

Supporting Information

Arylation of amines & monoarylation of symmetrical diamines in the presence brine solution with diheteroaryl halides

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General information:

All the starting materials were obtained from commercial supplies and used as received. Triple distilled water was used for the reaction. The reactions were performed in air atmosphere without any specific precautions. Column chromatography was performed with silica gel 200-400 mesh using ethylacetate and ethanol as eluents.

Synthesis of Benzothiazol-2-yl-morpholine (General Procedure 1).

In a 50 mL round-bottom flask, 0.87 gm (0.01 mol) of morpholine, 0.68 gm (0.01 mol) of Imidazole, 0.274 gm (0.001 mol) of tributylbenzyl ammonium choride and 1.69 gm (0.01 mol) 2-chlorobenzothiazole were added in 20 mL of 5% NaCl(aq) solution. The reaction mixture was refluxed for 6 hrs. The progress for reaction was monitored by TLC. After completion of the reaction, aqueous layer was washed with ethyl acetate (3 x 10 mL). The combined organic layer was dried over anhydrous Na₂SO₄ and concentrated at reduced pressure. Products were purified either by crystallizing or by flash chromatography.

Synthesis of Benzothiazol-2-yl-Piperazine (General Procedure 2).

In a 50 mL round-bottom flask, 1.22 gm (0.01 mol) of Piperazine mono hydrochloride, 0.68 gm (0.01 mol) of Imidazole, 0.274 gm (0.001 mol) of tributylbenzyl ammonium choride and 1.69 gm (0.01 mol) 2-chlorobenzothiazole were added. The reaction mixture was allowed to stir at room temperature for half hour. After stirring, 25 ml of 5% NaCl(aq) solution was added and refluxed for another 10 hrs. The progress for reaction was monitored by TLC using ethyl acetate/methanol(9:1). After completion of the reaction, aqueous layer was washed with ethyl acetate (3 x 10 ml). The combined organic layer was dried over anhydrous Na₂SO₄ and concentrated at reduced pressure. Products were purified either by crystallizing or by flash chromatography.

Synthesis of Benzothiazol-2-yl-Piperazine (General Procedure 3).

In a 50 mL round bottom flask, 0.86 gm (0.01 mol) of piperazine and 1.58 gm (0.01 mol) of piperazine dihydrochloride were added in 20 mL of water and stirred for half hour. 0.68 gm (0.01 mol) of Imidazole, 0.274 gm (0.001 mol) of tributylbenzyl ammonium chloride, 1.69 gm (0.01 mol) 2-chlorobenzothiazole and 2gm NaCl(aq) were added in the reaction mixture and refluxed for 10 hrs. The progress of reaction was monitored by TLC. After completion of the reaction, aqueous layer was washed with ethyl acetate (3 x 10 ml). The combined organic layer was dried over anhydrous Na₂SO₄ and concentrated at reduced pressure. Products were purified either by crystallizing or by flash chromatography.

All the products of table 2¹ and table 4 (entry 1-5¹, 6², 8³, 9⁴, 10⁵, 11-14⁶⁻⁷) are reported compounds. Reference data related entry 1-13 of table 2 and entry 1-5 of table 4 are available in the available in supporting information of reference 1.

1. 2-Morpholin-4-yl-benzothiazole (C₁₁H₁₂N₂OS)

White crystalline solid; FTIR, 654.5, 757.4, 861.1, 944.3, 1030.3, 1069.2, 1112.9, 1182, 1228, 1272, 1287, 1340, 1377, 1441, 1540, 1594, 2853.1 ¹H NMR (400 MHz, CDCl₃): δ 3.63.(t, 4H), 3.85 (t, 4H), 7.12 (t, 1H), 7.31 (t, 1H), 7.61(t, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 48.12, 66.26, 119.34, 120.79, 121.71, 126.12, 129.07, 129.33, 130.56, 150.12, 168.20; MS (ESI, MeOH): *m/z* 221 [M +H]⁺;

2. 1-benzothiazol-2-yl-homopiperazine (C₁₂H₁₅N₃S).

White crystalline solid; ¹H NMR (400 MHz, CDCl₃): δ 1.96 (m, 2H), 2.9 (t, 2H), 3.1 (t, 2H), 3.7 (t, 4H), 7.0 (t, 1H), 7.2 (t, 1H), 7.6 (dd, 2H) ; ¹³C NMR (100 MHz, CDCl₃): δ 27.67, 47.27, 47.74, 49.55, 51.15, 52.24, 52.77, 118.64, 120.36, 120.54, 125.65, 152.88, 167.43; MS(ESI, MeOH): *m/z* 234.10 [M +H]⁺.

3. 2-((2S,6S)-2,6-dimethylpiperazin-1-yl)benzothiazole (C₁₃H₁₇N₃S).

- White crystalline solid; ^1H NMR (400 MHz, CDCl_3): δ 1.25 (d, 3H), 1.37 (d, 3H), 2.6 (dd, 1H), 3.28 (m, 1H), 3.4 (dd, 1H), 3.5 (d, 2H), 4.2 (m, 1H), 7.0 (t, 1H), 7.28 (t, 2H), 7.6 (t, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 14.2, 17.15, 43.8, 47.1, 48.9, 51.7, 118.8, 120.4, 121.1, 125.8, 130.2, 152.6, 169.0; MS(ESI, MeOH): m/z 248.10 $[\text{M} + \text{H}]^+$.
- 4. 2-((3R, 5R)-3, 5-dimethylpiperazin-1-yl)benzothiazole ($\text{C}_{13}\text{H}_{17}\text{N}_3\text{S}$)**
- White crystalline solid; ^1H NMR (400 MHz, CDCl_3): δ 1.2-1.4 (m, 6H), 2.6 (dd, 1H), 3.3(m, 1H), 3.4 (dd, 1H), 3.5 (d, 2H), 4.2(m, 1H), 7.1 (t, 1H), 7.2 (m, 1H), 7.5 (dd, 2H) ; ^{13}C NMR (100 MHz, CDCl_3): δ 14.23, 17.15, 29.58, 43.86, 47.15, 48.95, 51.75, 118.82, 120.47, 121.09, 125.82, 130.25, 152.66, 169.05. ; MS (ESI, MeOH): m/z 247.11 $[\text{M} + \text{H}]^+$.
- 5. (1R, 4R)-N1-(benzothiazol-2-yl)cyclohexane-1,4-diamine($\text{C}_{13}\text{H}_{17}\text{N}_3\text{S}$)**
- White crystalline solid; ^1H NMR (400 MHz, CDCl_3): δ 1.2 (m, 4H), 1.9-2.2 (dd, 4H), 2.6(m, 1H), 3.5(m, 1H) 7.16 (t 1H), 7.2 (m, 1H), 7.6 (dd 2H), ; ^{13}C NMR (100 MHz, CDCl_3): δ 31.92, 35.14, 49.76, 54.18, 118.63, 120.65, 121.29, 125.80, 130.27, 152.41, 165.59; MS(ESI, MeOH): m/z 248.1 $[\text{M} + \text{H}]^+$.
- 6. (1S,2S)-N1-(benzothiazol-2-yl)cyclohexane-1,2-diamine($\text{C}_{13}\text{H}_{17}\text{N}_3\text{S}$)**
- White crystalline solid; ^1H NMR (400 MHz, CDCl_3): δ 1.2 (m, 4H), 1.9 (m, 4H), 2.6 (m 1H), 3.3 (m 1H), 7.1 (t, 1H), 7.3(t, 1H), 7.5(dd, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 24.62, 24.89, 32.34, 34.25, 55.22, 61.83, 118.52, 120.70, 121.48, 125.84, 130.25, 152.09, 167.72.; MS(ESI, MeOH): m/z 248.1 $[\text{M} + \text{H}]^+$.
- 7. N-(benzothiazol-2-yl) ethane-1,2-diamine ($\text{C}_9\text{H}_{11}\text{N}_3\text{S}$)**
- White crystalline solid; ^1H NMR (400 MHz, CDCl_3): δ 3.0 (t, 2H), 3.5 (t, 2H), 7.1 (t, 1H), 7.3 (d, 1H), 7. 6 (dd, 2H);, ^{13}C NMR (100 MHz, CDCl_3): δ 40.94, 47.47, 118.65, 120.77, 121.47, 125.91, 130.37, 152.41, 167.75; MS(ESI, MeOH): m/z 194.0 $[\text{M} + \text{H}]^+$.

