Copper-Catalyzed Synthesis of 2-Aminobenzothiazoles from Carbodiimide and Sodium Hydrosulfide

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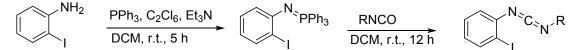
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1) General Information

NMR spectra of the products **2a**, **2k** were obtained using Bruker Avance-500 instruments, calibrated to TMS (¹H NMR spectra) and CD(H)Cl₃ (¹³C NMR spectra) as the internal reference (0.00 ppm for ¹H NMR spectra and 77.00 ppm for ¹³C NMR spectra). NMR spectra of the product **2b-2t** was recorded using Bruker Avance-500 instruments, calibrated to residual DMSO- d_6 as the internal reference (2.50 ppm for ¹H NMR spectra). High-resolution massspectra (HRMS) were recorded on a Bruker Apex IV FTMS mass spectrometer using ESI (electrospray ionization). Reactions were monitored by thin-layer chromatography. Column chromatography (petroleum ether/ethyl acetate) was performed on silica gel (200-300 mesh). Unless otherwise noted, all reactions were run under nitrogen atmosphere.

2) Synthesis of Starting Materials

Preparation of 1a-1t:



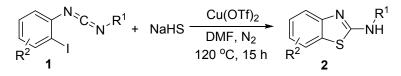
General Procedure for the Synthesis of Aza-Wittig Reagents

To a mixture of 2-iodoaniline (1.00 g, 4.57 mmol), PPh₃ (1.80 g, 6.86 mmol) and C_2Cl_6 (1.62 g, 6.86 mmol) in dry CH₂Cl₂ (40 mL), Et₃N (1.40 g, 13.84 mmol) was added dropwise at 25 °C. After being stirred for 5 h, the reaction mixture was concentrated under reduced pressure. The residue was extracted by EtOAc (100 mL), filtered through Celite (5 cm). All the volatiles were removed under reduced pressure. Isolation by silica gel column chromatography with EtOAc/ petroleum ether (v/v = 1:6) as the eluant afforded white solid (1.30 g, 98 %).

General Procedure for the Synthesis of O-iodoarylcarbodiimides 1a-1t.

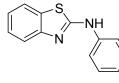
To a stirred solution of an aza-Wittig reagent (10 mmol) in CH_2Cl_2 (50 mL), an isocyanate R₂-NCO (10 mmol) was added dropwise, and then the resulting mixture was stirred at room temperature for 12 h. The solvent was evaporated under reduced pressure. Isolation by silica gel column chromatography with EtOAc/ petroleum ether (v/v = 1:12) as the eluent afforded the corresponding o-iodoarylcarbodiimides 1a-1t.

3) Typical Procedures



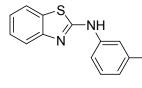
To a schlenk tube were added *o*-iodoarylcarbodiimides (0.3 mmol), NaHS (3equiv), $Cu(OTf)_2$ (20 mol%), and DMF (2 mL). Then under the protection of nitrogen, the mixture was stirred at 120 °C (oil bath temperature) for the indicated time until complete consumption of starting material as monitored by TLC. After the reaction was finished, the reaction mixture was cooled to room temperature, diluted in ethyl acetate, and washed with water. The aqueous phase was re-extracted with ethyl acetate. The combined organic extracts were dried over Na₂SO₄ and concentrated in vacuum, and the resulting residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 5:1) to afford the desired product.

4) Characterization Data



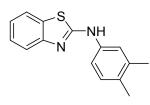
N-phenylbenzo[d]thiazol-2-amine(2a):¹ The product was purified by flash chromatography to give 63 mg (74%) as a yellow solid. ¹H NMR (CDCl₃, 500 MHz) δ = 7.60 (d, *J* = 8.0

Hz, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.49 (d, J = 8.0 Hz, 2H), 7.38 (t, J = 7.8 Hz, 2H), 7.30 (t, J = 7.5 Hz, 1H), 7.17-7.11 (m, 2H). ¹³C NMR (CDCl₃, 125 MHz) $\delta = 165.2$, 151.3, 140.0, 129.8, 129.5, 126.1, 124.4, 122.3, 120.8, 120.5, 119.2.



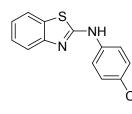
N-(m-tolyl)benzo[d]thiazol-2-amine(2b):¹ The product was purified by flash chromatography to give 66 mg (93%) as a yellow solid. ¹H NMR (DMSO-*D6*, 500 MHz) $\delta = 10.42$ (s,

1H), 7.79 (d, J = 7.5 Hz, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.62 (d, J = 8.0 Hz, 2H), 7.32 (td, J = 7.5 Hz, 1.0 Hz, 1H), 7.24 (t, J = 7.8 Hz, 1H), 7.14 (td, J = 8.0 Hz, 1.0 Hz, 1H), 6.84 (d, J = 7.5 Hz, 1H), 2.32 (s, 3H). ¹³C NMR (DMSO-*D6*, 125 MHz) $\delta = 162.2$, 152.6, 141.1, 138.7, 130.5, 129.3, 126.3, 123.4, 122.7, 121.5, 119.7, 118.8, 115.6, 21.8.



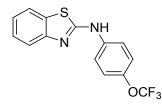
N-(3,4-dimethylphenyl)benzo[d]thiazol-2-amine(2c):⁸ The product was purified by flash chromatography to give 75 mg (95%) as a yellow solid. ¹H NMR (DMSO-*D6*, 500 MHz) δ = 10.30 (s, 1H), 7.76 (dd, *J* = 7.5 Hz, 1.0 Hz, 1H), 7.59-7.56 (m,

2H), 7.49 (d, J = 2.0 Hz, 1H), 7.30 (td, J = 8.0 Hz, 1.0 Hz, 1H), 7.14-7.10 (m, 2H), 2.22 (s, 3H), 2.17 (s, 3H). ¹³C NMR (DMSO-*D6*, 125 MHz) $\delta = 162.4$, 152.7, 139.0, 137.1, 130.5, 130.4, 130.3, 126.3, 122.5, 121.4, 119.8, 119.5, 116.1, 20.2, 19.2.



