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Electronic Supplementary Information

Structure-Dependent Tautomerization Induced Catalyst-Free Autocatalyzed N-Alkylation of Heteroaryl Amines with Alcohols

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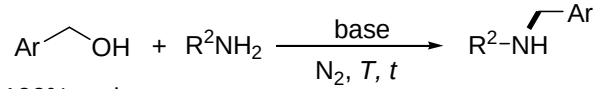
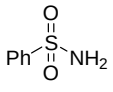
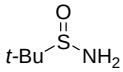
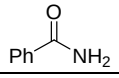
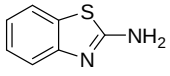
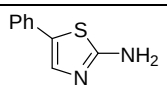
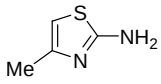
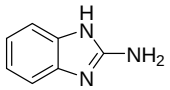
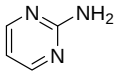
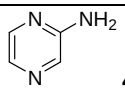
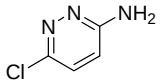
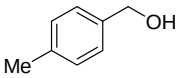
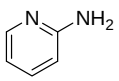
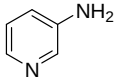
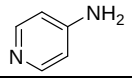
Table S1. Screening of Potential Amides and Amines for Catalyst-Free Autocatalyzed Dehydrative N-Alkylation Reaction using Pure Benzylic Alcohols.[a]

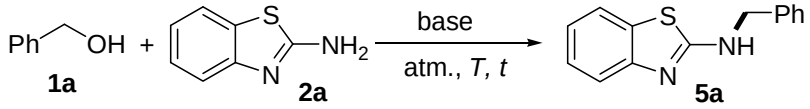


100% purity

entry	alcohol	amide or amine	base (mol%)	*T, t*	yield (%)[b]
1	$PhCH_2OH$ (**1a**)	4-$CH_3C_6H_4NH_2$ or $PhNH_2$	$CsOH·H_2O$ (40)	150 °C, 24 h	NR[c]
2	**1a**		K_2CO_3 (10)	135 °C, 18 h	NR
3	**1a**		K_2CO_3 (10)	135 °C, 18 h	NR
4			NaOH (100)	100 °C, 12 h	(47)
5	**1a**		K_2CO_3 (10)	135 °C, 18 h	NR
6	***1a***	 **2a**	***NaOH (20)***	***120 °C, 6 h***	***98 (95)***
7			***NaOH (20)***	***100 °C, 12 h***	***96 (84)***
8	**1a**		NaOH (20)	120 °C, 6 h	NR
9	**1a**		NaOH (20)	120 °C, 6 h	NR
10	**1a**		NaOH (20)	120 °C, 6 h	NR
11			K_2CO_3 (40)	135 °C, 24 h	NR
12	***1a***	 **3a**	***NaOH (40)***	***150 °C, 24 h***	***72 (60)***
13	***1a***	 **4**	***NaOH (40)***	***150 °C, 24 h***	***80 (70)***
14	**1a**		NaOH (40)	150 °C, 24 h	NR
15	 **1b**		NaOH (50)	150 °C, 22 h	44
16	**1b**		NaOH (50)	150 °C, 22 h	15
17	**1b**		NaOH (50)	150 °C, 22 h	NR

[a] The mixture of a pure alcohol (redistilled aldehyde-free, 100% purity as confirmed by GC analysis, 1.3-1.5 equiv.), an amide or an amine (1-3 mmol), and a base in a Schlenk tube (10 mL) was strictly degassed and then sealed under nitrogen. The mixture was then heated and monitored by GC-MS and/or TLC. [b] GC yields (isolated yields in parenthesis) based on the amides or amines. [c] NR: no reaction.

Table S2. Condition Optimization for Catalyst-Free Autocatalyzed Dehydrative N-Alkylation of 2-Aminobenzothiazole with Benzyl Alcohol.[a]

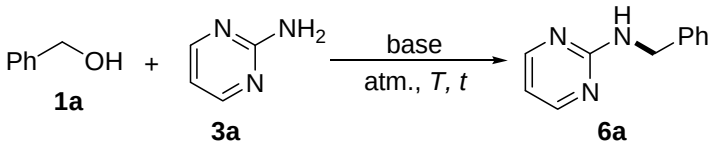


1a **2a** **5a**

entry	purity of **1a**	base (mol%)	additive (mol%)	atm., *T, t*	**5a**%[b]
1	100%[c]	NaOH (20)	-	N_2, 120 °C, 6 h	98 (95)
2	100%	NaOH (20)	-	N_2, 100 °C, 6 h	82 (78)
3	100%	NaOH (20)	-	N_2, 100 °C, 12 h	96 (84)
4	100%	LiOH (20)	-	N_2, 100 °C, 12 h	4
5	100%	KOH (20)	-	N_2, 100 °C, 12 h	16
6	100%	$CsOH·H_2O$ (20)	-	N_2, 100 °C, 12 h	52
7	100%	$CsCO_3$ (20)	-	N_2, 100 °C, 12 h	trace
8	100%	K_3PO_4 (20)	-	N_2, 100 °C, 12 h	trace
9	100%	*t*-BuOK (20)	-	N_2, 100 °C, 12 h	80
10	100%	NaOH (20)	--	air, 100 °C, 6 h	98 (92)
11	AR grade[d]	NaOH (20)	-	N_2, 100 °C, 6 h	97 (90)
12	***AR grade***	***NaOH (20)***	**-**	***air, 100 °C, 6 h***	***99 (93)***
13	AR grade	NaOH (20)	-	air, 100 °C, 5 h	97
14	AR grade	NaOH (20)	-	air, 100 °C, 3 h	86
15	AR grade	NaOH (10)	-	air, 100 °C, 6 h	23
16	AR grade	NaOH (20)	-	air, 80 °C, 6 h	86
17	100%	NaOH (20)	in dark	N_2, 100 °C, 6 h	(73)
18	100%	NaOH (20)	TEMPO (20 mol%)	N_2, 100 °C, 6 h	(93)
19	100%	NaOH (20)	$Ph_2C=CH_2$ (20 mol%)	N_2, 100 °C, 6 h	(80)

[a] The mixture of **1a** (1.5 mmol, 1.5 equiv.), **2a** (1 mmol) and a base sealed in a 10 mL Schlenk tube was heated and monitored by GC-MS and/or TLC. [b] GC yields (isolated yields in parenthesis) based **2a**. [c] Redistilled aldehyde-free **1a** (100% purity as confirmed by GC analysis) was used. [d] Commercial AR grade **1a** (≥99% purity) was directly used.

Table S3. Condition Optimization for Catalyst-Free Autocatalyzed Dehydrative N-Alkylation of 2-Aminopyrimidine with Benzyl Alcohol.[a]

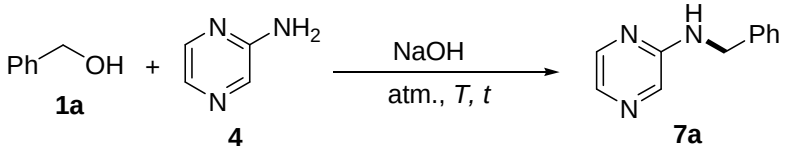


1a **3a** **6a**

entry	purity of **1a**	base (mol%)	atm. *T, t*	**6a**%[b]
1	100%[c]	NaOH (40)	N_2, 150 °C, 24 h	72 (60)
2	100%	NaOH (50)	N_2, 150 °C, 36 h	88 (72)
3	100%	NaOH (50)	air, 150 °C, 24 h	87 (73)
4	***AR grade***[d]	***NaOH (50)***	***air, 150 °C, 24 h***	***95 (82)***
5	AR grade	KOH (50)	air, 150 °C, 24 h	93 (80)
6	AR grade	LiOH (50)	air, 150 °C, 24 h	90
7	AR grade	$CsOH·H_2O$ (50)	air, 150 °C, 24 h	82
8	AR grade	K_2CO_3 (50)	air, 150 °C, 24 h	48
9	AR grade	*t*-BuOK (50)	air, 150 °C, 24 h	85
10	AR grade	NaOH (40)	air, 150 °C, 24 h	95 (80)
11	AR grade	NaOH (50)	air, 135 °C, 24 h	90
12	AR grade	NaOH (50)	air, 120 °C, 24 h	89

[a] The mixture of **1a** (3 mmol, 1.5 equiv.), **3a** (2 mmol), and a base was sealed in a Schlenk tube (10 mL) and then heated and monitored by GC-MS and/or TLC. [b] GC yields (isolated yields in parenthesis) based **3a**. [c] Redistilled aldehyde-free **1a** (100% purity as confirmed by GC analysis) was used. [d] Commercial AR grade **1a** (≥99% purity) was directly used.

Table S4. Condition Optimization for Catalyst-Free Autocatalyzed Dehydrative N-Alkylation of 2-Aminopyrazine with Benzyl Alcohol.[a]

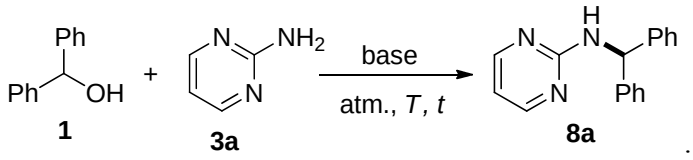


1a **4** **7a**

entry	purity of **1a**	NaOH (mol%)	atm. *T, t*	**7a**%[b]
1	100%[c]	40	N_2, 150 °C, 24 h	80 (70)
2	100%	50	N_2, 150 °C, 36 h	95 (84)
3	100%	50	air, 150 °C, 24 h	95 (80)
4	***AR grade***[d]	***50***	***air, 150 °C, 24 h***	***95 (86)***
5	AR grade	50	air, 125 °C, 24 h	(35)

[a] The mixture of **1a** (3 mmol, 1.5 equiv.), **4** (2 mmol), and NaOH (50 mol%) sealed in a 10 mL Schlenk tube was heated and monitored by GC-MS and/or TLC. [b] GC yields (isolated yields in parenthesis) based **4**. [c] Redistilled aldehyde-free **1a** (100% purity as confirmed by GC analysis) was used. [d] Commercial AR grade **1a** (≥99% purity) was directly used.

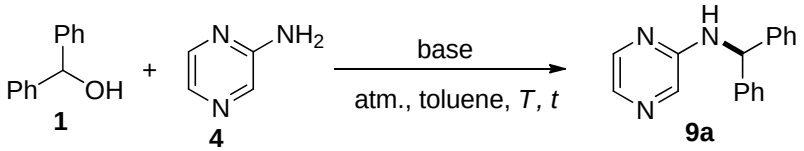
Table S5. Condition Optimization for Catalyst-Free Autocatalyzed Dehydrative N-Alkylation of 2-Aminopyrimidine with Benzohydrol.[a]



entry	solvent	base (mol%)	atm. *T, t*	**8a**%[b]
1	-	NaOH (50)	N_2, 150 °C, 24 h	NR
2	-	NaOH (50)	air, 150 °C, 24 h	NR
3	toluene (0.5 mL)	NaOH (50)	air, 150 °C, 24 h	NR
4	toluene (0.5 mL)	LiOH (100)	air, 150 °C, 24 h	NR
5	toluene (0.5 mL)	KOH (100)	air, 150 °C, 24 h	32
6	toluene (0.5 mL)	TBAOH (50)	air, 150 °C, 24 h	NR
7	toluene (0.5 mL)	*t*-BuONa (50)	air, 150 °C, 24 h	23
	toluene (0.5 mL)	*t*-BuOK (50)	air, 150 °C, 24 h	28
8	***toluene (0.5 mL)***	***CsOH·H₂O (30)***	***air, 150 °C, 24 h***	***95 (83)***
9	***toluene (0.5 mL)***	***CsOH·H₂O (30)***	***N_2, 150 °C, 24 h***	***96 (80)***
10	toluene (0.5 mL)	$CsOH·H_2O$ (30)	air, 130 °C, 24 h	90

[a] Unless otherwise indicated, the mixture of benzohydrol (1.3 mmol, 1.3 equiv.), **3a** (1 mmol) in toluene (0. 5 mL) was sealed in a Schlenk tube (10 mL) and then heated and monitored by GC-MS and/or TLC. [b] GC yields (isolated yields in parenthesis) based **3a**.

Table S6. Condition Optimization for Catalyst-Free Autocatalyzed Dehydrative N-Alkylation of 2-Aminopyrazine with Benzohydrol.[a]



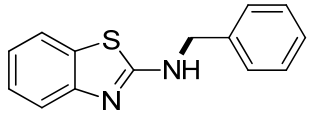
entry	base (mol%)	atm., *T, t*	**9a**%[b]
1	$CsOH·H_2O$ (30)	air, 150 °C, 24 h	***>99*** (95)
2	$CsOH·H_2O$ (30)	N_2, 150 °C, 24 h	(78)
3	NaOH (50)	air, 150 °C, 24 h	72
4	$CsOH·H_2O$ (30)	air, 130 °C, 18 h	>99
5	***$CsOH·H_2O$ (30)***	***air, 110 °C, 18 h***	***>99 (95)***

[a] The mixture of benzohydrol (1.3 mmol, 1.3 equiv.), **4** (1 mmol), and a base in toluene (0.5 mL) was sealed in a Schlenk tube (10 mL) and then heated and monitored by GC-MS and/or TLC. [b] GC yields (isolated yields in parenthesis) based on **4**.

Experimental

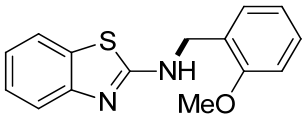
General. Unless otherwise noted, commercial alcohols (>99% purity), heteroaryl amines, bases, and solvents were all purchased and used without further purification. In certain reactions, pure alcohols and pure benzaldehyde were obtained by vacuum distillation of a commercial sample, with its purity confirmed by GC-MS analysis (100% as confirmed by GC analysis, and then degassed and stored under N_2 in a Schlenk flask). Most of the reactions were carried out in sealed 10 mL Schlenk tubes under air, and then heated and monitored by TLC and/or GC-MS. To test whether the amines and amides are suitable catalyst-free substrates, their reactions were investigated under catalyst-free conditions by using pure alcohols (100% purity) to avoid aldehyde contamination and performing the reactions under nitrogen after strict degassing to avoid air contamination in the reaction tubes. All the products were purified by column chromatography on silica gel using petroleum ether and ethyl acetate as the eluent. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance III AV500 instrument (500 MHz for ^{1}H and 125 MHz for ^{13}C NMR spectroscopy) by using $CDCl_3$, or d_6-DMSO, or d_6-actone as the solvent. Chemical shift values for ^{1}H and ^{13}C NMR were referred to internal Me_4Si (0 ppm). GC-MS and MS spectra were measured on a Shimadzu GCMS-QP2010 Plus or a Shimadzu GCMS-QP2010 Ultra spectrometer (EI). HRMS (ESI) analysis was measured on a Bruker microOTOF-Q II instrument.

Typical Procedure for Catalyst-Free Autocatalyzed Dehydrative *N*-Alkylation of 2-Aminobenzothiazoles with Primary Alcohols. The mixture of benzyl alcohol **1a** (0.155 mL, 1 mmol, 1.5 equiv), 2-aminobenzothiazole **2a** (0.1502 g, 1 mmol), and NaOH (0.0080 g, 0.2 mmol, 20 mol%) sealed in a 10 mL Schlenk tube was heated under air at 100 °C for 6 h and then monitored by TLC and/or GC-MS (>99% conversion by GC). The mixture was then quenched with ethyl acetate, the solvent evaporated under vacuum, and the residue purified by column chromatography using ethyl acetate and petroleum ether (60-90 ^{o}C) (v/v 1/5) as the eluent, giving *N*-benzylbenzo[*d*]thiazol-2-amine **5a** in 93% isolated yield.

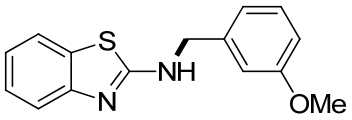


***N*-Benzylbenzo[*d*]thiazol-2-amine (5a).** White solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.56 (d, J = 7.8 Hz, 1H), 7.43-7.23 (m, 7H), 7.09-7.04 (m, 1H), 6.55 (b, 1H), 4.63 (s, 2H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 167.6, 152.3, 137.5, 130.4, 128.8, 127.9, 127.7, 126.0, 121.6, 120.8, 118.9, 49.4. MS (EI): m/z (%) 240 (46, M+), 239 (25), 212 (4), 136 (15), 106 (27), 92 (8), 91 (100), 65 (25). This compound

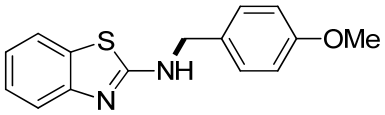
was known: Q. Li, S. Fan, Q. Sun, H. Tian, X. Yu, Q. Xu, *Org. Biomol. Chem.* **2012**, *10*, 2966.



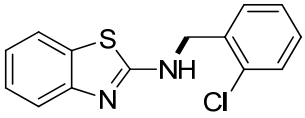
***N*-(2-Methoxybenzyl)benzo[*d*]thiazol-2-amine (5b).** Yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55 (d, J = 8.0 Hz, 1H), 7.46 (d, J = 8.0 Hz, 1H), 7.36 (dd, J = 7.5 Hz, J = 1.0 Hz, 1H), 7.28-7.23 (m, 2H), 7.06-7.02 (m, 1H), 6.92-6.86 (m, 2H), 6.48 (b, 1H), 4.59 (s, 2H), 3.82 (s, 3H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 167.8, 157.5, 152.4, 130.4, 129.4, 129.1, 125.8, 125.6, 121.3, 120.7, 120.5, 118.7, 110.4, 55.3, 45.4. MS (EI): *m/z* (%) 270 (37, M+), 255 (11), 239 (42), 207 (14), 131 (22), 121 (88), 91 (100), 69 (32), 65 (22). This compound was known: E. Feng, H. Huang, Y. Zhou, D. Ye, H. Jiang, H. Liu, *J. Comb. Chem.* **2010**, *12*, 422.



***N*-(3-Methoxybenzyl)benzothiazol-2-amine (5c).** White solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55 (d, J = 8.0 Hz, 1H), 7.38 (d, J = 8.0 Hz, 1H), 7.26-7.22 (m, 2H), 7.07-7.04 (m, 1H), 6.98-6.93 (m, 3H), 6.82 (dd, J = 8.5 Hz, J = 2.5 Hz, 1H), 4.58 (s, 2H), 3.74 (s, 3H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 168.0, 160.0, 152.2, 139.1, 130.4, 129.9, 126.0, 121.6, 120.9, 119.9, 118.8, 113.4, 113.2, 55.2, 49.4. MS (EI): m/z (%) 270 (76, M+), 269 (24), 136 (62), 121 (100), 91 (49), 78 (25), 77 (23), 65 (19). This compound was known: E. Feng, H. Huang, Y. Zhou, D. Ye, H. Jiang, H. Liu, *J. Comb. Chem.* **2010**, *12*, 422.

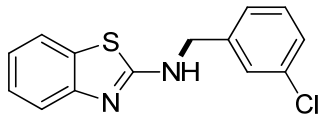


***N*-(4-Methoxybenzyl)benzothiazol-2-amine (5d).** Pale yellow solid. ^{1}H NMR (500 MHz, d_6-DMSO): δ 8.44 (t, J = 5.3 Hz, 1H), 7.67 (d, J = 8.0 Hz, 1H), 7.41 (d, J = 8.0 Hz, 1H), 7.33 (d, J = 9.0 Hz, 2H), 7.25-7.21 (m, 1H), 7.02 (t, J = 7.5 Hz, 1H), 6.92 (d, J = 8.5 Hz, 2H), 4.53 (d, J = 5.5 Hz, 2H), 3.74 (s, 3H). ^{13}C NMR (125.4 MHz, d_6-DMSO): δ 166.4, 158.6, 152.7, 131.0, 130.6, 129.0, 125.7, 121.07, 121.05, 118.2, 113.9, 55.2, 47.0. MS (EI): m/z (%) 270 (16, M+), 219 (4), 207 (3), 121 (100), 91 (5), 77 (8), 69 (7), 63 (5). This compound was known: E. Feng, H. Huang, Y. Zhou, D. Ye, H. Jiang, H. Liu, *J. Comb. Chem.* **2010**, *12*, 422.

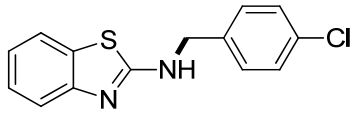


***N*-(2-Chlorobenzyl)benzo[*d*]thiazol-2-amine (5e).** White solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ

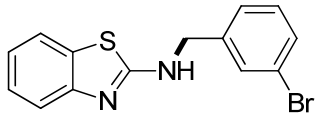
7.54 (d, *J* = 8.0 Hz, 1H), 7.50-7.48 (m, 1H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.38-7.36 (m, 1H), 7.24-7.18 (m, 3H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.97 (b, 1H), 4.71 (s, 2H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 167.7, 152.2, 135.0, 133.5, 130.4, 129.6, 129.4, 129.0, 127.1, 125.9, 121.6, 120.8, 118.8, 47.0. MS (EI): m/z (%) 274 (18, M+), 239 (100), 219 (22), 207 (21), 140 (13), 131 (20), 125 (56), 89 (19), 69 (35). This compound was known: F. Li, H. Shan, Q. Kang, L. Chen, *Chem. Commun.* **2011**, *47*, 5058.



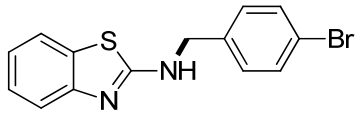
***N*-(3-Chlorobenzyl)benzo[*d*]thiazol-2-amine (5f).** White solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.58 (d, *J* = 7.5 Hz, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.39 (s, 1H), 7.31-7.28 (m, 4H), 7.12-7.08 (m, 1H), 6.18 (b, 1H), 4.63 (s, 2H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 167.2, 152.2, 139.6, 134.7, 130.5, 130.1, 128.0, 127.7, 126.1, 125.7, 121.9, 120.9, 119.1, 48.6. HRMS Calcd for $[C_{14}H_{11}ClN_2S + H]^+$: 275.0404; found: 275.0396.



***N*-(4-Chlorobenzyl)benzo[*d*]thiazol-2-amine (5g).** White solid. ^{1}H NMR (500 MHz, d_6-Actone): δ 7.67-7.65 (m, 1H), 7.60 (b, 1H), 7.50-7.44 (m, 3H), 7.40-7.37 (m, 2H), 7.28-7.25 (m, 1H), 7.09-7.05 (m, 1H), 4.74 (s, 2H). ^{13}C NMR (125.4 MHz, d_6-Actone): δ 167.2, 153.8, 139.1, 133.2, 131.9, 130.2, 129.3, 126.4, 122.2, 121.6, 119.6, 47.9. MS (EI): m/z (%) 274 (52, M+), 140 (27), 136 (17), 125 (100), 105 (5), 99 (7), 89 (22), 77 (4), 69 (10). This compound was known: F. Li, H. Shan, Q. Kang, L. Chen, *Chem. Commun.* **2011**, *47*, 5058.

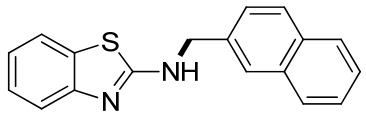


***N*-(3-Bromobenzyl)benzo[*d*]thiazol-2-amine (5h).** White solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.58 (d, *J* = 7.5 Hz, 1H), 7.55 (s, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.43 (d, *J* = 7.5 Hz, 1H), 7.33 (d, *J* = 7.5 Hz, 1H), 7.31-7.27(m, 1H), 7.23-7.20 (m, 1H), 7.11-7.08 (m, 1H), 6.28 (b, 1H), 4.62 (s, 2H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 167.2, 152.2, 139.9, 131.0, 130.6, 130.5, 130.4, 126.2, 126.1, 122.9, 121.9, 120.9, 119.1, 48.6. HRMS Calcd for $[C_{14}H_{11}BrN_2S + H]^+$: 318.9899; found: 318.9884.

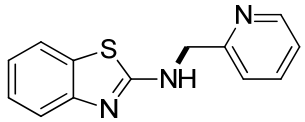


***N*-(4-Bromobenzyl)benzo[*d*]thiazol-2-amine (5i).** Pale yellow solid. ^{1}H NMR (500 MHz, d_6-DMSO): δ 8.53 (t, *J* = 5.5 Hz, 1H), 7.68 (d, *J* = 7.5 Hz, 1H), 7.54 (d, *J* = 8.5 Hz, 2H), 7.38 (dd, *J*

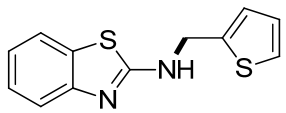
= 8.0 Hz, *J* = 20.0 Hz, 3H), 7.22 (t, *J* = 7.5 Hz, 1H), 7.03 (t, *J* = 7.5 Hz, 1H), 4.57 (d, *J* = 5.5 Hz, 2H). ^{13}C NMR (125.4 MHz, d_6-DMSO): δ 166.3, 152.5, 138.7, 131.4, 130.6, 129.7, 125.8, 121.3, 121.2, 120.2, 118.4, 46.7. MS (EI): m/z (%) 318 (53, M + 1), 317 (21, M+), 281 (31), 219 (74), 207 (65), 171 (83), 169 (91), 131 (63), 90 (52), 69 (100). This compound was known: F. Li, H. Shan, Q. Kang, L. Chen, *Chem. Commun.* **2011**, *47*, 5058.



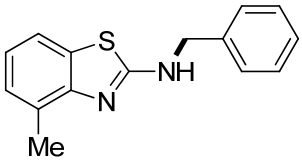
***N*-(Naphthalen-2-ylmethyl)benzo[*d*]thiazol-2-amine (5j).** White solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.86-7.82 (m, 4H), 7.59-7.55 (m, 2H), 7.52-7.47 (m, 3H), 7.32-7.29 (m, 1H), 7.12-7.09 (m, 1H), 5.85 (b, 1H), 4.81 (s, 2H). ^{13}C NMR (125.4 MHz, d_6-Actone): δ 166.5, 153.0, 136.7, 133.5, 132.9, 131.0, 128.2, 127.7, 127.6, 126.2, 126.0, 125.97, 125.7, 125.6, 121.2, 120.7, 118.7, 48.0. HRMS Calcd for $[C_{18}H_{14}N_2S + H]^+$: 291.0950; found: 291.0955.



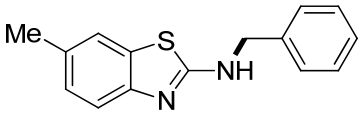
***N*-(Pyridin-2-ylmethyl)benzo[*d*]thiazol-2-amine (5k).** White solid. ^{1}H NMR (500 MHz, d_6-DMSO): δ 8.58 (d, *J* = 4.5 Hz, 1H), 7.70-7.67 (m, 1H), 7.59-7.57 (m, 2H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.31-7.28 (m, 1H), 7.23 (dd, *J* = 7.0 Hz, *J* = 5.5 Hz, 1H), 7.11-7.08 (m, 1H), 6.86 (b, 1H) 4.82 (s, 2H). ^{13}C NMR (125.4 MHz, d_6-DMSO): δ 166.6, 155.8, 152.5, 149.0, 136.8, 130.8, 125.9, 122.6, 121.9, 121.7, 120.8, 119.1, 49.2. MS (EI): m/z (%) 241 (86, M+), 163 (55), 136 (100), 135 (18), 107 (45), 93 (27), 79 (20), 78 (24), 65 (36). This compound was known: M. Bala, P. K. Verma, U. Sharma, N. Kumar, B. Singh, *Green Chem.* **2013**, *15*, 1687.



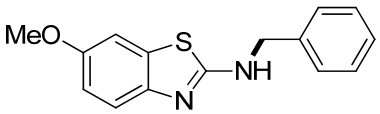
***N*-(Thiophen-2-ylmethyl)benzo[*d*]thiazol-2-amine (5l).** White solid. ^{1}H NMR (500 MHz, d_6-DMSO): δ 8.53 (t, *J* = 5.3 Hz, 1H), 7.68 (d, *J* = 7.5 Hz, 1H), 7.43-7.40 (m, 2H), 7.26-7.23 (m, 1H), 7.09 (d, *J* = 3.0 Hz, 1H), 7.06-7.03 (m, 1H), 6.99-6.98 (m, 1H), 4.76 (d, *J* = 6.0 Hz, 2H). ^{13}C NMR (125.4 MHz, d_6-DMSO): δ 166.2, 152.5, 142.1, 130.7, 127.0, 126.2, 125.9, 125.5, 121.5, 121.3, 118.5, 42.4. MS (EI): m/z (%) 248 (2, M+), 247 (4), 246 (26), 105 (3), 97 (100), 69 (5), 53 (11). HRMS Calcd for $[C_{12}H_{10}N_2S_2 + H]^+$: 247.0358; found: 247.0361.



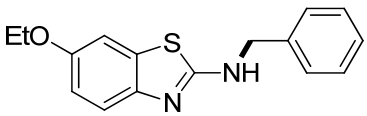
***N*-Benzyl-4-methylbenzo[*d*]thiazol-2-amine (5m).** Pale yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40 (d, J = 7.5 Hz, 1H), 7.36-7.22 (m, 5H), 7.09 (d, J = 7.5 Hz, 1H), 6.98 (t, J = 7.5 Hz, 1H), 6.15 (b, 1H), 4.56 (s, 2H), 2.54 (s, 3H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 166.8, 151.3, 137.6, 130.2, 128.73, 128.68, 127.7, 127.6, 126.7, 121.4, 118.3, 49.5, 18.3. MS (EI): m/z (%) 254 (64, M+), 226 (5), 163 (16), 150 (24), 136 (4), 106 (36), 91 (100), 77 (5). This compound was known: K. Inamoto, C. Hasegawa, J. Kawasaki, K. Hiroya, T. Doi, *Adv. Synth. Catal.* **2010**, *352*, 2643.



***N*-Benzyl-6-methylbenzo[*d*]thiazol-2-amine (5n).** White solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40-7.33 (m, 6H), 7.31-7.28 (m, 1H), 7.08 (dd, J= 8.0 Hz, J= 1.0 Hz, 1H), 6.01 (b, 1H), 4.62 (s, 2H), 2.38(s, 3H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 116.7, 150.1, 137.6, 131.4, 130.6, 128.8, 127.8, 127.7, 127.1, 120.9, 118.6, 49.4, 21.2. MS (EI): m/z (%) 254 (48, M+), 163 (6), 150 (23), 121 (6), 106 (27), 91 (100), 77 (7), 65 (25). This compound was known: F. Li, H. Shan, Q. Kang, L. Chen, *Chem. Commun.* **2011**, *47*, 5058.

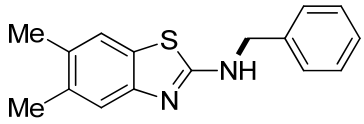


***N*-Benzyl-6-methoxybenzo[*d*]thiazol-2-amine (5o).** White solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36 (d, J = 7.5 Hz, 2H), 7.32-7.22 (m, 4H), 7.07 (d, J = 2.5 Hz, 1H), 6.89 (b, 1H), 6.82 (dd, J = 8.5 Hz, J = 2.5 Hz, 1H), 4.55 (s, 2H), 3.76 (s, 3H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 166.3, 155.0, 146.4, 137.6, 131.2, 128.7, 127.64, 127.57, 119.0, 113.5, 105.4, 55.8, 49.3. MS (EI): m/z (%) 270 (59, M+), 255 (4), 179 (27), 166 (20), 135 (12), 106 (14), 91 (100). This compound was known: E. Feng, H. Huang, Y. Zhou, D. Ye, H. Jiang, H. Liu, *J. Comb. Chem.* **2010**, *12*, 422.

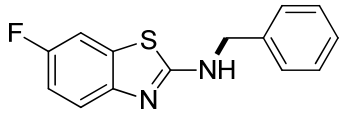


***N*-Benzyl-6-ethoxybenzo[*d*]thiazol-2-amine (5p).** White solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36 (d, J = 7.5 Hz, 2H), 7.32-7.24 (m, 3H), 7.21 (d, J = 9.0 Hz, 1H), 7.06 (d, J = 2.5 Hz, 1H), 6.94 (b, 1H), 6.81 (dd, J= 8.5 Hz, J= 2.5 Hz, 1H), 4.54 (s, 2H), 3.97 (q, J = 14.0 Hz, J = 7.0 Hz, 2H), 1.37 (t, J = 7.0 Hz, 3H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 166.3, 154.3, 146.3, 137.7, 131.1, 128.7, 127.62,

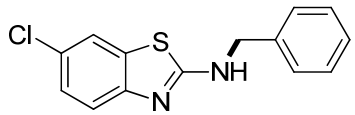
127.56, 119.0, 114.1, 106.2, 64.1, 49.3, 14.8. MS (EI): m/z (%) 284 (61, M+), 255 (20), 193 (6), 180 (19), 165 (27), 152 (5), 121 (6), 106 (9), 91 (100). HRMS Calcd for $[C_{16}H_{16}N_2OS + H]^+$: 285.1056; found: 285.1073.



***N*-Benzyl-5,6-dimethylbenzo[*d*]thiazol-2-amine (5q).** Pale yellow solid. ^{1}H NMR (500 MHz, d_6-DMSO): δ 8.33 (t, J = 5.8 Hz, 1H), 7.41 (s, 1H), 7.38-7.33 (m, 4H), 7.28-7.25 (m, 1H), 7.19 (b, 1H), 4.56 (d, J = 6.0 Hz, 2H), 2.23 (s, 3H), 2.22(s, 3H). ^{13}C NMR (125.4 MHz, d_6-DMSO): δ 165.9, 151.0, 139.3, 133.9, 129.4, 128.5, 127.7, 127.6, 127.2, 121.3, 119.2, 47.4, 19.8, 19.4. MS (EI): m/z (%) 268 (51, M+), 240 (5), 207 (18), 191 (6), 177 (10), 164 (24), 133 (9), 106 (36), 91 (100). HRMS Calcd for $[C_{16}H_{15}N_2S + H]^+$: 269.1062; found: 269.1101.



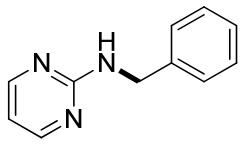
***N*-Benzyl-6-fluorobenzo[*d*]thiazol-2-amine (5r).** Pale red solid. ^{1}H NMR (500 MHz, d_6-DMSO): δ 8.49 (t, J = 5.8 Hz, 1H), 7.61 (dd, J = 8.8 Hz, J = 2.8 Hz, 1H), 7.40-7.34 (m, 5H), 7.29-7.26 (m, 1H), 7.06 (td, J = 9.3 Hz, J = 2.8 Hz, 1H), 4.59 (d, J = 6.0 Hz, 2H). ^{13}C NMR (125.4 MHz, d_6-DMSO): δ 166.3, 158.30 and 156.42 ($J_{C\text{-}F}$ = 235.8 Hz), 149.3, 139.0, 131.63 and 131.55 ($J_{C\text{-}F}$ = 10.0 Hz), 128.5, 127.5, 127.2, 118.68 and 118.61 ($J_{C\text{-}F}$ = 8.8 Hz), 113.07 and 112.88 ($J_{C\text{-}F}$ = 23.8 Hz), 108.13 and 107.92 ($J_{C\text{-}F}$ = 26.3 Hz), 47.4. MS (EI): m/z (%) 258 (39, M+), 154 (11), 123 (4), 106 (14), 91 (100), 77 (2). This compound was known: E. Feng, H. Huang, Y. Zhou, D. Ye, H. Jiang, H. Liu, *J. Comb. Chem.* **2010**, *12*, 422.



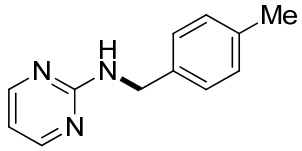
***N*-Benzyl-6-chlorobenzo[*d*]thiazol-2-amine (5s).** Pale red solid. ^{1}H NMR (500 MHz, d_6-DMSO): δ 8.62 (t, J = 5.5 Hz, 1H), 7.80 (d, J = 2.0 Hz, 1H), 7.39-7.34 (m, 5H), 7.29-7.26 (m, 1H), 7.23 (dd, J = 8.5 Hz, J = 2.0 Hz, 1H), 4.60 (d, J = 6.0 Hz, 2H). ^{13}C NMR (125.4 MHz, d_6-DMSO): δ 167.0, 151.6, 138.9, 132.3, 128.6, 127.6, 127.3, 125.9, 124.9, 120.8, 119.1, 47.5. MS (EI): m/z (%) 274 (25, M+), 246 (2), 170 (7), 106 (15), 91 (100), 77 (2). This compound was known: E. Feng, H. Huang, Y. Zhou, D. Ye, H. Jiang, H. Liu, *J. Comb. Chem.* **2010**, *12*, 422.

Typical Procedure for Catalyst-Free Autocatalyzed Dehydrative *N*-Alkylation of

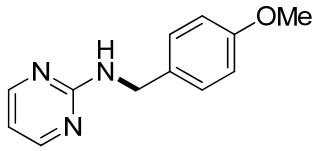
2-Aminopyrimidines or 2-Aminopyrazine with Primary Alcohols. The mixture of benzyl alcohol **1a** (0.31 mL, 3.0 mmol, 1.5 equiv), 2-aminopyrimidine **3a** (0.1902 g, 2.0 mmol), and NaOH (0.0400 g, 1.0 mmol, 50 mol%) sealed in a 10 mL Schlenk tube was heated under air at 150°C for 24 h and then monitored by TLC and/or GC-MS (95% conversion by GC). The mixture was then quenched with ethyl acetate, solvent evaporated under vacuum, and the residue purified by column chromatography using ethyl acetate and petroleum ether (60-90 ^{o}C) (v/v 1/5) as the eluent, giving *N*-Benzyl-(2-pyrimidyl)amine **6a** in 82% isolated yield.



***N*-Benzyl-(2-pyrimidyl)amine (6a).** White solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.21 (b, 2H), 7.40-7.34 (m, 4H), 7.31-7.28 (m, 1H), 6.52 (t, J = 4.8 Hz, 1H), 6.12 (b, 1H), 4.66 (d, J = 6.0 Hz, 2H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 162.3, 158.1, 139.1, 128.6, 127.6, 127.2, 110.7, 45.5. MS (EI): m/z (%) 186 (13, M+1), 185 (100, M+), 184 (68), 106 (54), 91 (22), 79 (18), 65 (11), 53 (6). This compound was known: D. S. Ermolat'ev, E. V. Van der Eycken, *J. Org. Chem.* **2008**, *73*, 6691.

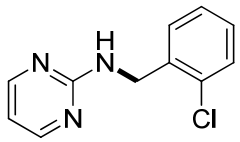


***N*-(4-Methylbenzyl)-(2-pyrimidyl)amine (6b).** White solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.22 (b, 2H), 7.25 (d, J = 9.0 Hz, 2H), 7.14 (d, J = 7.5 Hz, 2H), 6.51 (t, J = 4.8 Hz, 1H), 5.80 (b, 1H), 4.58 (d, J = 6.0 Hz, 2H), 2.33 (s, 3H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 162.3, 158.1, 136.9, 136.0, 129.3, 127.5, 110.7, 45.2, 21.1. MS (EI): m/z (%) 200 (13, M+1), 199 (100, M+), 198 (48), 184 (63), 120 (57), 105 (49), 106 (32), 91 (22), 79 (41), 77 (33), 65 (11), 53 (15). This compound was known: Q. Li, S. Fan, Q. Sun, H. Tian, X. Yu, Q. Xu, *Org. Biomol. Chem.* **2012**, *10*, 2966.

