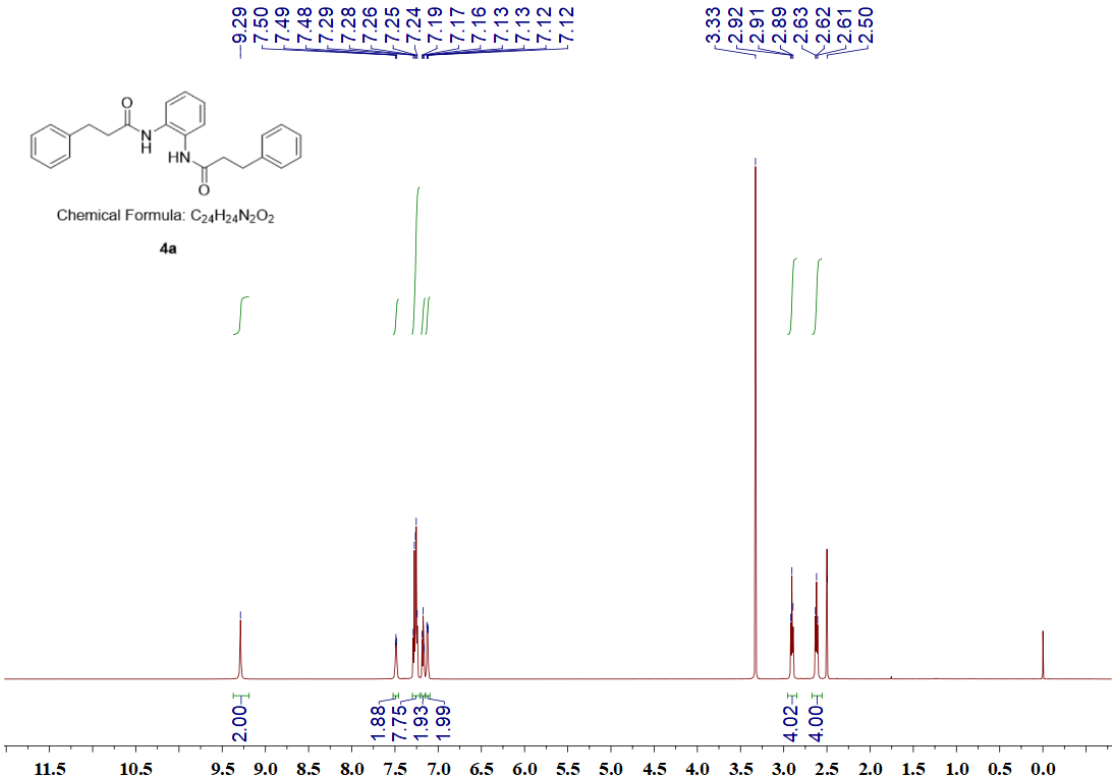
8. ^{1}H and ^{13}C NMR chromatograms

3a





4a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7.28
7.26
7.25
7.24
7.19
7.17
7.16
7.13
7.12
7.12
3.33
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2.91
2.89
2.63
2.62
2.61
2.50
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4a
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1.99
4.02
4.00
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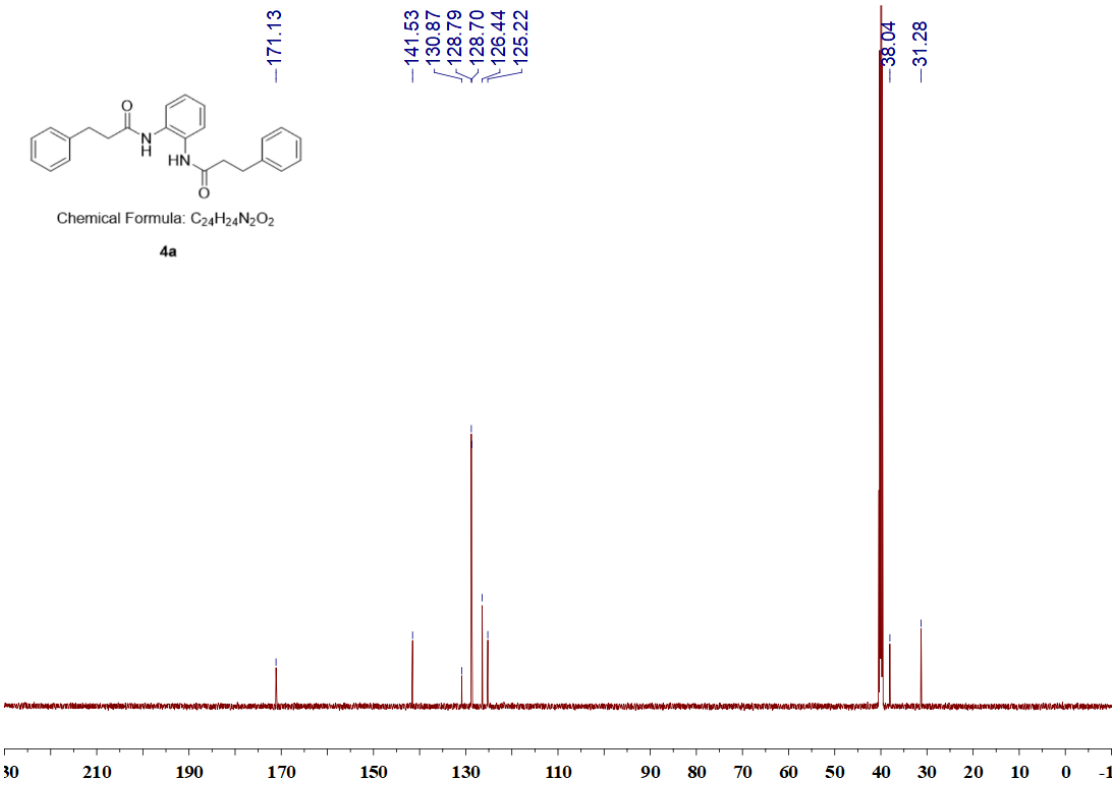
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38.04
31.28
Chemical Formula: C24H24N2O2
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130
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90
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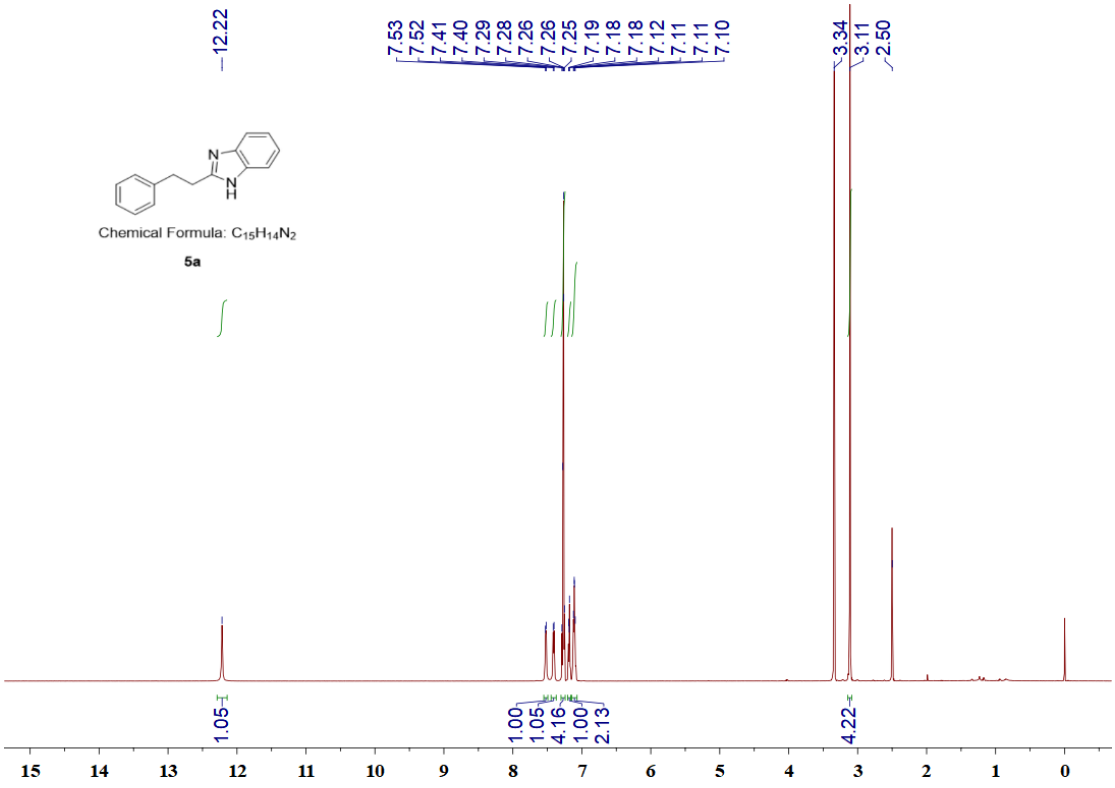
50
40
30
20
10
0
-1

5a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7.12
7.11
7.11
7.10
3.34
3.11
2.50
Chemical Formula: C15H14N2
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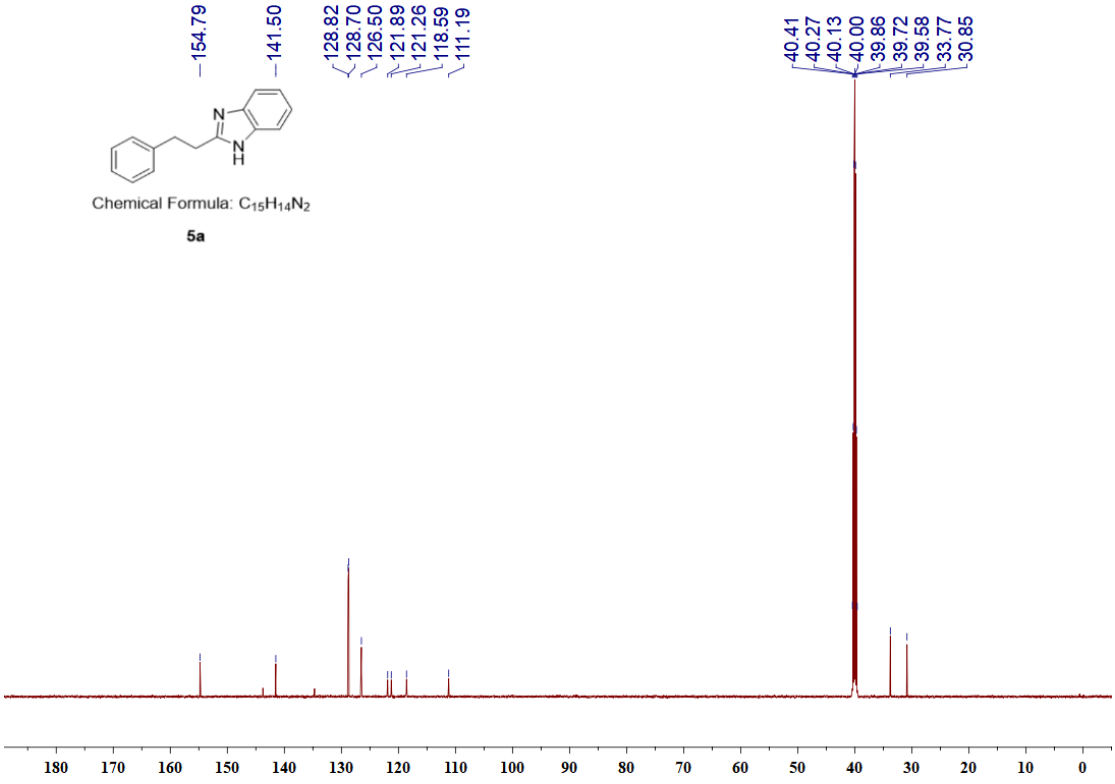
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111.19
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40.27
40.13
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39.86
39.72
39.58
33.77
30.85
Chemical Formula: C15H14N2
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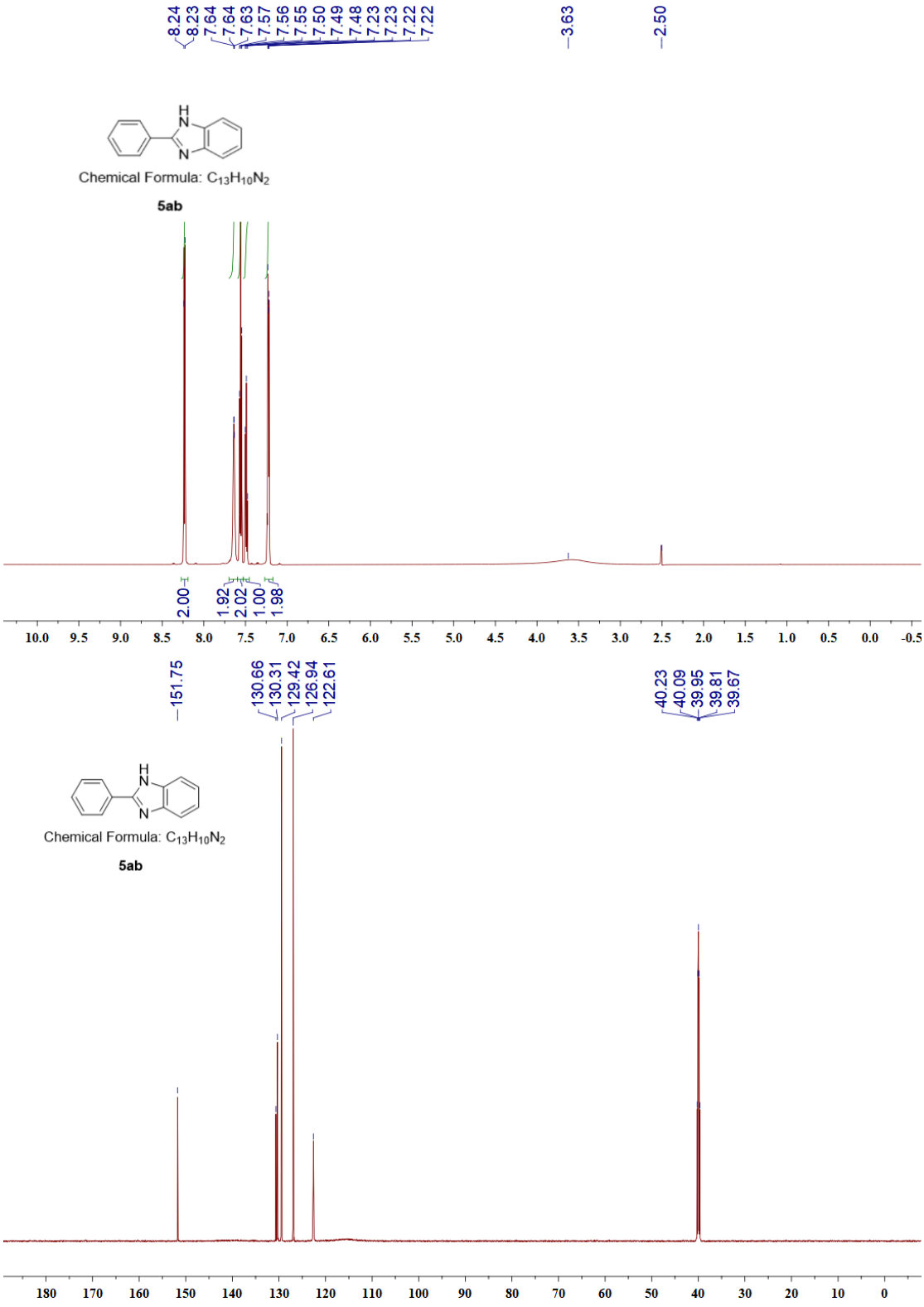
40
30
20
10
0

5ab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7.22
3.63
2.50
Chemical Formula: C13H10N2
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130.31
129.42
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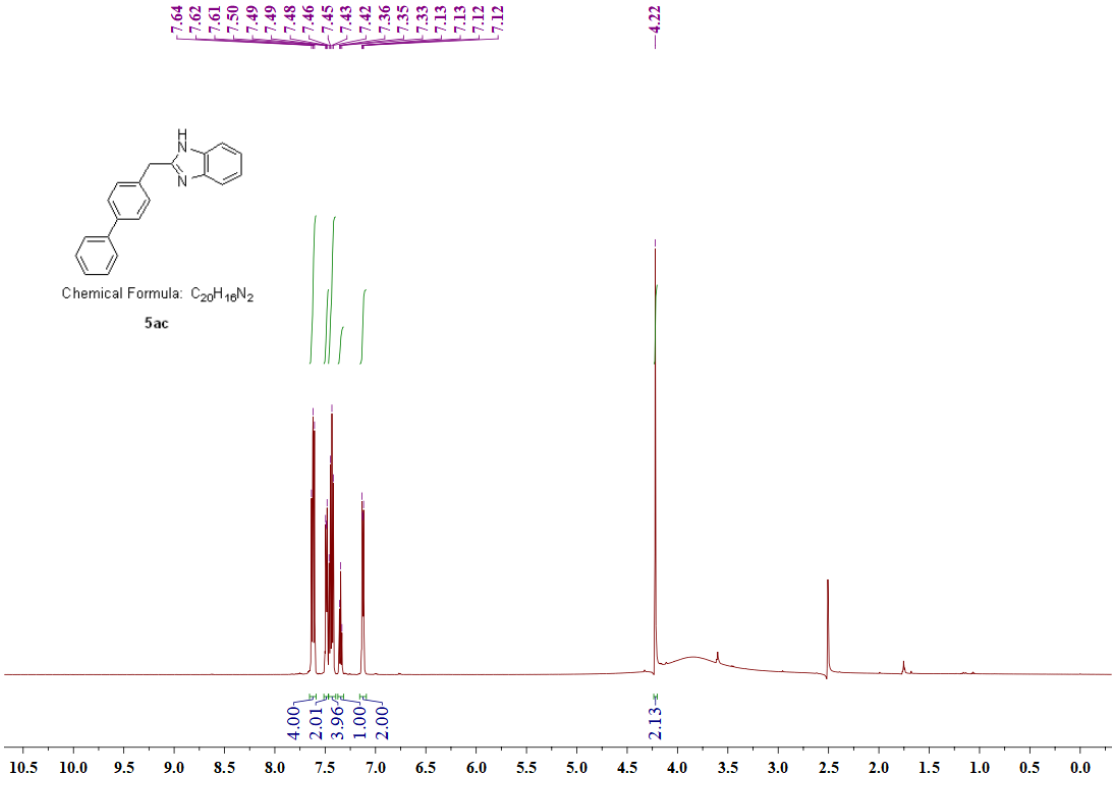
39.67
Chemical Formula: C13H10N2
5ab