N-(4-chlorophenyl)benzo[d]thiazol-2-amine(2d):¹ The product was purified by flash chromatography to give 76 mg (82%) as a yellow solid. ¹H NMR (DMSO-*D6*, 500 MHz) δ = 10.62 (s, 1H), 7.84-7.81 (m, 3H), 7.62 (d, *J* = 7.5 Hz, 1H), 7.41

(d, *J* = 9.0 Hz, 2H), 7.34 (td, *J* = 8.0 Hz, 1.0 Hz, 1H), 7.16 (td, *J* = 8.0 Hz, 1.0 Hz, 1H). ¹³C NMR (DMSO-*D6*, 125 MHz) δ = 161.8, 152.4, 140.0, 130.5, 129.3, 126.5, 126.0, 123.0, 121.6, 119.9, 119.7.



N-(4-(trifluoromethoxy)phenyl)benzo[d]thiazol-2-

amine(2e): The product was purified by flash chromatography to give 72 mg (82%) as a yellow solid. mp: 168.7-170.0 °C. ¹H NMR (DMSO-D6, 500 MHz) $\delta = 10.68$

(s, 1H), 7.94-7.91 (m, 2H), 7.80 (dd, J = 8.0 Hz, 1.0 Hz, 1H), 7.63 (d, J = 7.5 Hz, 1H), 7.36-7.31 (m, 3H), 7.16 (td, J = 8.0 Hz, 1.0 Hz, 1H). ¹³C NMR (DMSO-D6, 125 MHz) $\delta = 161.9$, 152.4, 143.2, 140.3, 130.6, 126.4, 123.0, 122.3, 121.5, 120.7 (q, J = 254 Hz), 119.9, 119.4. HRMS (ESI, m/z) calcd for [C₁₄H₁₀F₃N₂OS]H⁺: 311.0460; found 311.0462.

N-benzylbenzo[d]thiazol-2-amine(2f):⁵ The product was purified by flash chromatography to give 61 mg (95%) as a

yellow solid. ¹H NMR (DMSO-D6, 500 MHz) δ = 8.53 (s, 1H), 7.67 (d, J = 7.5 Hz,

1H), 7.41 (t, J = 8.5 Hz, 3H), 7.34 (t, J = 7.5 Hz, 2H), 7.27-7.21 (m, 2H), 7.02 (td, J = 7.5 Hz, 0.5 Hz, 1H), 4.62 (d, J = 5.0 Hz, 2H). ¹³C NMR (DMSO-D6, 125 MHz) $\delta = 166.8, 153.0, 139.4, 131.0, 128.8, 127.9, 127.5, 126.0, 121.5, 121.4, 118.6, 47.7.$

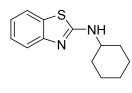
N-(3-methylbenzyl)benzo[d]thiazol-2-amine(2g):⁷ The product was purified by flash chromatography to give 73 mg (91%) as a yellow solid. ¹H NMR (DMSO-D6, 500 MHz) $\delta = 8.53$ (s, 1H), 7.66 (d, J = 7.5 Hz, 1H), 7.41 (d, J = 8.0 Hz, 1H), 7.23-7.16 (m, 4H), 7.07-7.00 (m, 2H), 4.57 (d, J = 5.0 Hz, 2H), 2.27 (s, 3H). ¹³C NMR (DMSO-D6, 125 MHz) $\delta = 166.9$, 153.1, 139.4, 138.1, 131.0, 129.0, 128.6, 128.3, 126.2, 125.1, 121.6, 121.6, 118.7, 47.9, 21.7.

N-(4-fluorobenzyl)benzo[d]thiazol-2-amine(2h):⁷ The product was purified by flash chromatography to give 63 mg (84%) as a yellow solid. ¹H NMR (DMSO-D6, 500 MHz) $\delta = 8.52$ (s, 1H), 7.66 (dd, J = 8.0 Hz, 1.0 Hz, 1H), 7.44-7.40 (m, 3H), 7.22 (td, J = 7.5 Hz, 1.5 Hz, 1H), 7.16 (td, J = 6.5 Hz, 2.0 Hz, 2H), 7.02 (td, J = 7.5 Hz, 1.0 Hz, 1H), 4.59 (d, J = 5.0 Hz, 2H). ¹³C NMR (DMSO-D6, 125 MHz) $\delta = 166.7$, 161.8 (d, J = 241.3 Hz), 152.9, 135.6 (d, J = 3.0 Hz), 130.9, 129.9 (d, J = 8.1 Hz), 126.0, 121.5, 121.4, 118.6, 115.5 (d, J = 21.3 Hz), 47.0.

N-ethylbenzo[d]thiazol-2-amine(2i):³ The product was purified by flash chromatography to give 44 mg (90%) as a yellow solid. ¹H NMR (DMSO-D6, 500 MHz) δ = 7.98 (s, 1H), 7.64 (dd, *J* = 7.5 Hz, 1.0 Hz, 1H), 7.38 (d, *J* = 7.5 Hz, 1H), 7.20 (td, *J* = 8.0 Hz, 1.5 Hz, 1H), 7.00 (td, *J* = 8.0 Hz, 1.0 Hz, 1H), 3.40-3.36 (m, 2H), 1.19 (t, *J* = 7.0 Hz, 3H). ¹³C NMR (DMSO-D6, 125 MHz) δ = 166.5, 153.2, 130.7, 126.0, 121.3, 121.2, 118.4, 39.2, 14.9.

yellow solid. ¹H NMR (DMSO-D6, 500 MHz) δ = 7.90 (s, 1H), 7.63 (d, *J* = 7.5 Hz, 1H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.00 (t, *J* = 7.5 Hz, 1H), 4.02-3.96 (m, 1H), 1.21 (d, *J* = 6.5 Hz, 6H). ¹³C NMR (DMSO-D6, 125 MHz) δ = 165.8, 153.3, 130.7, 125.9, 121.2, 121.2, 118.4, 46.3, 22.8.

