Supporting Information

Dehydrative amination of benzhydrols with electron-withdrawing group-substituted 2-aminopyridines utilizing Au(III)/TPPMS catalyst system in water

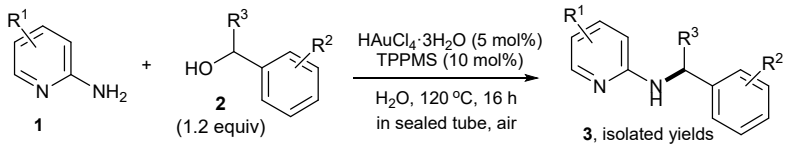
Hidemasa Hikawa*, Taku Nakayama, Shunki Nakamura, Shoko Kikkawa, and Isao Azumaya*

Faculty of Pharmaceutical Sciences, Toho University, Funabashi, Chiba 274-8510, Japan
hidemasa.hikawa@phar.toho-u.ac.jp and isao.azumaya@phar.toho-u.ac.jp

General Considerations

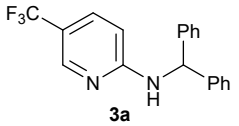
All of the starting materials and solvents were purchased from Sigma–Aldrich Japan, FUJIFILM Wako Pure Chemical Co., Nacalai Tesque, Inc., and TCI Co., Ltd. All commercially available reagents and solvents (guaranteed reagents) were used without further purification. CHROMATOREX Q-PACK SI50 (Fuji Silysia Chemical Ltd, Japan) was used for flash column chromatography. All melting points were determined using a Yanako micro melting point apparatus without correction. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a JEOL ECS400 spectrometer. IR spectra were measured with a JASCO FT/IR-4100 spectrometer. Mass spectra were obtained using a JEOL the JMS-700 MStation Mass Spectrometer.

Scheme S1. Substrate scope.



General procedure: A mixture of 2-aminopyridines **1** (1 mmol), $HAuCl_4 \cdot 4H_2O$ (20.6 mg, 0.05 mmol), $HAuCl_4 \cdot 4H_2O$ (20.6 mg, 0.05 mmol), TPPMS (36.4 mg, 10 mol%), and benzhydroles **2** (1.2 mmol) in water (1 mL) was heated at 120 °C for 16 h in a sealed tube under air. After cooling, the reaction mixture was poured into water and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, *n*-hexane/EtOAc) to give desired product **3**.

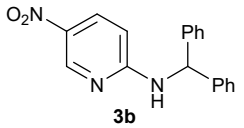
***N*-Benzhydryl-5-(trifluoromethyl)pyridin-2-amine 3a**



Prepared according to the general procedure by using 5-(trifluoromethyl)pyridine -2-amine (162 mg) and benzhydrol (221 mg).

White solid, 236 mg (72%); mp 142-144 °C; IR (KBr) (cm^{-1}) 3269, 1618, 1522; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.65 (brd, *J*=6.0 Hz, 1H), 5.91 (d, *J*=6.0 Hz, 1H), 6.32 (d, *J*=9.2 Hz, 1H), 7.26-7.37 (m, 10H), 7.53 (dd, *J*=8.7, 2.3 Hz, 1H), 8.25 (brs, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 60.6, 106.0, 116.0 (q, *J*=33.6 Hz), 124.5 (q, *J*=270.3 Hz), 127.4, 127.7, 128.9, 134.6 (q, *J*=3.8 Hz), 141.5, 146.1 (q, *J*=3.8 Hz), 159.5; MS (FAB): *m/z* 329 $[M+H]^+$; HRMS (FAB): *m/z* $[M+H]^+$ calcd. for $C_{19}H_{16}F_3N_2$ 329.1266, found 329.1266.

_N_-Benzhydryl-5-nitropyridin-2-amine 3b

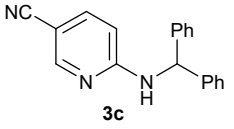


3b

Prepared according to the general procedure by using 2-amino-5-nitropyridine (139 mg) and benzhydrol (221 mg).

Pale yellow solid, 298 mg (98%); mp 138–140 °C; IR (KBr) (cm^{-1}) 3223 1598; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.00 (brs, 1H), 6.15-6.40 (m, 1H), 6.30 (d, *J*=9.2 Hz, 1H), 7.27-7.40 (m, 10H), 8.13 (dd, 9.6, 2.3 Hz, 1H), 8.82 (brd, *J*=2.3 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 60.7, 105.6, 127.4, 128.0, 129.0, 133.2, 136.2, 140.6, 146.7, 160.4; MS (FAB): *m/z* 306 $[M+H]^+$; HRMS (FAB): *m/z* $[M+H]^+$ calcd. for $C_{18}H_{16}N_3O_2$ 306.1243, found 306.1243.

6-(Benzhydrylamino)nicotinonitrile 3c

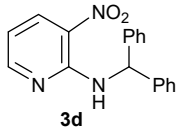


3c

Prepared according to the general procedure by using 2-amino-5-cyanopyridine (119 mg) and benzhydrol (221 mg).

White solid, 234 mg (82%); mp 152–154 °C; IR (KBr) (cm^{-1}) 3248 2218 1608 1506; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.93 (brs, 1H), 5.99 (brs, 1H), 6.30 (d, *J* = 8.7 Hz, 1H), 7.27–7.38 (m, 10H), 7.52 (dd, *J* = 8.7, 2.3 Hz, 1H), 8.14 (s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 60.4, 97.5, 106.5, 118.3, 127.5, 127.9, 128.9, 140.0, 140.9, 152.9, 159.0; MS (EI): *m/z* (%) 285 (M^+, 86), 167 (100); Anal. Calcd for $C_{19}H_{15}N_3$: C, 79.98; H, 5.30; N, 14.73. Found: C, 79.91; H, 5.30; N, 14.67.

_N_-Benzhydryl-3-nitropyridin-2-amine 3d

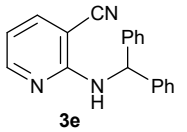


3d

Prepared according to the general procedure by using 3-nitropyridin-2-amine (139 mg) and benzhydrol (221 mg).

Yellow solid, 293 mg (96%); mp 82-84 °C; IR (KBr) (cm^{-1}) 3389, 1613, 1573, 1495; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.66 (dd, *J*=8.2, 4.6 Hz, 1H), 6.73 (d, *J*=7.8 Hz, 1H), 7.24-7.37 (m, 10H), 7.37 (dd, *J*=4.6, 1.4 Hz, 1H), 8.44 (dd, *J*=8.7, 1.8 Hz, 1H), 8.88 (d, *J*=7.3 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 58.4, 112.4, 127.4, 127.5, 128.7, 135.2, 141.9, 151.5, 155.8; MS (FAB): *m/z* 306 $[M+H]^+$; Anal. Calcd for $C_{18}H_{15}N_3O_2$: C, 70.81; H, 4.95; N, 13.76. Found: C, 70.94; H, 4.92; N, 13.67.

2-(Benzhydrylamino)nicotinonitrile 3e

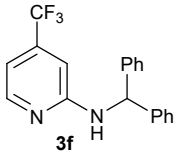


3e

Prepared according to the general procedure by using 2-aminonicotinonitrile (119 mg) and benzhydrol (221 mg).

White solid, 228 mg (80%); mp 133-134 °C; IR (KBr) (cm^{-1}) 3349, 2227, 1590, 1513; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.69 (brd, *J*=7.3 Hz, 1H), 6.52 (d, *J*=7.3 Hz, 1H), 6.62 (dd, *J*=7.8, 4.6 Hz, 1H), 7.24-7.37 (m, 10H), 7.67 (dd, *J*=7.8, 1.8 Hz, 1H), 8.24 (dd, *J*=4.6, 2.3 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 58.6, 91.7, 112.6, 116.7, 127.4, 127.5, 128.7, 141.3, 141.8, 152.9, 157.3; MS (FAB): *m/z* 286 $[M+H]^+$; Anal. Calcd for $C_{19}H_{15}N_3$: C, 79.98; H, 5.30; N, 14.73. Found: C, 80.27; H, 5.33; N, 14.62.

***N*-Benzhydryl-4-(trifluoromethyl)pyridin-2-amine 3f**

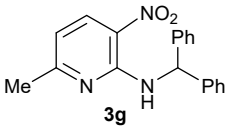


3f

Prepared according to the general procedure by using 4-(trifluoromethyl)pyridine -2-amine (162 mg) and benzhydrol (221 mg).

White solid, 269 mg (82%); mp 106-108 °C; IR (KBr) (cm^{-1}) 3269, 1617, 1574; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.39 (brd, *J*=6.0 Hz, 1H), 5.97 (d, *J*=6.4 Hz, 1H), 6.50 (s, 1H), 6.76 (dd, *J*=5.5, 0.9 Hz, 1H), 7.26-7.37 (m, 10H), 8.19 (d, *J*=5.5 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 60.4, 102.9 (q, *J*=3.8 Hz), 108.7 (q, *J*=2.9 Hz), 123.0 (q, *J*=273.2 Hz), 127.4, 127.6, 128.8, 139.6 (q, *J*=32.6 Hz), 141.8, 149.5, 158.0; MS (FAB): *m/z* 329 $[M+H]^+$; Anal. Calcd for $C_{19}H_{15}F_3N_2$: C, 69.50; H, 4.61; N, 8.53. Found: C, 69.48; H, 4.64; N, 8.52.

***N*-Benzhydryl-6-methyl-3-nitropyridin-2-amine 3g**

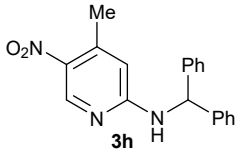


3g

Prepared according to the general procedure by using 6-methyl-3-nitropyridin-2-amine (153 mg) and benzhydrol (221 mg).

Yellow solid, 240 mg (75%); mp 106-108 °C; IR (KBr) (cm^{-1}) 3384, 1598, 1581, 1516; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.50 (d, *J*=8.7 Hz, 1H), 6.80 (d, *J*=8.2 Hz, 1H), 7.23-7.40 (m, 10H), 8.30 (d, *J*=8.7 Hz, 1H), 8.97 (d, *J*=7.8 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 25.2, 58.0, 112.6, 127.3, 127.5, 128.6, 135.3, 142.1, 151.0, 166.5; MS (FAB): *m/z* 320 $[M+H]^+$; Anal. Calcd for $C_{19}H_{17}N_3O_2$: C, 71.46; H, 5.37; N, 13.16. Found: C, 71.67; H, 5.33; N, 12.94.

***N*-Benzhydryl-4-methyl-5-nitropyridin-2-amine 3h**

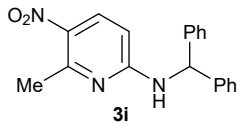


3h

Prepared according to the general procedure by using 4-methyl-5-nitropyridin-2-amine (153 mg) and benzhydrol (221 mg).

Pale yellow solid, 281 mg (88%); mp 191-193 °C; IR (KBr) (cm^{-1}) 3218, 1609, 1574; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.52 (s, 3H), 5.86 (brs, 1H), 5.99 (brs, 1H), 6.12 (s, 1H), 7.27-7.39 (m, 10H), 8.86 (s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 21.8, 60.5, 108.0, 127.4, 127.9, 128.9, 137.4, 141.0, 145.6, 148.3, 159.6; MS (FAB): *m/z* 320 $[M+H]^+$; Anal. Calcd for $C_{19}H_{17}N_3O_2 \cdot H_2O$: C, 67.64; H, 5.08; N, 12.46. Found: C, 67.33; H, 5.10; N, 12.23.

***N*-Benzhydryl-6-methyl-5-nitropyridin-2-amine 3i**

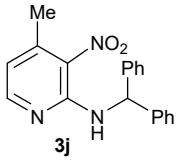


3i

Prepared according to the general procedure by using 6-methyl-5-nitropyridin-2-amine (153 mg) and benzhydrol (221 mg).

Yellow solid, 266 mg (83%); mp 110-112 °C; IR (KBr) (cm^{-1}) 3326, 1591, 1536; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.74 (s, 3H), 5.82 (brs, 1H), 5.95 (brs, 1H), 6.17 (d, *J*=9.2 Hz, 1H), 7.27-7.39 (m, 10H), 8.16 (d, *J*=9.2 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 25.4, 60.7, 104.0, 127.4, 127.9, 128.9, 135.6, 136.7, 141.0, 156.4, 158.5; MS (FAB): *m/z* 320 $[M+H]^+$; Anal. Calcd for $C_{19}H_{17}N_3O_2$: C, 71.46; H, 5.37; N, 13.16. Found: C, 71.35; H, 5.32; N, 13.07.

***N*-Benzhydryl-4-methyl-3-nitropyridin-2-amine 3j**

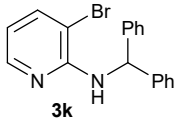


3j

Prepared according to the general procedure by using 4-methyl-3-nitropyridin-2-amine (153 mg) and benzhydrol (221 mg).

Yellow solid, 236 mg (74%); mp 90-92 °C; IR (KBr) (cm^{-1}) 3410, 1604, 1557; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.54 (s, 3H), 6.49 (d, *J*=5.0 Hz, 1H), 6.62 (d, *J*=7.3 Hz, 1H), 7.23-7.35 (m, 10H), 8.09 (d, *J*=5.0 Hz, 1H), 8.12 (brd, *J*=6.9 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 21.8, 58.7, 116.4, 127.4, 128.7, 130.6, 142.2, 146.6, 151.6, 152.4; MS (FAB): *m/z* 320 $[M+H]^+$; Anal. Calcd for $C_{19}H_{17}N_3O_2$: C, 71.46; H, 5.37; N, 13.16. Found: C, 71.62; H, 5.38; N, 13.03.

***N*-Benzhydryl-3-bromopyridin-2-amine 3k**

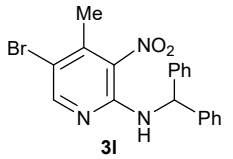


3k

Prepared according to the general procedure by using 2-amino-3-bromopyridine (173 mg) and benzhydrol (221 mg).

White solid, mp 49–52 °C; IR (KBr) (cm^{-1}) 3418 1589 1492; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* (ppm): 5.60 (brd, *J* = 7.3 Hz, 1H), 6.44–6.47 (m, 2H), 7.23–7.35 (m, 10H), 7.62 (dd, *J* = 7.6, 1.6 Hz, 1H), 8.00 (dd, *J* = 4.8, 1.6 Hz, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 58.8, 105.4, 114.7, 127.5, 127.8, 129.0, 140.6, 143.4, 147.2, 153.9; MS (EI): *m/z* (%) 338 (M^+, 78), 340 (M^++2, 78), 167 (100); Anal. Calcd for $C_{18}H_{15}BrN_2$: C, 63.73; H, 4.46; N, 8.26. Found: C, 64.11; H, 4.51; N, 8.05.

***N*-Benzhydryl-5-bromo-4-methyl-3-nitropyridin-2-amine 3l**

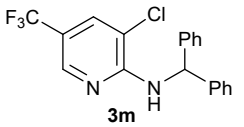


3l

Prepared according to the general procedure by using 5-bromo-4-methyl-3-nitropyridin-2-amine (232 mg) and benzhydrol (221 mg).

Yellow solid, 323 mg (81%); mp 102-104 °C; IR (KBr) (cm^{-1}) 3418, 1592, 1541, 1518; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.50 (d, *J*=6.9 Hz, 1H), 7.22-7.42 (m, 10H), 8.28 (brs, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 20.7, 59.0, 111.1, 127.5, 127.6, 132.4, 141.8, 144.1, 149.7, 153.5; MS (FAB): *m/z* 398 $[M+H]^+$; Anal. Calcd for $C_{19}H_{16}BrN_3O_2$: C, 57.30; H, 4.05; N, 10.55. Found: C, 57.34; H, 3.96; N, 10.51.

***N*-Benzhydryl-3-chloro-5-(trifluoromethyl)pyridin-2-amine 3m**

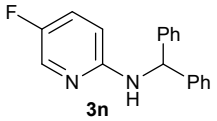


3m

Prepared according to the general procedure by using 2-amino-3-chloro-5-(trifluoroehtyl) pyridine (197 mg) and benzhydrol (221 mg).

White solid, 293 mg (81%); mp 103–105 °C; IR (KBr) (cm^{-1}) 3330 1613 1569 1509; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* (ppm): 5.89 (brd, *J* = 7.3 Hz, 1H), 6.49 (d, *J* = 7.3 Hz, 1H), 7.27–7.38 (m, 8H), 7.66 (d, *J* = 2.3 Hz, 1H), 8.24 (q, *J* = 0.9 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 59.1, 80.2, 115.0, 116.5 (q, *J*=33.6 Hz), 123.9 (q, *J*=271.3 Hz), 127.4, 127.6, 127.7, 128.6, 128.9, 133.1 (q, *J*=2.9 Hz), 142.0, 142.4, 144.2 (q, *J*=4.8 Hz), 154.9; MS (FAB): *m/z* 363 $[M+H]^+$; HRMS (FAB): *m/z* $[M+H]^+$ calcd. for $C_{19}H_{15}ClF_3N_2$ 363.0876, found 363.0876.

***N*-Benzhydryl-5-fluoropyridin-2-amine 3n**

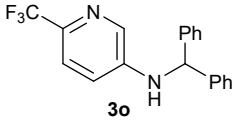


3n

Prepared according to the general procedure by using 2-amino-5-fluoropyridine (112 mg) and benzhydrol (221 mg).

White solid, 224 mg (80%); mp 130–132 °C; IR (KBr) (cm^{-1}) 3345, 1614, 1577; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.09 (brd, J = 5.2 Hz, 1H), 5.77 (d, J = 5.5 Hz, 1H), 6.24 (dd, J = 9.0, 3.4 Hz, 1H), 7.13 (td, J = 3.0, 0.9 Hz, 1H), 7.22-7.35 (m, 10H), 7.93 (d, J = 3.0 Hz, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 58.8, 110.2 (d, J_{CF}=3.8 Hz), 125.6 (d, J_{CF}=21.1 Hz), 127.2, 127.8, 128.8, 133.8 (d, J_{CF}=24.0 Hz), 144.2, 153.2 (d, J_{CF}=237.7 Hz), 155.4; MS (EI): *m/z* (%) 278 (M^+, 92%), 167 (100); Anal. Calcd for $C_{18}H_{15}FN_2$: C, 77.68; H, 5.43; N, 10.07. Found: C, 77.77; H, 5.43; N, 9.98.

***N*-Benzhydryl-6-(trifluoromethyl)pyridin-3-amine 3o**

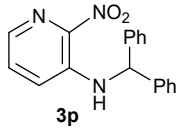


3o

Prepared according to the general procedure by using 6-(trifluoromethyl)pyridin-3-amine (162 mg) and benzhydrol (221 mg).

White solid, 315 mg, (96%); mp 203-205 °C; IR (KBr) (cm^{-1}) 3253, 1589, 1513; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 4.68 (d, J=4.1 Hz, 1H), 5.54 (d, J=4.6 Hz, 1H), 6.77 (dd, J=8.7, 2.8 Hz, 1H), 7.27-7.40 (m, 10H), 8.08 (d, J=2.8 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 62.5, 118.2, 121.1 (q, J=2.9 Hz), 122.2 (q, J=272.2 Hz), 127.3, 128.0, 129.1, 136.5, 136.8 (q, J=35.5 Hz), 141.0, 144.9; MS (FAB): *m/z* 329 $[M+H]^+$; HRMS (FAB): *m/z* $[M+H]^+$ calcd. for $C_{19}H_{16}F_3N_2$ 329.1266, found 329.1266.

***N*-Benzhydryl-2-nitropyridin-3-amine 3p**

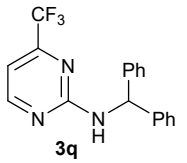


3p

Prepared according to the general procedure by using 2-nitropyridin-3-amine (139 mg) and benzhydrol (221 mg).

Yellow solid, 278 mg (91%); mp 134-136 °C; IR (KBr) (cm^{-1}) 3374, 1606, 1529; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.72 (d, J=5.5 Hz, 1H), 7.19 (dd, J=8.2, 1.4 Hz, 1H), 7.28-7.42 (m, 11H), 7.92 (dd, J=4.1, 1.4 Hz, 1H), 8.30 (brd, J=5.0 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 61.9, 124.7, 127.2, 128.2, 129.2, 130.3, 135.8, 139.7, 140.4, 141.3; MS (FAB): *m/z* 306 $[M+H]^+$; Anal. Calcd for $C_{18}H_{15}N_3O_2 \cdot 0.1H_2O$: C, 70.39; H, 4.92; N, 13.68. Found: C, 70.13; H, 4.94; N, 13.35.

***N*-Benzhydryl-4-(trifluoromethyl)pyrimidin-2-amine 3q**



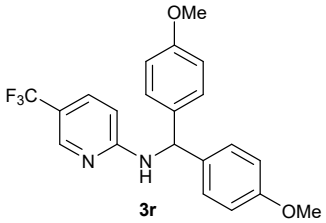
3q

Prepared according to the general procedure by using 4-(trifluoromethyl)pyrimidin-2-amine (163 mg) and benzhydrol (221 mg).

White solid, 247 mg (75%), mp 123-125 °C; IR (KBr) (cm^{-1}) 3236, 1603, 1581, 1545; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.10 (brs, 1H), 6.36 (d, J=7.8 Hz, 1H), 6.83 (d, J=5.0 Hz, 1H), 7.24-7.36 (m, 10H), 8.43 (brs, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 59.1, 106.2 (q, J=2.9 Hz), 120.4 (q, J=276.0 Hz), 127.5, 128.6, 141.8, 156.5 (q, J=35.5 Hz), 160.5, 161.5; MS (FAB): *m/z* 330 $[M+H]^+$, Anal. Calcd for $C_{18}H_{14}F_3N_3$: C, 65.65; H, 4.29; N, 12.76. Found: C, 65.75; H, 4.25; N, 12.72.

***N*-{Bis(4-methoxyphenyl)methyl}-5-(trifluoromethyl)pyridin-2-amine 3r**

Prepared according to the general procedure by using 2-amino-5-(trifluoromethyl)-pyridine (162 mg) and 4,4'-dimethoxybenzhydrol (293 mg).



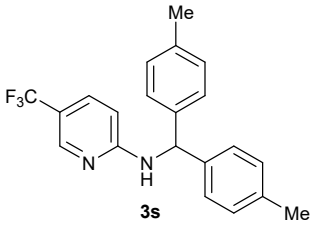
3r

White solid, 349 mg (90%); mp 128–131 °C; IR (KBr) (cm^{-1}) 3282, 1613, 1582, 1507; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 3.79 (s, 6H),5.66 (brd, J = 5.5 Hz, 1H), 5.78 (d, J = 5.5 Hz, 1H), 6.29 (d, J = 8.7 Hz, 1H), 6.86 (d, J = 8.7 Hz, 4H), 7.21 (d, J = 8.7 Hz, 4H), 7.52 (dd, J=8.7, 2.8 Hz, 1H), 8.22 (s, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ; 56.2, 59.4, 105.8, 114.1, 115.8 (q, J=33.6 Hz), 124.5 (q, J=271.3 Hz), 128.5, 133.8, 134.6 (q, J=3.8 Hz), 146.1 (q, J=3.8 Hz), 159.0, 159.6; MS (FAB): *m/z* 389 $[M+H]^+$; HRMS (FAB): *m/z* $[M+H]^+$ calcd. for $C_{21}H_{20}F_3N_2O_2$ 389.1477, found 389.1476.

***N*-(Di-*p*-tolylmethyl)-5-(trifluoromethyl)pyridin-2-amine 3s**

Prepared according to the general procedure by using 2-amino-5-(trifluoromethyl)-pyridine (162 mg) and 4,4'-dimethylbenzhydrol (254 mg).

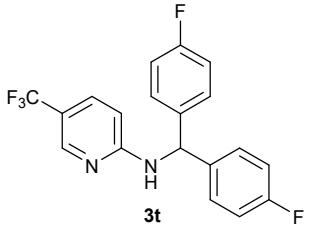


3s

White slid, 349 mg (98%); mp 149–152 °C; IR (KBr) (cm^{-1}) 3362, 1617, 1574, 1537; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 2.33 (s, 6H), 5.70 (brd, J = 5.5 Hz, 1H), 5.80 (d, J = 5.5 Hz, 1H), 6.29 (d, J = 8.7 Hz, 1H), 7.13 (d, J = 8.2 Hz, 4H), 7.19 (d, J=8.2 Hz, 4H), 7.52 (dd, J = 8.7, 2.8 Hz, 1H), 8.21 (q, J=1.4 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 21.1, 60.1, 105.8, 115.7 (q, J=33.6 Hz), 124.5 (q, J=270.3 Hz), 127.3, 129.5, 134.6 (q, J=3.8 Hz), 137.4, 138.7, 146.1 (q, J=4.8 Hz), 159.7; MS (FAB): *m/z* 357 $[M+H]^+$; HRMS (FAB): *m/z* $[M+H]^+$ calcd. for $C_{21}H_{20}F_3N_2$ 357.1579, found 357.1578.

***N*-{Bis(4-fluorophenyl)methyl}-5-(trifluoromethyl)pyridin-2-amine 3t**

Prepared according to the general procedure by using 2-amino-5-(trifluoromethyl)-pyridine (163 mg) and 4,4'-difluorobenzhydrol (265 mg).

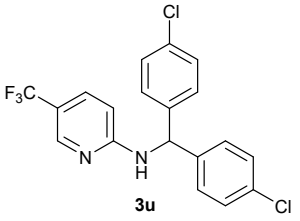


3t

White solid, 229 mg (63%); mp 197–200 °C; IR (KBr) (cm^{-1}) 3275, 1620, 1507; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 5.44 (brd, J = 5.5 Hz, 1H), 5.95 (d, J = 6.0 Hz, 1H), 6.33 (d, J = 8.9 Hz, 1H), 7.04 (dd, J = 8.7, 8.7 Hz, 4H), 7.26 (dd, J = 8.5, 5.5 Hz, 4H), 7.57 (dd, J = 8.7 , 2.3 Hz, 1H), 8.30 (s, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 56.8, 109.4, 113.9 (q, J_{CF}=31.6 Hz), 115.7 (d, J_{CF}=22.0 Hz), 125.5 (q, J_{CF}=270.3 Hz), 129.8 (d, J_{CF}=7.7 Hz), 134.1, 139.4 (d, J_{CF}=3.8 Hz), 145.9 (q, J_{CF}=4.8 Hz), 160.5, 161.5 (d, J_{CF}=277.0 Hz); MS (FAB): *m/z* 365 $[M+H]^+$; HRMS (FAB): *m/z* $[M+H]^+$ calcd. for $C_{19}H_{14}F_5N_2$ 365.1077, found 365.1076.

***N*-{Bis(4-chlorophenyl)methyl}-5-(trifluoromethyl)pyridin-2-amine 3u**

Prepared according to the general procedure by using 5-(trifluoromethyl)pyridin-2-amine (162 mg) and 4,4'-dichlorobenzhydrol (304 mg).

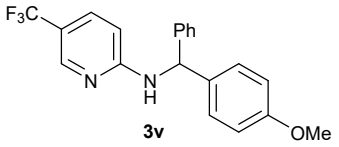


3u

White solid, 203 mg (51%); mp 180-182 °C; IR (KBr) (cm^{-1}) 3281, 1620, 1581, 1518; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.37 (brd, *J*=6.0 Hz, 1H), 5.96 (d, *J*=6.0 Hz, 1H), 6.34 (d, *J*=9.2 Hz, 1H), 7.22 (d, *J*=8.7 Hz, 2H), 7.32 (d, *J*=8.7 Hz, 2H), 7.57 (dd, *J*=9.2, 2.8 Hz, 1H), 8.31 (s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 59.1, 106.6, 116.6 (q, *J*=33.6 Hz), 124.3 (q, *J*=270.3 Hz), 128.7, 129.1, 133.8, 134.7 (q, *J*=3.8 Hz), 139.7, 146.1 (q, *J*=3.8 Hz), 159.0; MS (FAB): *m/z* 397 $[M+H]^+$, 399 $[M+H+2]^+$, 401 $[M+H+4]^+$, HRMS (FAB): *m/z* $[M+H]^+$ calcd. for $C_{19}H_{13}Cl_2F_3N_2$ 397.0486, found 397.0486.

***N*-{(4-Methoxyphenyl)(phenyl)methyl}-5-(trifluoromethyl)pyridin-2-amine 3v**

Prepared according to the general procedure by using 2-amino-5-(trifluoromethyl)pyridine (162 mg) and 4-methoxybenzhydrol (258 mg).

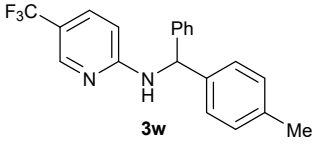


3v

White solid, 263 mg (73%); mp 121–123 °C; IR (KBr) (cm^{-1}) 3255, 1618, 1537; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* (ppm): 3.79 (s, 3H), 5.56 (brd, *J* = 5.7 Hz, 1H), 5.85 (d, *J* = 6.0 Hz, 1H), 6.31 (d, *J* = 8.7 Hz, 1H), 6.86 (d, *J* = 8.7 Hz, 2H), 7.22 (d, *J* = 8.7 Hz, 2H), 7.27–7.37 (m, 6H), 7.53 (dd, *J* = 8.7, 2.5 Hz, 1H), 8.28 (s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 55.4, 60.1, 106.1, 114.3, 116.0 (q, *J*=32.6 Hz), 124.6 (q, *J*=271.3 Hz), 127.2, 127.4, 127.7, 128.6, 128.7, 128.8, 128.9, 133.8, 146.2 (q, *J*=3.8 Hz), 159.2, 159.6; MS (FAB): *m/z* 359 $[M+H]^+$, HRMS (FAB): *m/z* $[M+H]^+$ calcd. for $C_{20}H_{18}F_3N_2O$ 359.1371, found 359.1371.

***N*-{Phenyl(*p*-tolyl)methyl}-5-(trifluoromethyl)pyridin-2-amine 3w**

Prepared according to the general procedure by using 2-amino-5-(trifluoromethyl)-pyridine (163 mg) and 4-methylbenzhydrol (238 mg).

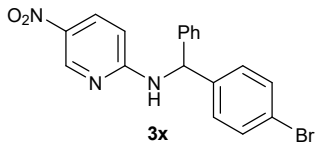


3w

White solid, 340 mg (99%); mp 141–143 °C; IR (KBr) (cm^{-1}) 3258, 1620, 1573, 1537; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* (ppm): 2.33 (s, 3H), 5.63 (brd, *J* = 5.5 Hz, 1H), 5.86 (d, *J* = 6.0 Hz, 1H), 6.31 (d, *J* = 9.2 Hz, 1H), 7.14 (d, *J* = 8.2 Hz, 2H), 7.20 (d, *J* = 7.8 Hz, 2H), 7.27–7.37 (m, 5H), 7.53 (dd, *J* = 8.7 Hz, 1H), 8.25 (q, *J*=0.9 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 21.1, 60.3, 106.0, 116.0 (q, *J*=32.6 Hz), 124.5 (q, *J*=270.3 Hz), 127.3, 127.6, 128.8, 129.5, 134.6 (q, *J*=2.9 Hz), 137.5, 138.6, 141.7, 146.2 (q, *J*=3.8 Hz), 159.5; MS (FAB): *m/z* 343 $[M+H]^+$, HRMS (FAB): *m/z* $[M+H]^+$ calcd. for $C_{20}H_{18}F_3N_2$ 343.1422, found 343.1422.

***N*-{(4-Bromophenyl)(phenyl)methyl}-5-nitropyridin-2-amine 3x**

Prepared according to the general procedure by using 5-nitropyridin-2-amine (139 mg) and 4-chlorobenzhydrol (262 mg).

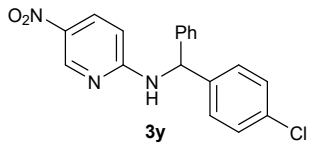


3x

Pale yellow solid, 327 mg (85%); mp 171-173 °C; IR (KBr) (cm^{-1}) 3373, 1598, 1576, 1535; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.87 (brs, 1H), 6.03 (brs, 1H), 6.32 (d, *J*=9.2 Hz, 1H), 7.19 (d, *J*=8.2 Hz, 2H), 7.25-7.29 (m, 3H), 7.39-7.40 (m, 3H), 7.48 (d, *J*=8.7 Hz, 2H), 8.17 (dd, *J*=9.2, 2.8 Hz, 1H), ; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 60.0, 106.1, 121.9, 127.4, 128.3, 129.0, 129.1, 132.1, 133.2, 136.6, 139.9, 140.3, 146.8, 160.1; MS (FAB): *m/z* 384 $[M+H]^+$, 386 $[M+H+2]^+$; Anal. Calcd for $C_{18}H_{14}BrN_3O_2$: C, 56.27; H, 3.67; N, 10.94. Found: C, 56.26; H, 3.81; N, 10.69.

***N*-{(4-Chlorophenyl)(phenyl)methyl}-5-nitropyridin-2-amine 3y**

Prepared according to the general procedure by using 5-nitropyridin-2-amine (139 mg) and 4-chlorobenzhydrol (262 mg).

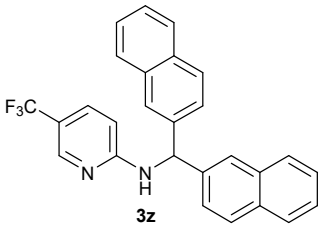


3y

Pale yellow solid, 282 mg (83%), mp 152–154 °C; IR (KBr) (cm^{-1}) 3373, 1599, 1577, 1530; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* (ppm): 8.96 (d, *J*=2.8 Hz, 1H), 8.17 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.30–7.40 (m, 5H), 7.22–7.29 (m, 5H), 6.32 (d, *J* = 9.2 Hz, 1H), 6.04 (brs, 1H), 5.91 (brs, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 59.9, 105.9, 127.5, 128.3, 128.7, 129.1, 133.2, 133.8, 136.3, 139.2, 140.3, 146.6, 160.2; MS (FAB): *m/z* 340 $[M+H]^+$; Anal. Calcd for $C_{18}H_{14}ClN_3O_2$: C, 63.63; H, 4.15; N, 12.37. Found: C, 63.75; H, 4.07; N, 12.34.

***N*-{Di(naphthalen-2-yl)methyl}-5-(trifluoromethyl)pyridin-2-amine 3z**

Prepared according to the general procedure by using 2-amino-5-(trifluoromethyl)-pyridine (163 mg) and di-1-naphthylemethanol (341 mg).

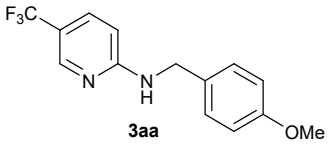


3z

White solid, 281 mg (66%); mp 215–217 °C; FT–IR (KBr, cm^{-1}): 3216, 1616, 1542, 1508; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.53 (d, *J*=6.0 Hz, 1H), 6.36 (d, *J*=8.7 Hz, 1H), 7.30-7.59 (m, 10H), 7.84 (d, *J*=7.8 Hz, 1H), 7.93 (d, *J*=8.2 Hz, 4H), 8.32 (s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 53.3, 106.1, 116.0 (q, *J*=32.6 Hz), 123.3, 124.5 (q, *J*=270.3 Hz), 125.4, 125.5, 126.8, 128.7, 128.9, 131.2, 134.1, 134.7 (q, *J*=2.9 Hz), 136.3, 146.3 (q, *J*=4.8 Hz), 159.2; MS (FAB): *m/z* 429 $[M+H]^+$; HRMS (FAB): *m/z* $[M+H]^+$ calcd. for $C_{27}H_{20}F_3N_2$ 429.1579, found 429.1579.

***N*-(4-Methoxybenzyl)-5-(trifluoromethyl)pyridin-2-amine 3aa [1)]**

Prepared according to the general procedure by using 2-amino-5-(trifluoromethyl)-pyridine (163 mg) and 4-methoxybenzylalchohol (166 mg).

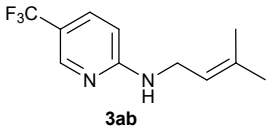


3aa

White solid, 203 mg (72%); mp 171–173 °C; IR (KBr) (cm^{-1}) 3229, 1620, 1579, 1552; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 3.80 (s, 3H), 4.48 (d, J = 5.5 Hz, 2H), 5.25 (brs, 1H), 6.39 (d, J = 9.2 Hz, 1H), 6.89 (d, J = 8.7 Hz, 2H), 7.27 (d, J = 8.7 Hz, 2H), 7.57 (dd, J = 8.7, 2.3 Hz, 1H), 8.32 (s, 1H). ^{13}C-NMR (100 MHz, DMSO-d_6) δ 44.0, 55.6, 113.1 (q, J_{CF}=32.6 Hz), 114.2, 125.6 (q, J_{CF}=270.3 Hz), 129.1, 132.0, 133.9, 146.0 (q, J_{CF}=4.8 Hz), 158.7, 161.1; MS (FAB): *m/z* 283 $[M+H]^+$.

***N*-(3-Methylbut-2-en-1-yl)-5-(trifluoromethyl)pyridin-2-amine 3ab**

Prepared according to the general procedure by using 2-amino-5-(trifluoromethyl)-pyridine (162 mg) and 2-methyl-3-buten-2-ol (315 µL, 3 equiv).

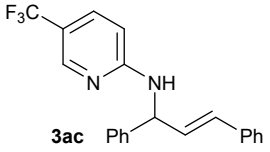


3ab

Pale yellow solid, 127 mg (55%); mp 73-75 °C; IR (KBr) (cm^{-1}) 3236, 1623, 1577, 1557; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.73 (s, 3H), 1.76 (d, J=0.9 Hz, 3H), 3.89 (t, J=6.0 Hz, 2H), 4.86 (brs, 1H), 5.30 (tsep, J=6.9, 1.4 Hz, 1H), 6.38 (d, J=8.7 Hz, 1H), 7.57 (dd, J=8.7, 2.3 Hz, 1H), 8.33 (t, J=0.92 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 18.0, 25.7, 40.1, 105.8, 115.3 (q, J=32.6 Hz), 120.3, 124.7 (q, J=270.3 Hz), 134.4 (q, J=2.9 Hz), 136.7, 146.1 (q, J=4.8 Hz), 160.3; MS (FAB): *m/z* 231 $[M+H]^+$; HRMS (FAB): *m/z* $[M+H]^+$ calcd. for $C_{11}H_{14}F_3N_2$ 231.1109, found 231.1109.