5ac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Chemical Formula: C20H16N2
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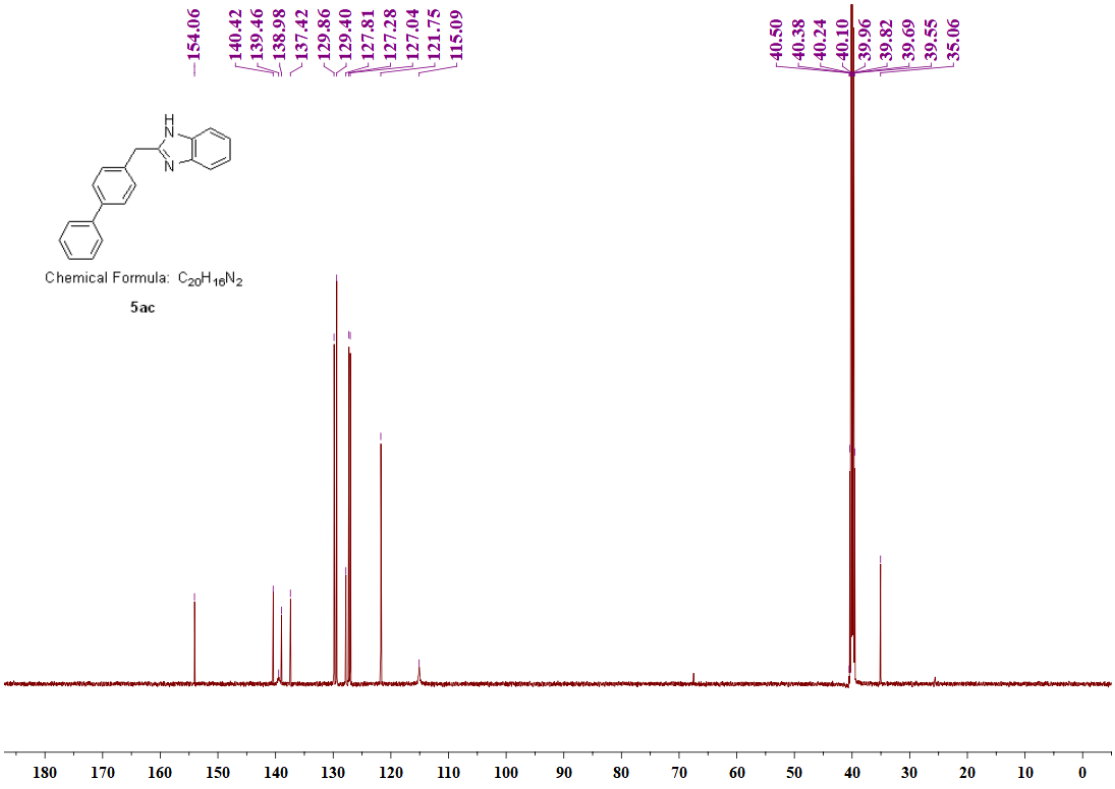
2.00
2.13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39.69
39.55
35.06
Chemical Formula: C20H16N2
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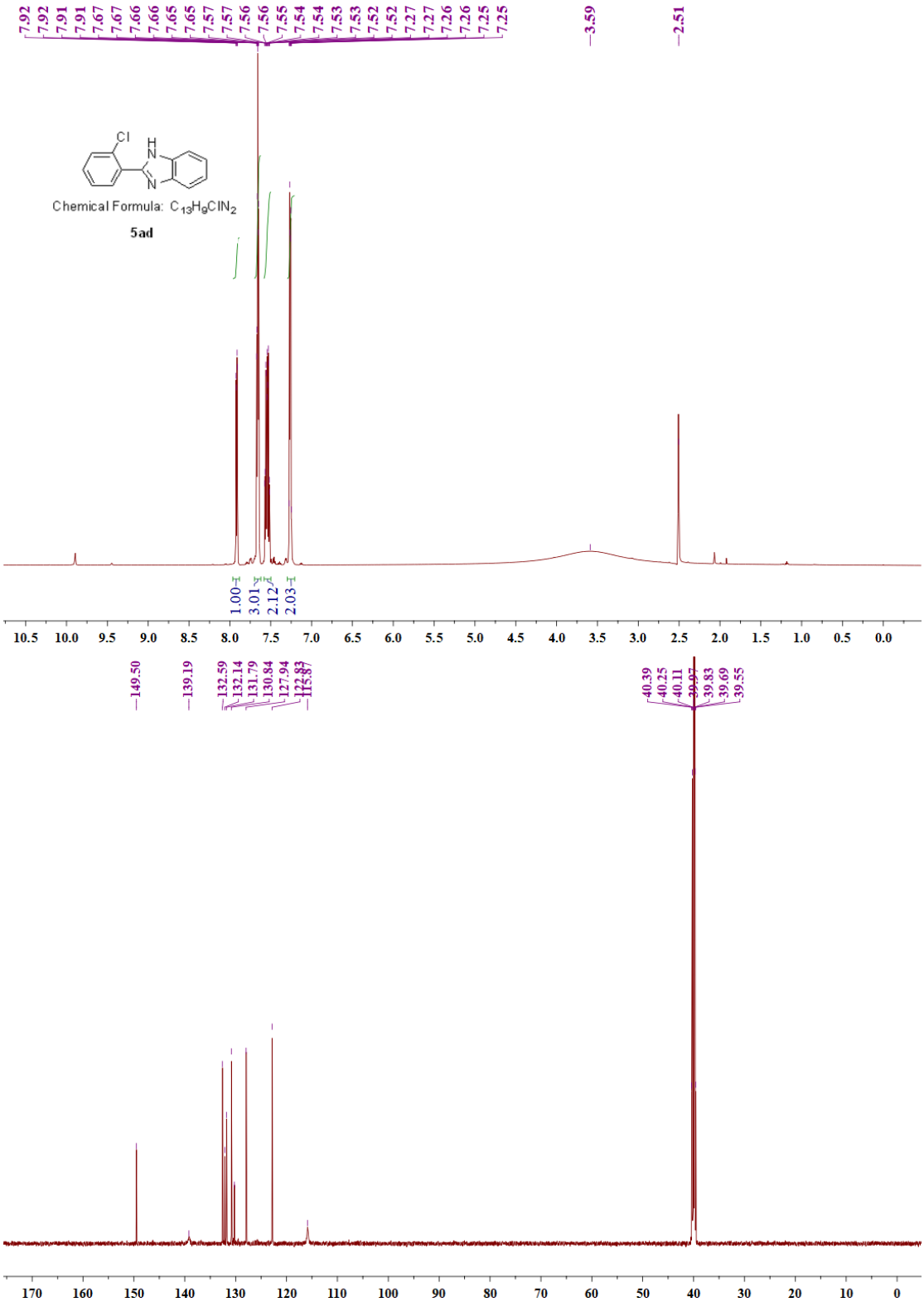
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7.55
7.54
7.54
7.53
7.53
7.52
7.52
7.27
7.27
7.26
7.26
7.25
7.25
3.59
2.51
Cl
H
N
N
Chemical Formula: C13H9ClN2
5ad
1.00
3.01
2.12
2.03
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
149.50
139.19
132.59
132.14
131.79
130.84
127.94
122.83
115.87
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40.11
39.97
39.83
39.69
39.55
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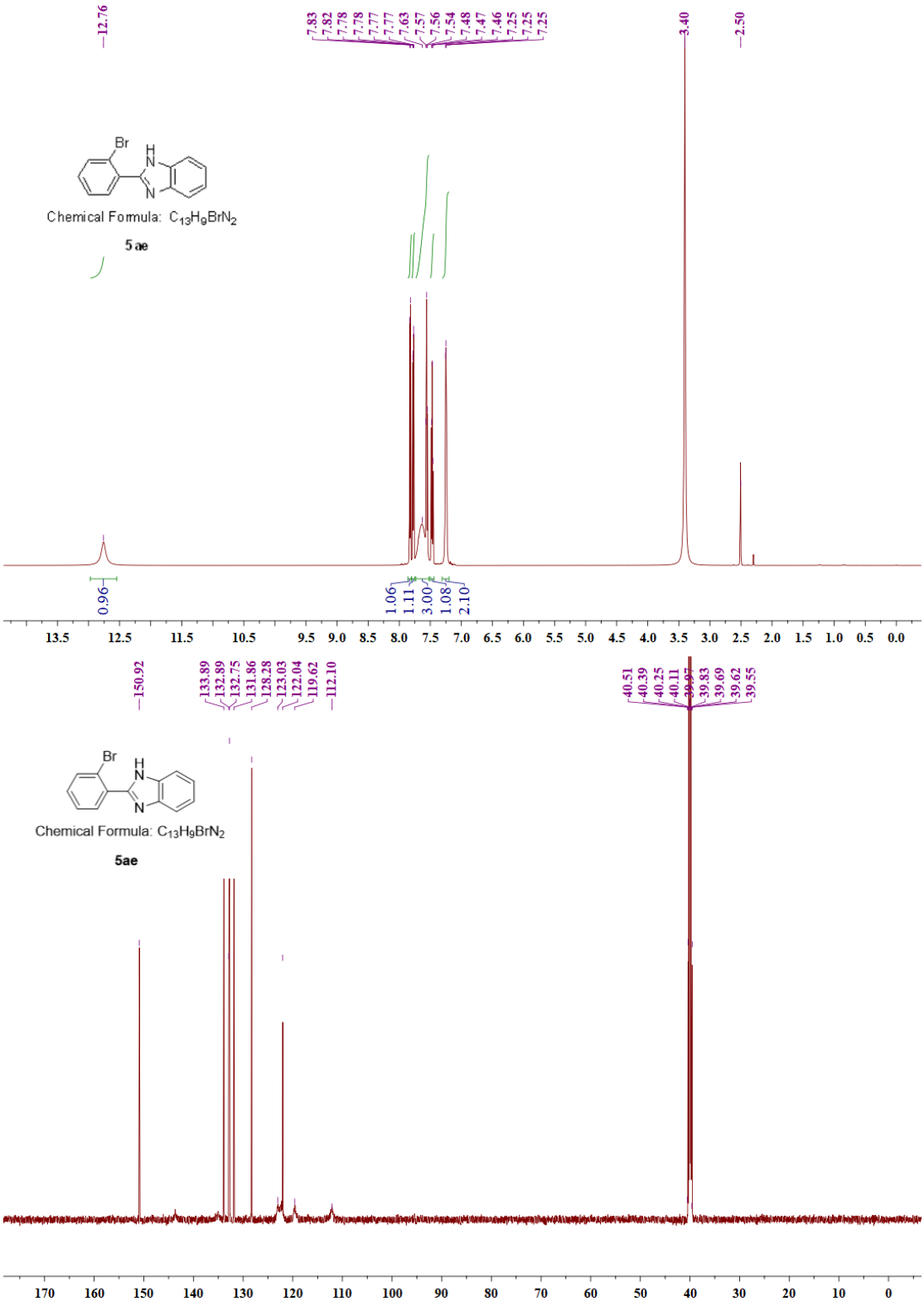
5ae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7.47
7.46
7.25
7.25
7.25
3.40
2.50
Br
H
N
N
Chemical Formula: C13H9BrN2
5ae
0.96
1.06
1.11
3.00
1.08
2.10
13.5 12.5 11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
150.92
133.89
132.89
132.75
131.86
128.28
123.03
122.04
119.62
112.10
40.51
40.39
40.25
40.11
39.97
39.83
39.69
39.62
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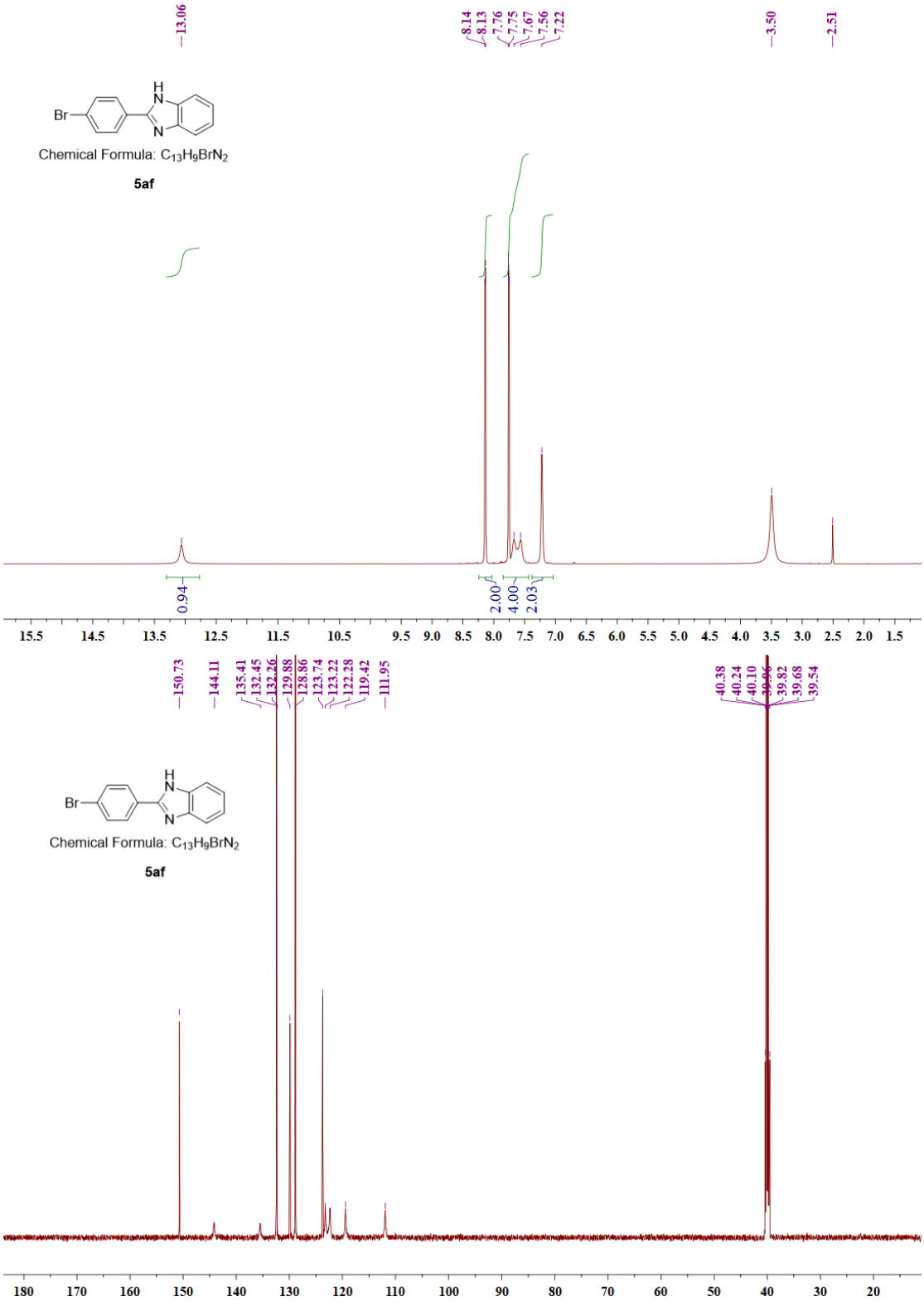
Br
H
N
N
Chemical Formula: C13H9BrN2
5ae
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

5af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7.67
7.56
7.22
3.50
2.51
Br
H
N
N
Chemical Formula: C13H9BrN2
5af
0.94
2.00
4.00
2.03
15.5 14.5 13.5 12.5 11.5 10.5 9.5 9.0 8.5 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
150.73
144.11
135.41
132.45
132.26
129.88
128.86
123.74
123.22
122.28
119.42
111.95
40.38
40.24
40.10
39.96
39.82
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H
N
N
Chemical Formula: C13H9BrN2
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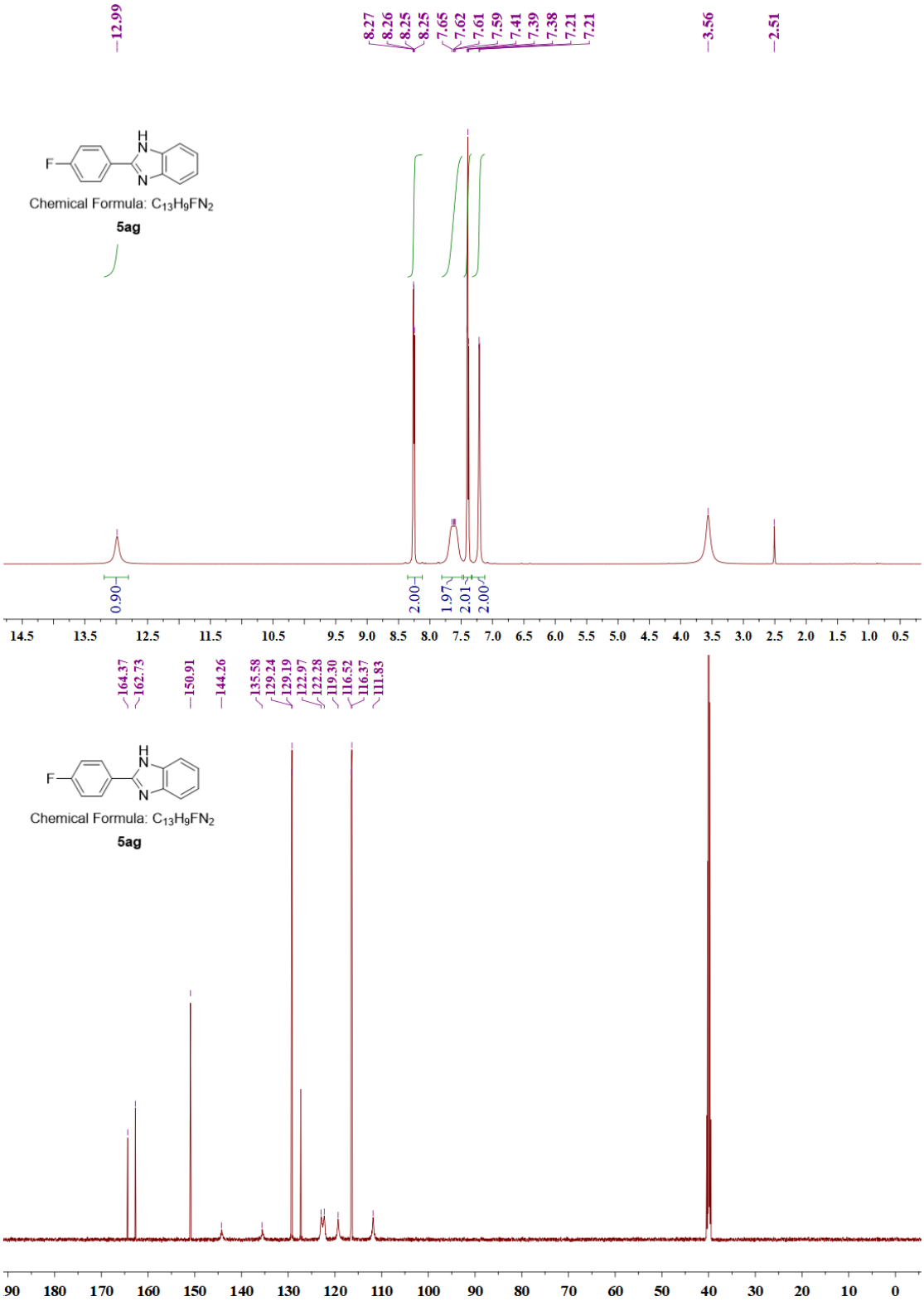
5ag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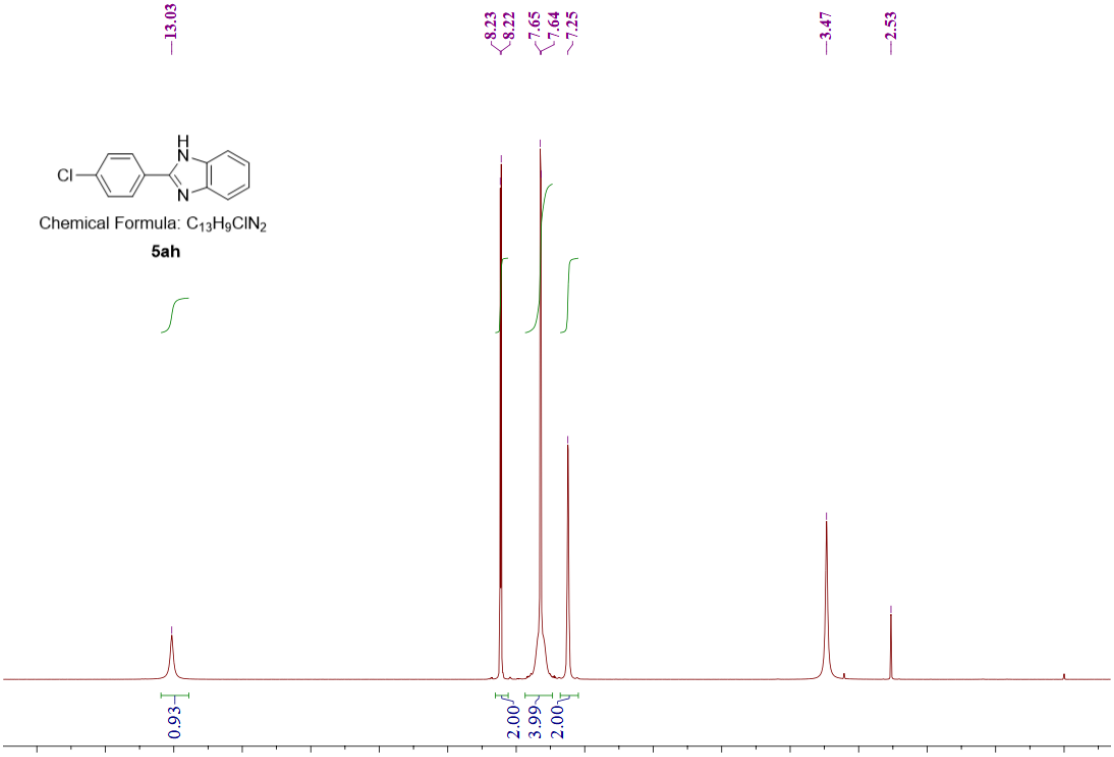
7.62
7.61
7.59
7.41
7.39
7.38
7.21
7.21
3.56
2.51
Chemical Formula: C13H9FN2
5ag
0.90
2.00
1.97
2.01
2.00
164.37
162.73
150.91
144.26
135.58
129.24
129.19
122.97
122.28
119.30
116.52
116.37
111.83
Chemical Formula: C13H9FN2
5ag