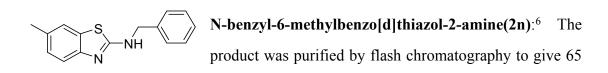
2-(tert-butyl)benzo[d]thiazole(2k):⁵ The product was purified by flash chromatography to give 57 mg (93%) as a yellow solid. ¹H NMR (CDCl3, 500 MHz) δ = 7.55 (t, *J* = 7.8 Hz, 2H), 7.28-7.23 (m, 1H), 7.05 (t, *J* = 7.5 Hz, 1H), 5.41 (s, 1H), 1.47 (s, 9H). ¹³C NMR (CDCl3, 125 MHz) δ = 164.6, 152.3, 130.7, 125.6, 121.4, 120.3, 119.0, 53.2, 29.0.



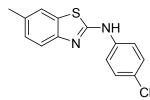
N-cyclohexylbenzo[d]thiazol-2-amine(2l):⁵ The product was purified by flash chromatography to give 63 mg (92%) as a yellow solid. ¹H NMR (DMSO-D6, 500 MHz) $\delta = 7.92$ (s, 1H),

7.18 (dd, J = 7.5 Hz, 1.0 Hz, 1H), 7.72 (dd, J = 8.0 Hz, 0.5 Hz, 1H), 7.19 (td, J = 8.0 Hz, 1.0 Hz, 1H), 6.98 (td, J = 7.5 Hz, 1.0 Hz, 1H), 3.70 (t, J = 3.3 Hz, 1H), 1.99 (d, J = 7 Hz, 2H), 1.73-1.70 (m, 2H), 1.58-1.55 (m, 1H), 1.34-1.25 (m, 4H), 1.20-1.15 (m, 1H). ¹³C NMR (DMSO-D6, 125 MHz) $\delta = 165.6$, 153.2, 130.6, 125.8, 121.1, 121.1, 118.3, 53.3, 32.8, 25.7, 24.9.

N-phenethylbenzo[d]thiazol-2-amine(2m):⁴ The product was purified by flash chromatography to give 68 mg (77%) as a yellow solid. ¹H NMR (DMSO-D6, 500 MHz) $\delta = 8.12$ (s, 1H), 7.65 (dd, J = 8.0 Hz, 1.0 Hz, 1H), 7.43 (dd, J = 8.0 Hz, 0.5 Hz, 1H), 7.31-7.26 (m, 4H), 7.24-7.20 (m, 2H), 7.01 (td, J = 8.0 Hz, 1.0 Hz, 1H), 3.64-3.60 (m, 2H), 2.93 (t, J = 7.3 Hz, 2H). ¹³C NMR (DMSO-D6, 125 MHz) $\delta = 166.5$, 153.2, 139.8, 130.8, 129.2, 128.8, 126.6, 126.0, 121.4, 118.5(2C), 45.9, 35.2.



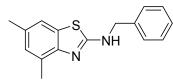
mg (85%) as a yellow solid. ¹H NMR (DMSO-D6, 500 MHz) δ = 8.38 (s, 1H), 7.45 (s, 1H), 7.38 (d, *J* = 7.0 Hz, 2H), 7.34 (t, *J* = 7.5 Hz, 2H), 7.28-7.24 (m, 2H), 7.02 (d, *J* = 8.0 Hz, 1H), 4.58 (d, *J* = 5.5 Hz, 2H), 2.30 (s, 3H). ¹³C NMR (DMSO-D6, 125 MHz) δ = 166.1, 150.8, 139.5, 131.0, 130.7, 128.9, 127.9, 127.5, 127.1, 121.4, 118.3, 47.7, 21.3.



N-(4-chlorophenyl)-6-methylbenzo[d]thiazol-2-

amine(20):¹ The product was purified by flash chromatography to give 79 mg (96%) as a yellow solid. ¹H NMR (DMSO-D6, 500 MHz) $\delta = 10.52$ (s, 1H), 7.81 (d, J =

8.5 Hz, 2H), 7.60 (s, 1H), 7.50 (d, J = 8.5 Hz, 1H), 7.41-7.39 (m, 2H), 7.14 (dd, J = 8.0 Hz, 1.0 Hz, 1H), 2.34(s, 3H). ¹³C NMR (DMSO-D6, 125 MHz) $\delta = 160.8$, 150.0, 139.9, 132.1, 130.3, 129.0, 127.3, 125.6, 121.2, 119.4, 119.3, 21.1.



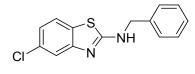
N-benzyl-4,6-dimethylbenzo[d]thiazol-2-amine(2p):7

The product was purified by flash chromatography to give 70 mg (87%) as a yellow solid. ¹H NMR (DMSO-

D6, 500 MHz) $\delta = 8.37$ (s, 1H), 7.40 (d, J = 7.5 Hz, 2H), 7.33 (t, J = 7.8 Hz, 2H), 7.25 (t, J = 5.0 Hz, 2H), 6.85 (s, 1H), 4.57 (d, J = 5.0 Hz, 2H), 2.41 (s, 3H), 2.26 (s, 3H). ¹³C NMR (DMSO-D6, 125 MHz) $\delta = 165.5$, 149.8, 139.6, 130.5, 130.4, 128.8, 128.2, 128.0, 127.6, 127.4, 118.8, 48.0, 21.3, 18.6.

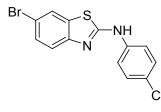
 $F_{3}C_{N} + K_{N} +$

Cl N-benzyl-6-chlorobenzo[d]thiazol-2-amine(2r):⁷ The product was purified by flash chromatography to give 75 mg (90%) as a yellow solid. ¹H NMR (DMSO-D6, 500 MHz) $\delta = 8.60$ (s, 1H), 7.78 (d, J = 2.0 Hz, 1H), 7.38-7.32 (m, 5H), 7.27-7.21 (m, 2H), 4.59 (d, J = 5.5 Hz, 2H). ¹³C NMR (DMSO-D6, 125 MHz) $\delta = 167.4$, 151.9, 139.2, 132.6, 128.9, 127.9, 127.6, 126.2, 125.2, 121.1, 119.4, 47.8.