8. N1-(benzothiazol-2-yl)-N1,N2-dimethylethane-1,2-diamine (C₁₁H₁₅N₃S)

White crystalline solid; ¹H NMR (400 MHz, CDCl₃): δ 2.7 (s, 3H), 3.1 (t, 2H), 3.2 (s 1H), 3.3 (s, NH), 3.7(t, 2H), 7.1 (t, 1H), 7.3 (t, 1H), 7.6 (dd, 2H), ; ¹³C NMR (100 MHz, CDCl₃): δ 32.56, 41.61, 50.83, 54.69, 119.35, 121.87, 122.54, 128.87, 131.70, 153.70, 170.72; MS(ESI, MeOH): m/z 222.10 [M +H]⁺.

9. N1-(benzothiazol-2-yl)-N1, N2-diethylethane-1,2-diamine (C₁₃H₁₉N₃S)

White crystalline solid; ¹H NMR (400 MHz, CDCl₃): δ 1.1 (t, 3H), 1.3 (t, 3H), 2.7(m, 2H), 2.9(t, 2H), 3.6(m, 4H), 7.0(t, 1H), 7.2(t, 1H), 7.6(dd, 7.6) ; ¹³C NMR (100 MHz, CDCl₃): δ 12.46, 15.17, 41.35, 43.99, 44.89, 46.89, 47.18, 50.79, 118.58, 120.38, 121.04, 128.67, 130.67, 153.04, 167.59. MS(ESI, MeOH): m/z 250.0[M +H]⁺.

10. 1-(benzothiazol-2-yl)-N1,N2-diethylpropane-1,2-diamine (C₁₄H₂₁N₃S)

White crystalline solid; ¹H NMR (400 MHz, CDCl₃): δ 1.1 (t, 3H), 1.3 (t, 3H), 1.9 (m, 2H), 2.6 (m, 4H), 3.5 (q, 2H), 3.6 (t, 2H), 7.0 (t, 1H), 7.2 (m 1H), 7.5(dd, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 12.60, 15.17, 28.18, 44.01, 45.99, 46.59, 48.26, 118.54, 120.53, 125.85, 130.65, 153.14, 167.75. ; MS(ESI, MeOH): m/z 264.13 [M +H]⁺.

11. 2,2'-((2R,5S)-2,5-dimethylpiperazine-1,4-diyl)dibenzothiazole (C₂₀H₂₀N₄S₂)

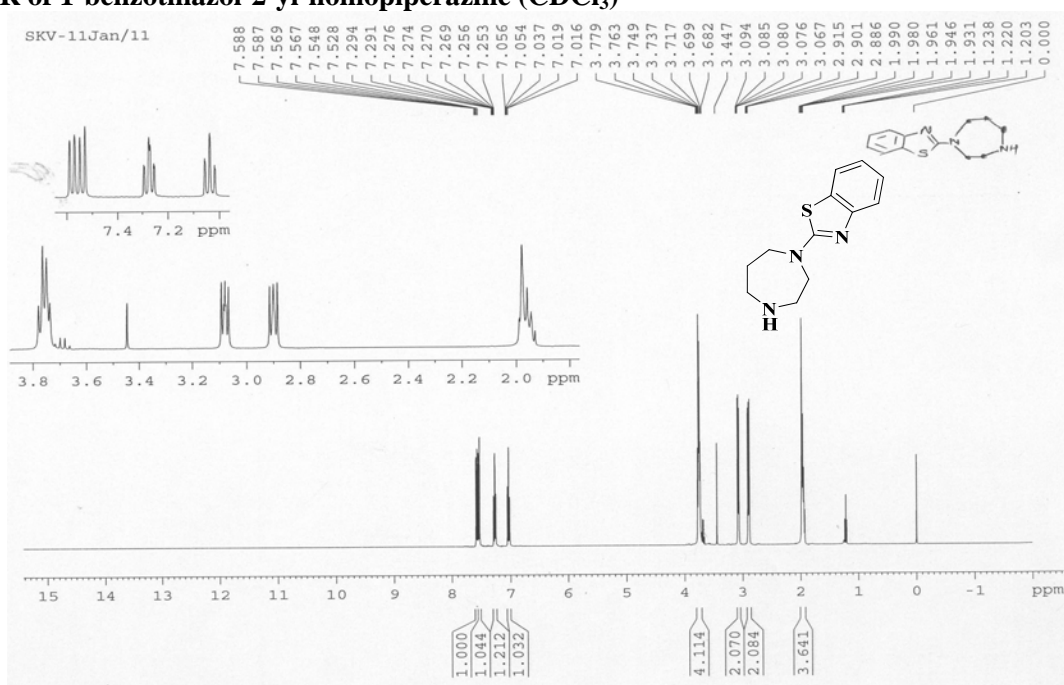
White crystalline solid; ¹H NMR (400 MHz, CDCl₃): δ 1.1 (d, 6H), 2.7 (t, 2H), 3.0 (m, 2H), 3.9 (d, 2H), 7.1 (t, 1H), 7.3 (m 1H), 7.6(dd, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 19.28, 50.34, 54.93, 118.97, 120.59, 121.25, 125.93, 130.48, 152.71, 168.61. ; MS(ESI, MeOH): m/z 381.1 [M +H]⁺.

References.