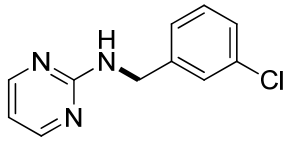


***N*-(4-Methoxybenzyl)-(2-pyrimidyl)amine (6c).** White solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.25 (d, J = 4.8 Hz, 2H), 7.32-7.28 (m, 2H), 6.89 (d, J = 8.1 Hz, 2H), 6.54 (t, J = 4.7 Hz, 1H), 5.73 (b, 1H), 4.58 (d, J = 5.7 Hz, 2H), 3.82 (s, 3H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 162.3, 158.9, 158.1, 131.1, 128.9, 114.0, 110.7, 55.3, 45.0. MS (EI): m/z (%) 215 (59, M+), 214 (22), 200 (7), 184 (18), 136 (20), 121 (100), 106 (19), 91 (11), 77 (17), 65 (6), 53 (8). This compound was known: D. S.

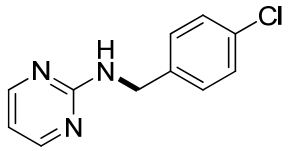
Ermolat'ev, E. V. Van der Eycken, *J. Org. Chem.* **2008**, *73*, 6691.



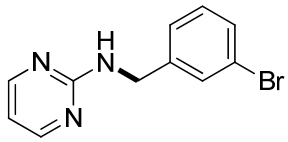
***N*-(2-Chlorobenzyl)-(2-pyrimidyl)amine (6d).** White solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.21(d, J = 4.2 Hz, 2H), 7.44-7.41 (m, 1H), 7.37-7.33 (m, 1H), 7.22-7.17 (m, 2H), 6.50 (t, J = 4.8 Hz, 1H), 6.29 (b, 1H), 4.73 (d, J = 6.3 Hz, 2H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 162.3, 158.1, 136.6, 133.6, 129.5, 129.3, 128.5, 126.8, 110.9, 43.2. This compound was known: X. Yu, C. Liu, L. Jiang, Q. Xu, *Org. Lett.* **2011**, *13*, 23.



***N*-(3-Chlorobenzyl)-(2-pyrimidyl)amine (6e).** White solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.24 (d, J = 4.8 Hz, 2H), 7.35-7.24 (m, 4H), 6.55 (t, J = 4.8Hz, 1H), 5.97 (b, 1H), 4.63 (d, J = 6.0 Hz, 2H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 162.2, 158.1, 141.4, 134.4, 129.8, 127.5, 127.3, 125.5, 111.1, 44.8. MS (EI): m/z (%) 221 (29, M+2). 220 (26, M+1), 219 (89, M+), 218 (43), 184 (29), 142 (33), 140 (100), 125 (26), 108 (31), 106 (15), 92(11), 89 (33), 80 (40), 79 (26), 63 (14), 53 (25), 52 (8). HRMS Calcd for $[C_{11}H_{10}ClN_3 + H]^+$: 220.0636; found: 220.0631.

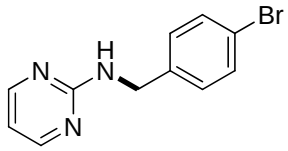


***N*-(4-Chlorobenzyl)-(2-pyrimidyl)amine (6f).** White solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.20 (d, J = 4.2 Hz, 2H), 7.28-7.27 (m, 4H), 6.53 (t, J = 4.8 Hz, 1H), 6.13 (b, 1H), 4.60 (d, J = 6.0 Hz, 2H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 162.2, 158.1, 137.7, 132.9, 128.8, 128.7, 111.0, 44.7. MS (EI): m/z (%) 221 (33, M+2), 220 (28, M+1), 219 (100, M+), 218 (46), 184 (44), 142 (31), 140 (94), 127 (16), 125 (50), 106 (23), 92 (12), 89 (41), 80 (43), 77 (17), 63 (15), 53 (27). This compound was known: A. Paio, A. Zaramella, R. Ferritto, N. Conti, C. Marchioro, P. Seneci, *J. Comb. Chem.* **1999**, *1*, 317.

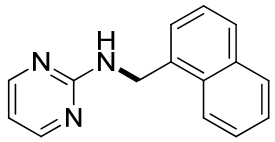


***N*-(3-Bromobenzyl)-(2-pyrimidyl)amine (6g).** White solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.19 (d,

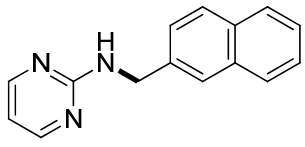
J = 4.2 Hz, 2H), 7.50 (s, 1H), 7.38 (d, J = 8.1 Hz, 1H), 7.28 (d, J = 6.0 Hz, 1H), 7.20-7.15 (m, 1H), 6.53 (t, J = 4.8 Hz, 1H), 6.31 (b, 1H), 4.62 (d, J = 6.0 Hz, 2H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 162.2, 158.1, 141.7, 130.4, 130.2, 130.1, 126.0, 122.7, 111.0, 44.7. MS (EI): m/z (%) 265 (68, M+2), 264 (39, M+1), 263 (71, M+), 262 (31), 186 (49), 184 (100), 108 (41), 106 (24), 92 (36), 90 (47), 81 (23), 80 (51), 79 (39), 77 (20), 63 (20), 89 (46), 53 (33). HRMS Calcd for $[C_{11}H_{10}BrN_3 + H]^+$: 264.0131; found: 264.0131.



***N*-(4-Bromobenzyl)-(2-pyrimidyl)amine (6h).** White solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.22 (d, J = 4.5 Hz, 2H), 7.44 (d, J = 8.4 Hz, 2H), 7.23 (d, J = 8.1 Hz, 2H), 6.54 (t, J = 4.8 Hz, 1H), 5.99 (b, 1H), 4.59 (d, J = 6.0 Hz, 2H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 162.2, 158.1, 138.3, 131.6, 129.1, 121.0, 111.0, 44.7. MS (EI): m/z (%) 265 (63, M+2), 264 (37, M+1), 263 (65, M+), 262 (30), 186 (38), 184 (100), 171 (16), 169 (19), 108 (22), 106 (25), 91 (29), 90 (47), 89 (46), 80 (44), 79 (34), 78 (10), 77 (18), 63 (17), 53 (27), 51 (11). This compound was known: V. Martínez-Barrasa, F. Delgado, C. Burgos, J. L. García-Navío, M. L. Izquierdo, J. Alvarez-Builla, *Tetrahedron*, **2000**, *56*, 2481.

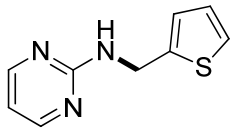


***N*-(Naphthalen-1-ylmethyl)-(2-pyrimidyl)amine (6i).** White solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.10-8.06 (m, 3H), 7.90-7.87 (m, 1H), 7.81 (d, J = 8.1 Hz, 1H), 7.53-7.49 (m, 3H), 7.46-741 (m, 1H), 6.46 (t, J = 4.8 Hz, 1H), 6.24 (b, 1H), 5.06 (d, J = 5.7 Hz, 2H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 162.1, 158.0, 134.2, 133.8, 131.5, 128.7, 128.2, 126.3, 125.8, 125.4, 123.6, 110.6, 43.6. MS (EI): m/z (%) 236 (17, M+1), 235 (100, M+), 234 (52), 156 (65), 141 (76), 139 (18), 129 (26), 128 (18), 127 (21), 115 (56), 106 (25), 80 (20), 79 (19). HRMS Calcd for $[C_{15}H_{13}N_3 + H]^+$: 236.1182; found: 236.1181.

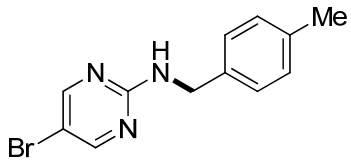


***N*-(Naphthalen-2-ylmethyl)-(2-pyrimidyl)amine (6j).** White solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.20 (b, 2H), 7.81-7.77 (m, 4H), 7.47-1.42 (m, 3H), 6.47 (t, J = 4.8 Hz, 1H), 6.10 (b, 1H), 4.79 (d, J = 6.0 Hz, 2H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 162.4, 158.1, 136.6, 133.5, 132.8, 128.4, 127.8,

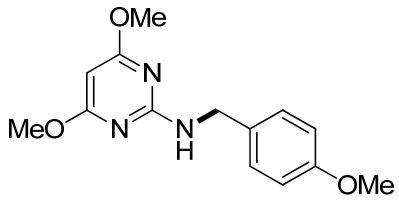
127.7, 126.2, 125.9, 125.8, 125.7, 110.8, 45.6. MS (EI): m/z (%) 236 (17, M+1), 235 (100, M+), 234 (51), 156 (60), 141 (41), 139 (9), 129 (15), 115 (23), 106 (11), 79 (9). This compound was known: A. Paio, A. Zaramella, R. Ferritto, N. Conti, C. Marchioro, P. Seneci, *J. Comb. Chem.* **1999**, *1*, 317.



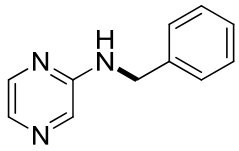
***N*-(Thiophen-2-ylmethyl)-(2-pyrimidyl)amine (6k).** White solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.25 (d, J = 3.0 Hz, 2H), 7.20 (dd, J = 5.0 Hz, J = 1.0 Hz, 1H), 7.02-7.00 (m, 1H), 6.96-6.94 (m, 1H), 6.55 (t, J = 4.8 Hz, 1H), 5.96 (b, 1H), 4.80 (d, J = 6.0 Hz, 2H)**.** ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 161.9, 158.1, 142.1, 126.8, 125.4, 124.8, 111.1, 40.4. MS (EI): m/z (%) 192 (13, M+1), 191 (100, M+), 190 (25), 158 (30), 112 (23), 106 (13), 97 (67), 79 (12), 53 (17). This compound was known: A. Ballistreri, A. Bottion, G. Musumarm, R. Fiofuvanti, M. Biava, G. C. Porretta, N. Simonetti, A. Villa, *J. Phys. Org. Chem.* **1995**, *9*, 61.



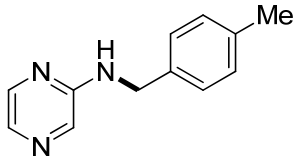
5-Bromo-*N*-(4-methylbenzyl)-(2-pyrimidyl)amine (6l). White solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.12 (b, 2H), 7.22 (d, J = 8.0 Hz, 2H), 7.15 (d, J = 8.0 Hz, 2H) , 6.01 (b, 1H), 4.52 (d, J = 5.5 Hz, 2H), 2.35 (s, 3H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 160.5, 158.3, 137.2, 135.5, 129.4, 127.7, 106.4, 45.6, 21.1. MS (EI): m/z (%) 279 (34, M+2), 278 (19, M+1), 277 (34, M+), 276 (15), 264 (33), 262 (33), 120 (36), 105 (100), 104 (19), 103 (19), 91 (16), 79 (32), 78 (12), 77 (34), 65 (10). HRMS Calcd for $[C_{12}H_{12}BrN_3 + H]^+$: 278.0287; found: 278.0315.



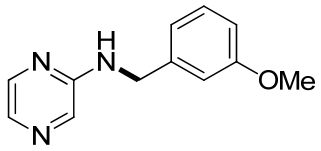
4,6-Dimethoxy-*N*-(4-methoxybenzyl)-(2-pyrimidyl)amine (6m). White solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.28 (d, J = 8.4 Hz, 2H), 6.86 (d, J = 8.7 Hz, 2H), 5.42 (s, 1H), 5.26 (b, 1H), 4.53 (d, J = 5.7 Hz, 2H), 3.84 (s, 6H), 3.80 (s, 3H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 172.2, 161.6, 158.8, 131.6, 128.9, 113.9, 78.9, 55.3, 53.5, 45.0. MS (EI): m/z (%) 276 (17, M+1),275 (100, M+), 274 (17), 260 (31), 244 (7), 139 (14), 136 (56), 125 (9), 121 (69), 91 (6), 77 (7). HRMS Calcd for $[C_{14}H_{17}N_3O_3 + H]^+$: 276.1343; found: 276.1331.



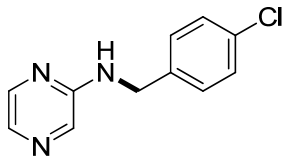
***N*-Benzylpyrazin-2-amine (7a).** Pale yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.00 (dd, J = 2.5 Hz, J = 1.5 Hz, 1H), 7.90 (d, J = 1.0 Hz, 1H), 7.83 (d, J = 2.5 Hz, 1H), 7.37-7.35 (m, 4H), 7.32-7.29 (m, 1H), 5.22 (b, 1H), 4.57 (d, J = 6.0 Hz, 2H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 154.5, 142.0, 138.5, 133.0, 132.1, 128.8, 127.58, 127.55, 45.6. MS (EI): m/z (%) 186 (11, M+1), 185 (85, M+), 184 (38), 106 (68), 91 (100), 79 (18), 65 (23), 52 (6). This compound was known: B. J. Tardiff, M. Stradiotto, *Eur. J. Org. Chem.* **2012**, *21*, 3972.



***N*-(4-Methylbenzyl)pyrazin-2-amine (7b).** Pale yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.98 (dd, J = 2.5 Hz, J = 1.5 Hz, 1H), 7.86 (d, J = 1.0 Hz, 1H), 7.80 (d, J = 3.0 Hz, 1H), 7.23 (d, J = 8.0 Hz, 2H), 7.15 (d, J = 7.5 Hz, 2H), 5.04 (b, 1H), 4.50 (d, J = 5.5 Hz, 2H), 2.34 (s, 3H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 154.5, 142.0, 137.3, 135.4, 133.0, 132.1, 129.4, 127.6, 45.4, 21.1. MS (EI): m/z (%) 199 (39, M+), 198 (9), 184 (11), 120 (18), 105 (100), 103 (12), 79 (25), 77 (21), 52 (7). This compound was known: V. Martínez-Barrasa, F. Delgado, C. Burgos, J. L. García-Navío, M. L. Izquierdo, J. Alvarez-Builla, *Tetrahedron*, **2000**, *56*, 2481.

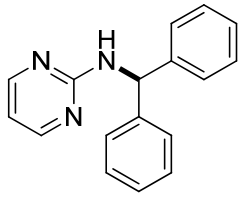


***N*-(3-Methoxybenzyl)pyrazin-2-amine (7c).** Pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.98-7.97 (m, 1H), 7.87 (d, J = 1.0 Hz, 1H), 7.80 (d, J = 2.5 Hz, 1H), 7.27-7.24 (m, 1H), 6.92 (d, J = 7.5 Hz, 1H), 6.89 (s, 1H), 6.82 (dd, J = 8.5 Hz, J = 2.5 Hz, 1H), 5.19 (b, 1H), 4.52 (d, J = 5.5 Hz, 2H), 3.78 (s, 3H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 160.0, 154.5, 142.0, 140.2, 133.1, 132.1, 129.8, 119.8, 113.2, 112.8, 55.2, 45.5. MS (EI): m/z (%) 215 (100, M+), 214 (30), 200 (10), 184 (11), 136 (66), 121 (73), 106 (9), 91 (27), 77 (12), 65 (9). HRMS Calcd for $[C_{12}H_{13}N_3O + H]^+$: 216.1131; found: 216.1126.

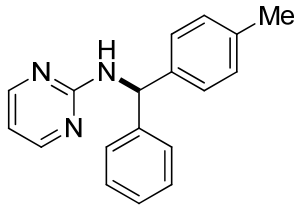


***N*-(4-Chlorobenzyl)pyrazin-2-amine (7d).** Yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.80-7.99 (m, 1H), 7.88 (s, 1H), 7.82 (d, J = 2.7 Hz, 1H), 7.33-7.27 (m, 4H), 5.08 (b, 1H), 4.54 (d, J = 6.0 Hz, 2H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 154.3, 142.0, 137.1, 133.34, 133.33, 133.26, 132.2, 128.9, 44.8. MS (EI): m/z (%) 221(14, M+2), 220 (10, M+1), 219 (44, M+), 218 (13), 184 (9), 142 (13), 140 (42), 127 (32), 125 (100), 99 (9), 89 (32), 80 (11), 79 (11), 63 (11), 52 (11). This compound was known: S. G. Durón, A. Lindstromf, C. Bonnefous, H. Zhang, X. H. Chen, K. T. Symons, M. Sablad, N. Rozenkrants, Y. Zhang, L. Wang, N. Yazdani, A. K. Shiau, S. A. Noble, P. Rix, T. S. Rao, C. A. Hassig, N. D. Smith, *Bioorg. Med. Chem. Lett.* **2012**, *22*, 1237.

Typical Procedure for Catalyst-Free Autocatalyzed Dehydrative *N*-Alkylation of 2-Aminopyrimidines with Secondary Alcohols. The mixture of benzohydrol (0.2395g, 1.3 mmol, 1.3 equiv), 2-aminopyrimidine **3a** (0.0951 g, 1 mmol), and $CsOH{\cdot}H_2O$ (0.0504 g, 0.3 mmol, 30 mol%) in toluene (0.5 ml) was sealed in a 10 mL Schlenk tube and then heated under air at 150°C for 24 h. The mixture was then monitored by TLC and/or GC-MS (95% conversion by GC). The mixture was quenched with ethyl acetate, solvent evaporated under vacuum, and the residue purified by column chromatography using ethyl acetate and petroleum ether (60-90 ^{o}C) (v/v 1/5) as the eluent, giving *N*-benzhydrylpyrimidin-2-amine **8a** in 83% isolated yield.

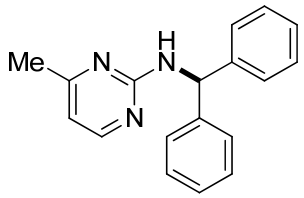


***N*-Benzhydrylpyrimidin-2-amine (8a).** ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.19 (d, J= 4.5 Hz, 2H), 7.32-7.23 (m, 10H), 6.51 (t, J = 4.8 Hz, 1H), 6.33 (d, J = 8.0 Hz, 1H), 6.07 (d, J = 7.5 Hz, 1H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 161.6, 158.1, 142.5, 128.6, 127.5, 127.2, 111.1, 58.9. HRMS Calcd for $[C_{17}H_{15}N_3 + H]^+$: 262.1339; found: 262.1329. This compound was known: J. Goerdeler, W. Roth, *Chem. Ber.* **1963**, *96*, 534.



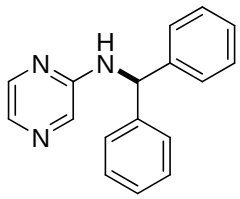
***N*-(Phenyl(*p*-tolyl)methyl)pyrimidin-2-amine (8b).** ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.07 (b, 2H), 7.32-7.28 (m, 4H), 7.25-7.21 (m, 1H), 7.20 (d, J = 8.0 Hz, 2H), 7.11 (d, J = 8.0 Hz, 2H), 6.57 (d, J =

8.0 Hz, 1H), 6.43 (t, J = 4.8 Hz, 1H), 6.31 (d, J = 8.0 Hz, 1H), 2.31 (s, 3H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 161.6, 157.9, 142.7, 139.6, 136.7, 129.2, 128.4, 127.48, 127.47, 127.0, 110.7, 58.4, 21.0. HRMS Calcd for $[C_{18}H_{17}N_3 + H]^+$: 276.1495; found: 276.1487.

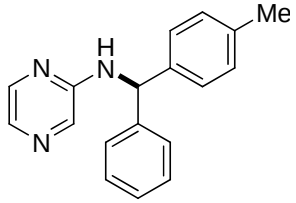


***N*-Benzhydryl-4-methylpyrimidin-2-amine (8c).** ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.06 (b, 1H), 7.33-7.21 (m, 11H), 6.40-6.39 (m, 1H), 6.37 (d, J = 7.0 Hz, 1H), 5.85 (b, 1H), 2.28 (s, 3H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 168.0, 161.4, 157.6, 142.7, 128.5, 127.4, 127.1, 110.7, 58.7, 24.1. HRMS Calcd for $[C_{18}H_{17}N_3 + H]^+$: 276.1495; found: 276.1490.

Typical Procedure for Catalyst-Free Autocatalyzed Dehydrative *N*-Alkylation of 2-Aminopyrazine with Secondary Alcohols. The mixture of benzohydrol (0.2395g, 1.3 mmol, 1.3 equiv), 2-aminopyrazine **4** (0.0951 g, 1 mmol) and $CsOH{\cdot}H_2O$ (0.0504 g, 0.3 mmol, 30 mol%) in toluene (0.5 ml) was sealed in a 10 mL Schlenk tube and then heated under air at 110 °C for 18 h. The mixture was then monitored by TLC and/or GC-MS (>99% conversion by GC). The mixture was quenched with ethyl acetate, solvent evaporated under vacuum, and the residue purified by column chromatography using ethyl acetate and petroleum ether (60-90 ^{o}C) (v/v 1/5) as the eluent, giving *N*-benzhydrylpyrazin-2-amine **9a** in 95% isolated yield.



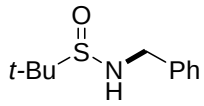
***N*-Benzhydrylpyrazin-2-amine (9a).** ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.89 (b, 1H), 7.82 (s, 1H), 7.78 (d, J = 2.5 Hz, 1H), 7.34-7.25 (m, 10H), 6.01 (d, J = 6.5 Hz, 1H), 5.43 (b, 1H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 153.6, 142.1, 141.8, 133.5, 131.8, 128.8, 127.6, 127.4, 59.7. HRMS Calcd for $[C_{17}H_{15}N_3 + H]^+$:262.1339; found: 262.1343.



***N*-(Phenyl(*p*-tolyl)methyl)pyrazin-2-amine (9b).** ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.94 (s, 1H), 7.83 (d, J = 1.5 Hz, 1H), 7.81 (d, J = 2.5 Hz, 1H), 7.35-7.31 (m, 4H), 7.29-7.25 (m, 1H), 7.21 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 8.0 Hz, 2H), 5.97 (d, J = 6.0 Hz, 1H), 5.25 (d, J = 6.0 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 153.7, 142.2, 142.0, 138.9, 137.4, 133.6, 131.8, 129.5, 128.8, 127.5, 127.3, 59.6, 21.1. HRMS Calcd for $[C_{18}H_{17}N_3 + H]^+$: 276.1495; found: 276.1491. This compound was known: T. Ishiyama, J. Hartwig, *J. Am. Chem. Soc.* **2000**, *122*, 12043.

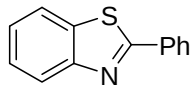
Control Reaction of Mechanistic Studies

Detailed Procedure for Dehydrative N-Alkylation of *tert*-Butanesulfinamide with Benzyl Alcohol (eq. 2 in the text). The mixture of pure benzyl alcohol **1a** (0.4217 g, 3.9 mmol, 1.3 equiv.), *tert*-butanesulfinamide **12** (0.3636 g, 3.0 mmol), and NaOH (0.1200 g, 3.0 mmol, 100 mol%) was degassed and sealed under nitrogen in a 10 mL Schlenk tube. The mixture was then stirred at 100 ^{o}C for 12 h and monitored by TLC and/or GC-MS. The crude product was purified by column chromatography using ethyl acetate and petroleum ether as the eluent, affording **13** in 47% isolated yield. The reaction at 125 ^{o}C gave 66% yield of **13**. The reaction at 100 ^{o}C with addition of 10 mol% 2-aminobenzothiazole **2a** gave 83% yield of **13**.



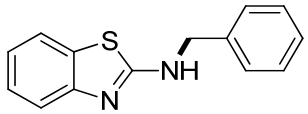
N-Benzyl-*tert*-butanesulfinamide (13). White solid. ^{1}H NMR (500 MHz, CDCl3): δ 7.35 (d, J = 4.0 Hz, 4H), 7.31-7.28(m, 1H), 4.36 (dd, J = 14.0, 4.5 Hz, 1H), 4.26 (dd, J = 14.0, 8.0 Hz, 1H), 3.49 (s, br, 1H), 1.25 (s, 9H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 138.5, 128.6, 128.1, 127.7, 55.9, 49.4, 22.7. MS (EI): m/z (%) 212 (18%), 211 (6%), 155 (34), 92 (12), 91 (100), 77 (28), 57 (40), 51 (4). This compound was known: R. Cano, D. J. Ramon and M. Yus, *J. Org. Chem.* **2011**, *76*, 5547.

Detailed Procedure for Reactions of 2-Aminothiophenol and Benzaldehyde (eq. 3 in the text). The mixture of pure PhCHO (3 mmol, 1.5 equiv., 100% purity as confirmed by GC-MS analysis) and 2-aminothiophenol **15** (2 mmol) in toluene (2 mL) was heated at 100 ^{o}C under air in a 100 mL Schlenk tube or under N_2 in a 20 mL Schlenk tube for 24 h, and then monitored by GC-MS and/or TLC. The mixture was concentrated by rotary evaporation and the residue purified by column chromatography by using ethyl acetate and petroleum ether (v/v 1/10) as the eluent. Product 2-phenylbenzothiazole **16** was obtained in 93% yield from the reaction under air and in 91% yield from the reaction under N_2, respectively.



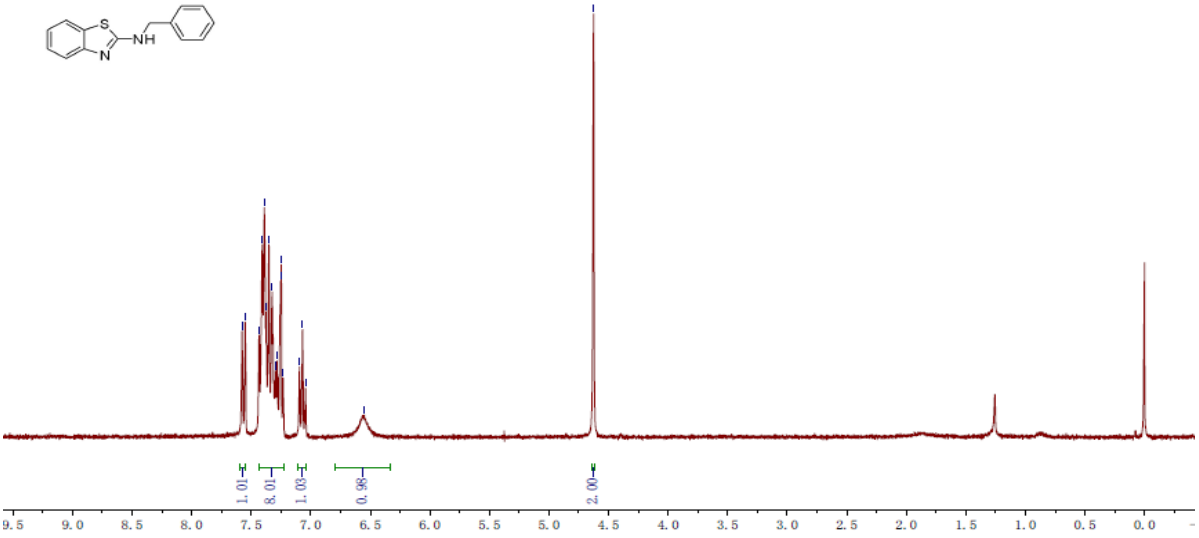
2-Phenylbenzo[d]thiazole (16). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.12-8.10 (m, 3H), 7.89-7.88 (m, 1H), 7.52-7.48 (m, 4H), 7.40-7.36 (m, 1H). ^{13}C NMR (125.4 MHz, $CDCl_3$): δ 167.9, 154.1, 135.0, 133.5, 130.8, 128.9, 127.5, 126.2, 125.1, 123.1, 121.5. MS (EI): m/z (%) 212 (17), 211 (100), 210 (22), 184 (6), 108 (24), 106 (6), 92 (5), 82 (8), 69 (13), 63 (6), 58 (4). This compound was known: Azizi, N.; Amiri, A. K.; Baghi, R.; Bolourtchian, M.; Hashemi, M. M. *Monatsh Chem.* **2009**, *140*, 1471-1473.

^{1}H and ^{13}C NMR of All Products

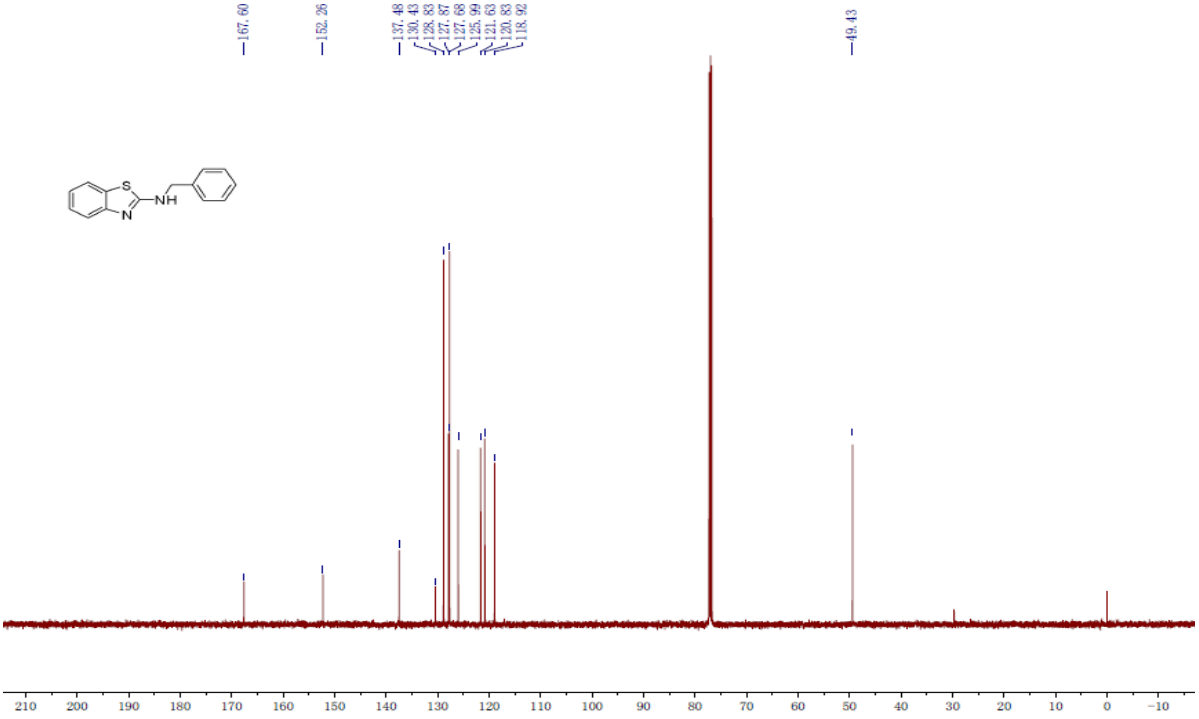


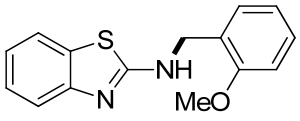
5a

^{1}H NMR



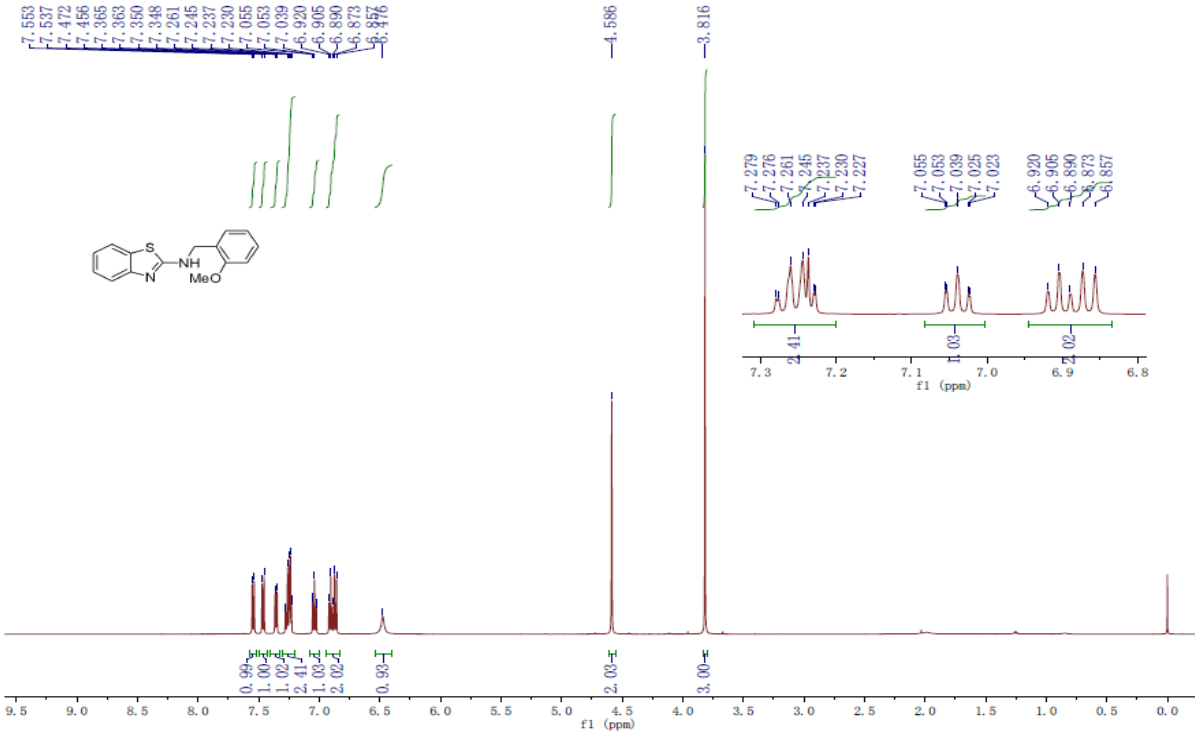
^{13}C NMR





5b

^{1}H NMR



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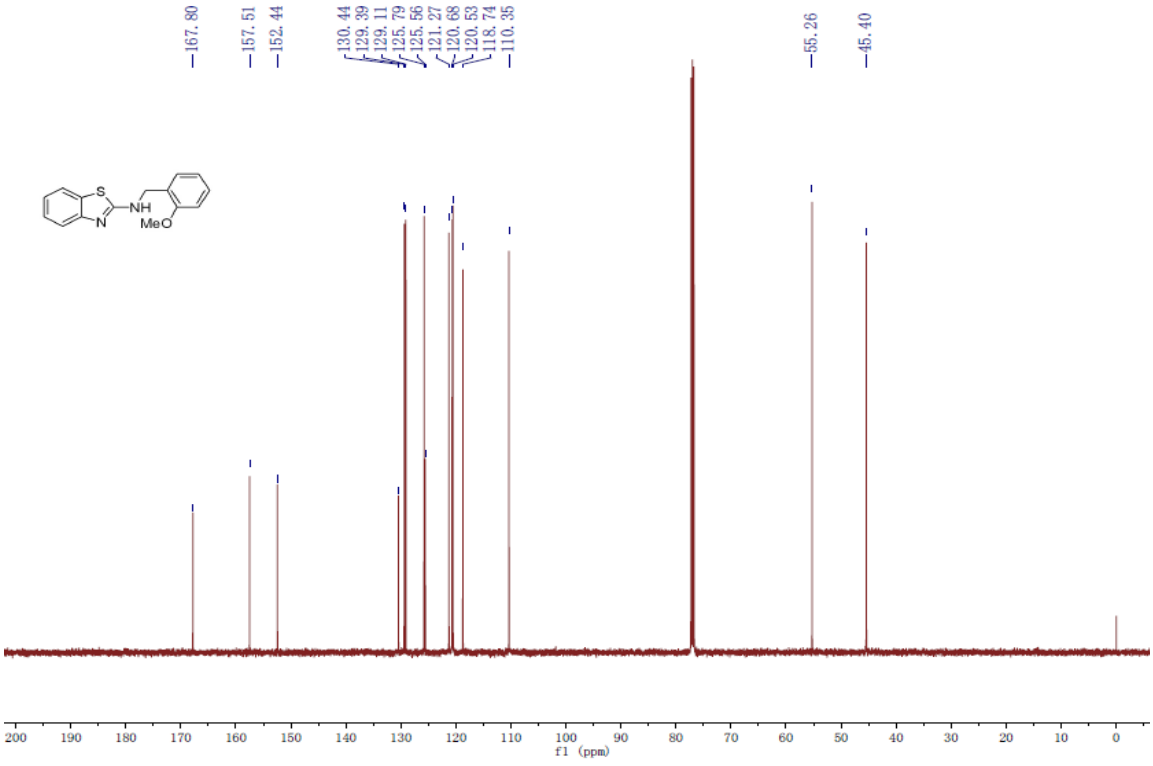

