

Supporting information

Solid-Phase Synthesis with Resin-Bound Triarylbismuthanes: Traceless and Multidirectional Cleavage of Unsymmetrical Biphenyls

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Table of contents:

Experimental section:	S3
Preparation of tris(3-bromophenyl)bismuthane	S3
Preparation of complex 3	S3
Preparation of resin 5	S3
Typical procedure for Suzuki coupling on resin 5	S4
Typical procedure for traceless cleavage with TFA	S4
Typical procedure for cleavage with bromine	S5
Typical procedure for cleavage with iodine	S6
¹ H-NMR and ¹³ C-NMR for 2	S8-S9
¹ H-NMR and ¹³ C-NMR for 8a	S10-S11
¹ H-NMR and ¹³ C-NMR for 8b	S12-S13
¹ H-NMR and ¹³ C-NMR for 8c	S14-S15
¹ H-NMR and ¹³ C-NMR for 8d	S16-S17
¹ H-NMR and ¹³ C-NMR for 9a	S18-S19
¹ H-NMR and ¹³ C-NMR for 9b	S20-S21
¹ H-NMR and ¹³ C-NMR for 9c	S22-S23
¹ H-NMR and ¹³ C-NMR for 9d	S24-S25
¹ H-NMR and ¹³ C-NMR for 10a	S26-S27
¹ H-NMR and ¹³ C-NMR for 10b	S28-S29
¹ H-NMR and ¹³ C-NMR for 10c	S30-S31
¹ H-NMR and ¹³ C-NMR for 10d	S32-S33
Reference list	S34

Experimental

General. All reactions were carried out in oven-dried glassware under an argon atmosphere. Chemicals and solvents were obtained from commercial suppliers and used as received unless otherwise stated. THF was distilled from sodium and benzophenone. ^1H -NMR and ^{13}C -NMR spectra were recorded at 500.13 MHz and 125.67 MHz, respectively, with TMS (^1H) or the residual solvent signal (^{13}C) as internal standards. Merrifield resin was purchased from Argonaut Technologies (loading: 2.38 mmol/g, 200 mesh, cross-linked with 1-2% divinylbenzene). The starting resin 4-iodophenoxymethyl polystyrene was prepared as previously described.¹ Products are colorless unless otherwise stated.

Tris(3-bromophenyl)bismuthane 2 – To a solution of 1,3-dibromobenzene (5.0 g, 21 mmol) in THF (50 mL) at $-78\text{ }^\circ\text{C}$ was slowly added a 1.6 M solution of *n*-BuLi in hexanes (8.8 mL, 19 mmol). After stirring at $-78\text{ }^\circ\text{C}$ for 1.5 h, a suspension of BiCl_3 (2.0 g, 6.4 mmol) in THF (30 mL) was added slowly keeping the temperature below $-65\text{ }^\circ\text{C}$. The mixture was warmed to room temperature over 4 h and stirred at room temperature for a further 10 h. The crude mixture was concentrated *in vacuo* and diluted with toluene (150 mL). The resulting suspension was filtered through celite, and the solvent removed by evaporation. The crude product was purified by flash chromatography (heptane) to yield 3.2 g (74%) of **2** as viscous oil. $\delta_{\text{H}}(\text{CDCl}_3)$ 7.3 (1H, t, $J = 7.5$ Hz), 7.5 (1H, d, $J = 8.0$ Hz), 7.6 (1H, d, $J = 7.1$ Hz), 7.9 (1H, s). ^{13}C -NMR $\delta_{\text{C}}(\text{CDCl}_3)$ 126.2, 131.4, 132.6, 135.6, 139.7.

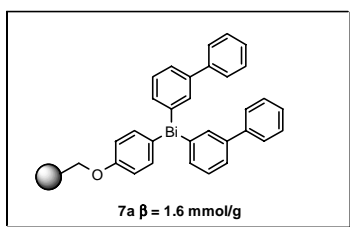
Preparation of complex 3 – To a solution of **2** (8.6 g, 13 mmol) in CH_2Cl_2 (80 mL) and MeOH (10 mL) at $0\text{ }^\circ\text{C}$ were added hexamethylphosphortriamide (4.6 g, 26 mmol) and trimethylsilyl trifluoromethanesulfonate (2.9 g, 13 mmol). The reaction was stirred at room temperature for 4 h. The solvent was removed by evaporation, and the product was dried *in vacuo* overnight. The crude product was used directly for the preparation of resin **5**.