5ah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7.25
3.47
2.53
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N
N
Chemical Formula: C13H9ClN2
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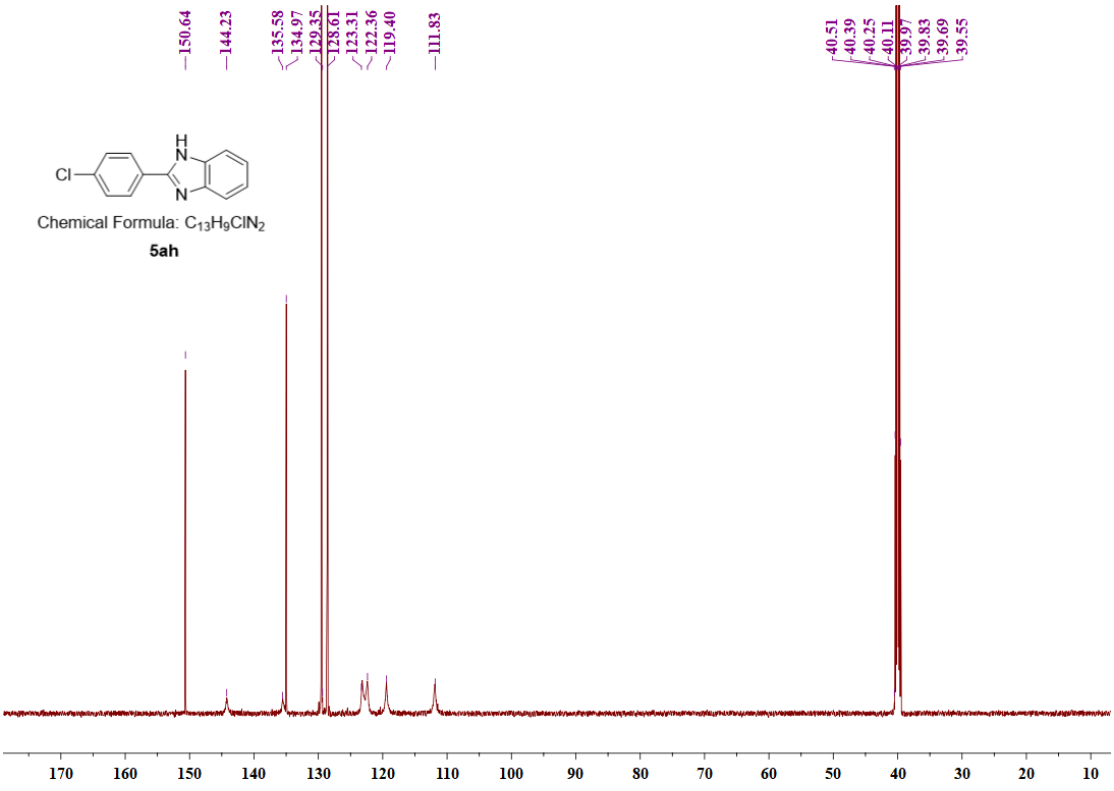
2.00
3.99
2.00
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0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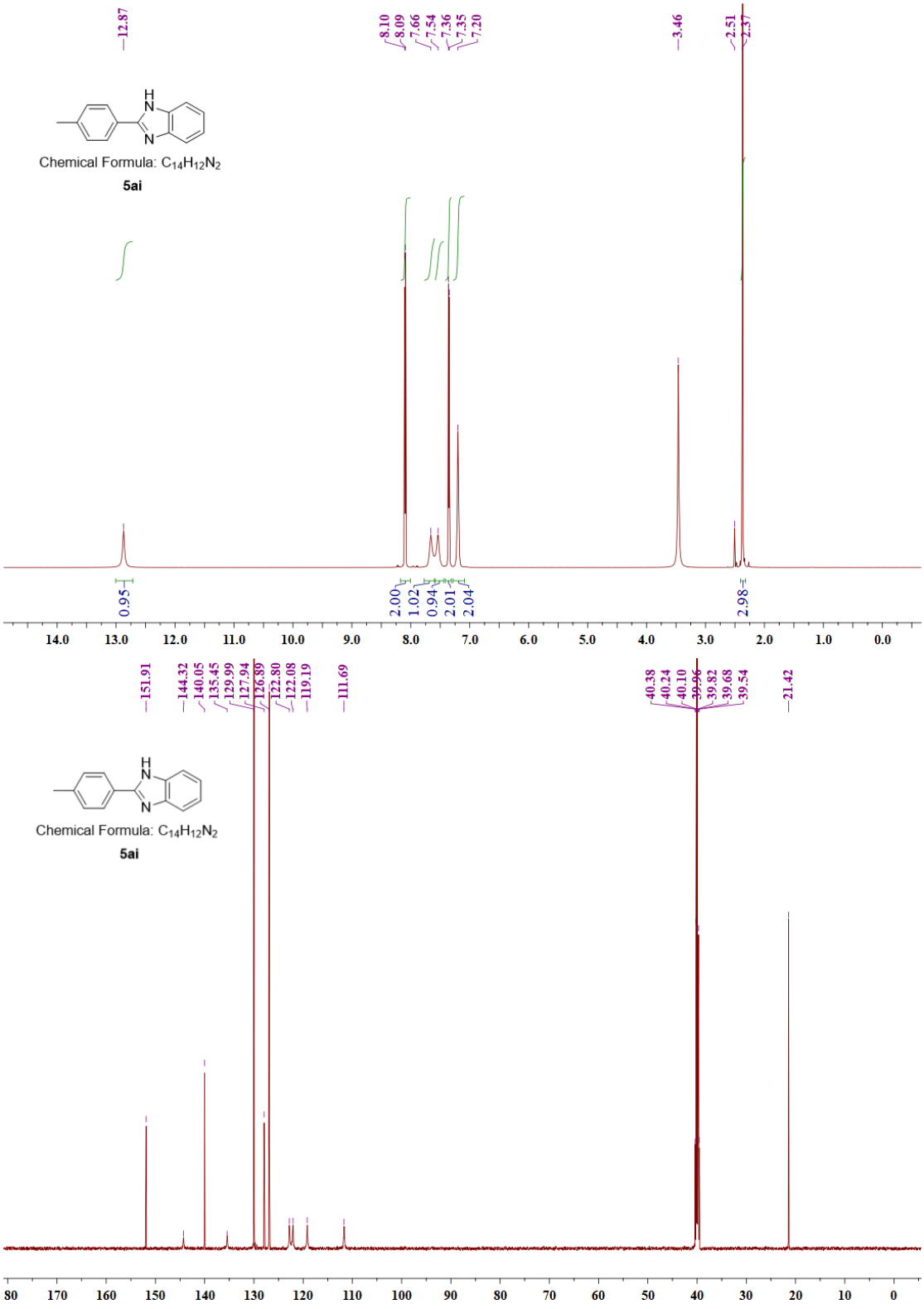
134.97
129.35
128.61
123.31
122.36
119.40
111.83
40.51
40.39
40.25
40.11
39.97
39.83
39.69
39.55
Cl
H
N
N
Chemical Formula: C13H9ClN2
5ah
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10

5ai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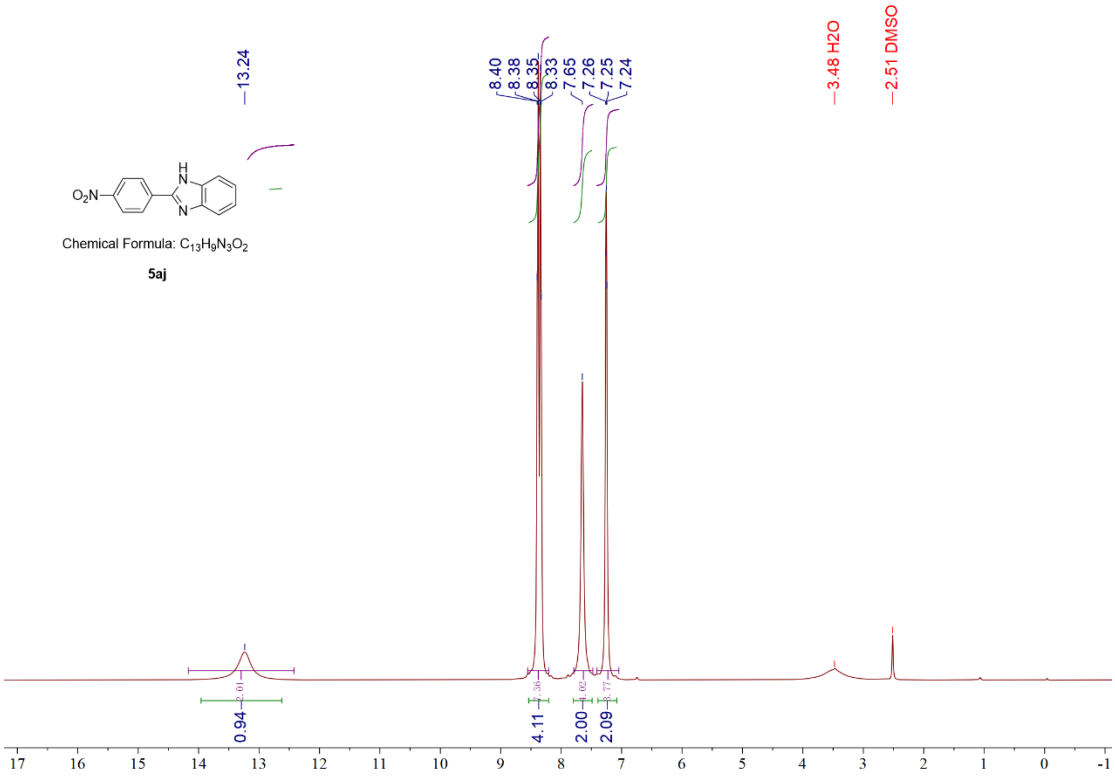
8.10
8.09
7.66
7.54
7.36
7.35
7.20
3.46
2.51
2.37
Chemical Formula: C14H12N2
5ai
0.95
2.00
1.02
0.94
2.01
2.04
2.98
151.91
144.32
140.05
135.45
129.99
127.94
126.89
122.80
122.08
119.19
111.69
40.38
40.24
40.10
39.96
39.82
39.68
39.54
21.42
Chemical Formula: C14H12N2
5ai

5aj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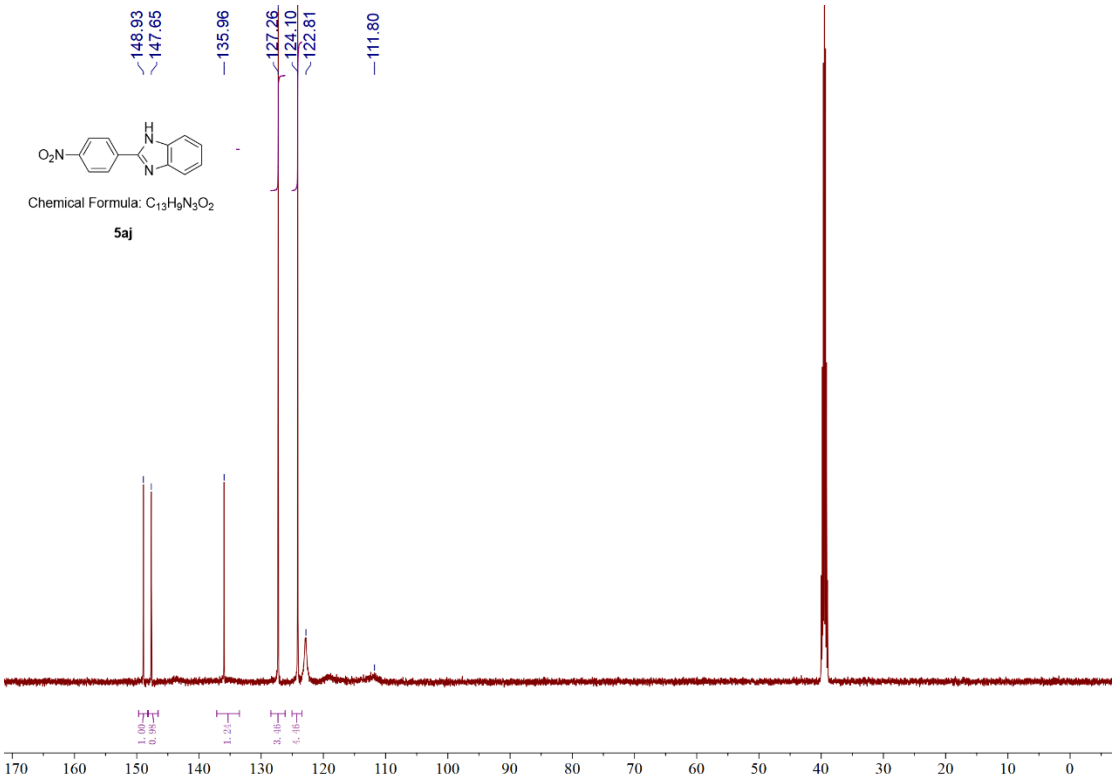
8.40
8.38
8.35
8.33
7.65
7.26
7.25
7.24
3.48 H2O
2.51 DMSO
Chemical Formula: C13H9N3O2
5aj
0.94
4.11
2.00
2.09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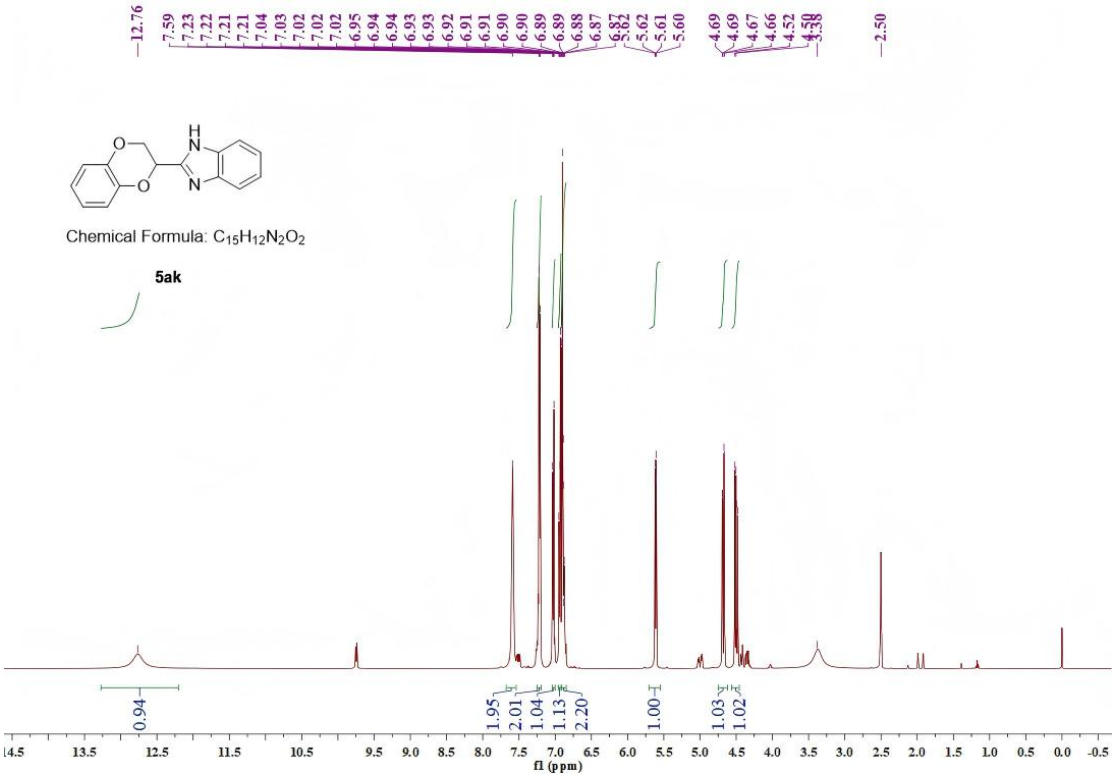
122.81
111.80
Chemical Formula: C13H9N3O2
5aj

5ak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7.23
7.22
7.21
7.21
7.04
7.03
7.02
7.02
7.02
6.95
6.94
6.94
6.93
6.93
6.92
6.91
6.91
6.90
6.90
6.89
6.89
6.88
6.87
5.62
5.61
5.60
4.69
4.69
4.67
4.66
4.52
2.50
Chemical Formula: C15H12N2O2
5ak
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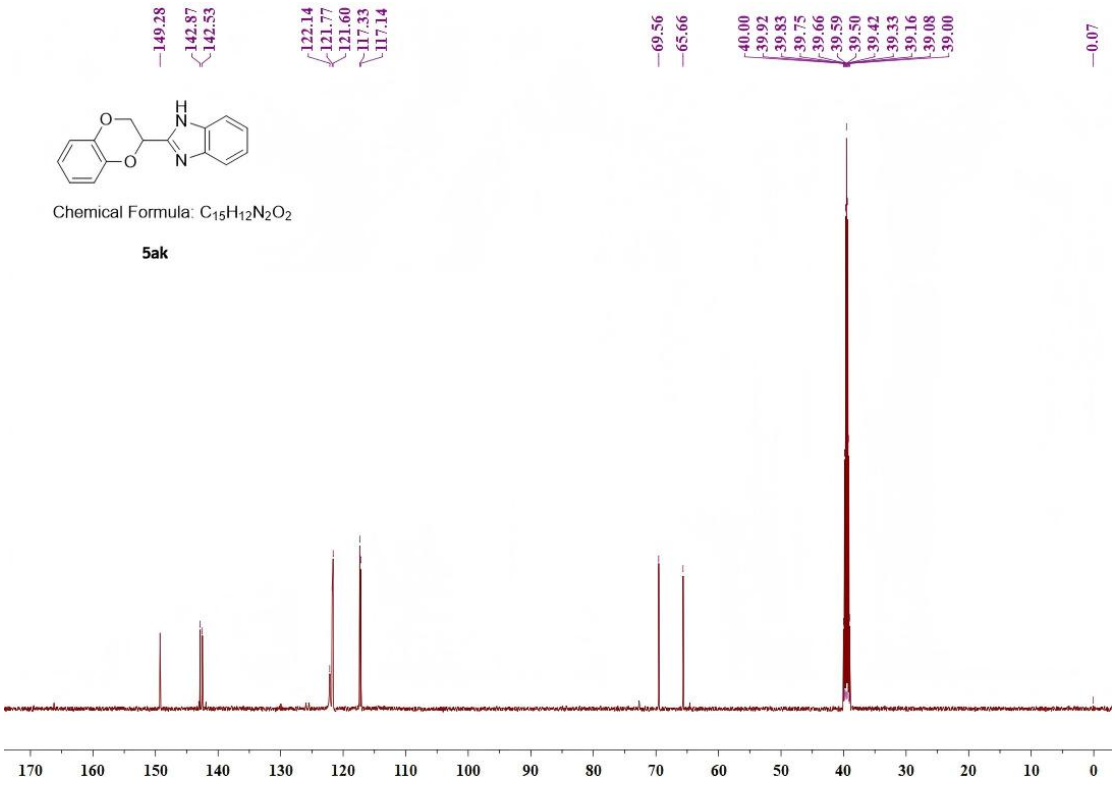
1.95
2.01
1.04
1.13
2.20
1.00
1.03
1.02
f1 (ppm)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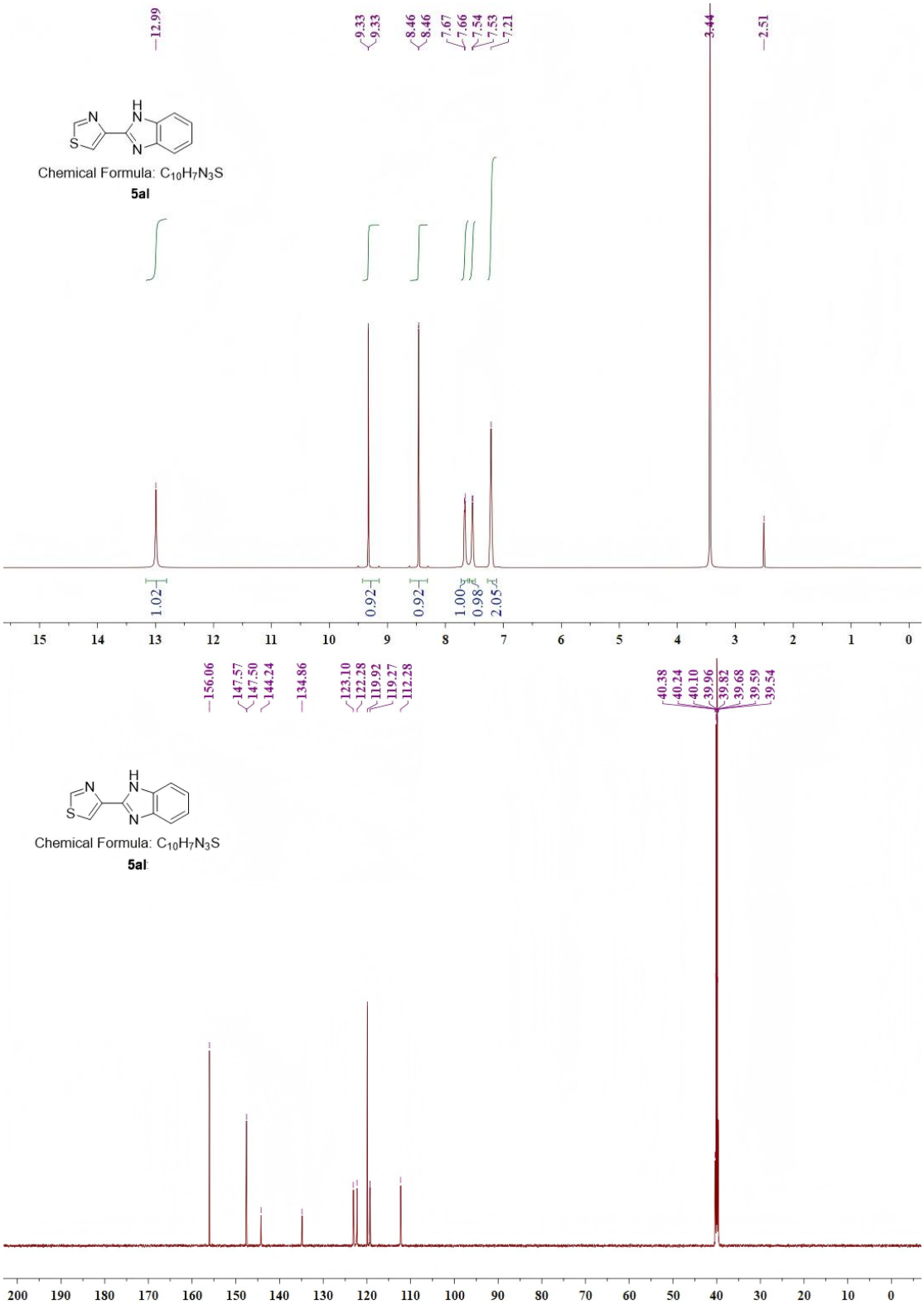
142.87
142.53
122.14
121.77
121.60
117.33
117.14
69.56
65.66
40.00
39.92
39.83
39.75
39.66
39.59
39.50
39.42
39.33
39.16
39.08
39.00
0.07
Chemical Formula: C15H12N2O2
5ak