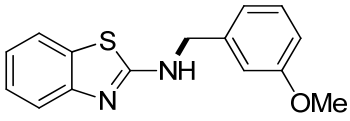

5c

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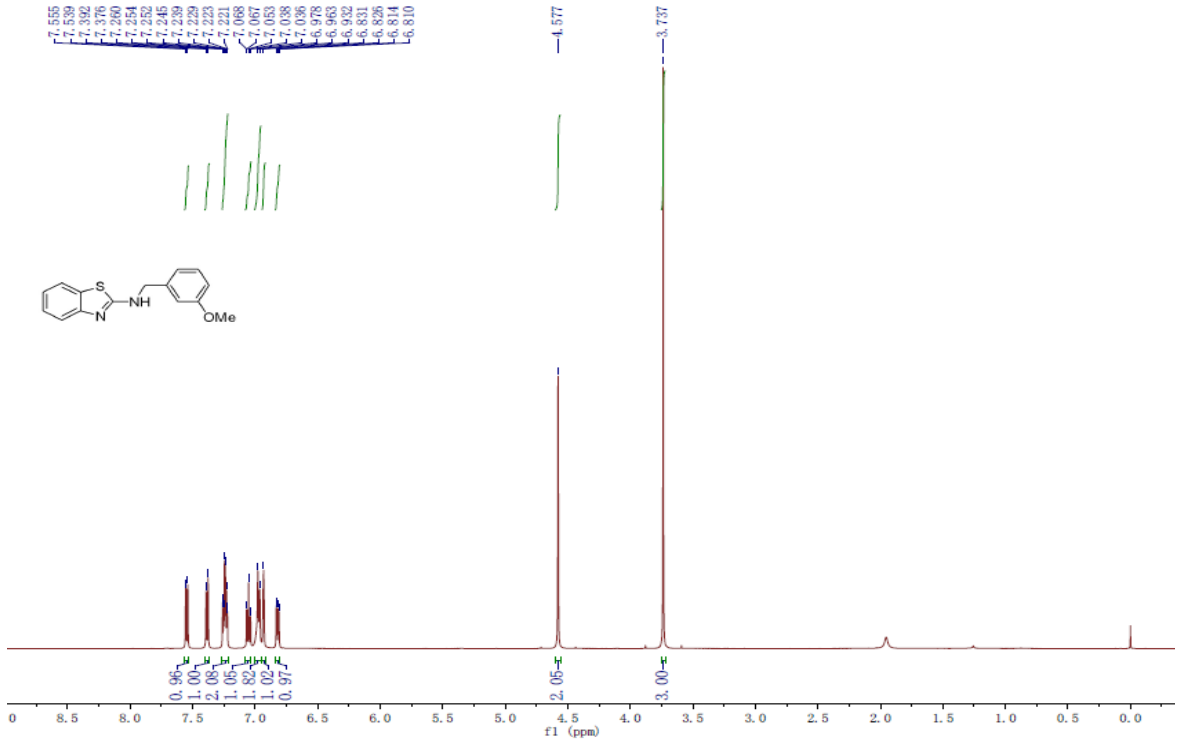
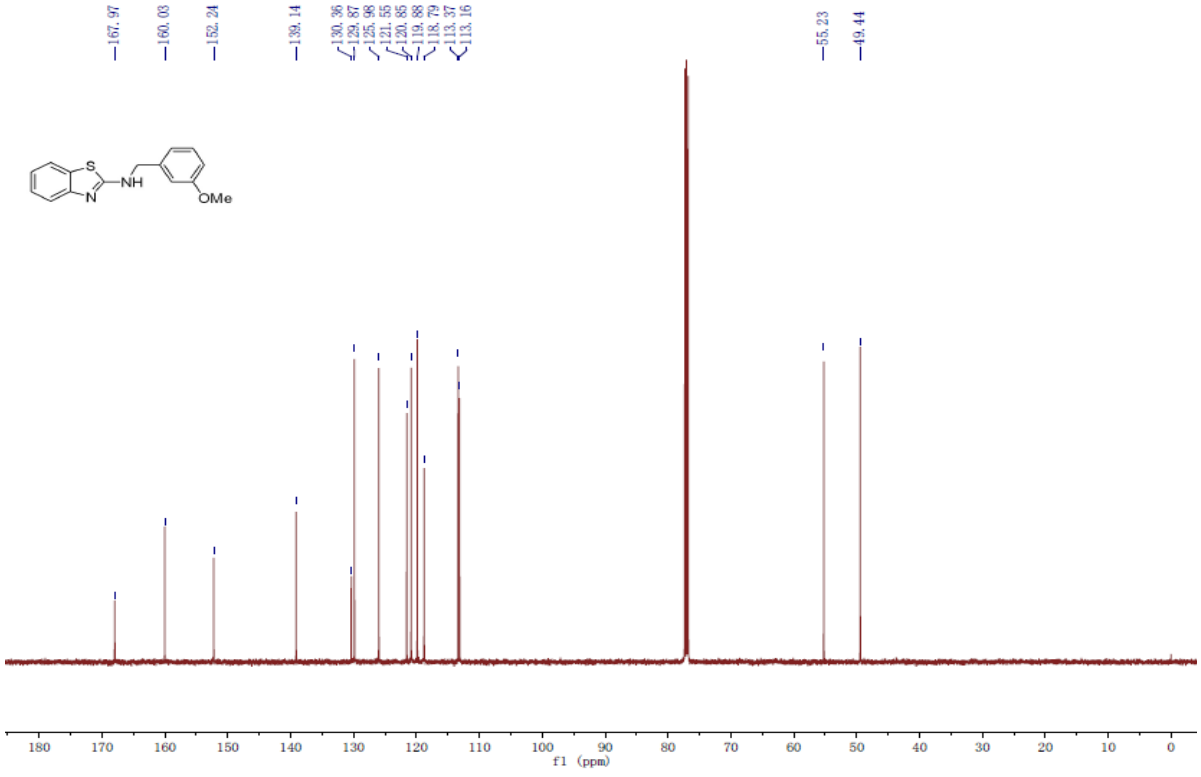
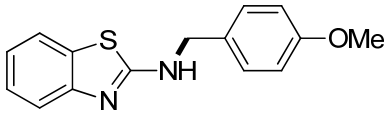


^{13}C NMR





5d

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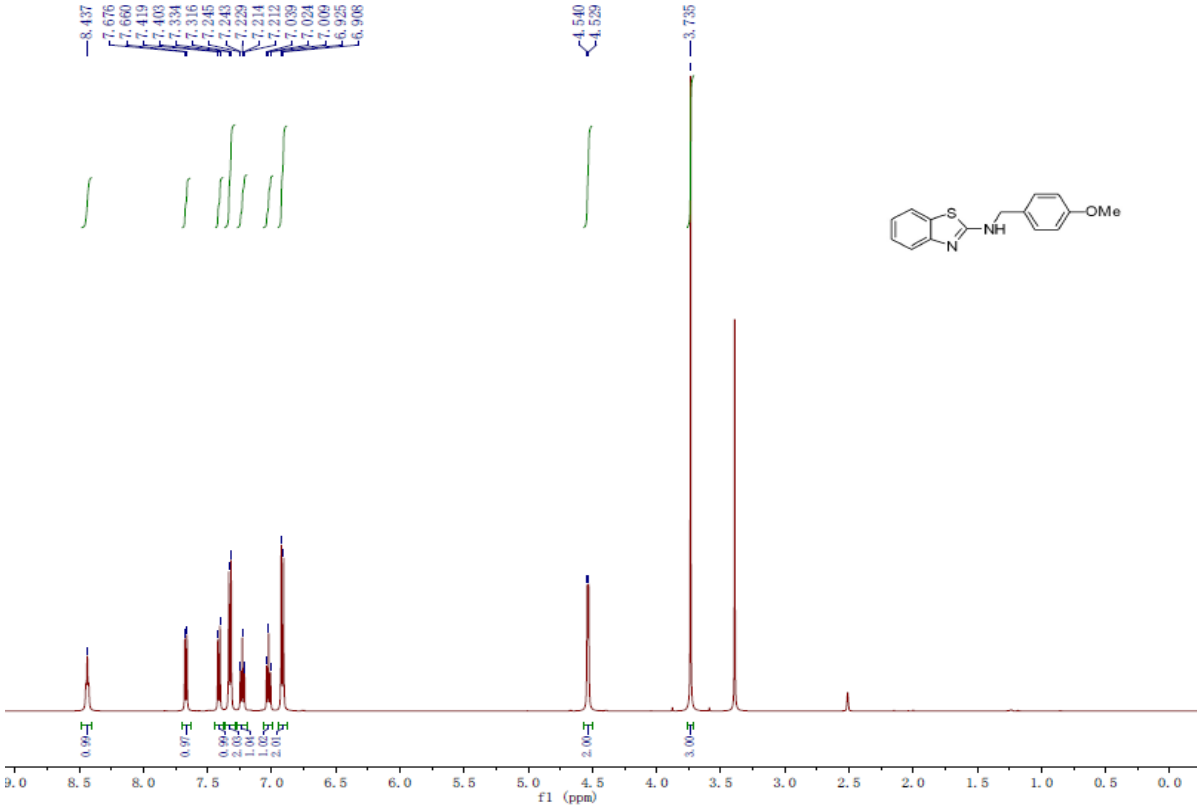

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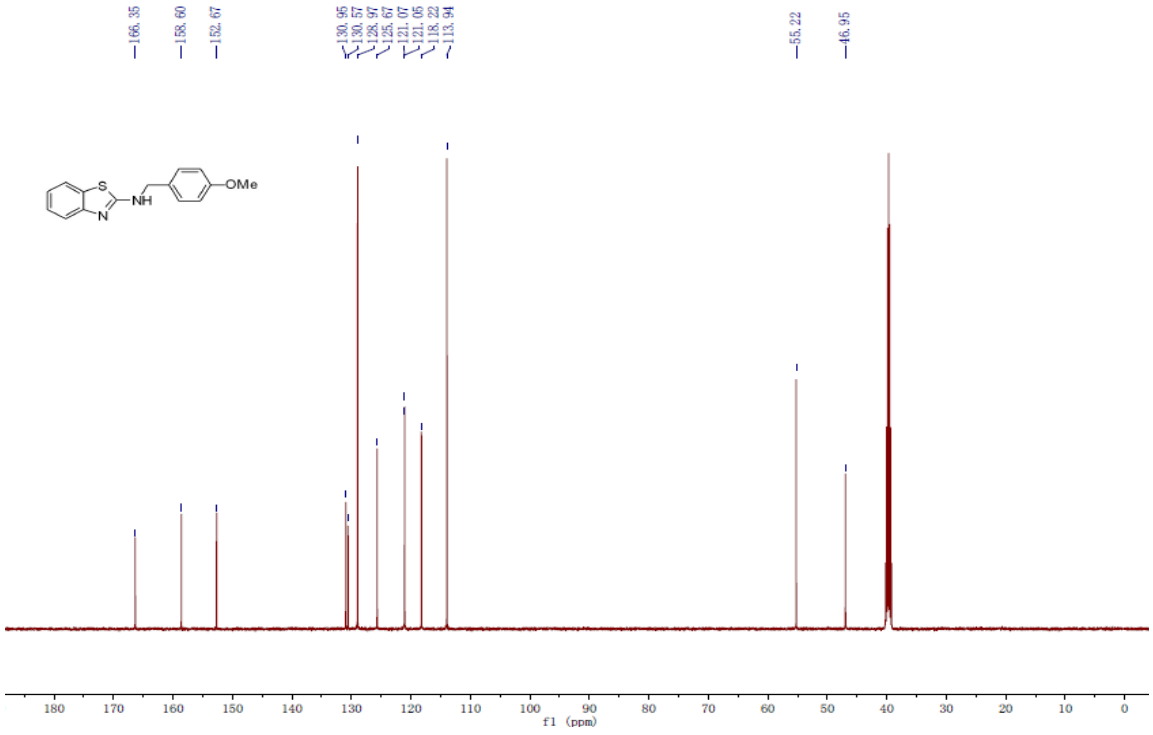

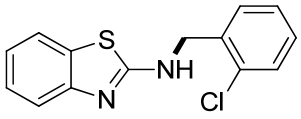

5e

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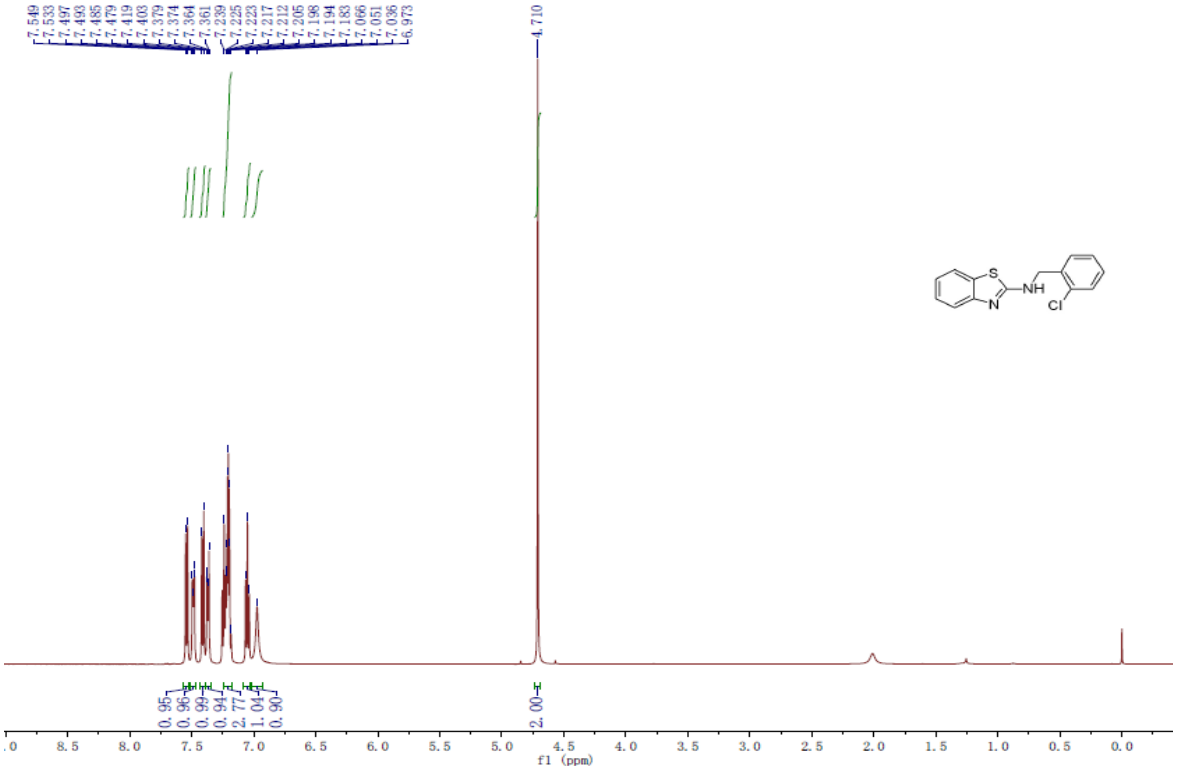
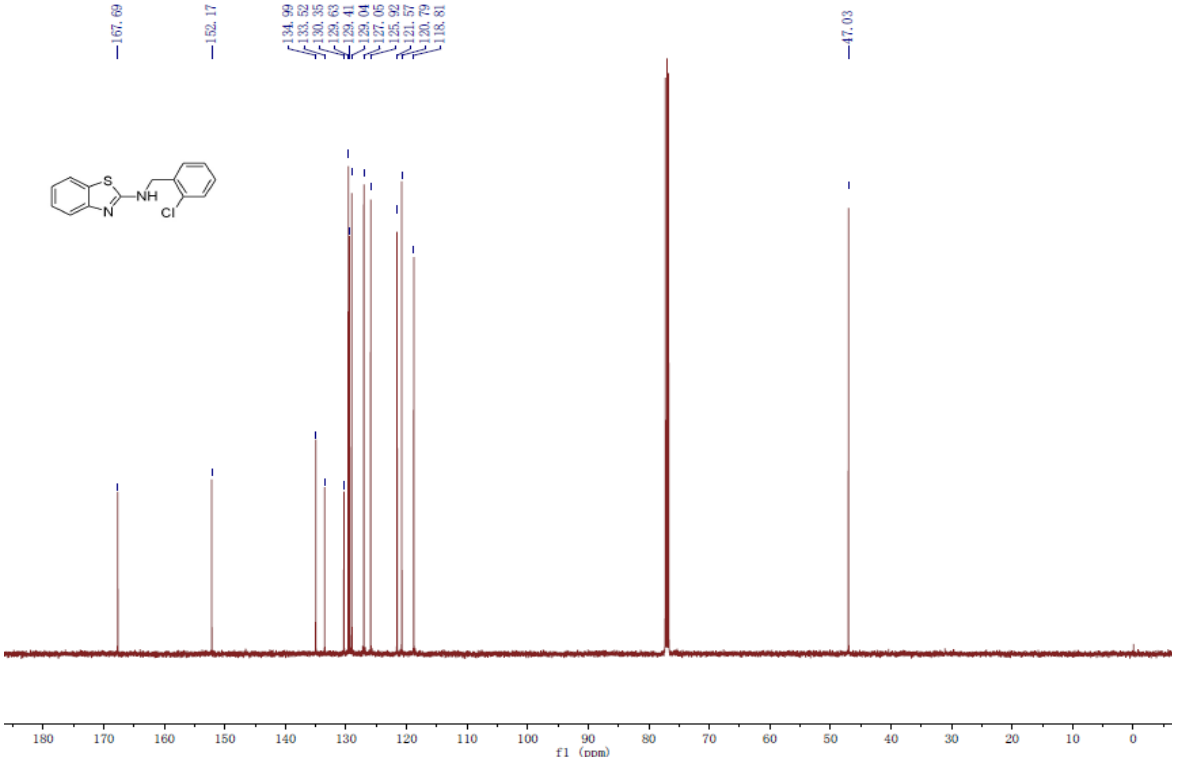
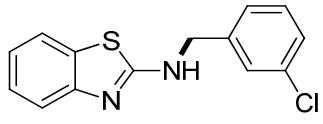


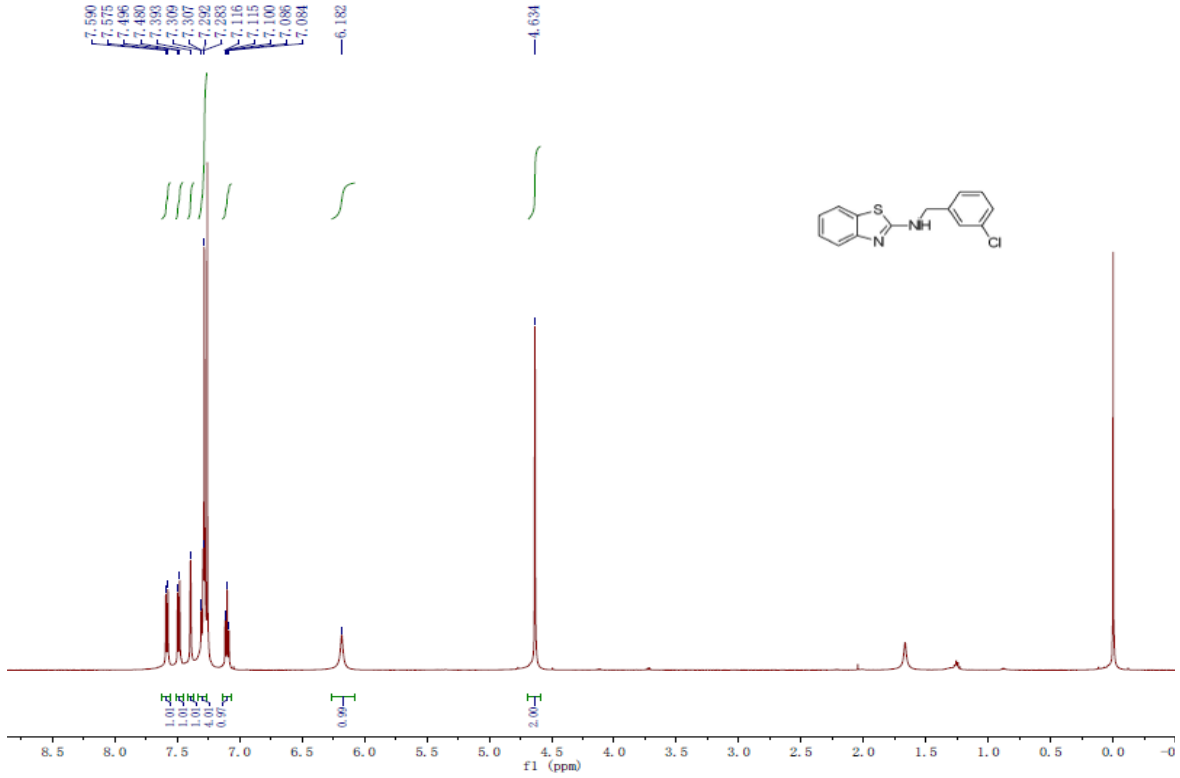
^{13}C NMR



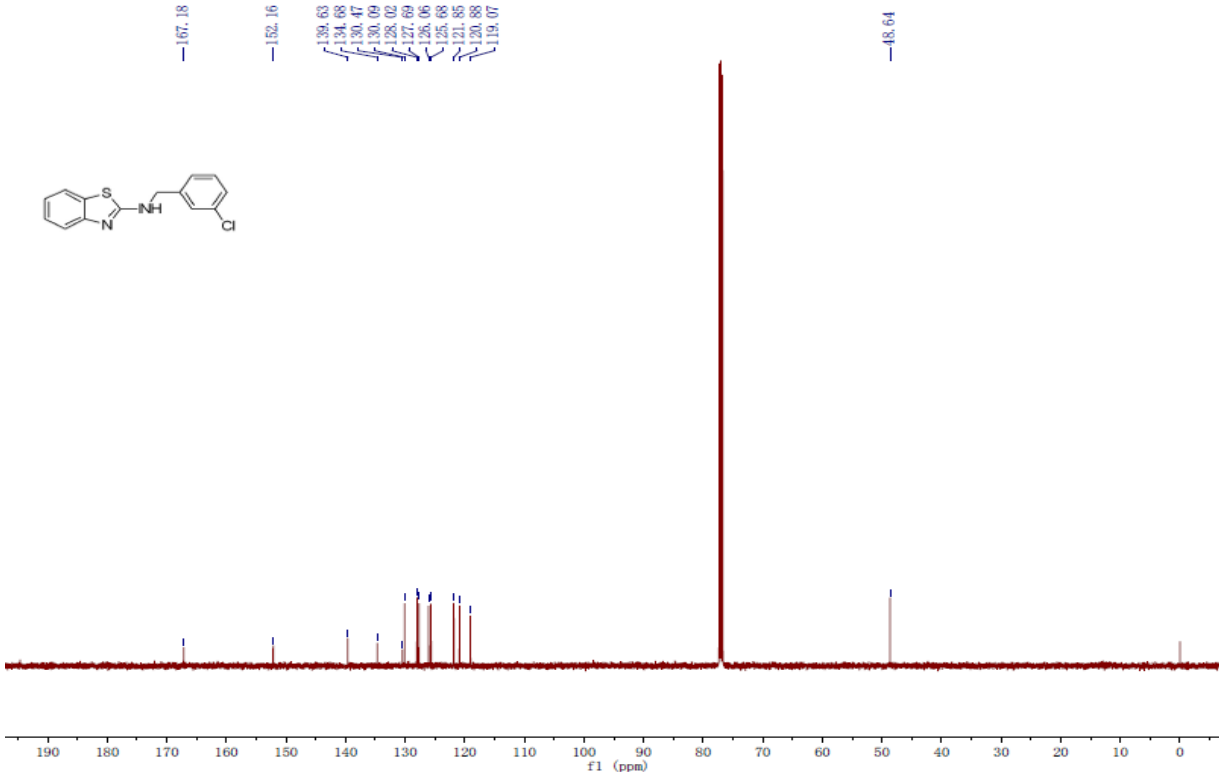


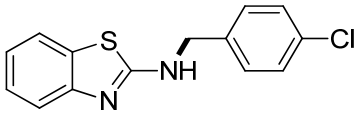
5f

^{1}H NMR



^{13}C NMR





5g

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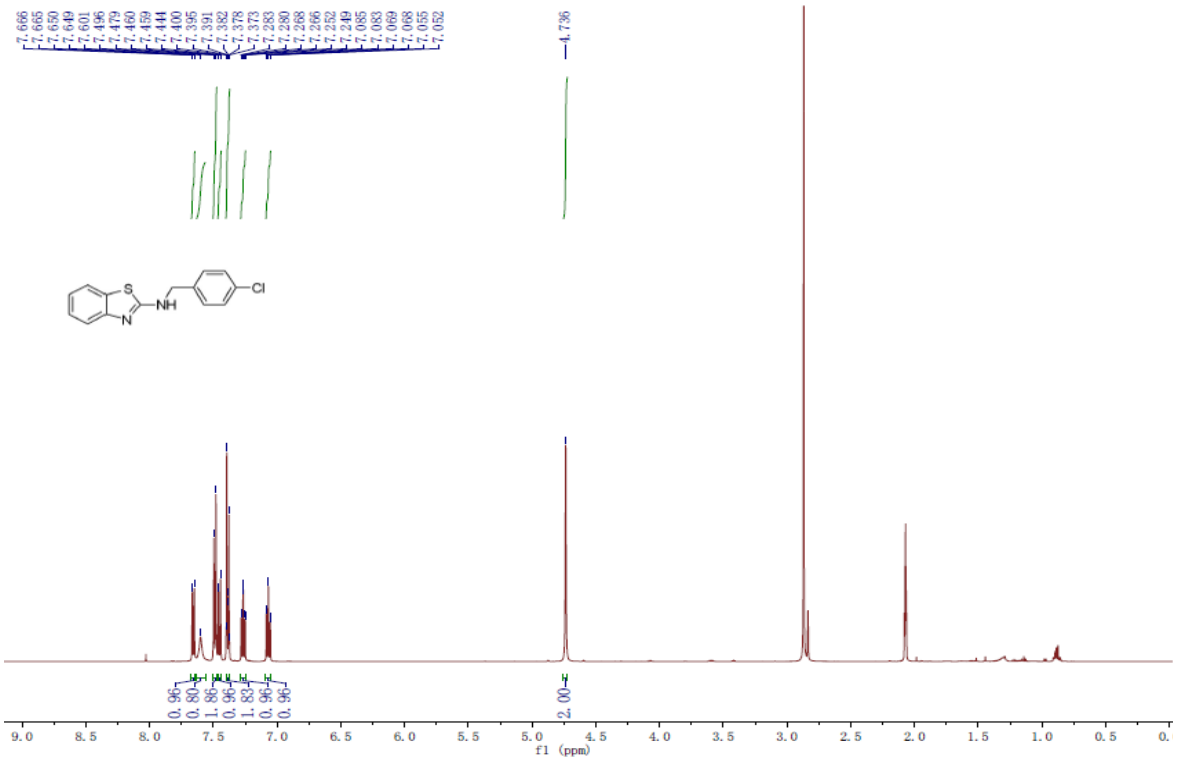
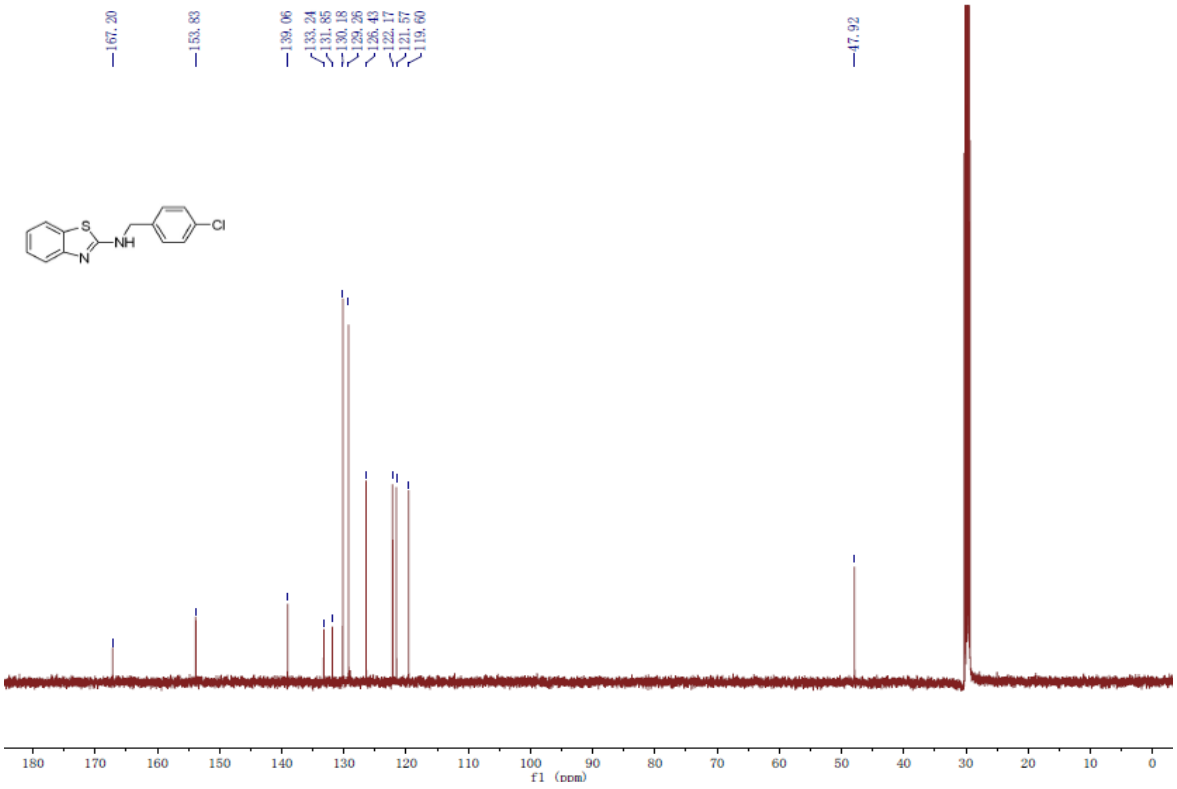
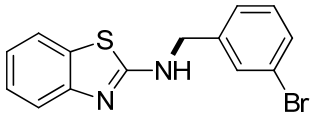