***(E)*-*N*-(1,3-Diphenylallyl)-5-(trifluoromethyl)pyridin-2-amine 3ac**

Prepared according to the general procedure by using 2-amino-5-(trifluoromethyl)-pyridine (162 mg) and *trans*-1,3-diphenyl-2-propen-1-ol (252 mg).

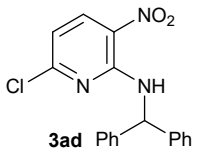


3ac

White solid, 301 mg (85%); mp 139-141 °C; IR (KBr) (cm^{-1}) 3224, 1616, 1579, 1549; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.47 (d, J=6.0 Hz, 1H), 5.54 (t, J=6.4 Hz, 1H), 6.40 (dd, J=16.0, 6.0 Hz, 1H), 6.42 (d, J=10.1 Hz, 1H), 6.60 (dd, J=15.6, 0.9 Hz, 1H), 7.21-7.27 (m, 1H), 7.27-7.34 (m, 3H), 7.34-7.45 (m, 6H), 7.57 (dd, J=8.7, 2.3 Hz, 1H), 8.32 (t, J=0.9 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 58.0, 106.3, 116.1 (q, J=33.6 Hz), 124.5 (q, J=270.3 Hz), 126.6, 127.2, 127.9, 128.6, 129.0, 129.1, 131.5, 134.6 (q, J=2.9 Hz), 136.3, 140.8, 146.2 (q, J=3.8 Hz), 159.5; MS (FAB): *m/z* 355 $[M+H]^+$; Anal. Calcd for $C_{21}H_{17}F_3N_2$: C, 71.18; H, 4.84; N, 7.91. Found: C, 71.09; H, 4.82; N, 7.79.

***N*-Benzhydryl-6-chloro-3-nitropyridin-2-amine 3ad**

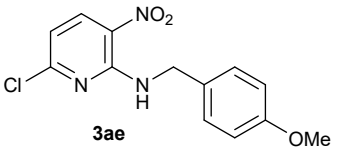
Prepared according to the general procedure by using 6-chloro-3-nitropyridin-2-amine (174 mg) and benzhydrol (221 mg).



Yellow solid, 241 mg (71%); mp 103-105 °C; IR (KBr) (cm^{-1}) 3374, 3357, 1604, 1568; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.63 (d, *J*=8.7 Hz, 1H), 6.68 (d, *J*=8.2 Hz, 1H), 7.26-7.39 (m, 10H), 8.36 (d, J=8.7 Hz, 1H), 9.03 (brd, *J*=7.8 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 58.5, 112.6, 126.8, 127.4, 127.7, 128.8, 137.7, 141.2, 151.1, 156.8; MS (FAB): *m/z* 340 $[M+H]^+$, 342 $[M+H+2]^+$; Anal. Calcd for $C_{18}H_{14}ClN_3O_2$: C, 63.63; H, 4.15; N, 12.37. Found: C, 63.74; H, 4.21; N, 12.32.

6-Chloro-*N*-(4-methoxybenzyl)-3-nitropyridin-2-amine 3ae

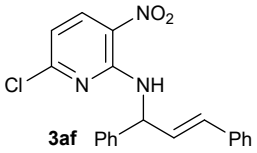
Prepared according to the general procedure by using 6-chloro-3-nitropyridin-2-amine (174 mg) and 4-methoxybenzyl alcohol (207 mg, 1.5 mmol).



Yellow solid, 220 mg (75%); mp 99-101 °C; IR (KBr) (cm^{-1}) 3370, 1605, 1568, 1510; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 3.81 (s, 3H), 4.74 (d, *J*=5.5 Hz, 2H), 6.64 (d, *J*=8.7 Hz, 1H), 6.90 (d, *J*=8.7 Hz, 2H), 7.31 (d, *J*=8.7 Hz, 2H), 8.36 (d, *J*=8.7 Hz, 1H), 8.54 (brs, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 45.0, 55.3, 112.1, 114.2, 129.4, 129.5, 137.7, 151.8, 156.8, 159.2; MS (FAB): *m/z* 294 $[M+H]^+$; Anal. Calcd for $C_{13}H_{12}ClN_3O_3$: C, 53.16; H, 4.12; N, 14.31. Found: C, 53.29; H, 4.18; N, 14.10.

(*E*)-6-Chloro-*N*-(1,3-diphenylallyl)-3-nitropyridin-2-amine 3af

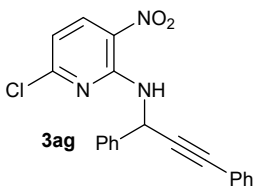
Prepared according to the general procedure by using 6-chloro-3-nitropyridin-2-amine (174 mg) and *trans*-1,3-diphenyl-2-propen-1-ol (315 mg, 1.5 mmol).



Yellow solid, 267 mg (73%); mp 94-96 °C; IR (KBr) (cm^{-1}) 3376, 1604, 1565, 1515; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.24 (ddd, *J*=7.8, 6.9, 0.9 Hz, 1H), 6.43 (dd, *J*=16.0, 6.4 Hz, 1H), 6.64 (d, *J*=8.7 Hz, 1H), 6.65 (dd, *J*=16.0, 0.9 Hz, 1H), 7.22-7.27 (m, 1H), 7.28-7.35 (m, 3H), 7.36-7.42 (m, 4H), 7.43-7.48 (m, 2H), 8.36 (d, *J*=8.2 Hz, 1H), 8.81 (brd, *J*=7.8 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 56.6, 112.6, 126.6, 126.9, 127.2, 127.9, 128.0, 128.5, 128.6, 128.9, 131.8, 136.3, 137.7, 140.4, 151.1, 156.7; MS (FAB): *m/z* 366 $[M+H]^+$, 368 $[M+H+2]^+$; Anal. Calcd for $C_{20}H_{16}ClN_3O_2$: C, 65.67; H, 4.41; N, 11.49. Found: C, 65.92; H, 4.42; N, 11.49.

6-Chloro-*N*-(1,3-diphenylprop-2-yn-1-yl)-3-nitropyridin-2-amine 3ag

Prepared according to the general procedure by using 6-chloro-3-nitropyridin-2-amine (174 mg) and 1,3-diphenylprop-2-yn-1-ol (312 mg, 1.5 mmol).

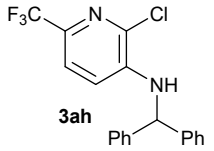


Pale yellow solid, 255 mg (70%); mp 125-128 °C; IR (KBr) (cm^{-1}) 3409, 1604, 1563; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.67 (d, *J*=8.2 Hz, 1H), 6.71 (d, *J*=8.7

Hz, 1H), 7.28-7.38 (m, 4H), 7.41 (t, *J*=7.8 Hz, 2H), 7.46-7.51 (m, 2H), 7.66 (dd, *J*=7.3 Hz, 2H), 8.38 (d, *J*=8.2 Hz, 1H), 8.75 (brd, *J*=7.8 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 47.0, 85.2, 86.7, 113.0, 122.3, 126.9, 127.4, 128.3, 128.4, 128.7, 128.9, 131.9, 137.8, 138.5, 150.4, 156.6; MS (FAB): *m/z* 364 $[M+H]^+$, 366 $[M+H+2]^+$; Anal. Calcd for $C_{20}H_{14}ClN_3O_2$: C, 66.03; H, 3.88; N, 11.55. Found: C, 66.36; H, 4.20; N, 11.36.

***N*-Benzhydryl-2-chloro-6-(trifluoromethyl)pyridin-3-amine 3ah**

Prepared according to the general procedure by using 2-chloro-6-(trifluoromethyl)pyridin-3-amine (197 mg) and benzhydrol (221 mg).

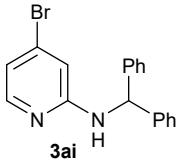


3ah

White solid, 243 mg (67%); mp 108-110 °C; IR (KBr) (cm^{-1}) 3430, 1590, 1574, 1507; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.32 (brd, *J*=4.1 Hz, 1H), 5.57 (d, *J*=4.6 Hz, 1H), 6.72 (d, *J*=8.2 Hz, 1H), 7.29-7.35 (m, 7H), 7.35-7.41 (m, 4H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 62.3, 118.1, 120.6 (q, *J*=2.9 Hz), 121.4 (q, *J*=272.2 Hz), 127.2, 128.2, 129.2, 134.9 (q, *J*=36.4 Hz), 136.8, 140.4, 141.7; MS (FAB): *m/z* 363 $[M+H]^+$, 365 $[M+H+2]^+$, Anal. Calcd for $C_{19}H_{14}ClF_3N_2$: C, 62.91; H, 3.89; N, 7.72. Found: C, 62.66; H, 3.90; N, 7.70.

***N*-Benzhydryl-4-bromopyridin-2-amine 3ai**

Prepared according to the general procedure by using 4-bromopyridin-2-amine (173 mg) and benzhydrol (221 mg).

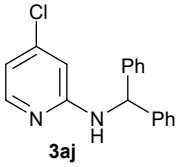


3ai

White solid, 207 mg (61%); mp 128-130 °C; IR (KBr) (cm^{-1}) 3287, 1583, 1552, 1508; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.26 (brd, *J*=6.0 Hz, 1H), 5.84 (d, *J*=6.0 Hz, 1H), 6.47 (d, *J*=1.4 Hz, 1H), 6.73 (dd, *J*=5.5, 1.8 Hz, 1H), 7.24-7.36 (m, 10H), 7.85 (d, *J*=5.5 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 60.5, 109.6, 116.7, 127.4, 127.6, 128.8, 133.5, 141.9, 149.0, 158.5; MS (FAB): *m/z* 339 $[M+H]^+$, 341 $[M+H+2]^+$, Anal. Calcd for $C_{18}H_{15}BrN_2$: C, 63.73; H, 4.46; N, 8.26. Found: C, 63.73; H, 4.45; N, 8.12.

***N*-Benzhydryl-4-chloropyridin-2-amine 3aj**

Prepared according to the general procedure by using 4-chloropyridin-2-amine (129 mg) and benzhydrol (221 mg).

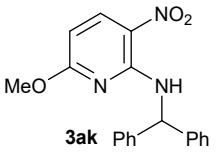


3aj

White solid, 156 mg (53%); mp 114-116 °C; IR (KBr) (cm^{-1}) 3283, 1588, 1555, 1510; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.29 (d, *J*=6.0 Hz, 1H), 5.82 (d, *J*=6.0 Hz, 1H), 6.29 (d, *J*=1.4 Hz, 1H), 6.58 (dd, *J*=5.0, 1.8 Hz, 1H), 7.24-7.40 (m, 10H), 7.93 (d, *J*=5.5 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 60.6, 106.5, 114.0, 126.5, 127.4, 127.6, 128.5, 128.8, 141.9, 144.8, 149.2, 158.7; MS (FAB): *m/z* 295 $[M+H]^+$, 297 $[M+H+2]^+$, Anal. Calcd for $C_{18}H_{15}ClN_2$: C, 73.34; H, 5.13; N, 9.50. Found: C, 73.37; H, 5.11; N, 9.27.

_N_-Benzhydryl-6-methoxy-3-nitropyridin-2-amine 3ak

Prepared according to the general procedure by using 6-methoxy-3-nitropyridin-2-amine (169 mg) and benzhydrol (221 mg).

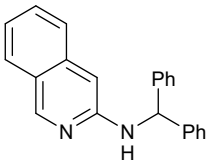


3ak

Yellow solid, 285 mg (85%); mp 154-156 ℃; IR (KBr) (cm^{-1}) 3376, 1607, 1588; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 3.75 (s, 3H), 6.06 (d, *J*=9.2 Hz, 1H), 6.48 (d, *J*=6.9 Hz, 1H), 7.26-7.40 (m, 10H), 8.32 (d, *J*=8.7 Hz, 1H), 9.30 (brd, *J*=6.4 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 54.4, 59.6, 101.2, 122.3, 127.3, 127.5, 128.8, 137.9, 141.6, 152.1, 166.7; MS (FAB): *m/z* 336 $[M+H]^+$; Anal. Calcd for $C_{19}H_{17}N_3O_3$: C, 68.05; H, 5.11; N, 12.53. Found: C, 68.12; H, 4.94; N, 12.36.

_N_-Benzhydrylisoquinolin-3-amine 4a

Prepared according to the general procedure by using isoquinolin-3-amine (144 mg) and benzhydrol (221 mg).



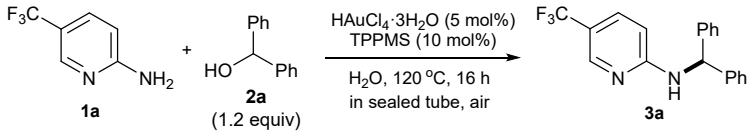
4a

White solid, 155 mg (50%); mp 172-174 ℃; IR (KBr) (cm^{-1}) 3239, 1629, 1594, 1581, 1523; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.32 (brd, *J*=5.0 Hz, 1H), 5.72 (d, *J*=5.0 Hz, 1H), 6.34 (s, 1H), 7.19 (ddd, *J*=7.8, 4.6, 3.2 Hz, 1H), 7.27 (tt, *J*=6.9, 1.4 Hz, 2H), 7.34 (t, *J*=7.8 Hz, 4H), 7.38-7.44 (m, 6H), 7.74 (d, *J*=7.3 Hz, 1H), 8.83 (s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 62.0, 76.2, 97.0, 122.7, 123.7, 125.0, 126.5, 127.4, 127.5, 127.6. 127.8, 128.5, 128.8, 130.3, 138.8, 142.3, 143.8, 151.8, 154.5; MS (FAB): *m/z* 311 $[M+H]^+$; Anal. Calcd for $C_{22}H_{18}N_2$: C, 85.13; H, 5.85; N, 9.03. Found: C, 84.88; H, 5.84; N, 8.74.

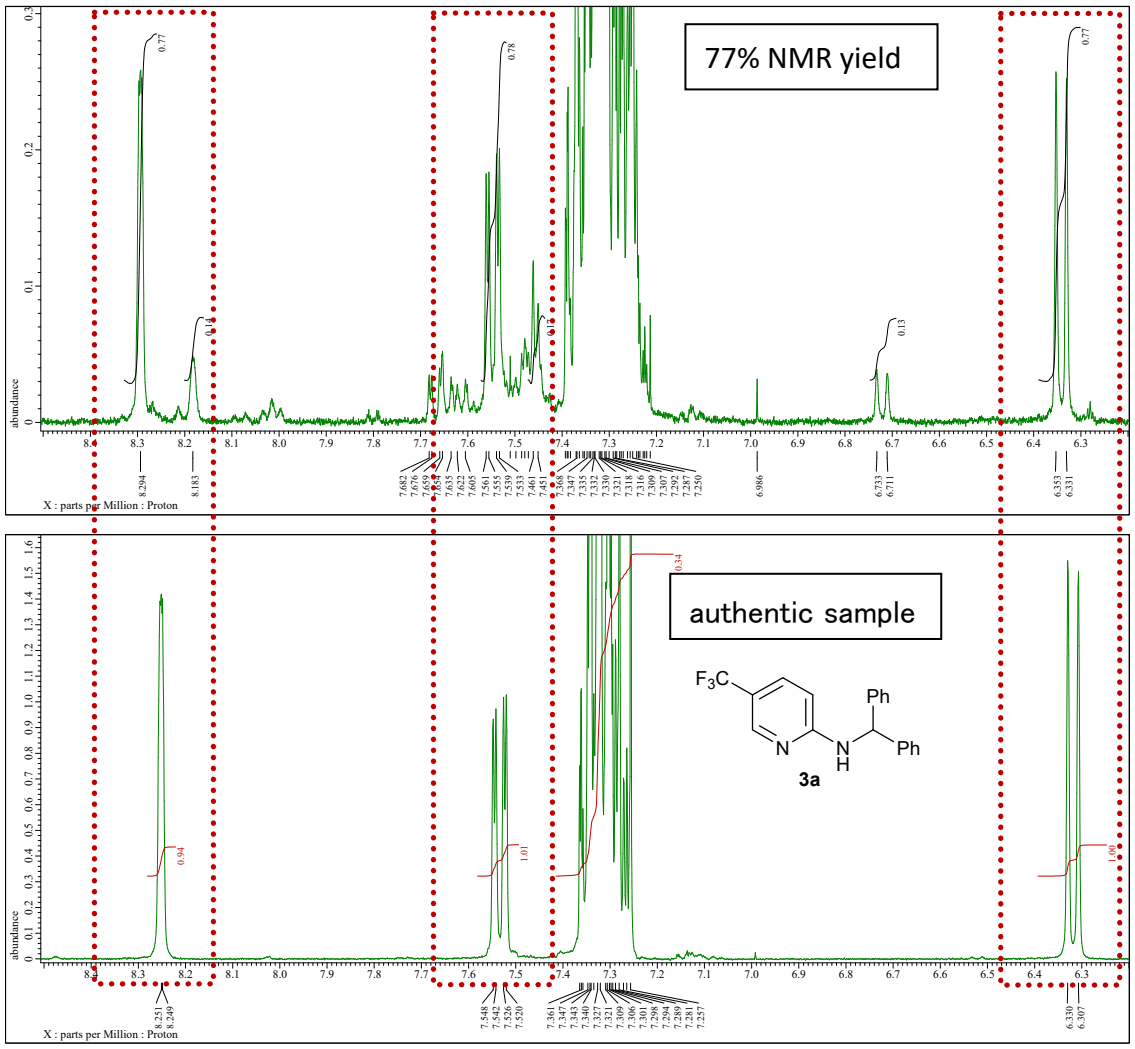
References

1) K. Walsh, H. F. Sneddon, C. J. Moody, *ChemSusChem,* 2013, **6**, 1455-1460.

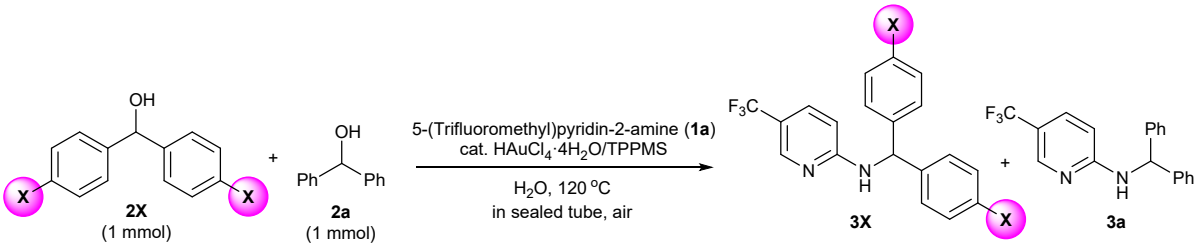
Scheme S2. Effects of catalysts and solvents.



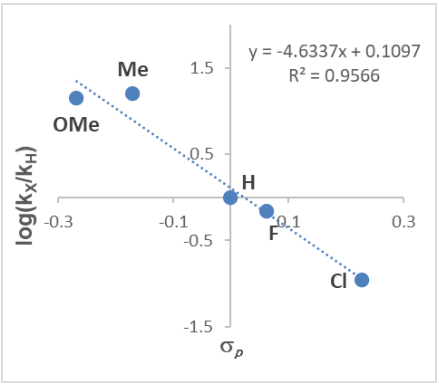
A mixture of 5-(trifluoromethyl)pyridin-2-amine (**1a**) (163 mg, 1 mmol), $HAuCl_4 \cdot 3H_2O$ (20 mg, 0.05 mmol), TPPMS (36 mg, 0.1 mmol) and benzhydrole **2a** (221 mg, 1.2 mmol) in H_2O (1 mL) was heated at 120 °C for 16 h in a sealed tube under air. After the reaction mixture was cooled, 1,3,5-trimethoxybenzene (168 mg, 1 mmol, internal standard) was added to the reaction mixture, which was extracted with EtOAc. The organic layer was concentrated in vacuo. The residue was analyzed by ^{1}H-NMR spectroscopy.



Scheme S3. Hammett study.



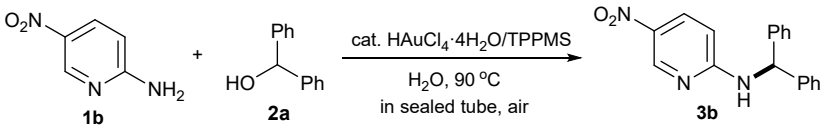
A mixture of 5-(trifluoromethyl)pyridine-2-amine **1a** (162 mg, 1 mmol), $HAuCl_4 \cdot 4H_2O$ (21 mg, 0.05 mmol), sodium diphenylphosphinobenzene-3-sulfonate (36 mg, 0.1 mmol), benzhydryl alcohols **2X** (1 mmol), and benzhydrol **2a** (184 mg, 1 mmol) in H_2O (1 mL) was heated at 120 °C in a sealed tube under air. After the reaction mixture was cooled, 1,3,5-trimethoxybenzene (168 mg, 1 mmol, internal standard) was added to the reaction mixture, which was extracted with CH_2Cl_2. The organic layer was concentrated in vacuo. The residue was analyzed by ^{1}H-NMR spectroscopy.



	σ_p	$\log(k_X/k_H)$
OMe	-0.268	1.1486
Me	-0.17	1.20358
H	0	0
F	0.06	-0.1549
Cl	0.227	-0.9586

Figure S1. Hammett plot for the reaction of 4-substituted benzhydroles **2.**

Scheme S4. Rate law measurements.



A mixture of 5-nitropyridin-2-amine **1b** (3-5 mmol), $HAuCl_4 \cdot 4H_2O$ (0.1-0.28 mmol), sodium diphenylphosphinobenzene-3-sulfonate (0.2-0.56 mmol), benzhydrol **2a** (3-6 mmol), and *p*-nitroanisole (153 mg, 1 mmol, internal standard) in H_2O (4 mL) was heated at 90 °C in a sealed tube under air. Every hour, a few drops of the reaction mixture were transferred into a test tube. The sample was extracted with $CDCl_3$, which was analyzed by ^{1}H-NMR spectroscopy.

Table S1. Molarities and volumes for kinetic experiments.

5-Nitropyridin-2-amine **1b**	Benzhydrol **2a**	$HAuCl_4 \cdot 4H_2O$	TPPMS	H_2O
417 mg (3 mmol) 0.75 M	884 mg (4.8 mmol) 1.2 M	82 mg (0.2 mmol) 0.05 M	144 mg (0.4 mmol) 0.1 M	4 mL
556 mg (4 mmol) 1 M	884 mg (4.8 mmol) 1.2 M	82 mg (0.2 mmol) 0.05 M	144 mg (0.4 mmol) 0.1 M	4 mL
696 mg (5 mmol) 1.25 M	884 mg (4.8 mmol) 1.2 M	82 mg (0.2 mmol) 0.05 M	144 mg (0.4 mmol) 0.1 M	4 mL
556 mg (4 mmol) 1 M	553 mg (3 mmol) 0.75 M	82 mg (0.2 mmol) 0.05 M	144 mg (0.4 mmol) 0.1 M	4 mL
556 mg (4 mmol) 1 M	737 mg (4 mmol) 1 M	82 mg (0.2 mmol) 0.05 M	144 mg (0.4 mmol) 0.1 M	4 mL
556 mg (4 mmol) 1 M	1105 mg (6 mmol) 1.5 M	82 mg (0.2 mmol) 0.05 M	144 mg (0.4 mmol) 0.1 M	4 mL
556 mg (4 mmol) 1 M	884 mg (4.8 mmol) 1.2 M	41 mg (0.1 mmol) 0.025 M	73 mg (0.2 mmol) 0.05 M	4 mL
556 mg (4 mmol) 1 M	884 mg (4.8 mmol) 1.2 M	66 mg (0.16 mmol) 0.04 M	117 mg (0.32 mmol) 0.1 M	4 mL
556 mg (4 mmol) 1 M	884 mg (4.8 mmol) 1.2 M	115 mg (0.28 mmol) 0.07 M	204 mg (0.56 mmol) 0.14 M	4 mL

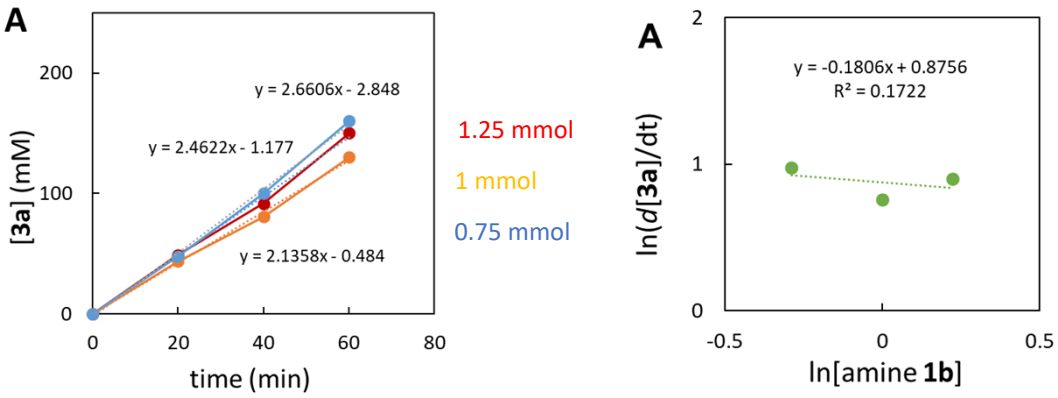


Figure S2. Initial rates obtained when 5-nitropyridin-2-amine **1b** was varied.

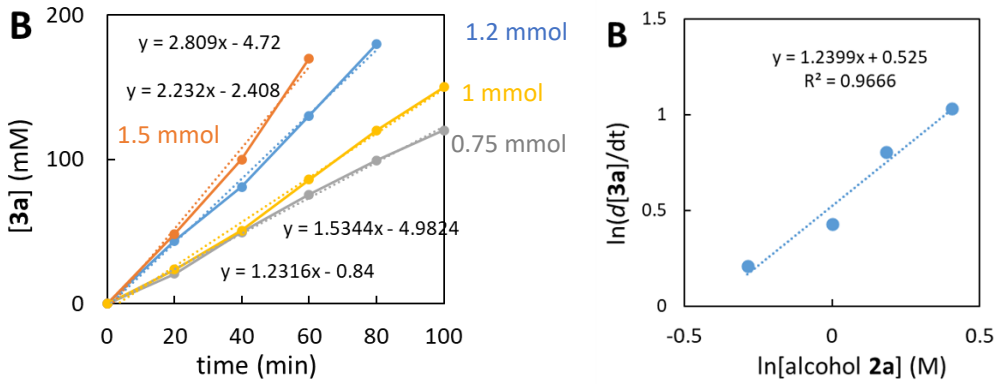


Figure S3. Initial rates obtained when benzhydrol **2a** was varied.

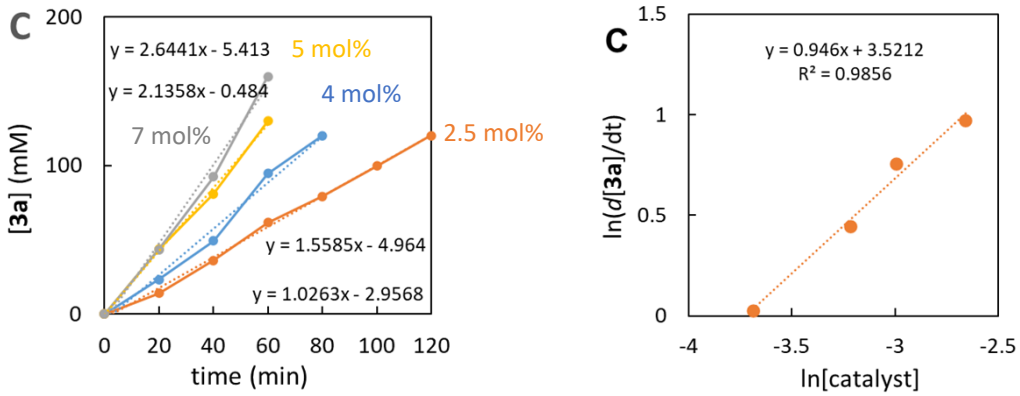
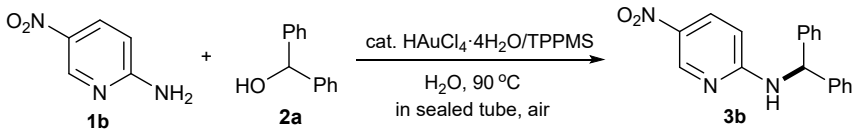


Figure S4. Initial rates obtained when $HAuCl_4 \cdot 4H_2O$ and TPPMS were varied.

Scheme S5. Comparison of reaction rates in H_2O *versus* in D_2O.



A mixture of 5-(trifluoromethyl)pyridin-2-amine **1a** (648 mg, 4 mmol) or 5-nitropyridin-2-amine **1b** (556 mg, 4 mmol), $HAuCl_4 \cdot 4H_2O$ (78.4 mg, 0.2 mmol), sodium diphenylphosphinobenzene-3-sulfonate (144 mg, 0.4 mmol), benzhydrol **2a** (884 mg, 4.8 mmol), and *p*-nitroanisole (153 mg, 1 mmol, internal standard) in H_2O or D_2O (4 mL) was heated at 120 °C in a sealed tube under air. Every hour, a few drops of the reaction mixture were transferred into a test tube. The sample was extracted with $CDCl_3$, which was analyzed by ^{1}H-NMR spectroscopy.

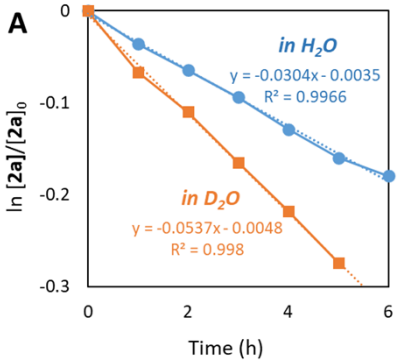
Table S2. Reaction of 5-(trifluoromethyl)pyridin-2-amine **1a**.

In H_2O

Time (h)	ln [**2a**]/[**2a**]$_0$
0	0
1	-0.03605905
2	-0.064538521
3	-0.093852909
4	-0.12878079
5	-0.160070948
6	-0.179824677

In D_2O

Time (h)	ln [**2a**]/[**2a**]$_0$
0	0
1	-0.066763216
2	-0.110000895
3	-0.164972918
4	-0.217948734
5	-0.27388875



KSIE (k_{H_2O}/k_{D_2O}) = 0.0304/0.0537 =0.6

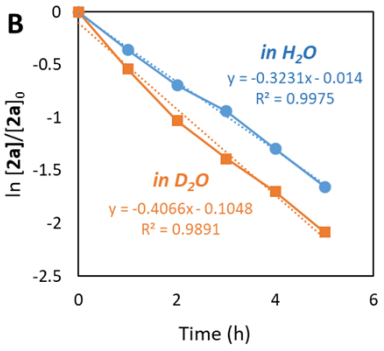
Table S3. Reaction of 5-nitropyridin-2-amine **1b**.

in H_2O

Time (h)	ln [**2a**]/[**2a**]$_0$
0	0
1	-0.356674944
2	-0.693147181
3	-0.937344141
4	-1.290984181
5	-1.651997527

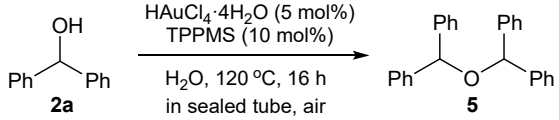
in D_2O

Time (h)	ln [**2a**]/[**2a**]$_0$
0	0
1	-0.538996501
2	-1.026291627
3	-1.386294361
4	-1.696449289
5	-2.079441542



KSIE (k_{H_2O}/k_{D_2O}) = 0.3231/0.4066 =0.8

Scheme S6. Homocoupling of alcohol **2a**

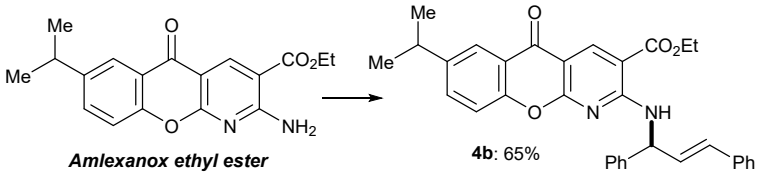


A mixture of benzhydrol **2a** (884 mg, 4.8 mmol), $HAuCl_4 \cdot 4H_2O$ (80 mg, 0.2 mmol), and TPPMS (144 mg, 0.4 mmol), in water (4 mL) was heated at 120 °C for 16 h in a sealed tube under air. After cooling, the reaction mixture was poured into water and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, hexane/EtOAc) to give diphenylmethyl ether **5** (510 mg, 1.46 mmol) as a white solid.

Diphenylmethyl ether **5**

mp 105-107 °C; IR (KBr) (cm^{-1}) 1493; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.39 (s, 2H), 7.25 (tt, *J*=6.0, 1.4 Hz, 4H), 7.31 (dd, *J*=7.3, 7.3 Hz, 8H), 7.31 (dd, *J*=7.3, 7.3 Hz, 8H), 7.36 (dd, *J*=8.7, 1.4 Hz, 8H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 79.9, 127.2, 127.4, 128.4, 142.2; MS (FAB): *m/z* 373 $[M+Na]^+$.

Scheme S7. A. Late-stage direct modification.

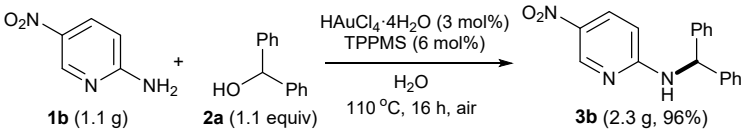


A mixture of ethyl 2-amino-7-isopropyl-5-oxo-5*H*-chromeno[2,3-b]pyridine-3-carboxylate (298 mg, 1 mmol), $HAuCl_4 \cdot 4H_2O$ (98.9 mg, 0.24 mmol), TPPMS (175 mg, 0.48 mmol), and *trans*-1,3-diphenyl-2-propen-1-ol (315 mg, 1.5 mmol) in water (5 mL) was heated at 110 °C for 16 h in a sealed tube under air. After cooling, the reaction mixture was poured into water and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, hexane/EtOAc) to give desired product **4b** 337 mg (65%) as a white solid.

Ethyl (*E*)-2-(1,3-diphenylallylamino)-7-isopropyl-5-oxo-5*H*-chromeno[2,3-b]pyridine-3-carboxylate 4b

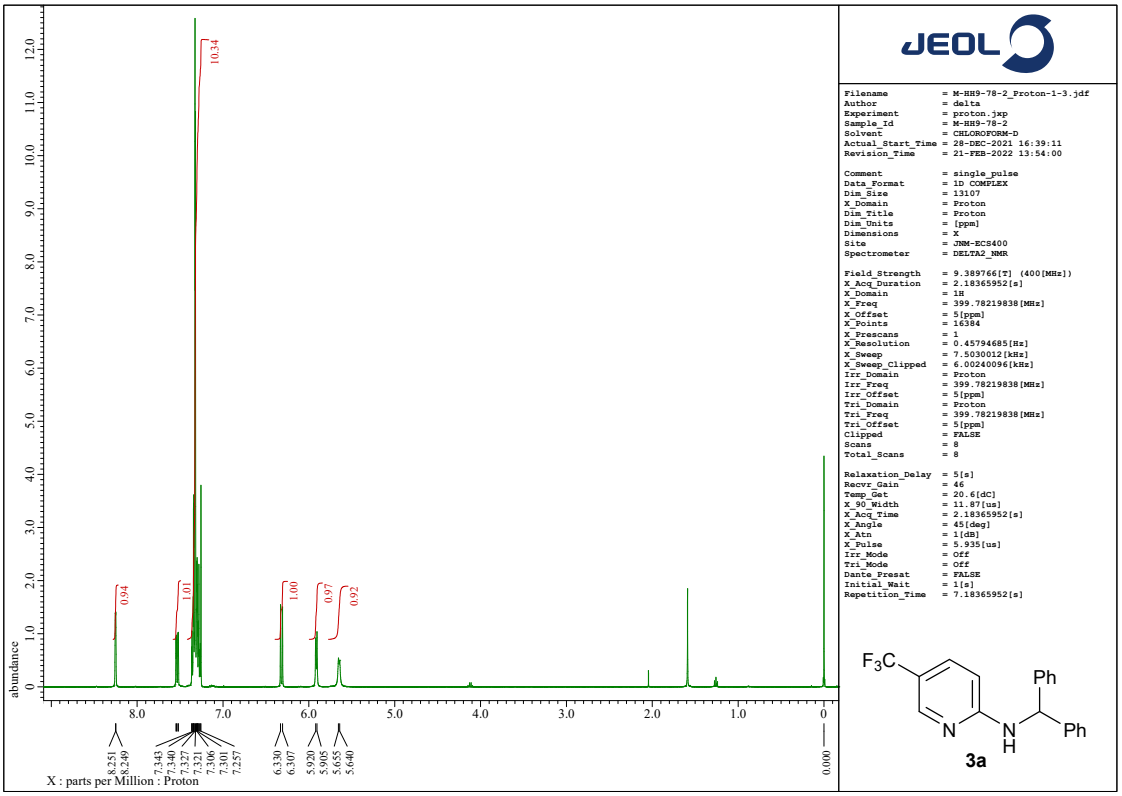
mp 153-155 °C; IR (KBr) (cm^{-1}) 3290, 1691, 1660, 1611; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 1.26 (d, *J*=6.9 Hz, 6H), 1.38 (t, *J*=7.3 Hz, 3H), 3.06 (sep, *J*=6.9 Hz, 1H), 4.39 (q, *J*=6.9 Hz, 2H), 6.17 (d, *J*=7.3 Hz, 1H), 6.69 (d, *J*=2.3 Hz, 2H), 7.24 (t, *J*=6.9 Hz, 1H), 7.32 (t, *J*=7.8 Hz, 3H), 7.37-7.52 (m, 6H), 7.58 (d, *J*=8.7 Hz, 1H), 7.73 (d, *J*=8.7 Hz, 1H), 7.93 (s, 1H), 8.87 (s, 1H), 9.27 (d, *J*=7.8 Hz, 1H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 14.6, 24.3, 33.3, 57.0, 62.1, 106.4, 106.8, 118.7, 121.4, 123.0, 127.1, 127.4, 128.1, 128.4, 129.2, 129.4, 130.0, 131.0, 134.4, 136.7, 141.4, 141.5, 145.8, 153.6, 158.7, 162.8, 166.4, 175.4; MS (FAB): *m/z* 519 $[M+H]^+$; Anal. Calcd for $C_{33}H_{30}N_2O_4$: C, 76.43; H, 5.83; N, 5.40. Found: C, 76.50; H, 5.85; N, 5.35.