5al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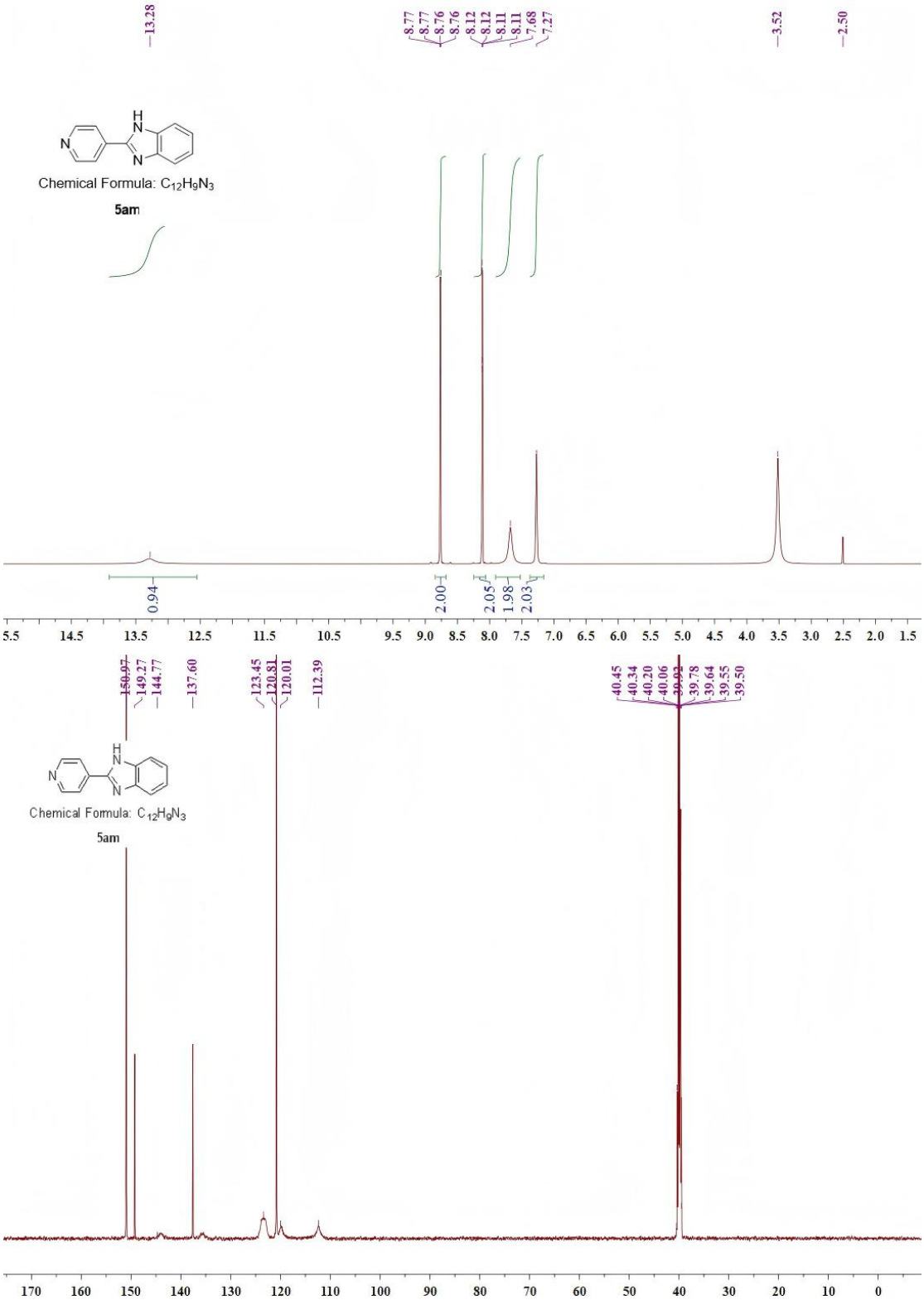
9.33
9.33
8.46
8.46
7.67
7.66
7.54
7.53
7.21
3.44
2.51
Chemical Formula: C10H7N3S
5al
1.02
0.92
0.92
1.00
0.98
2.05
156.06
147.57
147.50
144.24
134.86
123.10
122.28
119.92
119.27
112.28
40.38
40.24
40.10
39.96
39.82
39.68
39.59
39.54
Chemical Formula: C10H7N3S
5al

5am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8.77
8.76
8.76
8.12
8.12
8.11
8.11
7.68
7.27
3.52
2.50
Chemical Formula: C12H9N3
5am
0.94
2.00
2.05
1.98
2.03
150.97
149.27
144.77
137.60
123.45
120.81
120.01
112.39
40.45
40.34
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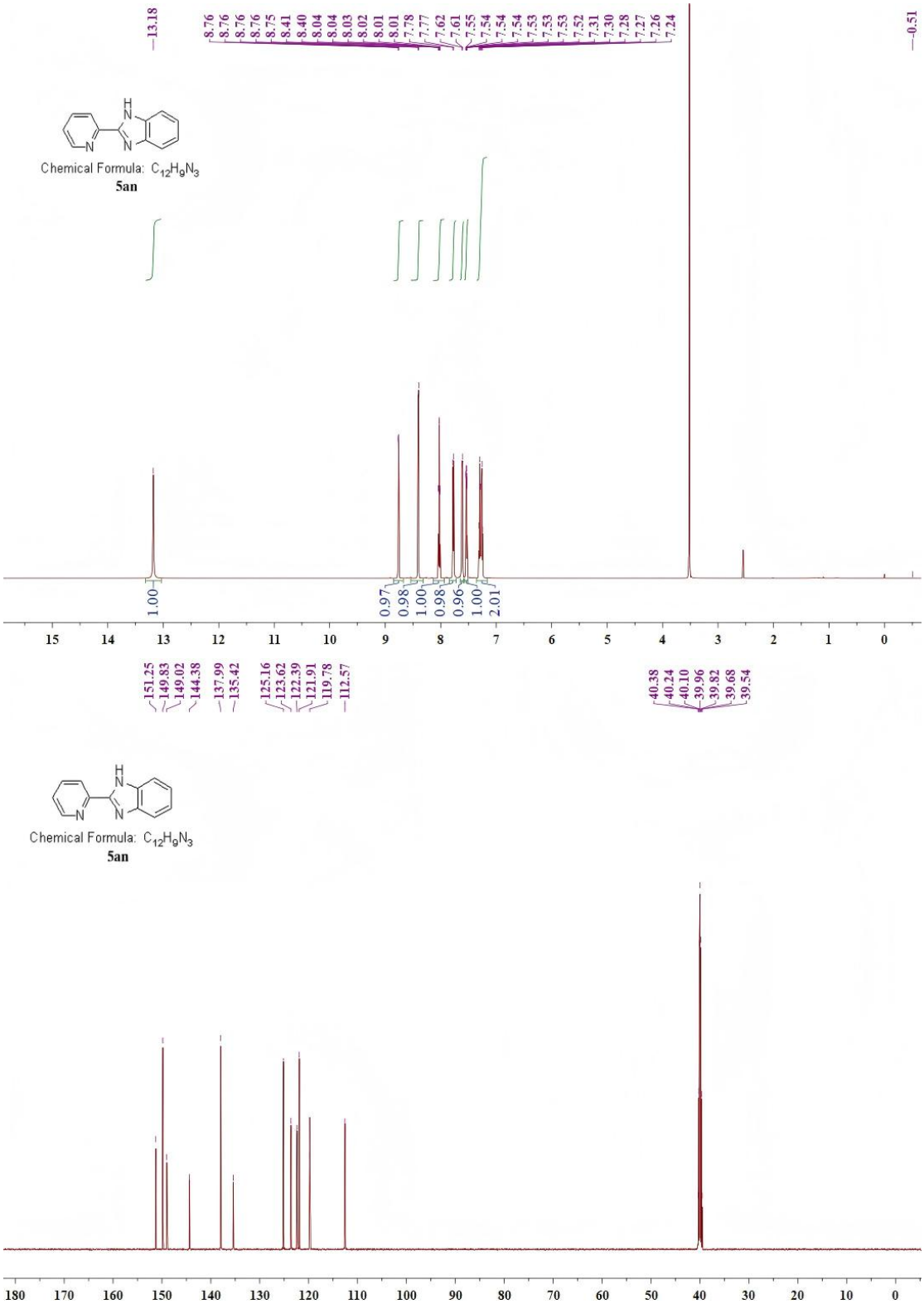
39.92
39.78
39.64
39.55
39.50
Chemical Formula: C12H9N3
5am

5an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8.75
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8.40
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8.04
8.03
8.02
8.01
8.01
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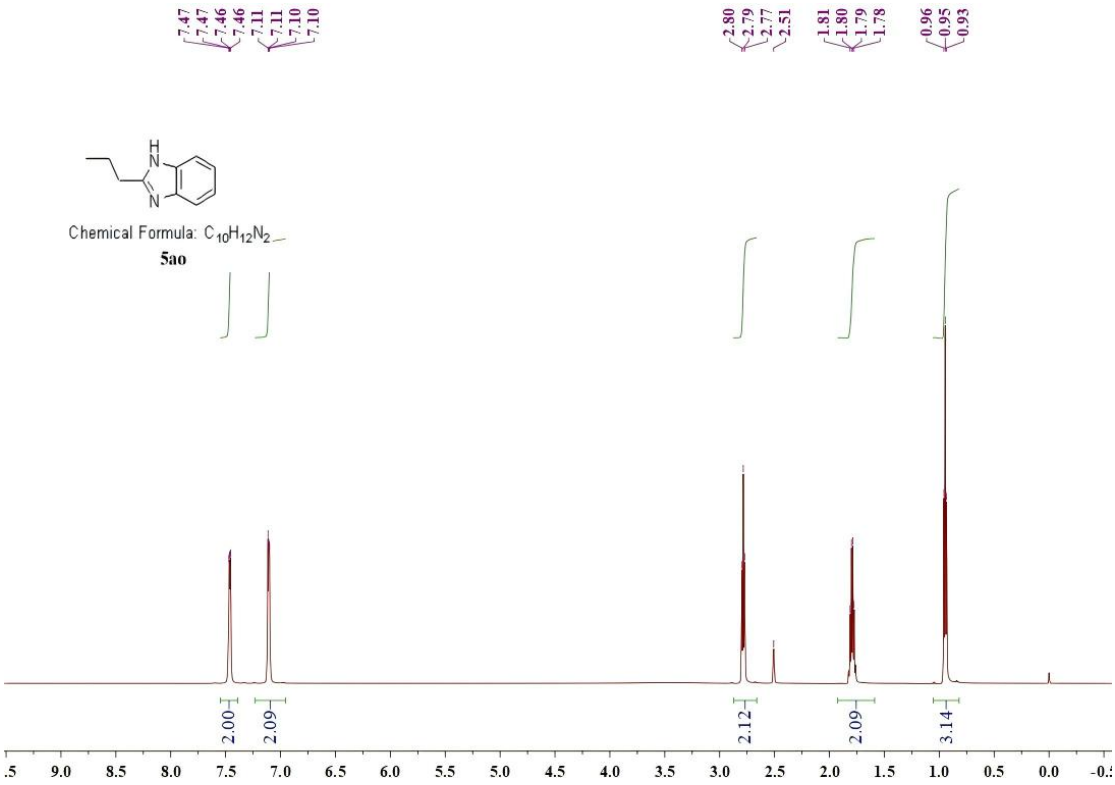
7.54
7.54
7.53
7.53
7.53
7.52
7.31
7.30
7.28
7.27
7.26
7.24
0.51
Chemical Formula: C12H9N3
5an
1.00
0.97
0.98
1.00
0.98
0.96
1.00
2.01
151.25
149.83
149.02
144.38
137.99
135.42
125.16
123.62
122.39
121.91
119.78
112.57
40.38
40.24
40.10
39.96
39.82
39.68
39.54
Chemical Formula: C12H9N3
5an

5ao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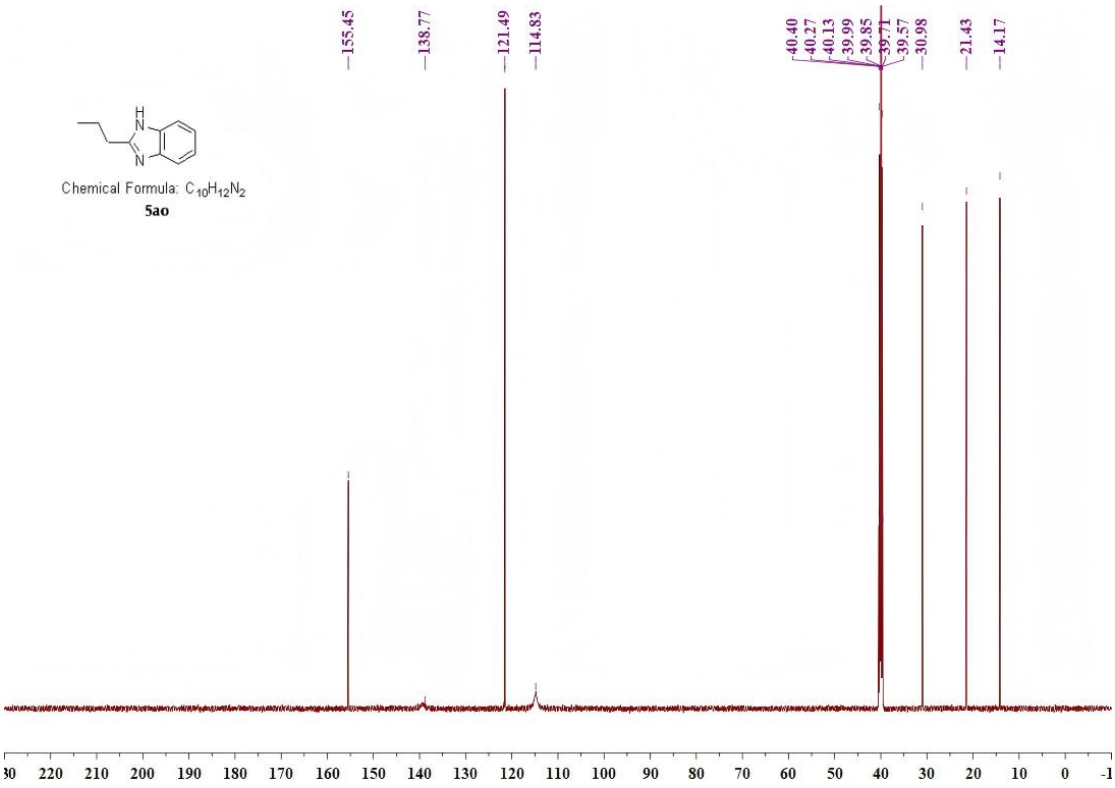
7.11
7.10
7.10
2.80
2.79
2.77
2.51
1.81
1.80
1.79
1.78
0.96
0.95
0.93
Chemical Formula: C10H12N2
5ao
2.00
2.09
2.12
2.09
3.14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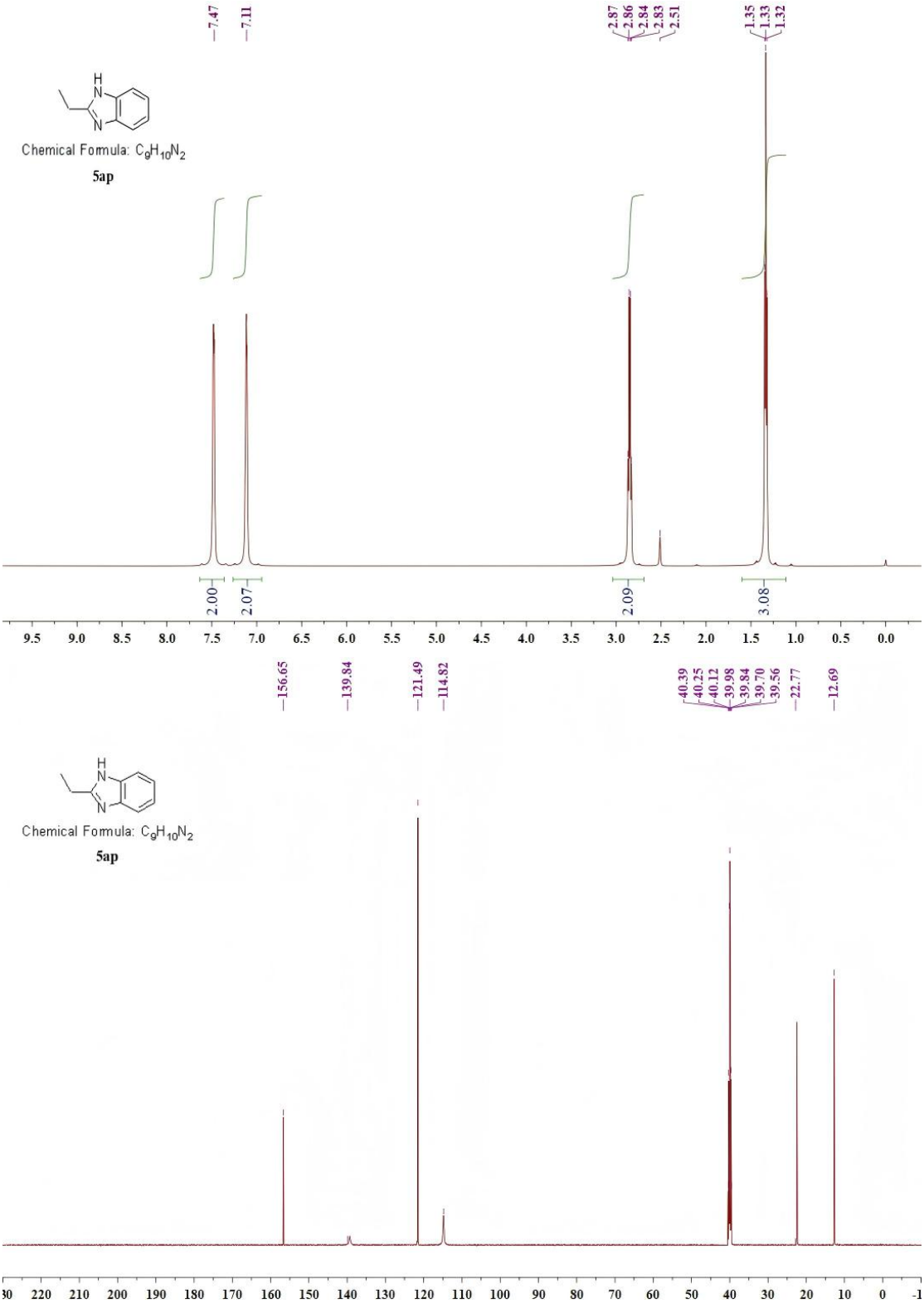
138.77
121.49
114.83
40.40
40.27
40.13
39.99
39.85
39.71
39.57
30.98
21.43
14.17
Chemical Formula: C10H12N2
5ao

5ap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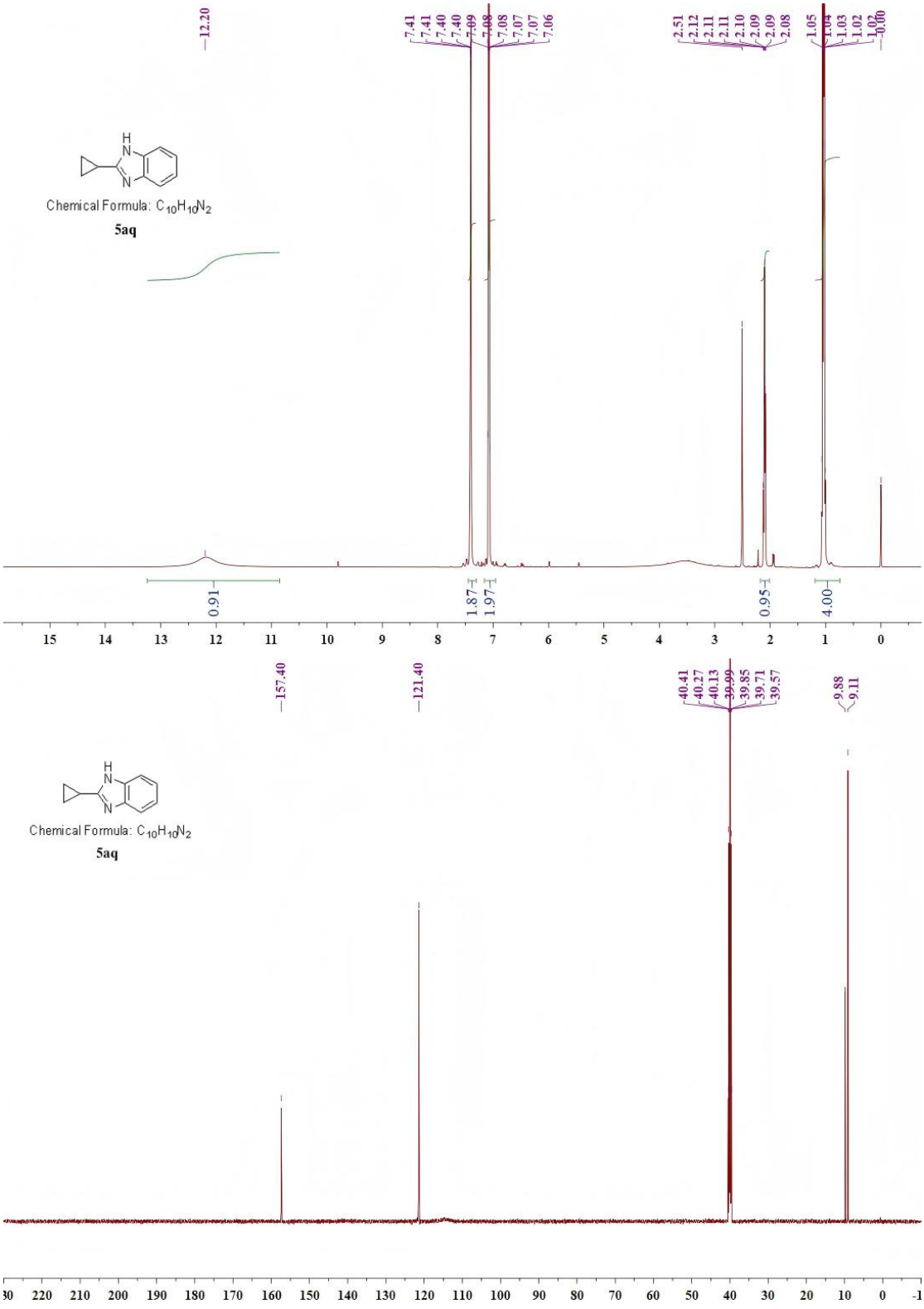
7.11
2.87
2.86
2.84
2.83
2.51
1.35
1.33
1.32
Chemical Formula: $C_9H_{10}N_2$
5ap
2.00
2.07
2.09
3.08
156.65
139.84
121.49
114.82
40.39
40.25
40.12
39.98
39.84
39.70
39.56
22.77
12.69
Chemical Formula: $C_9H_{10}N_2$
5ap