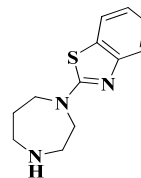
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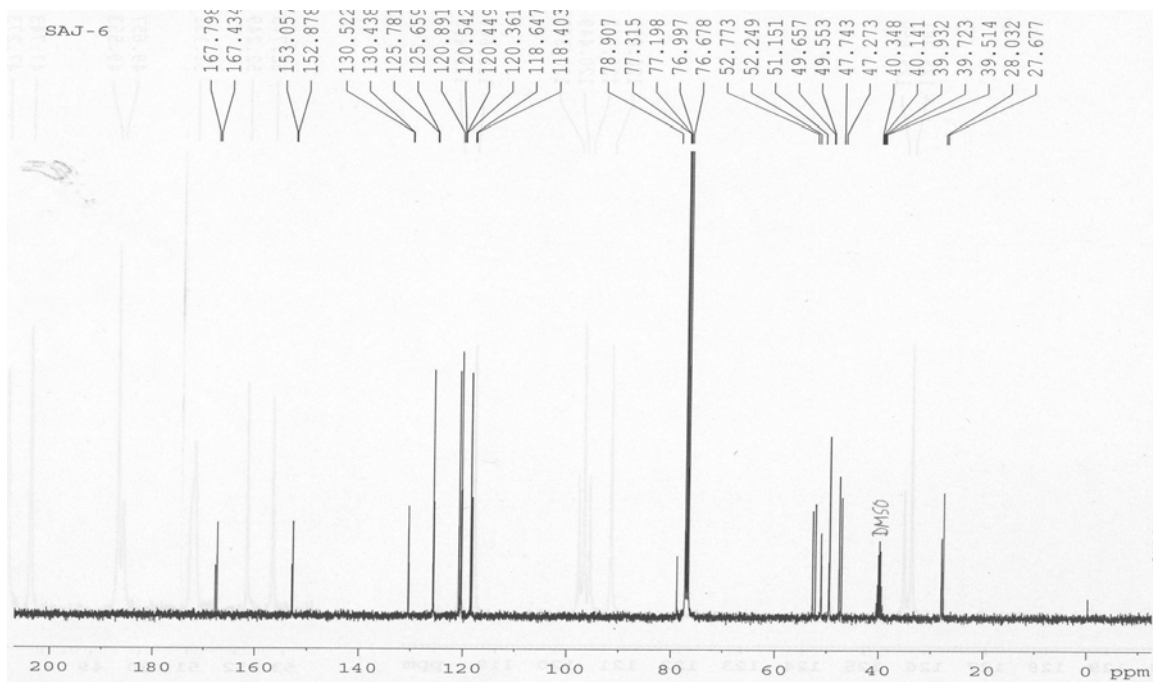
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¹H NMR of 1-benzothiazol-2-yl-homopiperazine (CDCl₃)

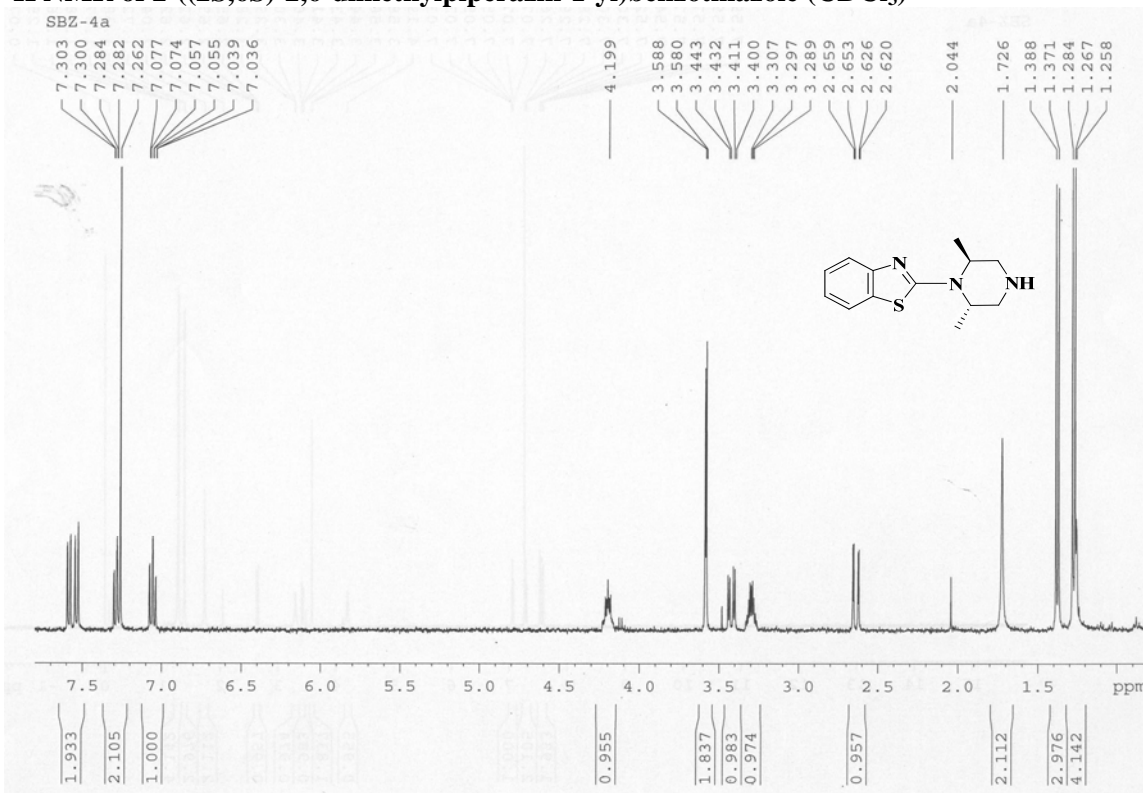


¹³C NMR of 1-benzothiazol-2-yl-homopiperazine (CDCl₃)