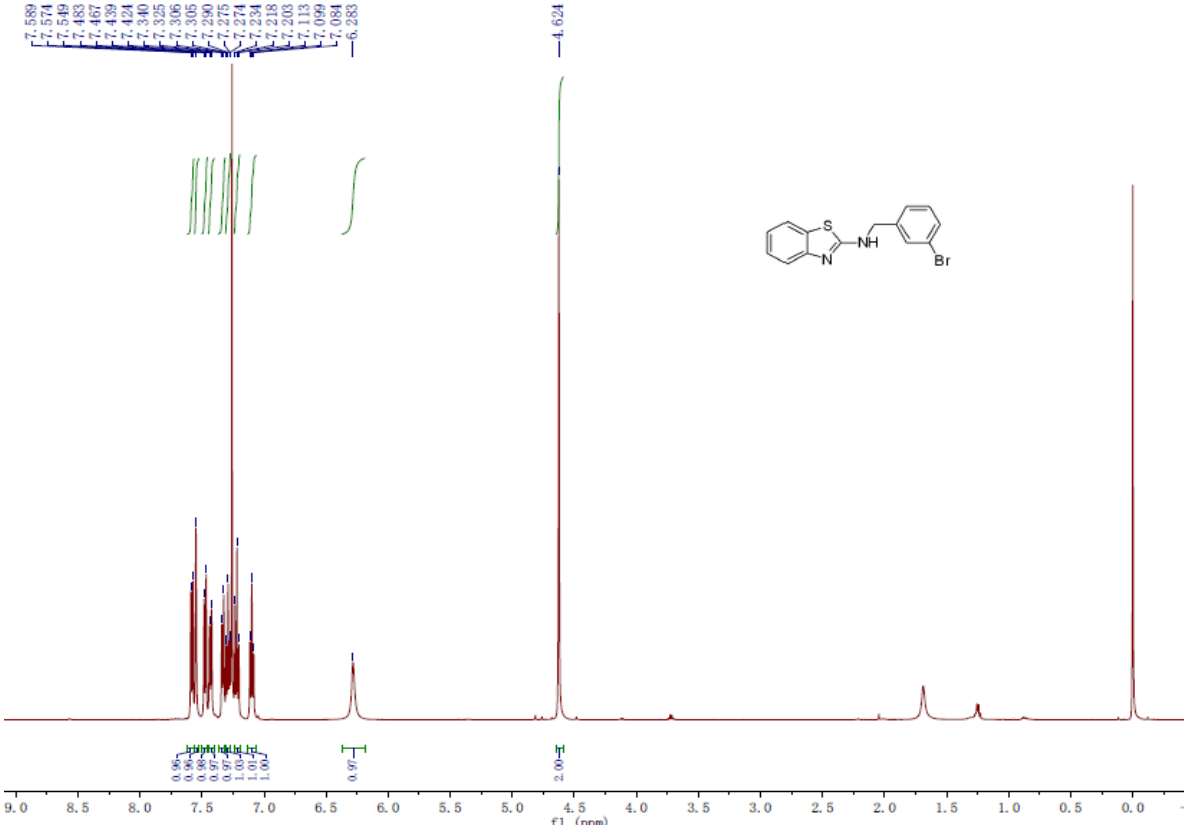
^{13}C NMR



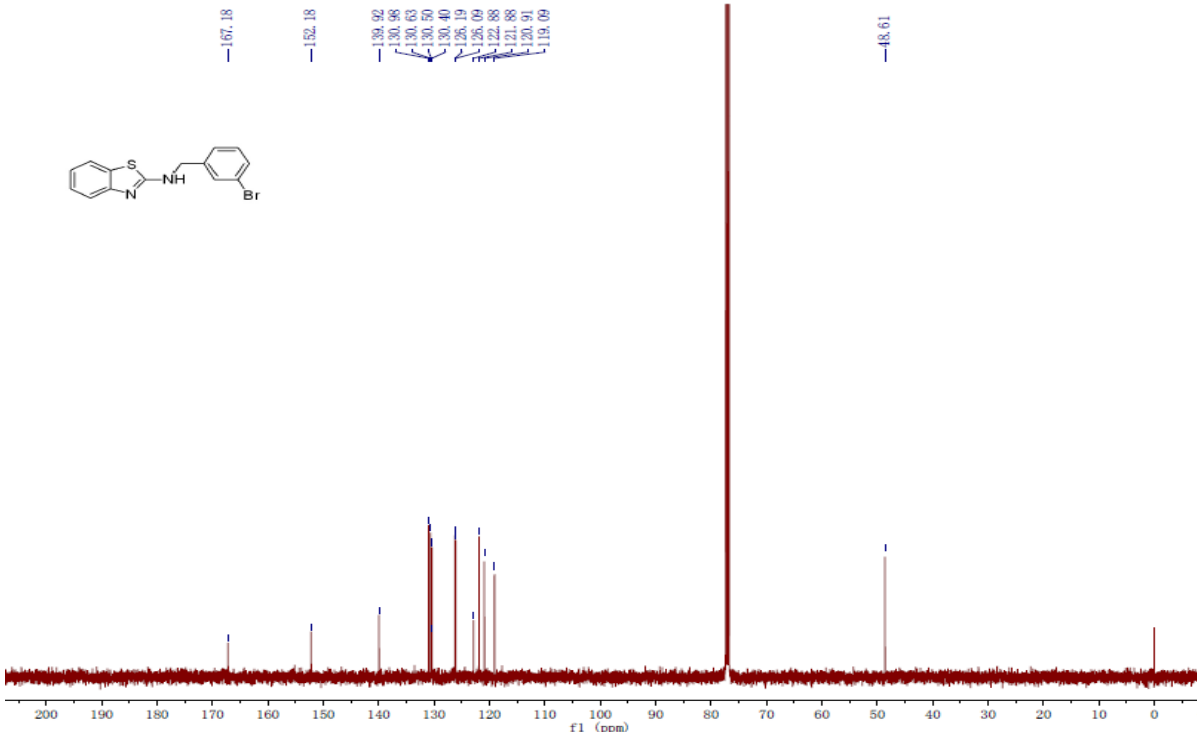


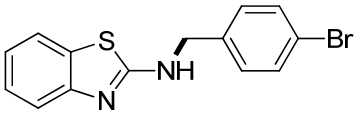
5h

^{1}H NMR



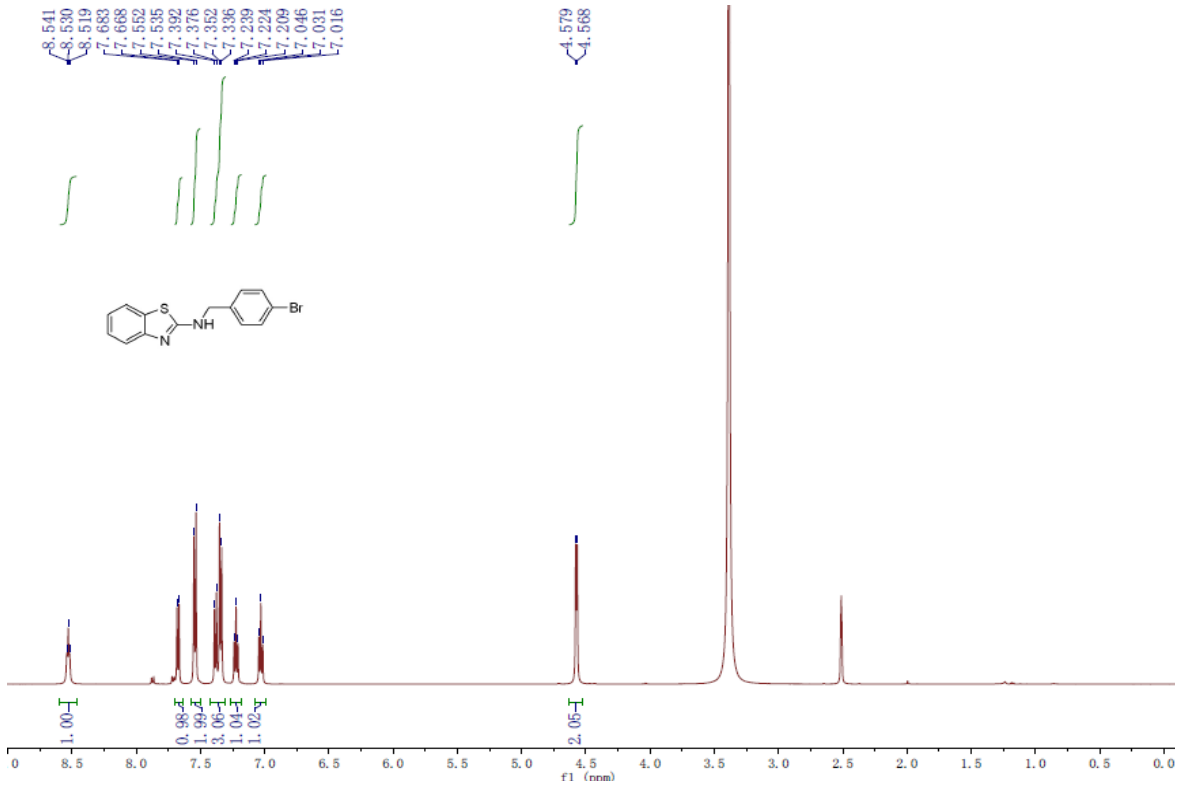
^{13}C NMR



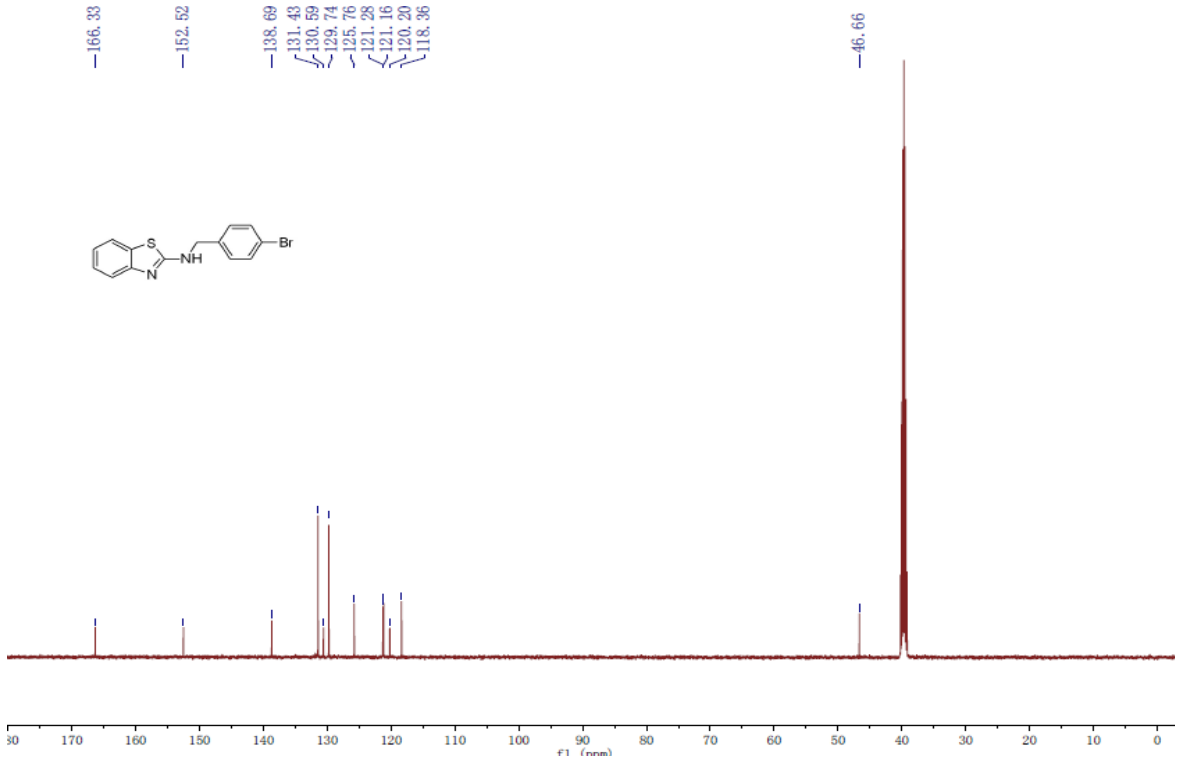


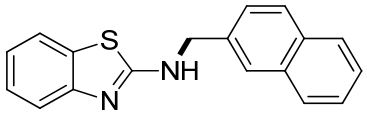
5i

^{1}H NMR



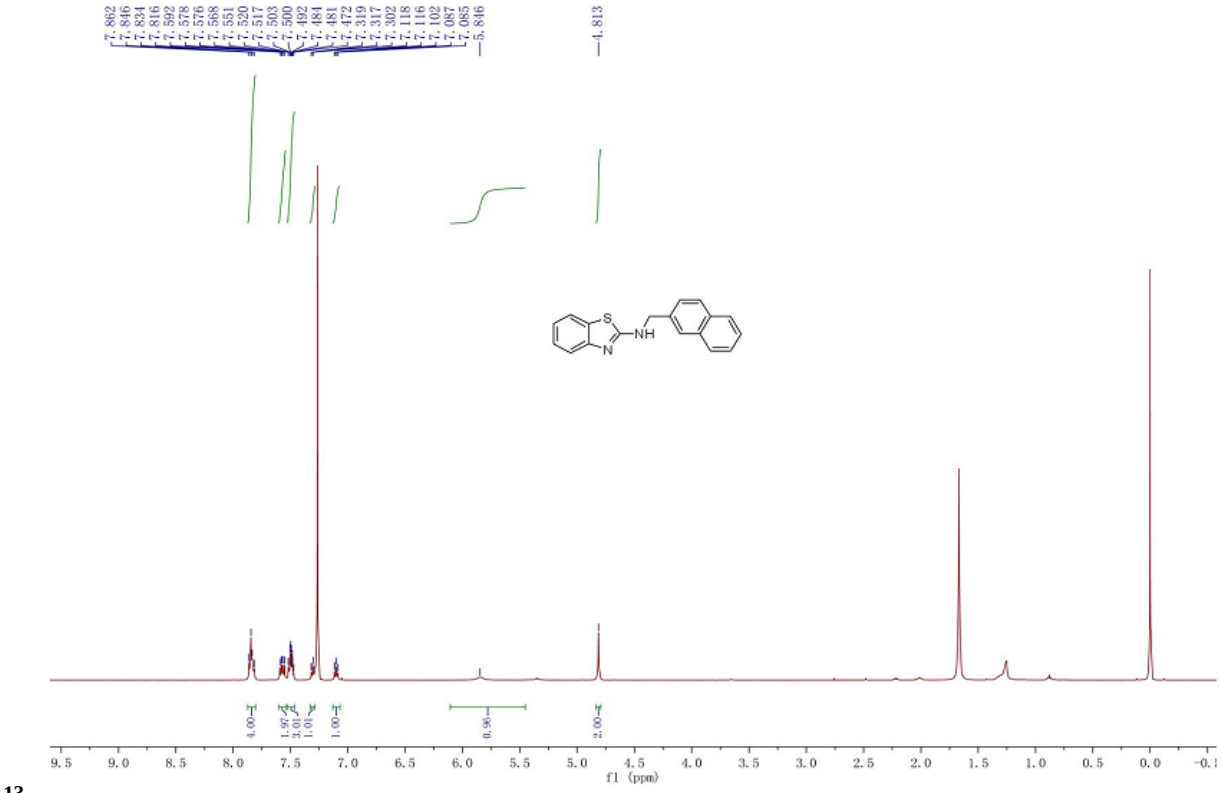
^{13}C NMR



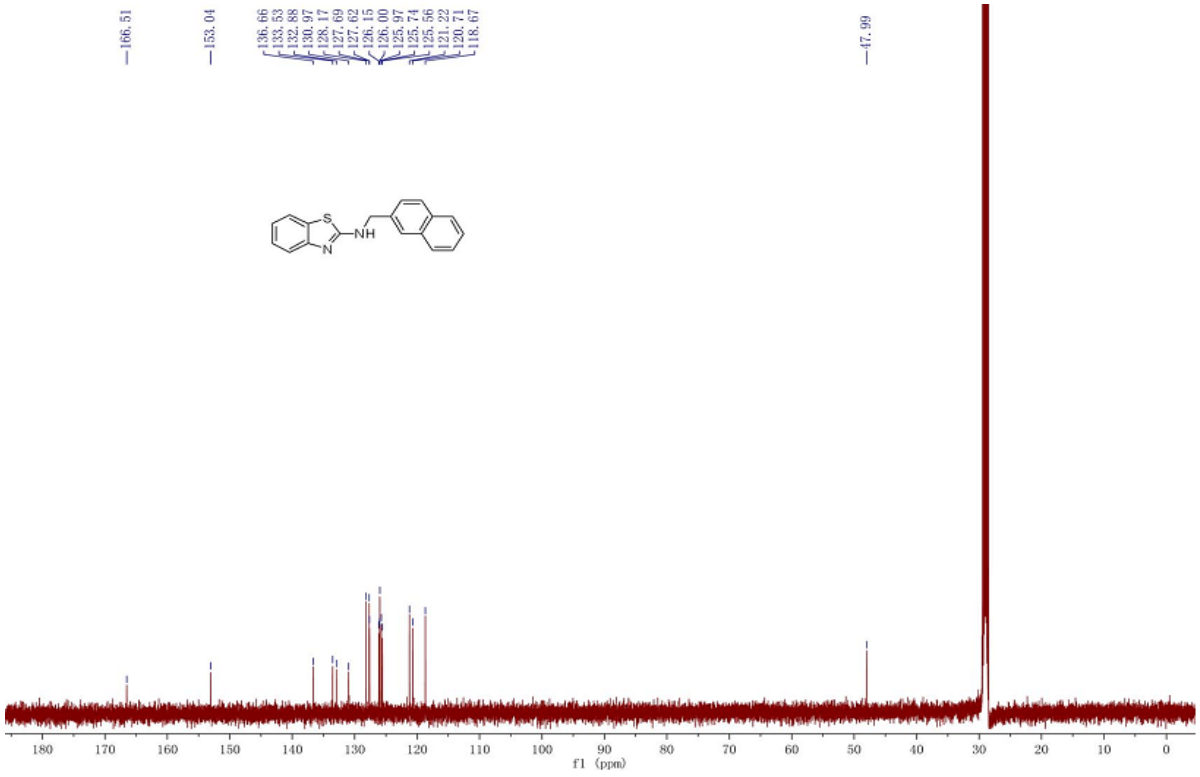


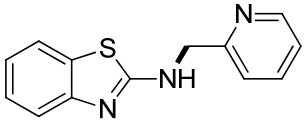
5j

^{1}H NMR



^{13}C NMR





5k

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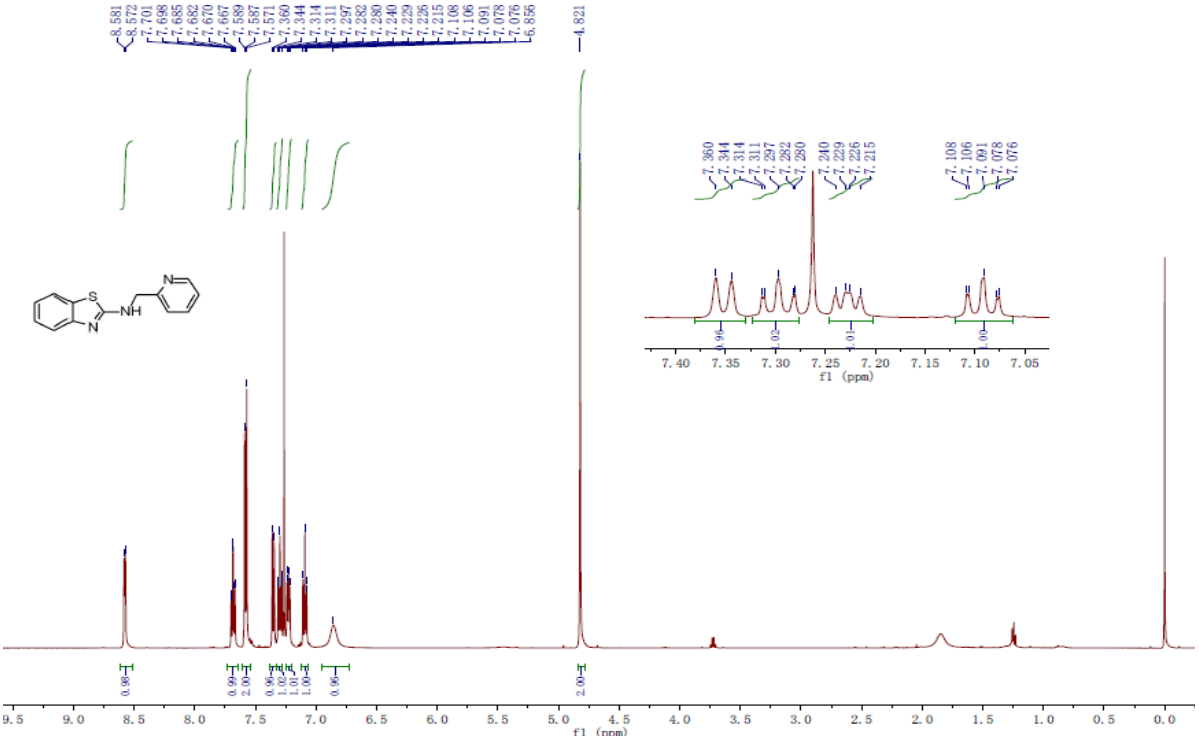
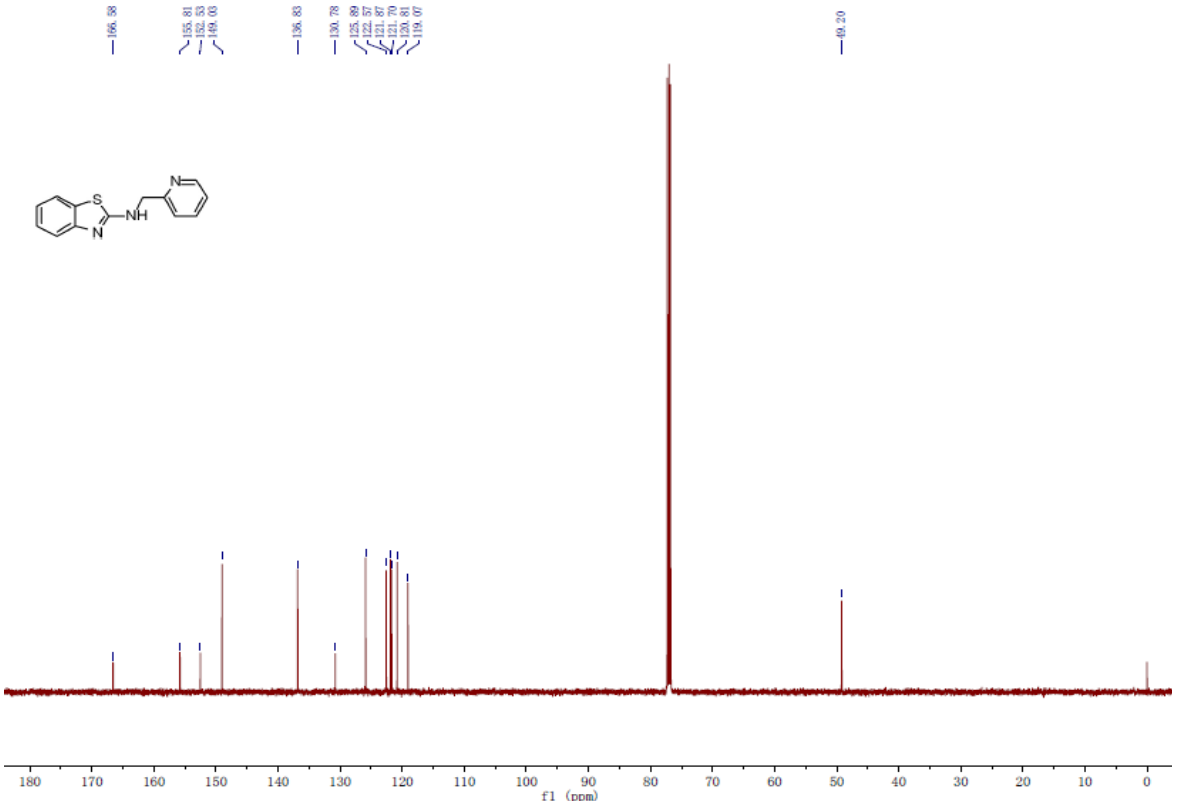
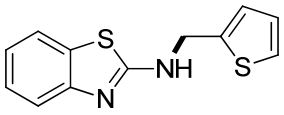