Preparation of resin 5 – *i*-PrMgBr (0.71 M in THF, 75 mL, 53 mmol) was added at $-30\text{ }^\circ\text{C}$ to a suspension of 4-iodophenoxymethyl polystyrene (7.1 g, 11 mmol) in THF (50 mL). Stirring was continued for 3 h at $-30\text{ }^\circ\text{C}$. The resin-bound Grignard reagent was filtered, washed with THF (30 mL) and then suspended in THF (30 mL). A solution of complex **3** (21 mmol) in THF (50 mL) was added to

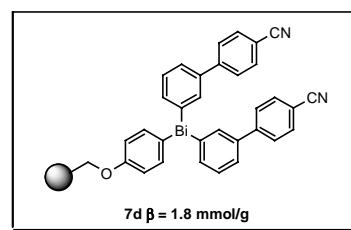
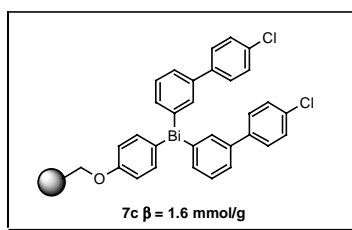
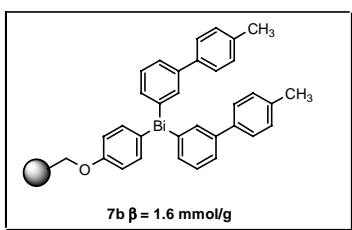
the suspension at -30°C. The reaction was allowed to warm slowly to room temperature overnight. The resin was isolated by filtration and washed with THF (3 x 20 mL), MeOH (3 x 20 mL), THF (3 x 20 mL), and finally with CH₂Cl₂ (3 x 20 mL) and dried overnight *in vacuo* at 40 °C to give 10.7 g of light yellow resin **5**. Calculated from the gain in weight, resin **5** had a loading of 1.9 mmol/g (based on Br).

Suzuki coupling on resin **5** – Typical procedure

To a suspension of resin **5** (2.0 g, 3.7 mmol) in THF (20 mL) was added phenylboronic acid (1.1 g, 9.3 mmol), potassium fluoride (3.2 g, 56 mmol), tris(dibenzylideneacetone)dipalladium (0.17 g, 0.19 mmol), and tri-*t*-butylphosphane (0.11 g, 0.56 mmol). The reaction was heated to 40 °C for 12 h. The resulting resin was filtered through a sintered glass filter (G3) and washed with THF (3 x 10 mL), H₂O (3 x 10 mL), MeOH-H₂O 1:1 (3 x 10 mL), THF-H₂O 1:1 (3 x 10 mL), THF (3x 10 mL), CH₂Cl₂ (3 x 10 mL) and dried overnight at 40 °C *in vacuo* to give **7a** as a black resin. Calculated from the gain in weight, resin **7a** had a loading of 1.6 mmol/g.



The resins **7b** (loading 1.6 mmol/g), **7c** (loading 1.6 mmol/g) and **7d** (loading 1.8 mmol/g) were prepared analogously.



Cleavage with trifluoroacetic acid (traceless cleavage) – Typical procedure

Biphenyl 8a² – To a suspension of resin **7a** (0.30 g, 0.48 mmol) in CH₂Cl₂ (1 mL) was added trifluoroacetic acid (1 mL). The suspension was stirred for 12 h at RT. The resin was filtered and, extracted with CH₂Cl₂ (3 x 5 mL). The combined organic phases were washed with H₂O (20 mL), brine

(20 mL) and dried over MgSO₄. The crude product was concentrated *in vacuo* and purified by column chromatography (heptane) to yield 49 mg (68%) of **8a** as a solid, mp 66.5-67.7 °C. $\delta_{\text{H}}(\text{CDCl}_3)$ 7.4 (2H, t, $J = 7.1$ Hz), 7.4 (4H, t, $J = 7.5$ Hz), 7.6 (4H, d, $J = 7.5$ Hz). $\delta_{\text{C}}(\text{CDCl}_3)$ 126.1, 126.2, 127.7, 140.2. GCMS-purity: 98%.