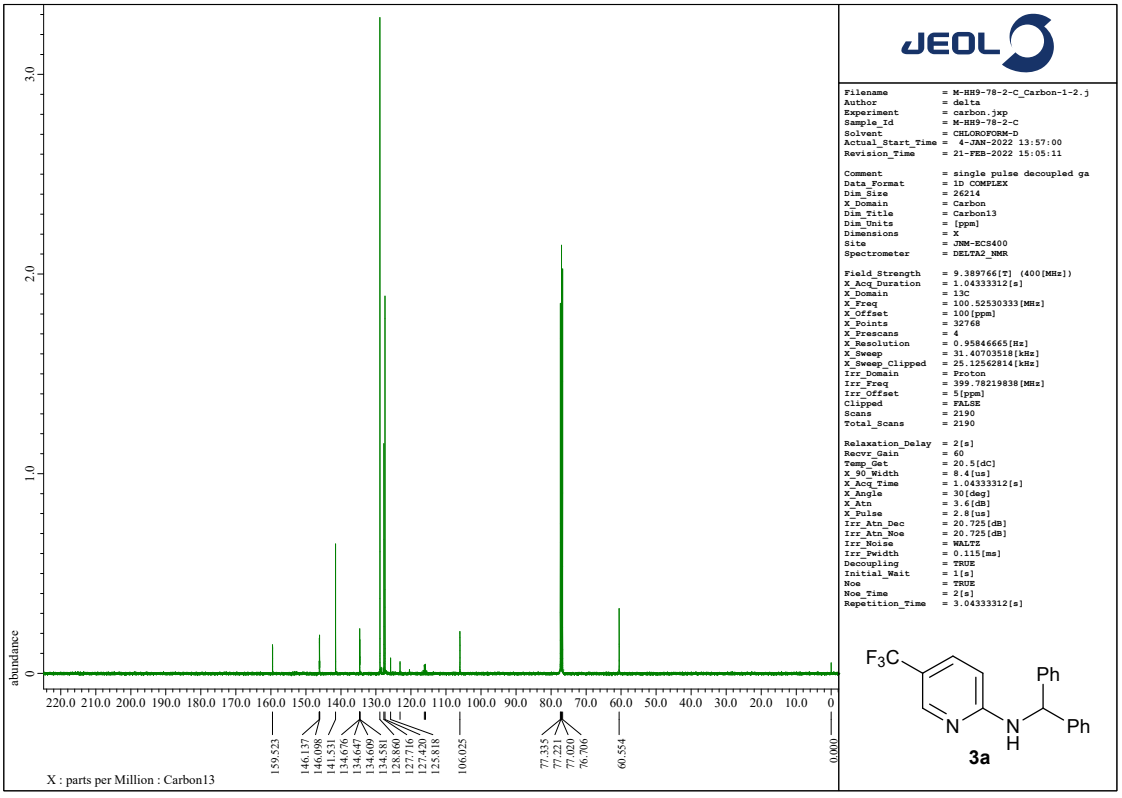
Scheme S8. Scale-up experiment.



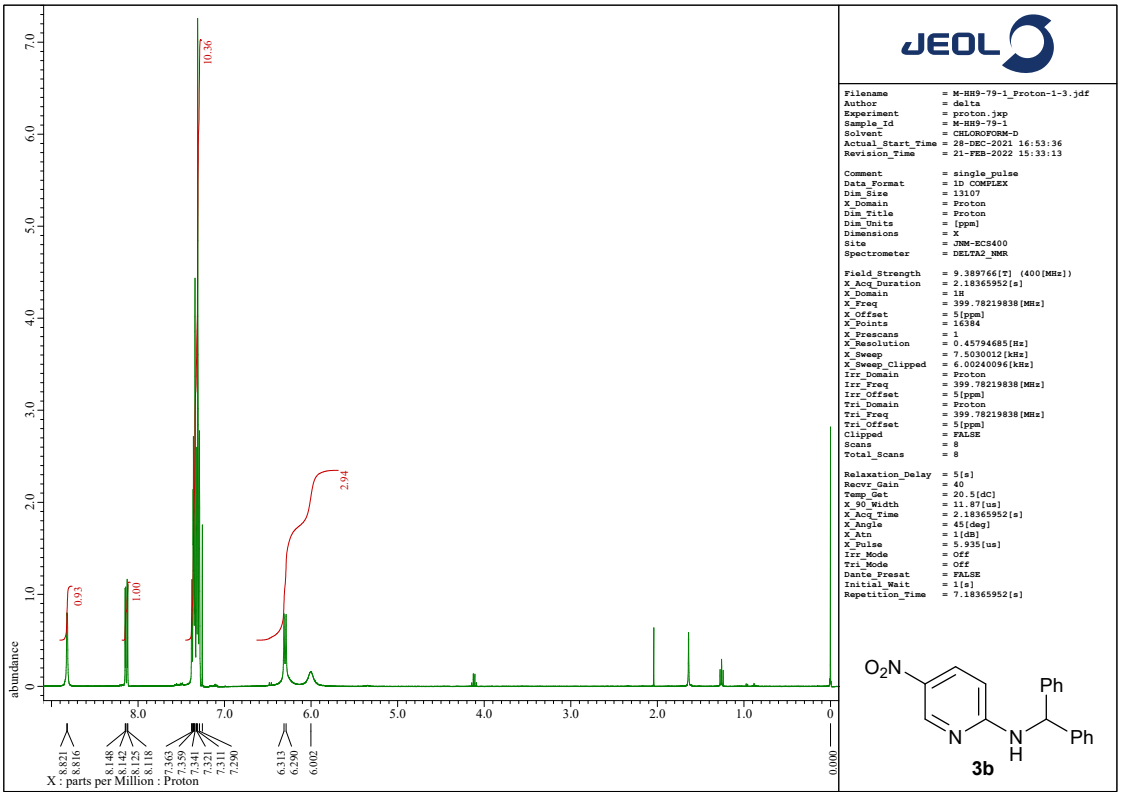
A mixture of 5-nitropyridin-2-amine **1b** (1.11 g, 8 mmol), $HAuCl_4 \cdot 4H_2O$ (98.9 mg, 0.24 mmol), TPPMS (175 mg, 0.48 mmol), and benzhydrol **2a** (1.62 g, 8.8 mmol) in water (5 mL) was heated at 110 °C for 16 h in a sealed tube under air. After cooling, the reaction mixture was poured into water and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was recrystallized from *n*-hexane and EtOAc to give desired product **3b** (2.34 g, 96%) as a white solid.

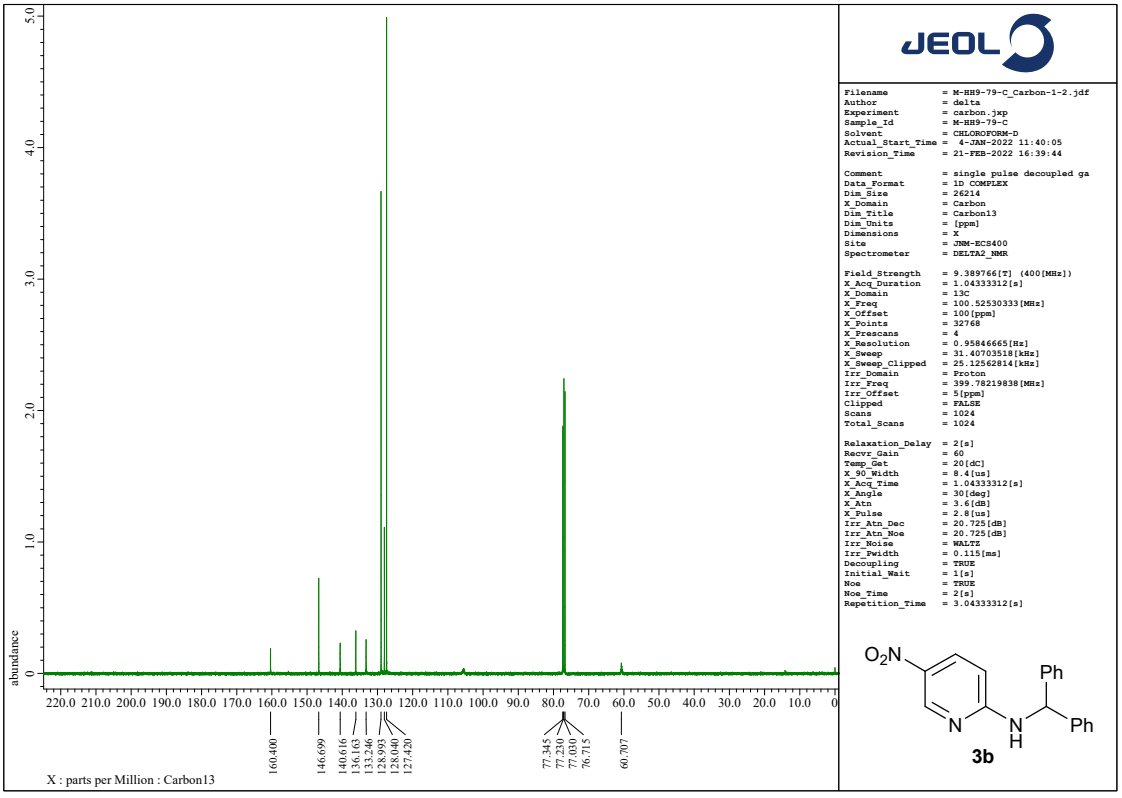
_N_-Benzhydryl-5-(trifluoromethyl)pyridin-2-amine 3a



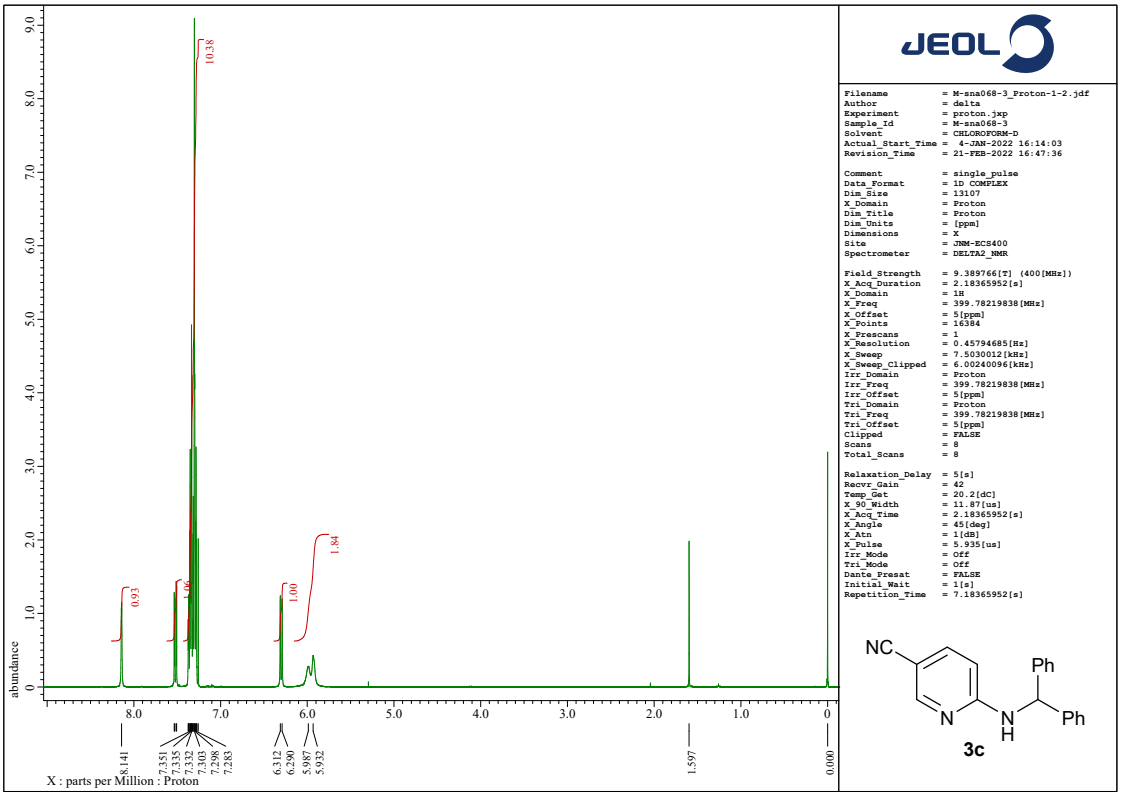


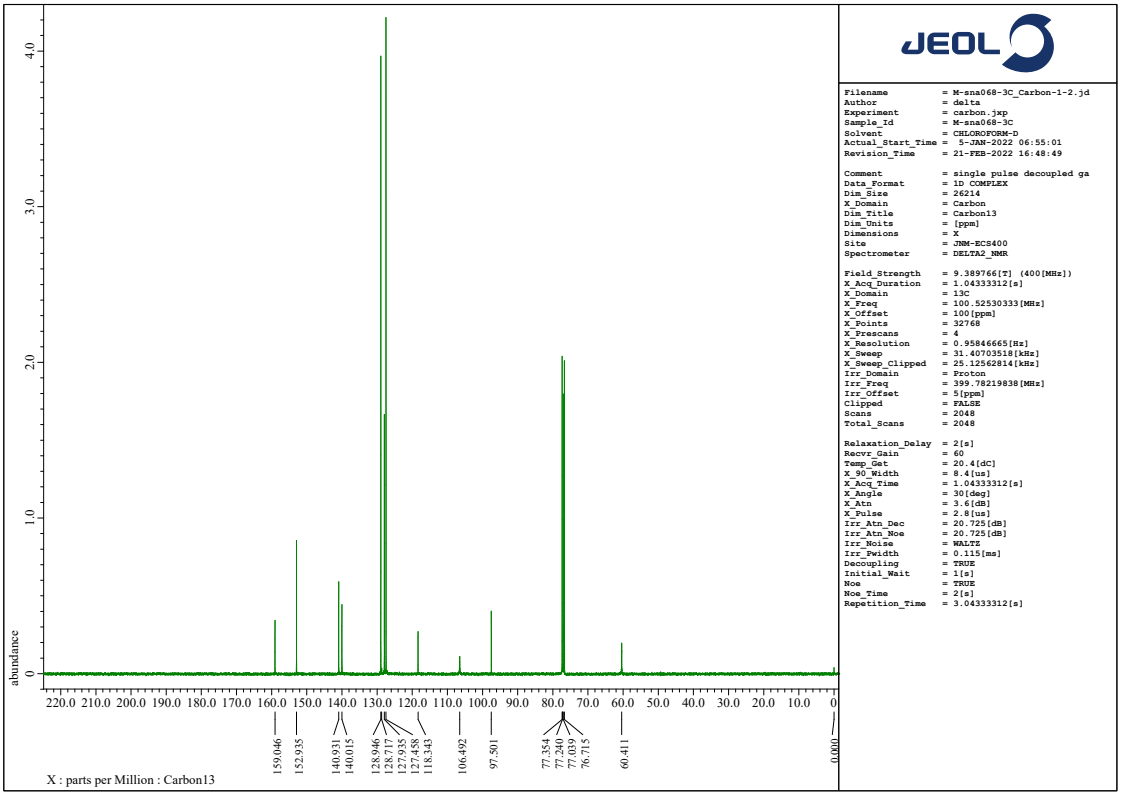
***N*-Benzhydryl-5-nitropyridin-2-amine 3b**



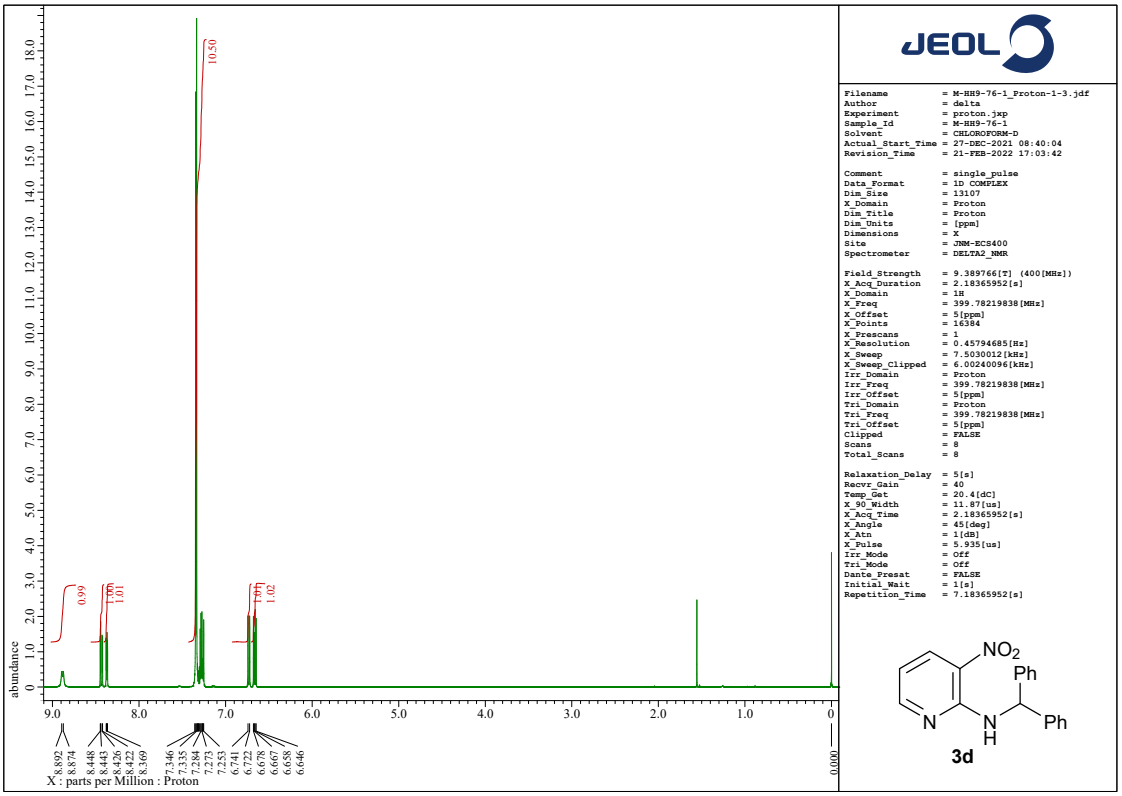


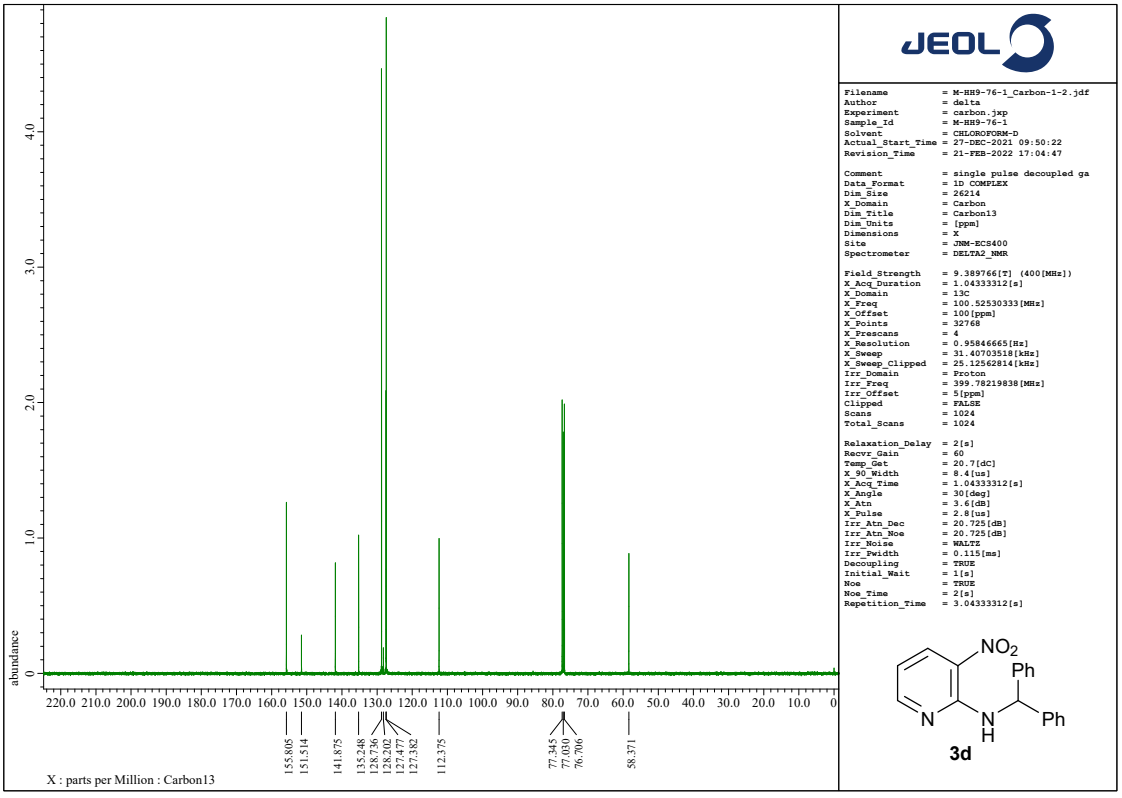
6-(Benzhydrylamino)nicotinonitrile 3c



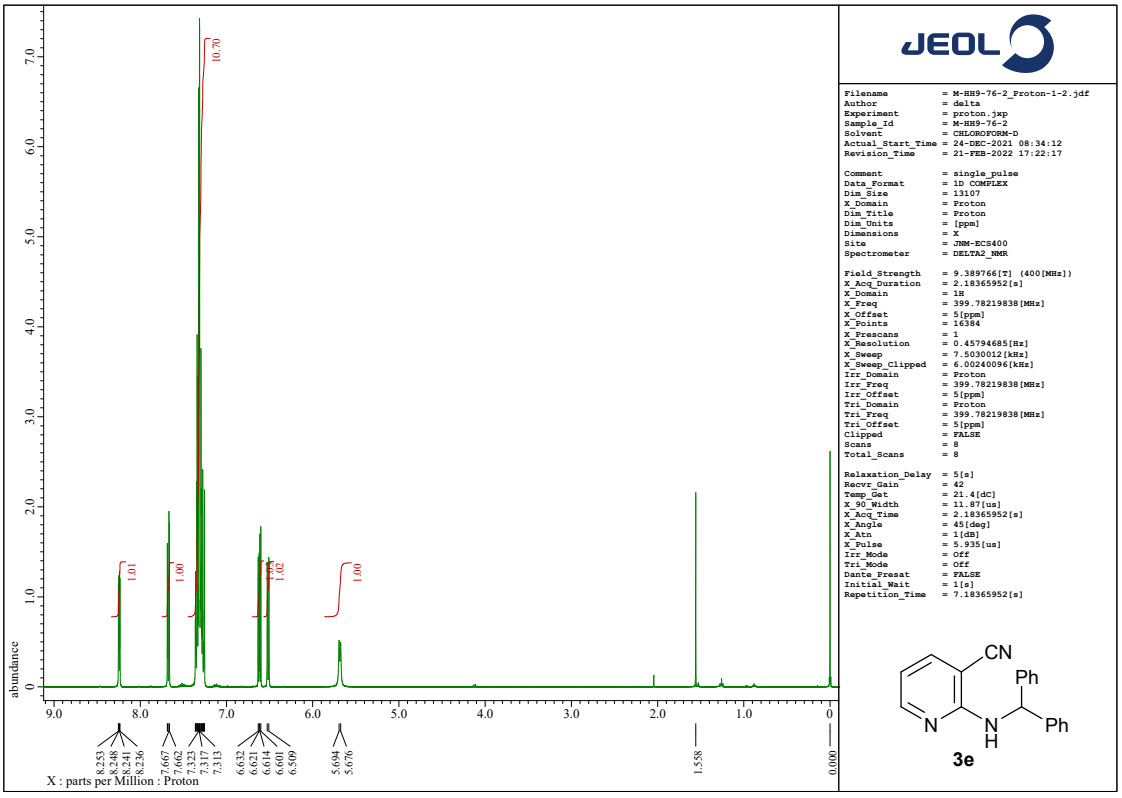


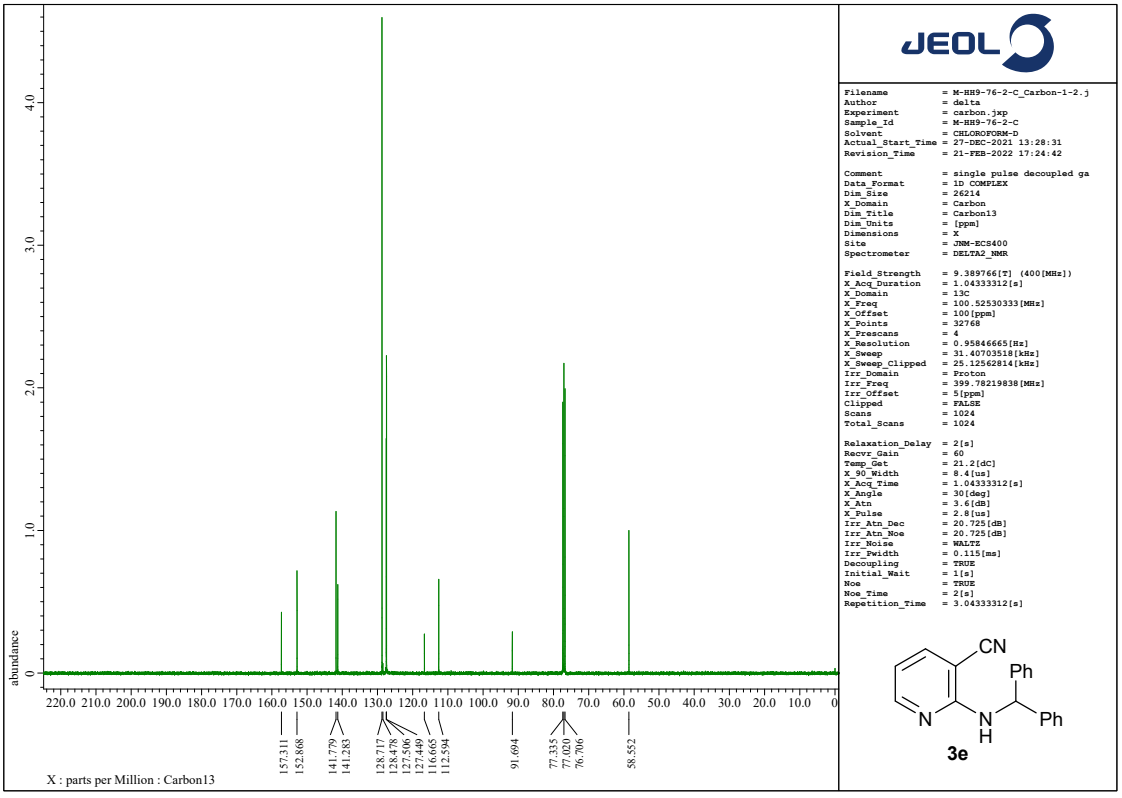
N-Benzhydryl-3-nitropyridin-2-amine 3d



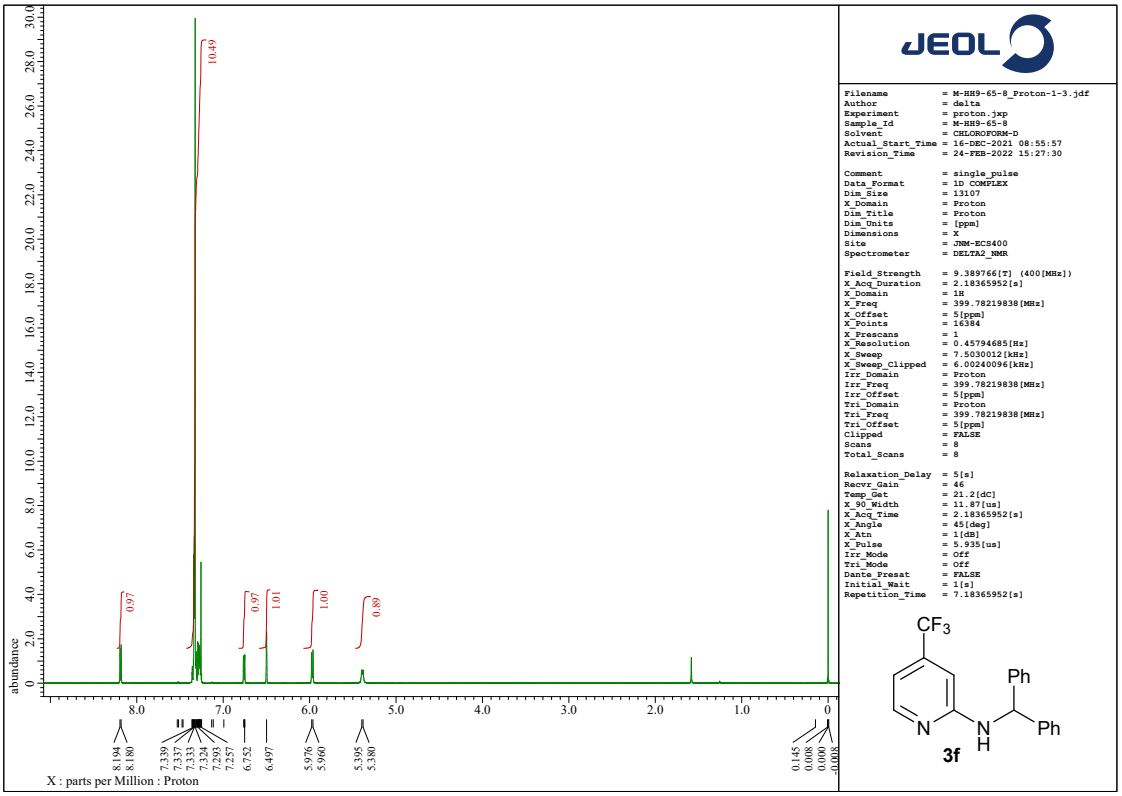


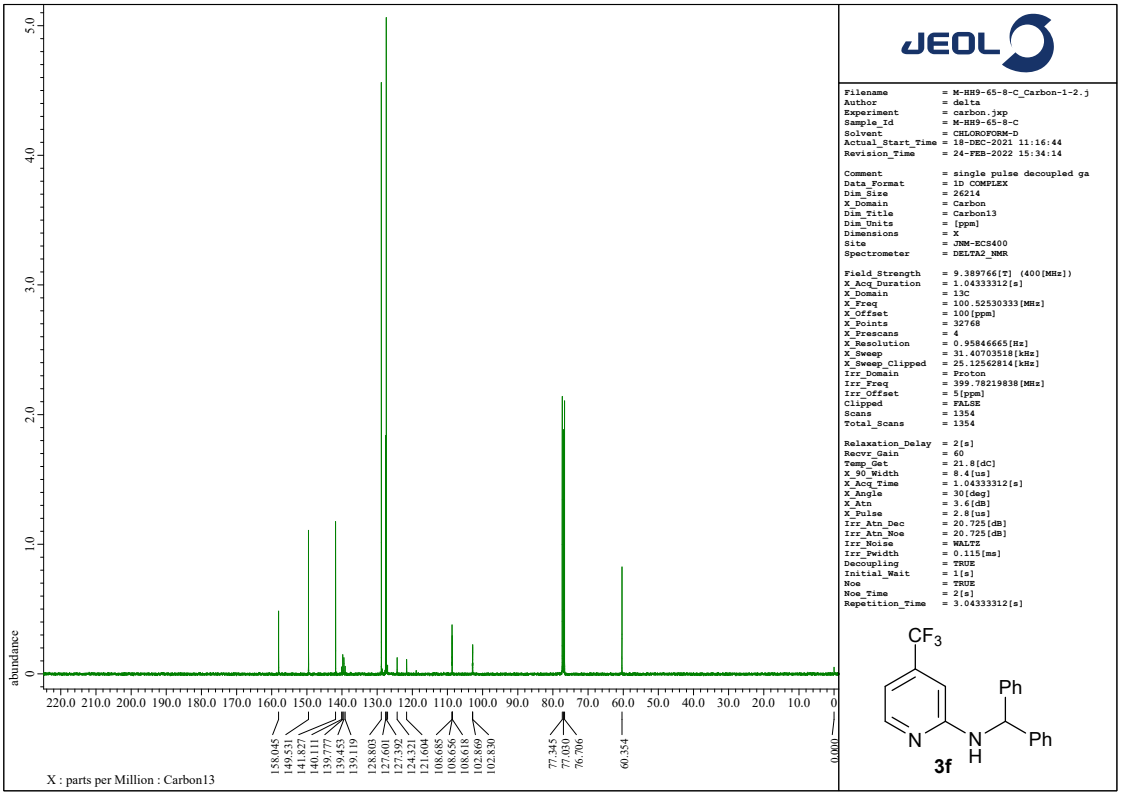
2-(Benzhydrylamino)nicotinonitrile 3e



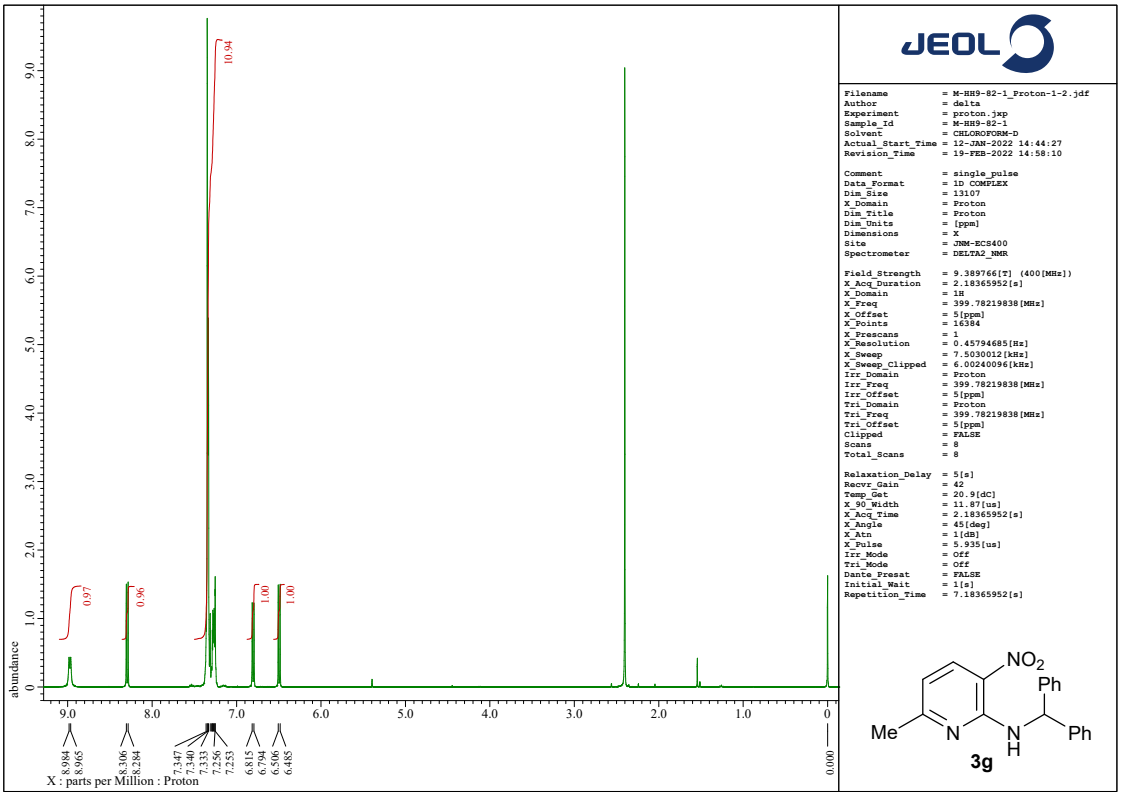


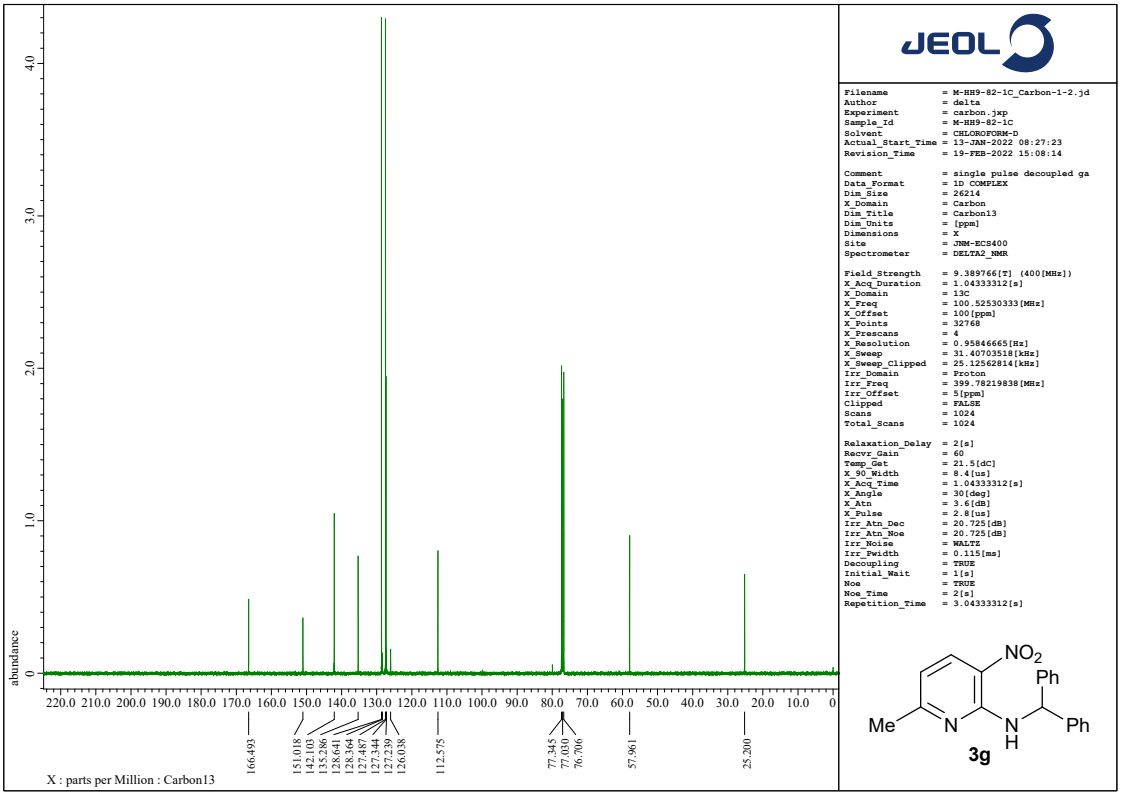
***N*-Benzhydryl-4-(trifluoromethyl)pyridin-2-amine 3f**