5aq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7.41
7.40
7.40
7.09
7.08
7.08
7.07
7.07
7.06
2.51
2.12
2.11
2.11
2.10
2.09
2.09
2.08
1.05
1.04
1.03
1.02
1.02
0.00
Chemical Formula: C10H10N2
5aq
0.91
1.87
1.97
0.95
4.00
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
157.40
121.40
40.41
40.27
40.13
39.99
39.85
39.71
39.57
9.88
9.11
Chemical Formula: C10H10N2
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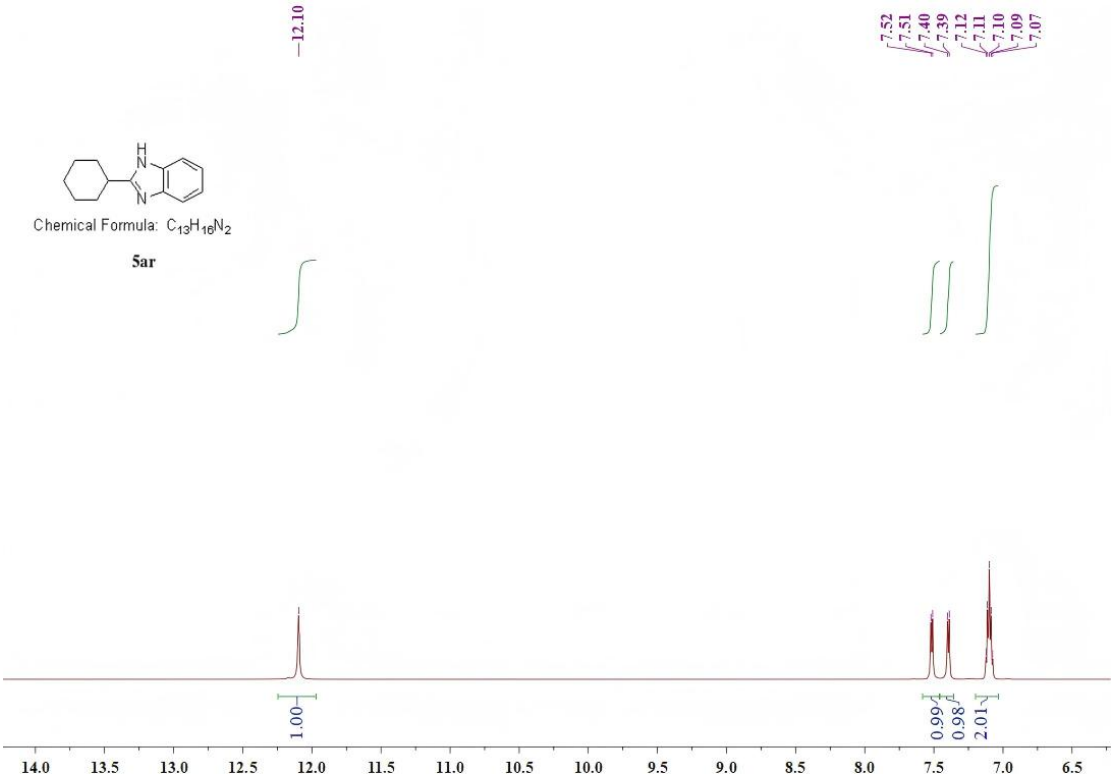
5ar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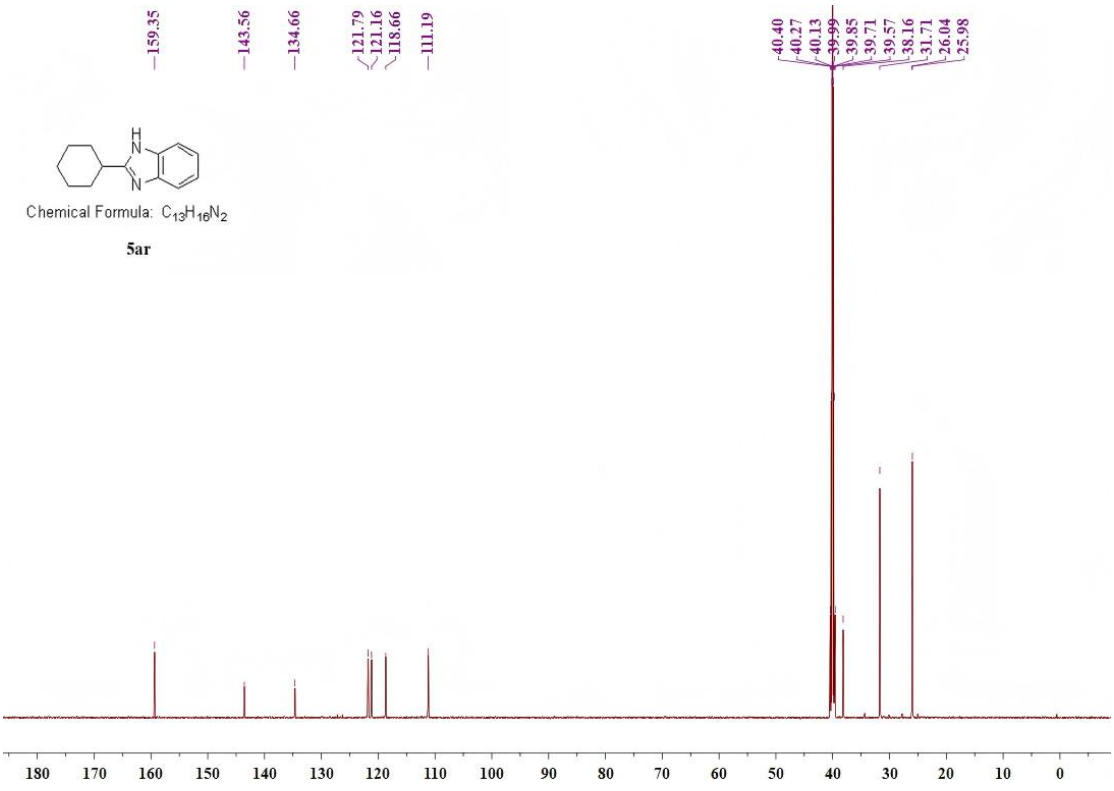
7.51
7.40
7.39
7.12
7.11
7.10
7.09
7.07
Chemical Formula: C13H16N2
5ar
1.00
0.99
0.98
2.01
14.0
13.5
13.0
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5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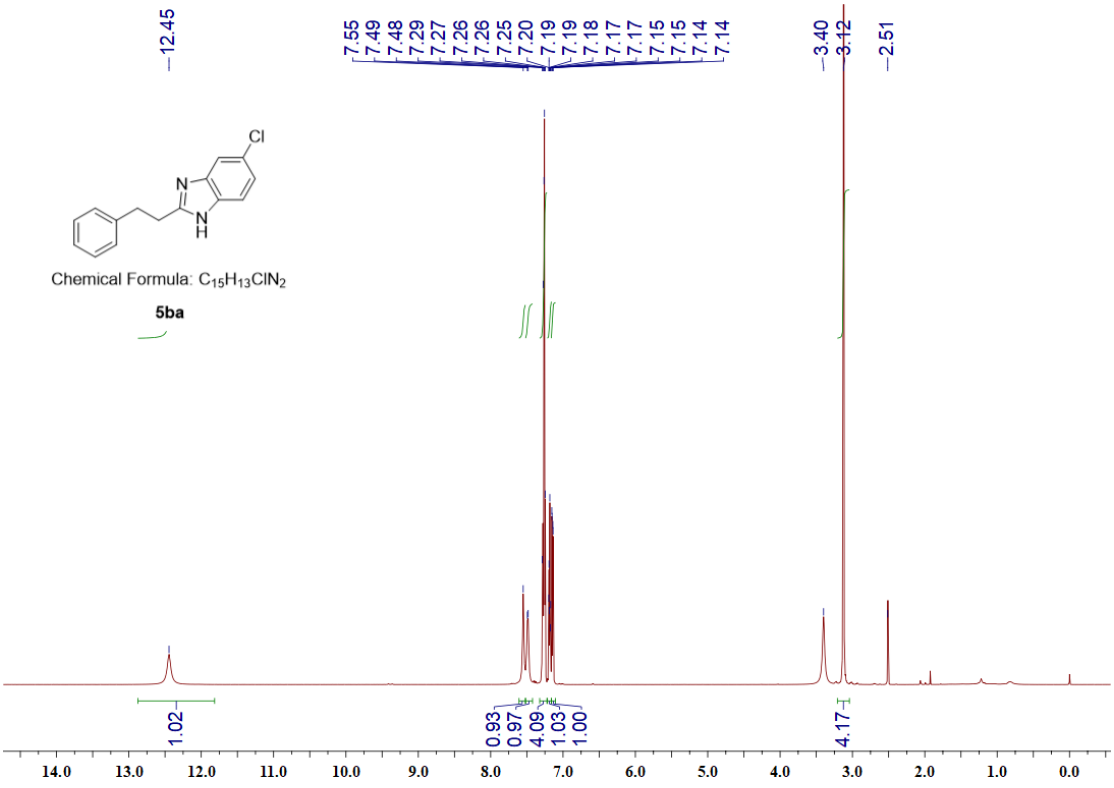
121.79
121.16
118.66
111.19
40.40
40.27
40.13
39.99
39.85
39.71
39.57
38.16
31.71
26.04
25.98
Chemical Formula: C13H16N2
5ar
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

5ba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7.20
7.19
7.19
7.18
7.17
7.17
7.15
7.15
7.14
7.14
3.40
3.12
2.51
Cl
N
N
H
Chemical Formula: C15H13ClN2
5ba
1.02
0.93
0.97
4.09
1.03
1.00
4.17
14.0
13.0
12.0
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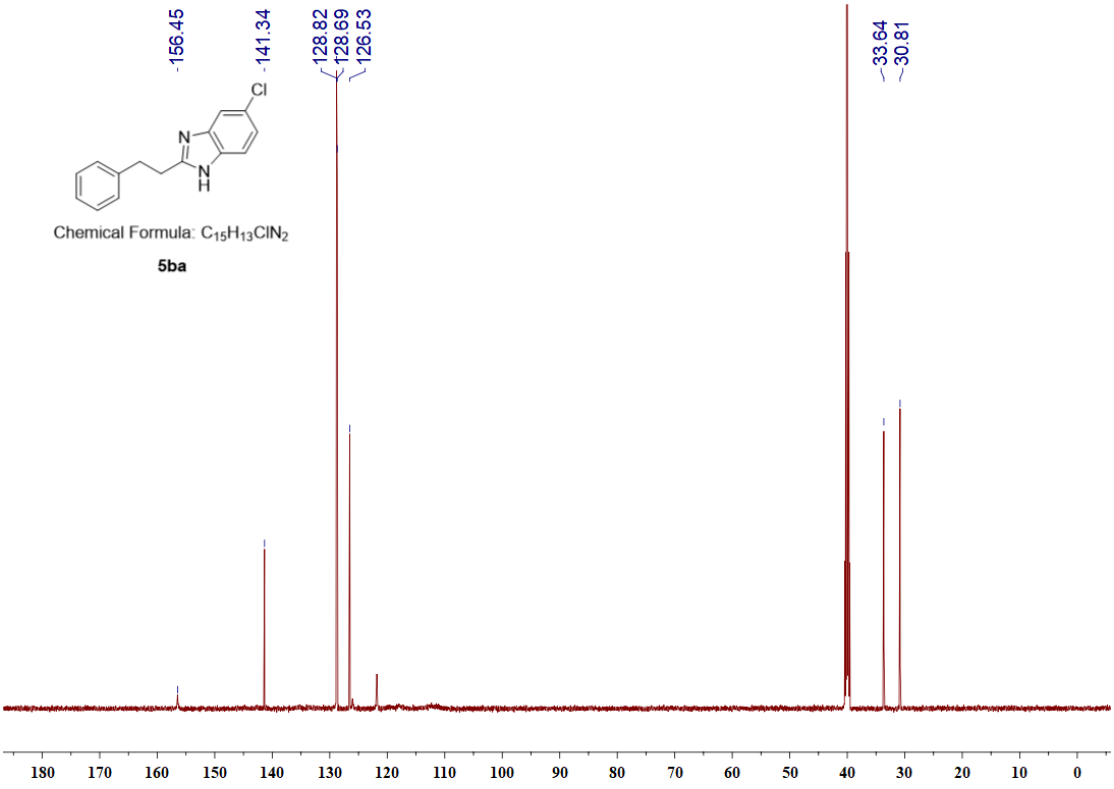
156.45
141.34
128.82
128.69
126.53
33.64
30.81
Cl
N
N
H
Chemical Formula: C15H13ClN2
5ba
180
170
160
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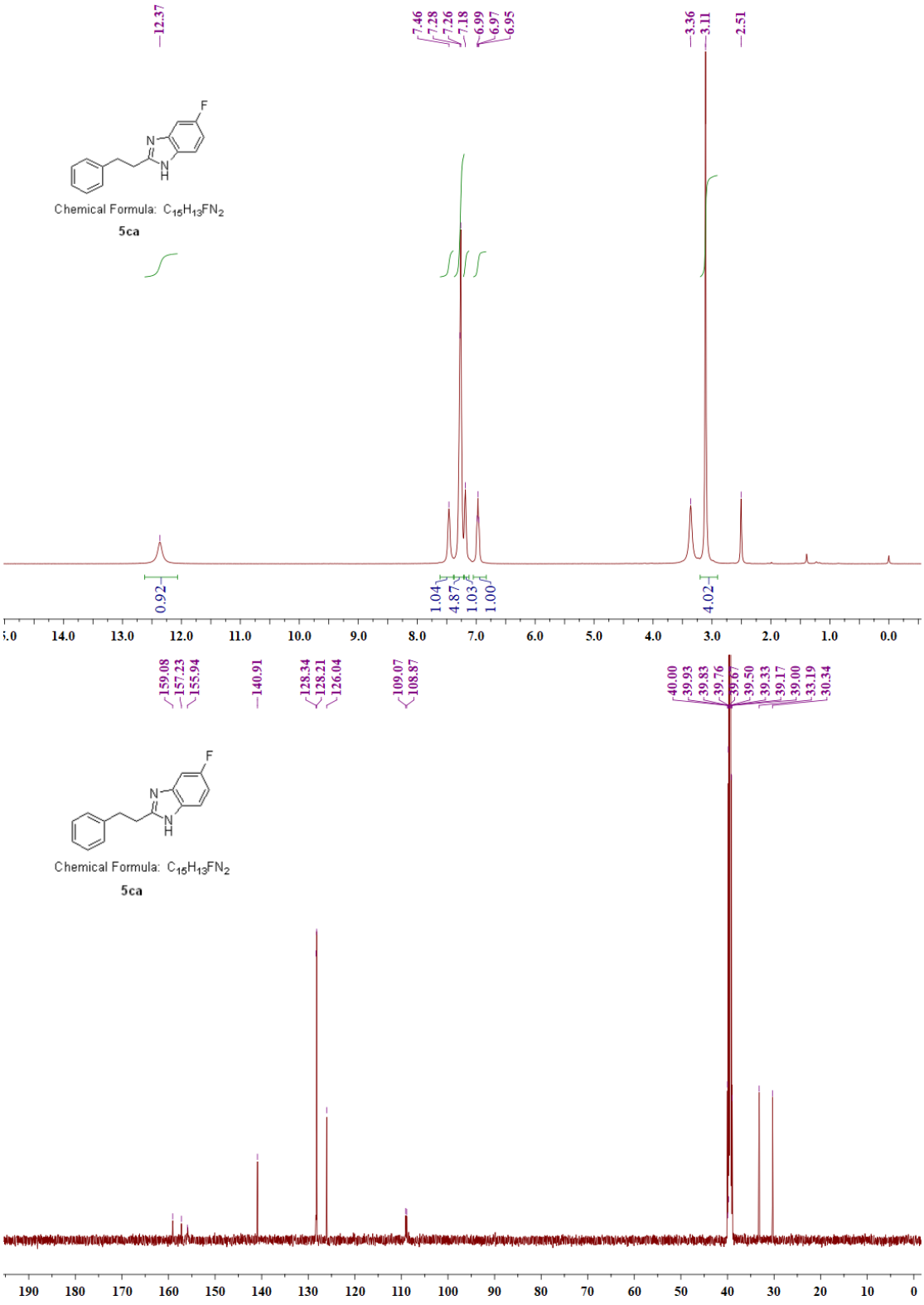
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