Compounds **8b-d** were prepared analogously.

4-Methylbiphenyl 8b,² (59 %), mp 46.5-46.9 °C $\delta_{\text{H}}(\text{CDCl}_3)$ 2.4 (3H, s), 7.2 (2H, d, $J = 8.0$ Hz), 7.3 (1H, t, $J = 7.5$ Hz), 7.4 (2H, t, $J = 7.5$ Hz), 7.5 (2H, d, $J = 8.0$ Hz), 7.6 (2H, d, $J = 7.5$ Hz). $\delta_{\text{C}}(\text{CDCl}_3)$ 20.1, 125.93, 125.95, 126.0, 127.7, 128.4, 136.0, 137.3, 140.1. GCMS-purity: >98%.

4-Chlorobiphenyl 8c,² (58 %). $\delta_{\text{H}}(\text{CDCl}_3)$ 7.4 (1H, t, $J = 7.5$ Hz), 7.39-7.46 (4H, m), 7.5 (2H, d, $J = 8.5$ Hz), 7.6 (2H, d, $J = 7.5$ Hz). $\delta_{\text{C}}(\text{CDCl}_3)$ 126.0, 126.6, 127.4, 127.85, 127.88, 132.4, 138.6, 139.0. GCMS-purity: >98%.

4-Cyanobiphenyl 8d,³ (62 %), mp. 83.4-85.0 °C. $\delta_{\text{H}}(\text{CDCl}_3)$ 7.4 (1H, t, $J = 7.5$ Hz), 7.5 (2H, t, $J = 7.1$ Hz), 7.6 (2H, d, $J = 7.1$ Hz), 7.68 (2H, d, $J = 8.0$ Hz), 7.72 (2H, d, $J = 8.5$ Hz). $\delta_{\text{C}}(\text{CDCl}_3)$ 109.9, 117.9, 126.2, 126.7, 127.6, 128.1, 131.6, 138.1, 144.6. GCMS-purity: >98%.

Cleavage with bromine – Typical procedure

3-Bromobiphenyl 9a⁴ – To a suspension of resin **7a** (0.50 g, 0.80 mmol) in dichloroethane (10 mL) was added bromine (0.50 g, 3.2 mmol). After stirring at 60 °C for 12 h, the reaction was filtered. The resin was extracted with CH₂Cl₂ (2 x 5 mL) and THF (2 x 5 mL). To the combined organic phases was added aq. Na₂S₂O₃ (1 M, 5 mL). The organic solvents were removed *in vacuo*, and to the residue were added H₂O (20 mL) and EtOAc (20 mL). The phases were separated and the aqueous phase extracted with EtOAc (2 x 20 mL). The combined organic phases were washed with brine (20 mL) and dried over MgSO₄. The crude product was concentrated *in vacuo* and purified by column chromatography (heptane) to yield 113 mg (62%) of **9a** as an oil. $\delta_{\text{H}}(\text{CDCl}_3)$ 7.3 (1H, t, $J = 7.5$ Hz), 7.4 (1H, t, $J = 7.0$ Hz), 7.42-7.48 (3H, m), 7.5 (1H, d, $J = 7.5$ Hz), 7.6 (2H, t, $J = 7.5$ Hz), 7.7 (1H, t, $J = 1.9$ Hz).

$\delta_{\text{C}}(\text{CDCl}_3)$ 123.3, 126.2, 127.5, 128.27, 129.29, 130.58, 130.63, 130.7, 140.1, 143.7. GCMS-purity: >98%.

Compounds **9b-d** were prepared analogously.

3-Bromo-4'-methylbiphenyl 9b, (48 %), mp 42.9-43.2 °C, $\delta_{\text{H}}(\text{CDCl}_3)$ 2.4 (3H, s), 7.16-7.20 (2H m), 7.2 (1H, d, $J = 7.5$ Hz), 7.34-7.44 (4H, m), 7.6 (1H, t, $J = 1.9$ Hz). $\delta_{\text{C}}(\text{CDCl}_3)$ 21.5, 123.3, 126.0, 127.3, 130.0, 130.3, 130.4, 130.6, 137.2, 138.2, 143.7. GCMS-purity: 98%. Anal. calcd for $\text{C}_{13}\text{H}_{11}\text{Br}$: C, 63.18; H, 4.49. Found: C, 63.27; H, 4.31.