N-benzyl-5-chlorobenzo[d]thiazol-2-amine(2s):⁶ The product was purified by flash chromatography to give 75 mg (92%) as a yellow solid. ¹H NMR (DMSO-D6,

500 MHz) δ = 8.72 (s, 1H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.42 (s, 1H), 7.39-7.32 (m, 4H), 7.26 (td, *J* = 8.0 Hz, 1.5 Hz, 1H), 7.04 (dd, *J* = 8.5 Hz, 2.0 Hz, 1H), 4.61 (d, *J* = 5.5 Hz, 2H). ¹³C NMR (DMSO-D6, 125 MHz) δ = 168.4, 154.2, 139.1, 130.8, 129.7, 128.9, 127.9, 127.6, 122.7, 121.2, 118.0, 47.8.



6-bromo-N-(4-chlorophenyl)benzo[d]thiazol-2-

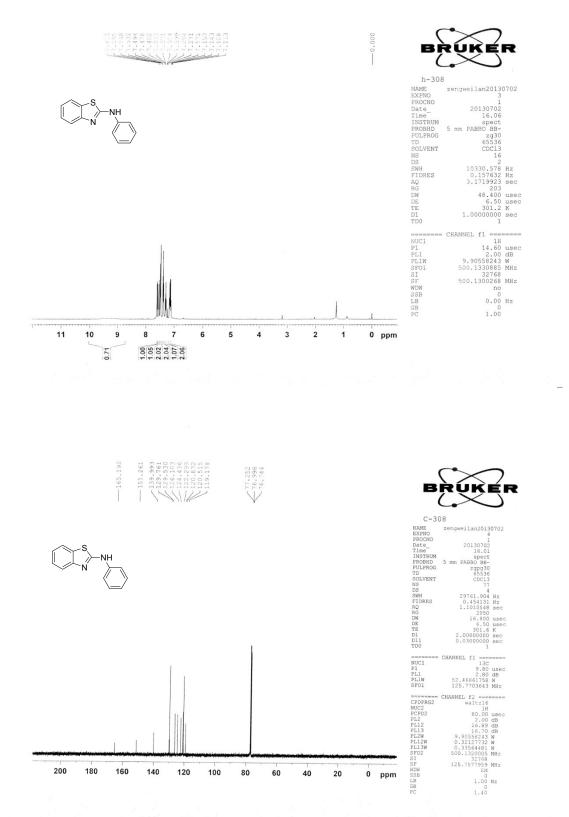
amine(2t):² The product was purified by flash chromatography to give 68 mg (66%) as a yellow solid. ¹H NMR (DMSO-D6, 500 MHz) $\delta = 10.70$ (s, 1H), 8.06 (d, J

= 2.0 Hz, 1H), 7.80 (d, J = 8.5 Hz, 2H), 7.53 (d, J = 8.5 Hz, 1H), 7.45 (dd, J = 8.5 Hz, 2.0 Hz, 1H), 7.41 (d, J = 8.5 Hz, 2H). ¹³C NMR (DMSO-D6, 125 MHz) δ = 162.5, 151.6, 139.7, 132.7, 129.3(2C), 126.3, 124.1, 121.3, 119.9, 114.5.

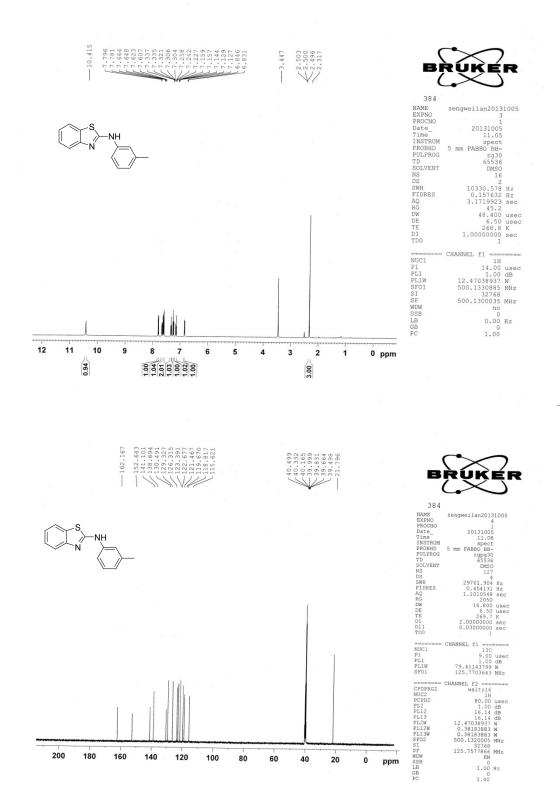
5) References

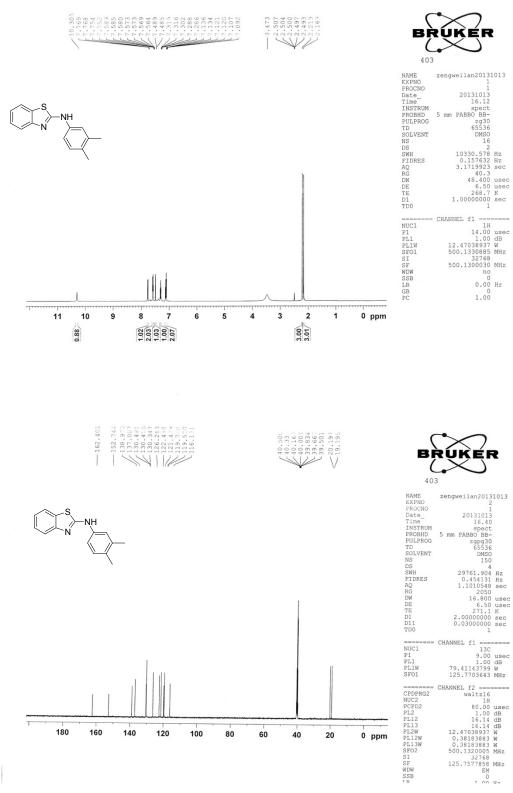
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6) Scanned ¹H NMR and ¹³C NMR Spectra of All New Compounds