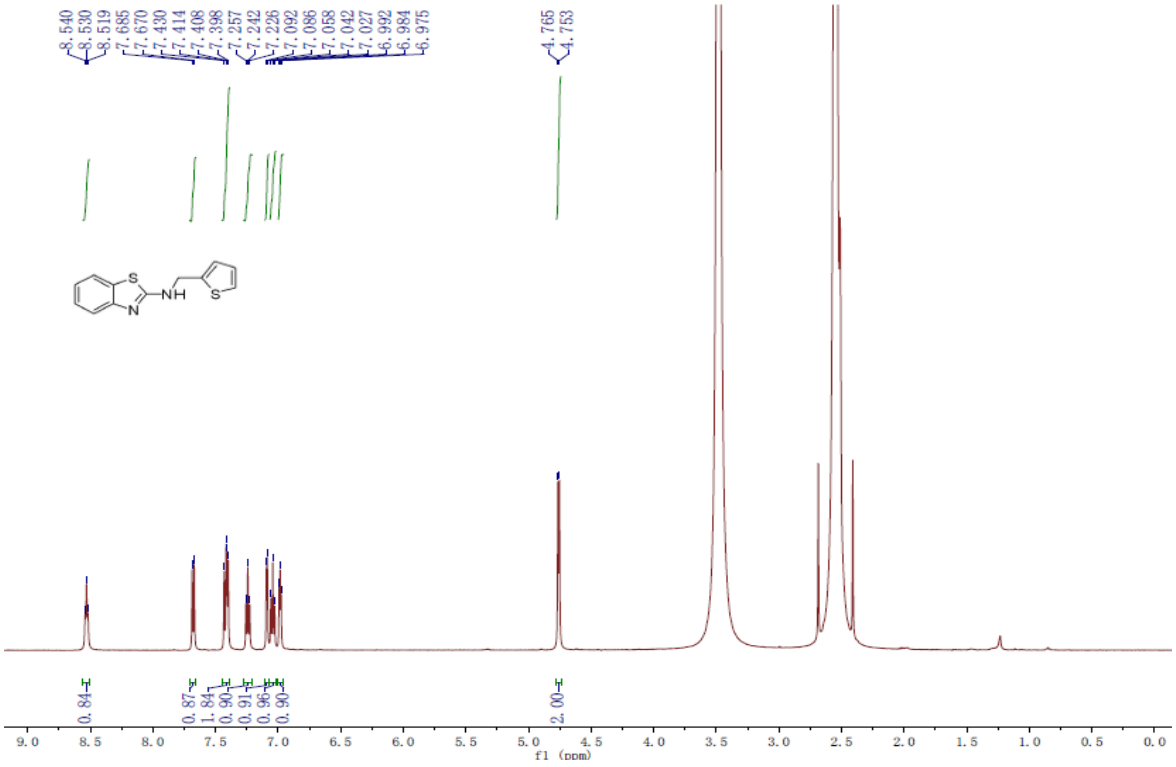
^{13}C NMR



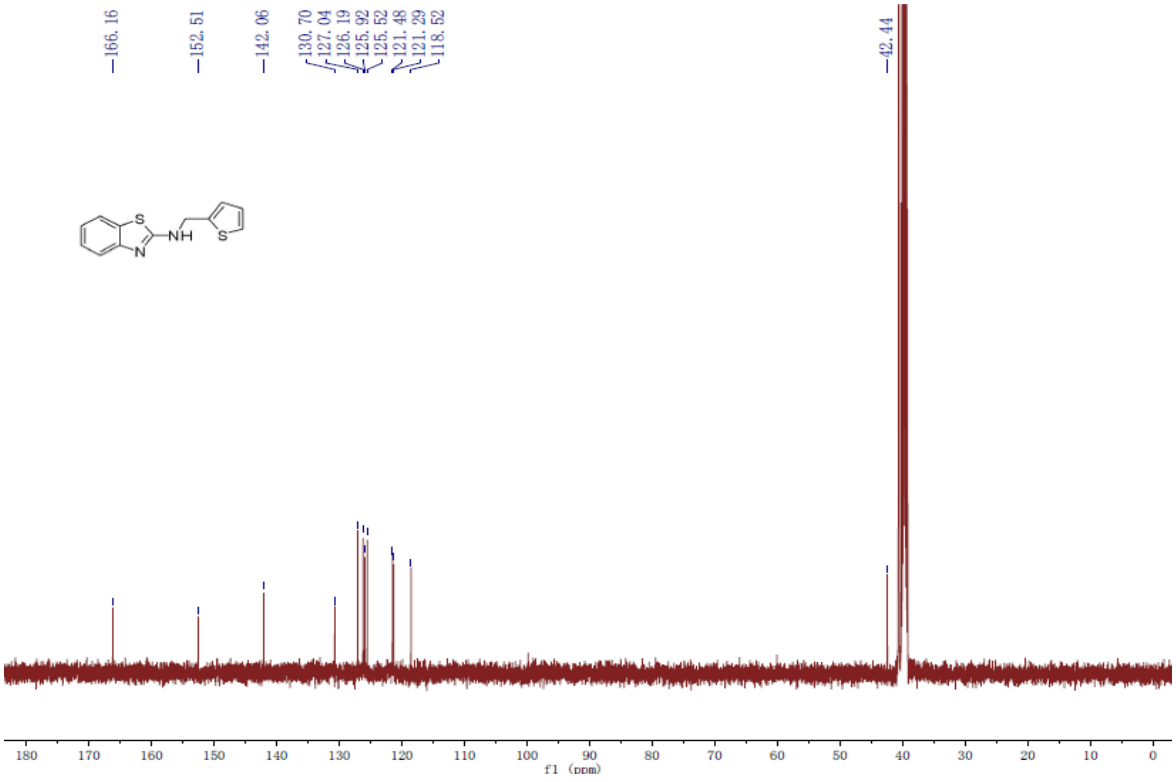


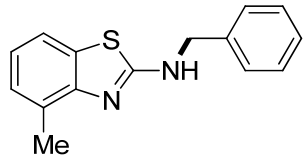
5l

^{1}H NMR



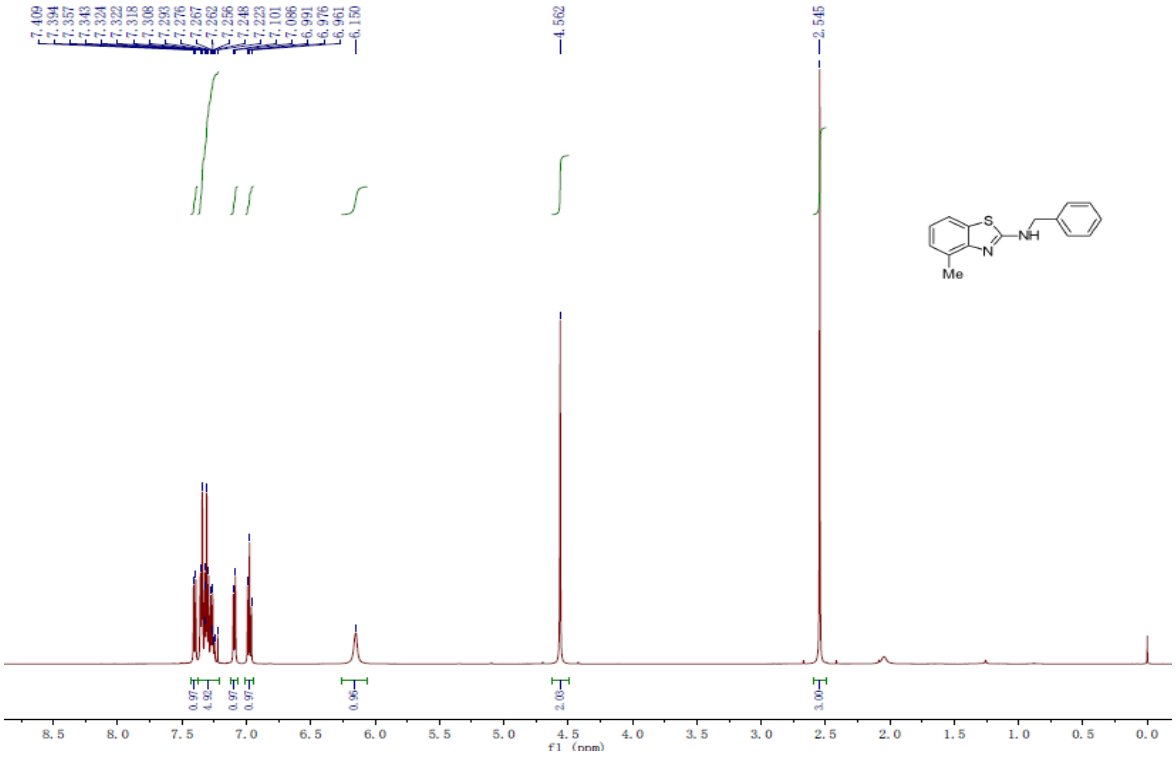
^{13}C NMR



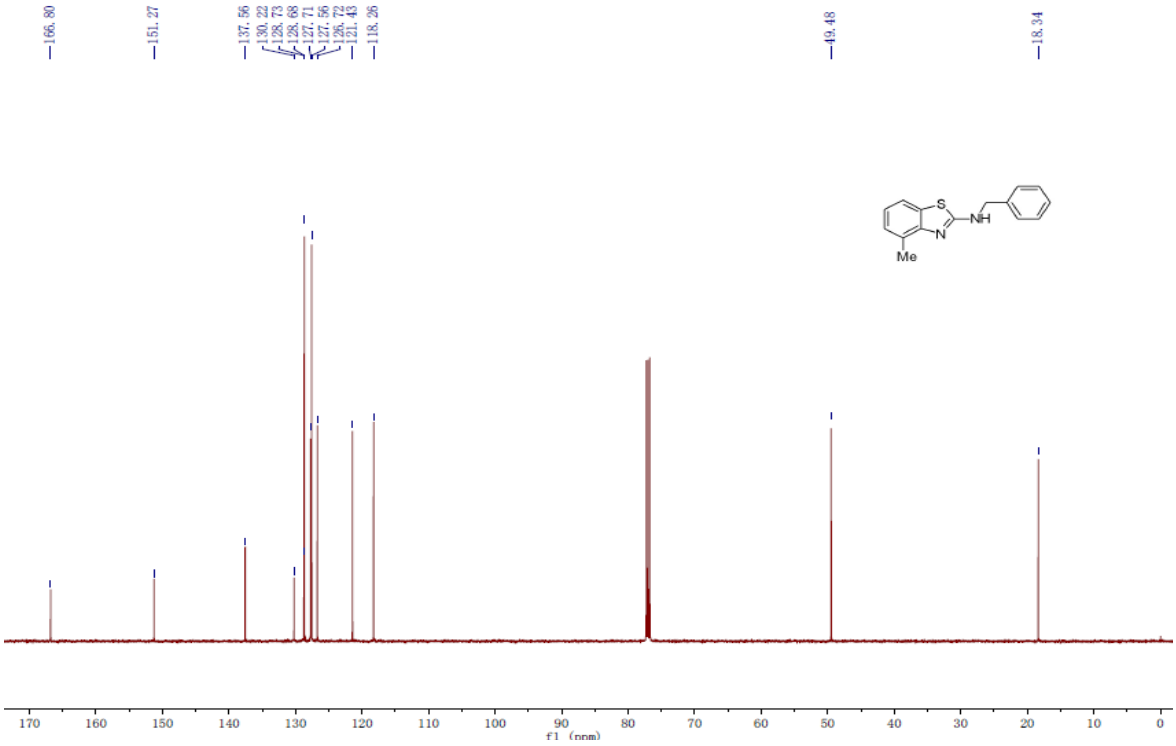


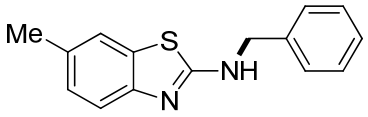
5m

^{1}H NMR



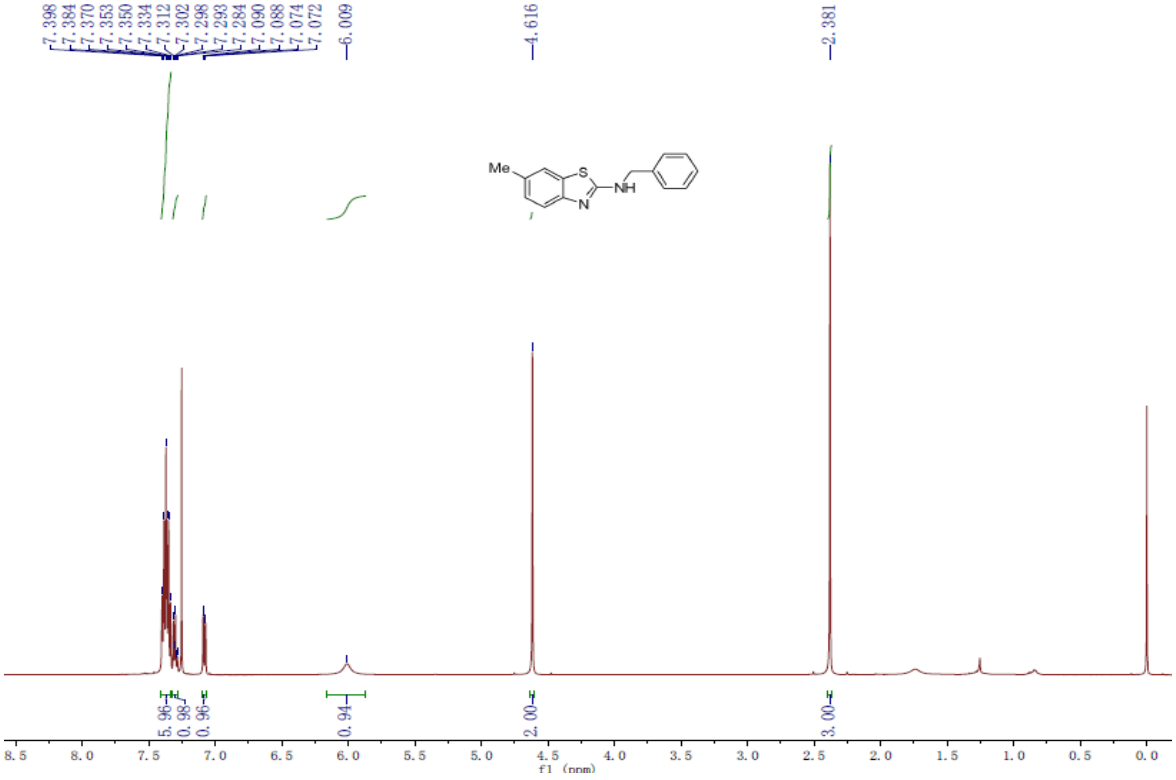
^{13}C NMR



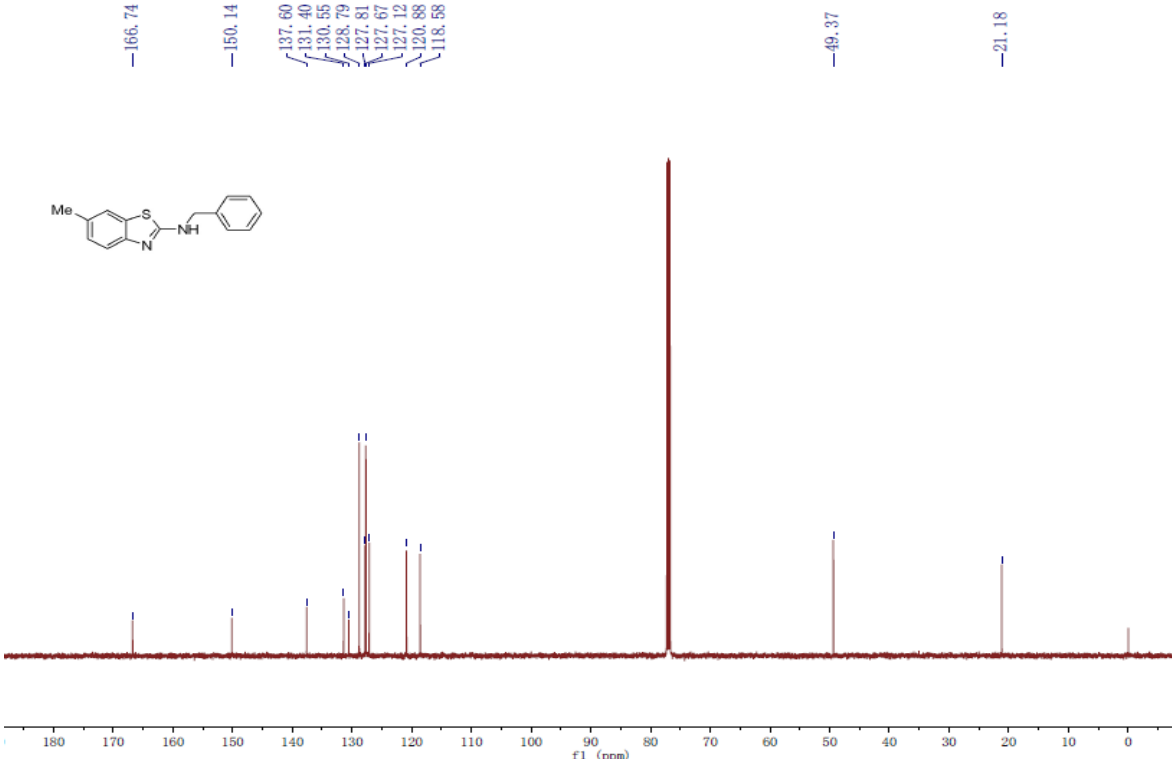


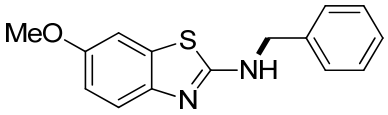
5n

^{1}H NMR



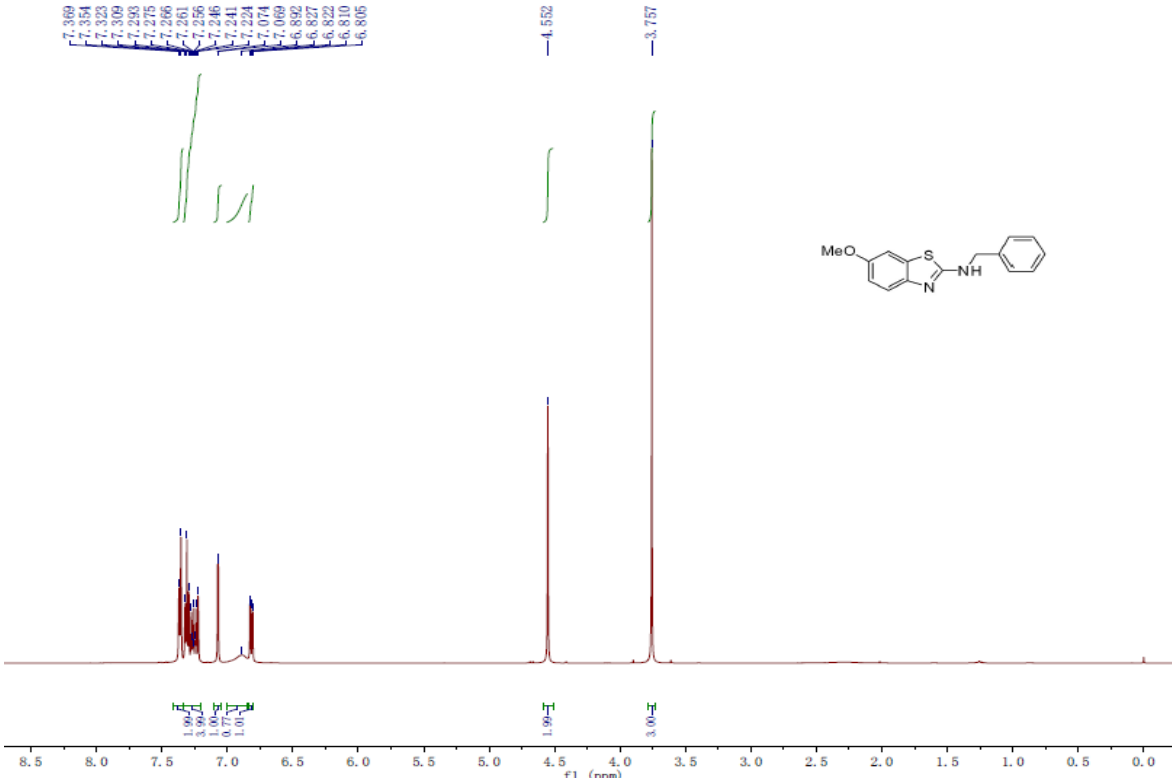
^{13}C NMR



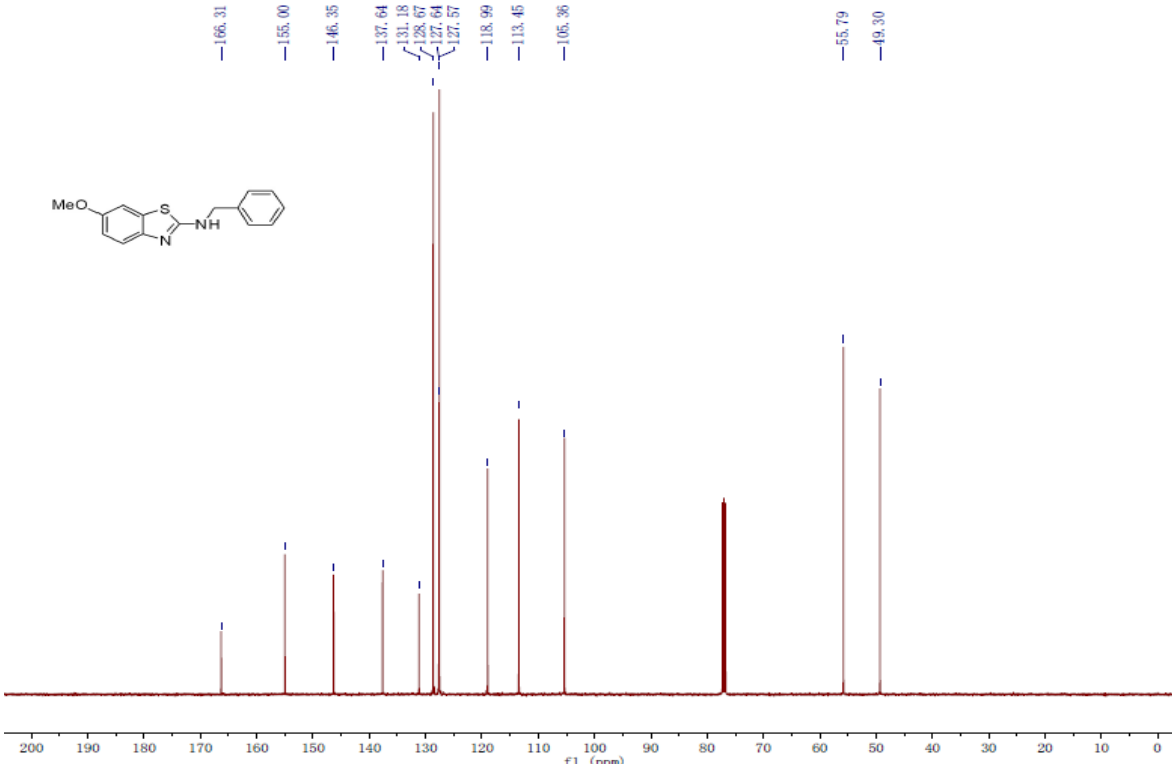


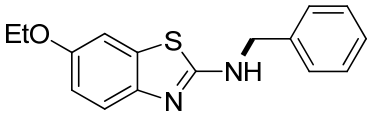
5o

^{1}H NMR



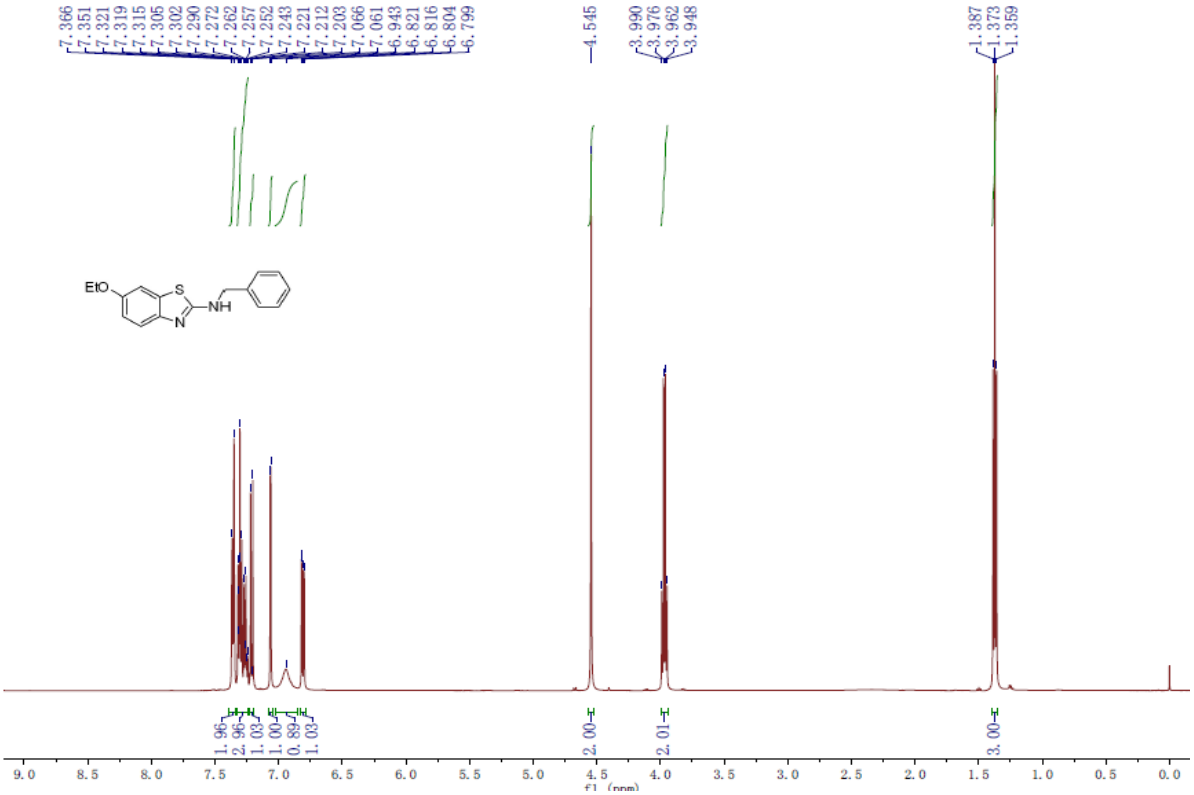
^{13}C NMR



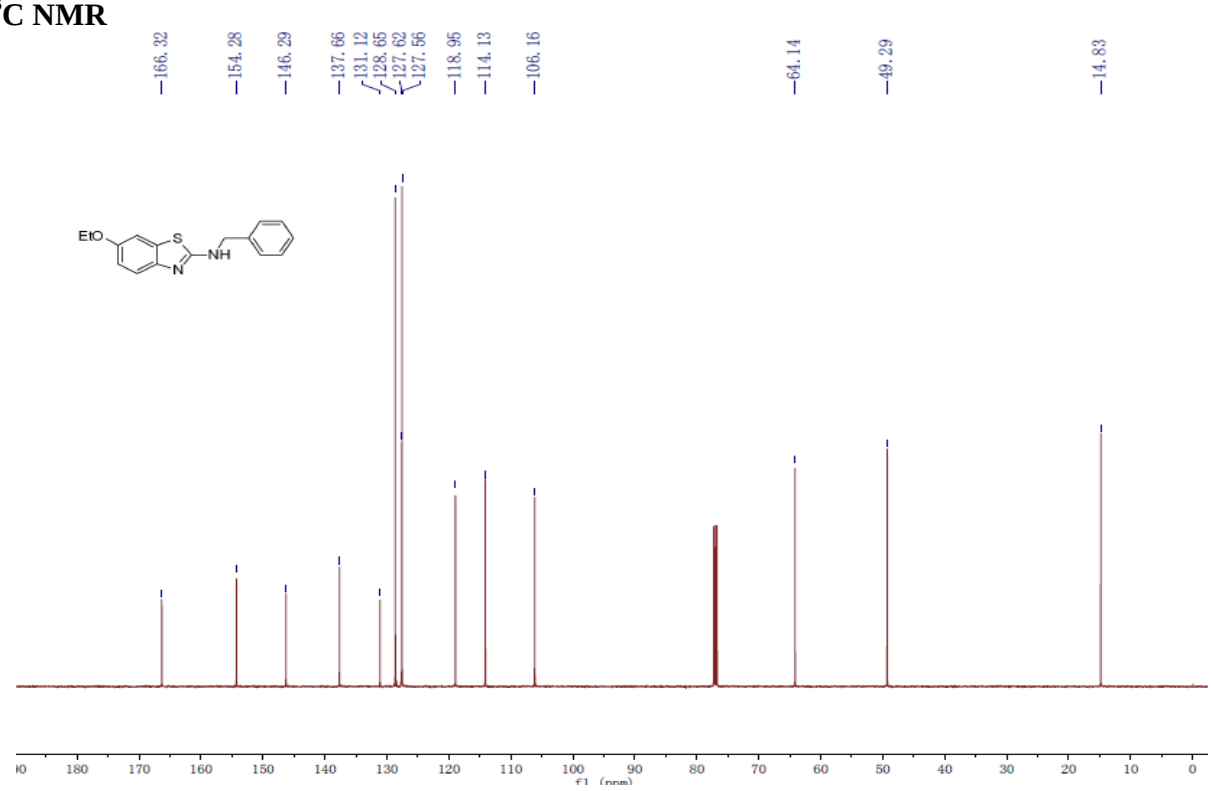


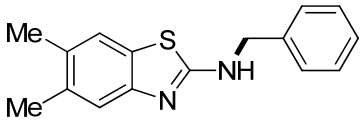
5p

^{1}H NMR



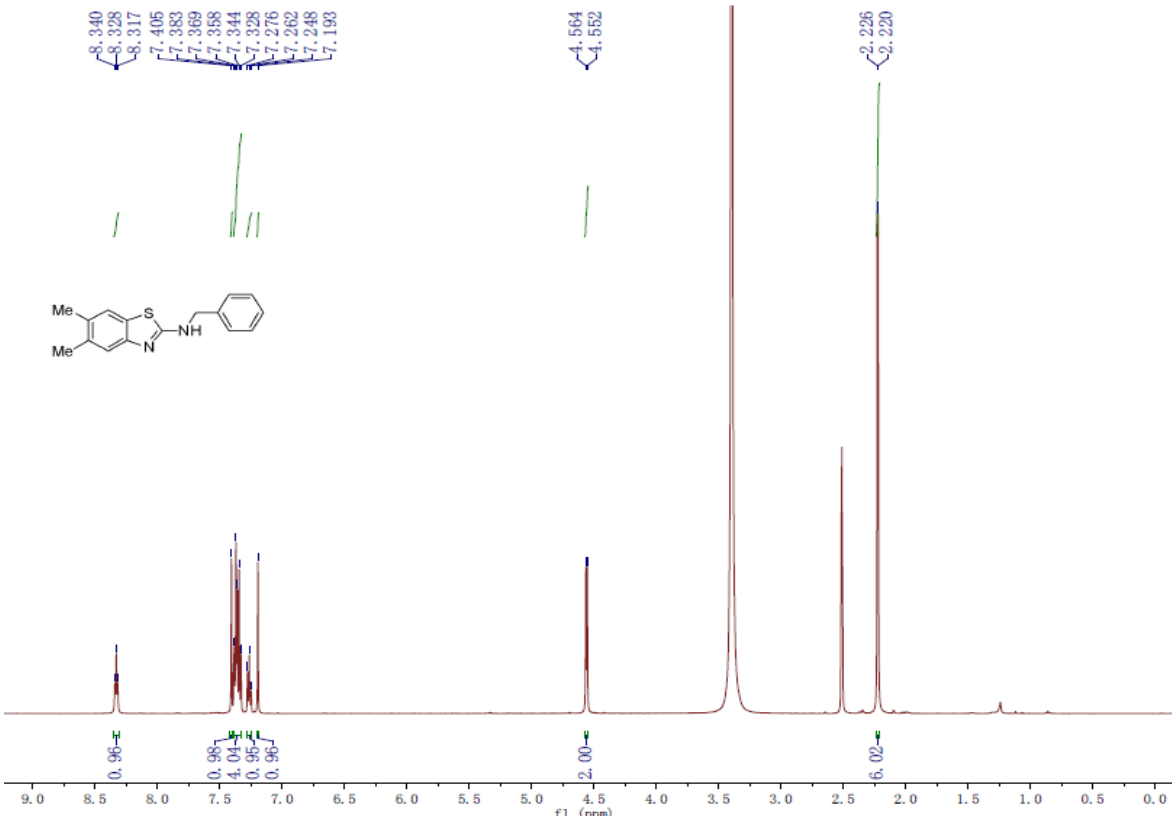
^{13}C NMR



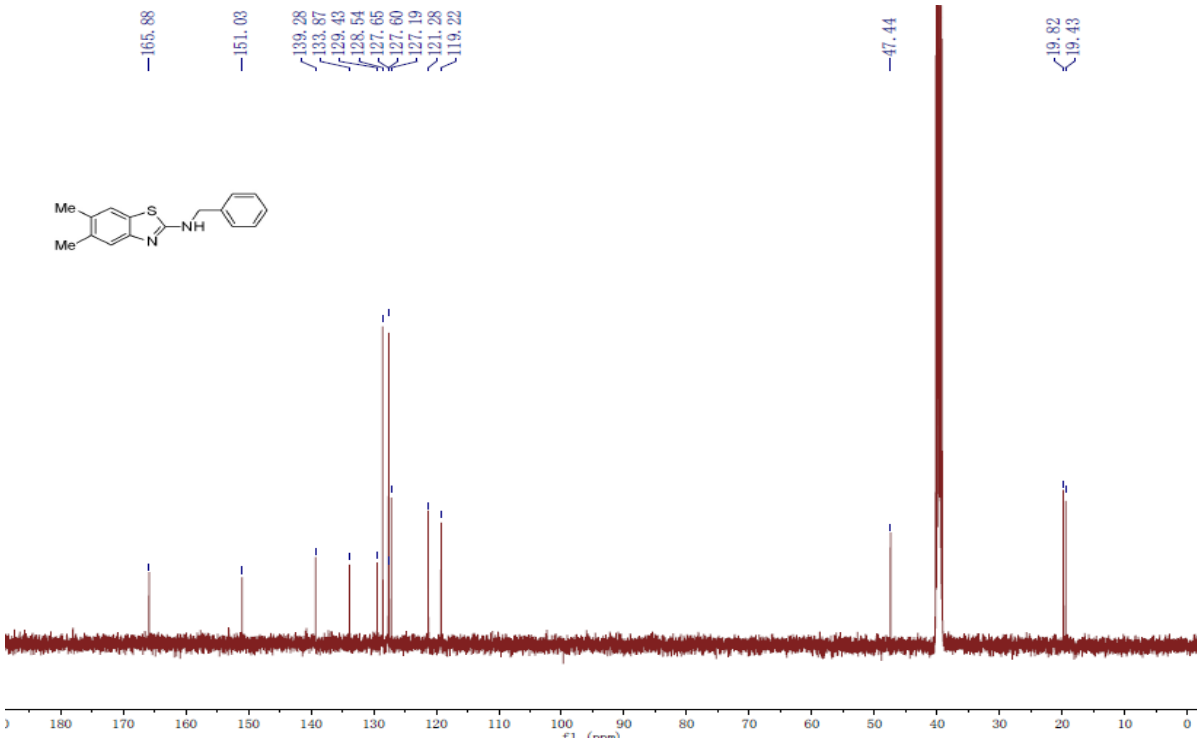


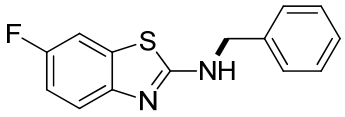
5q

^{1}H NMR



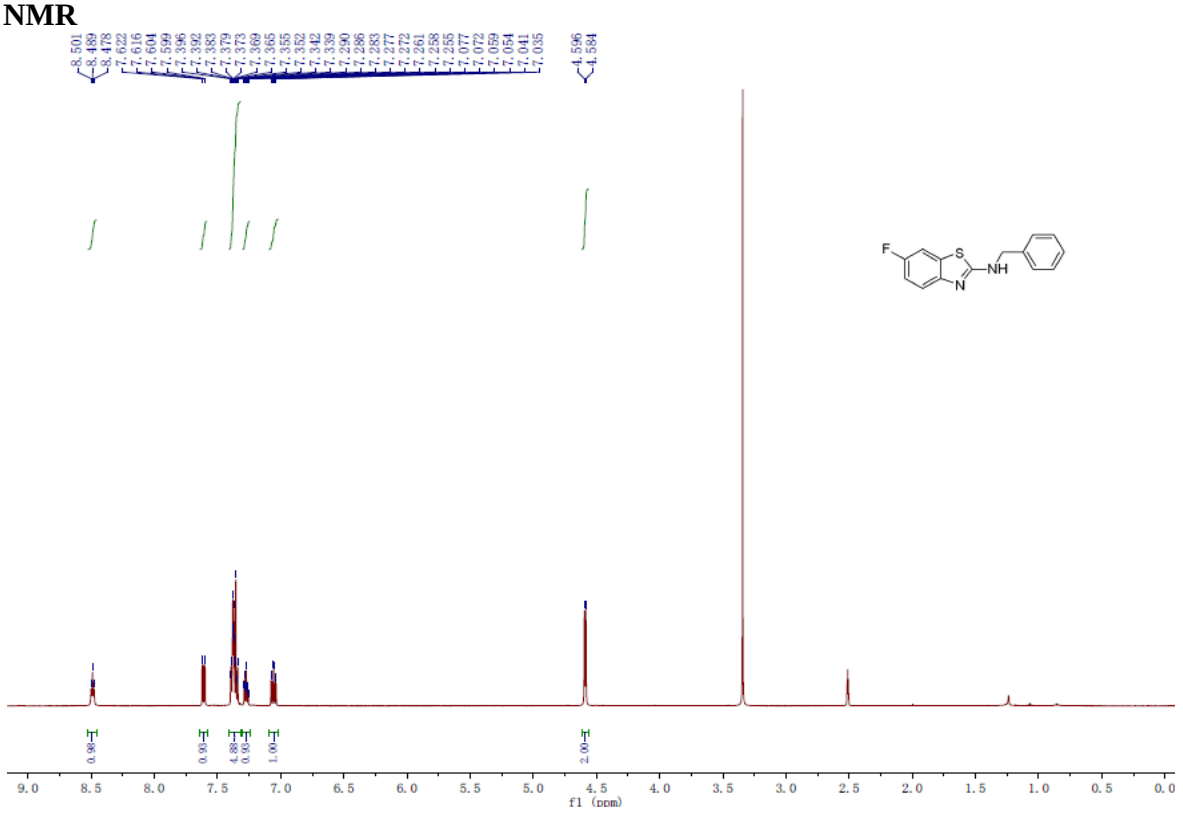
^{13}C NMR



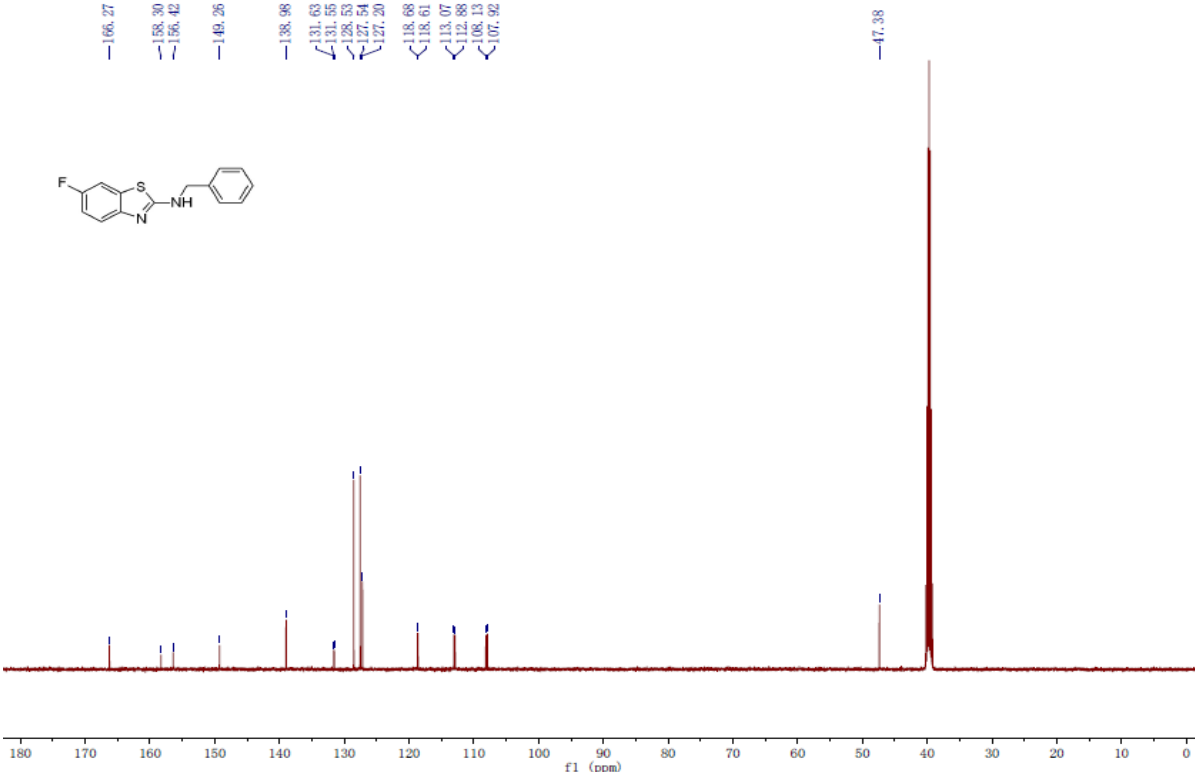


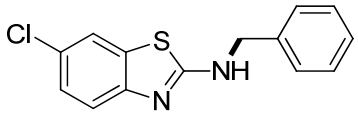
5r

^{1}H NMR



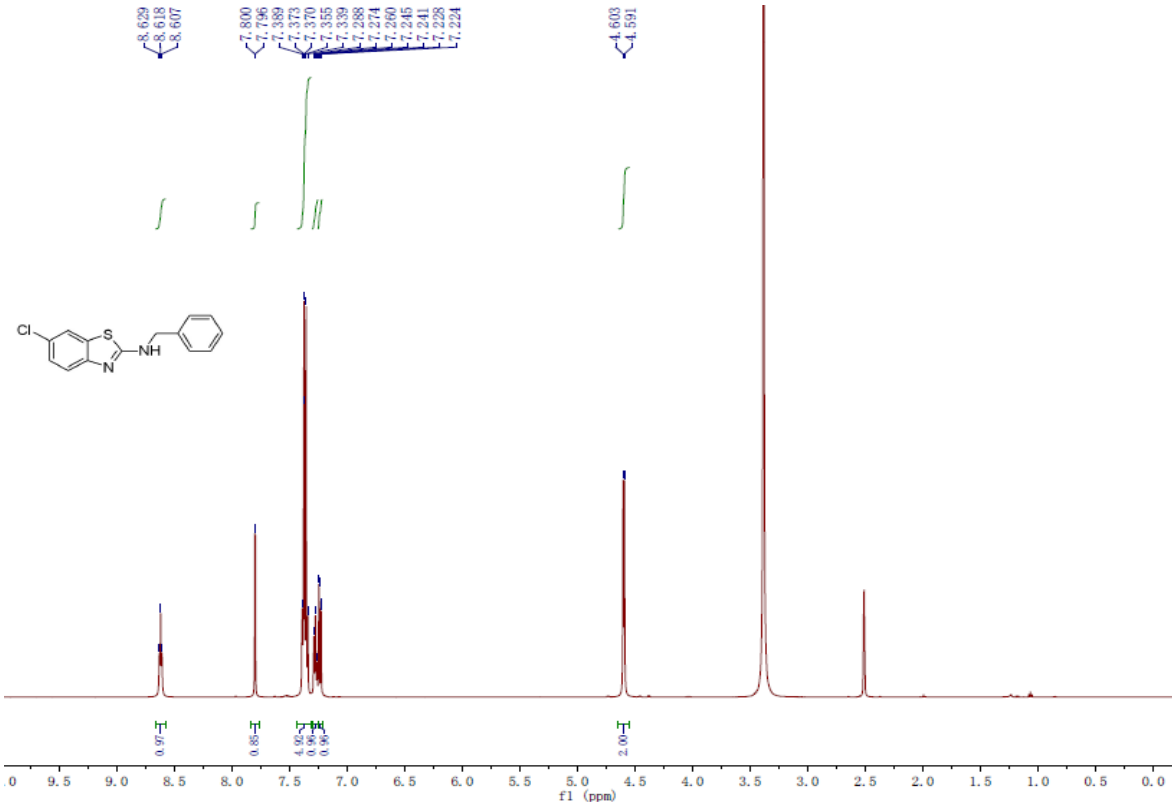
^{13}C NMR



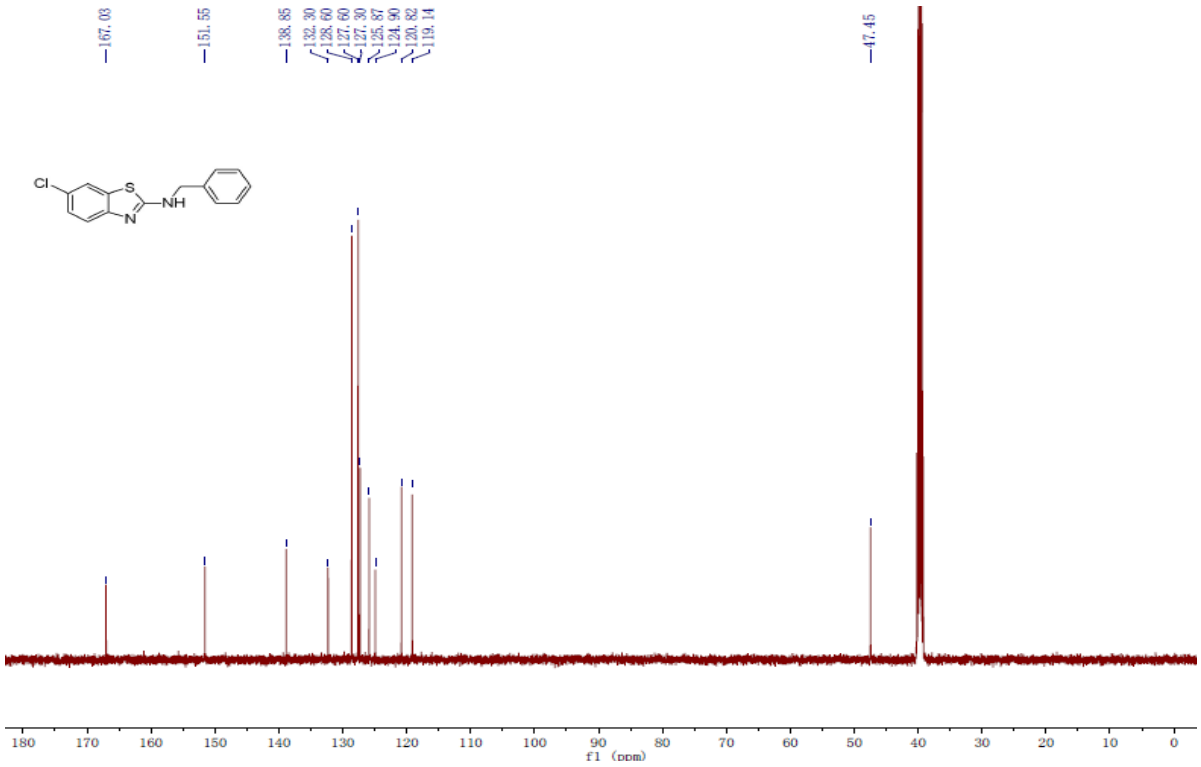


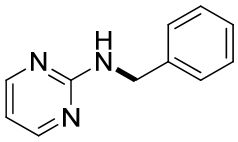
5s

^{1}H NMR



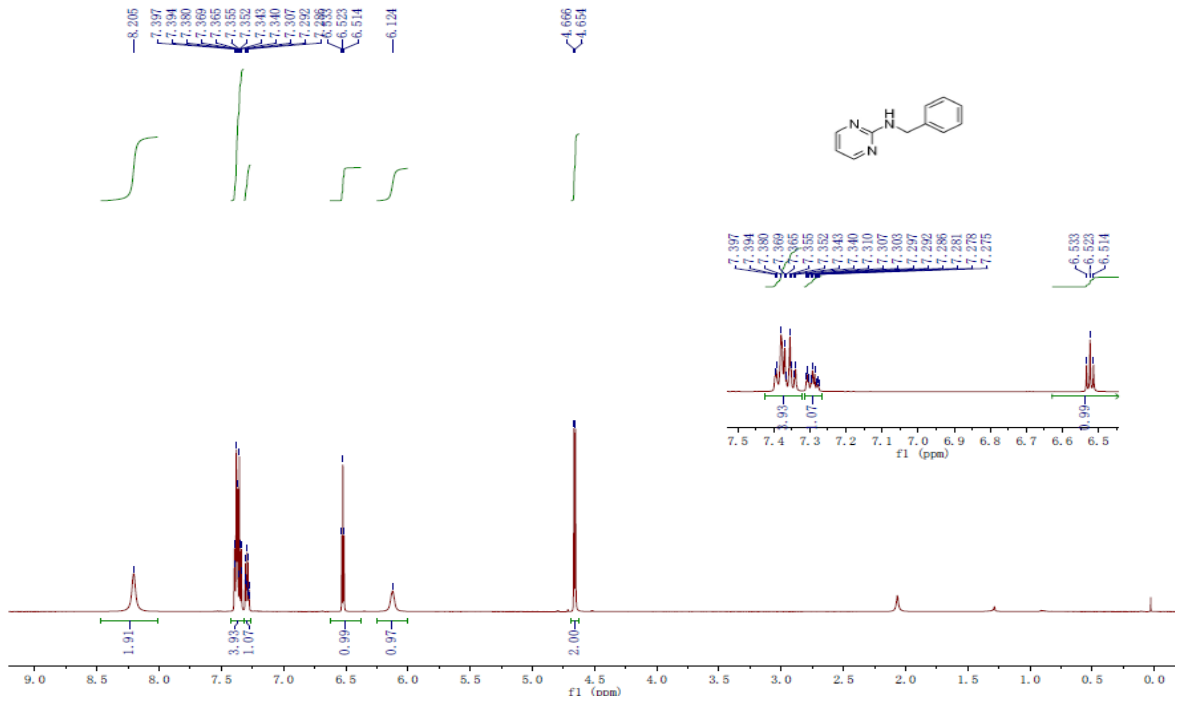
^{13}C NMR



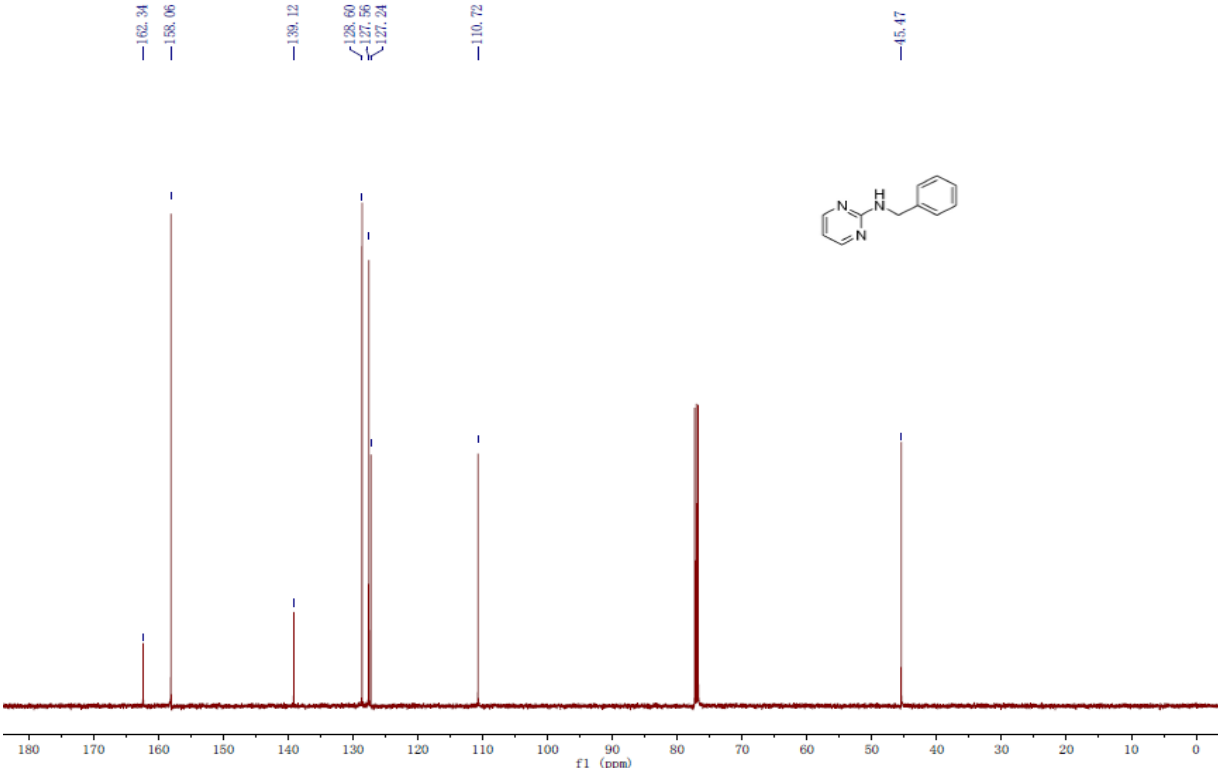


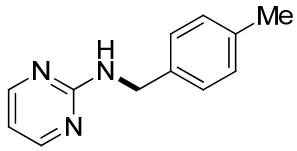
6a

^{1}H NMR



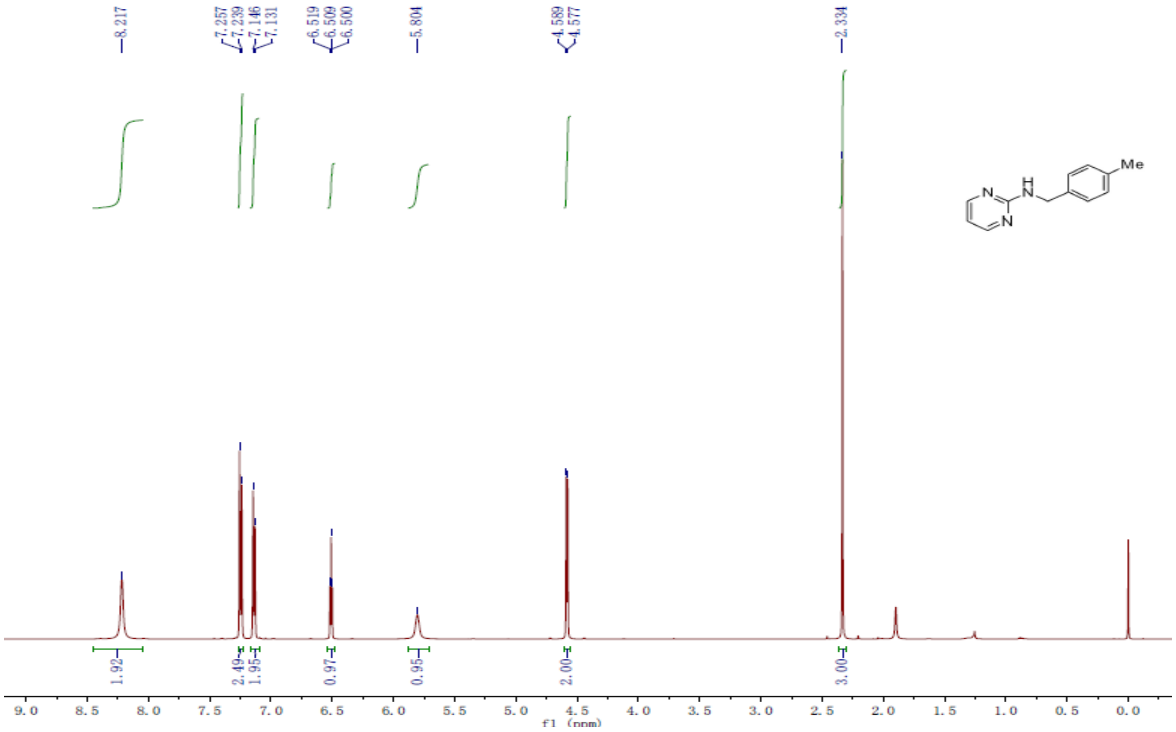
^{13}C NMR



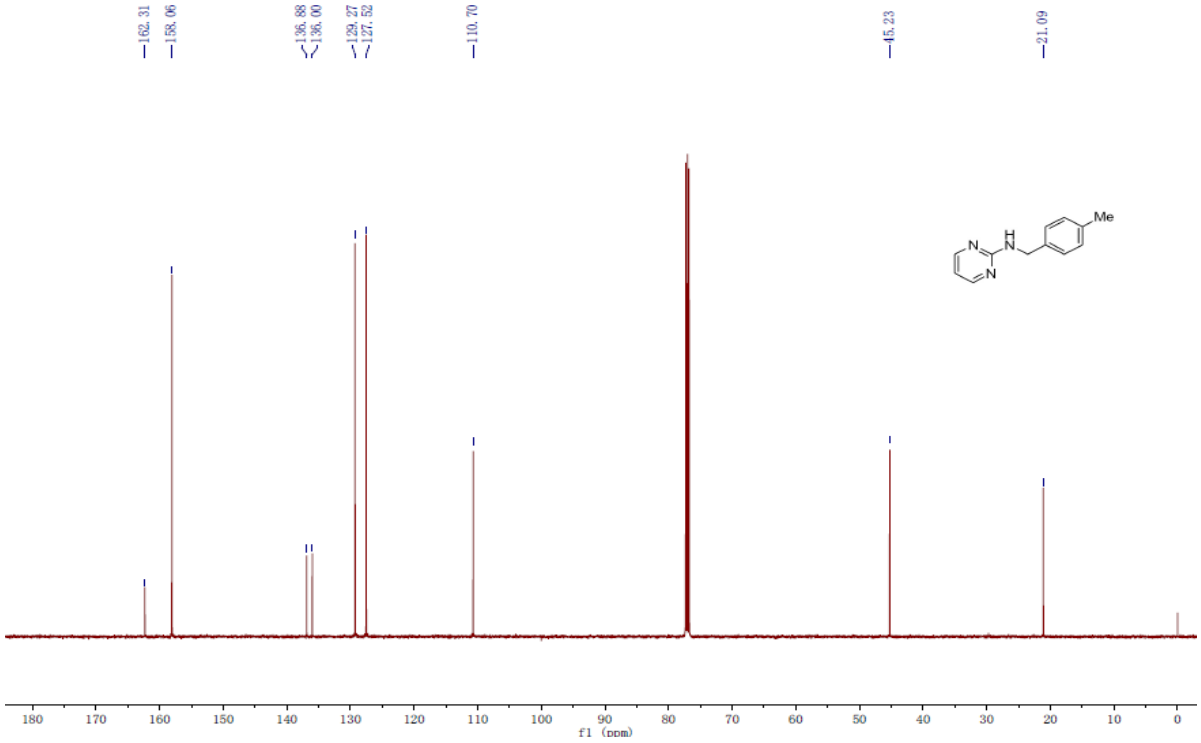


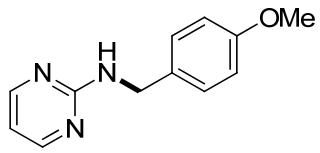
6b

^{1}H NMR



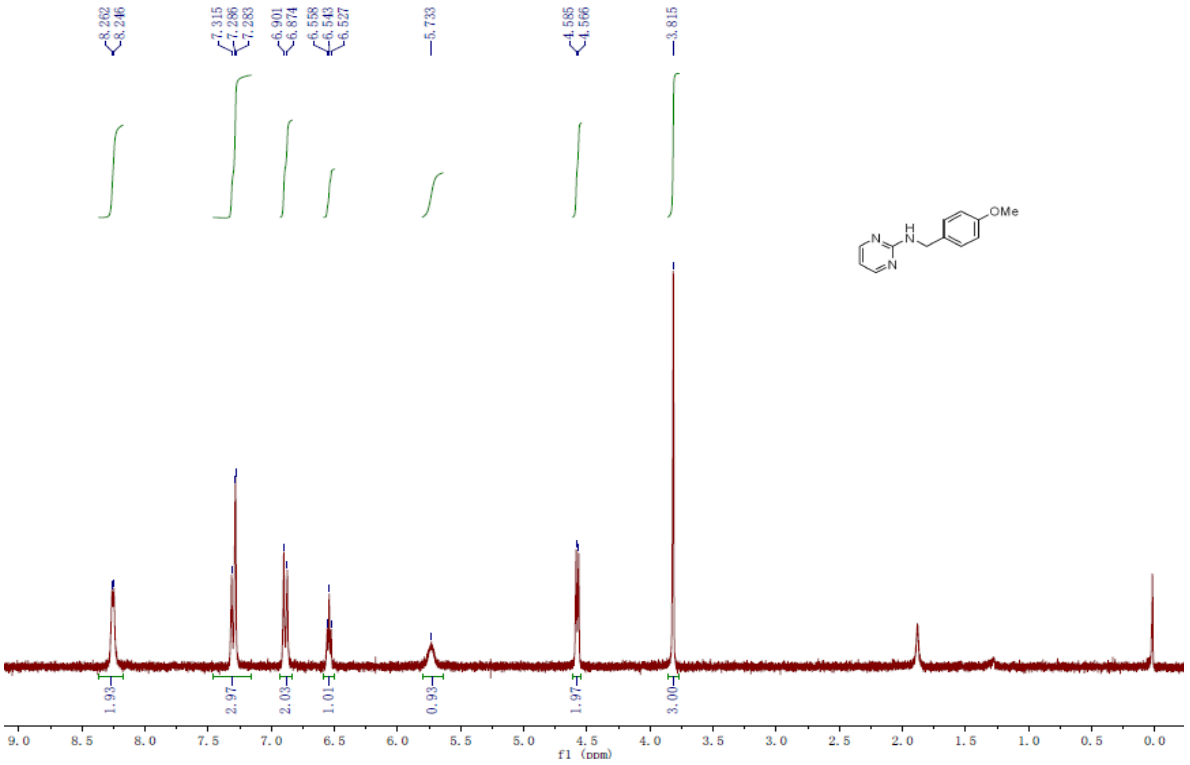
^{13}C NMR





6c

^{1}H NMR



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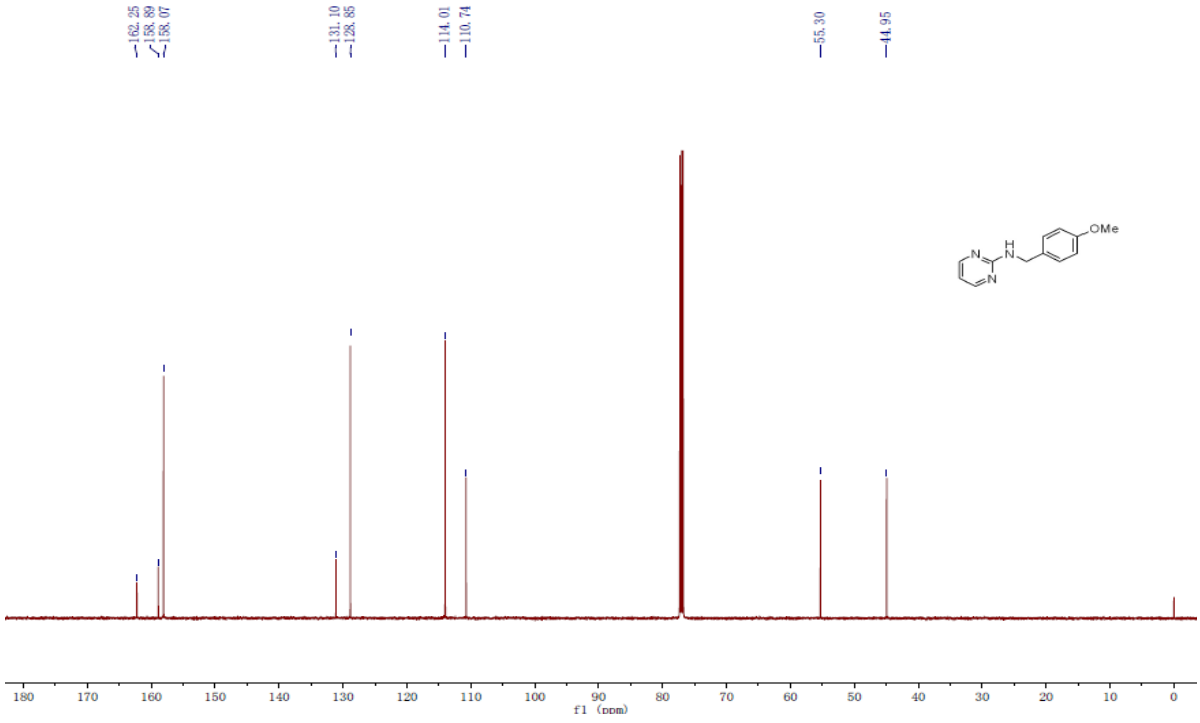
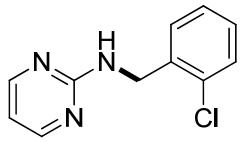
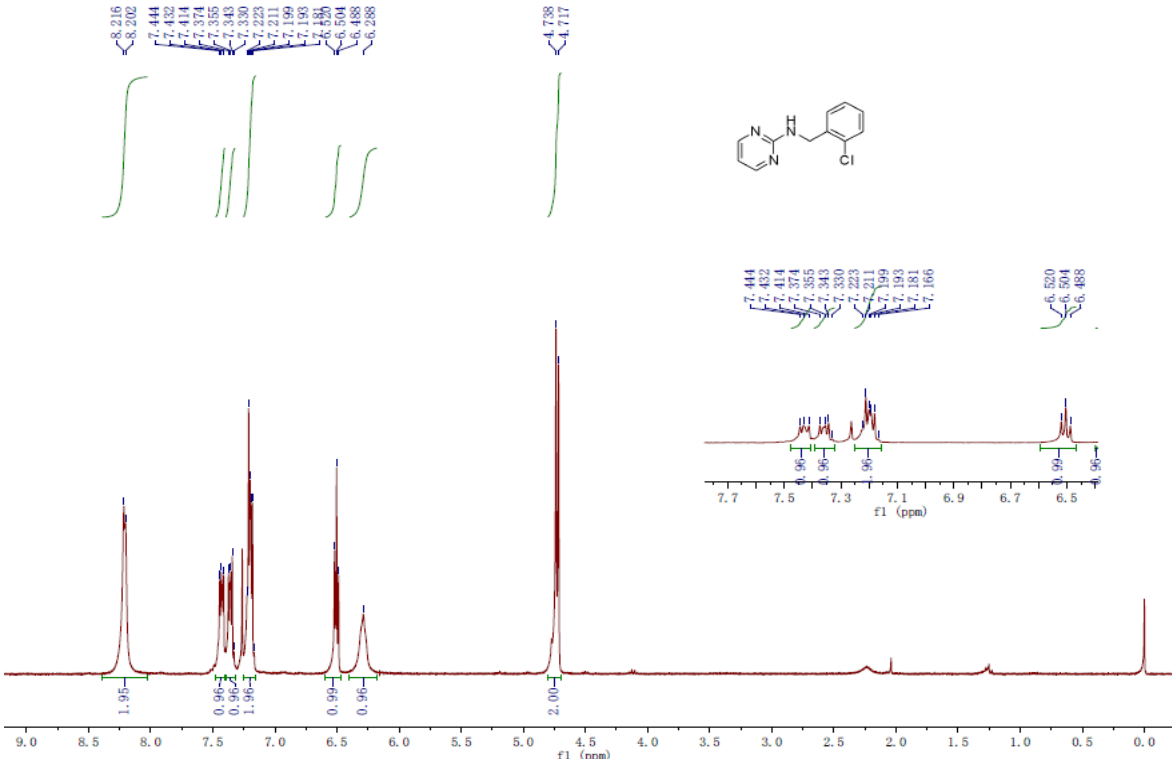