5ca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7.46
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7.26
7.18
6.99
6.97
6.95
3.36
3.11
2.51
F
N
N
H
Chemical Formula: C15H13FN2
5ca
0.92
1.04
4.87
1.03
1.00
4.02
159.08
157.23
155.94
140.91
128.34
128.21
126.04
109.07
108.87
40.00
39.93
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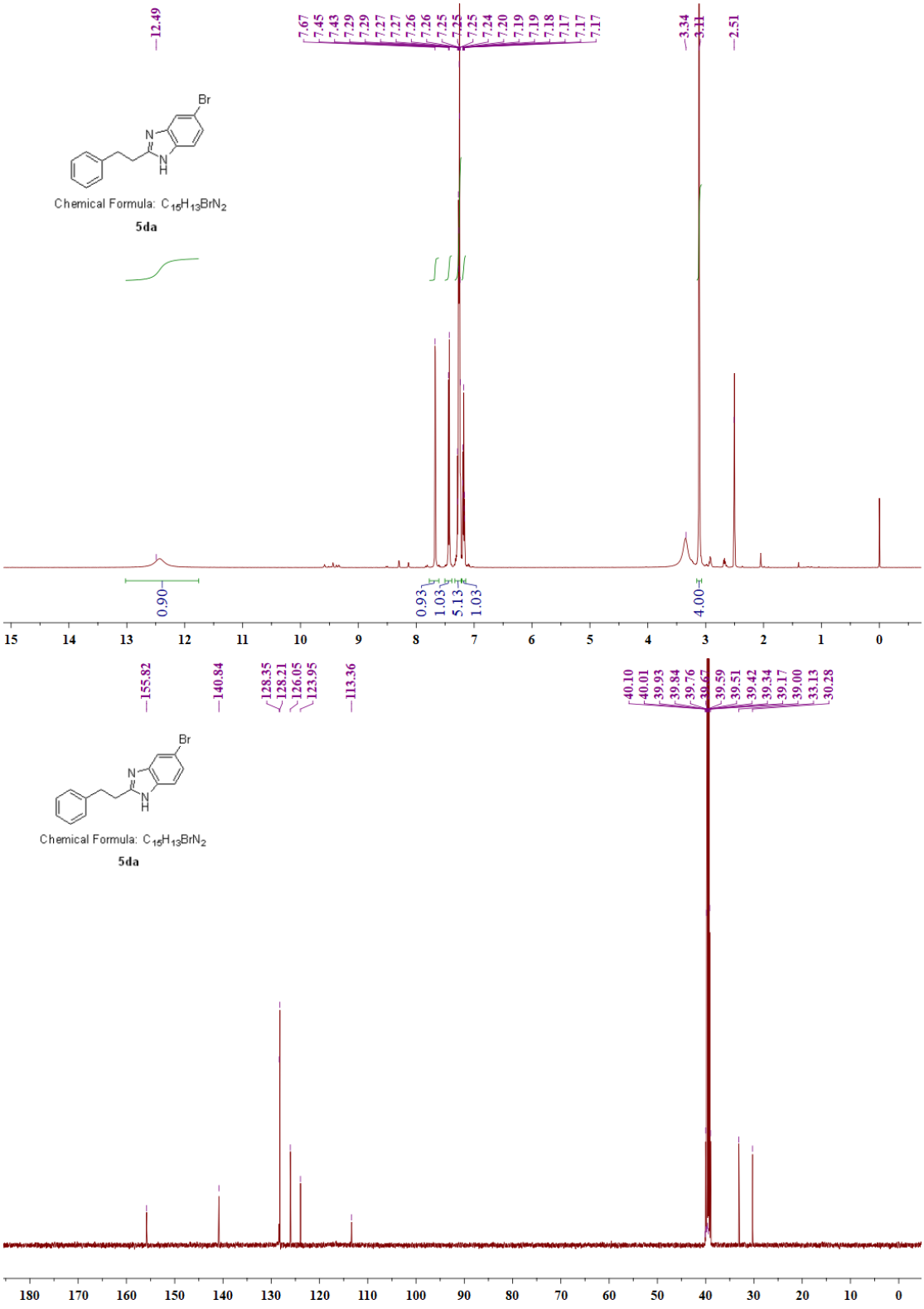
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Br
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N
H
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123.95
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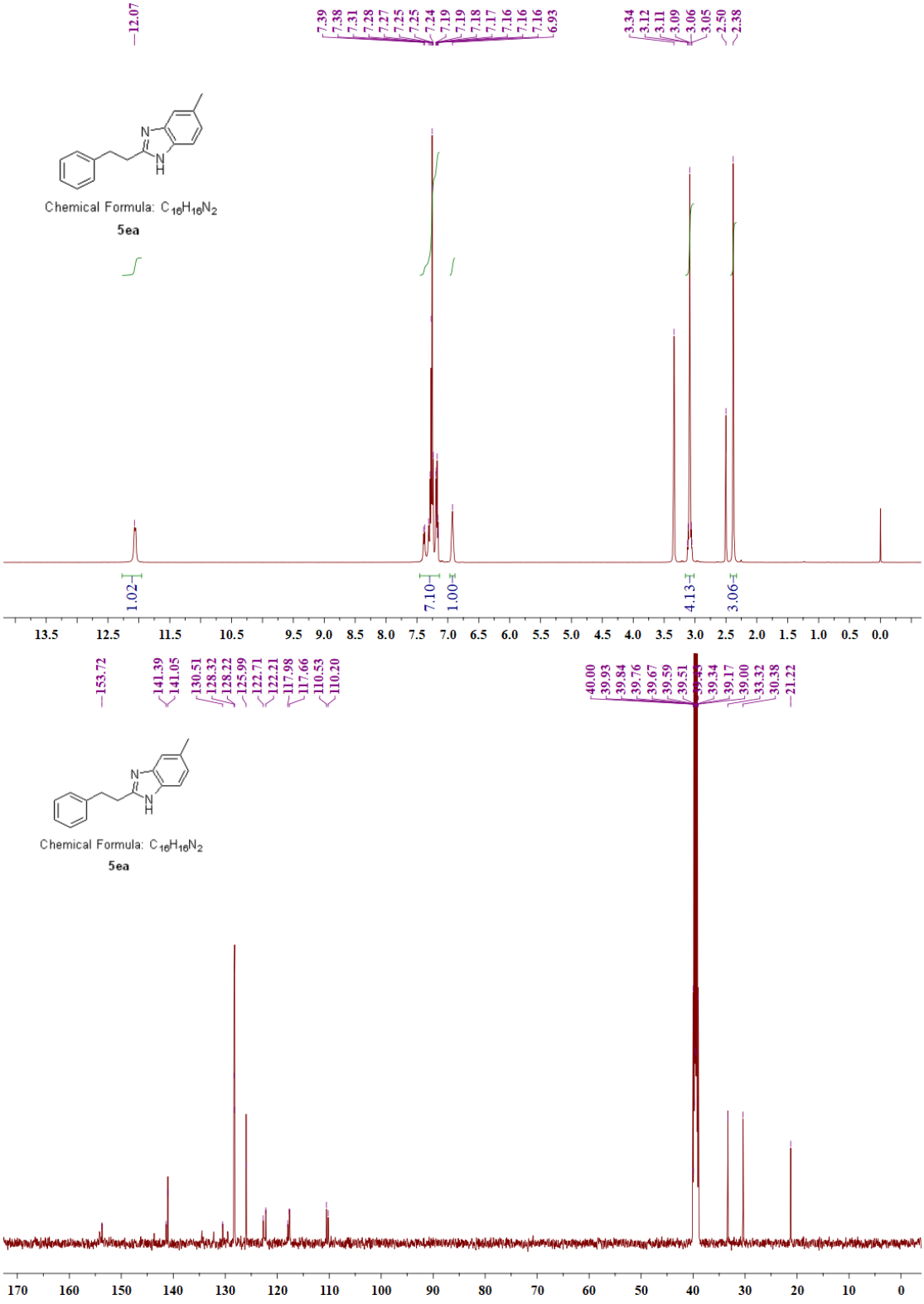
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2.38
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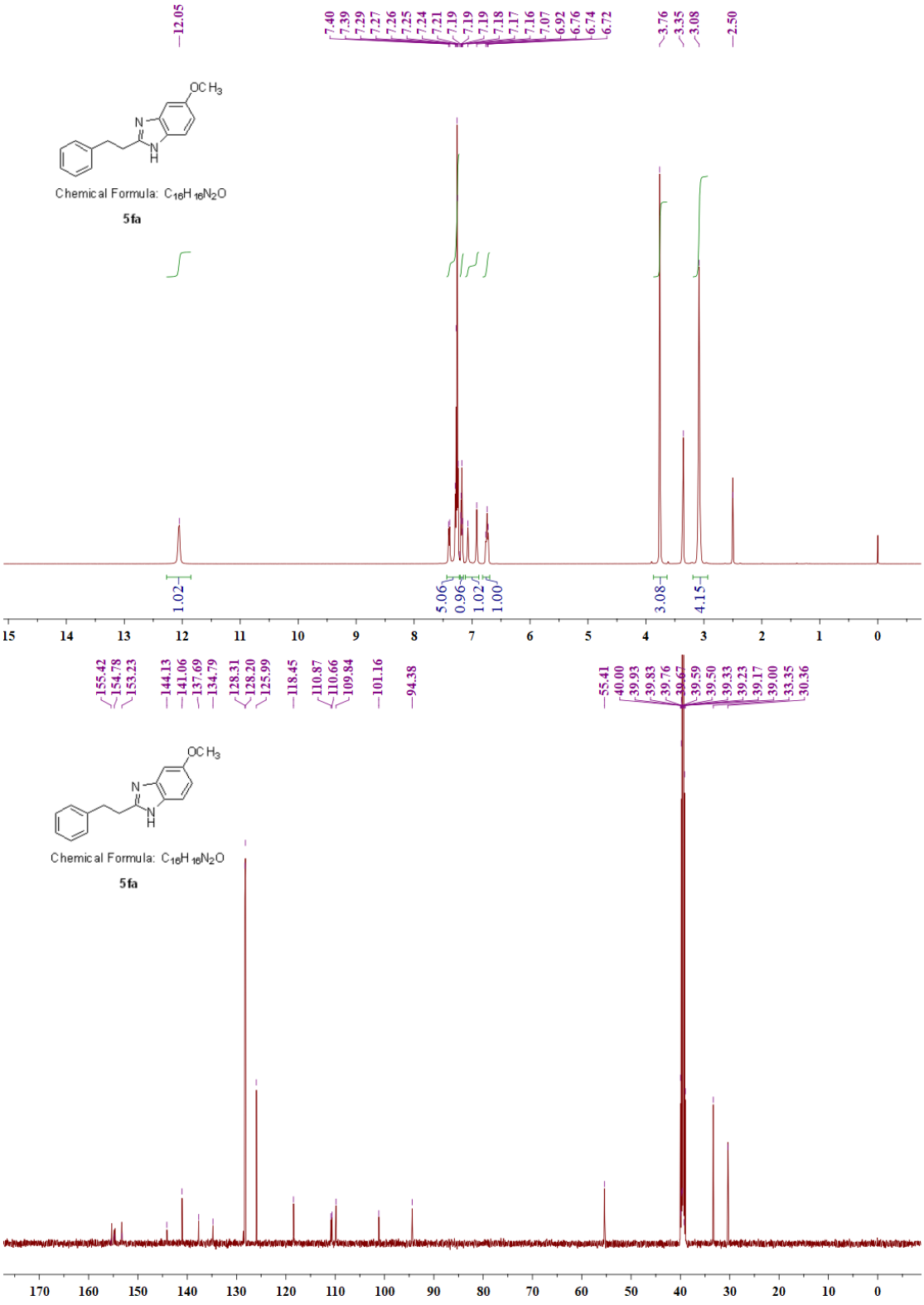
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7.17
7.16
7.07
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6.76
6.74
6.72
3.76
3.35
3.08
2.50
OCH3
N
N
H
Chemical Formula: C16H16N2O
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1.02
1.00
3.08
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154.78
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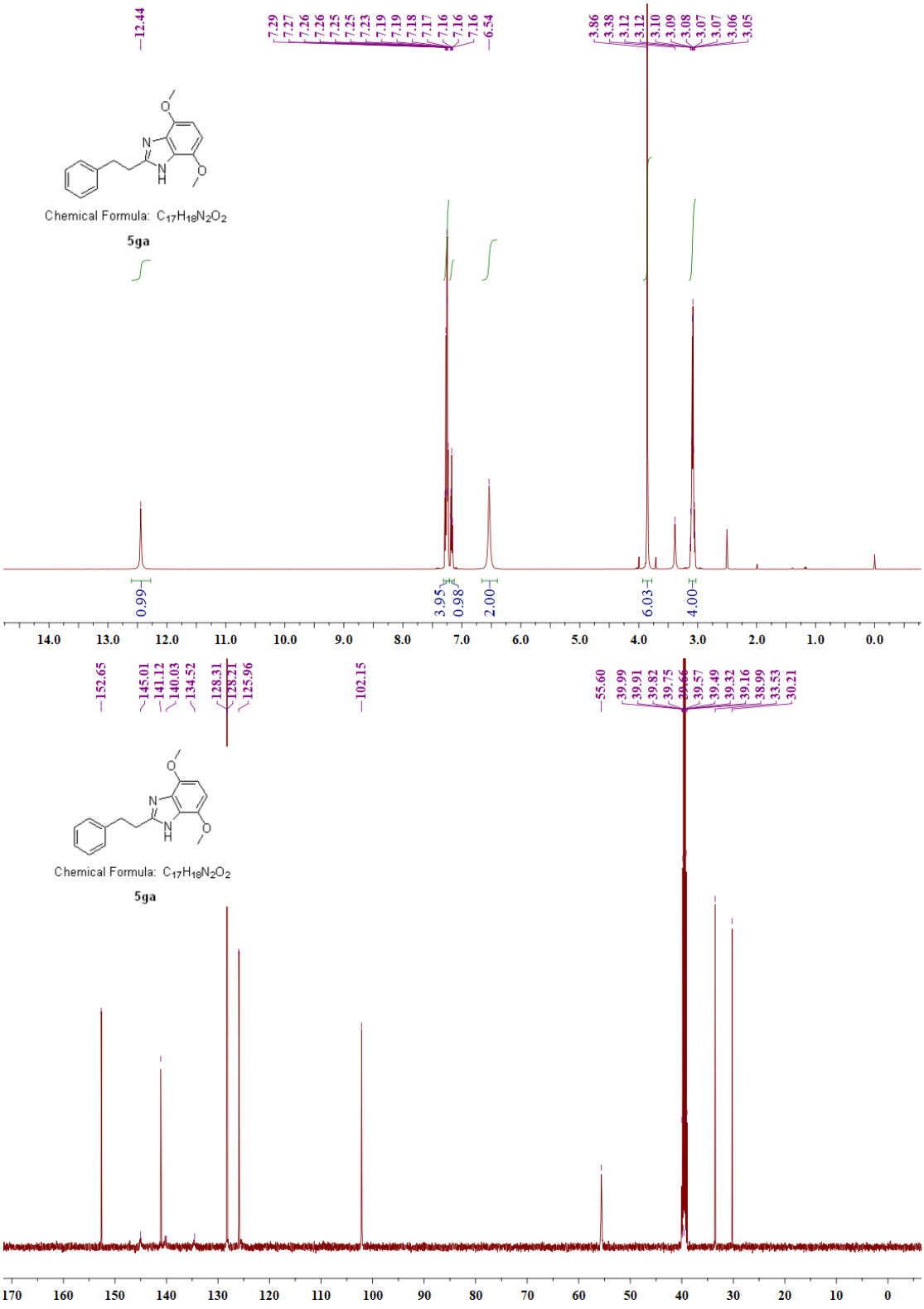
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3.08
3.07
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3.06
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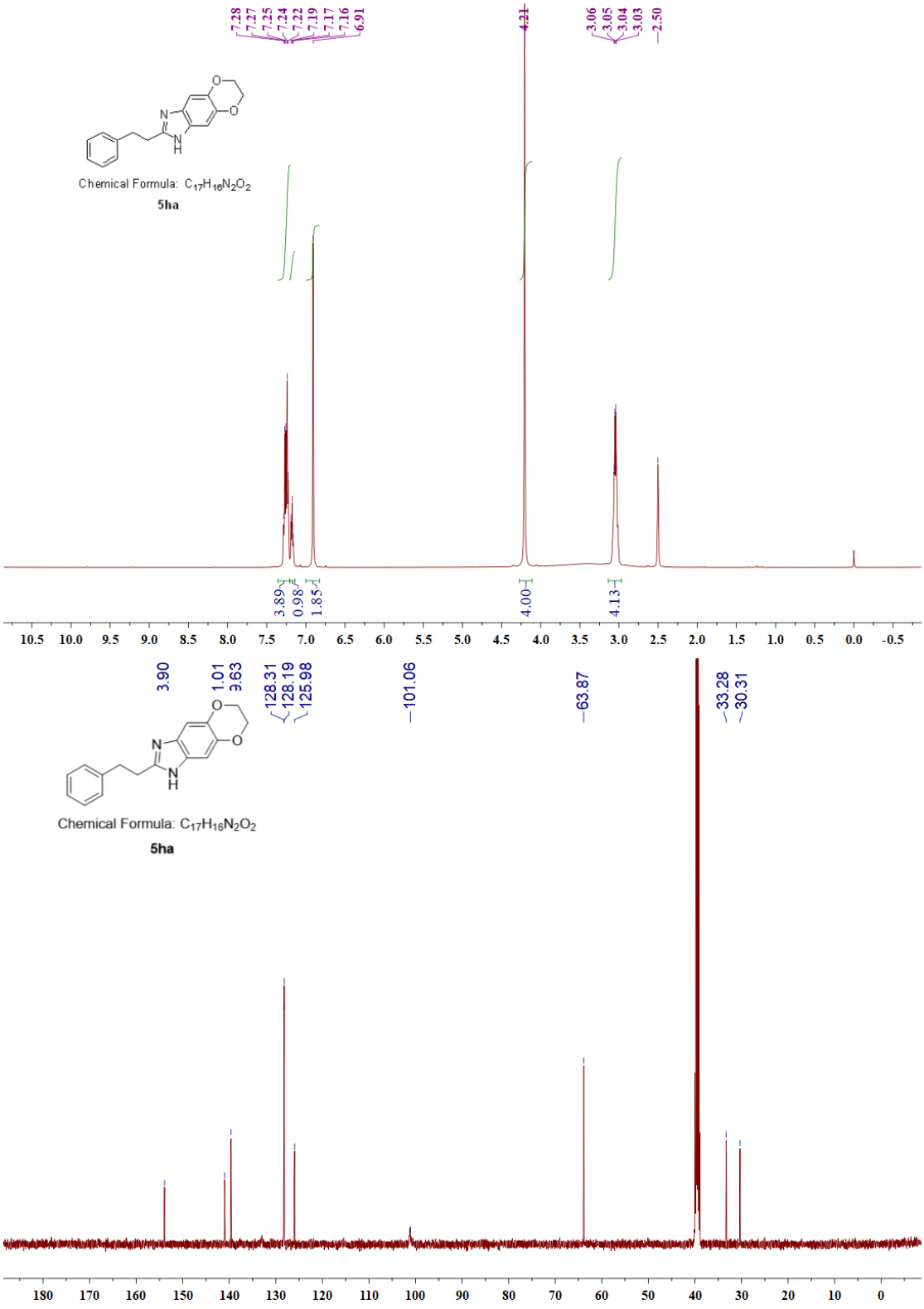
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3.06
3.05
3.04
3.03
2.50
Chemical Formula: C17H16N2O2
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4.00
4.13
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1.01
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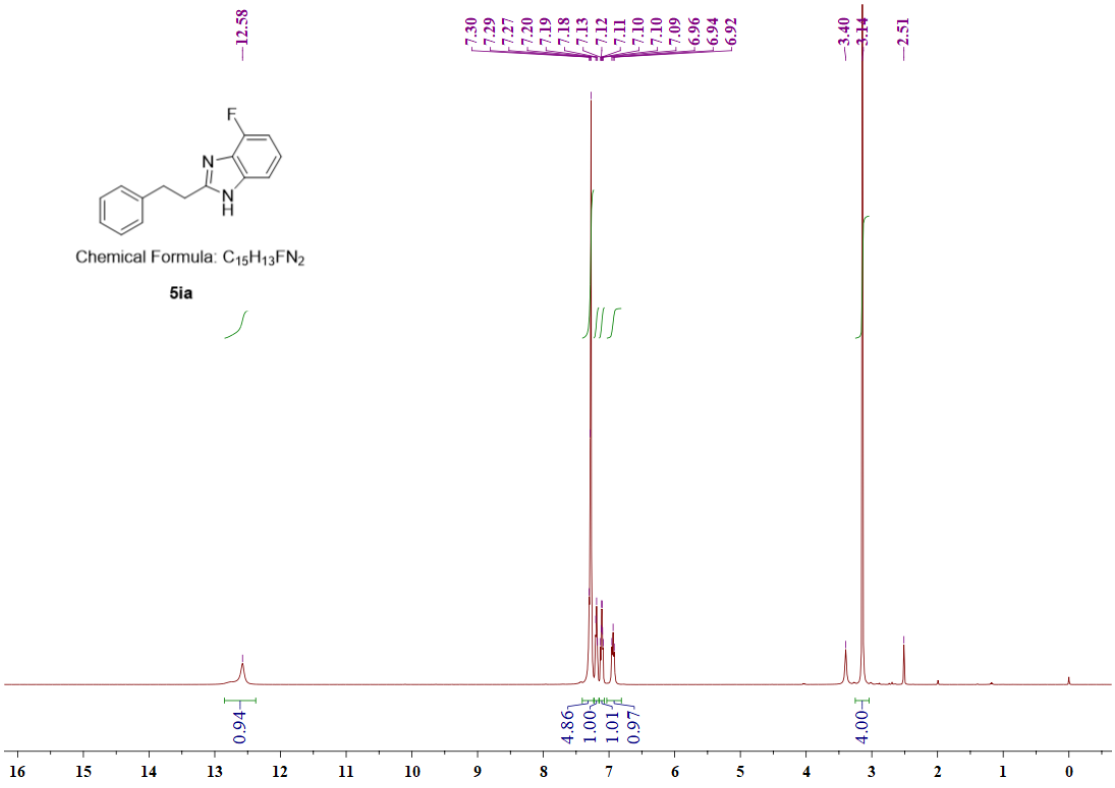
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6.94
6.92
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3.14
2.51
F
N
N
H
Chemical Formula: C15H13FN2
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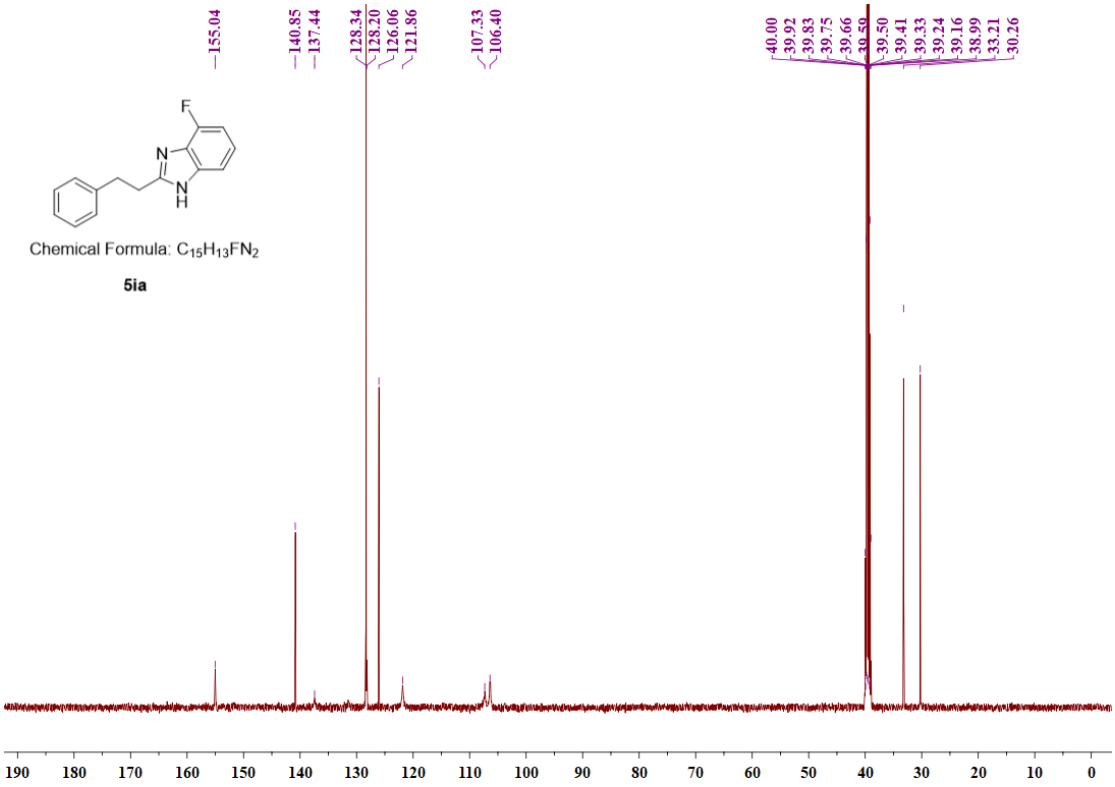
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39.66
39.50
39.50
39.41
39.33
39.24
39.16
38.99
33.21
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N
H
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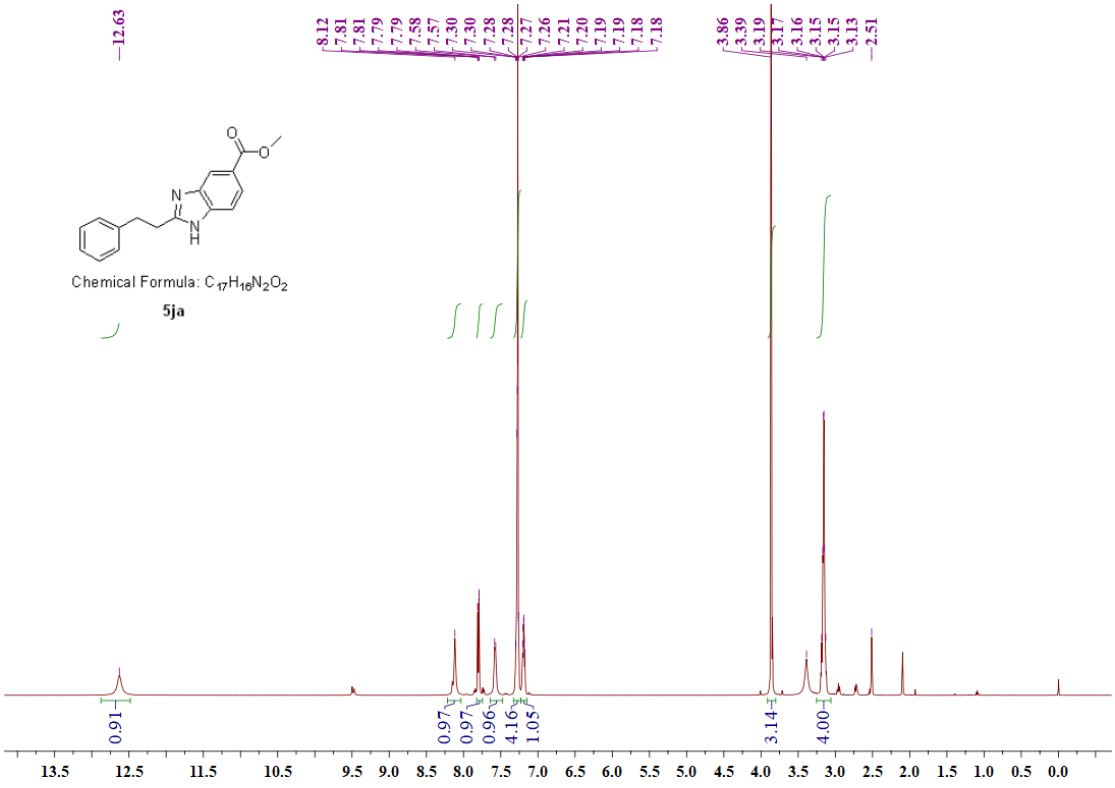
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7.18
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3.13
2.51
Chemical Formula: C17H16N2O2
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0.97
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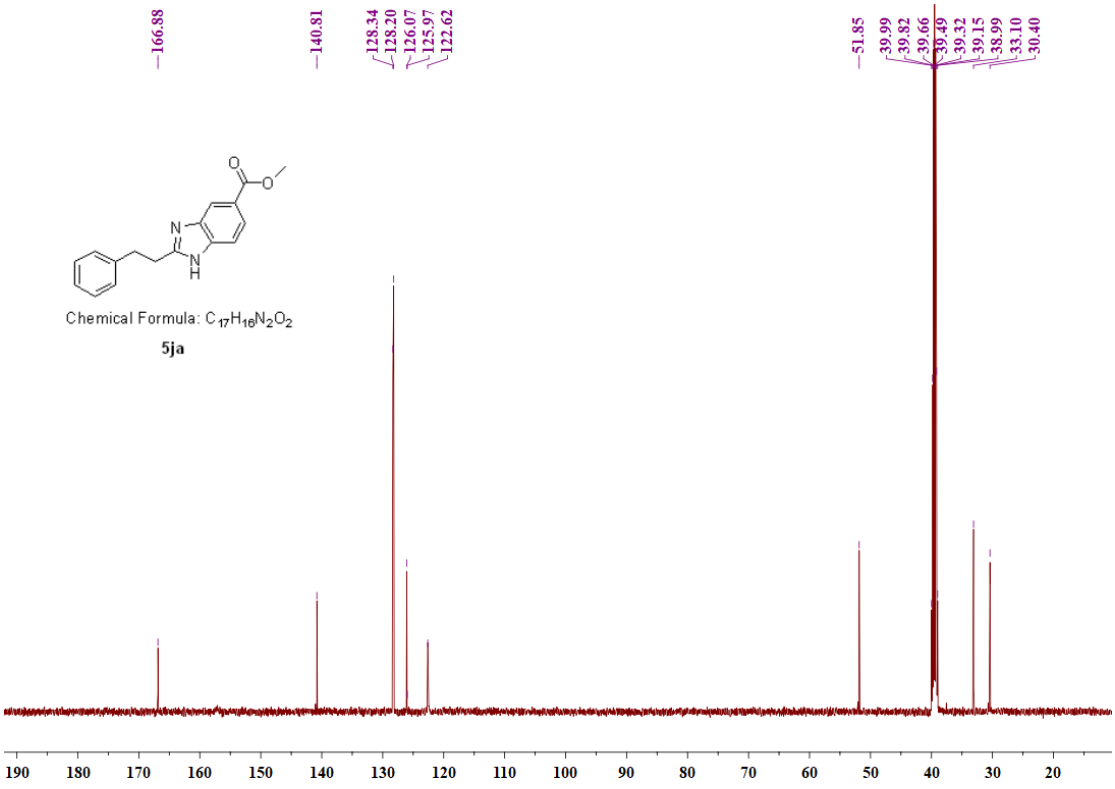
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38.99
33.10
30.40
Chemical Formula: C17H16N2O2
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80
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20