3-Bromo-4'-chlorobiphenyl 9c, (83 %), oil, $\delta_{\text{H}}(\text{CDCl}_3)$ 7.3 (1H, t, $J = 8.1$ Hz), 7.4 (2H, d, $J = 8.5$ Hz), 7.44-7.50 (4H, m), 7.7 (1H s). $\delta_{\text{C}}(\text{CDCl}_3)$ 123.4, 126.0, 128.8, 129.5, 130.4, 130.8, 130.9, 134.5, 138.5, 142.5. GCMS-purity: 98%. Anal. calcd for $\text{C}_{12}\text{H}_8\text{BrCl}$: C, 53.87; H, 3.01. Found: C, 53.88; H, 3.09.

3'-Bromobiphenyl-4-carbonitrile 9d, (77 %), mp 48.6-49.8 °C, $\delta_{\text{H}}(\text{CDCl}_3)$ 7.4 (1H, t, $J = 7.5$ Hz), 7.51 (1H, d, $J = 8.0$ Hz), 7.54 (1H, d, $J = 8.0$ Hz), 7.6 (2H, d, $J = 8.5$ Hz), 7.71-7.75 (3H, m) (signals of an unknown impurity found at 5.9 ppm and 7.6 ppm). $\delta_{\text{C}}(\text{CDCl}_3)$ 112.0, 119.1, 123.6, 126.3, 128.2, 130.7, 132.0, 133.1, 134.6, 141.6, 144.5 (signal of an unknown impurity found at 134.6 ppm).

Cleavage with iodine – Typical procedure

3-Iodobiphenyl 10a.⁵ – To a suspension of resin **7a** (0.50 g, 0.80 mmol) in THF (10 mL) was added iodine (0.39 g, 1.6 mmol). After stirring at 60 °C for 12 h, the reaction was filtered, and the resin was extracted with THF (3 x 5 mL). To the combined organic phases was added aq. $\text{Na}_2\text{S}_2\text{O}_3$ (1 M, 5 mL), and the organic solvent was removed *in vacuo*. To the residue were added H_2O (20 mL) and EtOAc (20 mL). The phases were separated, and the aqueous phase extracted with EtOAc (2 x 20 mL). The combined organic phases were washed with brine (20 mL) and dried over MgSO_4 . The crude product was purified by column chromatography (heptane) to yield 131 mg (60%) of **10a** as viscous oil. $\delta_{\text{H}}(\text{CDCl}_3)$ 7.2 (1H, t, $J = 8.0$ Hz), 7.36 (1H, t, $J = 7.5$ Hz), 7.43 (2H, t, $J = 7.1$ Hz), 7.51-7.55 (3H, m),

7.7 (1H, d, $J = 8.0$ Hz), 7.9 (1H, t, $J = 1.4$ Hz). $\delta_{\text{C}}(\text{CDCl}_3)$ 95.2, 126.8, 127.5, 128.3, 129.3, 130.8, 136.56, 136.60, 140.0, 143.8. GCMS-purity: 98%.

Compounds **10b-d** were prepared analogously.