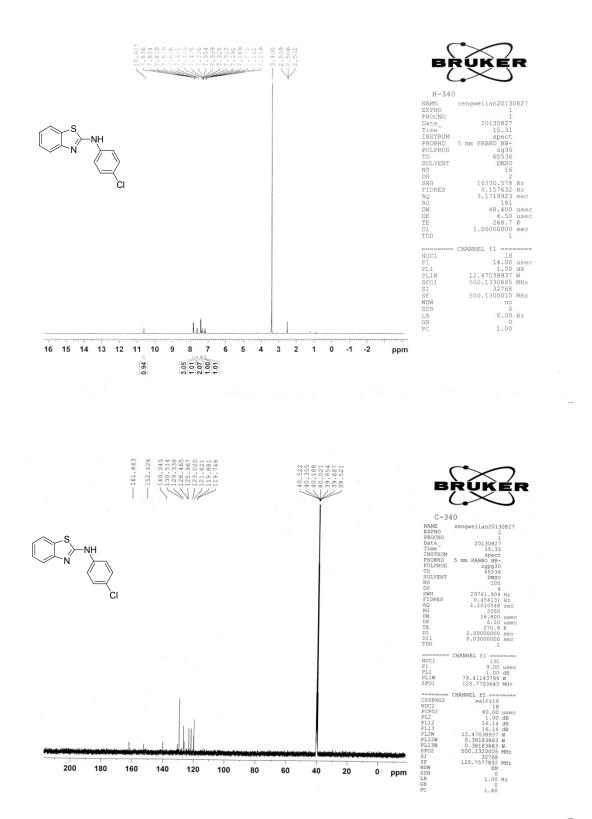


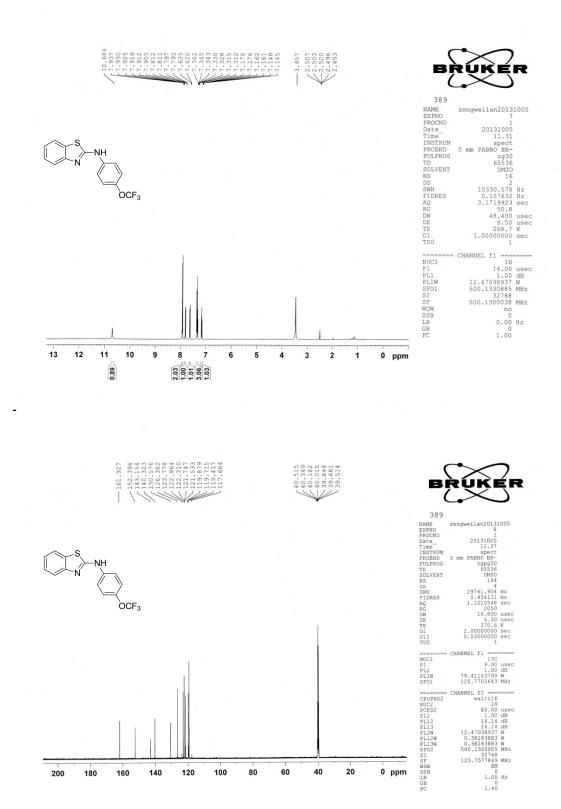
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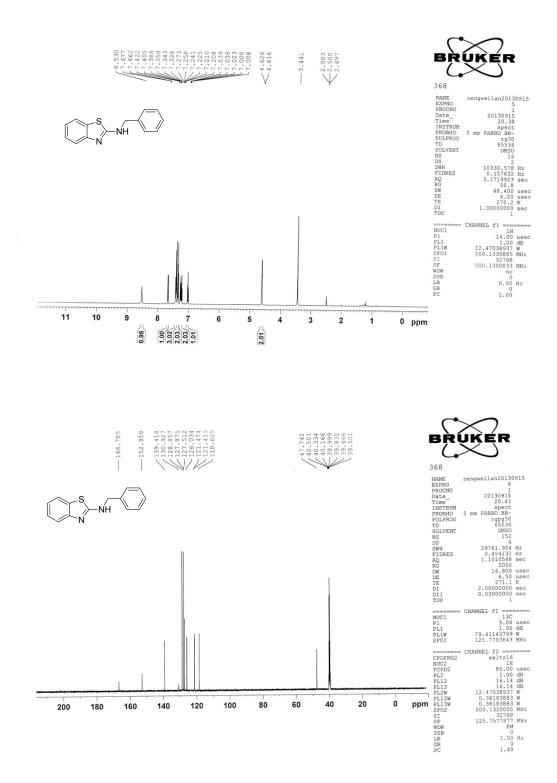