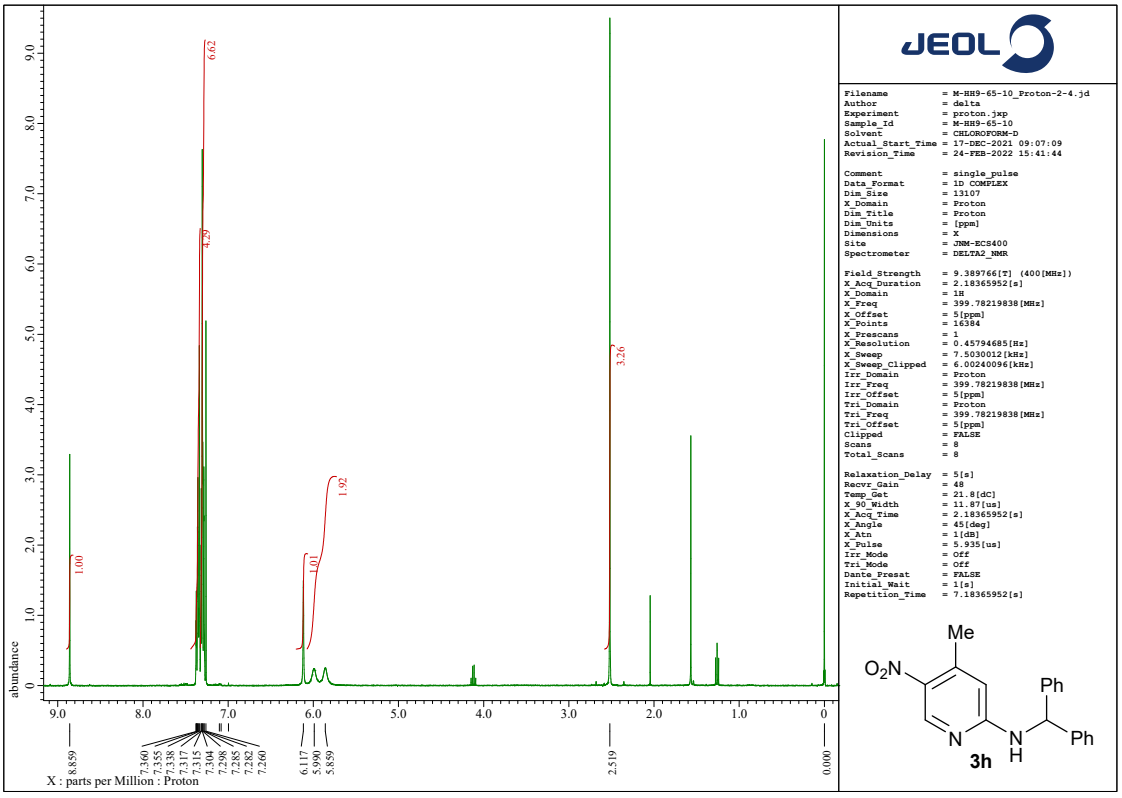


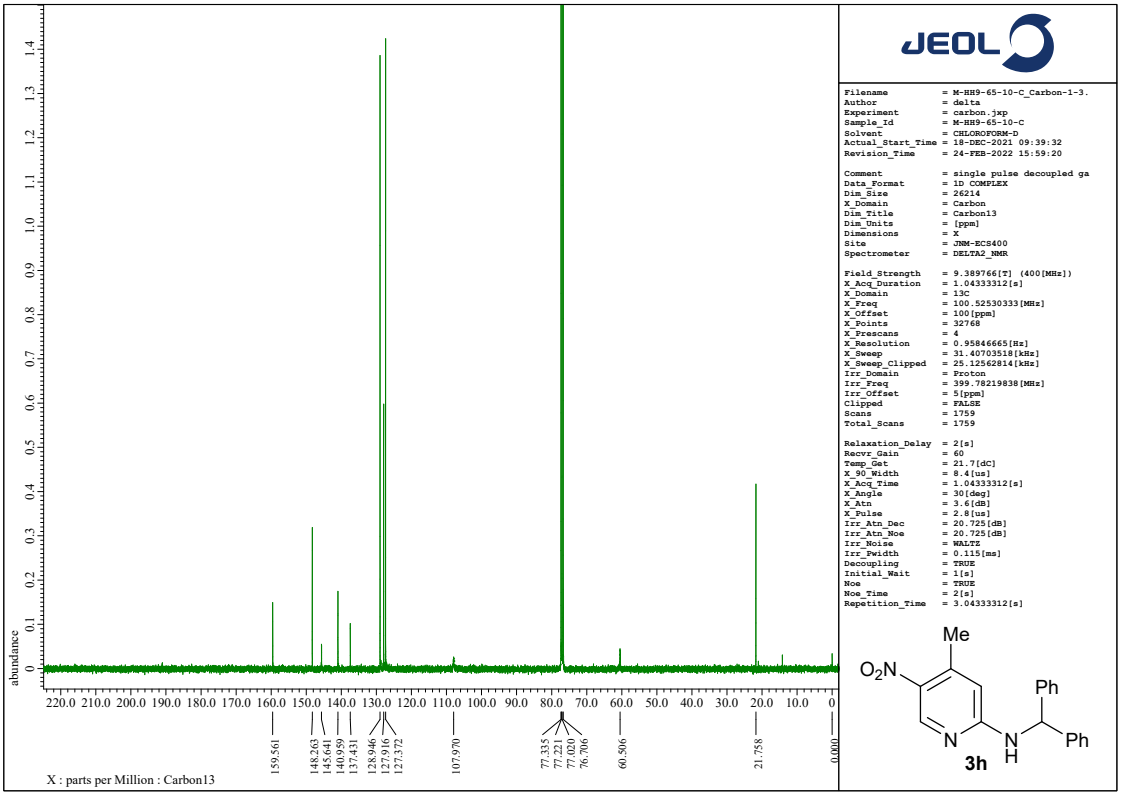
***N*-Benzhydryl-6-methyl-3-nitropyridin-2-amine 3g**



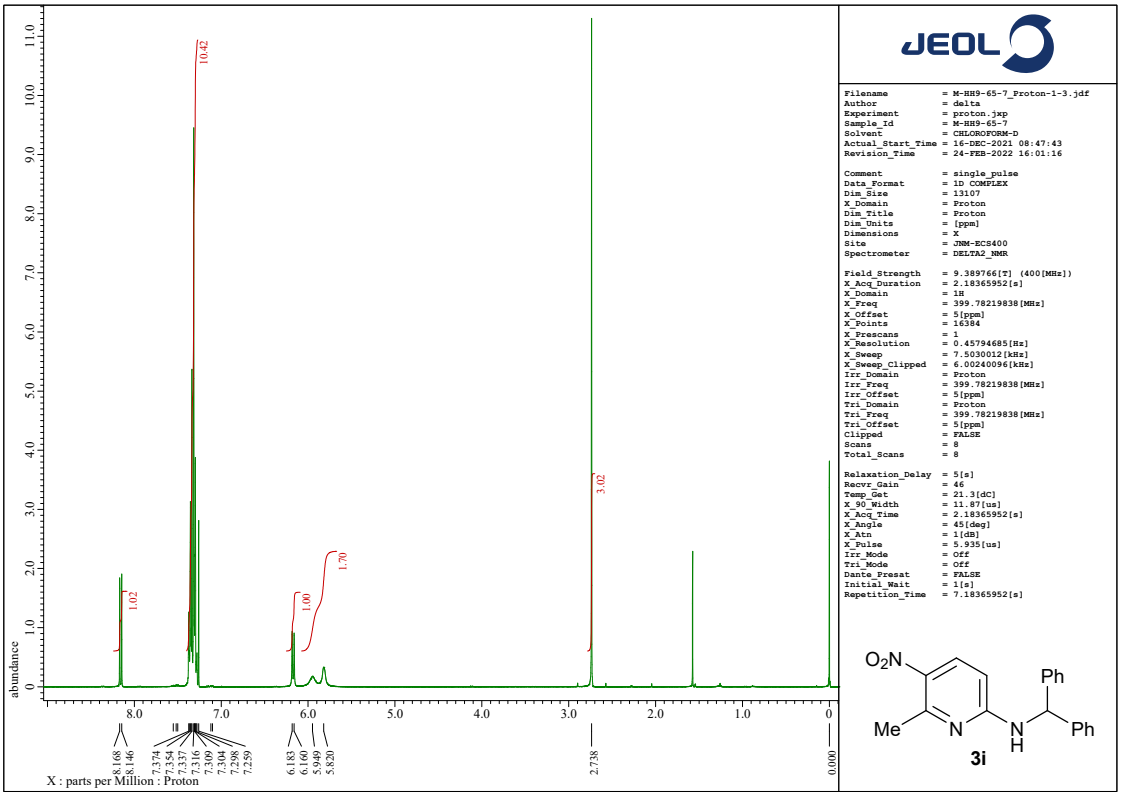


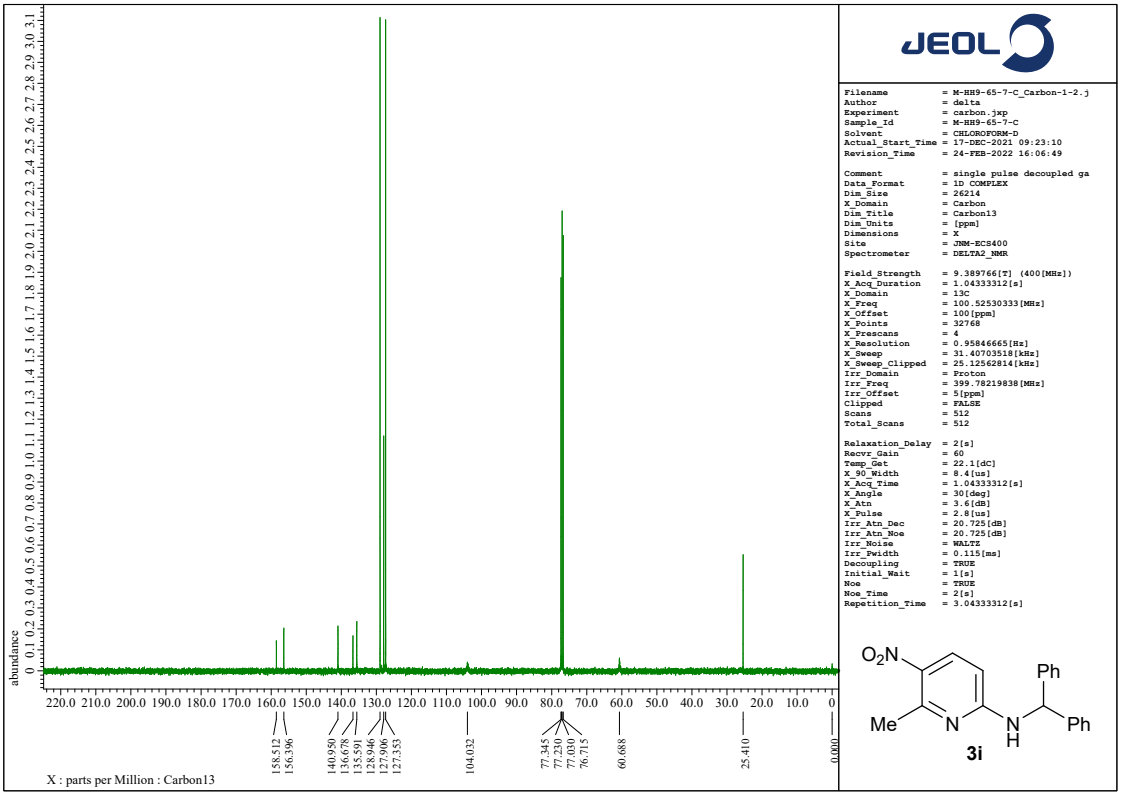
***N*-Benzhydryl-4-methyl-5-nitropyridin-2-amine 3h**



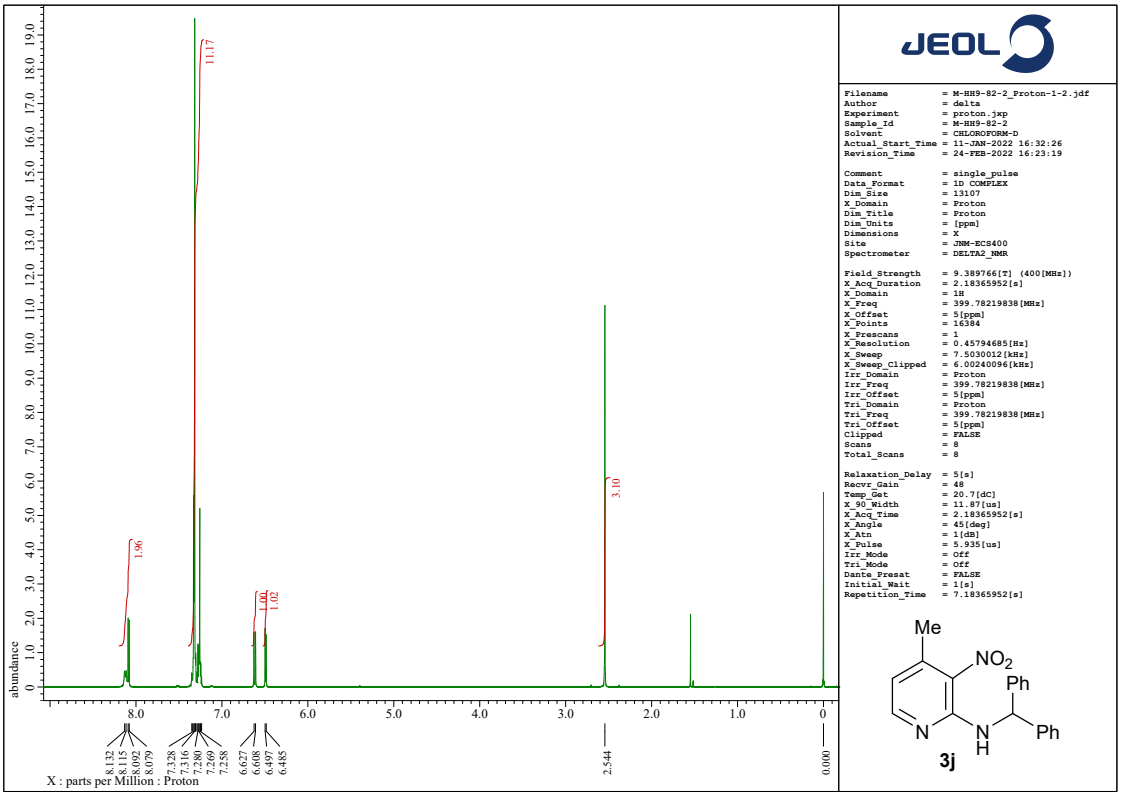


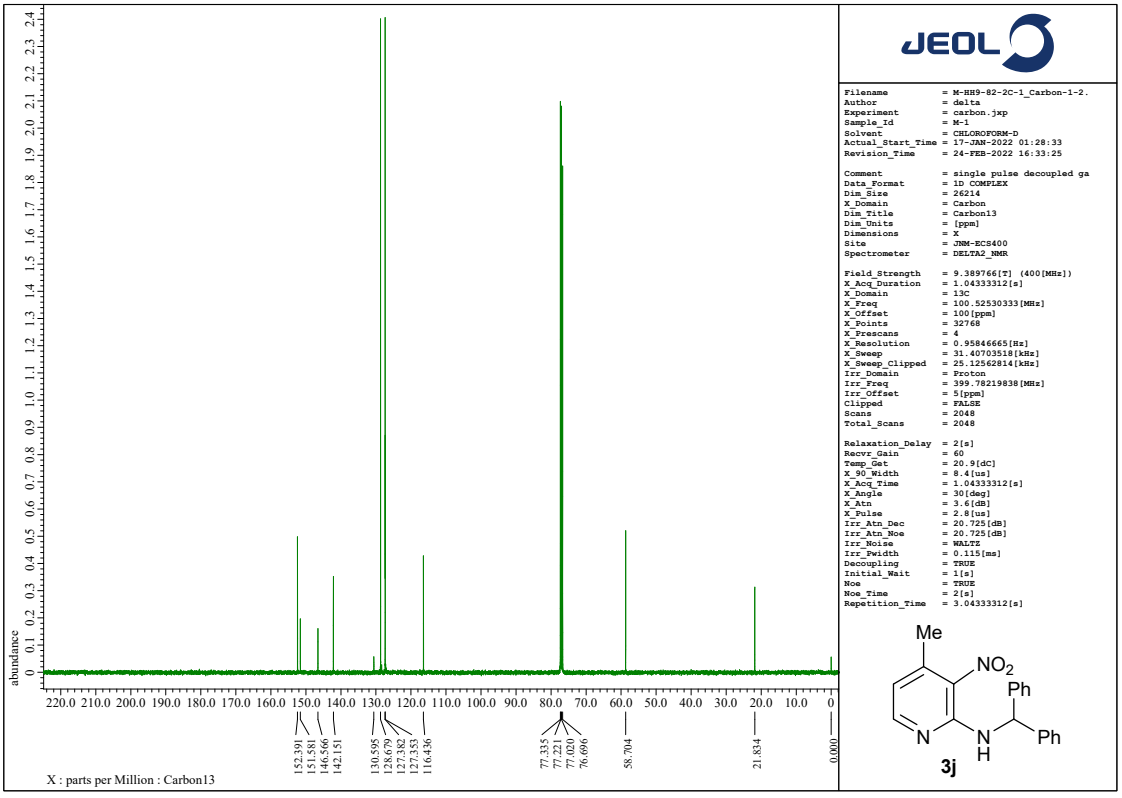
***N*-Benzhydryl-6-methyl-5-nitropyridin-2-amine 3i**



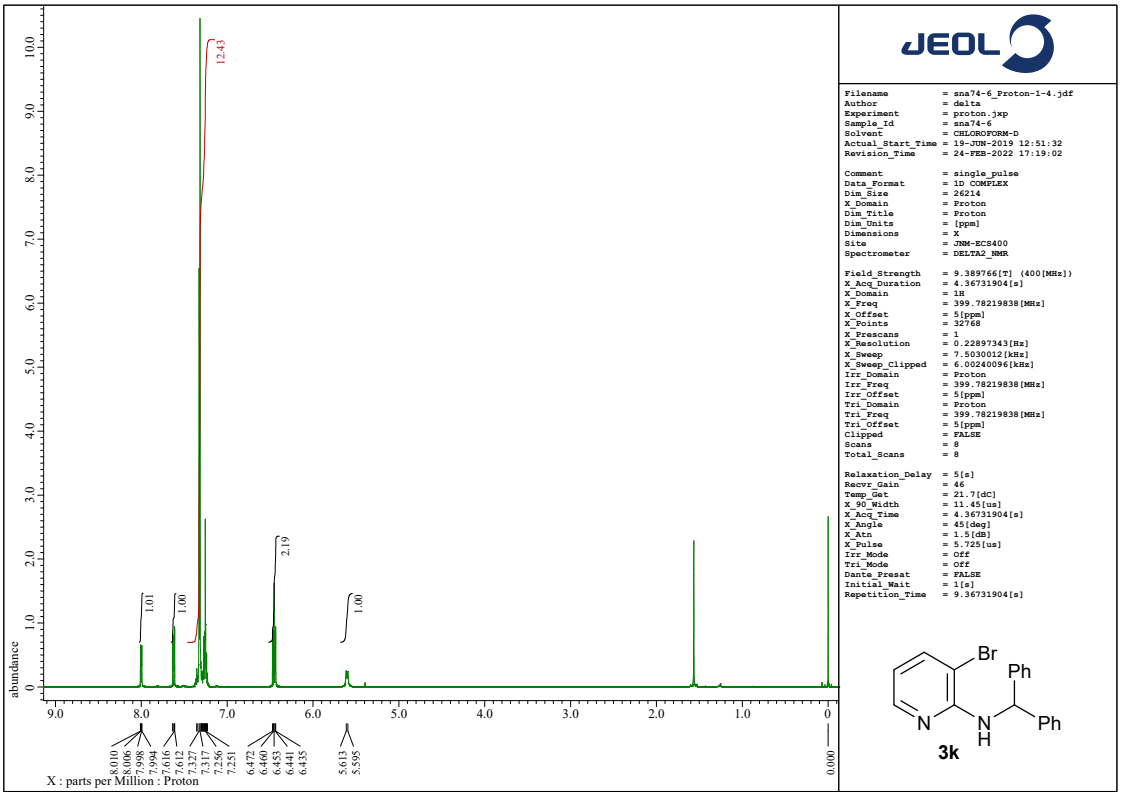


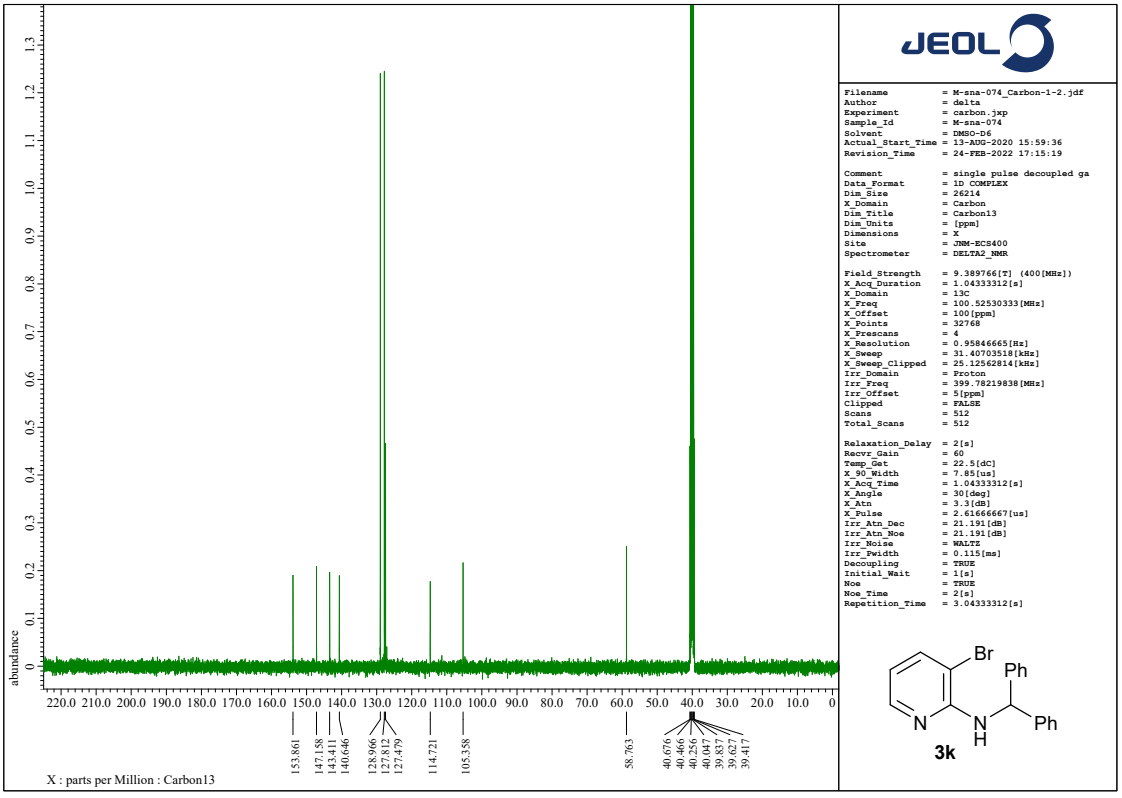
***N*-Benzhydryl-4-methyl-3-nitropyridin-2-amine 3j**



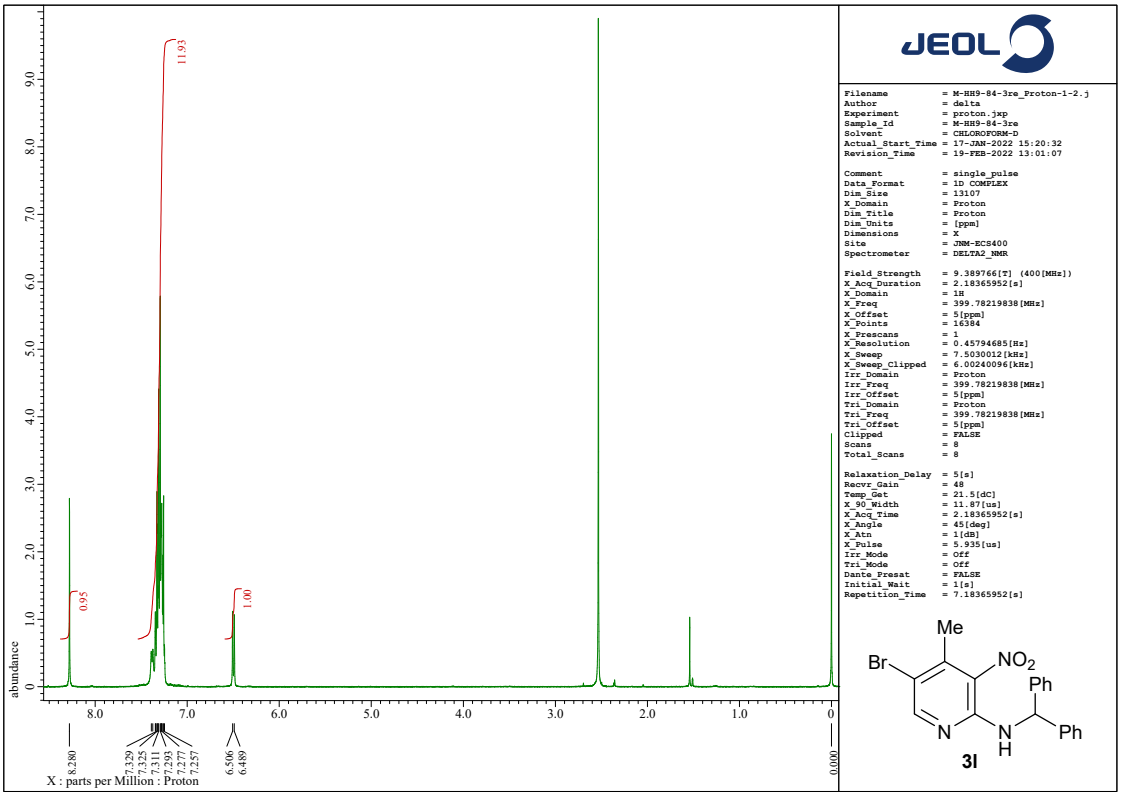


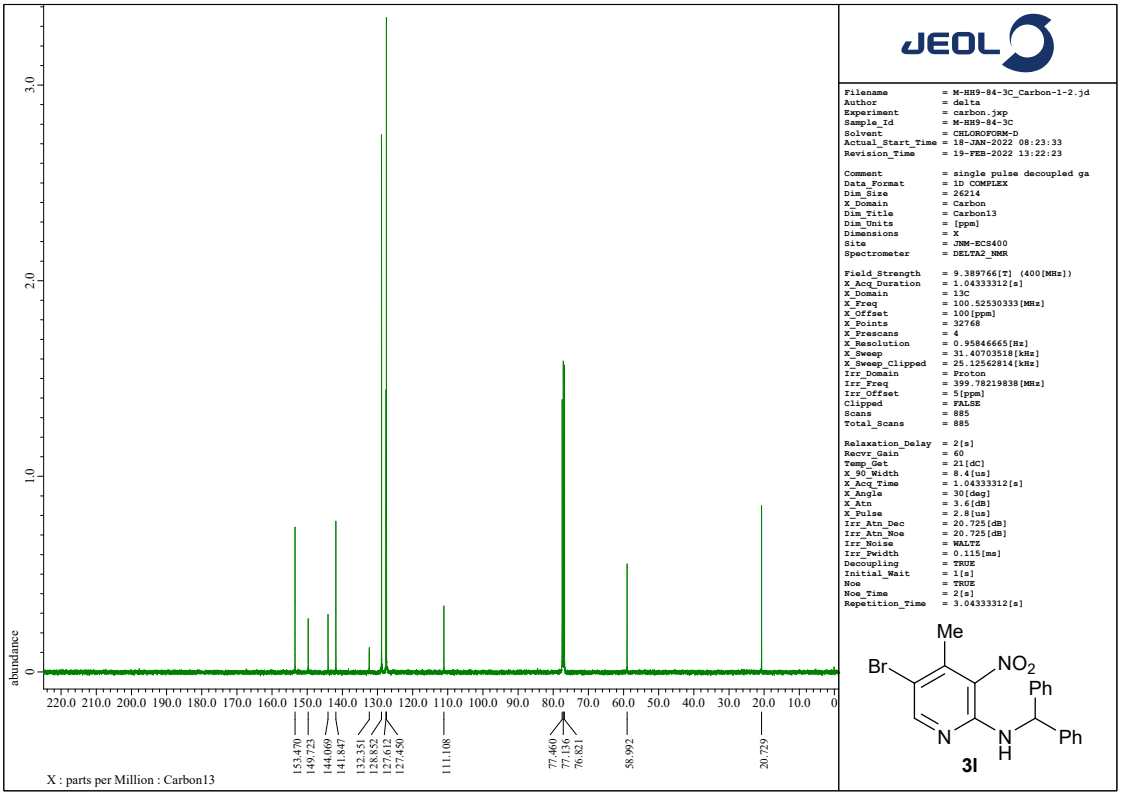
***N*-Benzhydryl-3-bromopyridin-2-amine 3k**



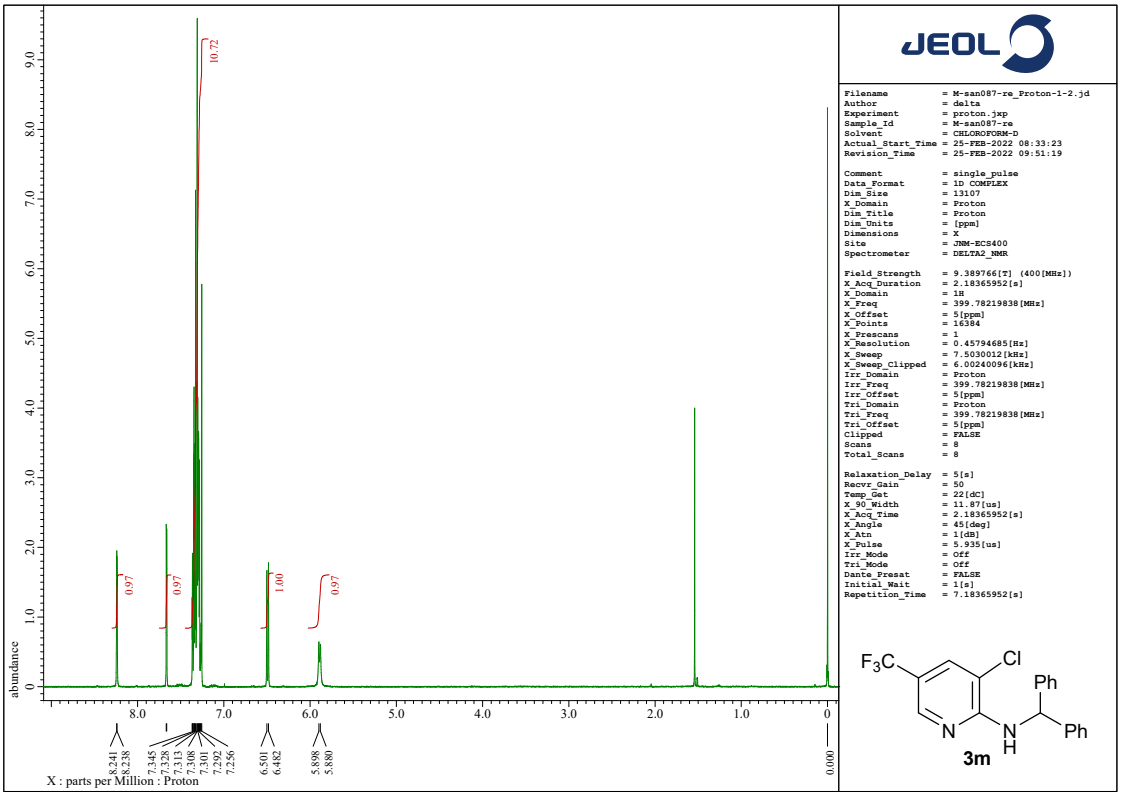


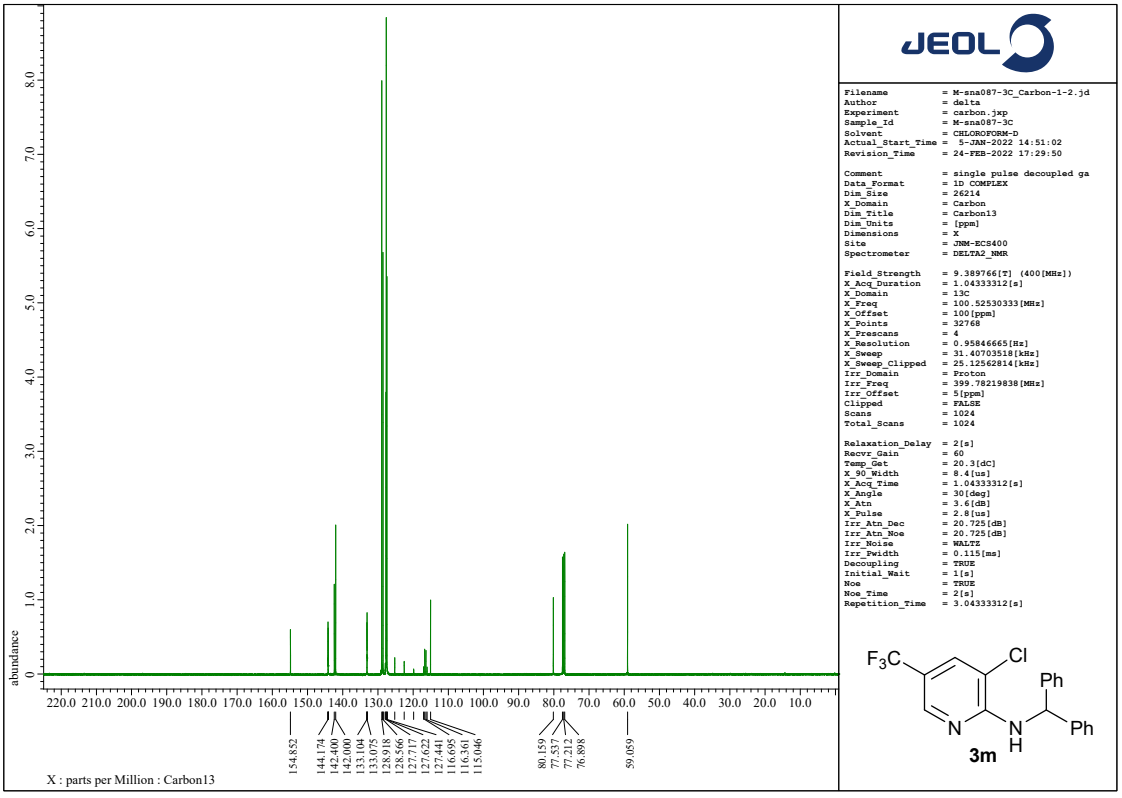
_N_-Benzhydryl-5-bromo-4-methyl-3-nitropyridin-2-amine 3l