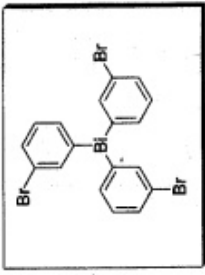
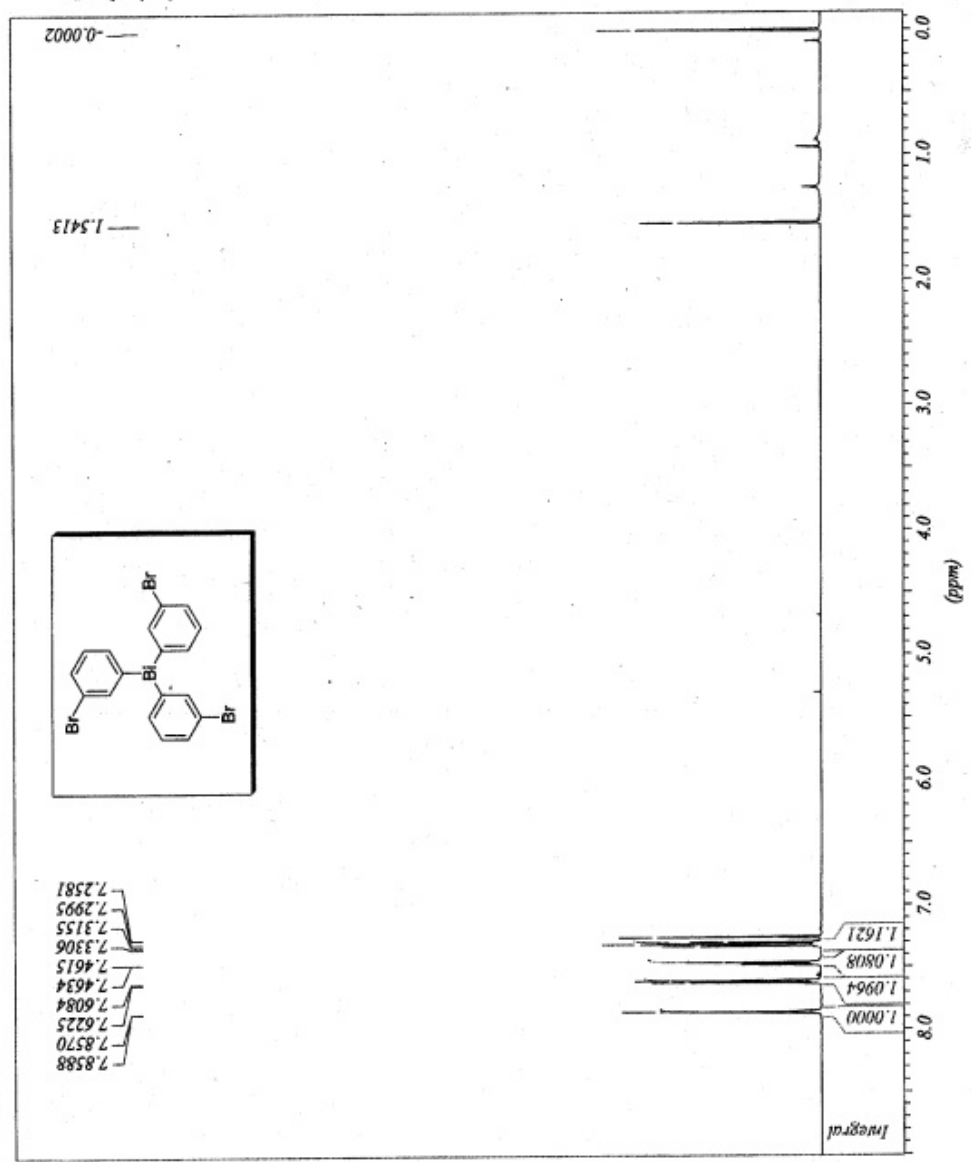
3-Iodo-4'-methylbiphenyl 10b, (69 %), oil, $\delta_{\text{H}}(\text{CDCl}_3)$ 2.4 (3H, s), 7.1 (1H, t, $J = 8.0$ Hz), 7.2 (2H, d, $J = 7.5$ Hz), 7.4 (2H, d, $J = 8.0$ Hz), 7.5 (1H, d, $J = 8.0$ Hz), 7.6 (1H, d, $J = 7.5$ Hz), 7.9 (1H, s). $\delta_{\text{C}}(\text{CDCl}_3)$ 21.5, 95.2, 126.6, 127.3, 130.0, 130.8, 136.3, 136.4, 137.1, 138.1, 143.8. GCMS-purity: >98%. Anal. calcd for $\text{C}_{13}\text{H}_{11}\text{I}$: C, 53.08; H, 3.77. Found: C, 53.09; H, 3.81.

4'-Chloro-3-iodobiphenyl 10c, (66 %), oil, $\delta_{\text{H}}(\text{CDCl}_3)$ 7.2 (1H, t, $J = 7.5$ Hz), 7.4 (2H, d, $J = 8.5$ Hz), 7.46 (2H, d, $J = 8.5$ Hz), 7.50 (1H, d, $J = 8.0$ Hz), 7.7 (1H, d, $J = 8.0$ Hz), 7.9 (1H, s). $\delta_{\text{C}}(\text{CDCl}_3)$ 95.3, 126.6, 128.8, 129.5, 130.9, 134.4, 136.4, 138.9, 138.5, 142.6. GCMS-purity: 97%. Anal. calcd for $\text{C}_{12}\text{H}_8\text{ClI}$: C, 45.82; H, 2.56. Found: C, 45.65; H, 2.42.