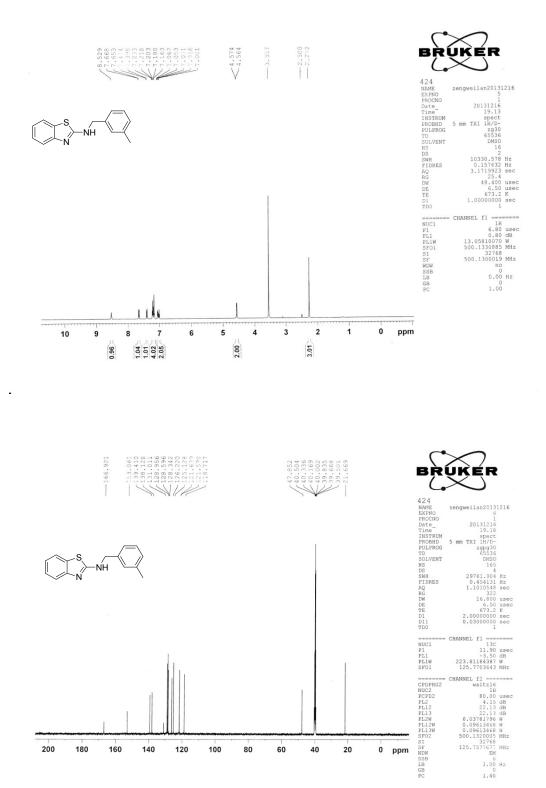


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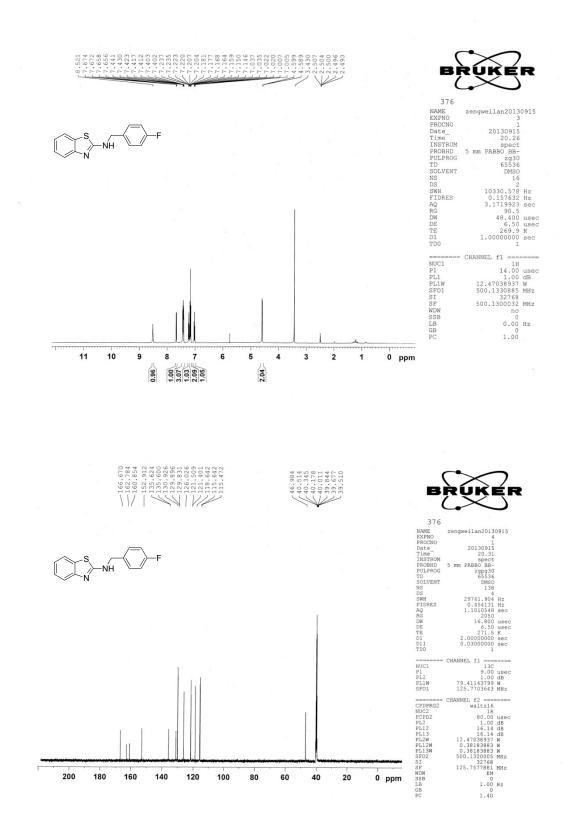