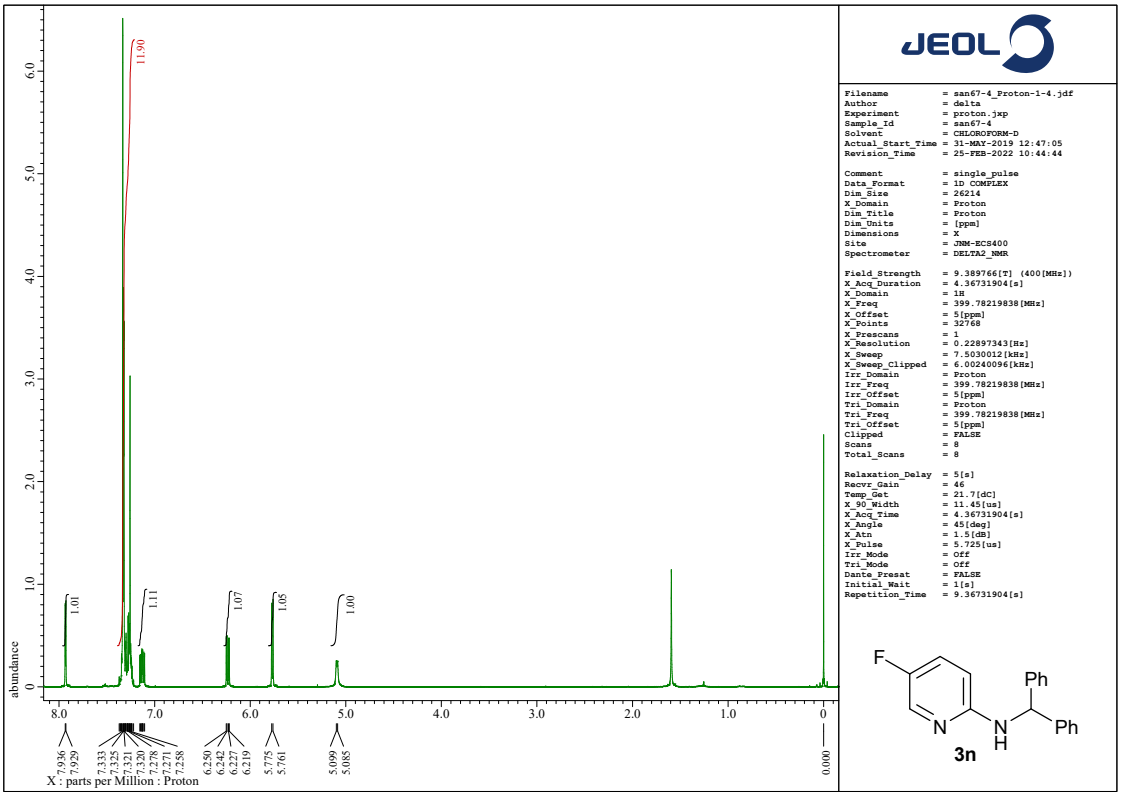


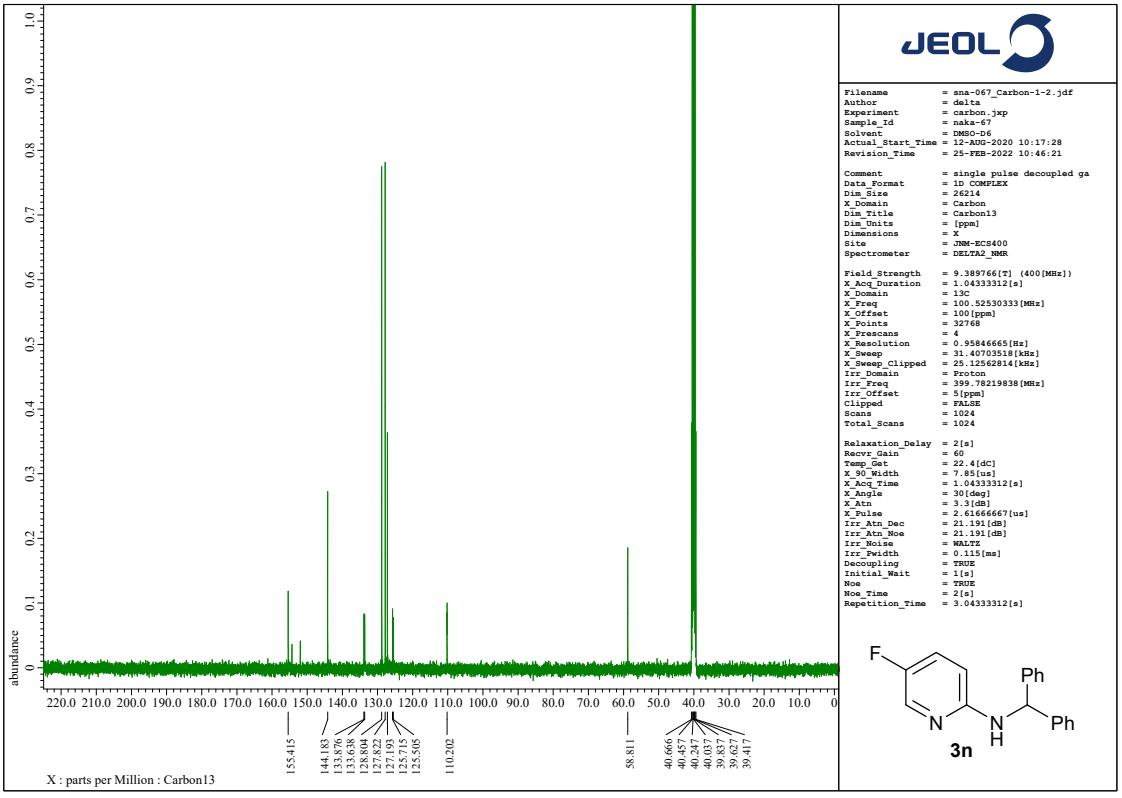
***N*-Benzhydryl-3-chloro-5-(trifluoromethyl)pyridin-2-amine 3m**



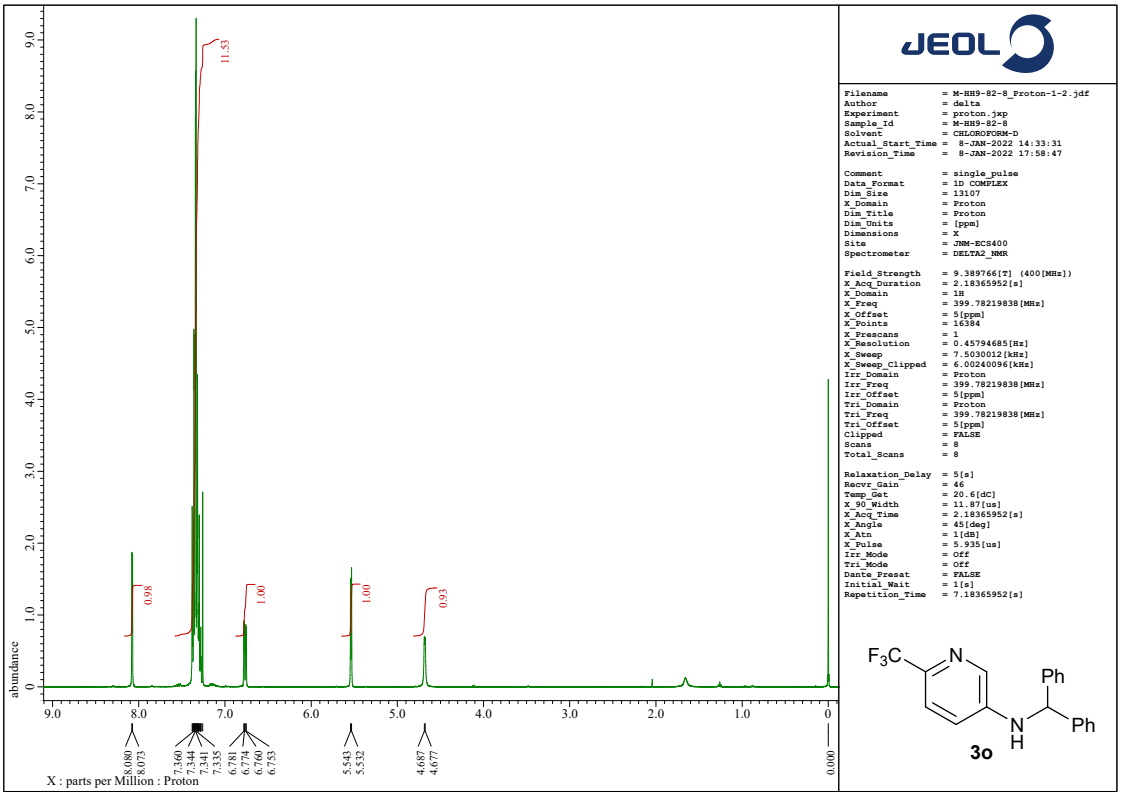


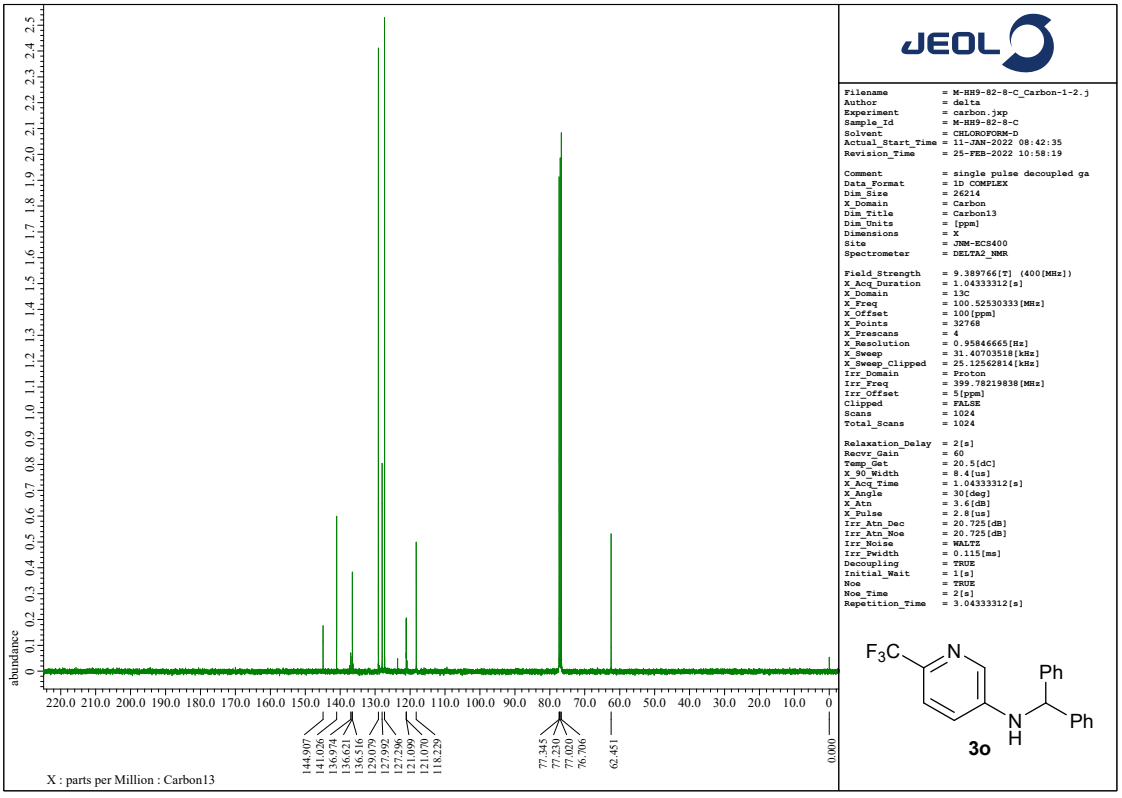
***N*-Benzhydryl-5-fluoropyridin-2-amine 3n**



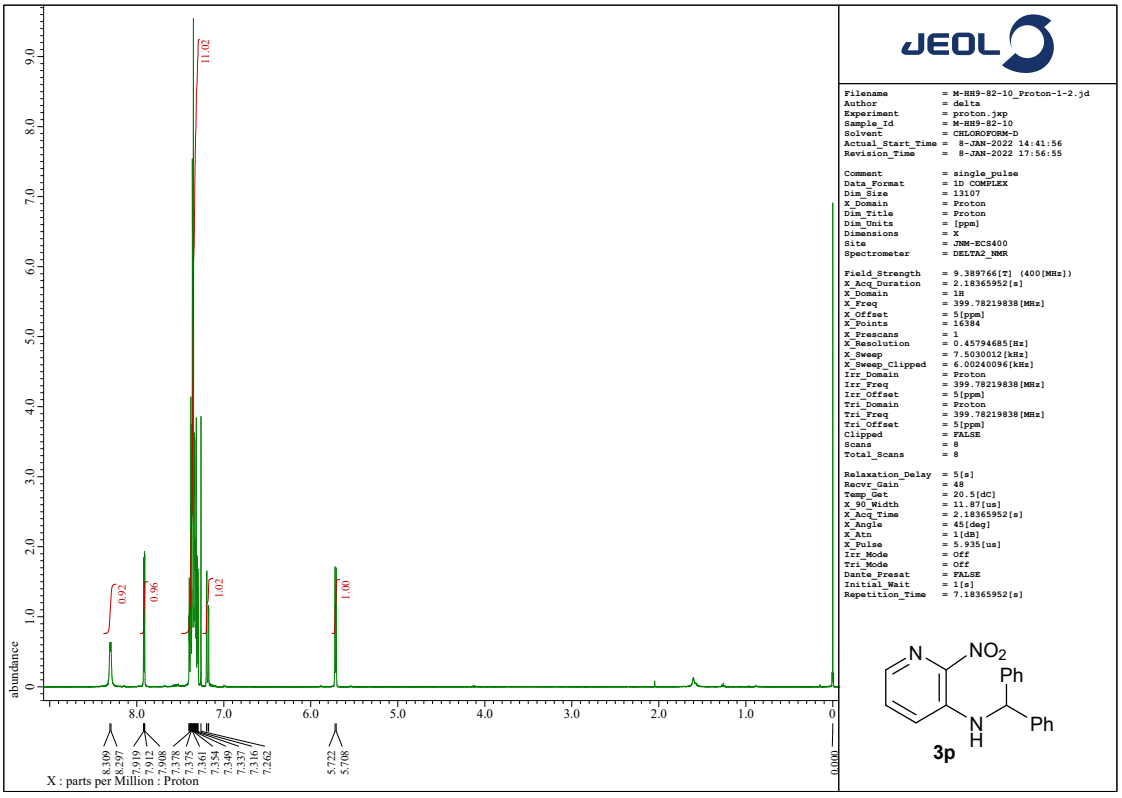


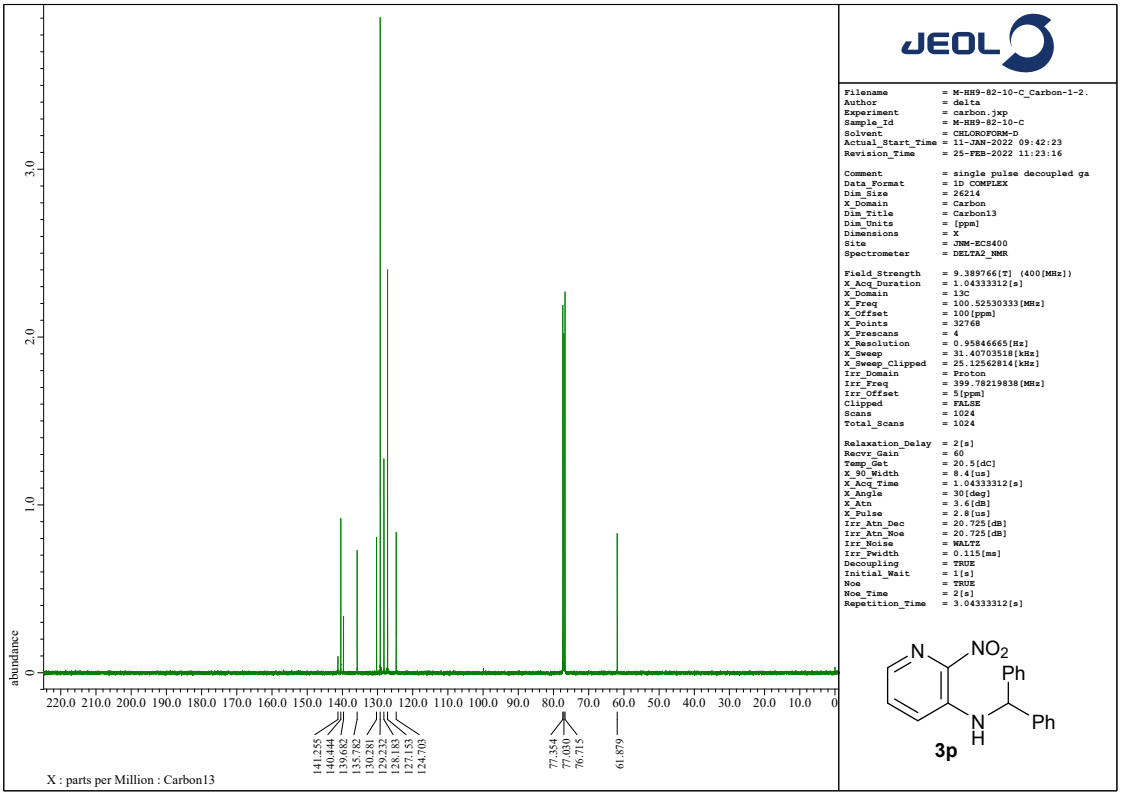
_N_-Benzhydryl-6-(trifluoromethyl)pyridin-3-amine 3o



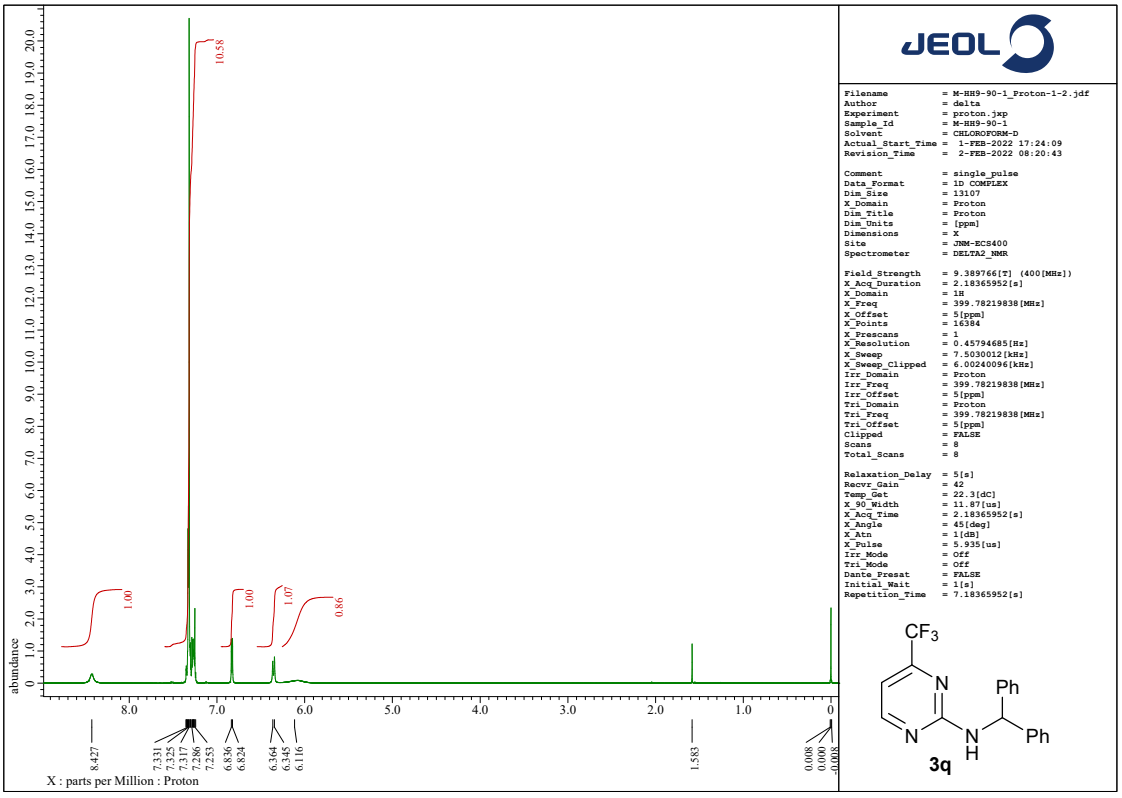


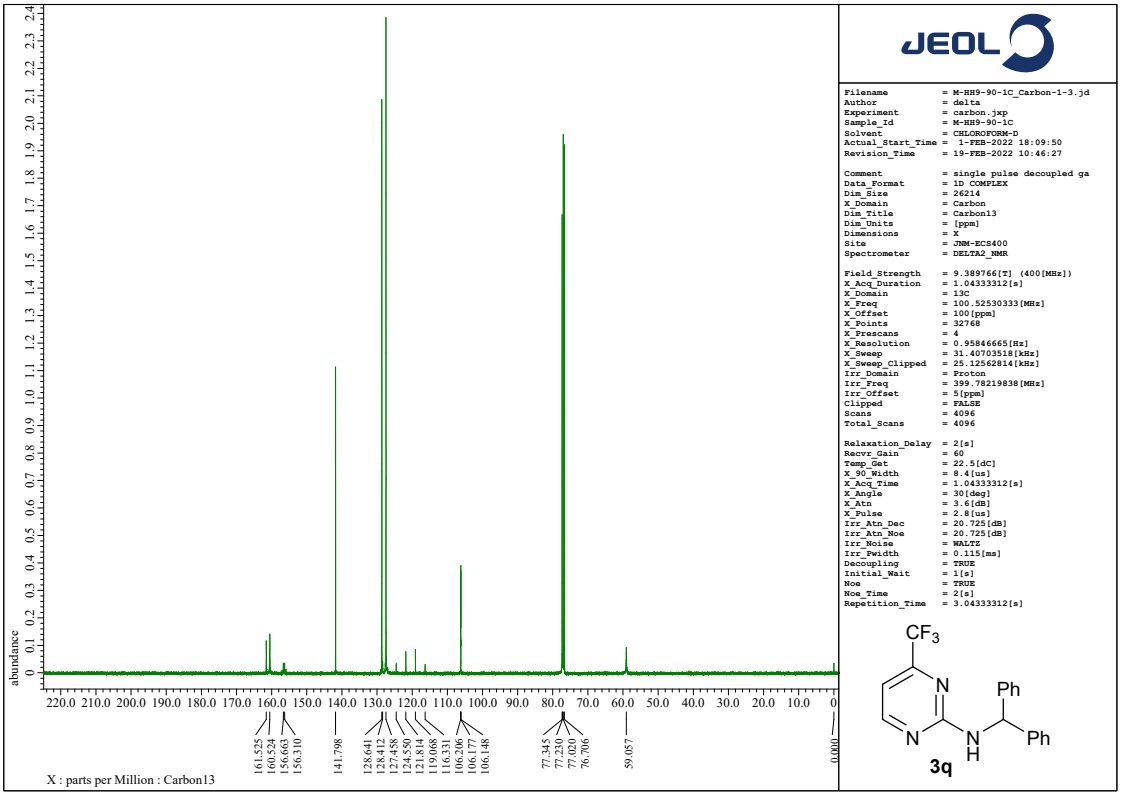
***N*-Benzhydryl-2-nitropyridin-3-amine 3p**



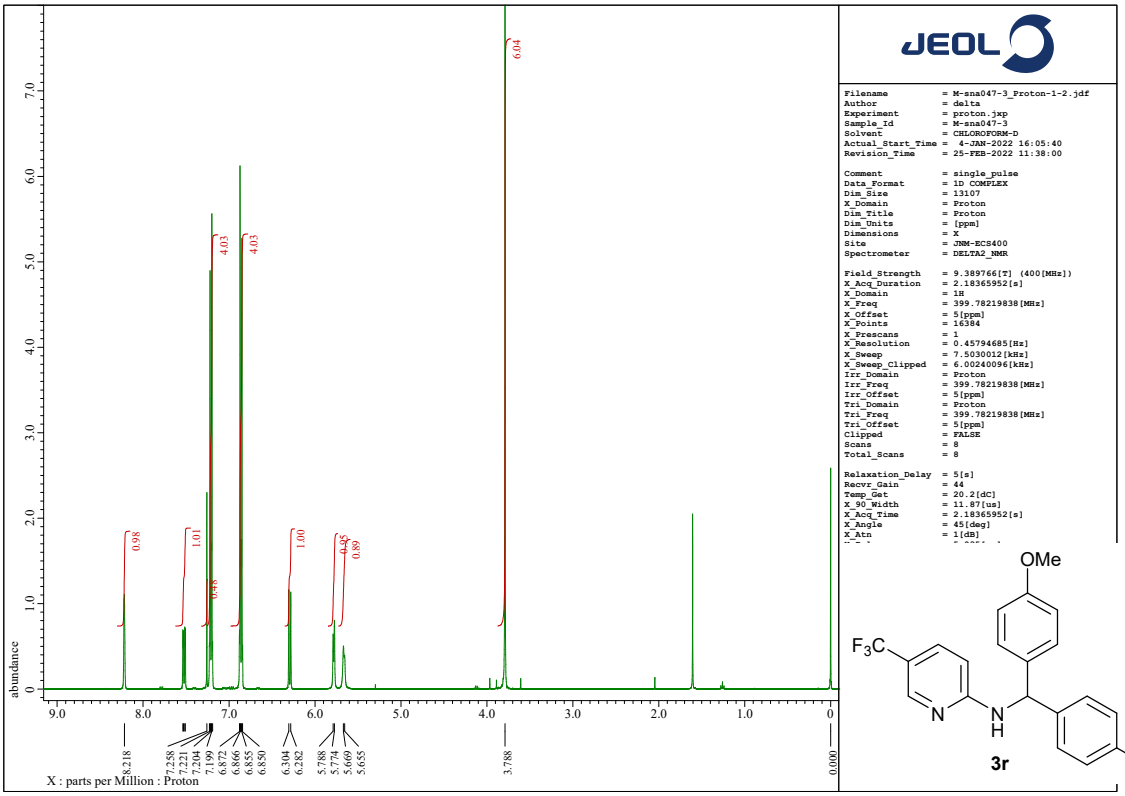


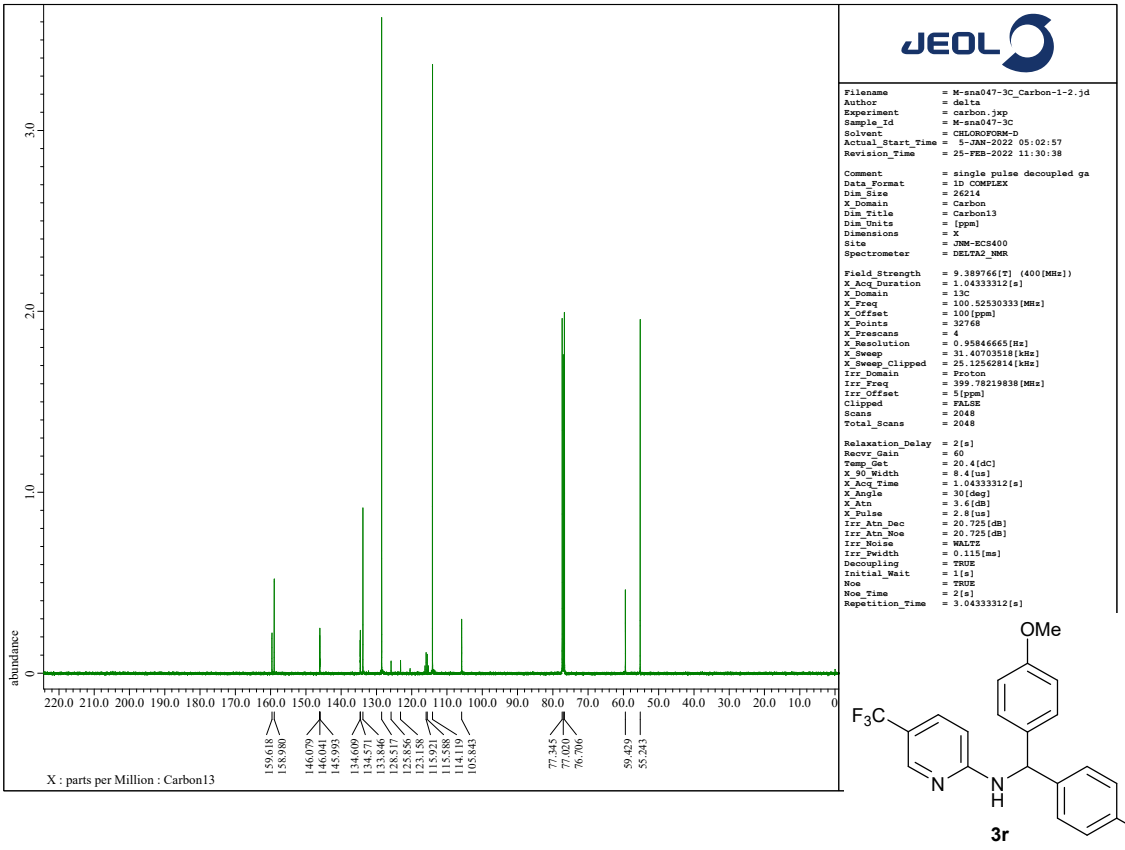
N-Benzhydryl-4-(trifluoromethyl)pyrimidin-2-amine 3q



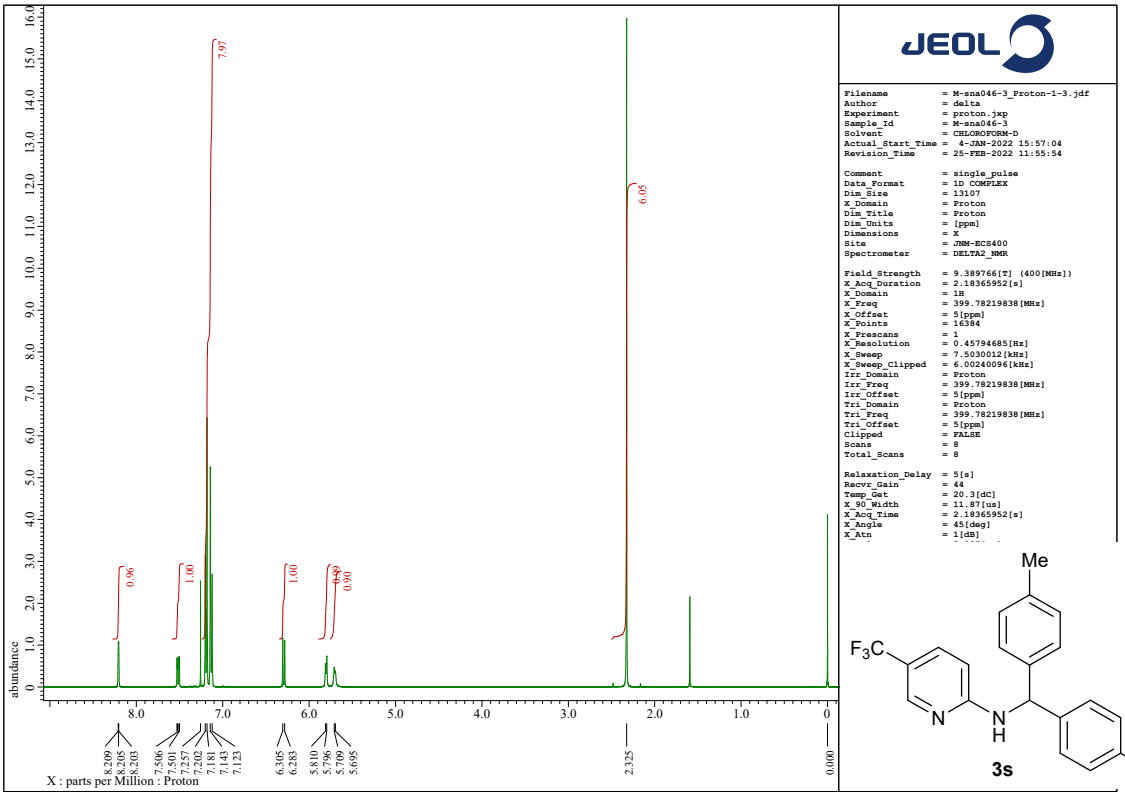


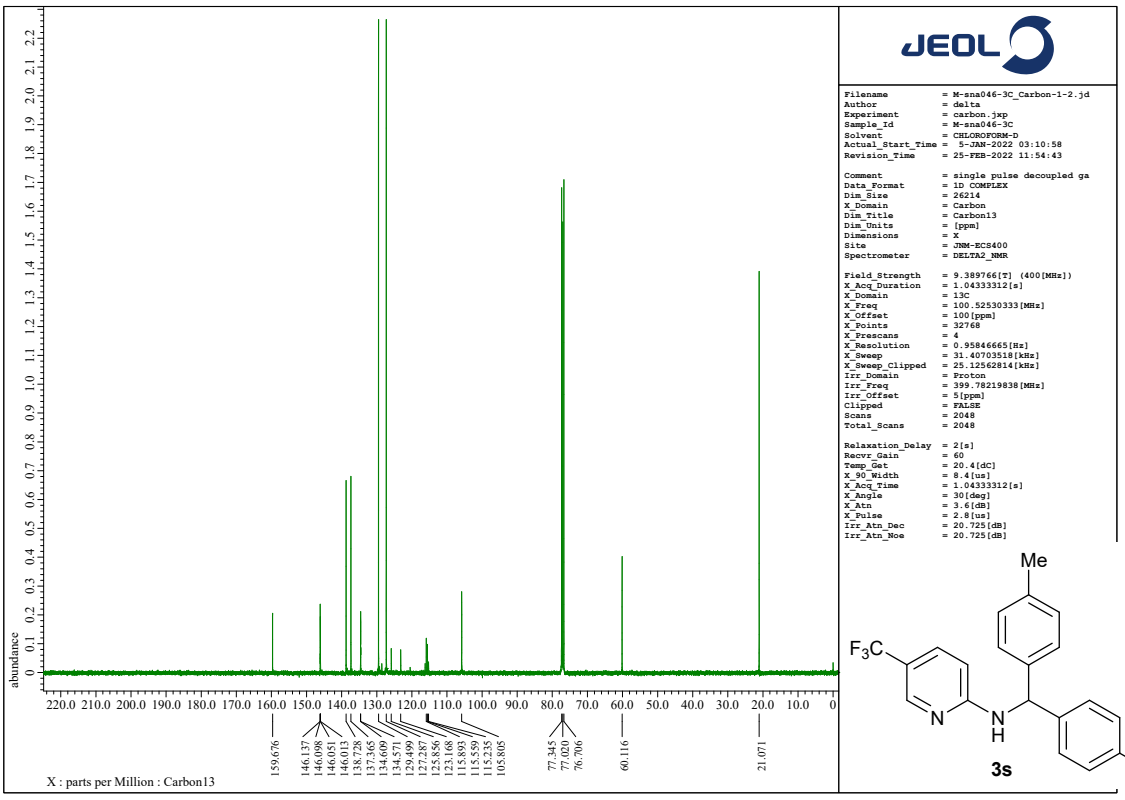
***N*-{Bis(4-methoxyphenyl)methyl}-5-(trifluoromethyl)pyridin-2-amine 3r**



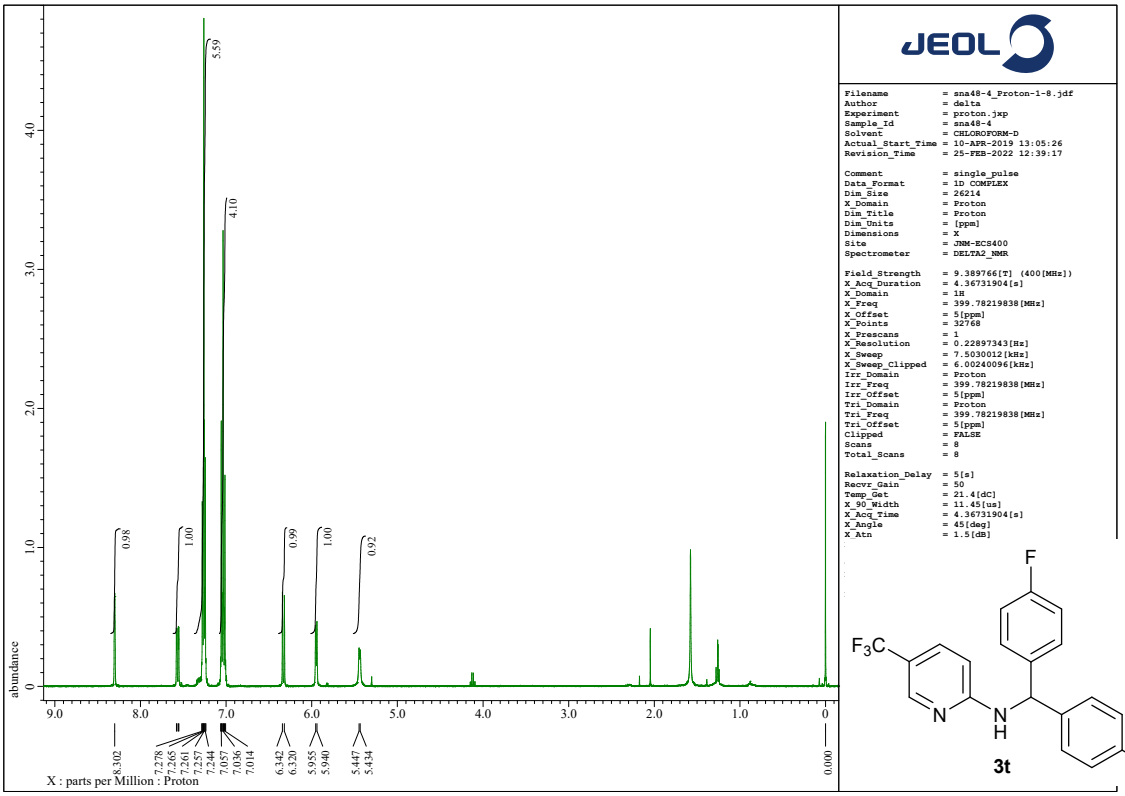


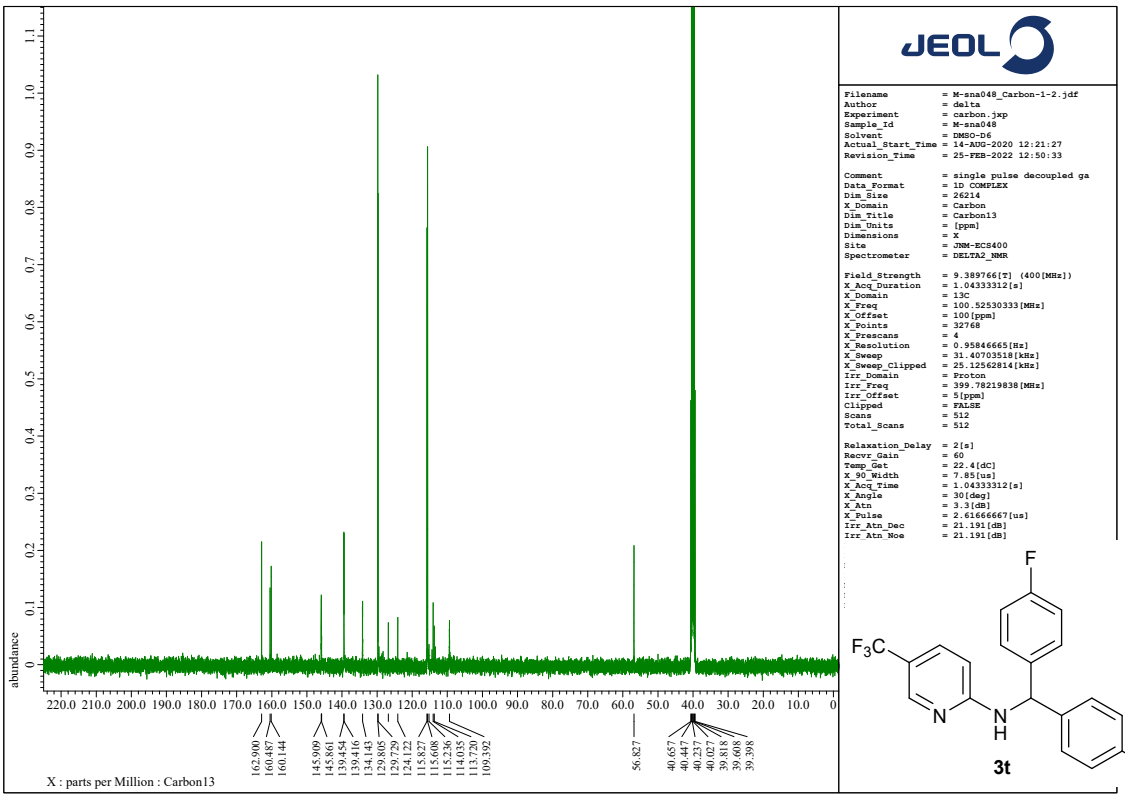
***N*-(Di-*p*-tolylmethyl)-5-(trifluoromethyl)pyridin-2-amine 3s**