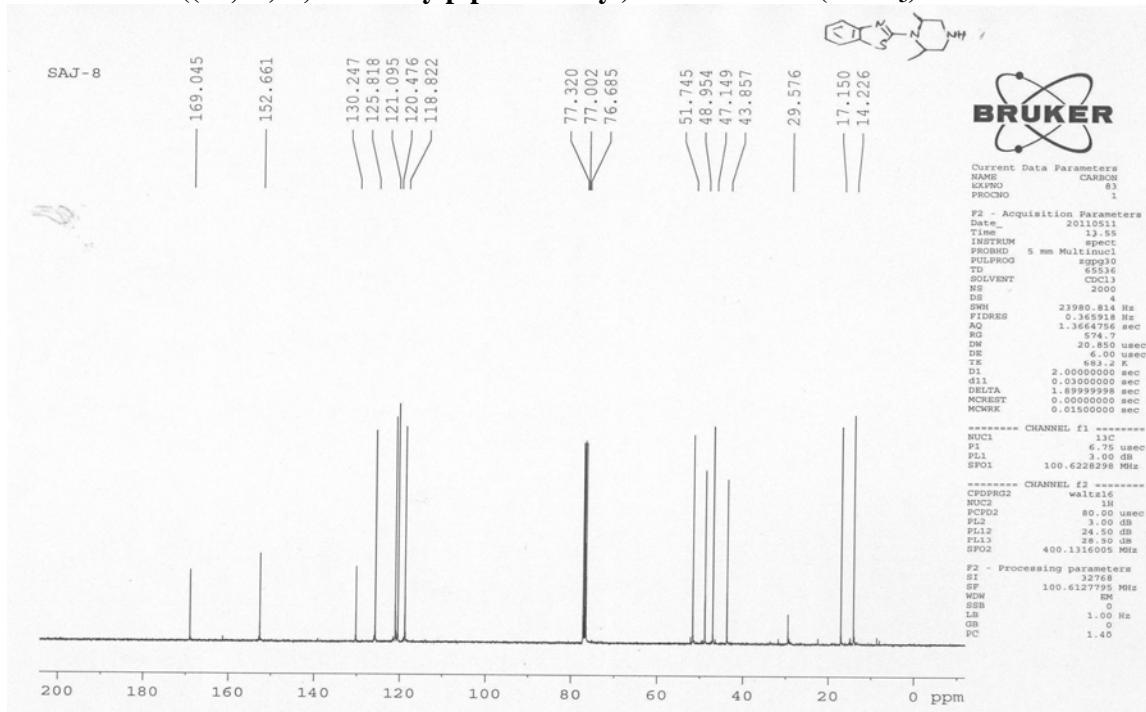




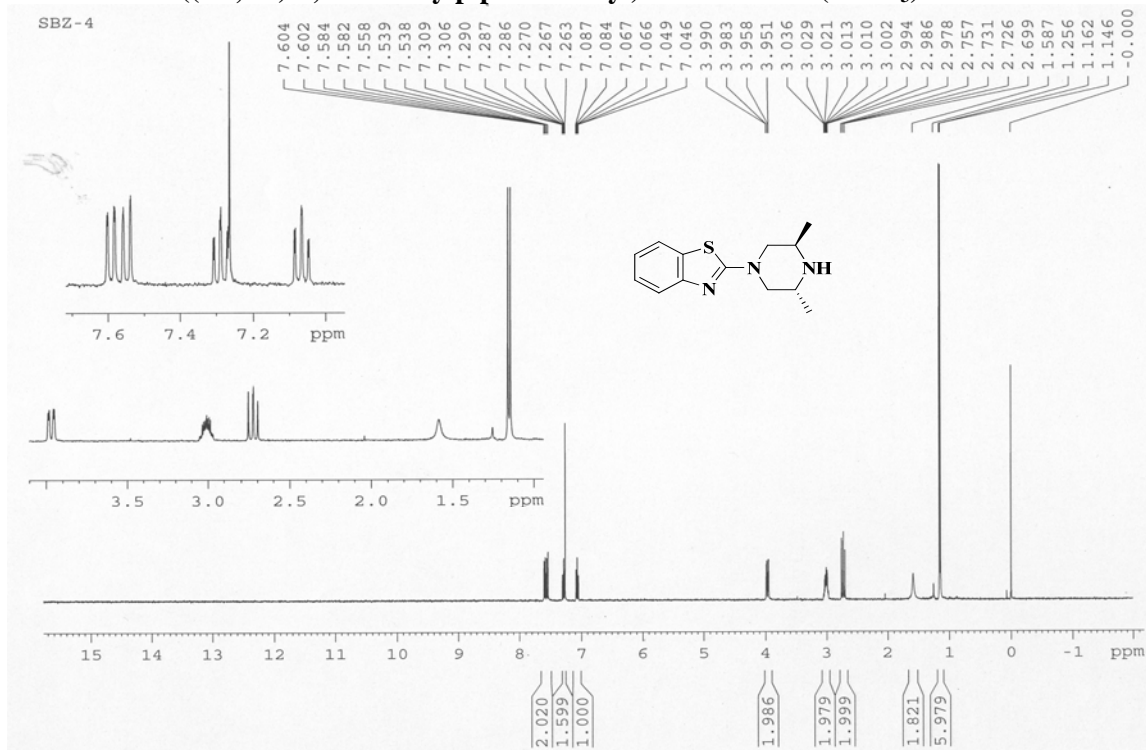
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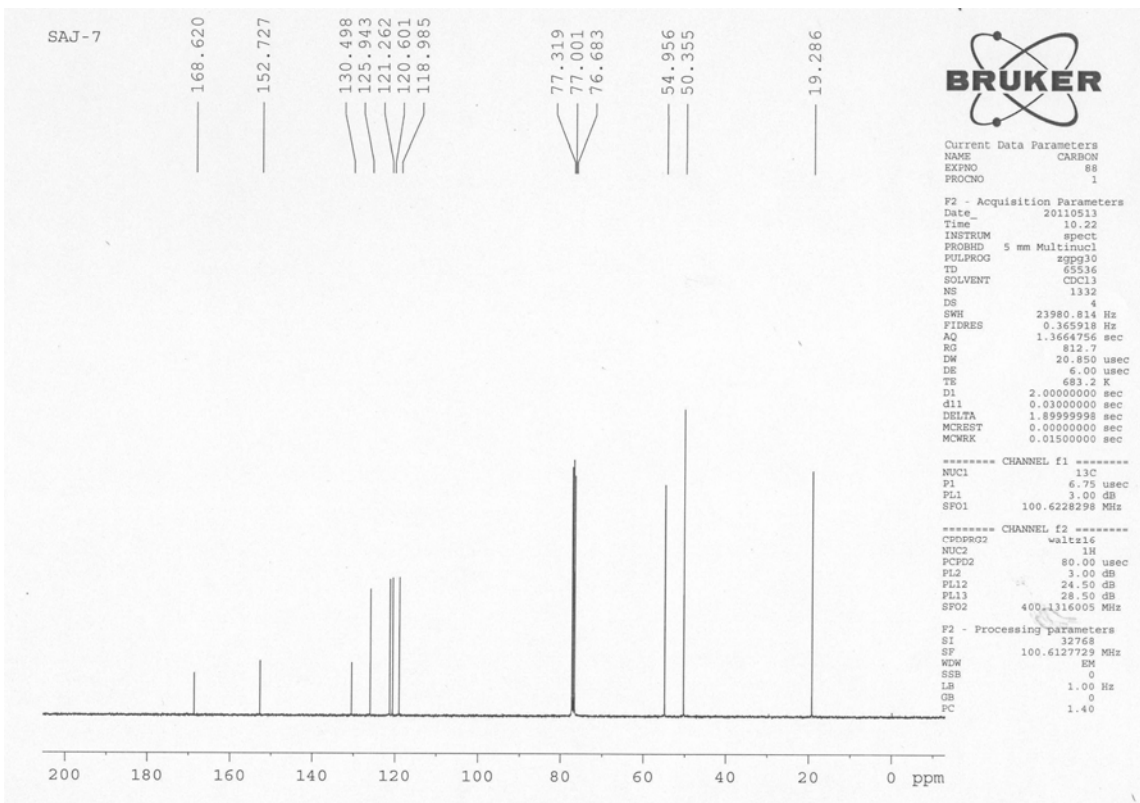
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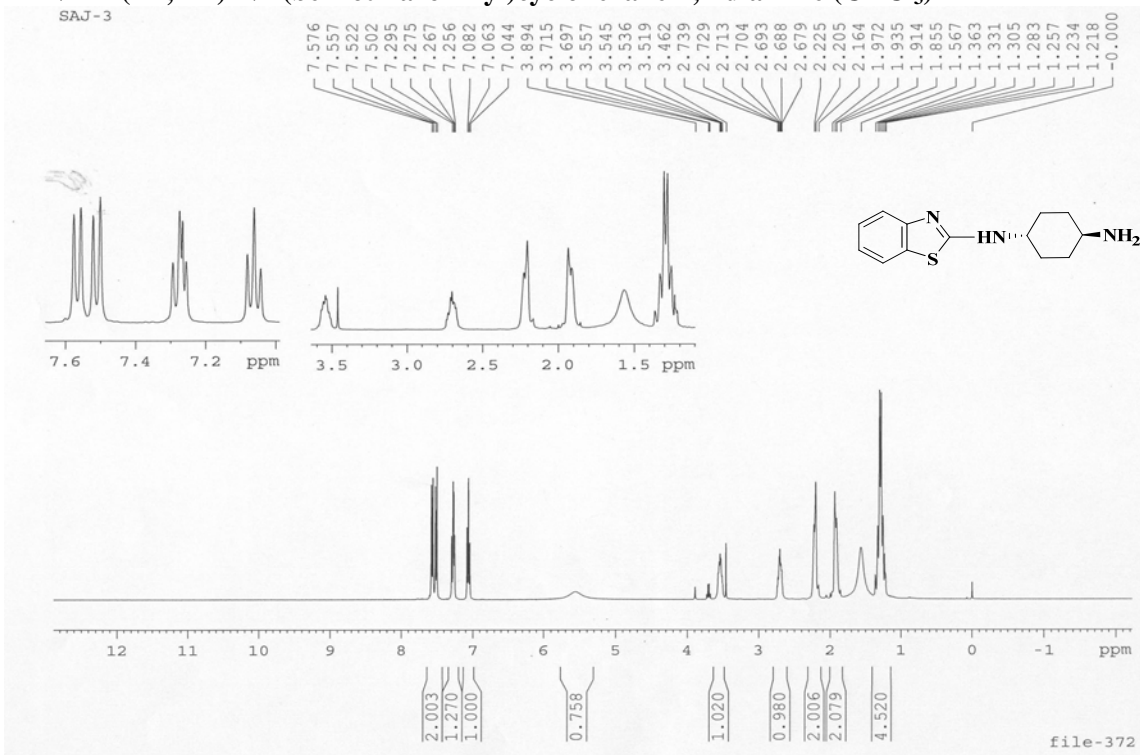