3'-Iodobiphenyl-4-carbonitrile 10d, (65 %), mp 90.0-90.6°C. $\delta_{\text{H}}(\text{CDCl}_3)$ 7.2 (1H, t, $J = 7.5$ Hz), 7.5 (1H, d, $J = 7.5$ Hz), 7.6 (2H, d, $J = 8.5$ Hz), 7.72-7.77 (3H, m), 7.9 (1H, s). $\delta_{\text{C}}(\text{CDCl}_3)$ 95.4, 112.0, 119.1, 126.9, 128.1, 131.1, 133.1, 136.6, 137.9, 141.7, 144.4. GCMS-purity: >98%. Anal. calcd for $\text{C}_{13}\text{H}_8\text{IN}$: C, 51.17; H, 2.64; N, 4.59. Found: C, 51.16; H, 2.46 N, 4.48.



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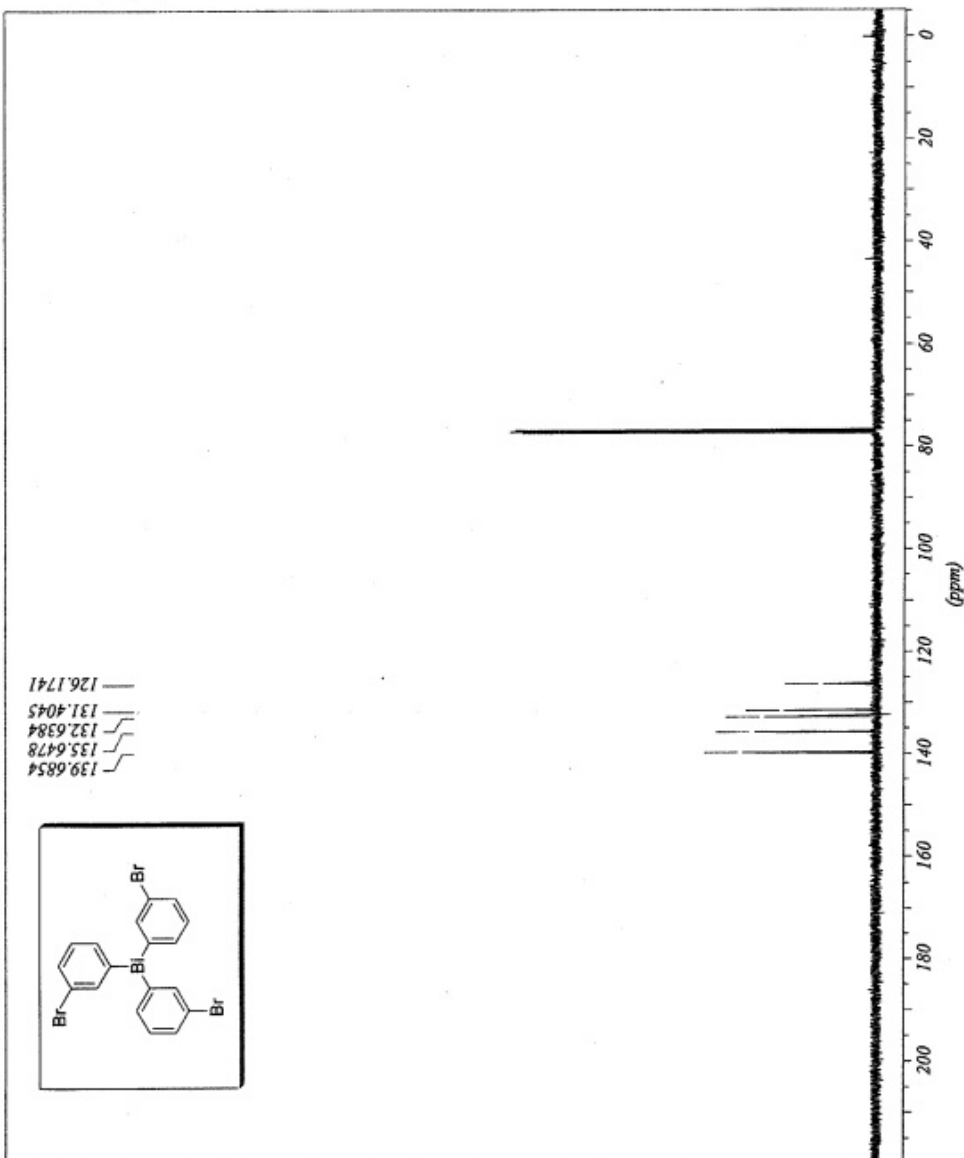