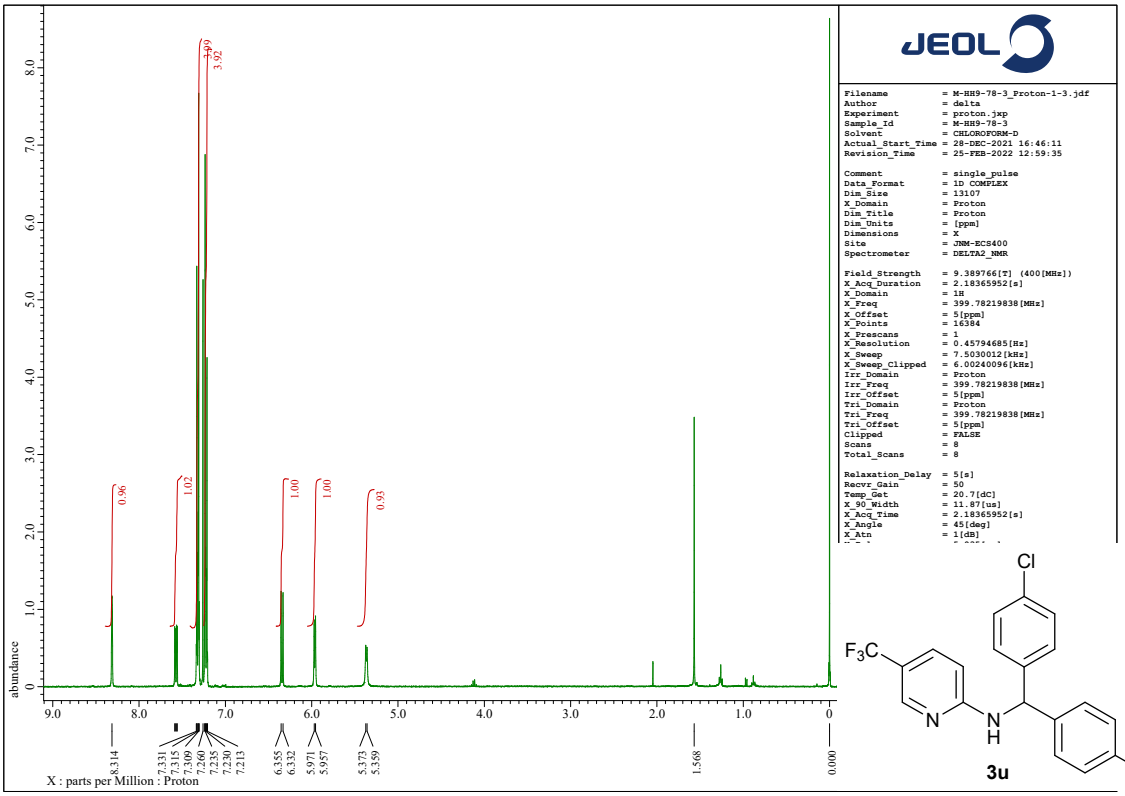


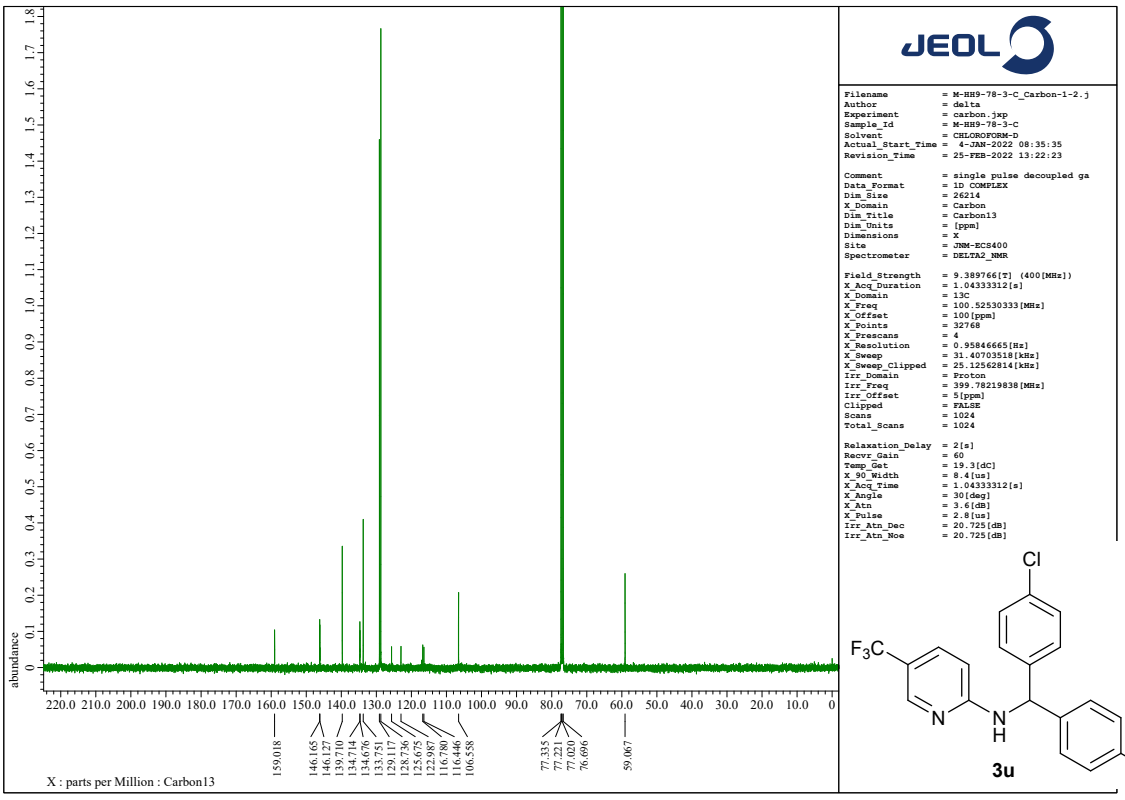
***N*-{Bis(4-fluorophenyl)methyl}-5-(trifluoromethyl)pyridin-2-amine 3t**



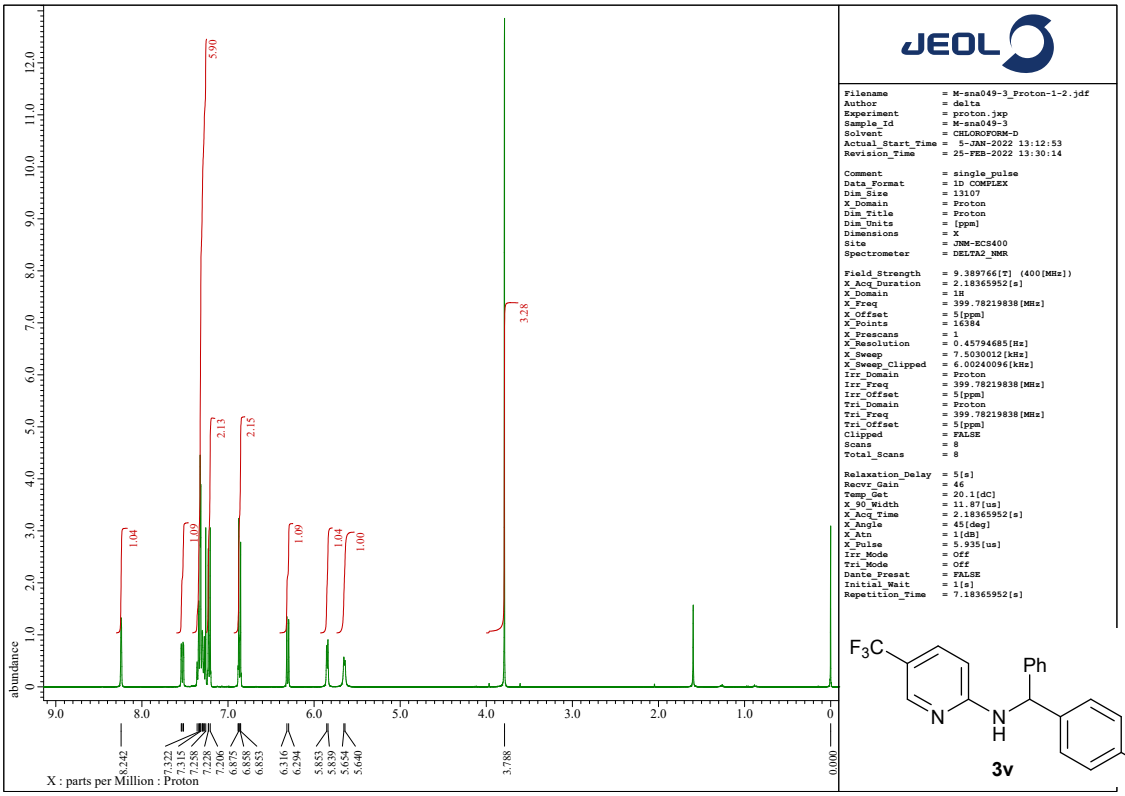


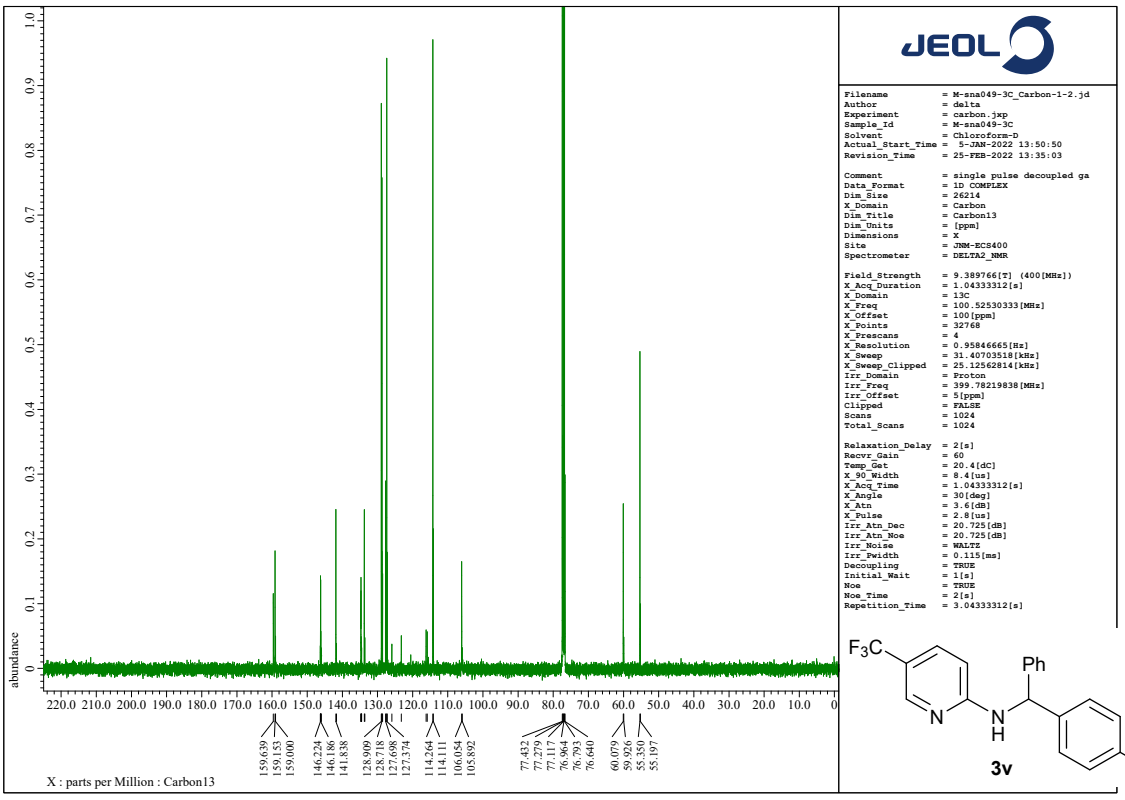
***N*-{Bis(4-chlorophenyl)methyl}-5-(trifluoromethyl)pyridin-2-amine 3u**



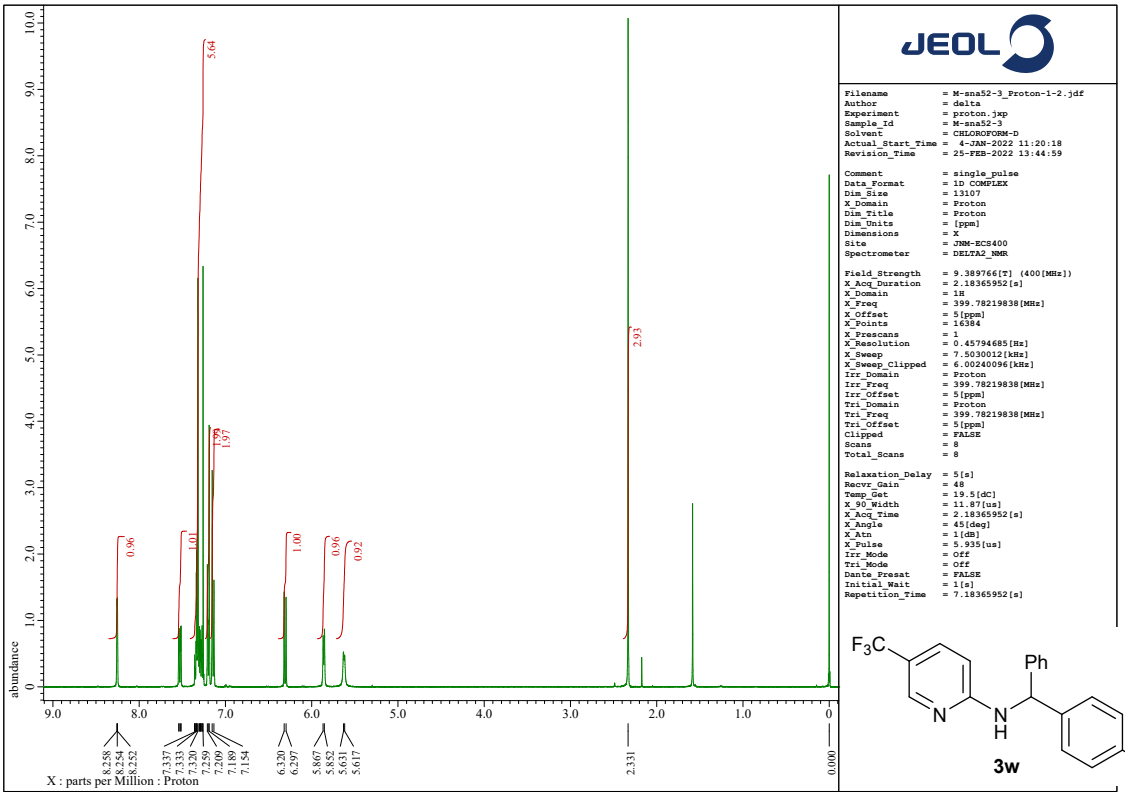


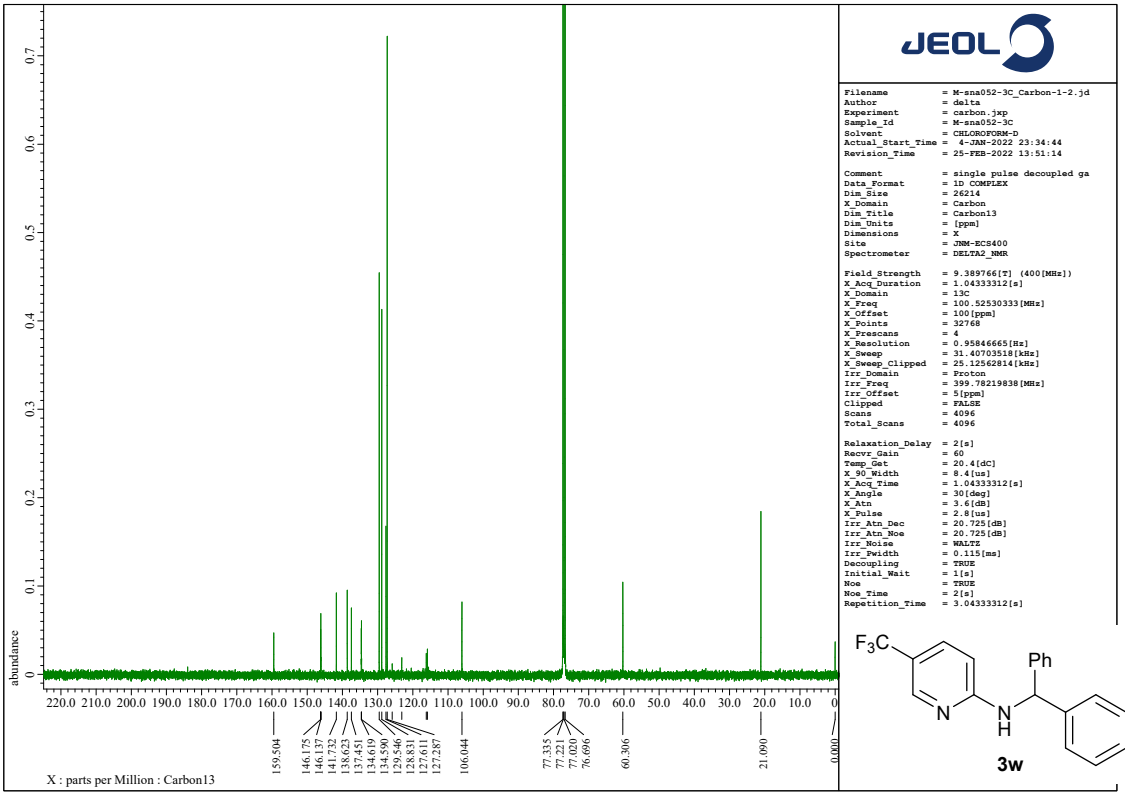
***N*-{(4-Methoxyphenyl)(phenyl)methyl}-5-(trifluoromethyl)pyridin-2-amine 3v**



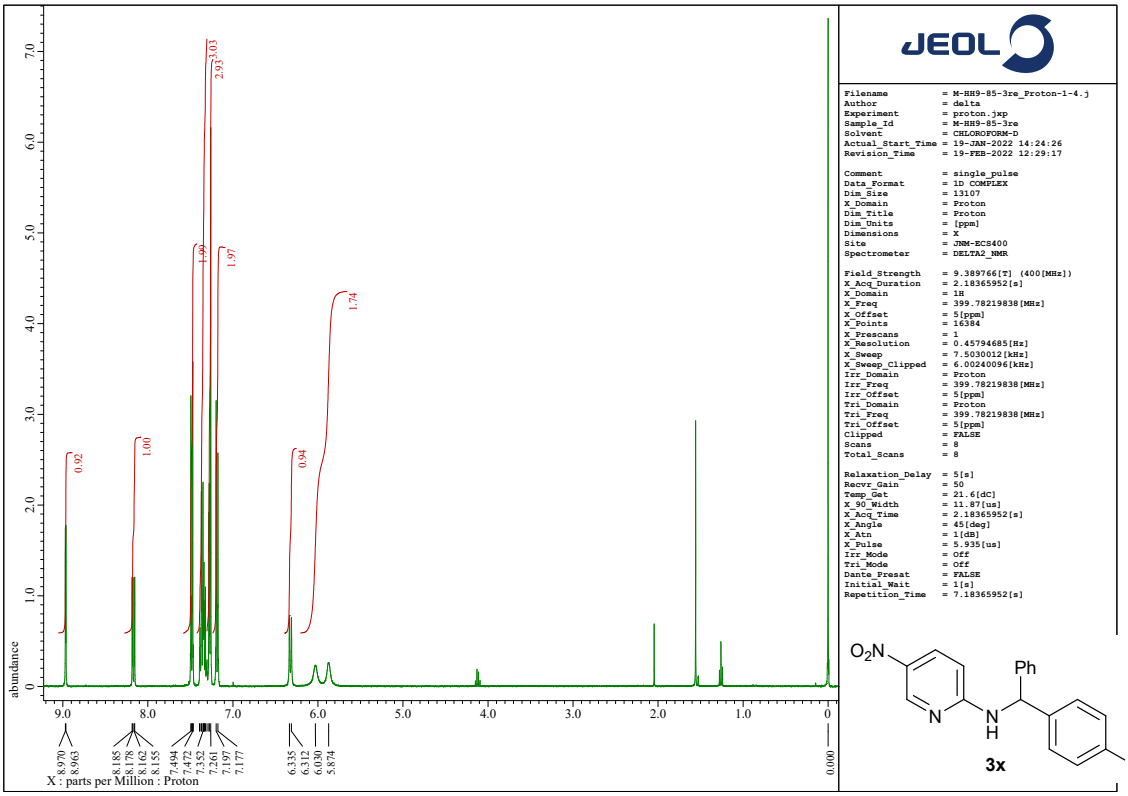


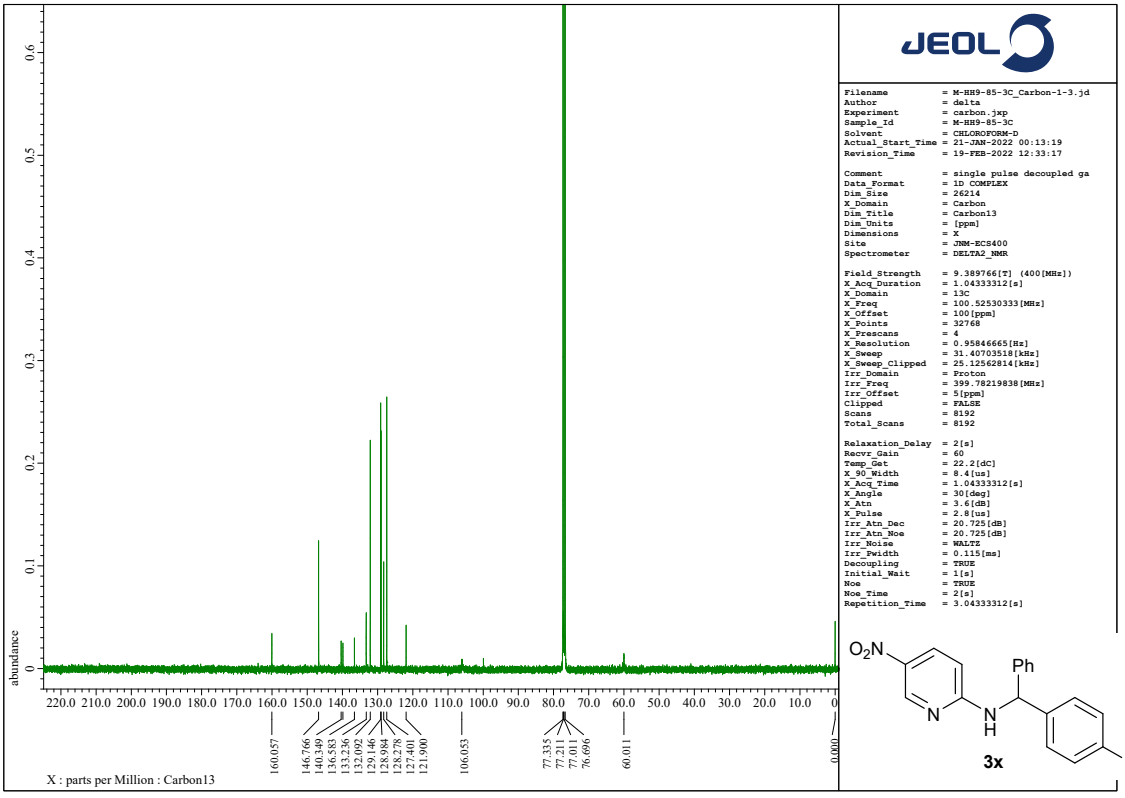
***N*-{Phenyl(*p*-tolyl)methyl}-5-(trifluoromethyl)pyridin-2-amine 3w**



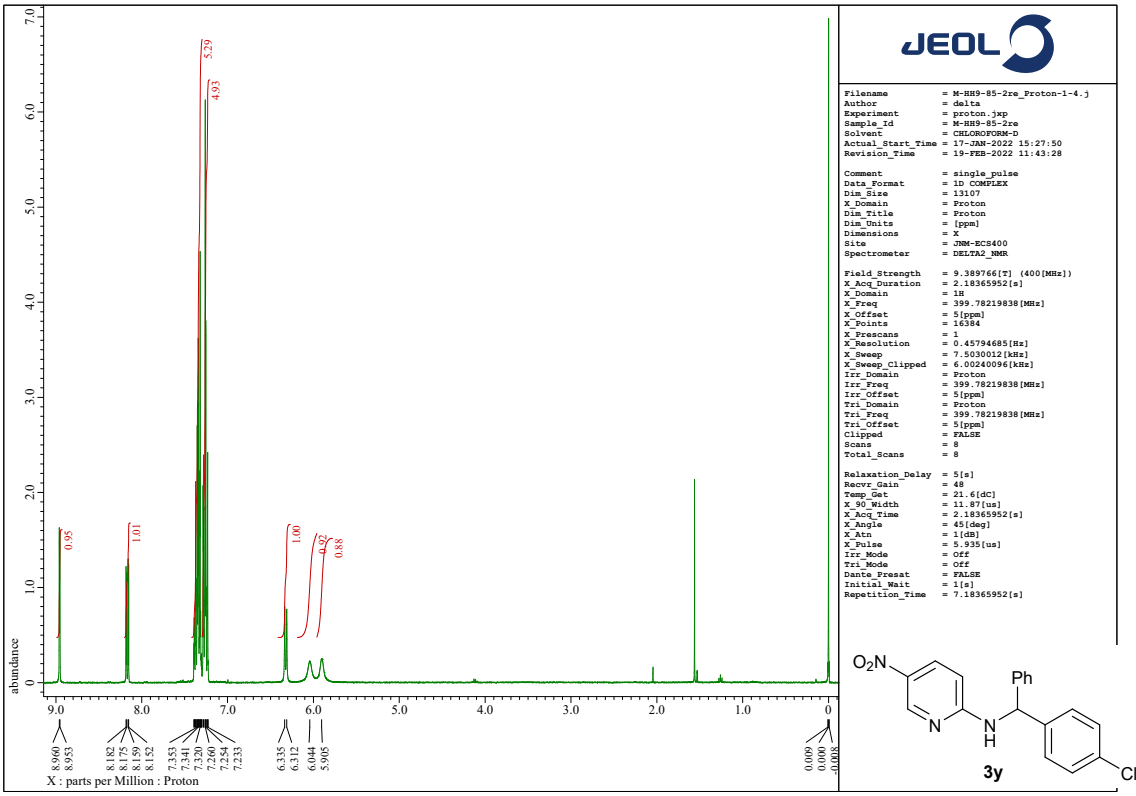


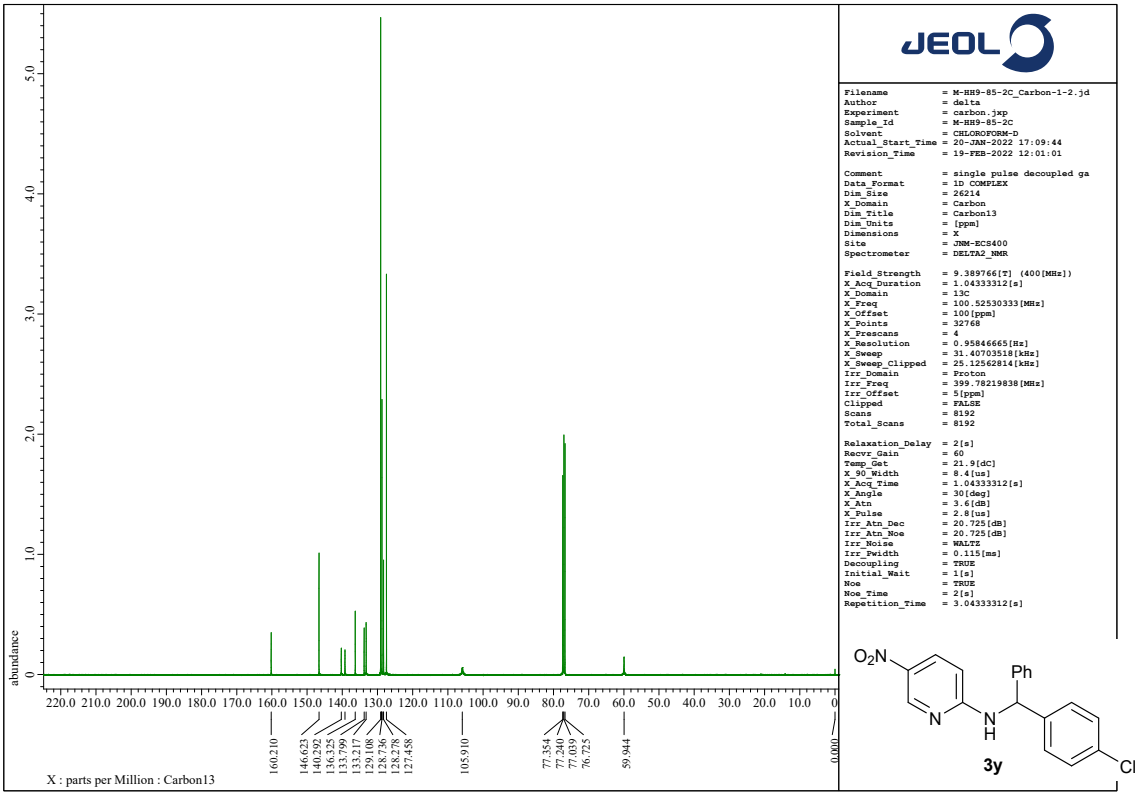
***N*-{(4-Bromophenyl)(phenyl)methyl}-5-nitropyridin-2-amine 3x**



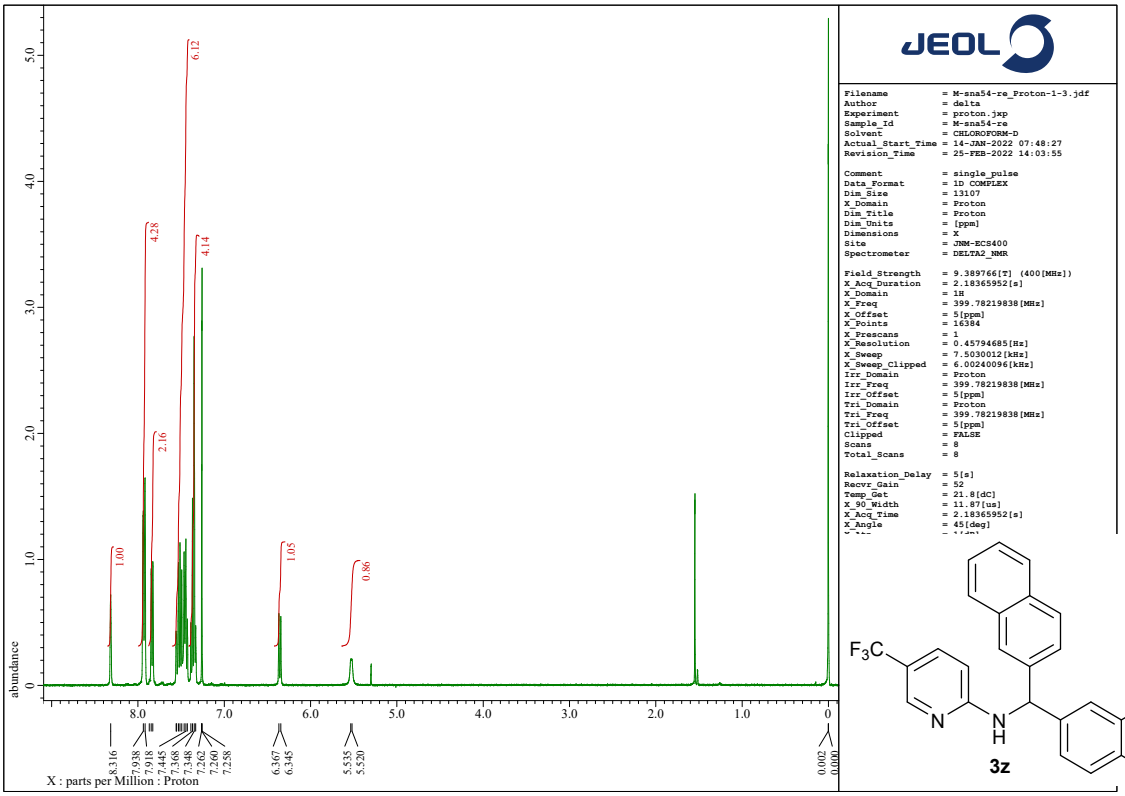


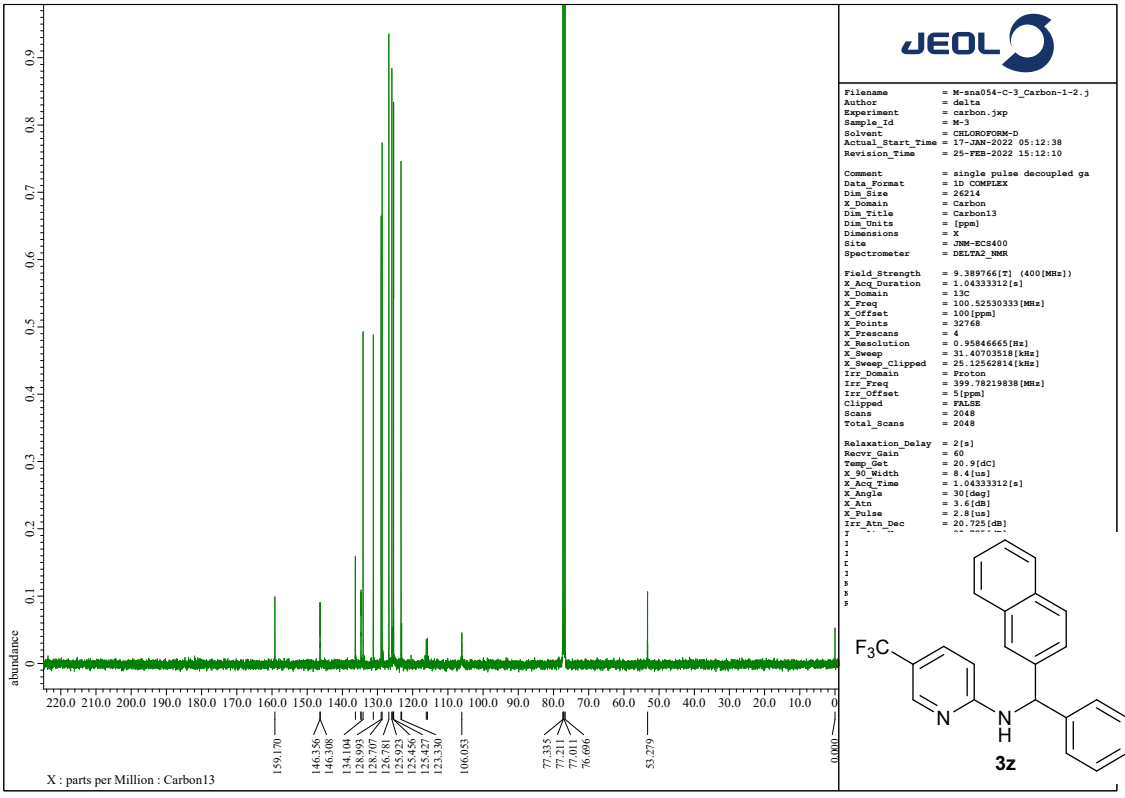
***N*-{(4-Chlorophenyl)(phenyl)methyl}-5-nitropyridin-2-amine 3y**