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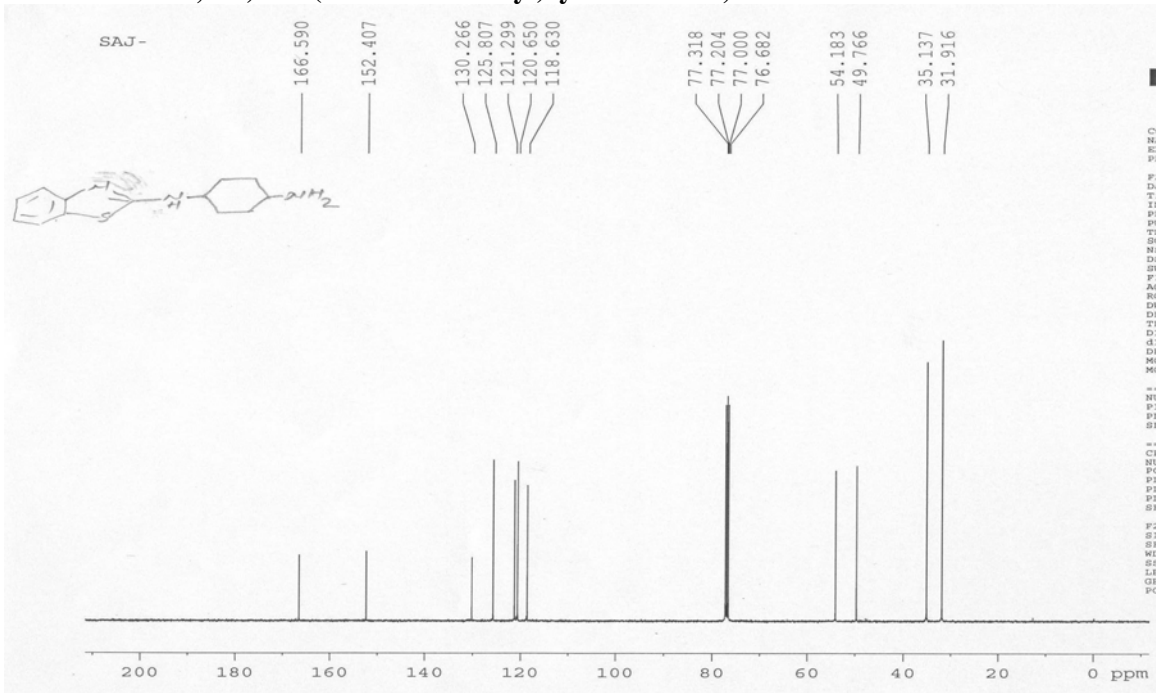
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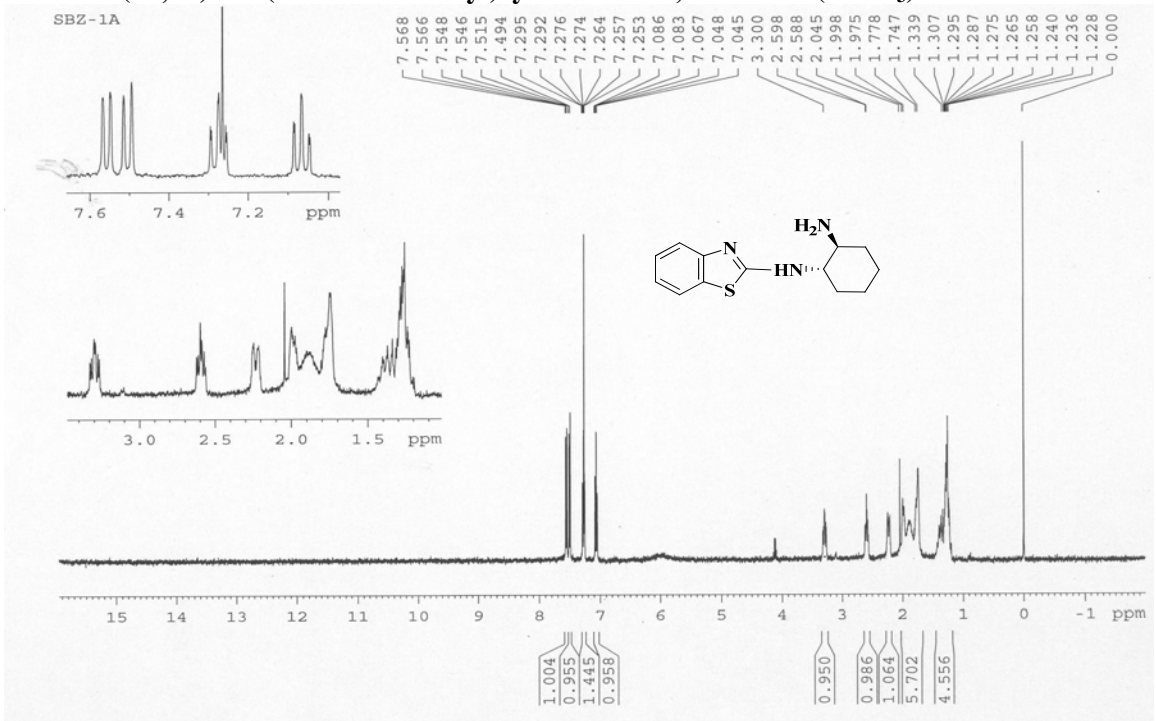
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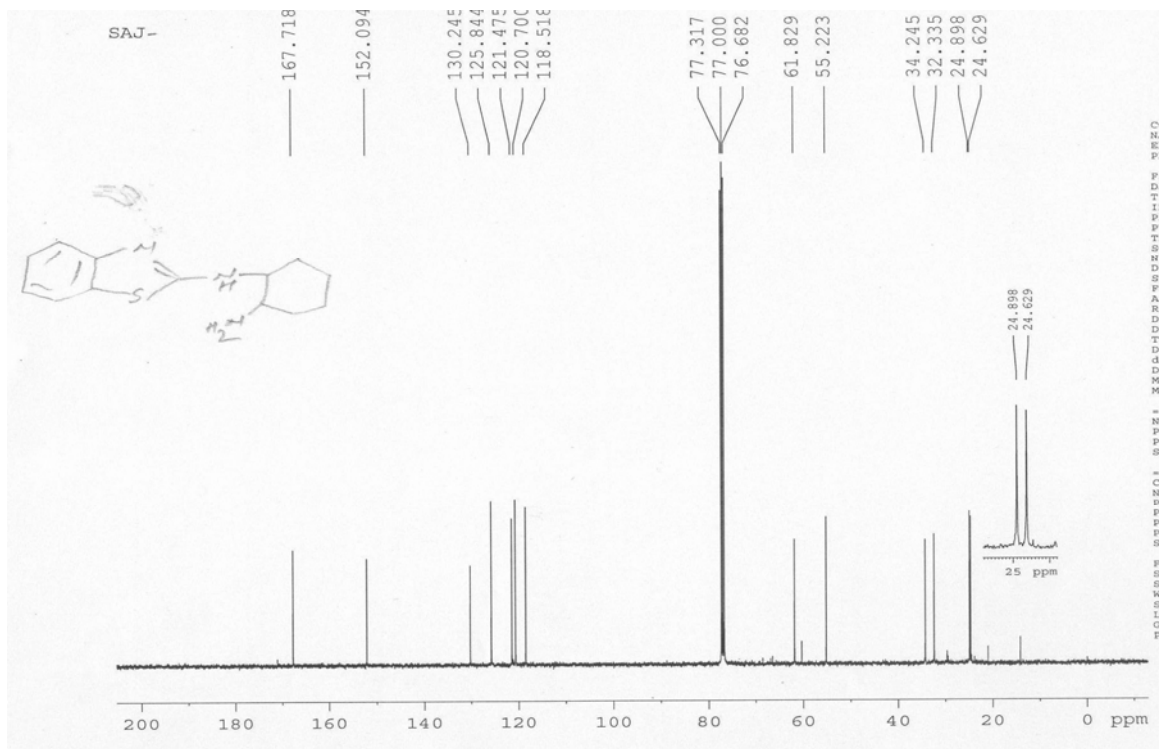