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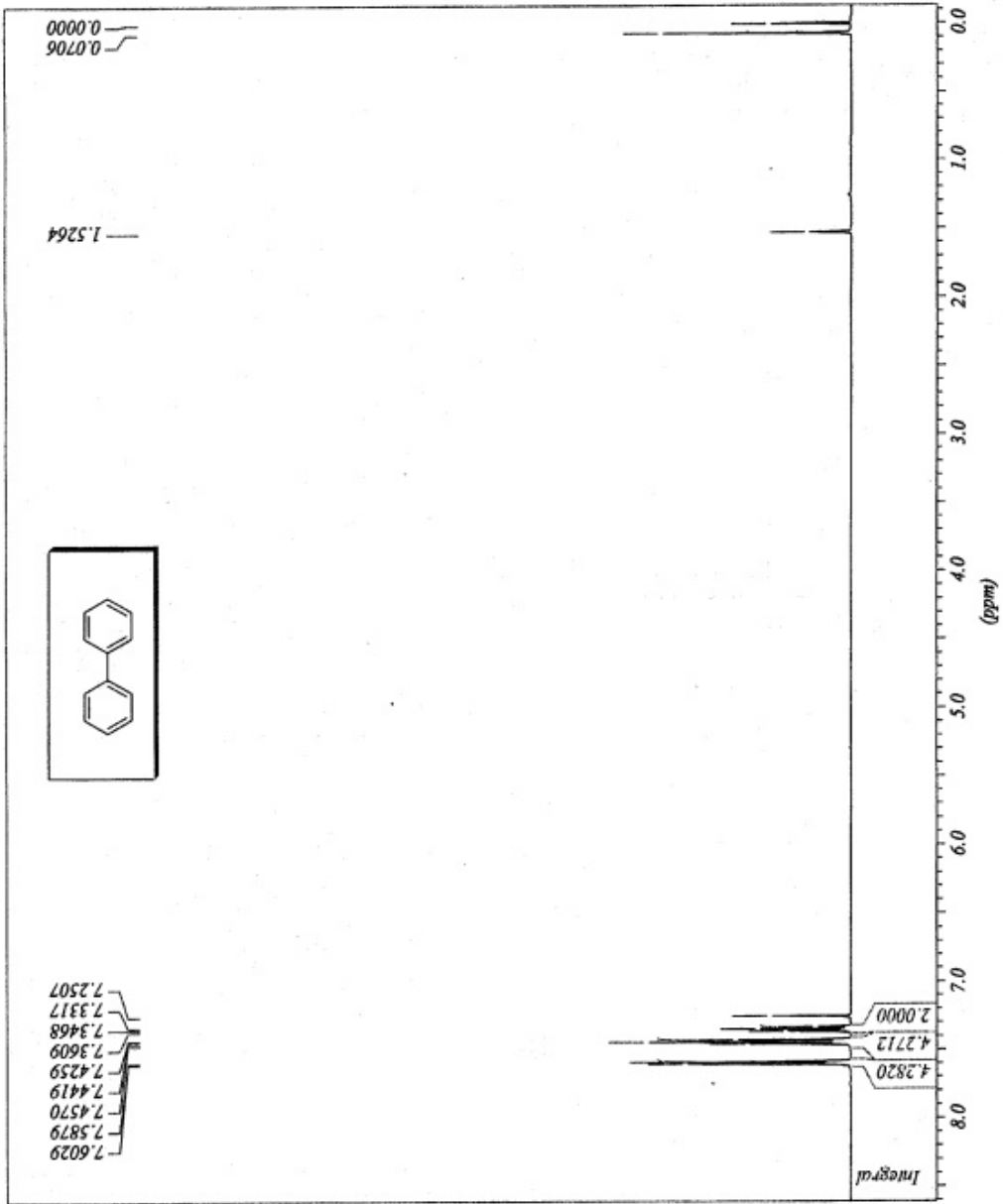