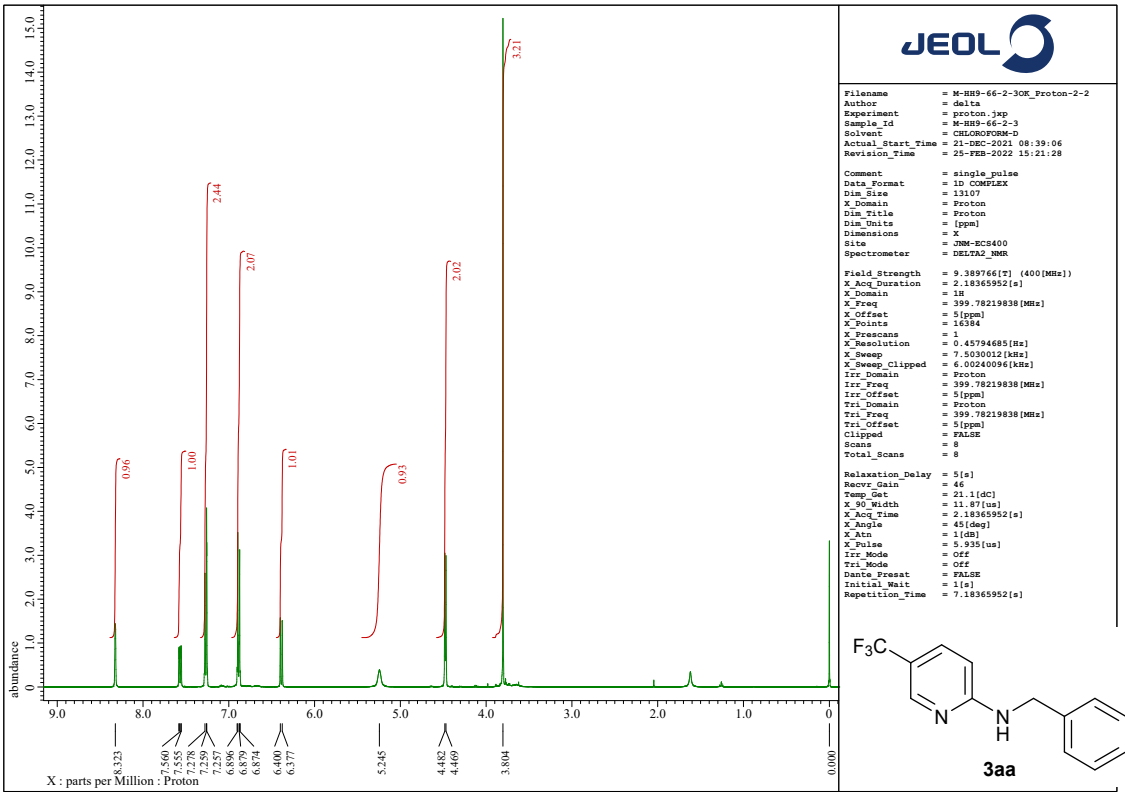


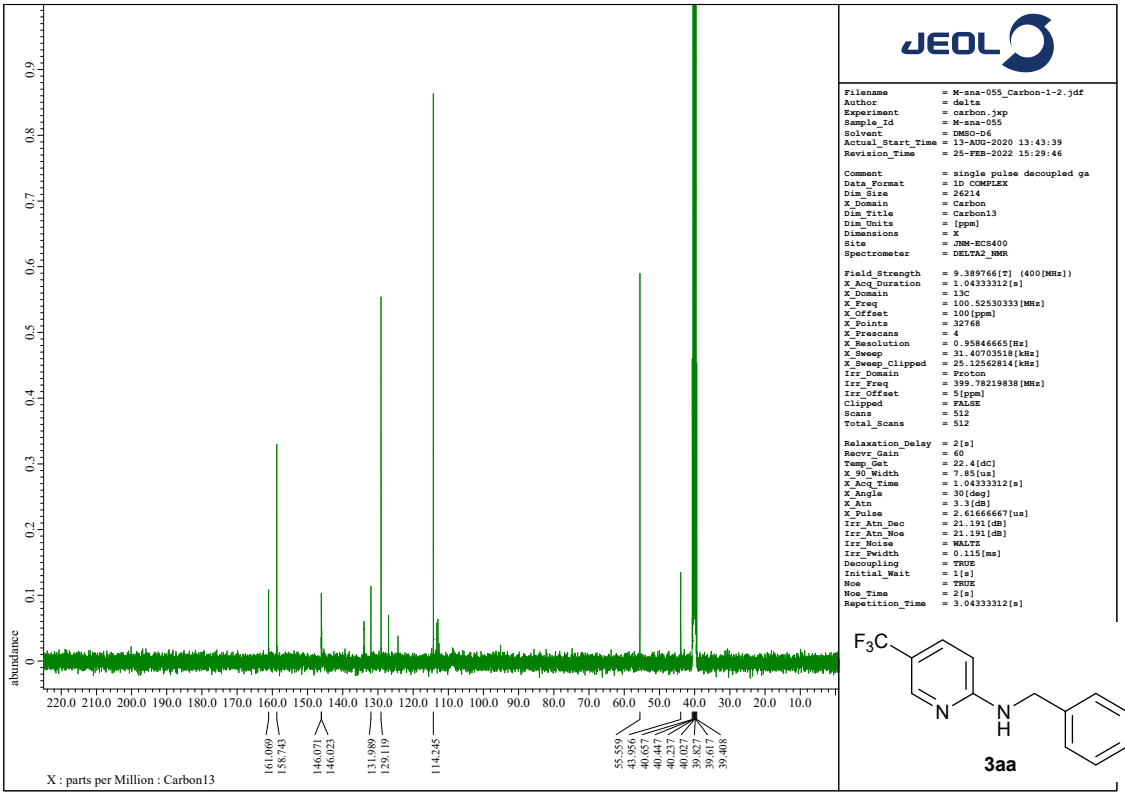
***N*-{Di(naphthalen-2-yl)methyl}-5-(trifluoromethyl)pyridin-2-amine 3z**



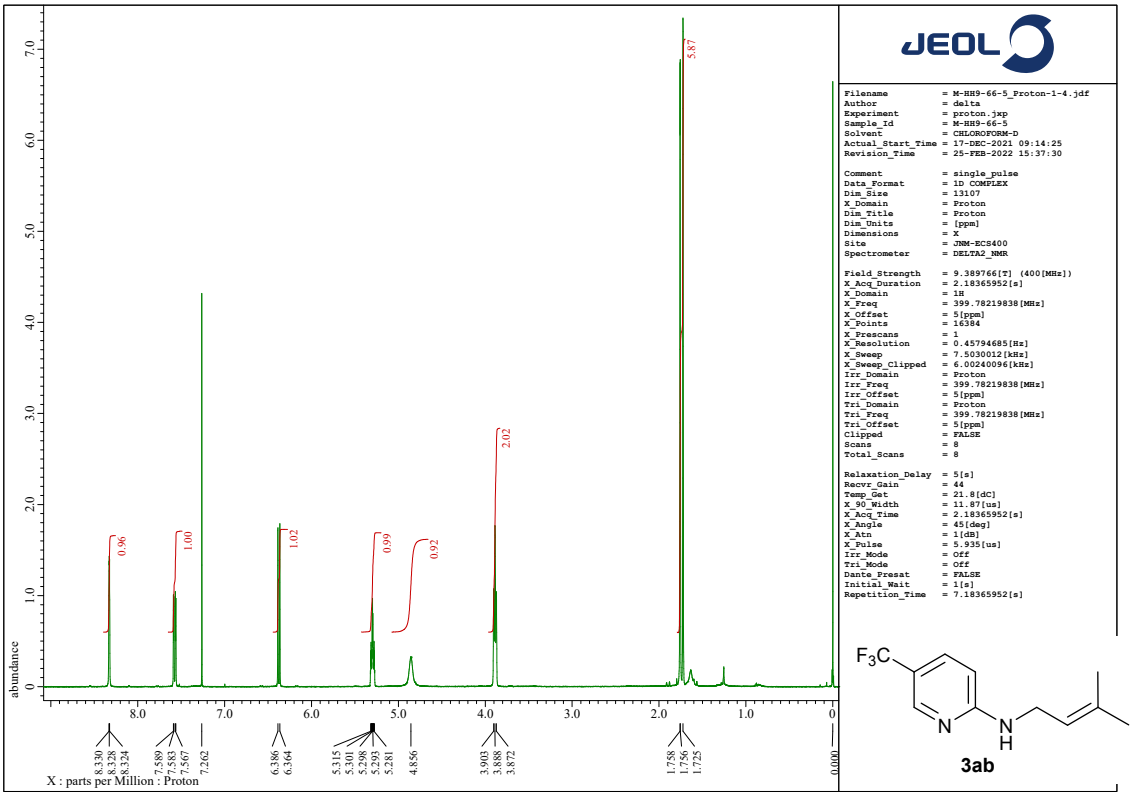


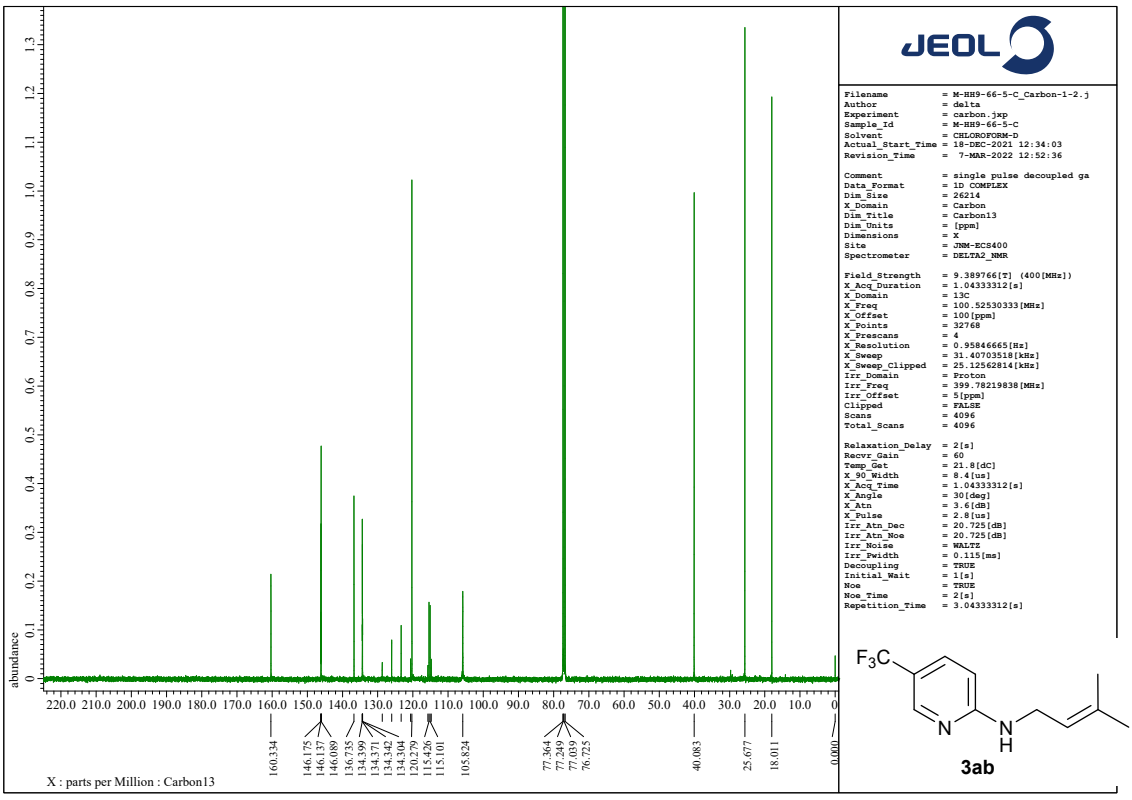
***N*-(4-Methoxybenzyl)-5-(trifluoromethyl)pyridin-2-amine 3aa**



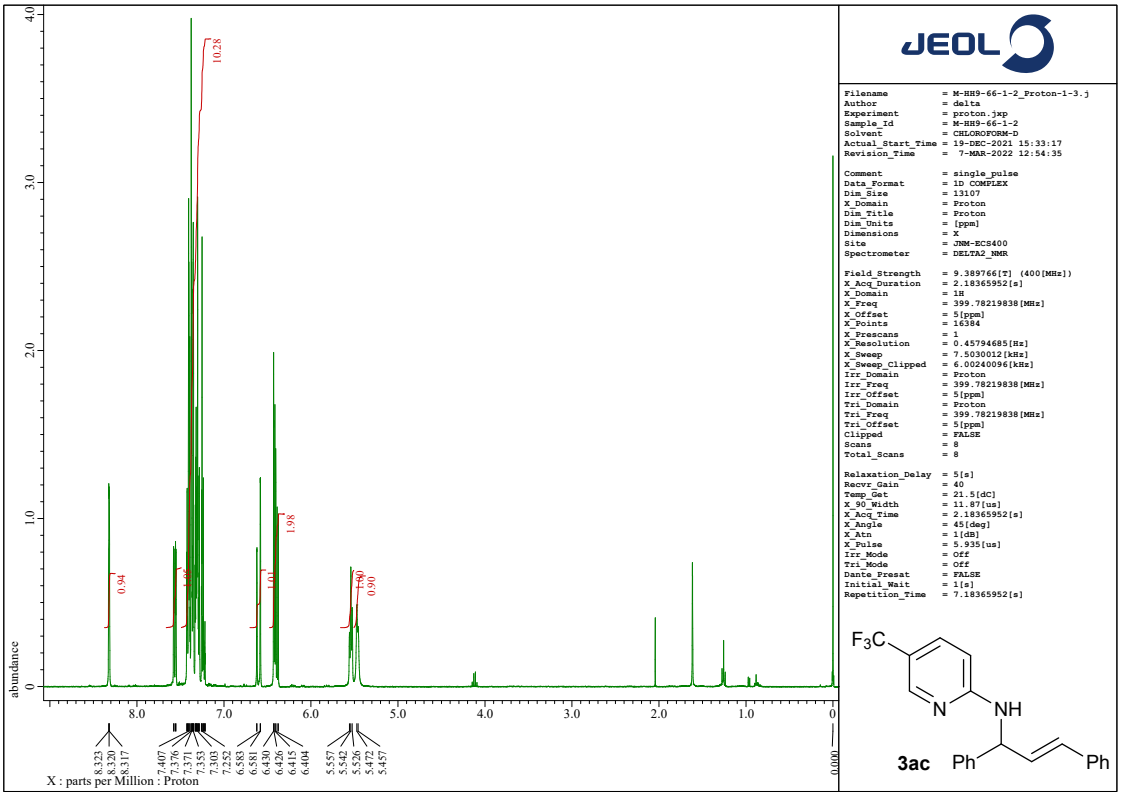


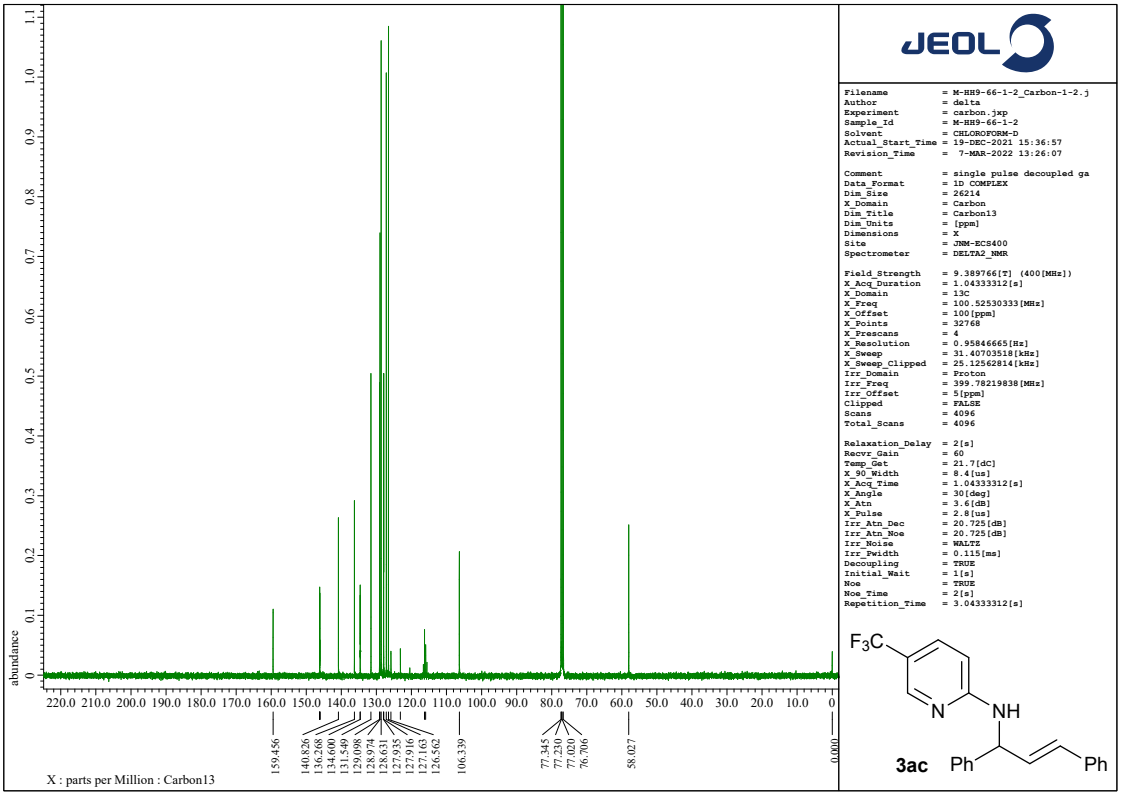
***N*-(3-Methylbut-2-en-1-yl)-5-(trifluoromethyl)pyridin-2-amine 3ab**



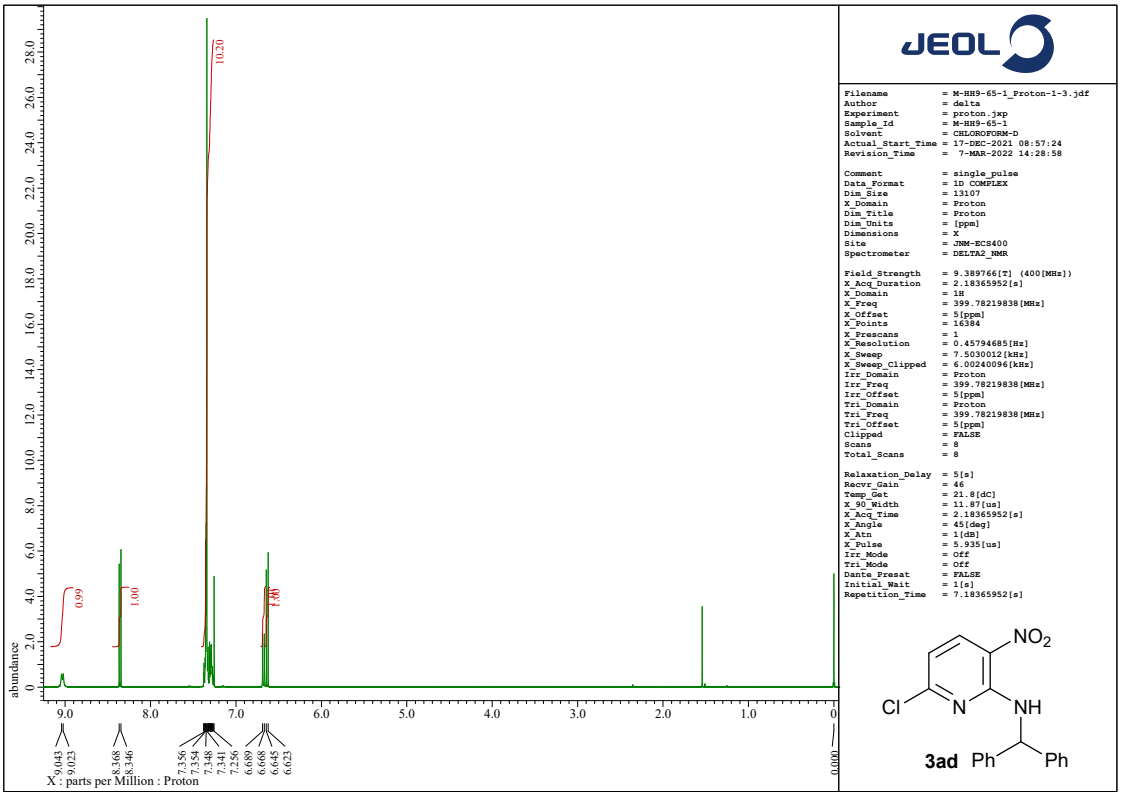


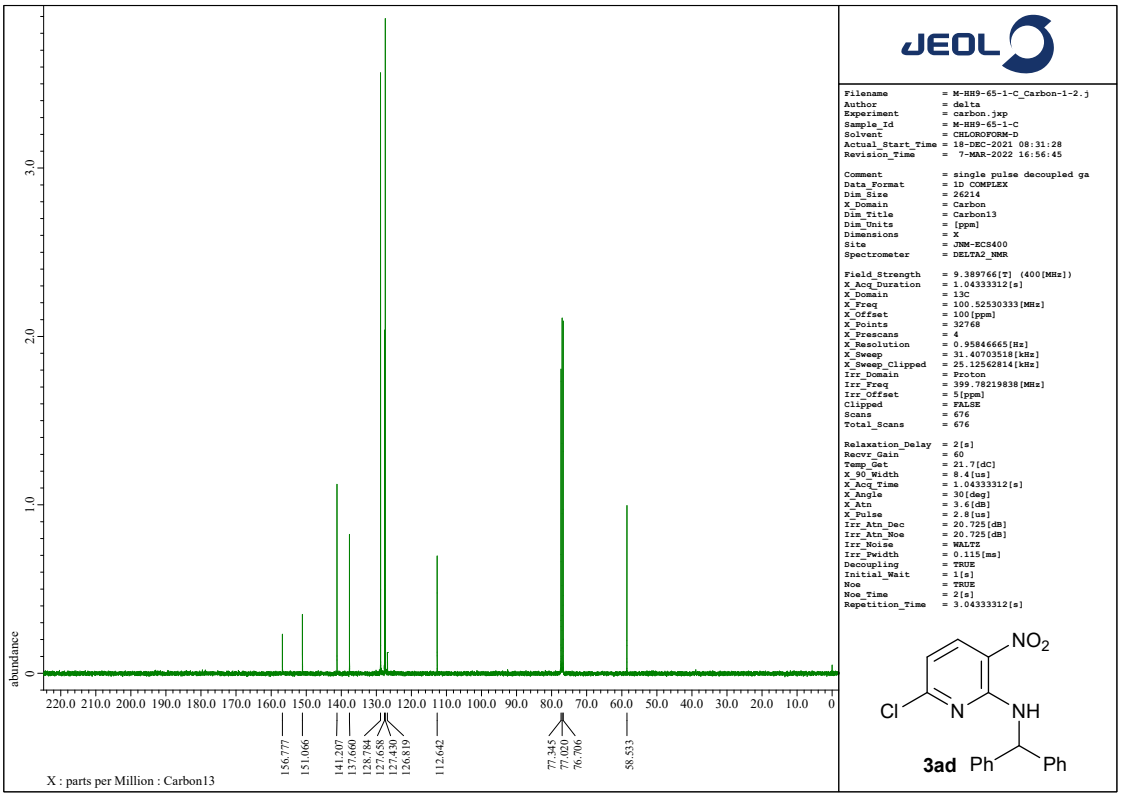
***(E)*-*N*-(1,3-Diphenylallyl)-5-(trifluoromethyl)pyridin-2-amine 3ac**



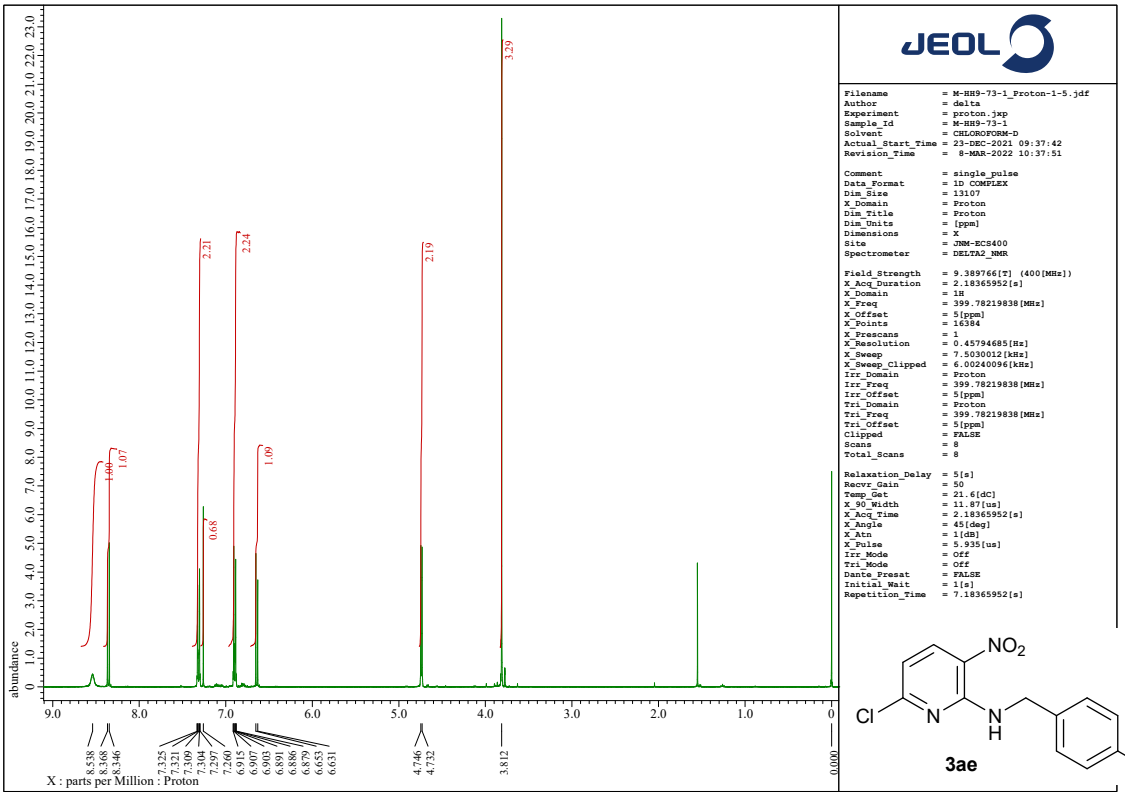


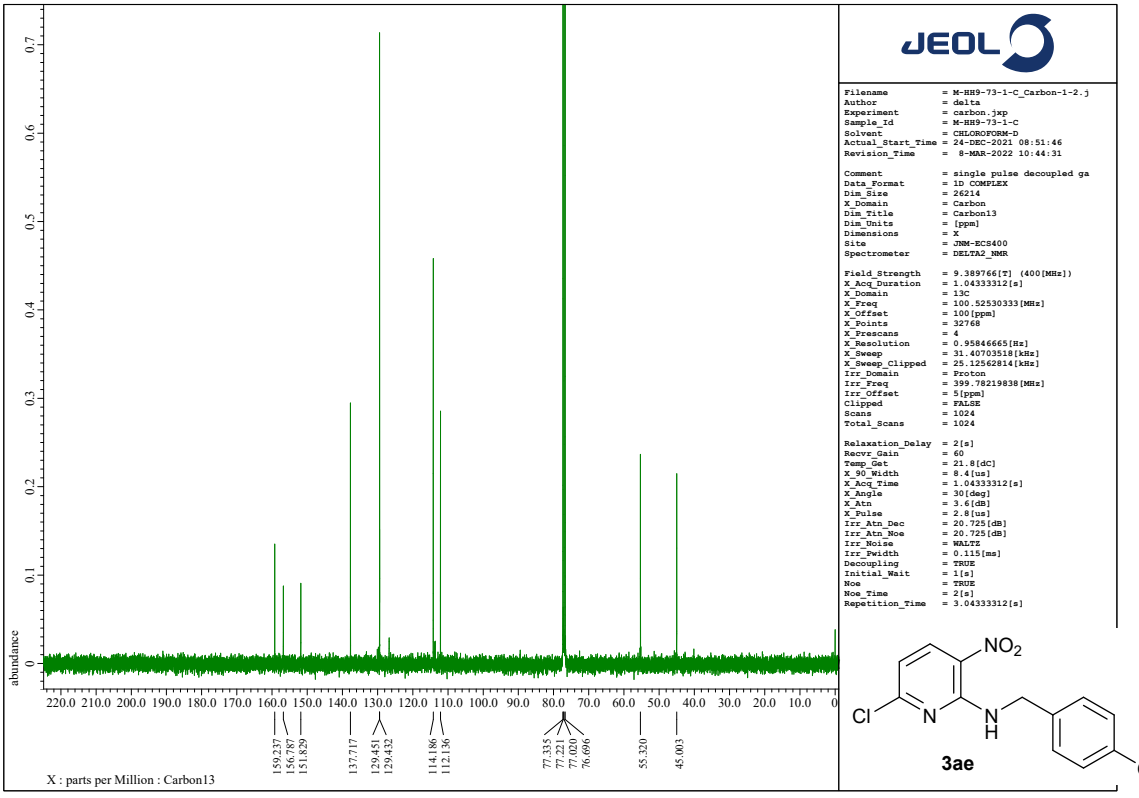
_N_-Benzhydryl-6-chloro-3-nitropyridin-2-amine 3ad



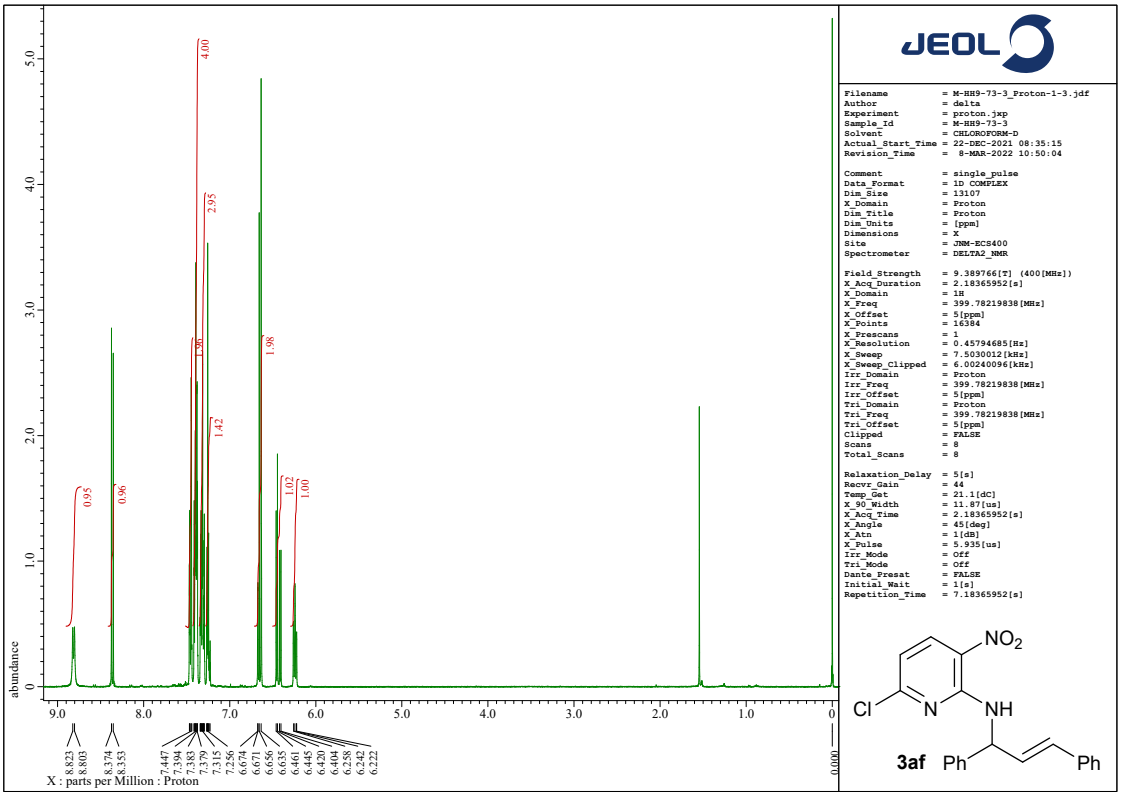


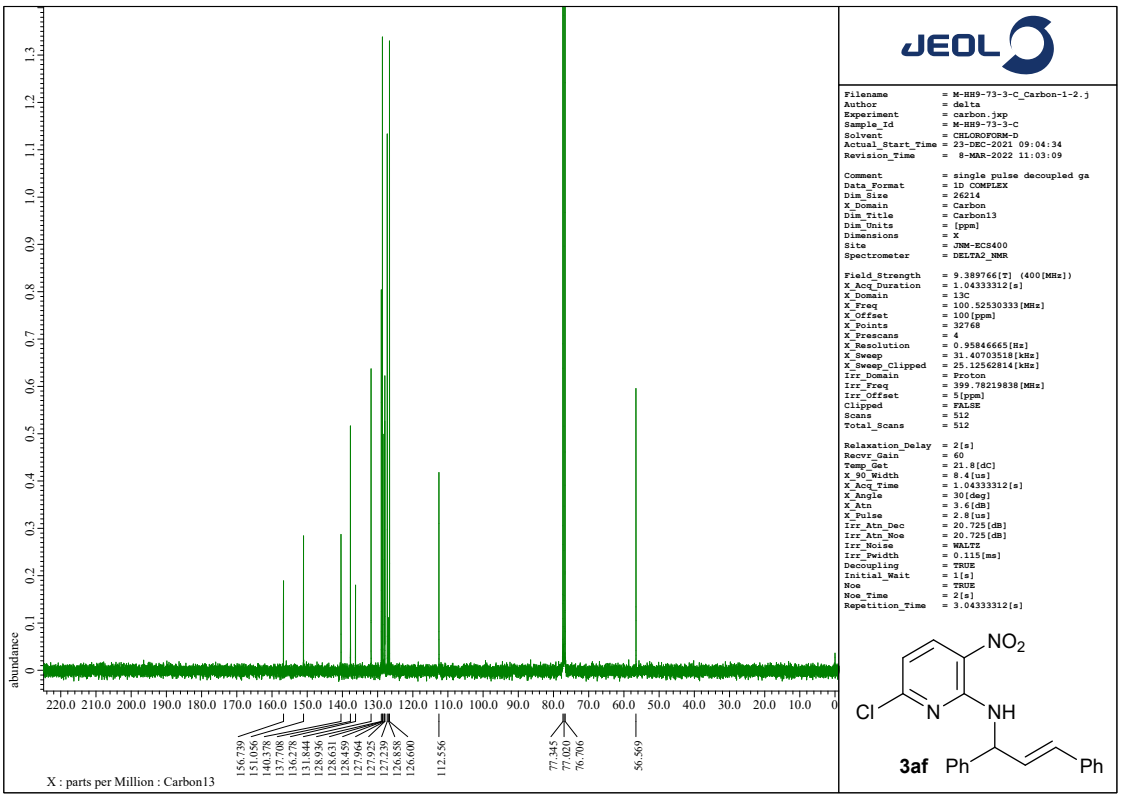
6-Chloro-*N*-(4-methoxybenzyl)-3-nitropyridin-2-amine 3ae



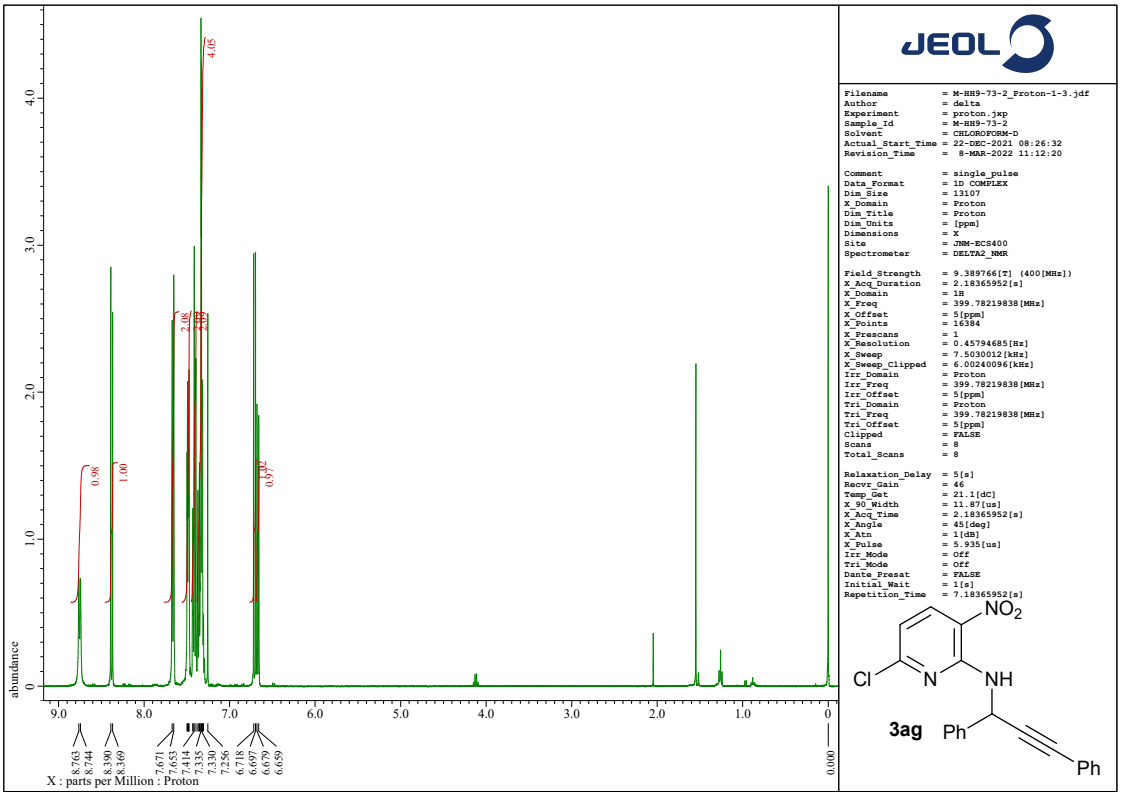


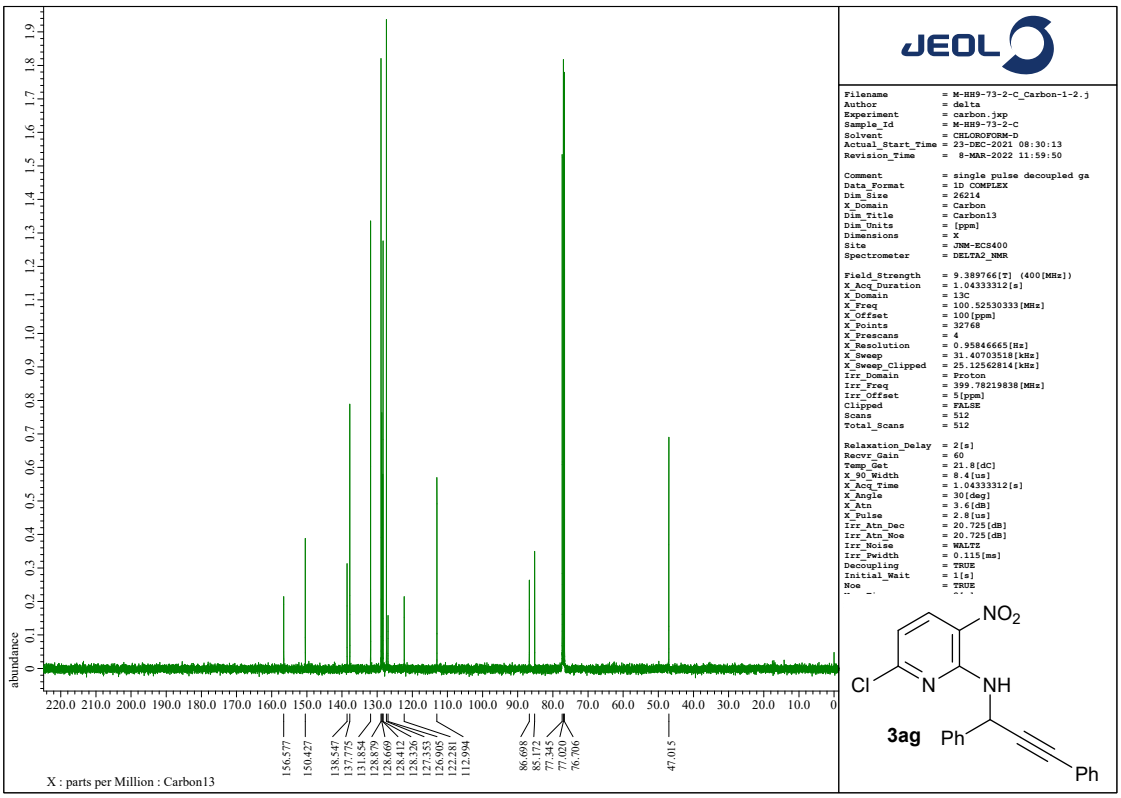
(*E*)-6-Chloro-*N*-(1,3-diphenylallyl)-3-nitropyridin-2-amine 3af