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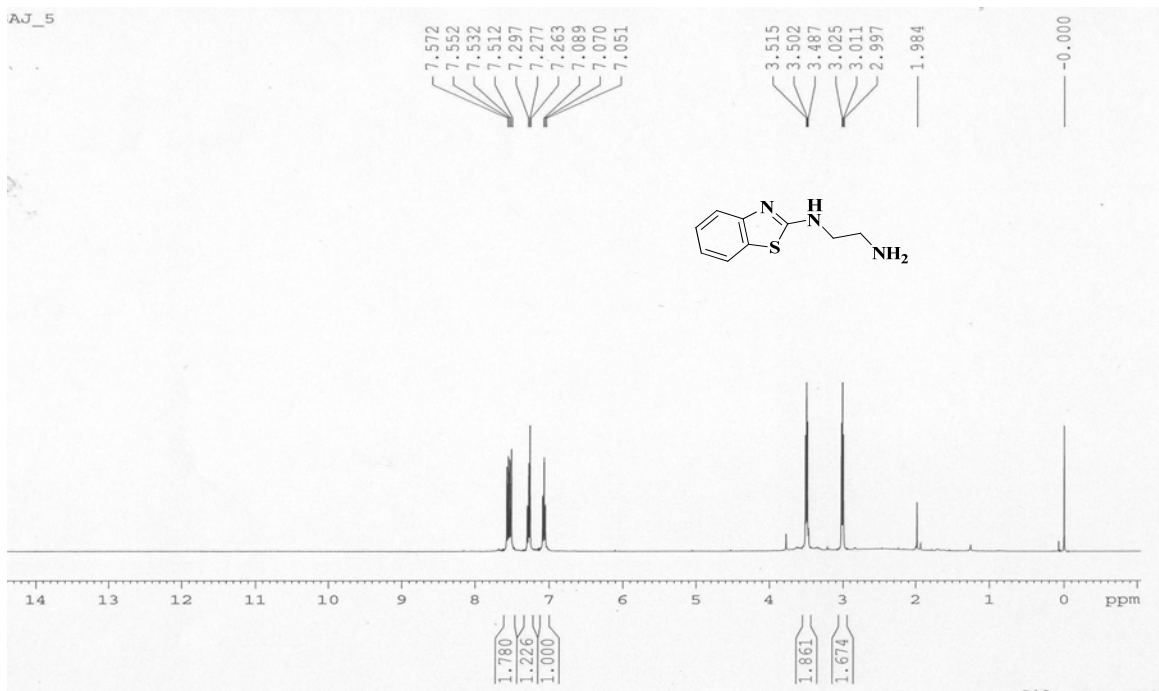
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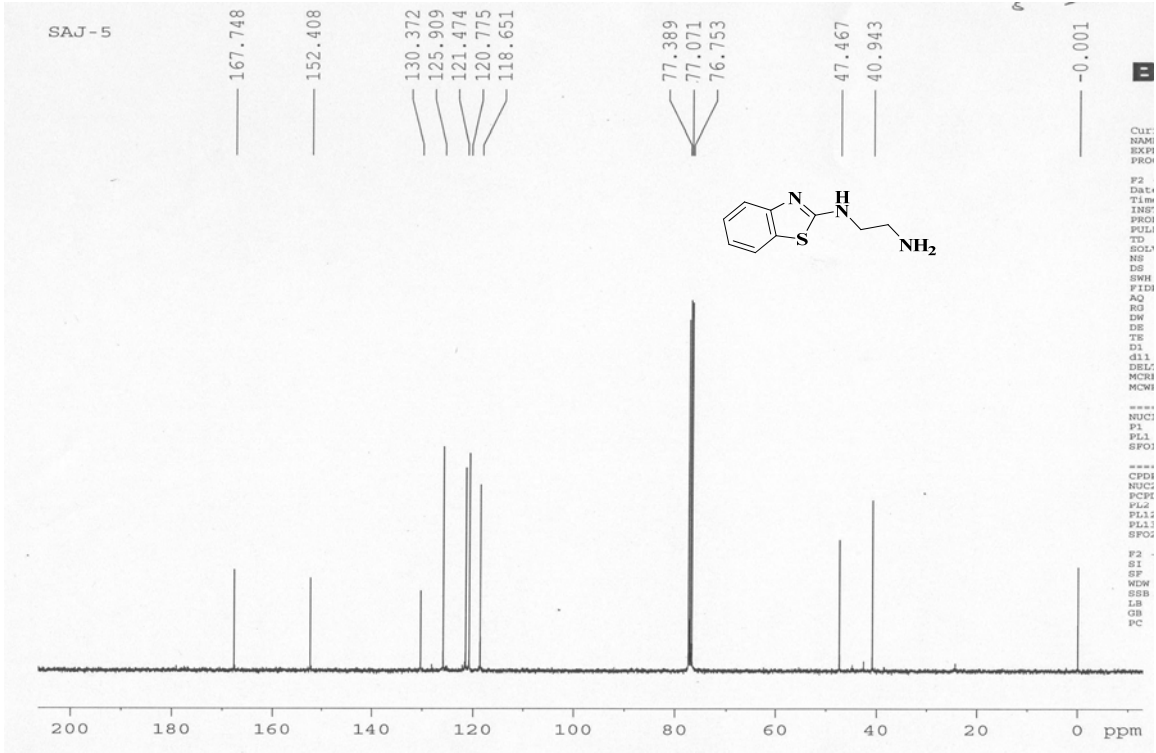
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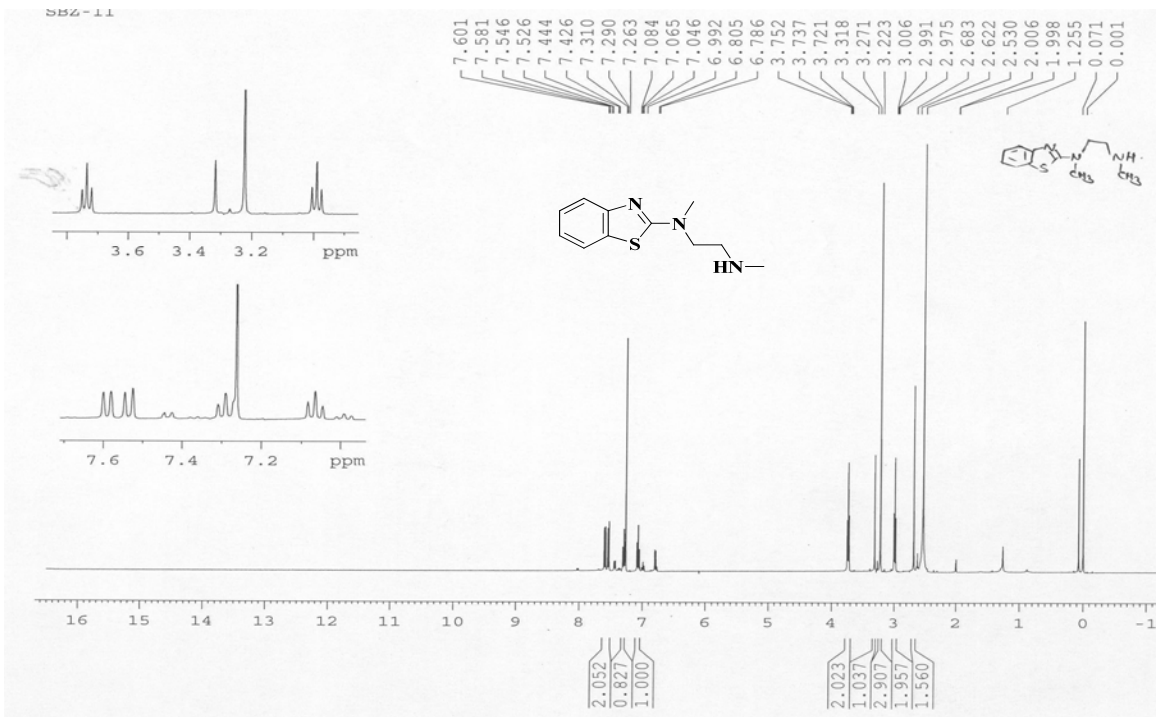