6d

^{1}H NMR



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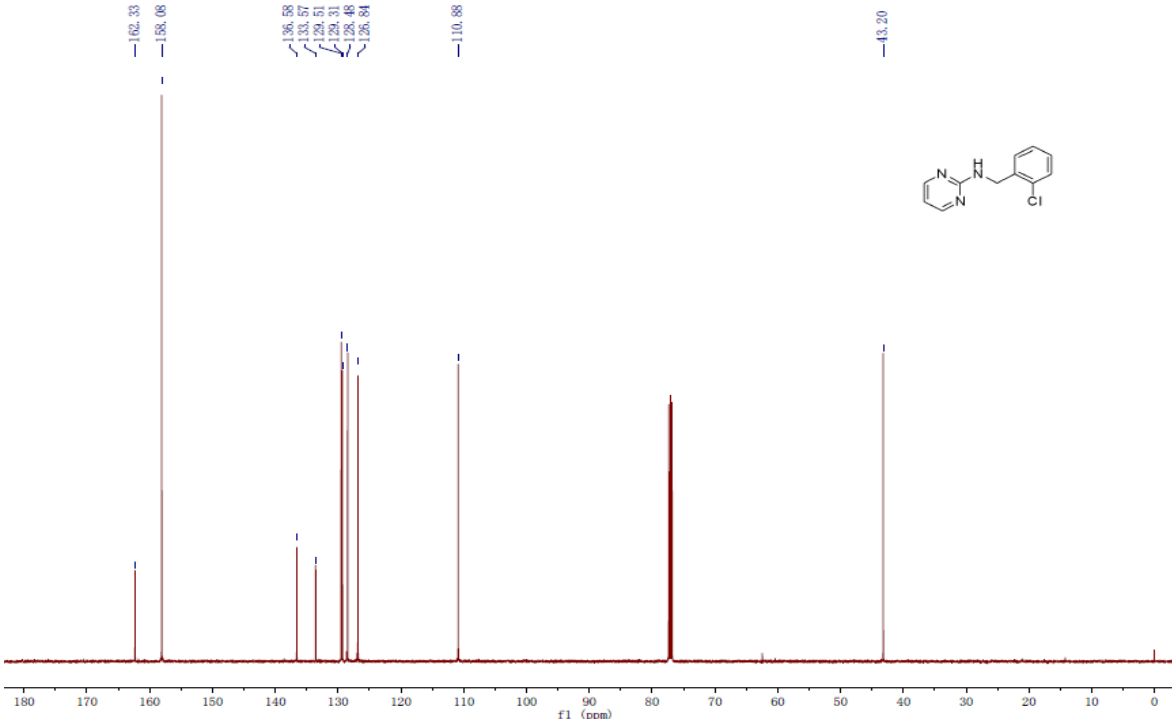
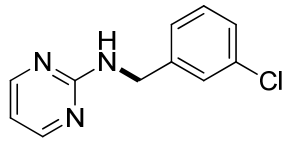
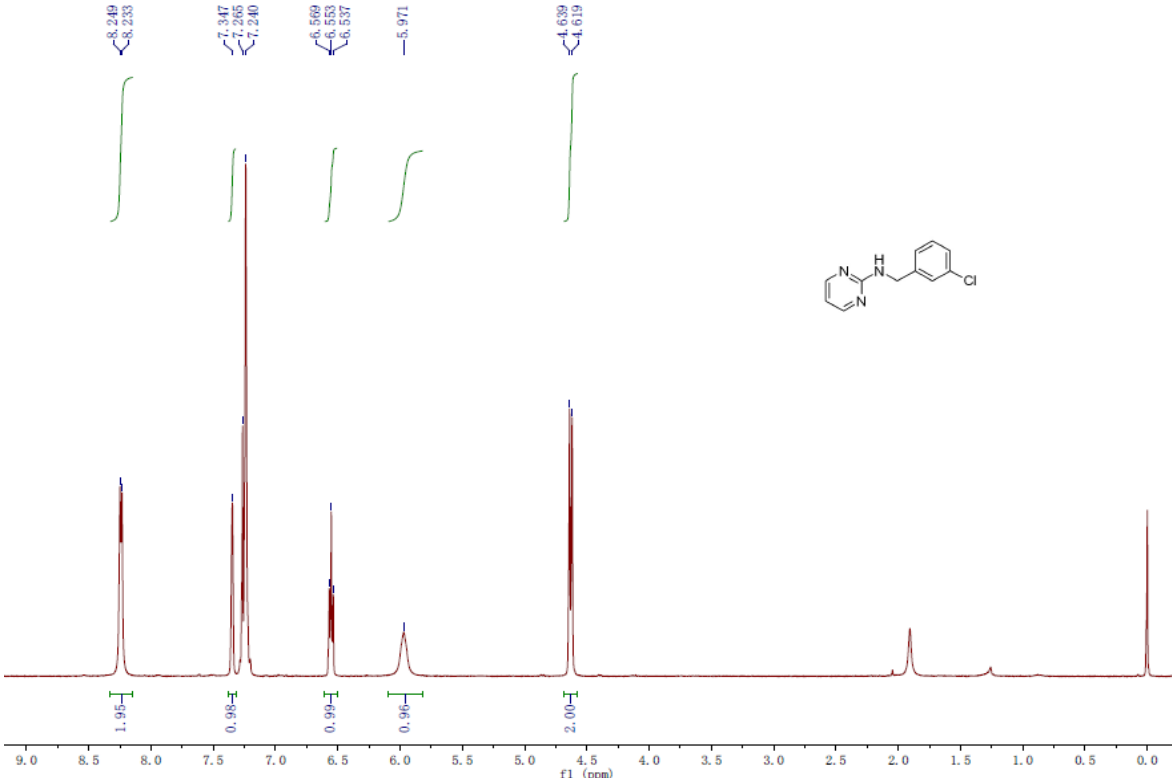