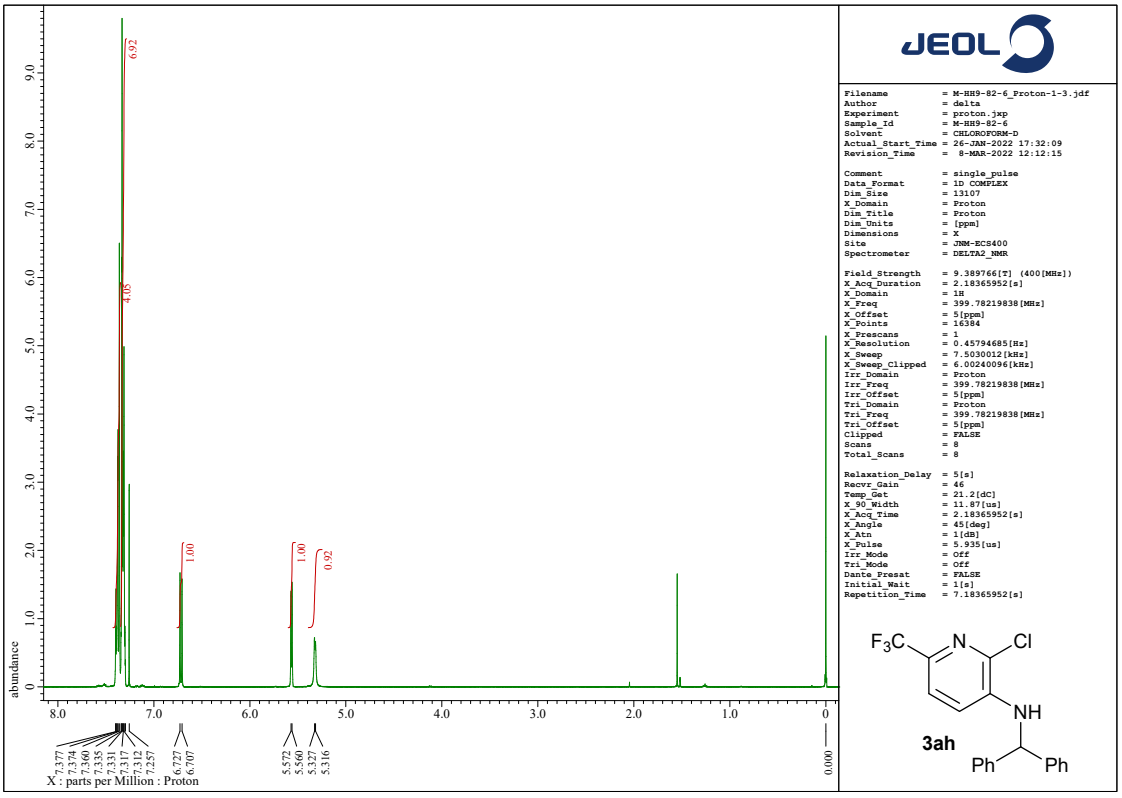


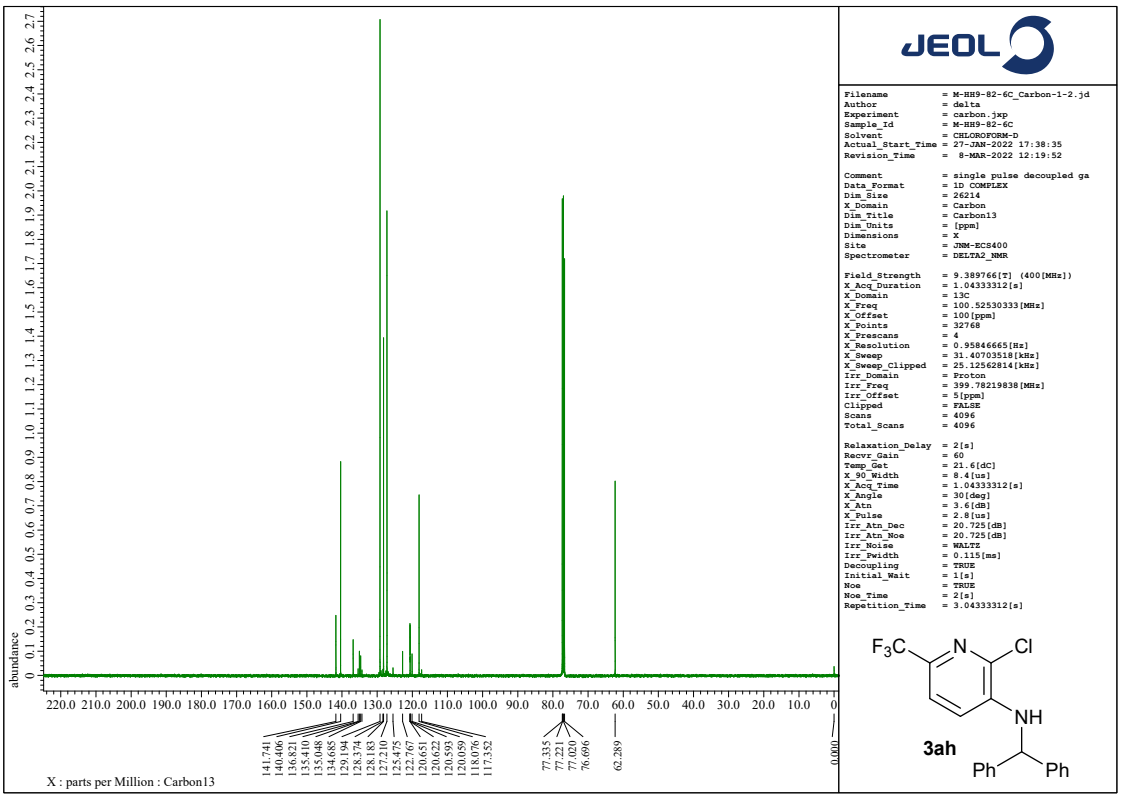
6-Chloro-*N*-(1,3-diphenylprop-2-yn-1-yl)-3-nitropyridin-2-amine 3ag



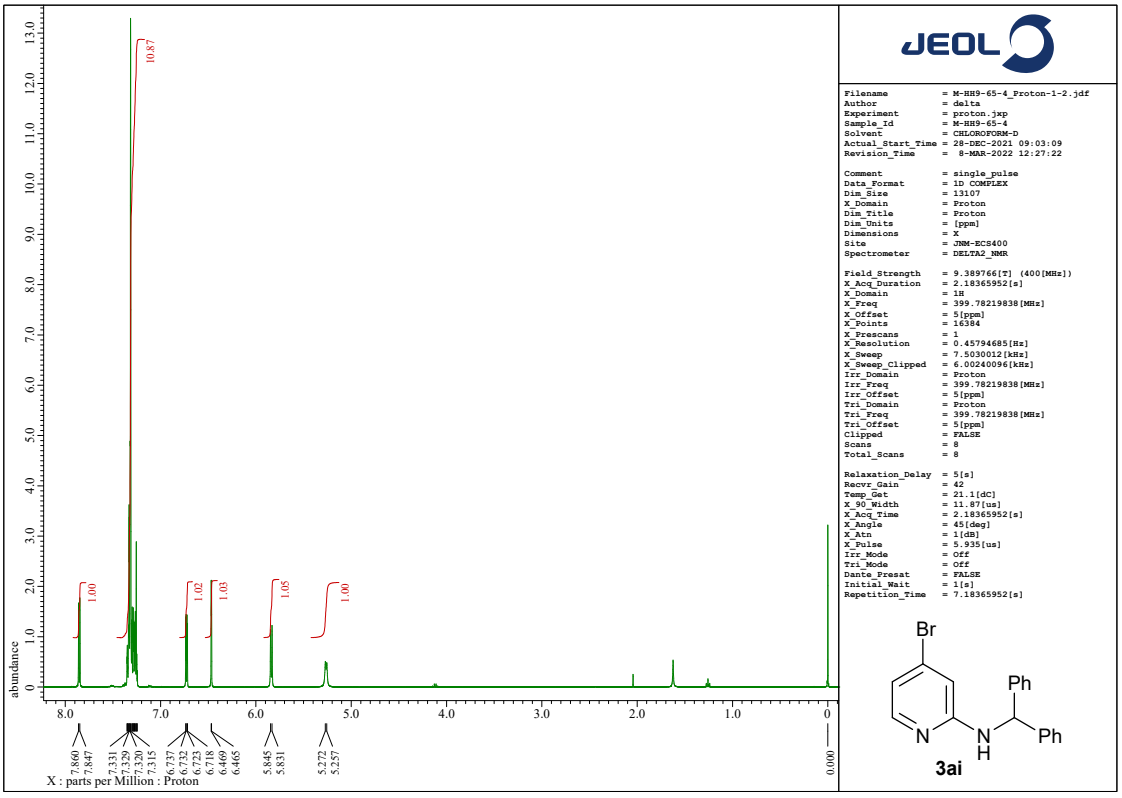


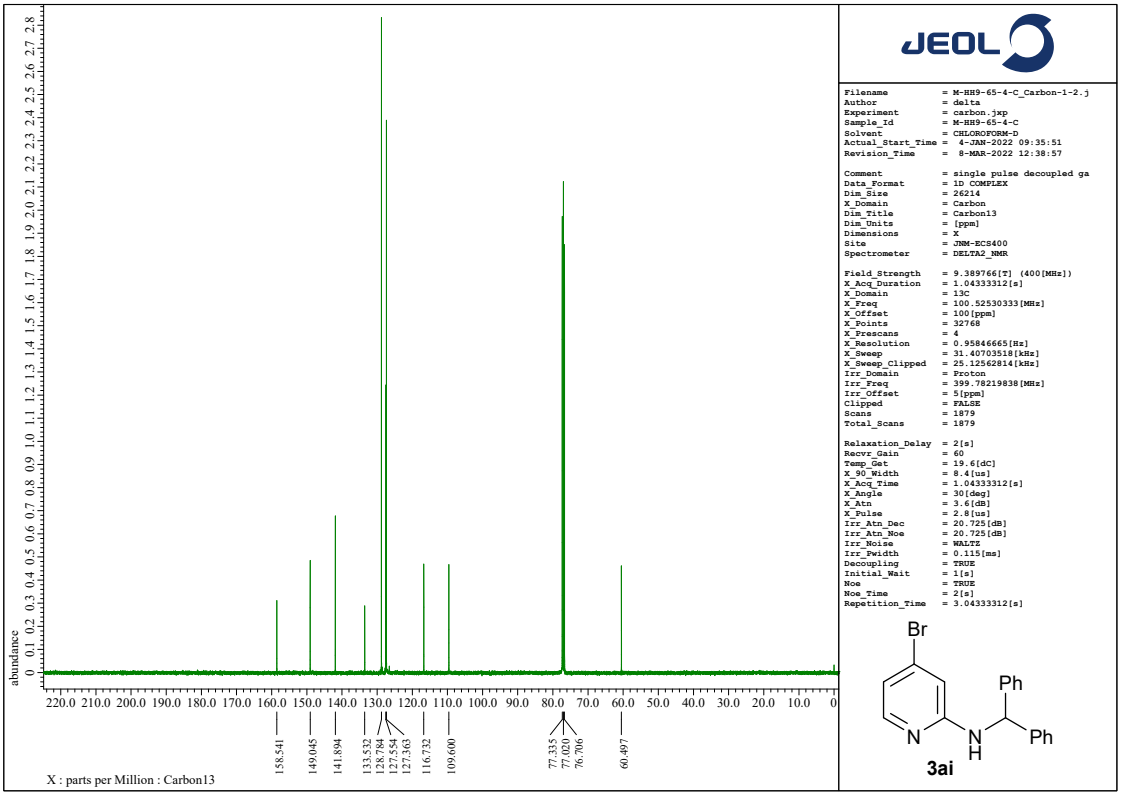
***N*-Benzhydryl-2-chloro-6-(trifluoromethyl)pyridin-3-amine 3ah**



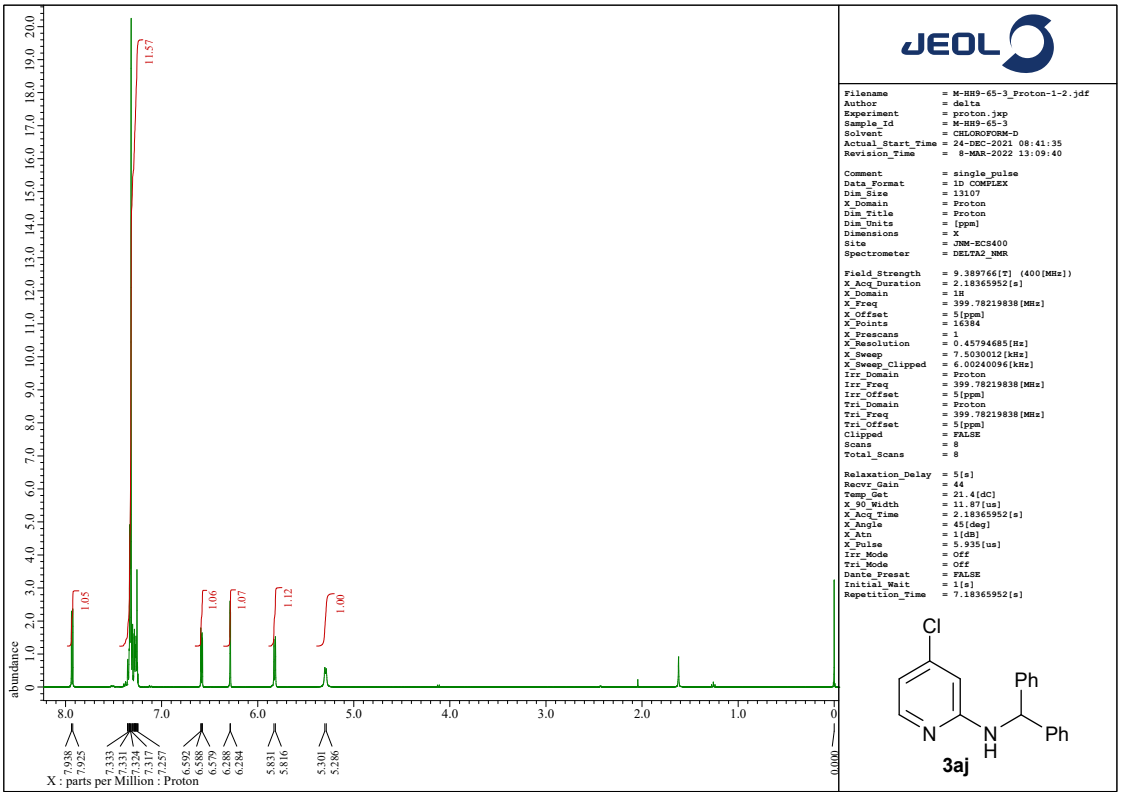


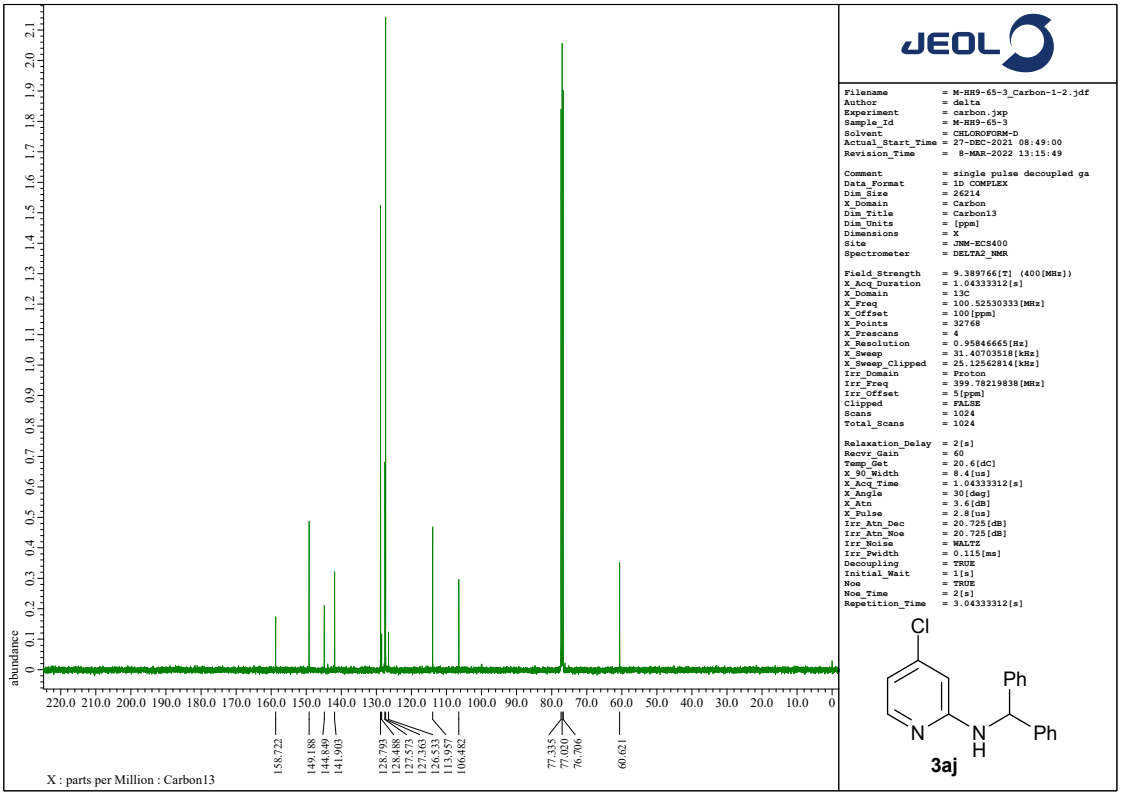
N-Benzhydryl-4-bromopyridin-2-amine 3ai



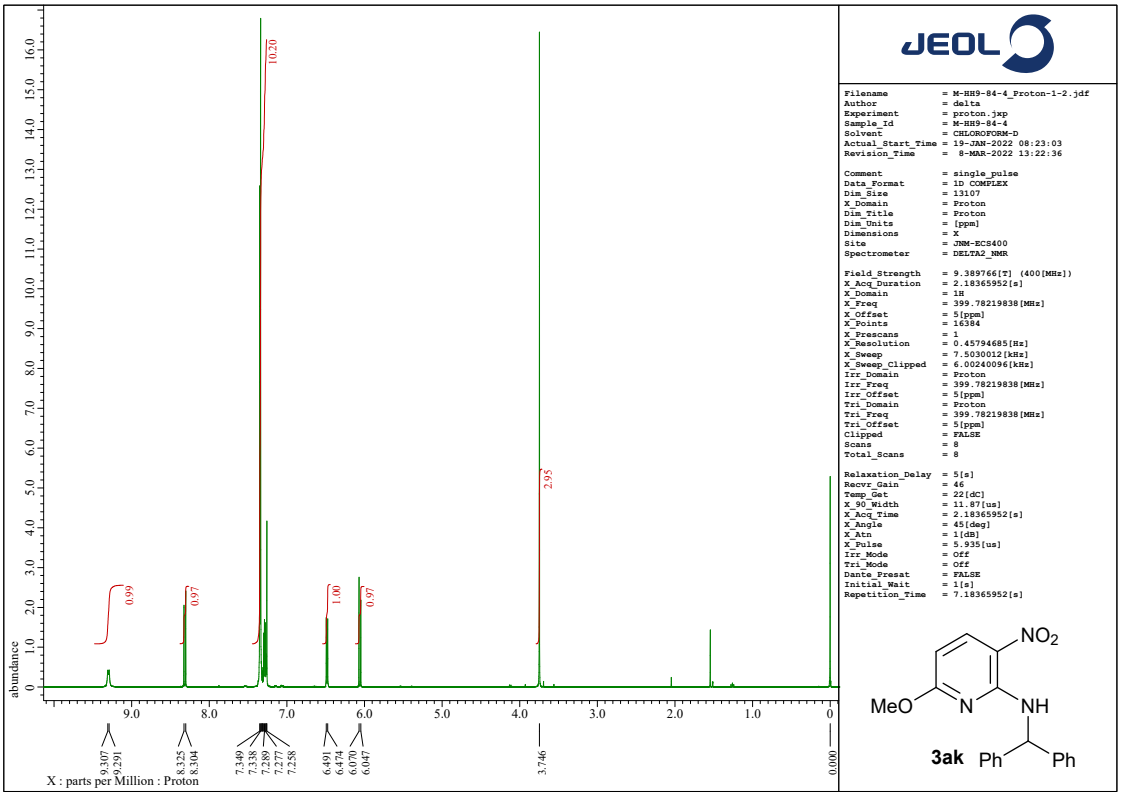


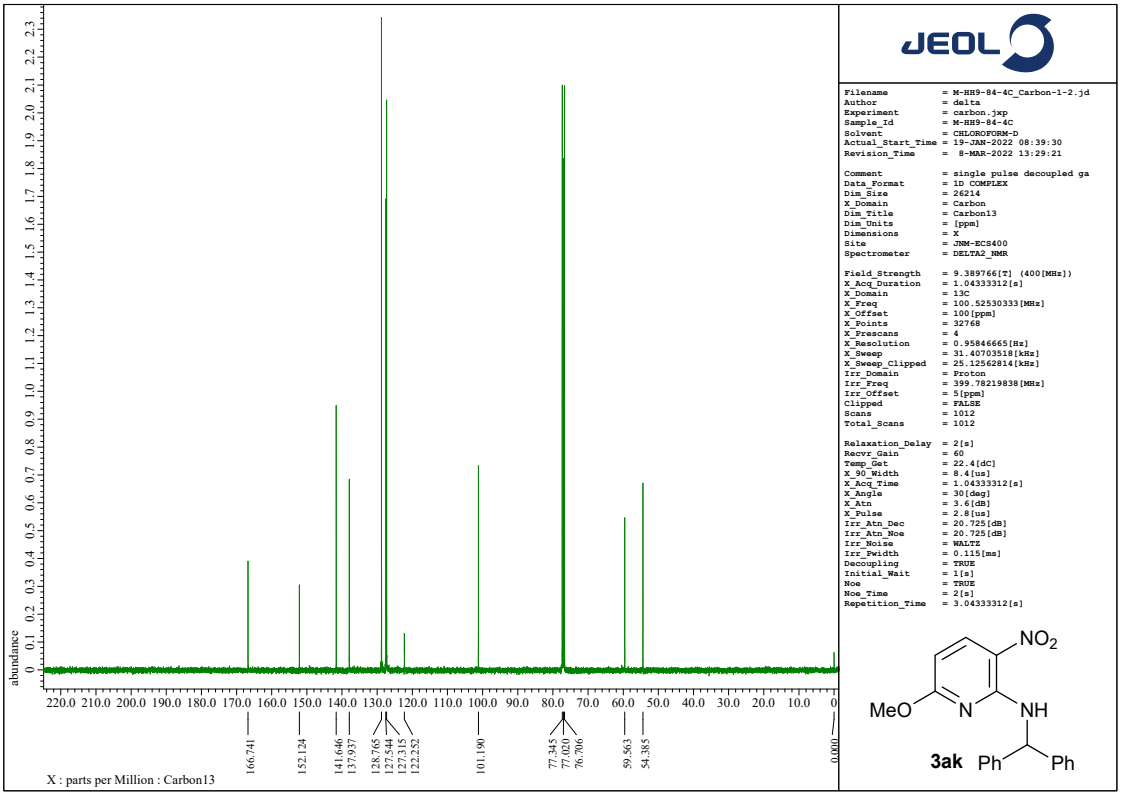
N-Benzhydryl-4-chloropyridin-2-amine 3aj



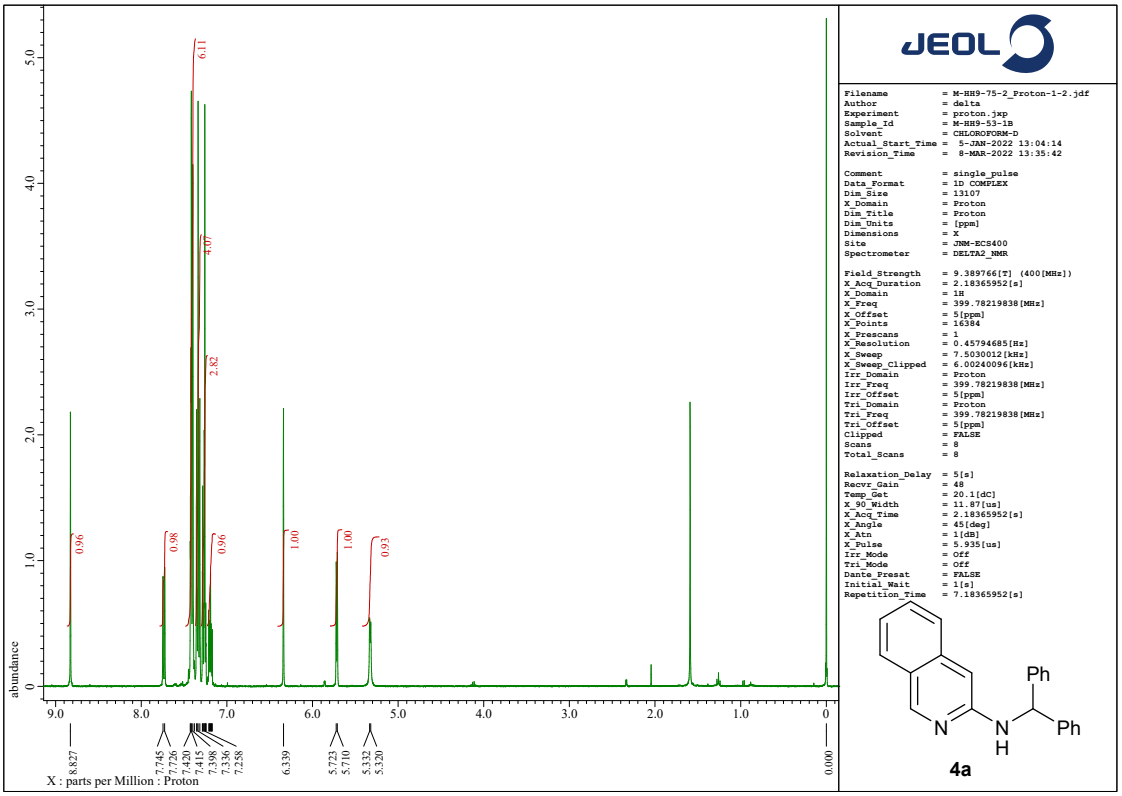


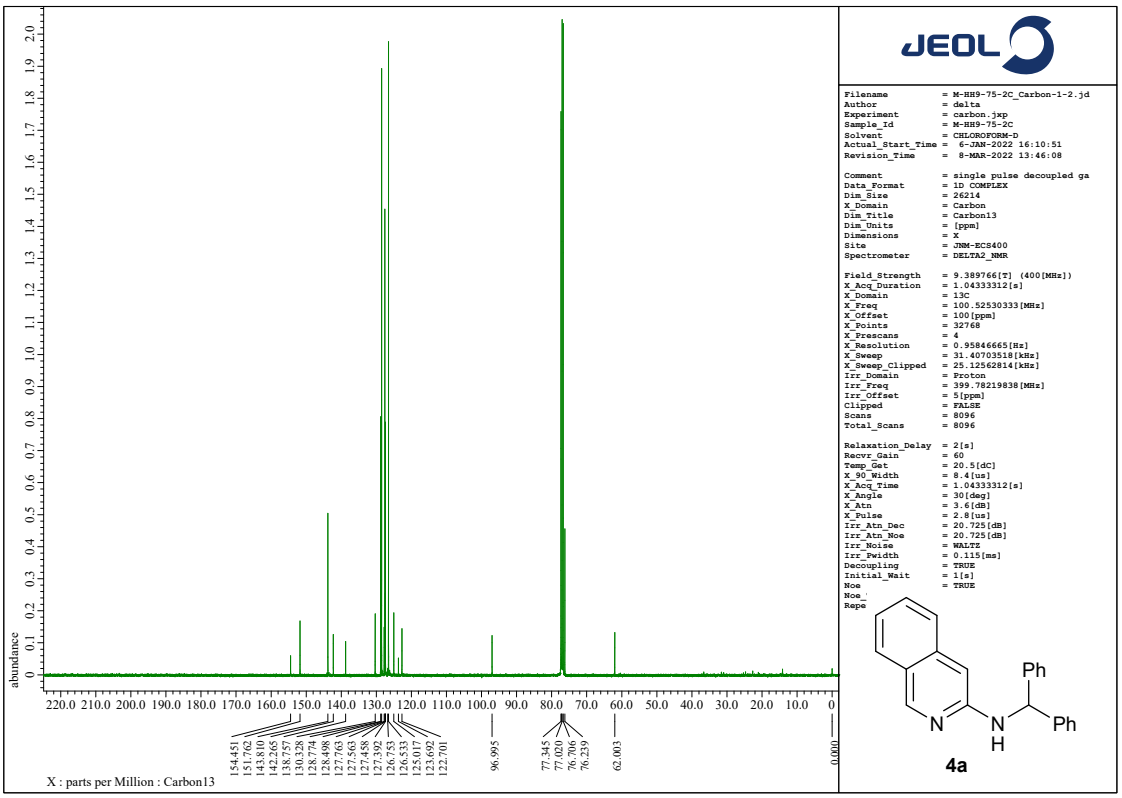
_N_-Benzhydryl-6-methoxy-3-nitropyridin-2-amine 3ak



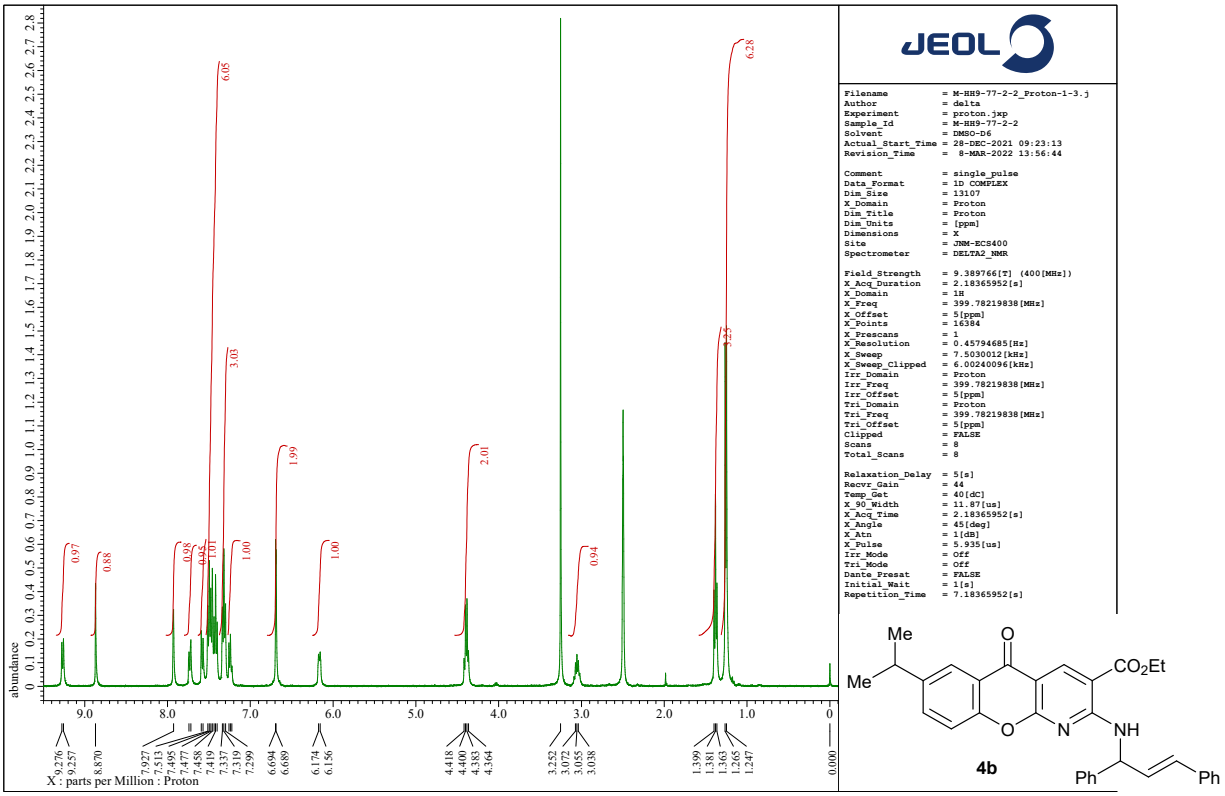


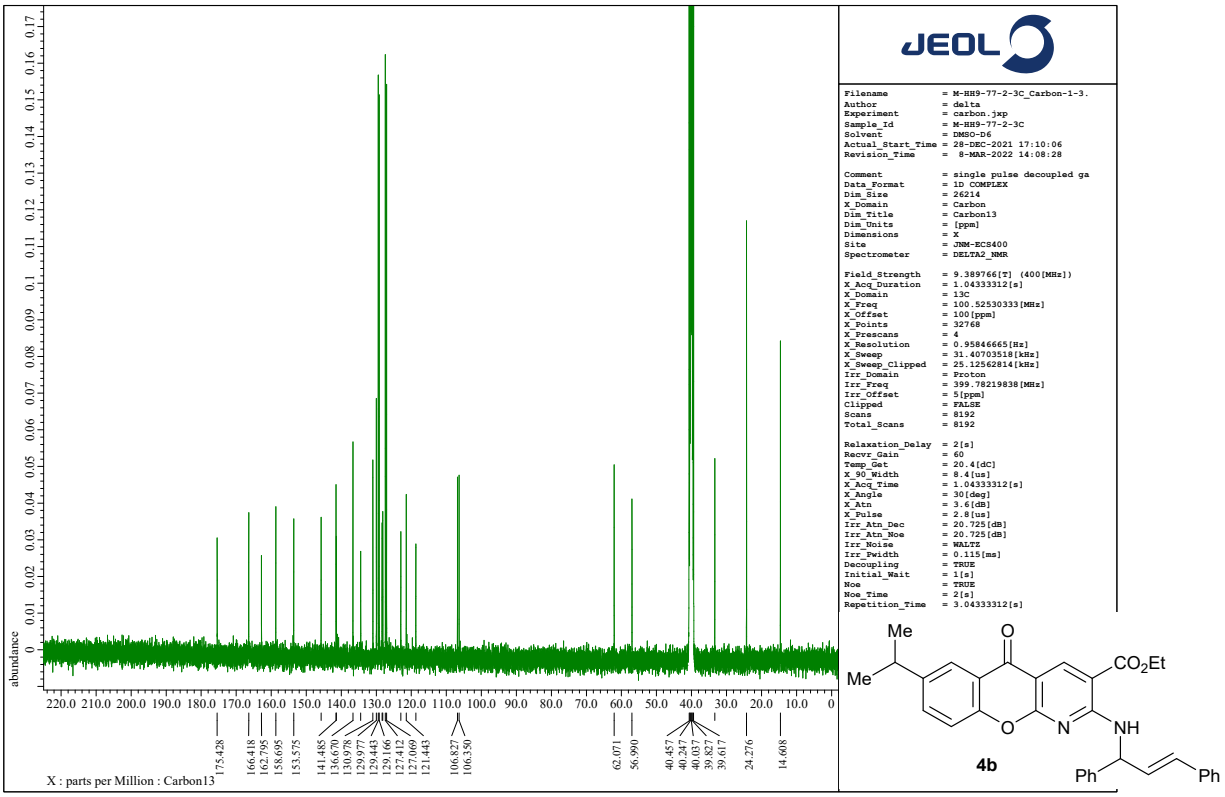
***N*-Benzhydrylisoquinolin-3-amine 4a**





Ethyl (*E*)-2-(1,3-diphenylallylamino)-7-isopropyl-5-oxo-5*H*-chromeno[2,3-b]pyridine-3-carboxylate 4b





Diphenylmethyl ether **5**