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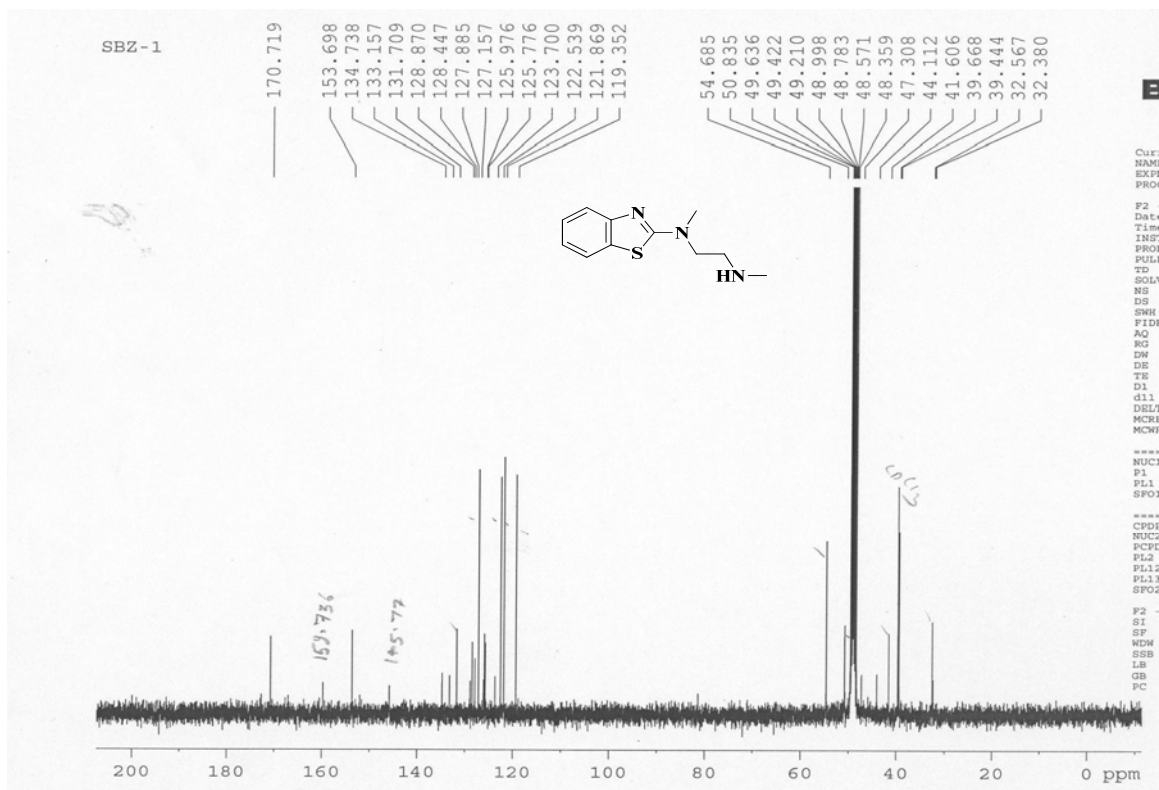
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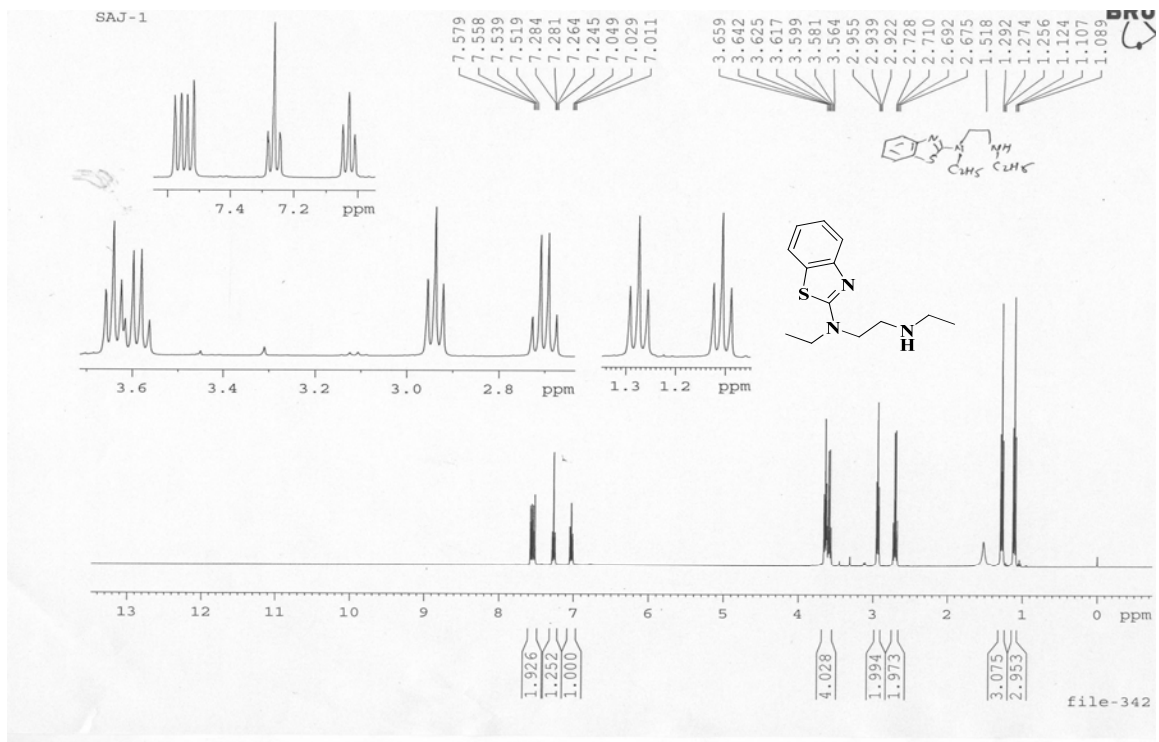
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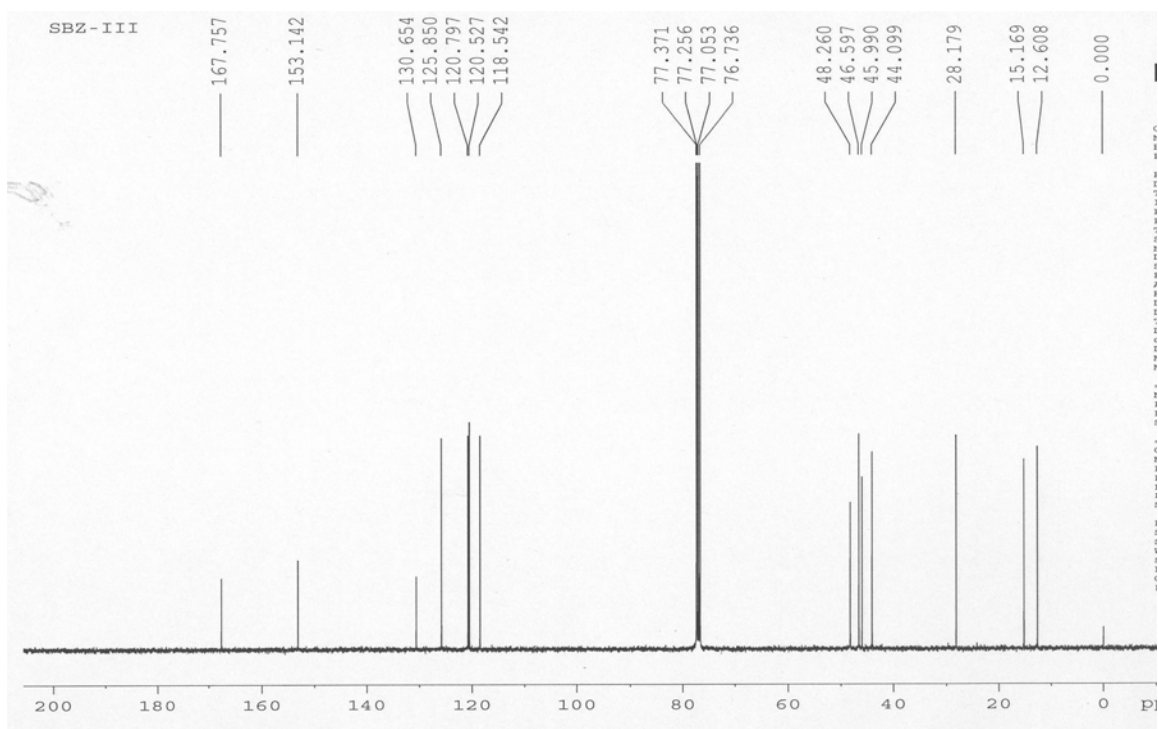