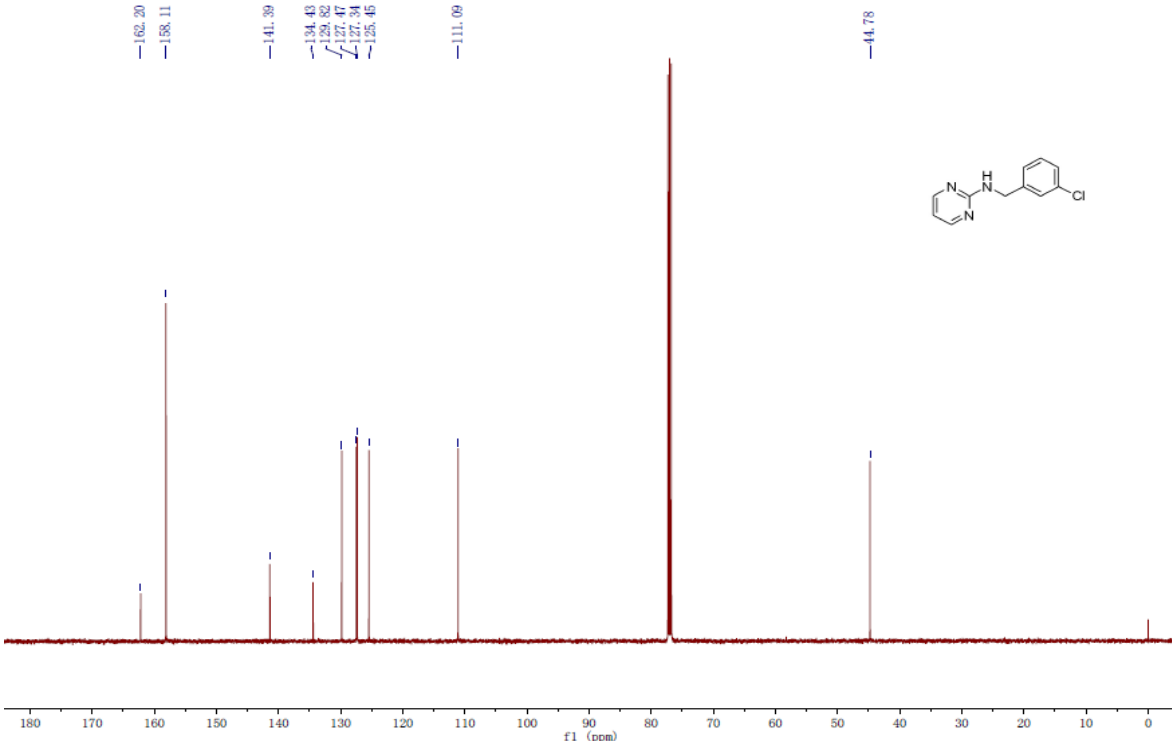


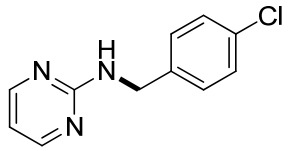
6e

^{1}H NMR



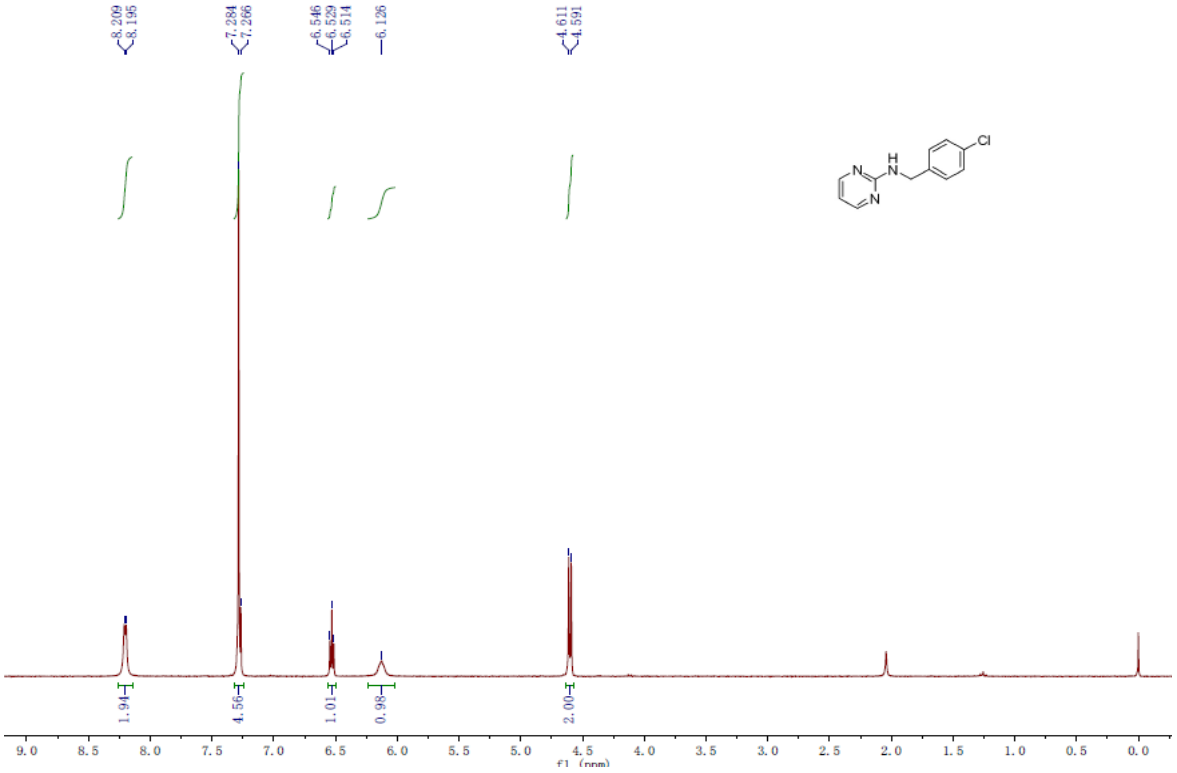
^{13}C NMR



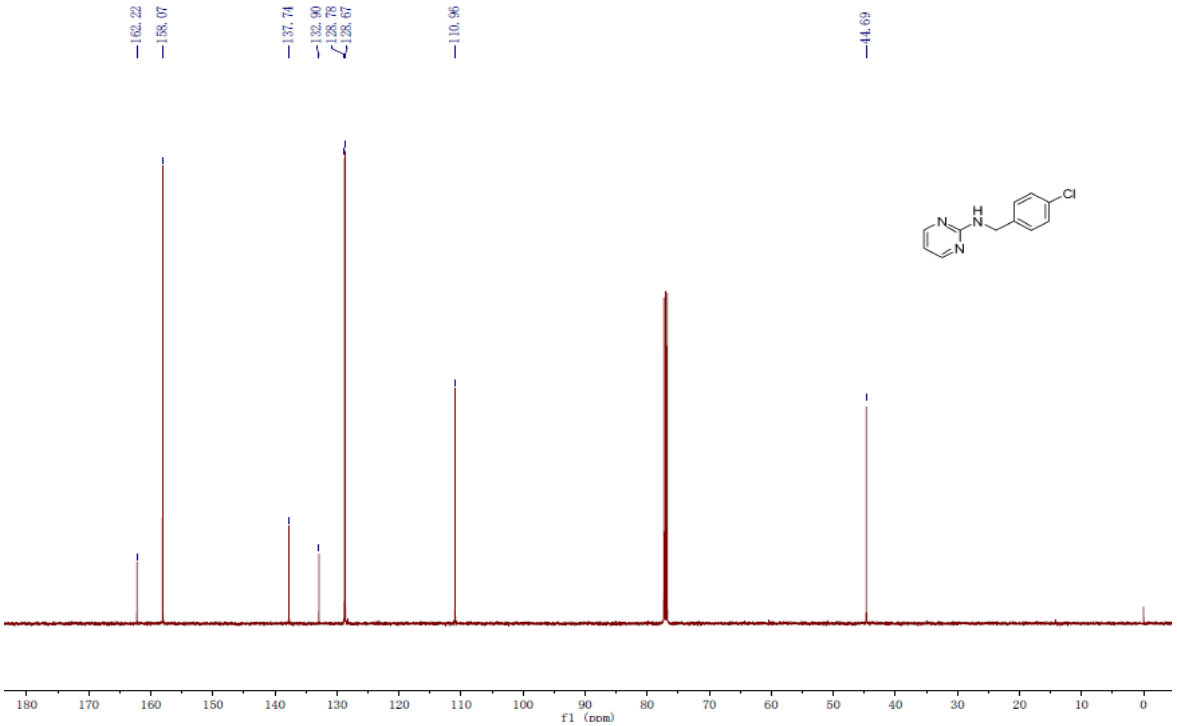


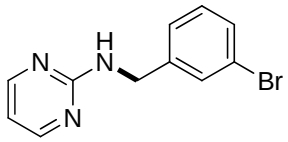
6f

^{1}H NMR



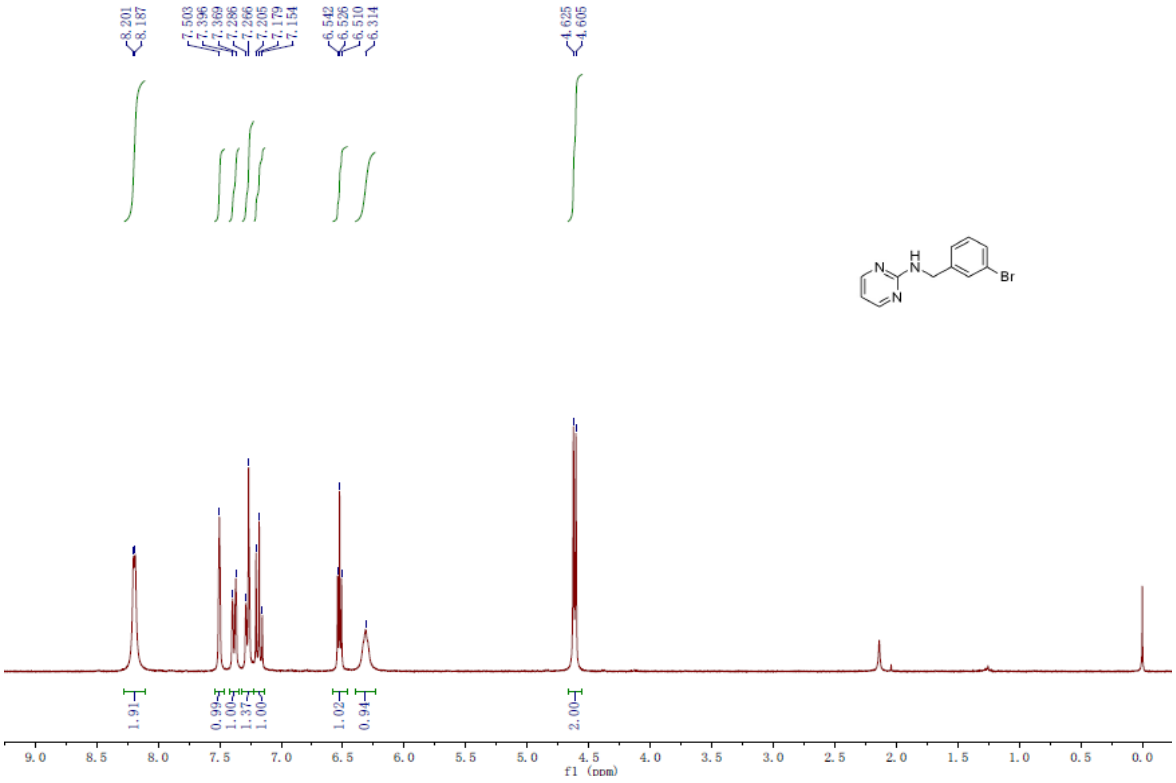
^{13}C NMR



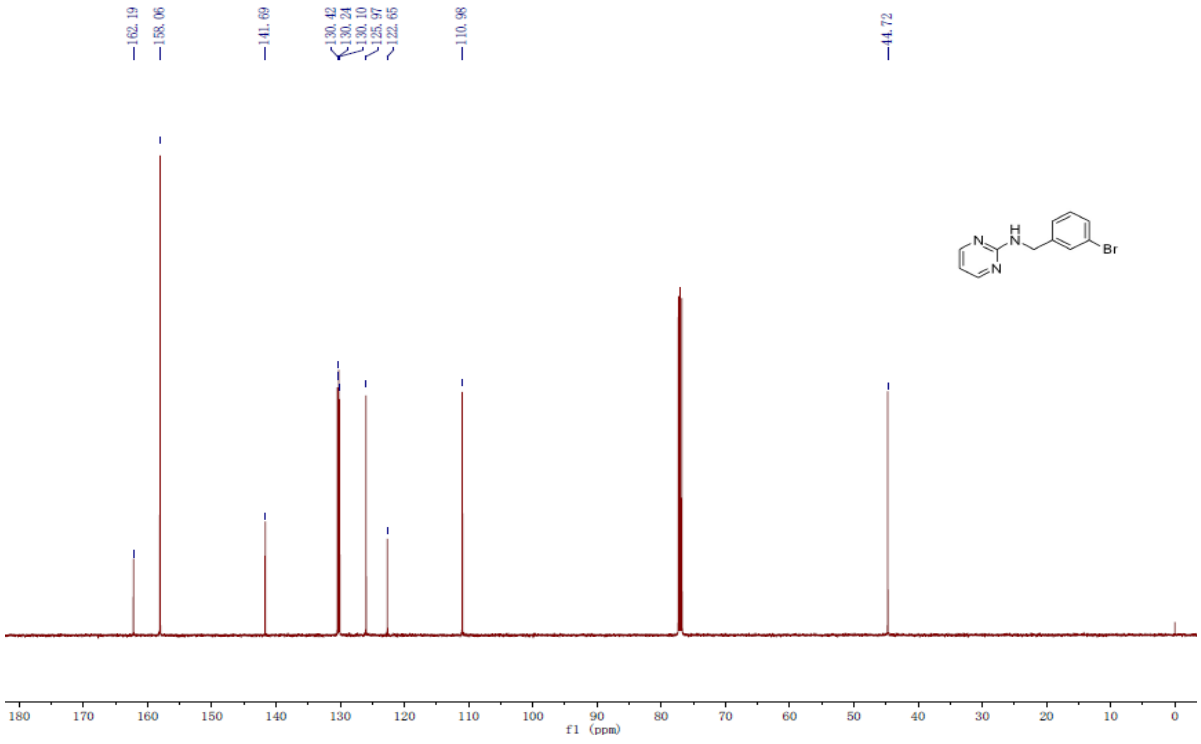


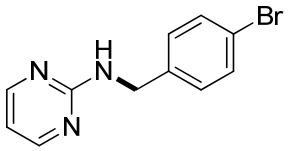
6g

^{1}H NMR



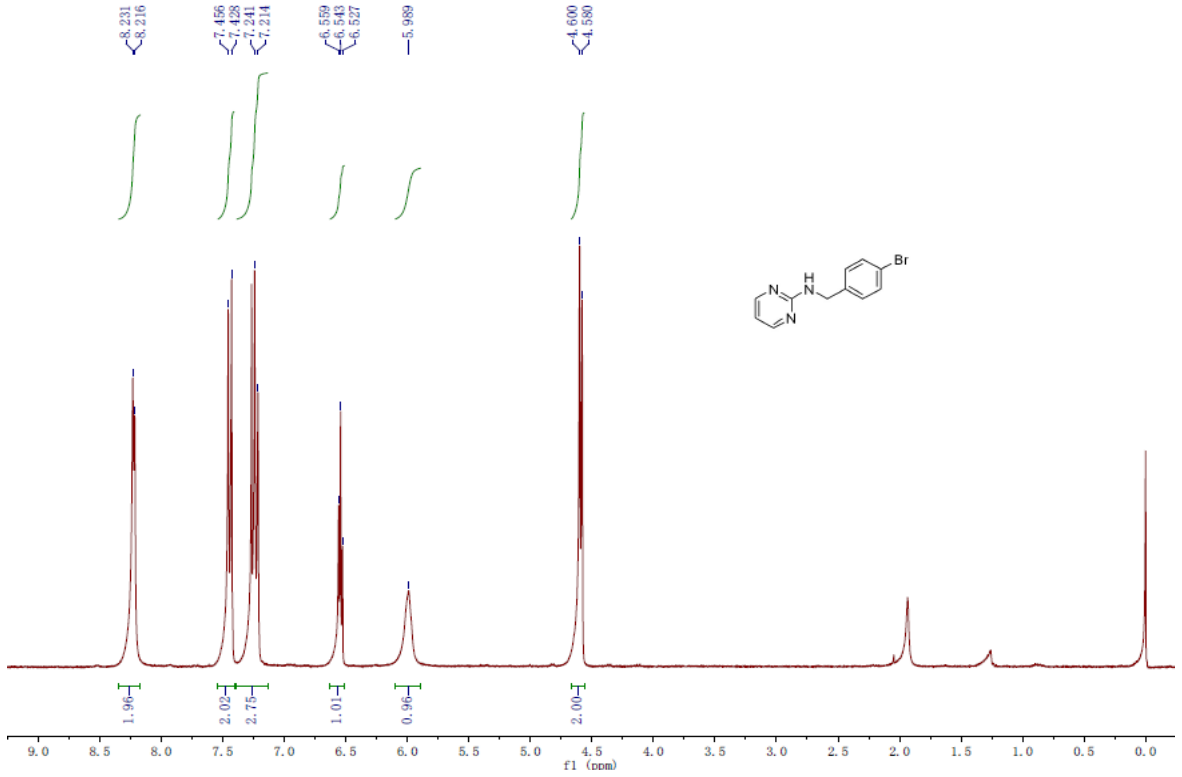
^{13}C NMR



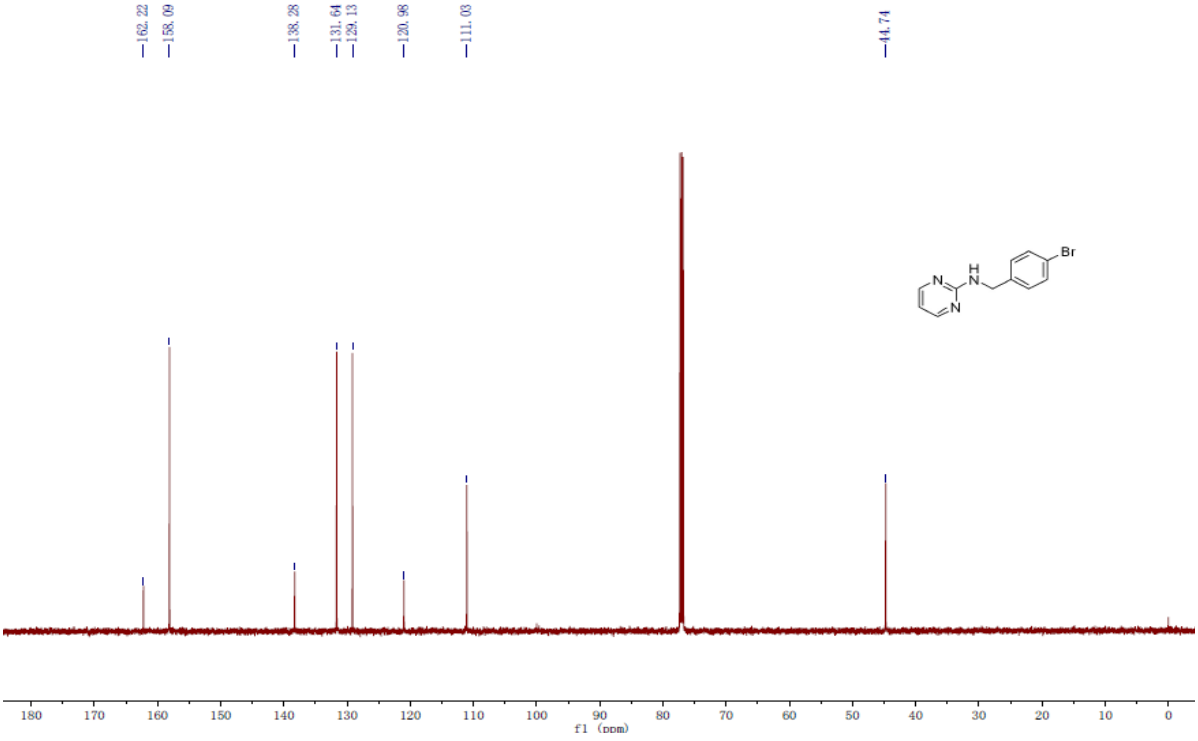


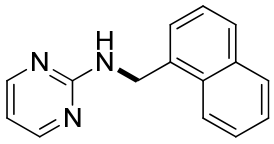
6h

^{1}H NMR



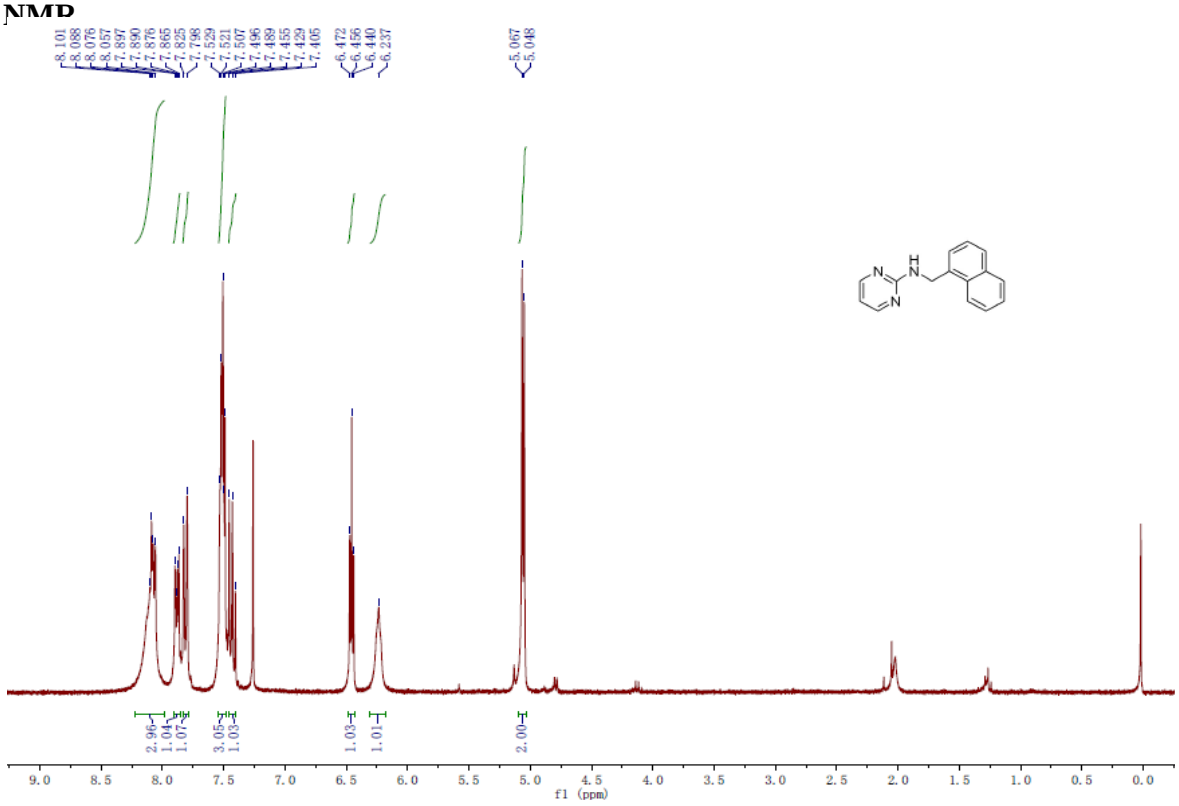
^{13}C NMR



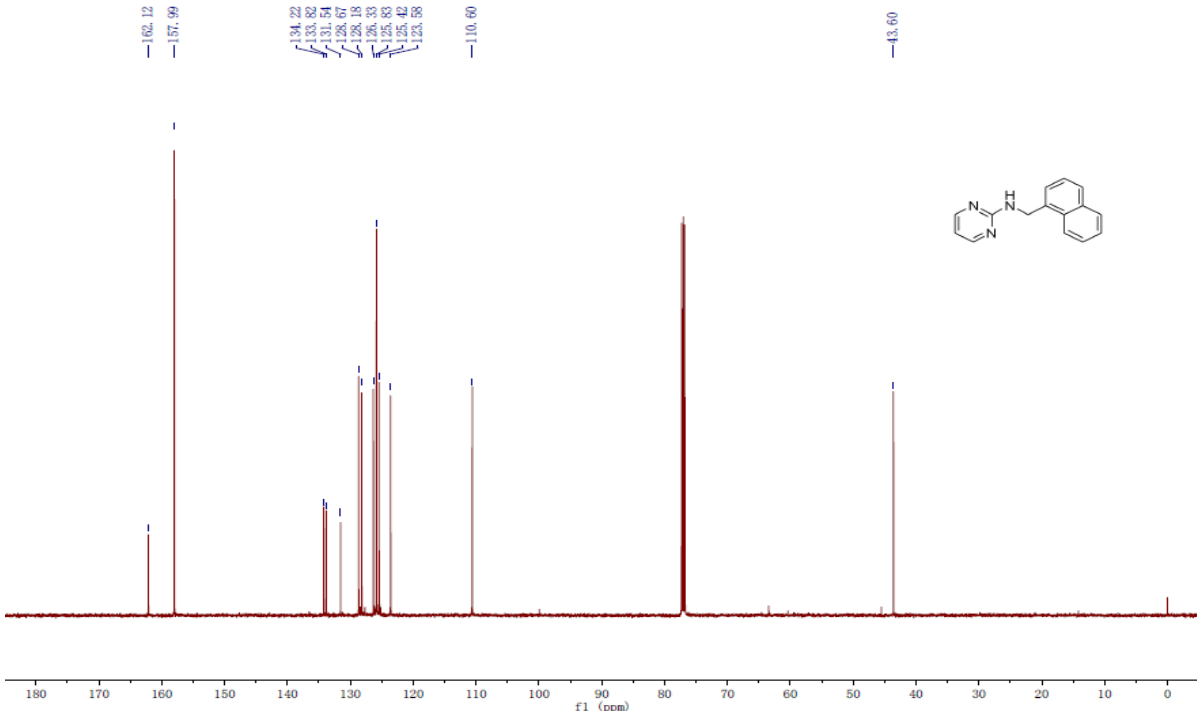


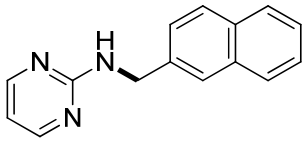
6i

^{1}H NMR



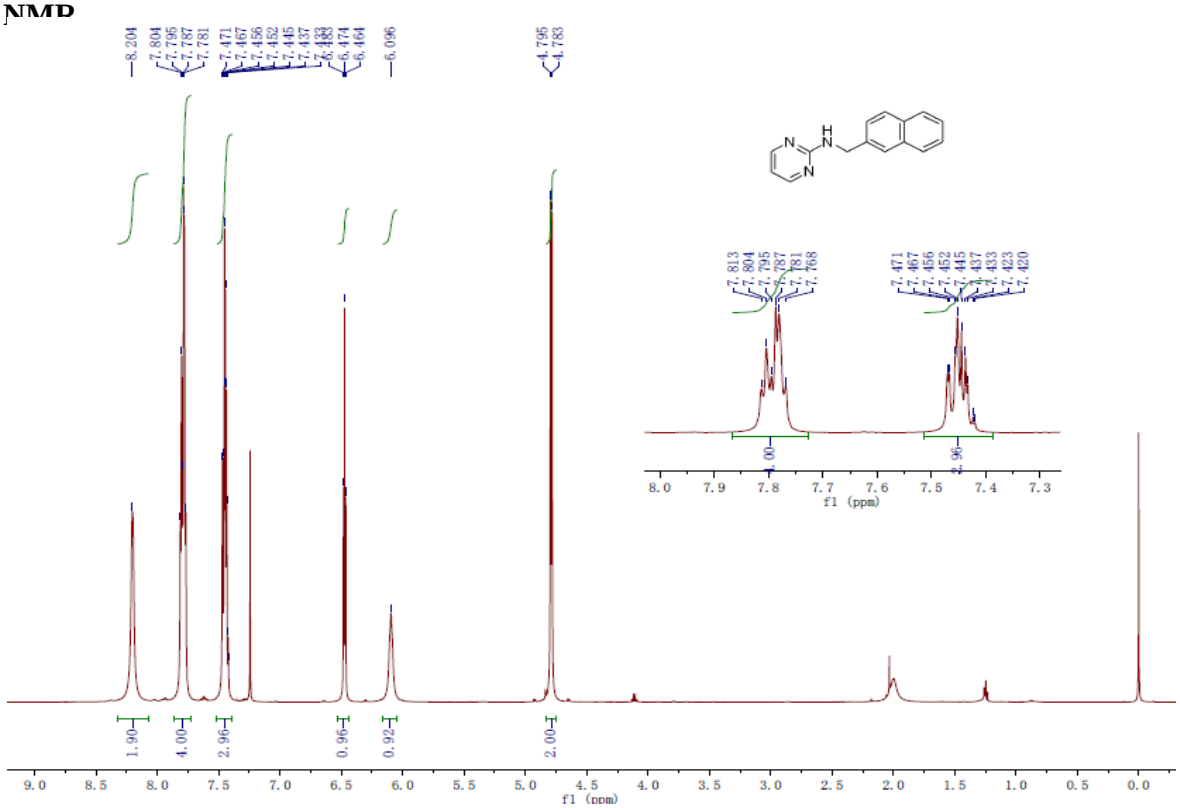
^{13}C NMR



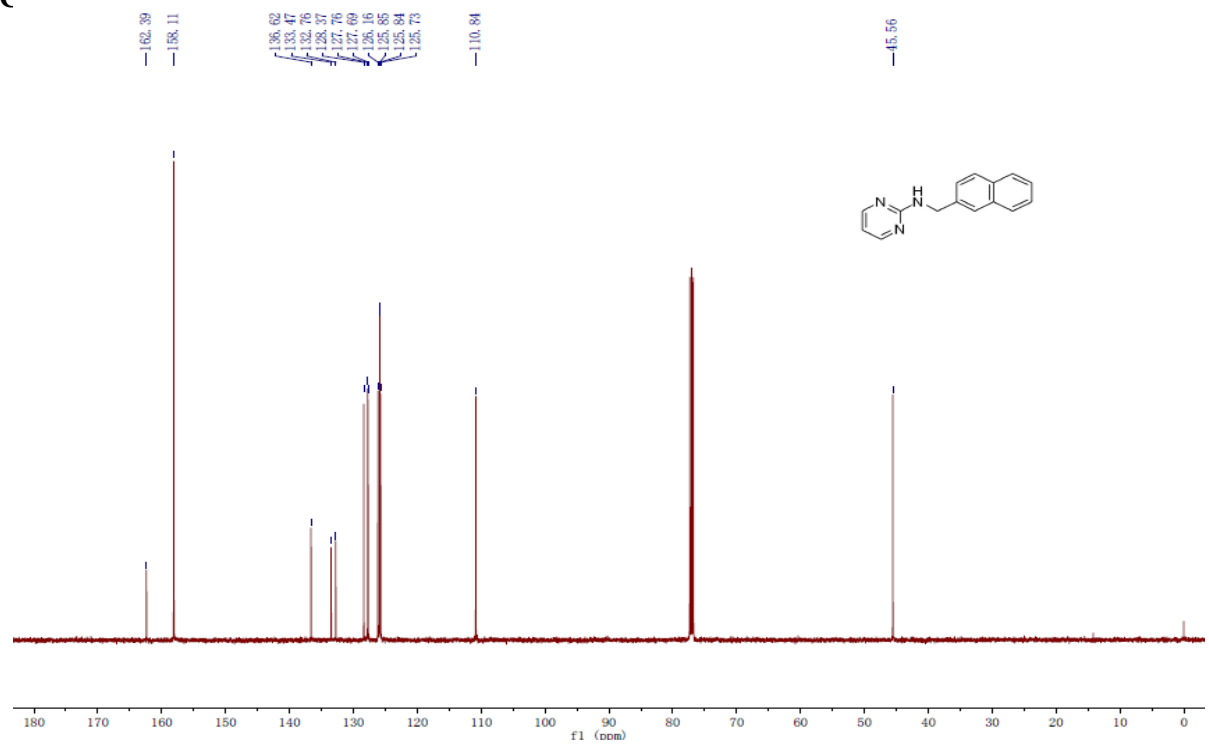


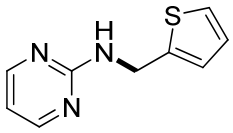
6j

^{1}H NMR



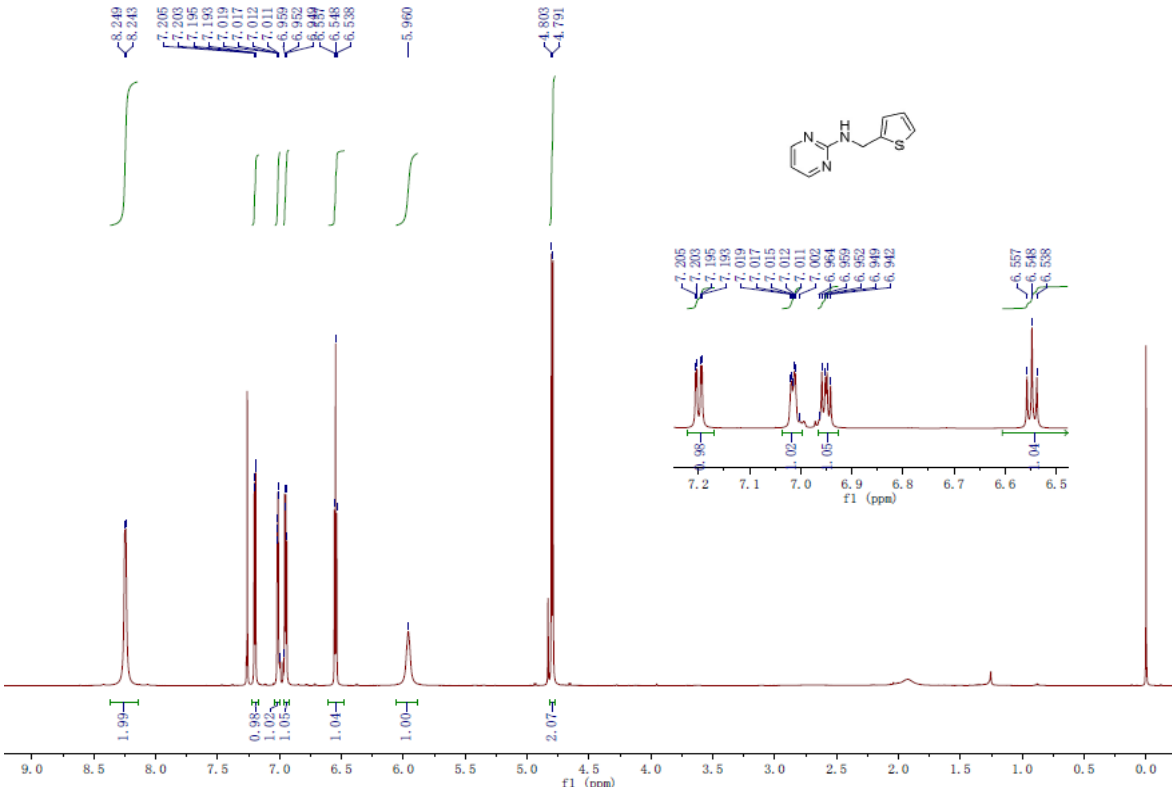
^{13}C NMR



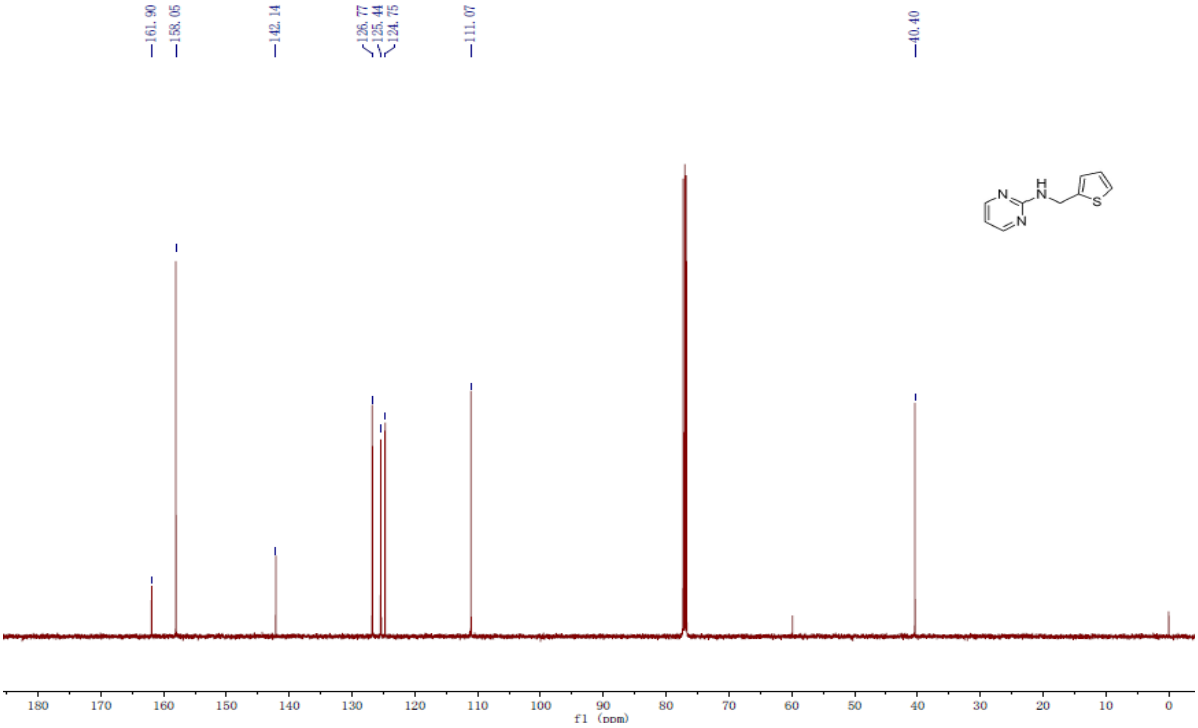


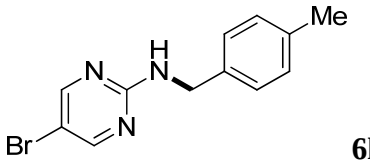
6k

^{1}H NMR



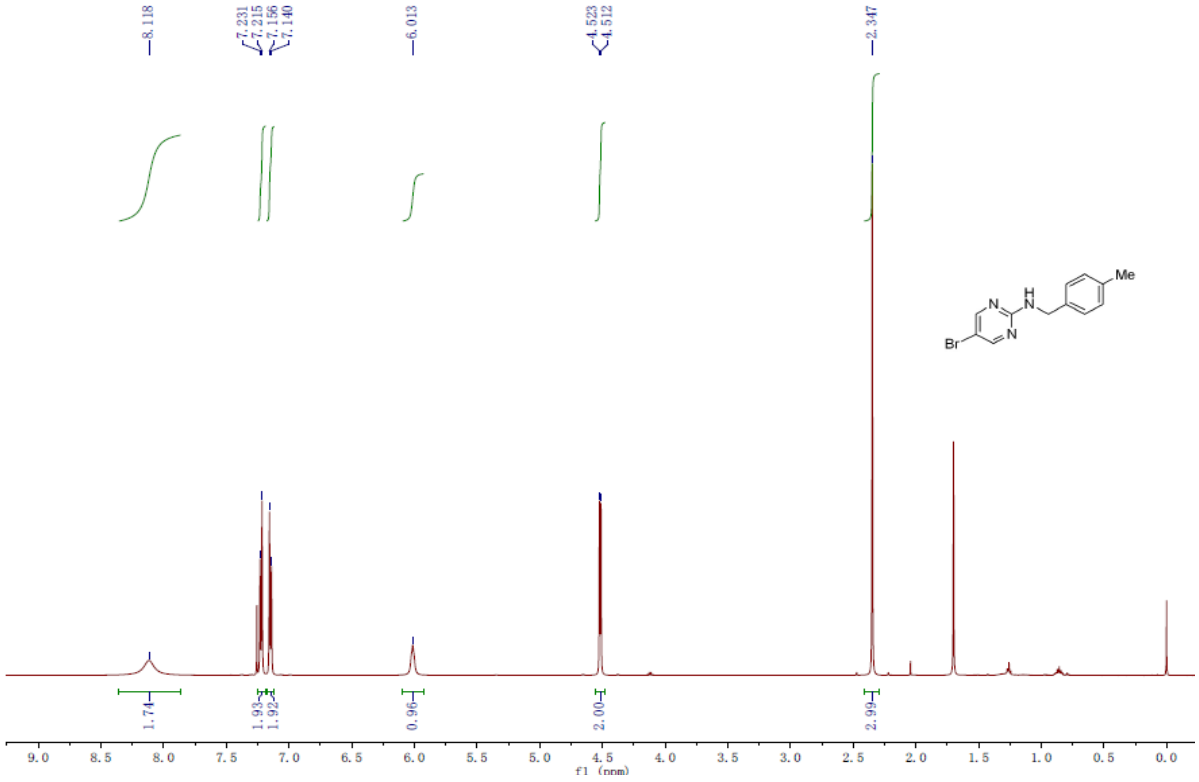
^{13}C NMR



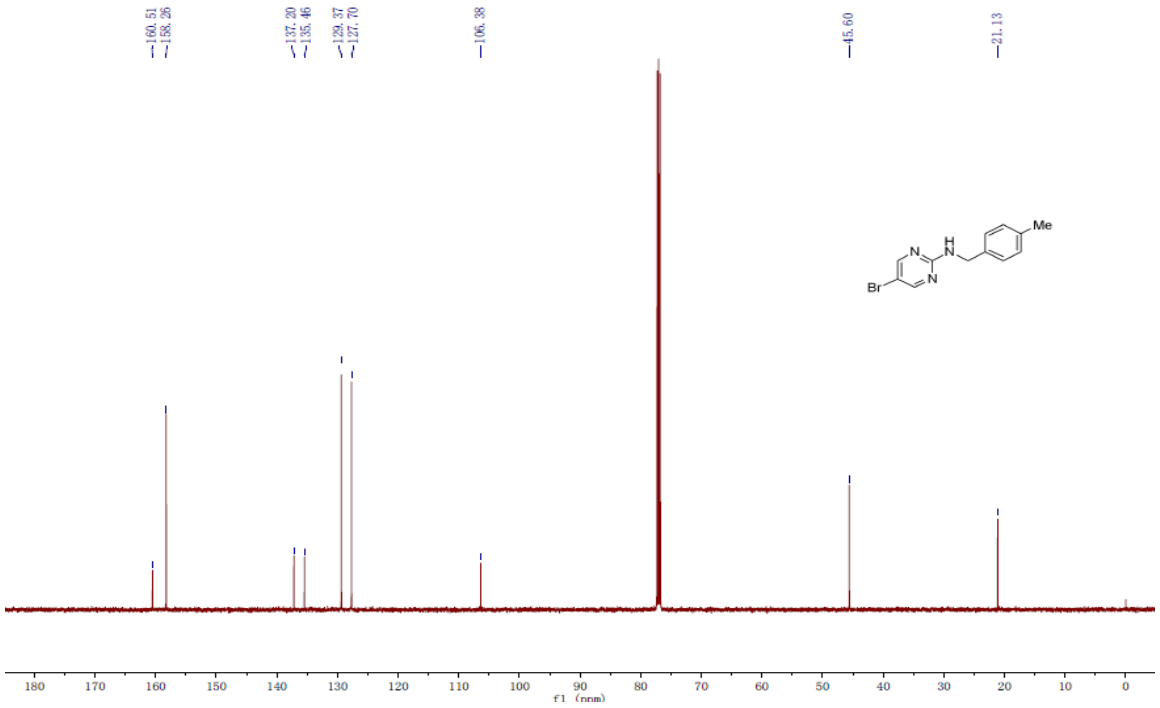


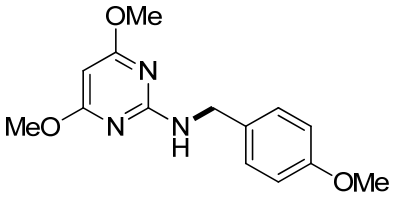
6l

^{1}H NMR



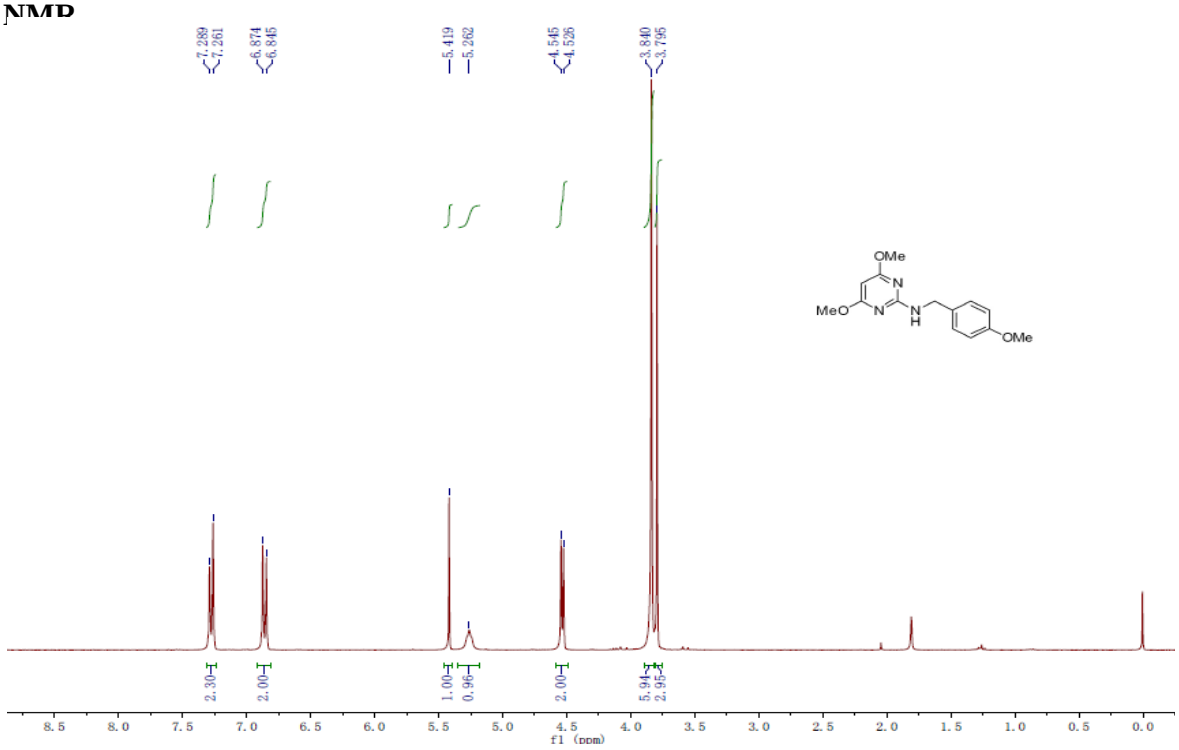
^{13}C NMR



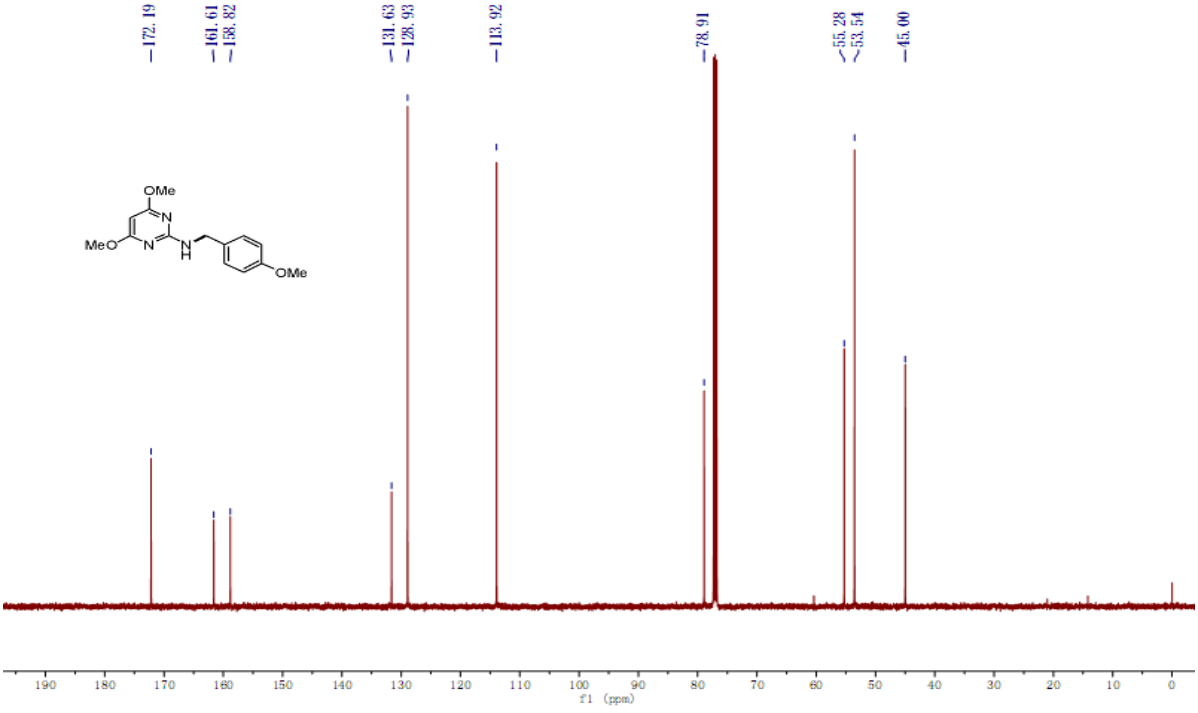


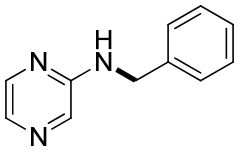
6m

^{1}H NMR



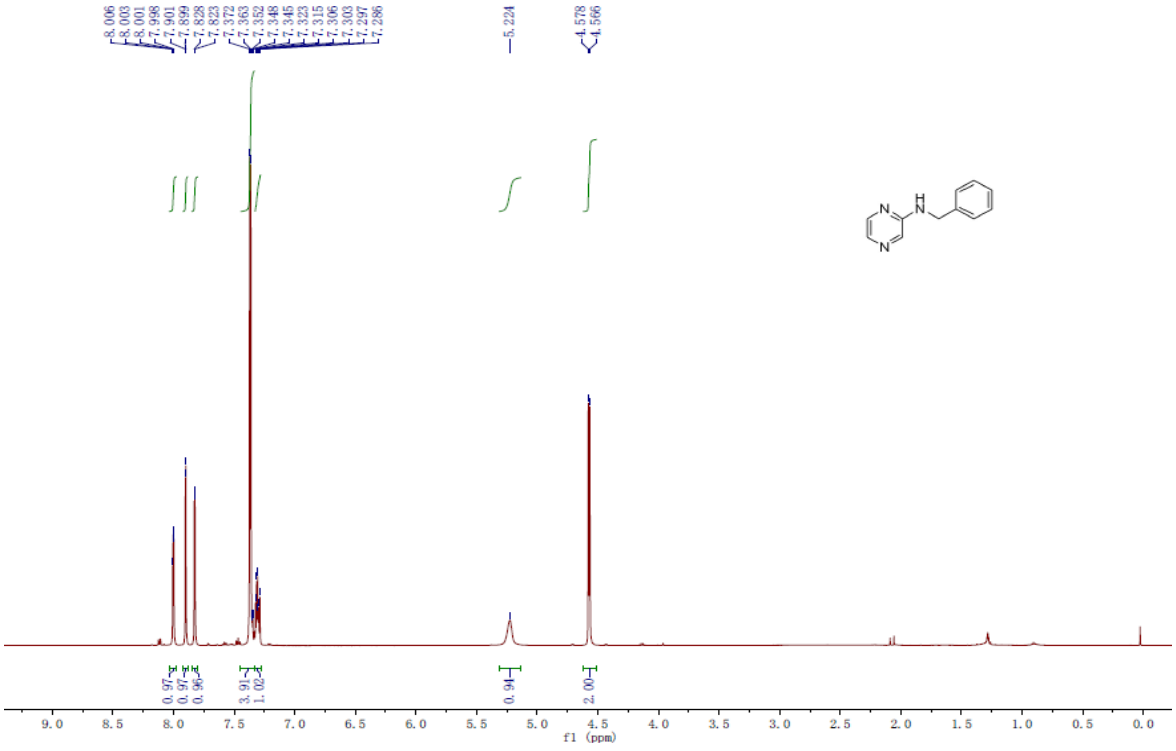
^{13}C NMR



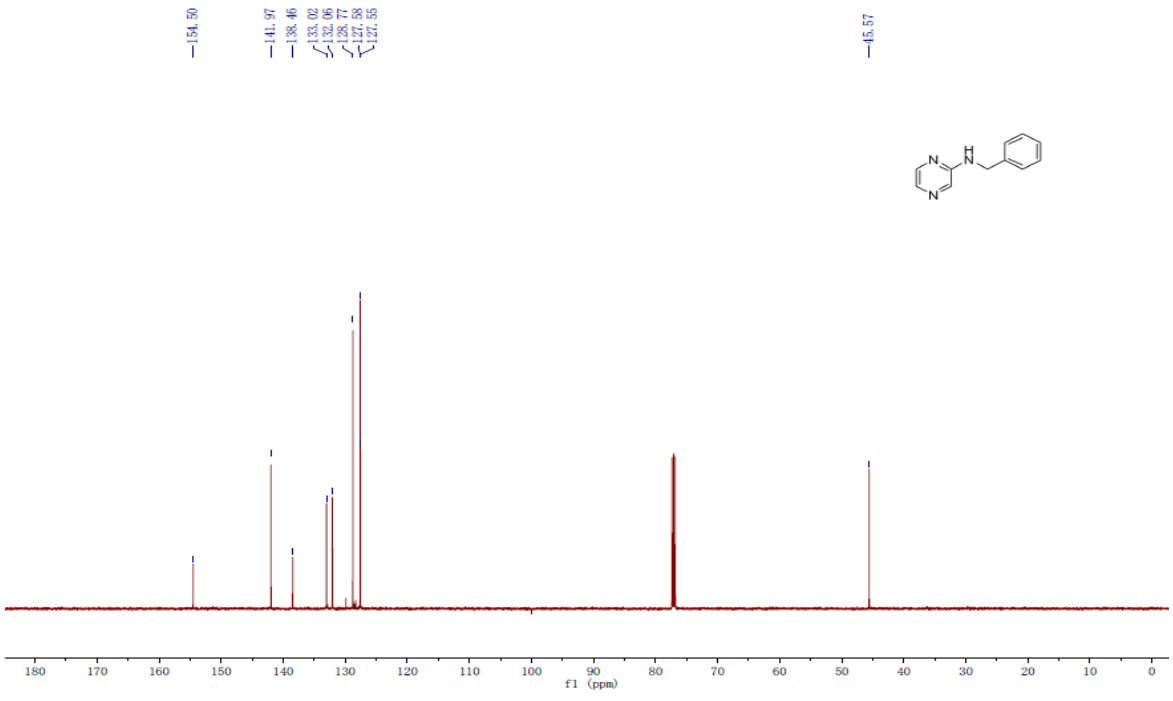


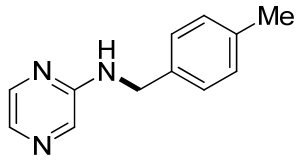
7a

^{1}H NMR



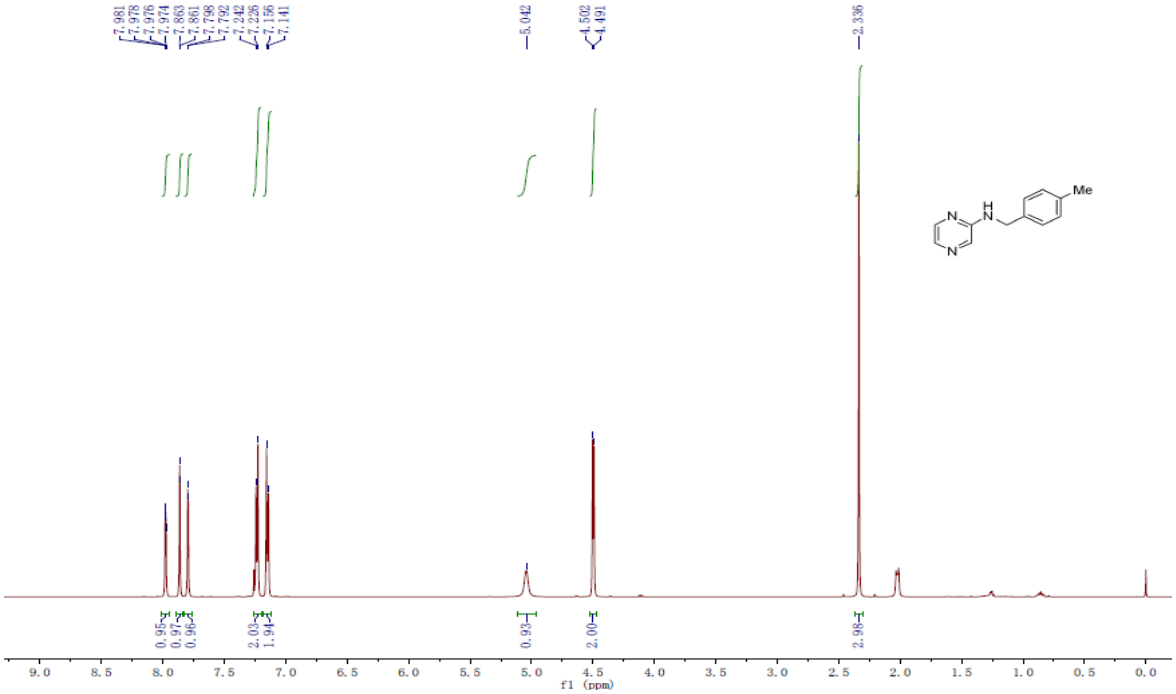
^{13}C NMR





7b

^{1}H NMR



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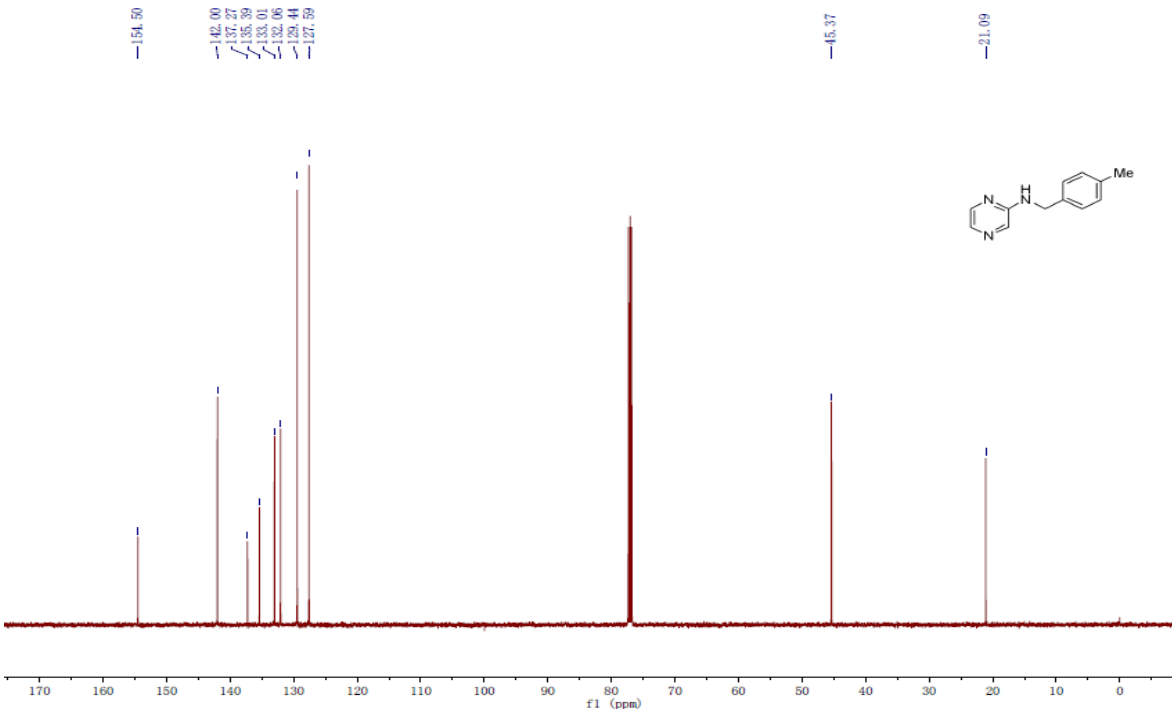
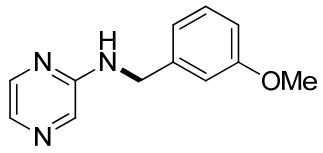
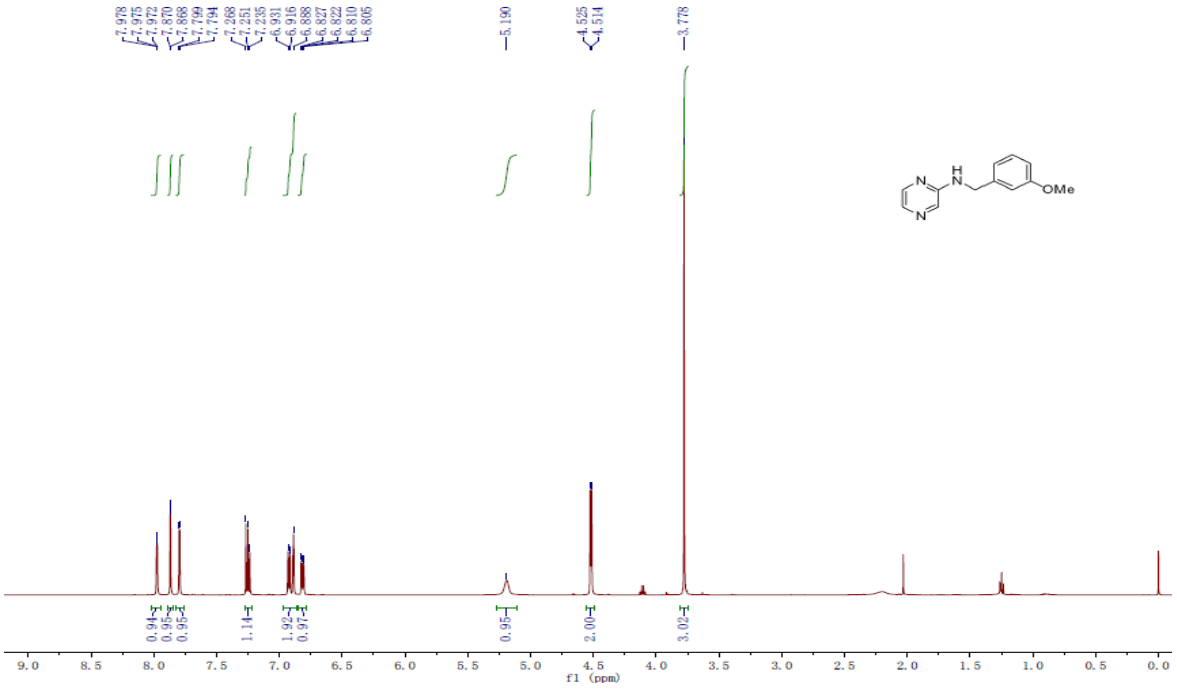




7c

^{1}H NMR



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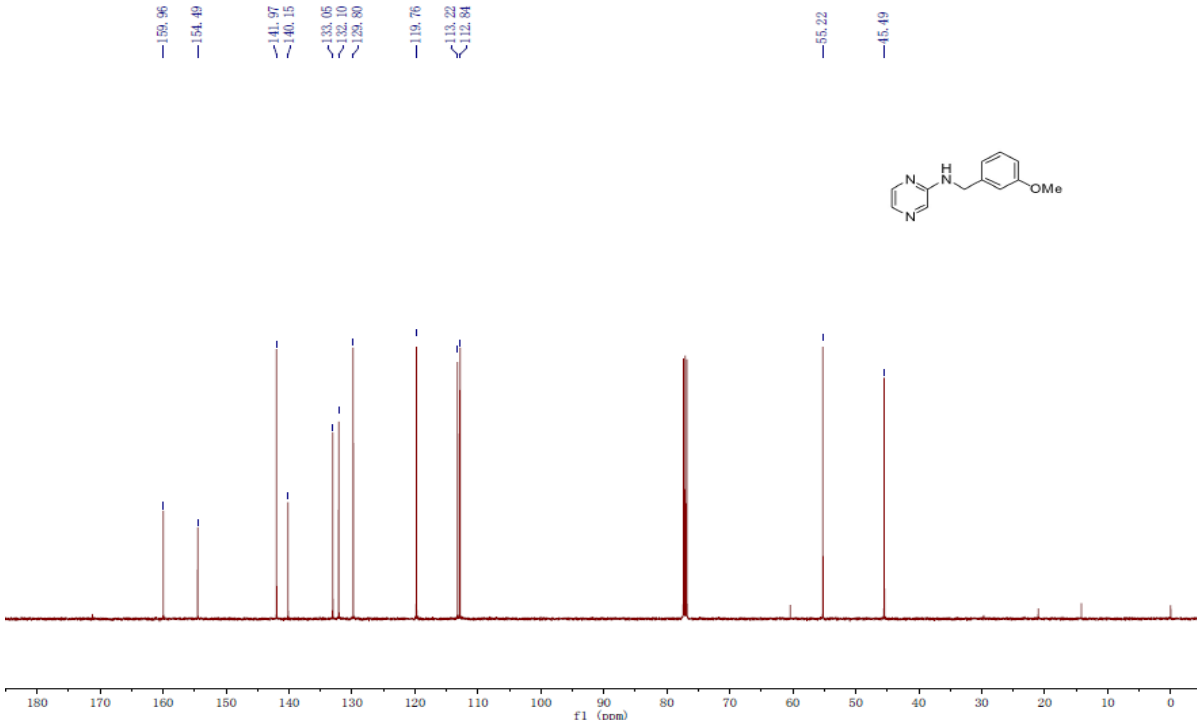
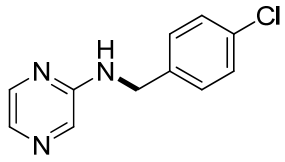
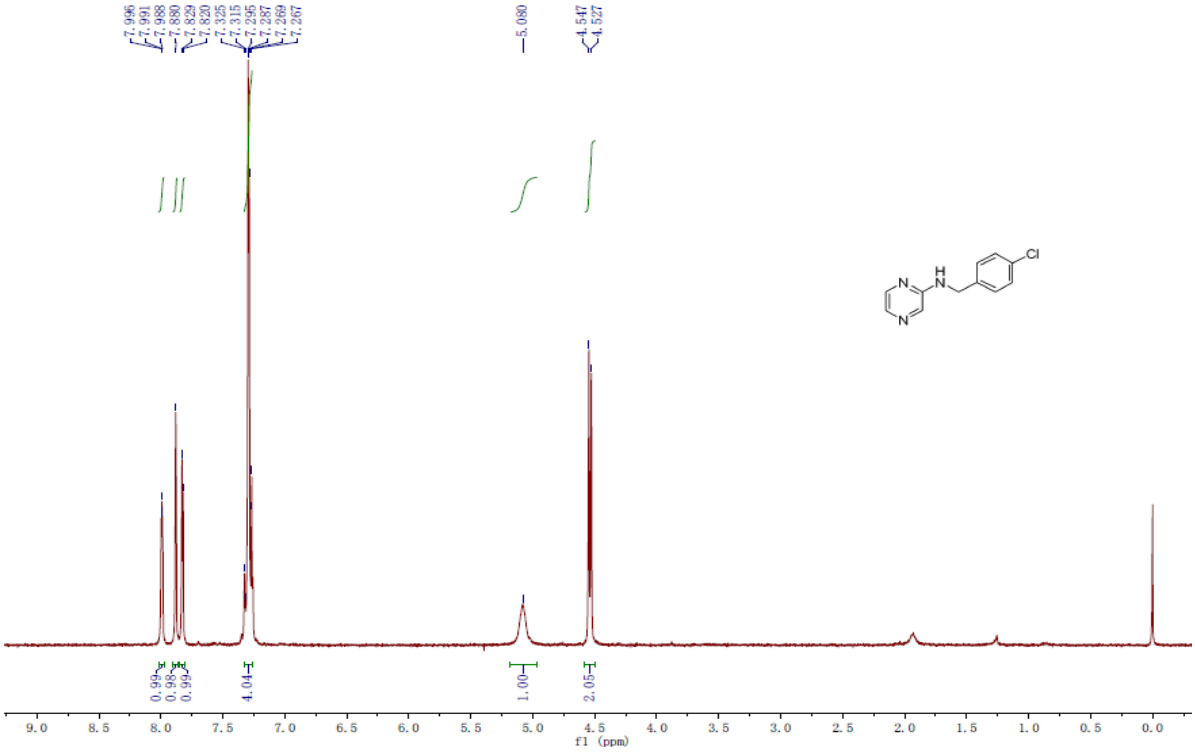