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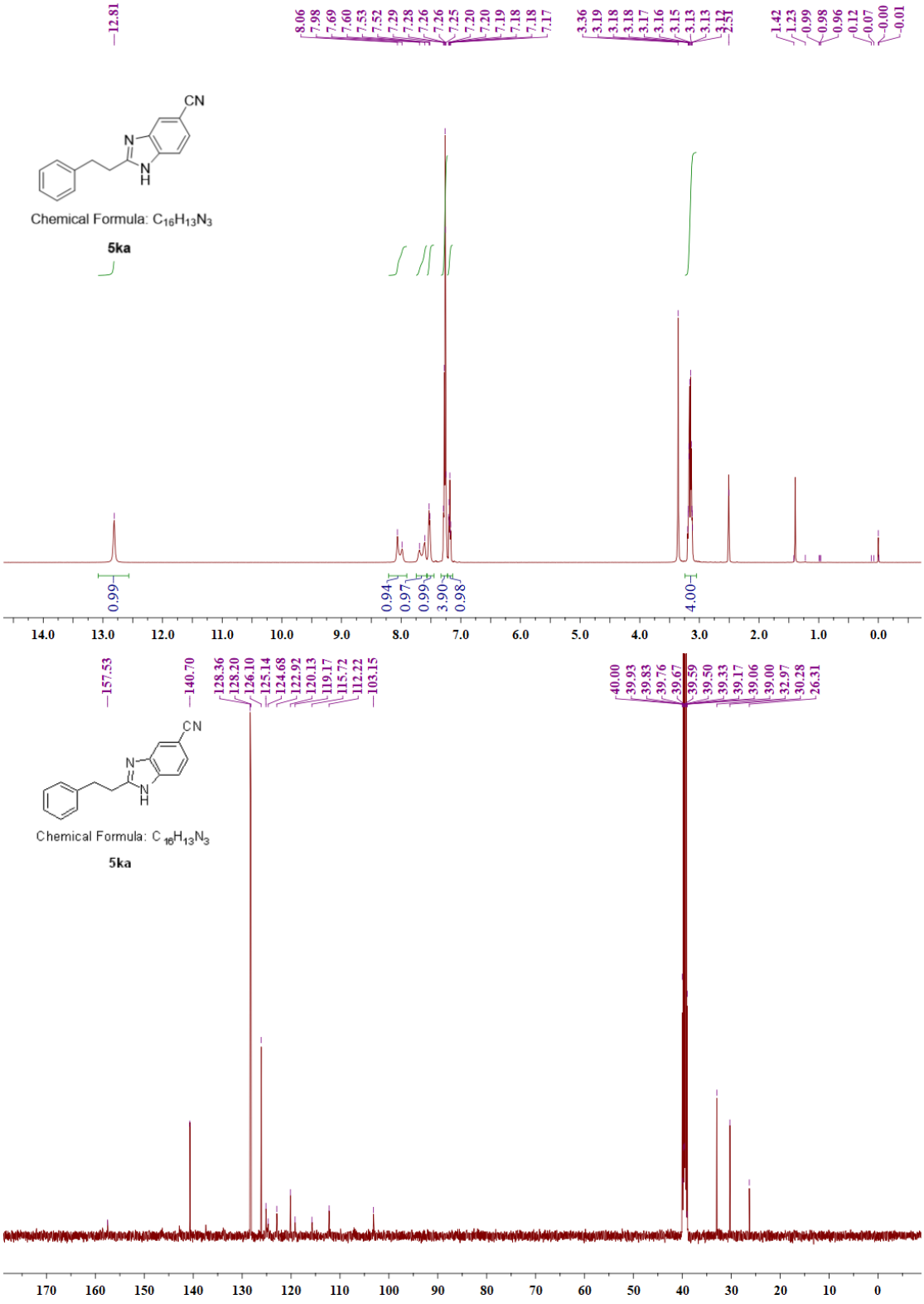
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3.13
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N
H
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4.0
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112.22
103.15
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39.76
39.67
39.59
39.50
39.33
39.17
39.06
39.00
32.97
30.28
26.31
CN
N
N
H
Chemical Formula: C16H13N3
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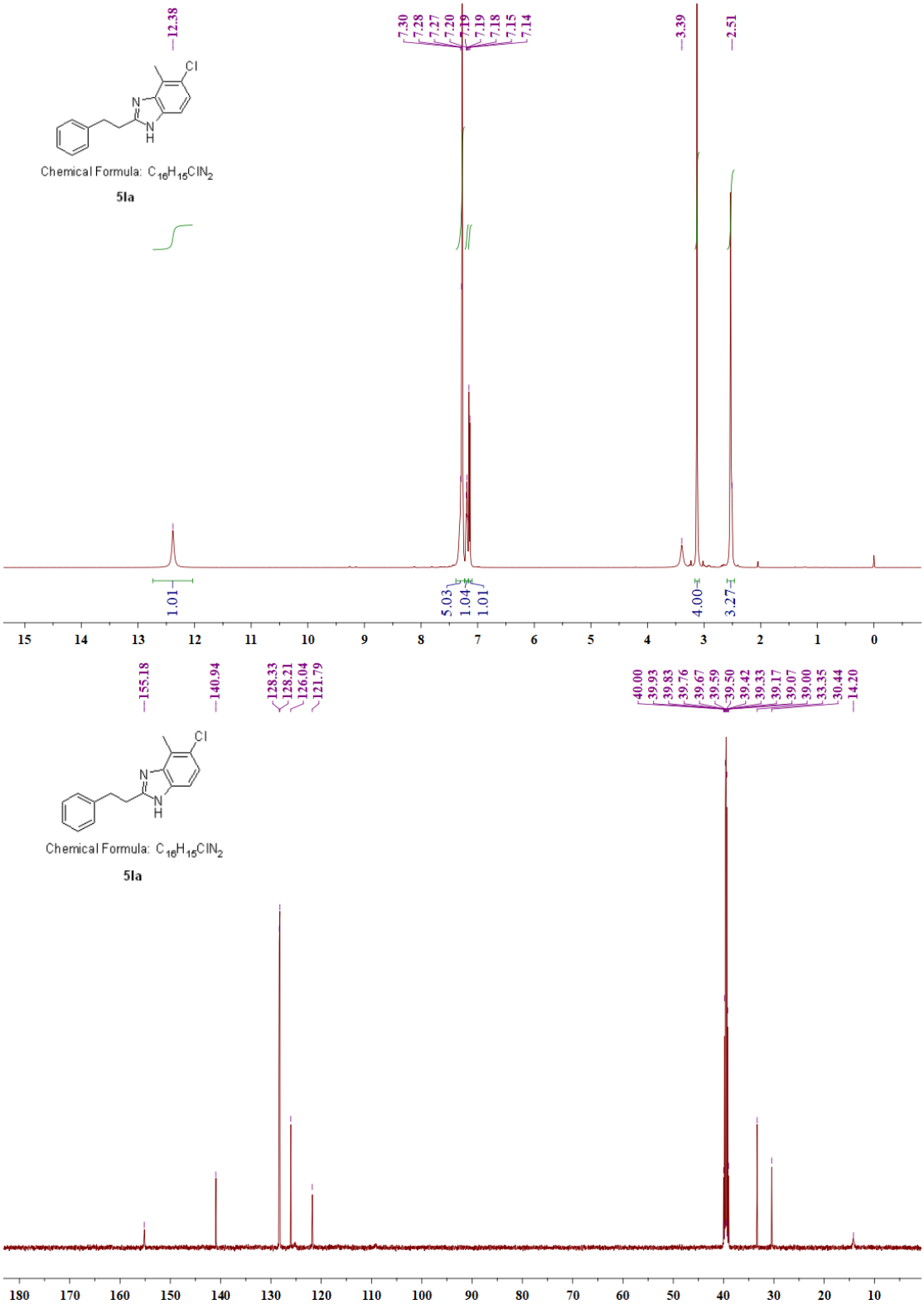
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N
N
H
Chemical Formula: C16H15ClN2
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5.03
1.04
1.01
4.00
3.27
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140.94
128.33
128.21
126.04
121.79
40.00
39.93
39.83
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39.50
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H
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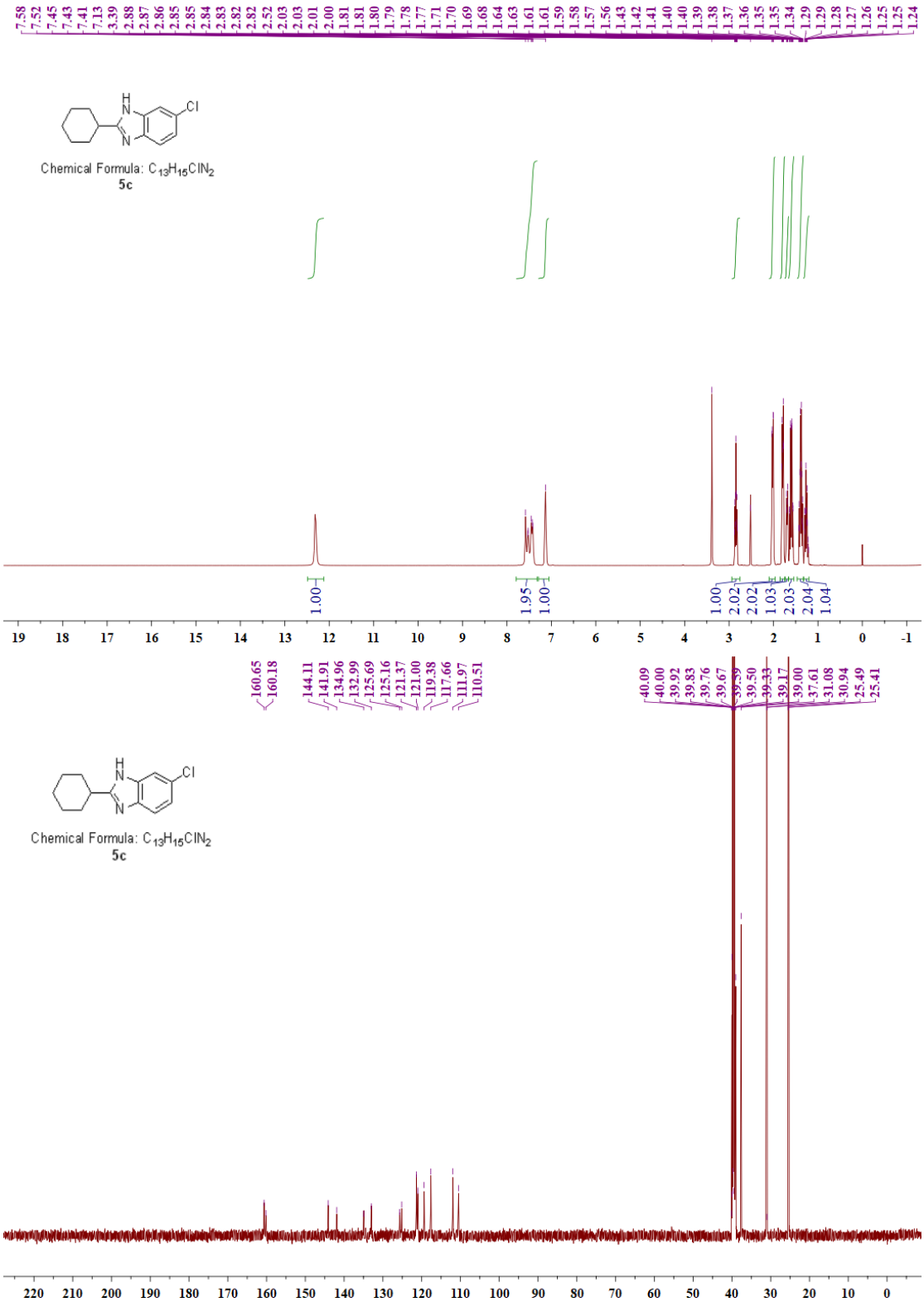
5c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Chemical Formula: C13H15ClN2
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40.09 40.00 39.92 39.83 39.76 39.67 39.59 39.50 39.33 39.17 39.00 37.61 31.08 30.94 25.49 25.41
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Chemical Formula: C13H15ClN2
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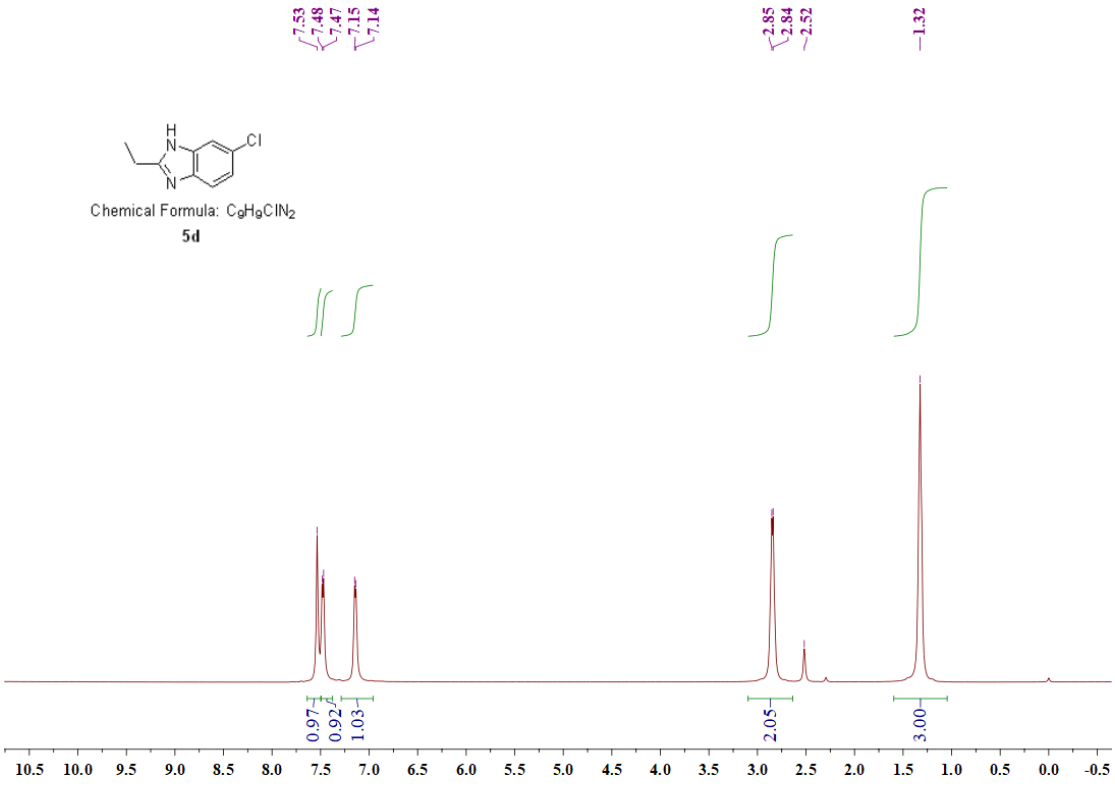
5d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0.92
1.03
2.05
3.00
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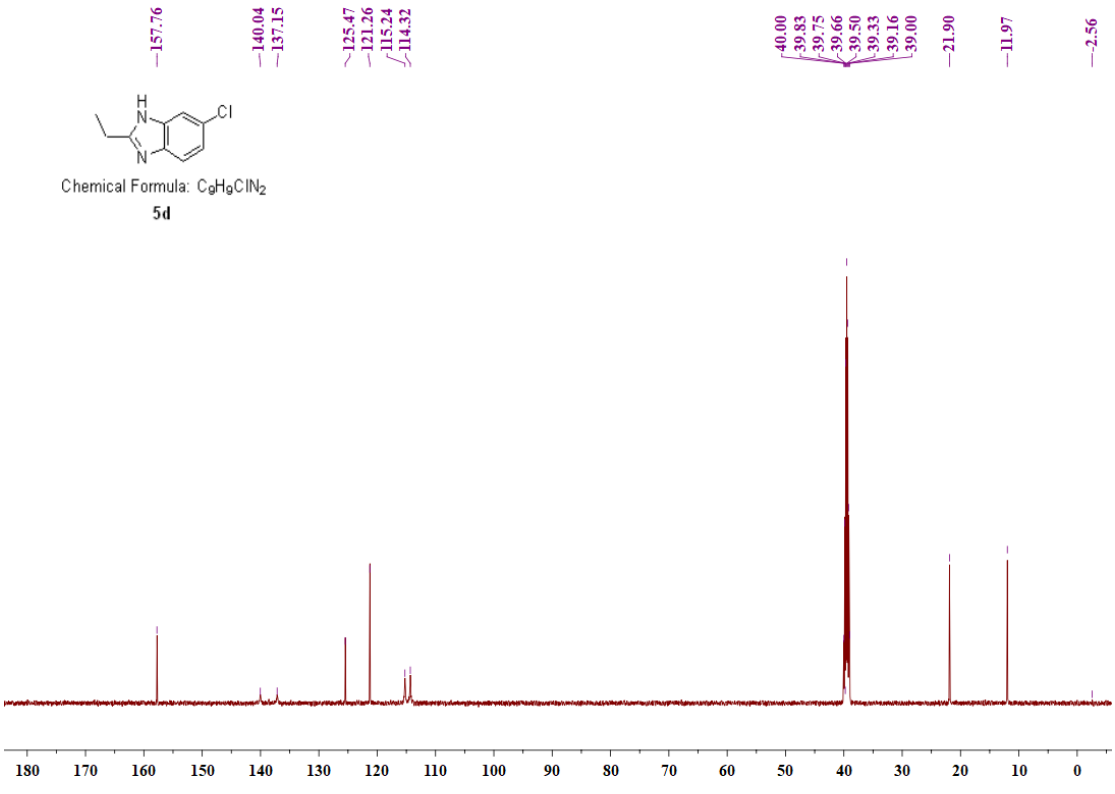
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39.16
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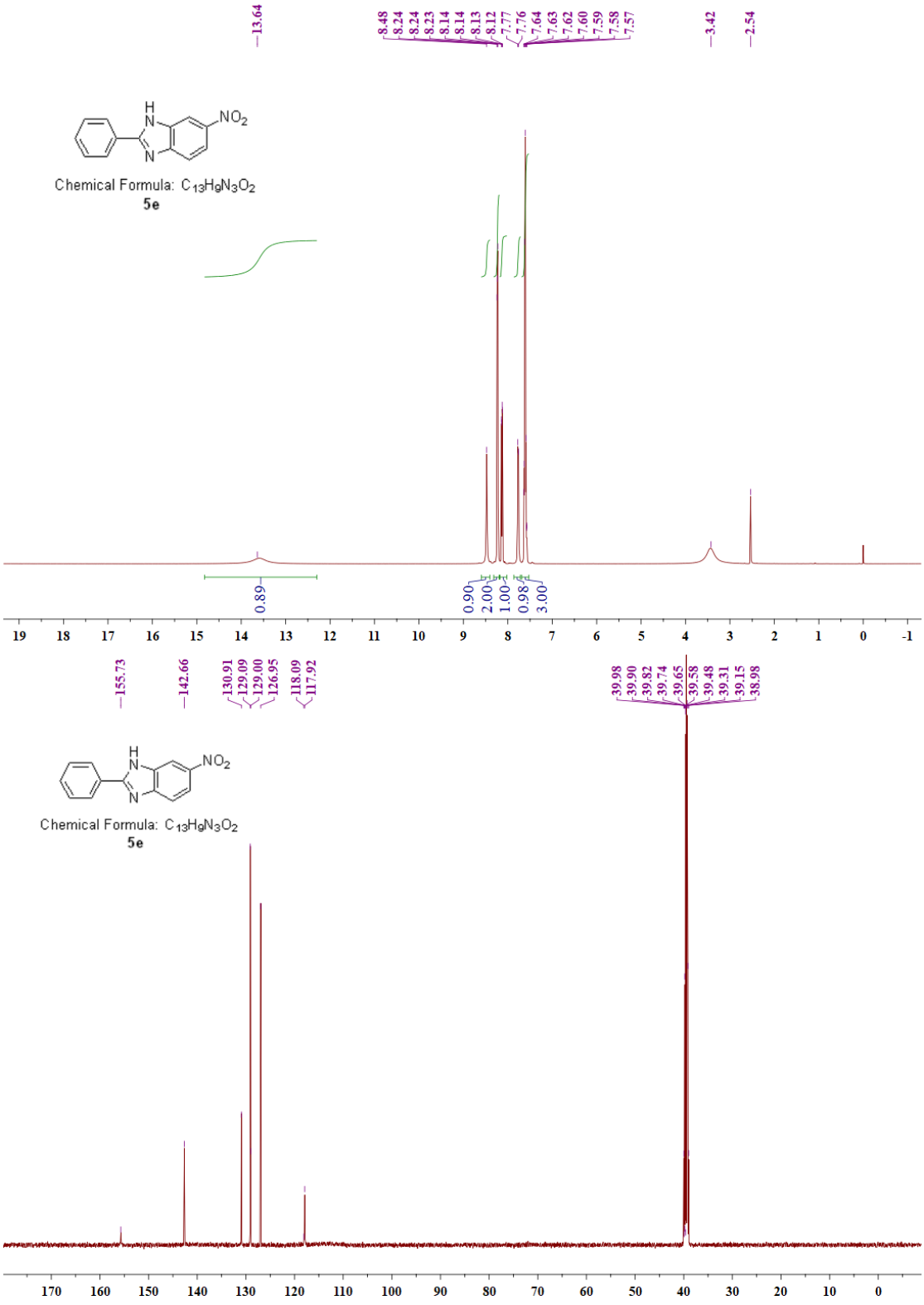