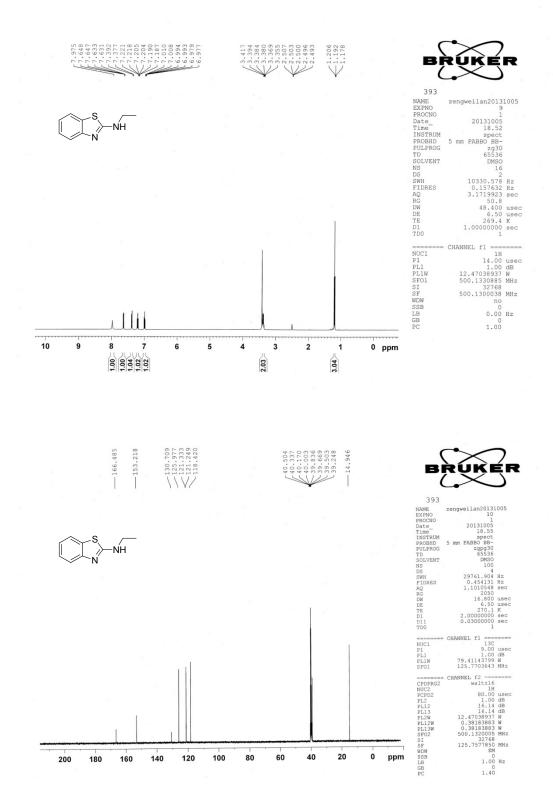


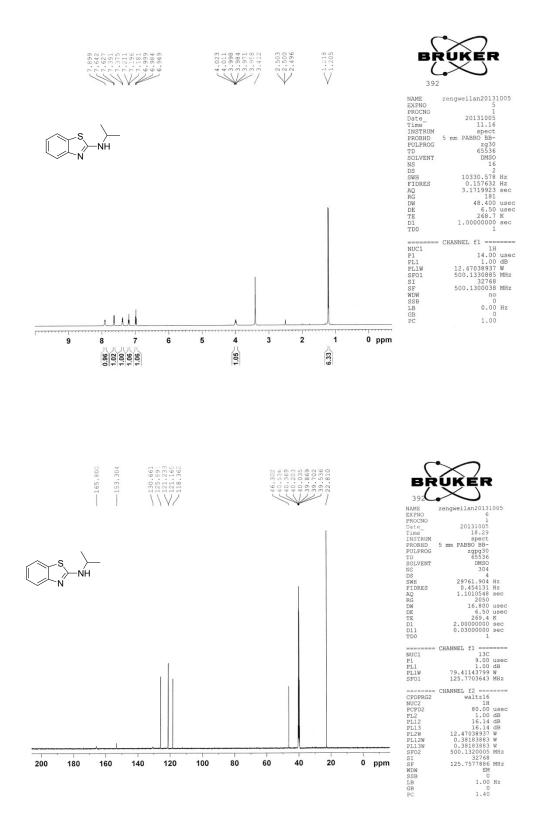


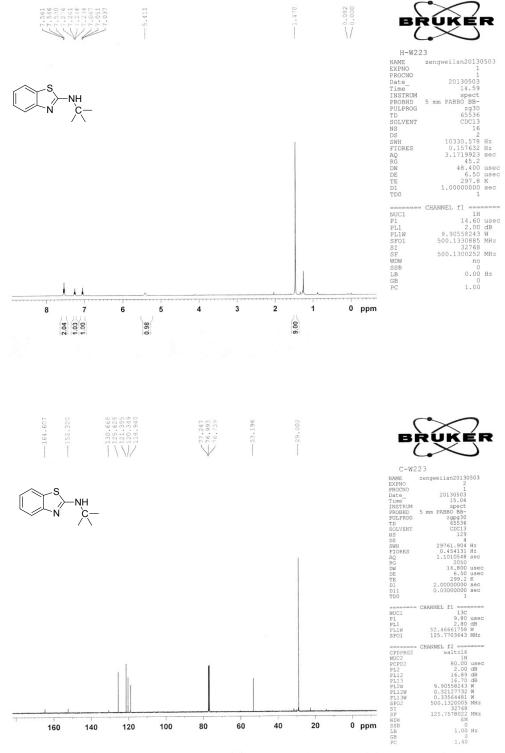


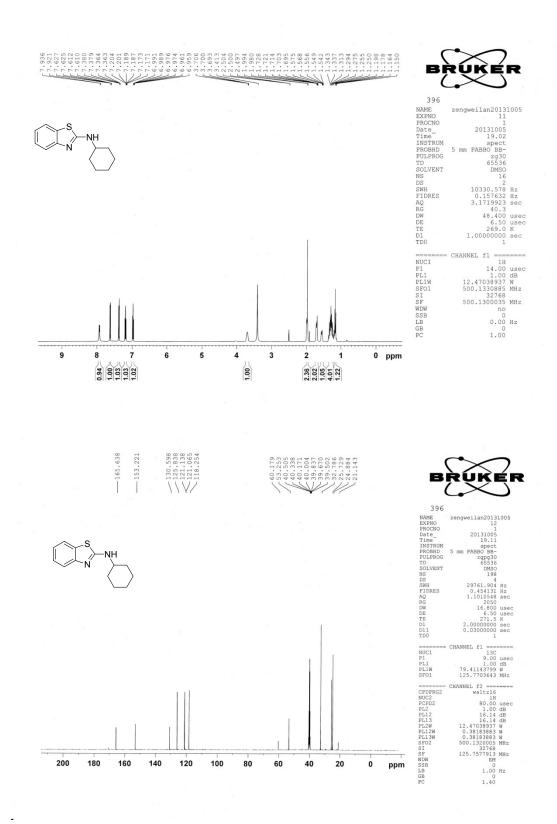
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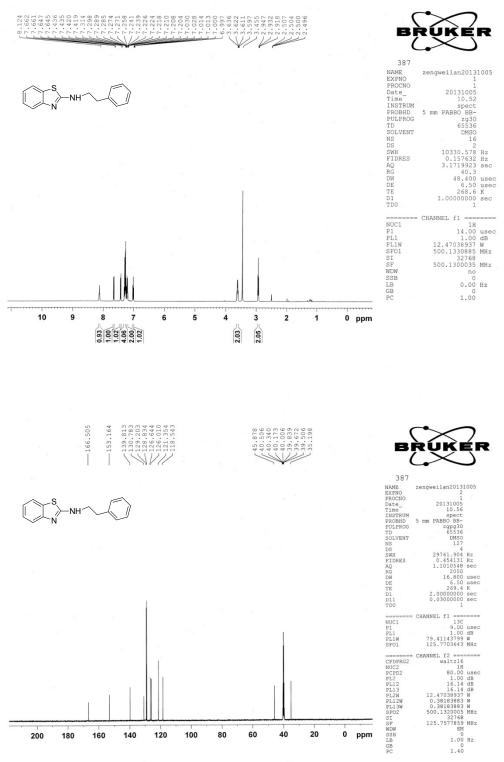