^{13}C NMR- N^1 -(benzothiazol-2-yl)- N^1,N^2 -dimethylethane-1,2-diamine (CDCl_3)

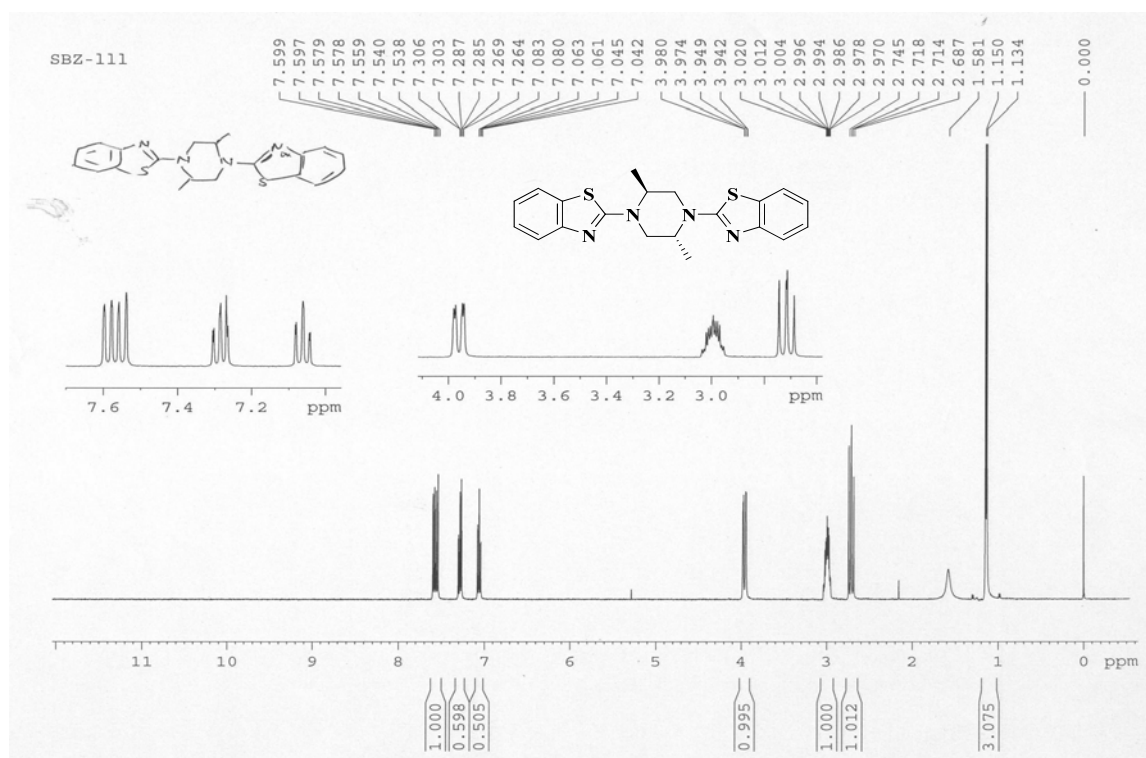


¹H NMR- N¹-(benzothiazol-2-yl)-N¹,N²-diethylethane-1,2-diamine (CDCl₃)





^{13}C NMR- 2,2'-((2R,5S)-2,5-dimethylpiperazine-1,4-diyl)dibenzothiazole (CDCl_3)



^1H NMR- 2,2'-((2R,5S)-2,5-dimethylpiperazine-1,4-diyl)dibenzothiazole (CDCl_3)