5e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7.58
7.57
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2.54
NO2
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1.00
0.98
3.00
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129.00
126.95
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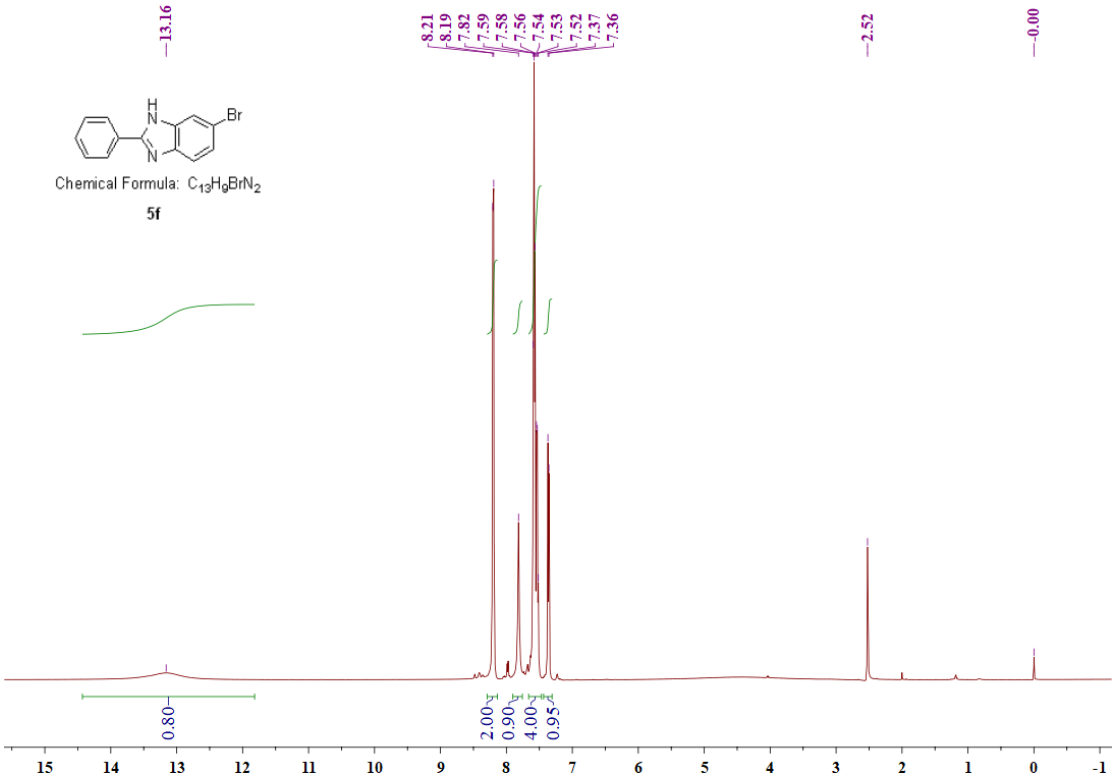
5f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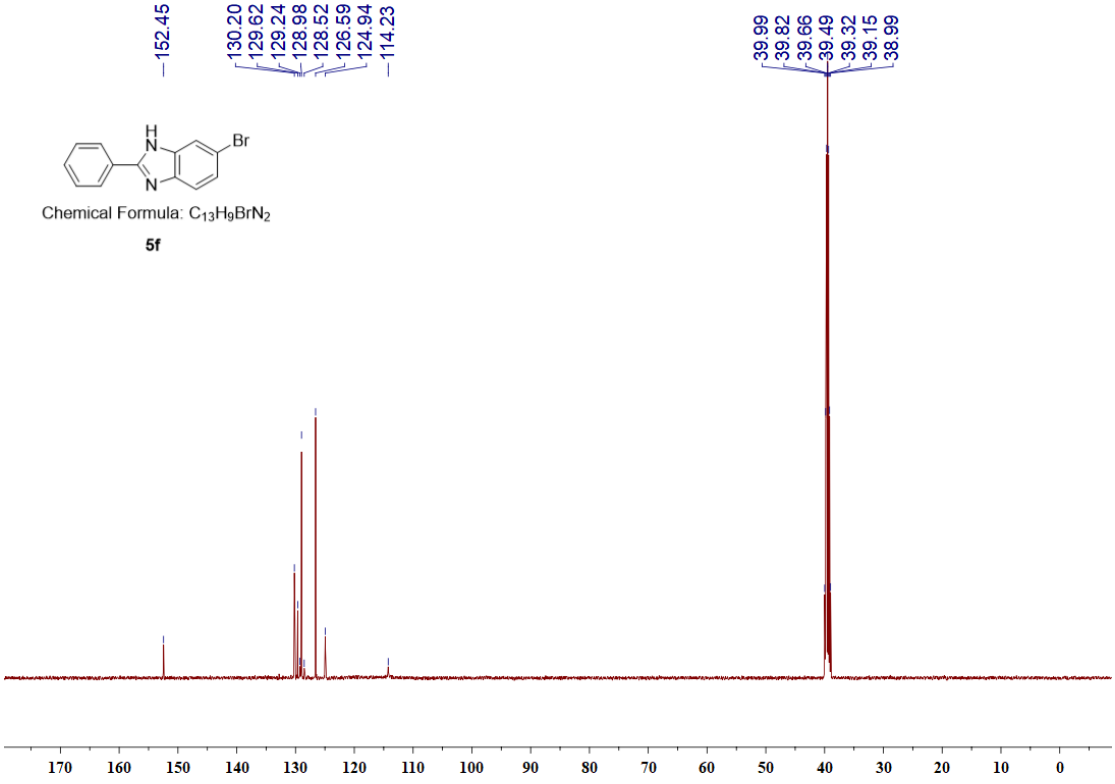
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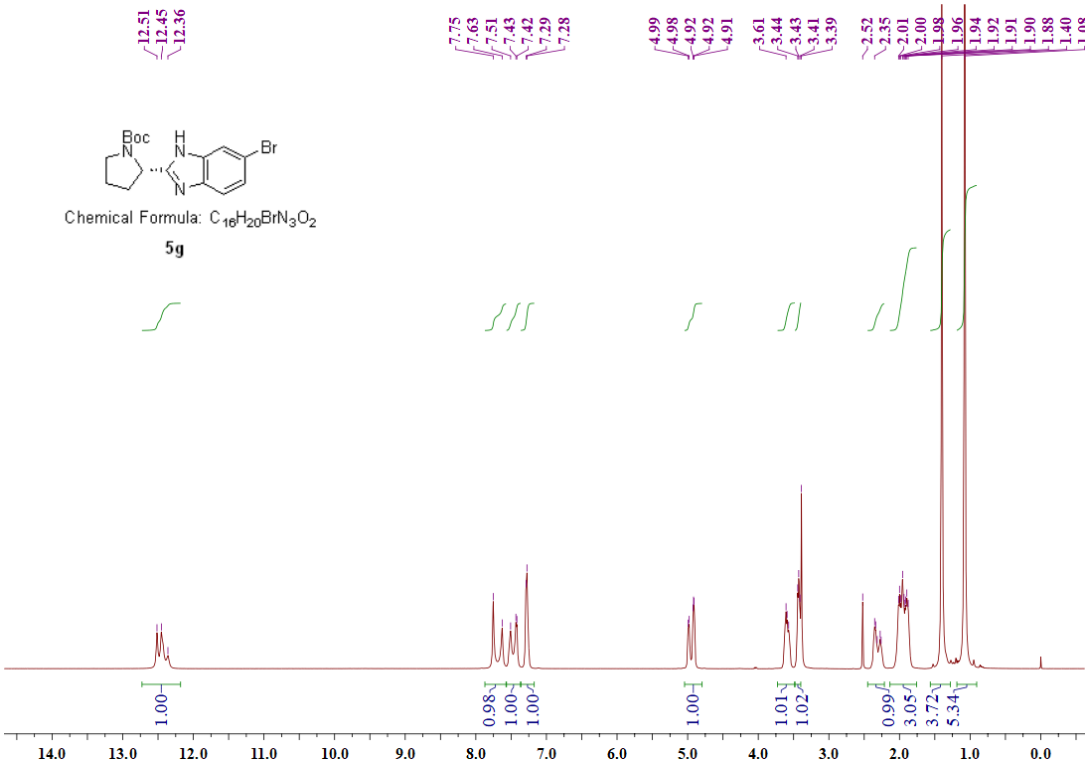
5g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Boc
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N
N
Br
Chemical Formula: C16H20BrN3O2
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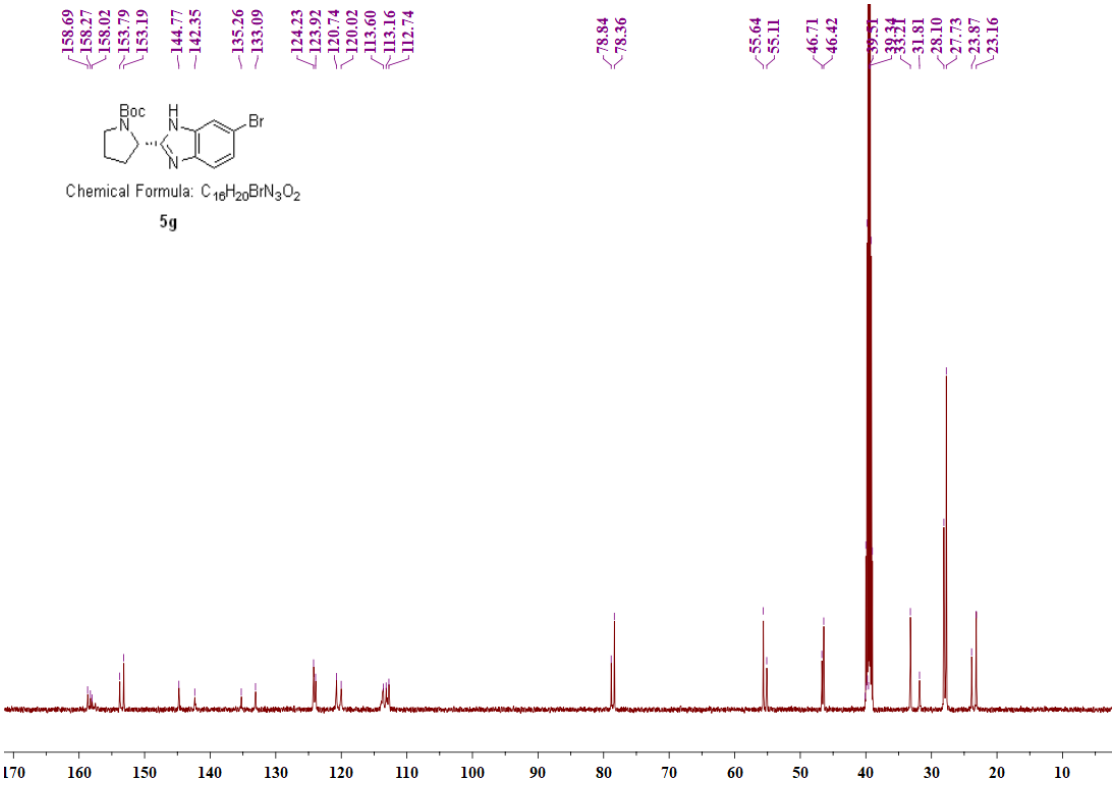
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Boc
H
N
N
Br
Chemical Formula: C16H20BrN3O2
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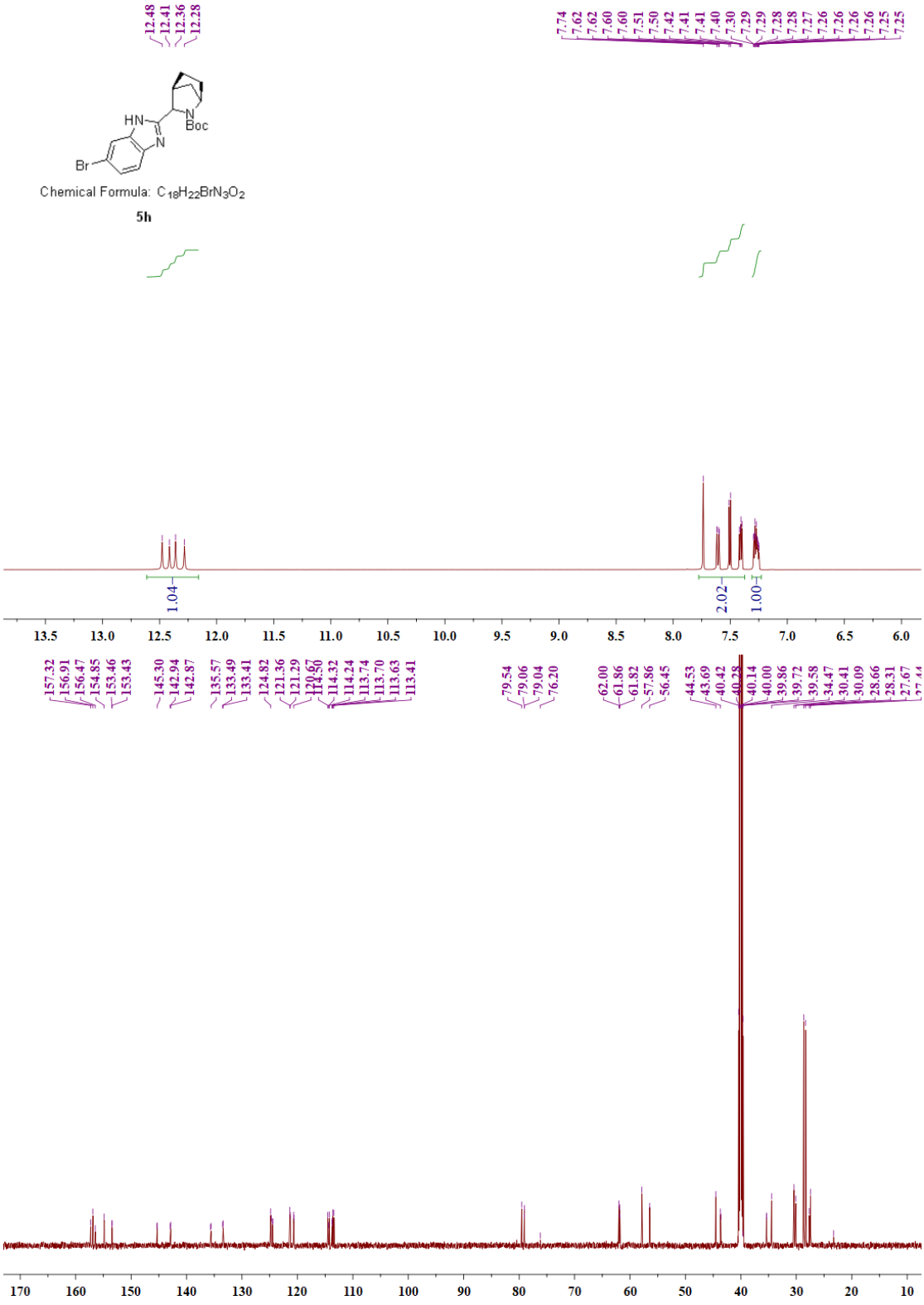
10

5h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Boc
N
Br
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156.47
154.85
153.46
153.43
145.30
142.94
142.87
135.57
133.49
133.41
124.82
121.36
121.29
120.67
114.50
114.32
114.24
113.74
113.70
113.63
113.41
79.54
79.06
79.04
76.20
62.00
61.86
61.82
57.86
56.45
44.53
43.69
40.42
40.28
40.14
40.00
39.86
39.72
39.58
34.47
30.41
30.09
28.66
28.31
27.67
170
160
150
140
130
120
110
100
90
80
70
60
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References

(1) Magano, J. Large-scale amidations in process chemistry: Practical considerations for reagent selection and reaction execution. *Org. Process Res. Dev.* **2022**, *26* (6), 1562-1689.

(2) Albericio, F.; El-Faham, A. Choosing the Right Coupling Reagent for Peptides: A Twenty-Five-Year Journey. *Org. Process Res. Dev.* **2018**, *22* (7), 760-772.