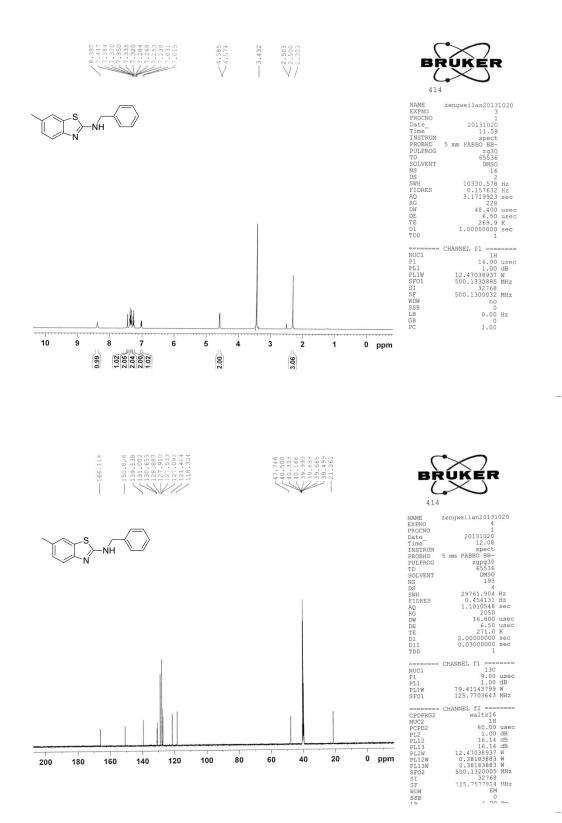


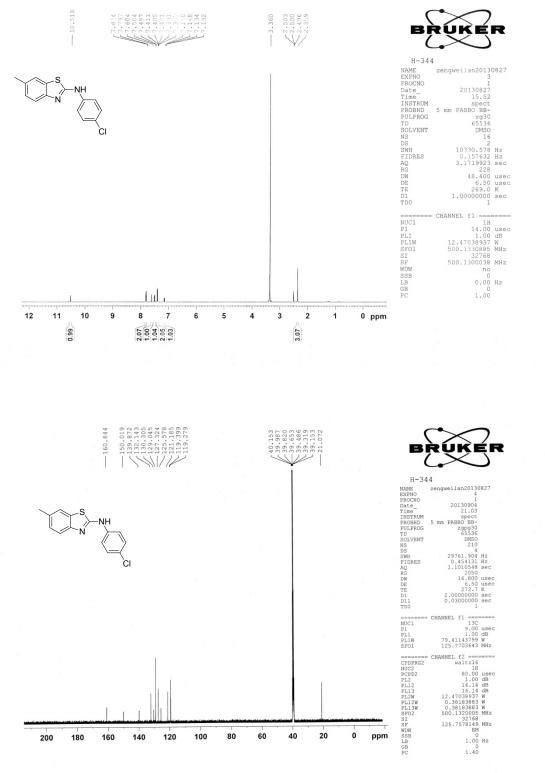




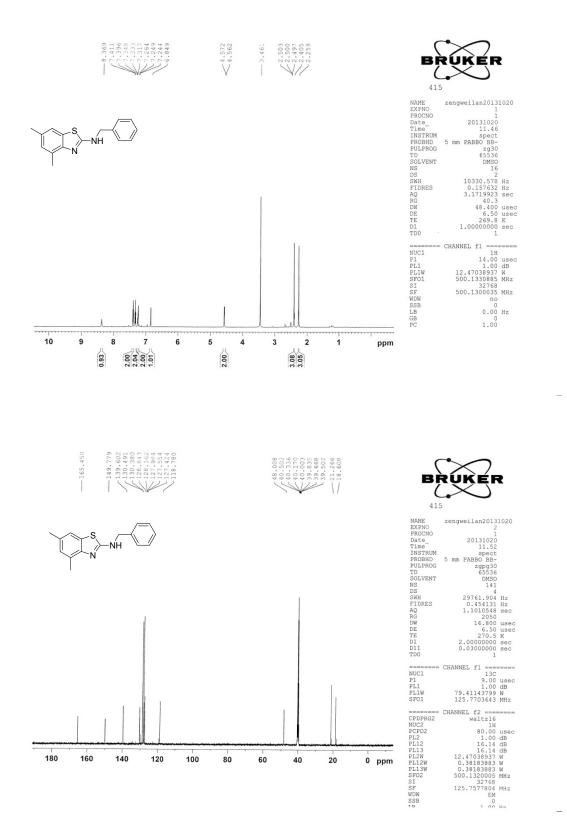


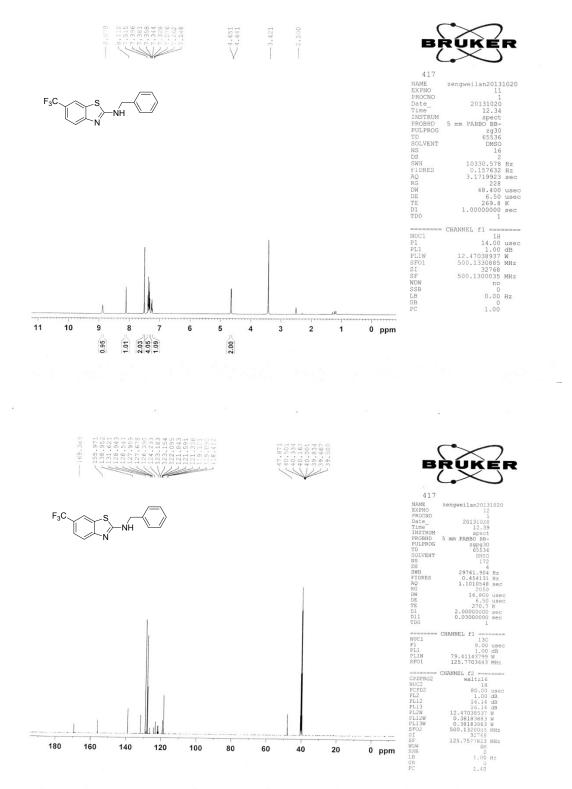


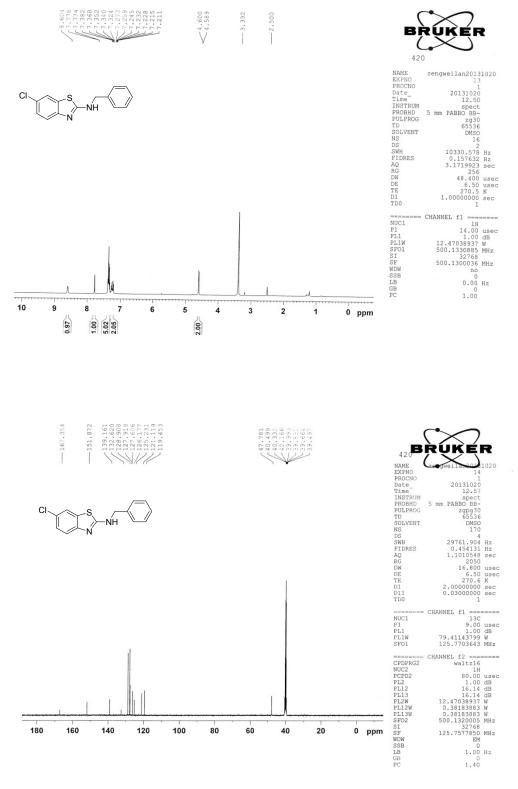




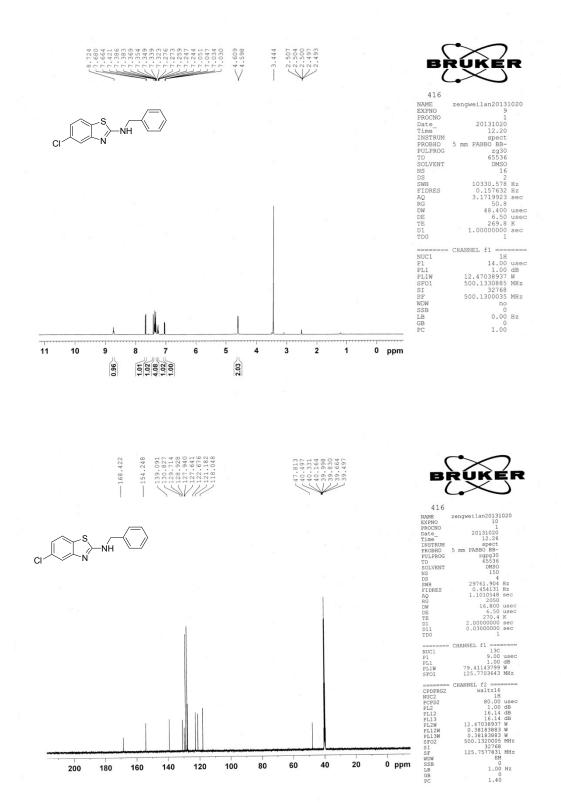
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