7d

^{1}H NMR



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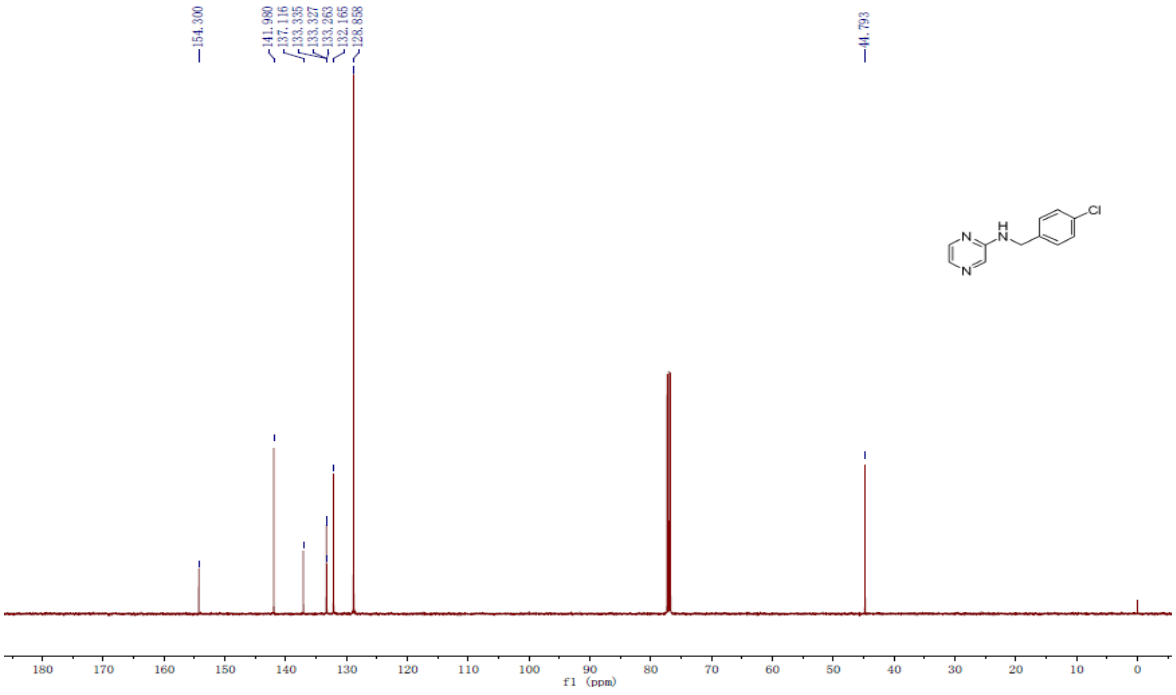
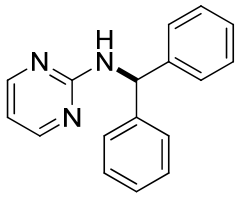
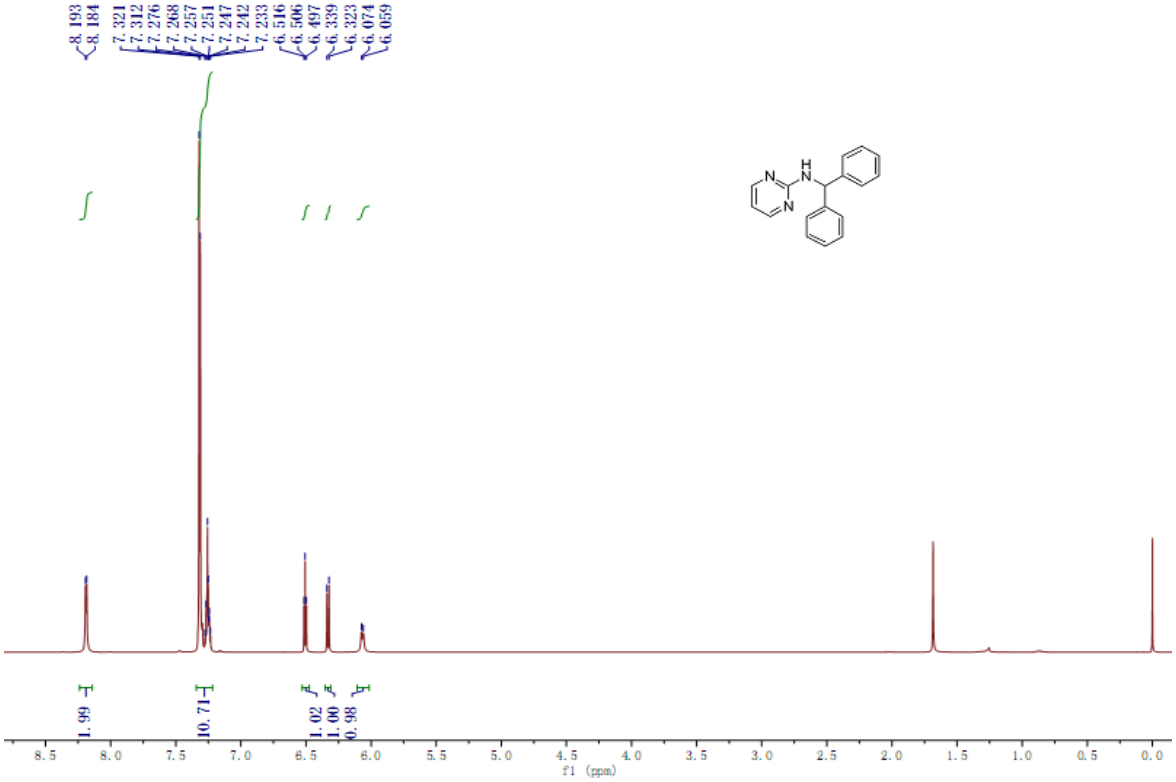




8a

^{1}H NMR



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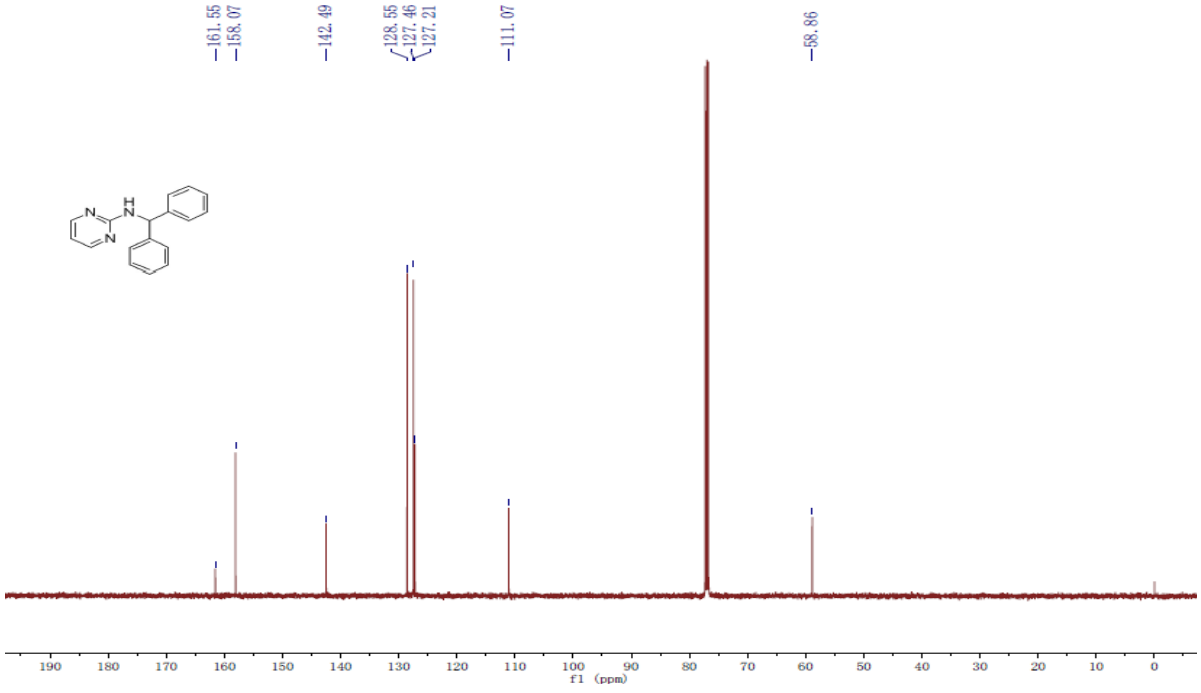
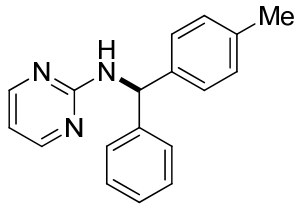
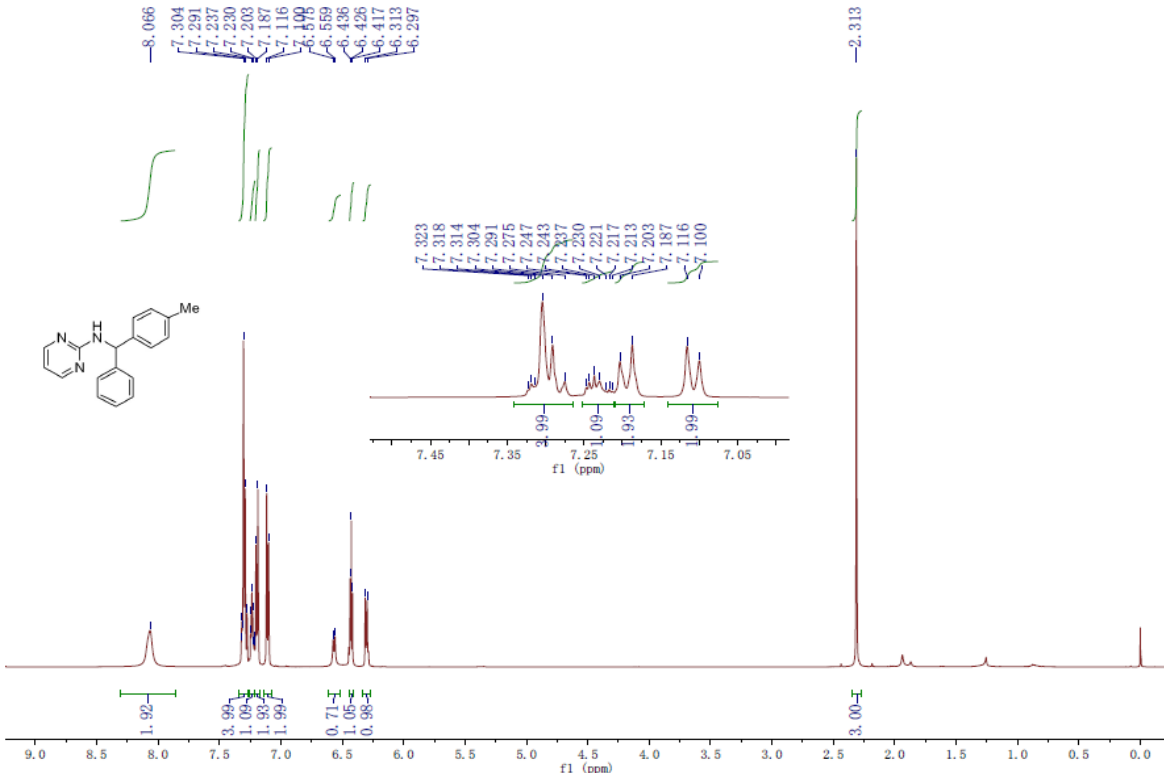




8b

^{1}H NMR



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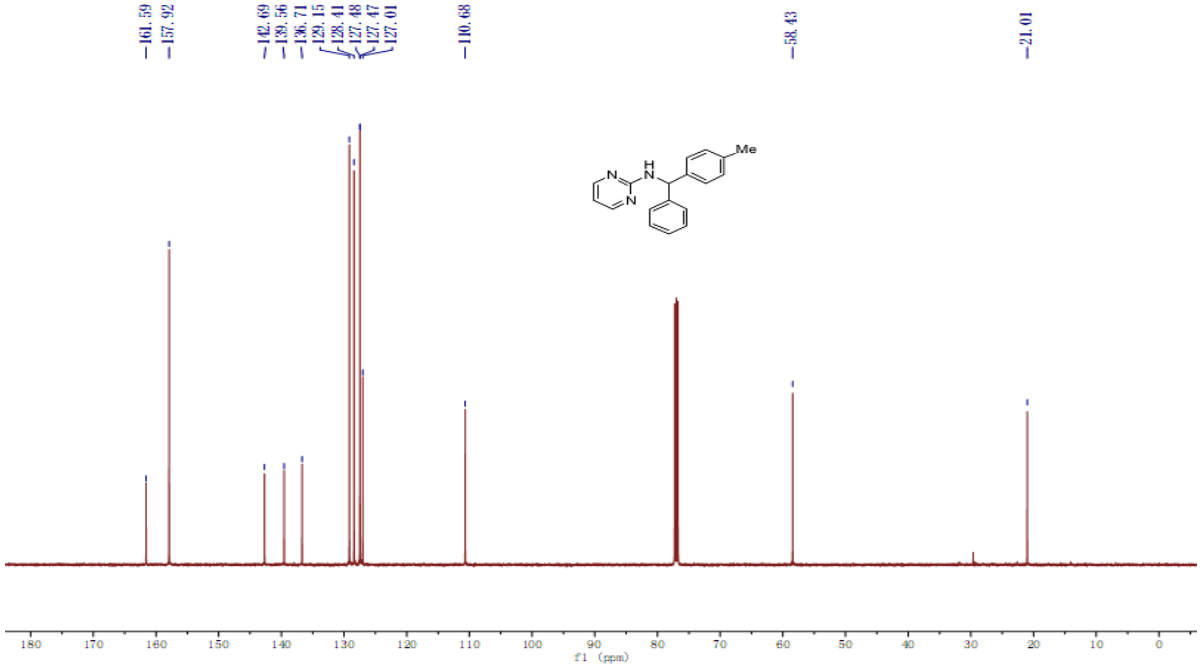
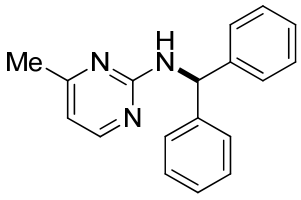
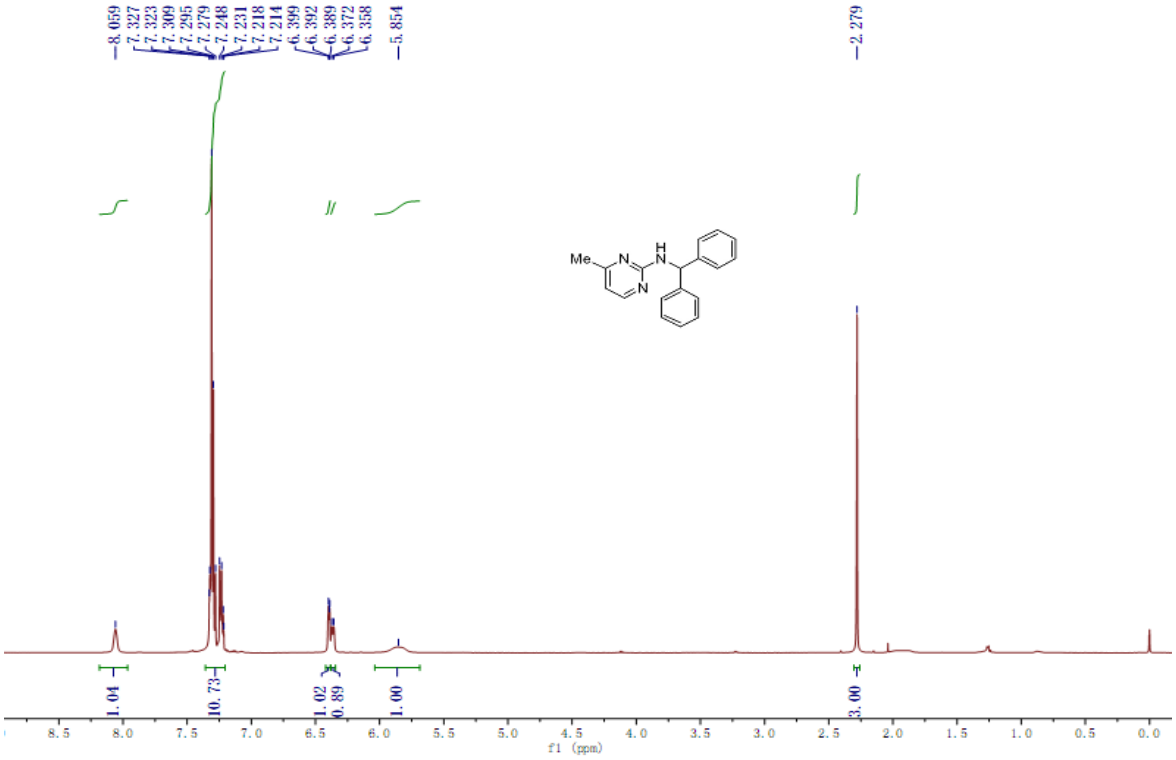




8c

^{1}H NMR



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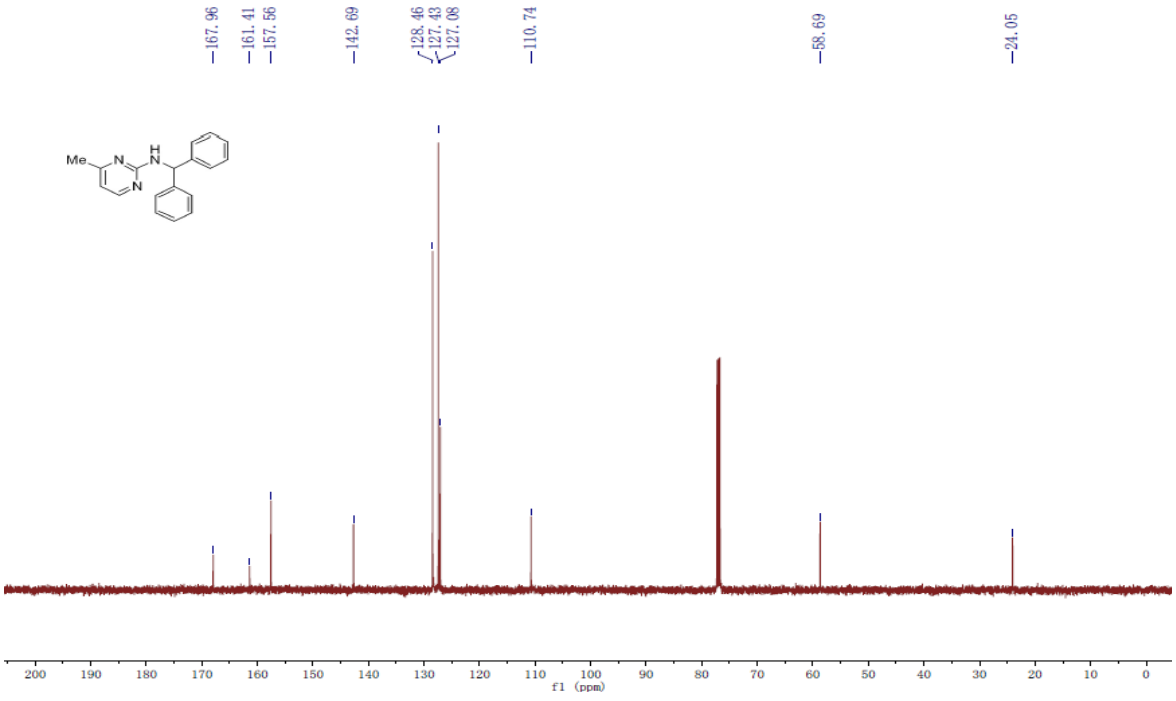
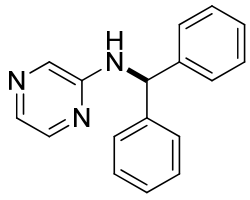
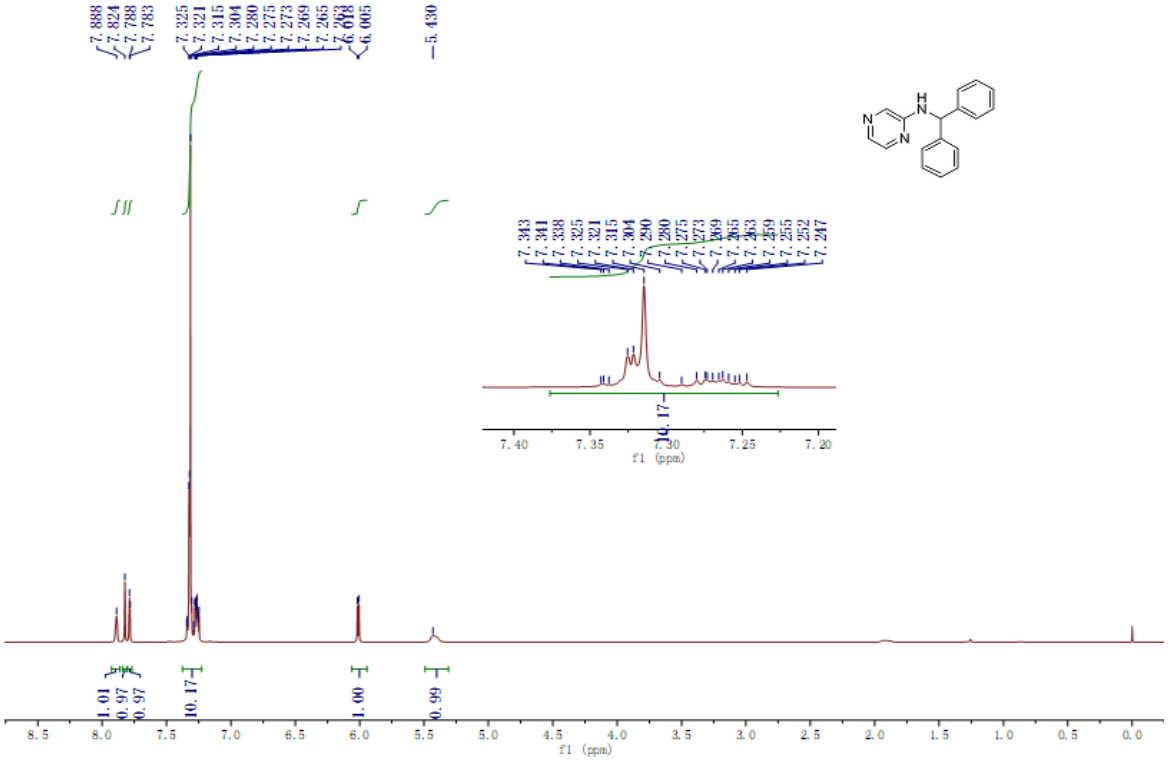




9a

^{1}H NMR



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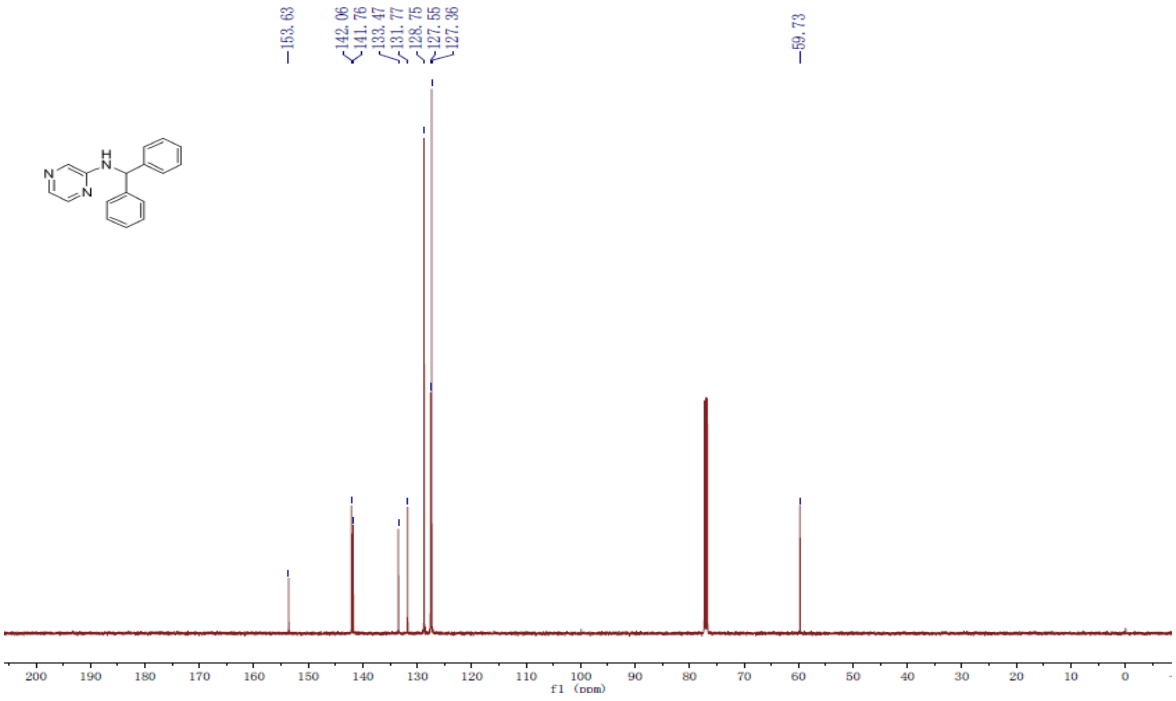

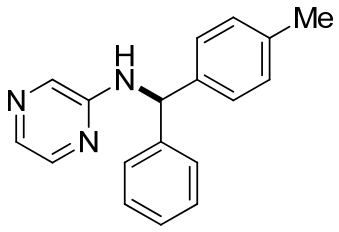

9b

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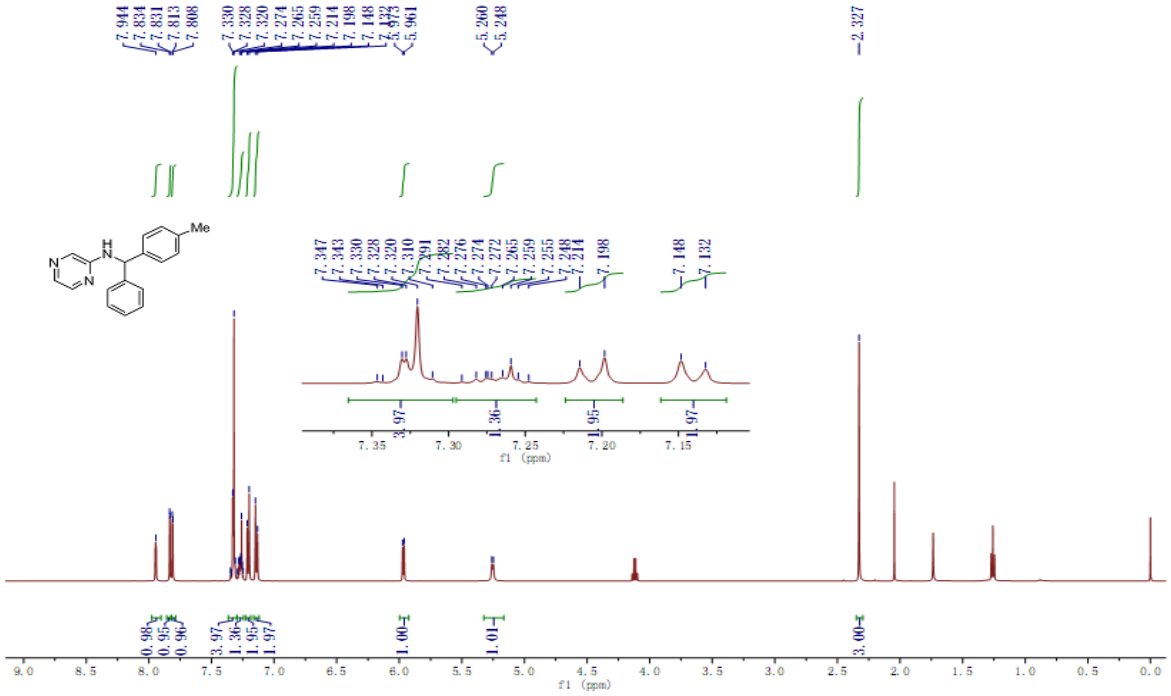

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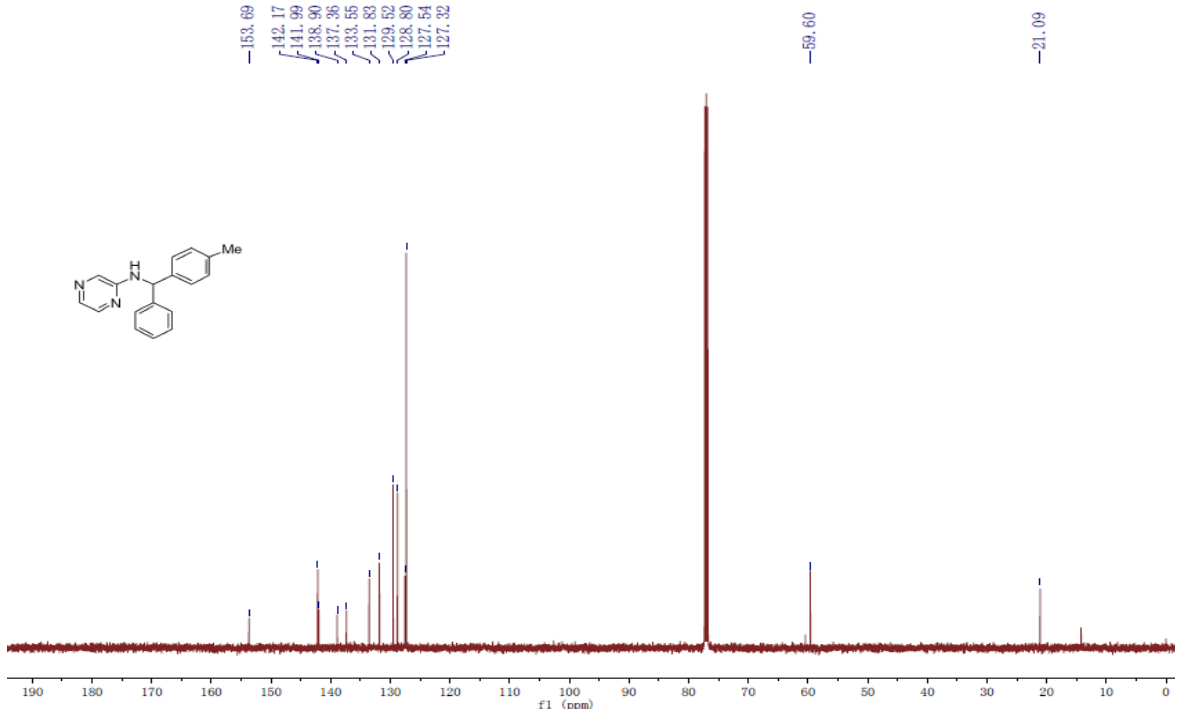
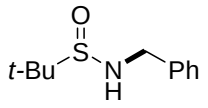
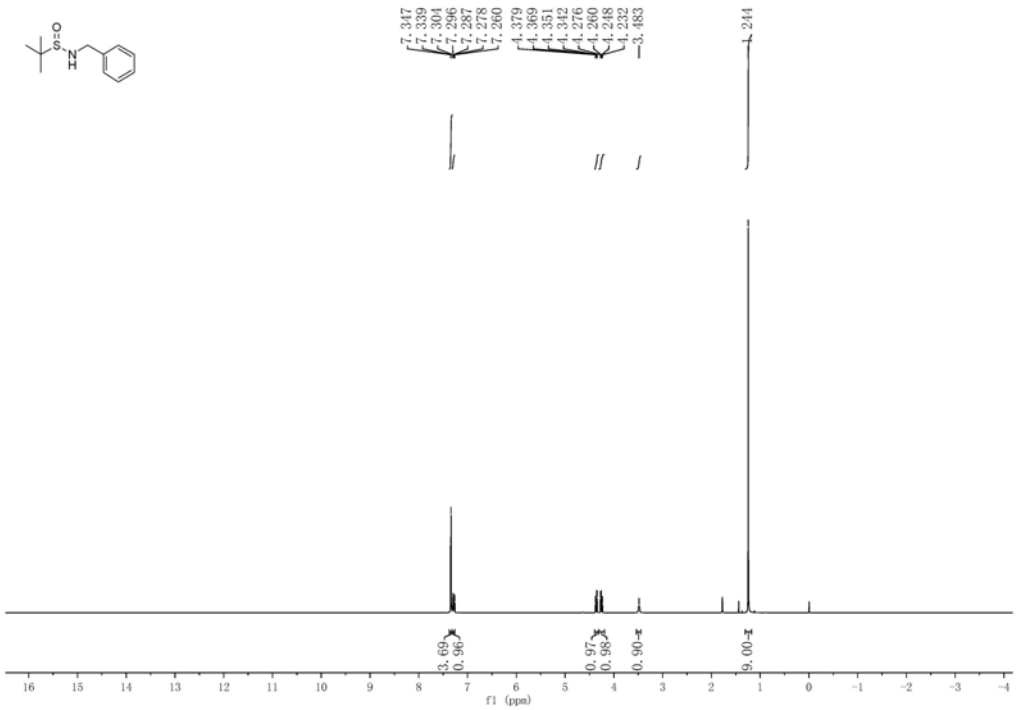




13

^{1}H NMR



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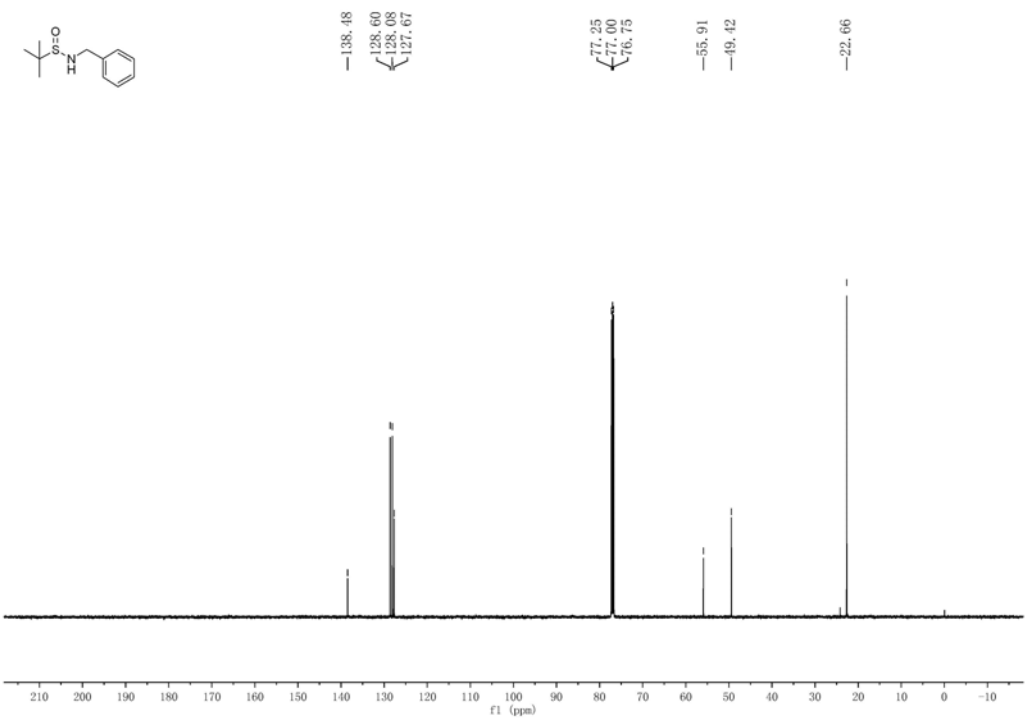
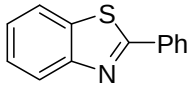
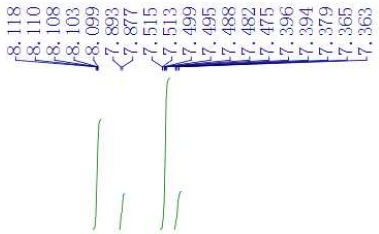
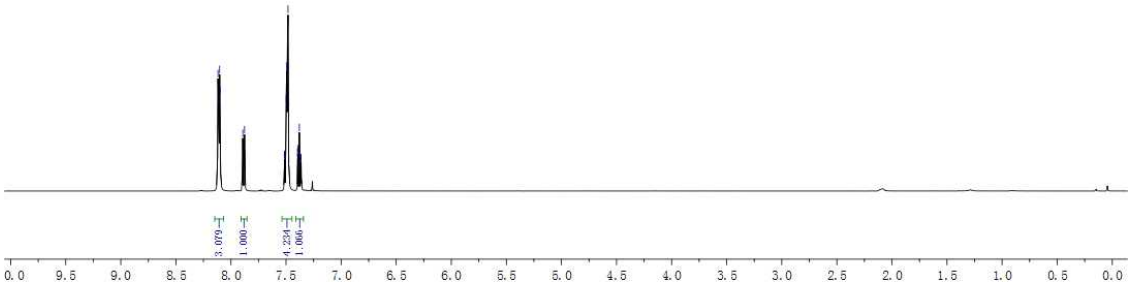




16

^{1}H NMR





^{13}C NMR