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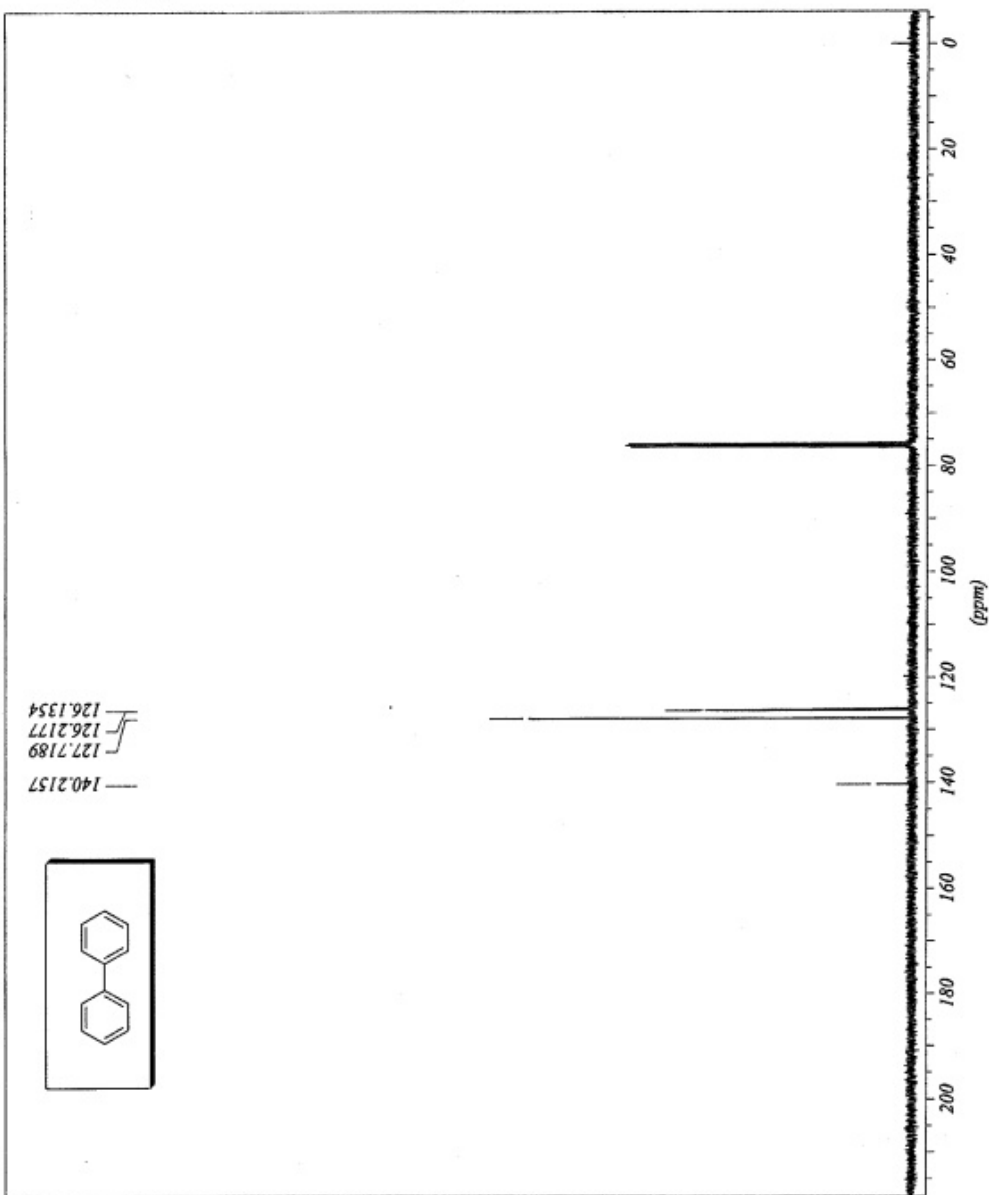
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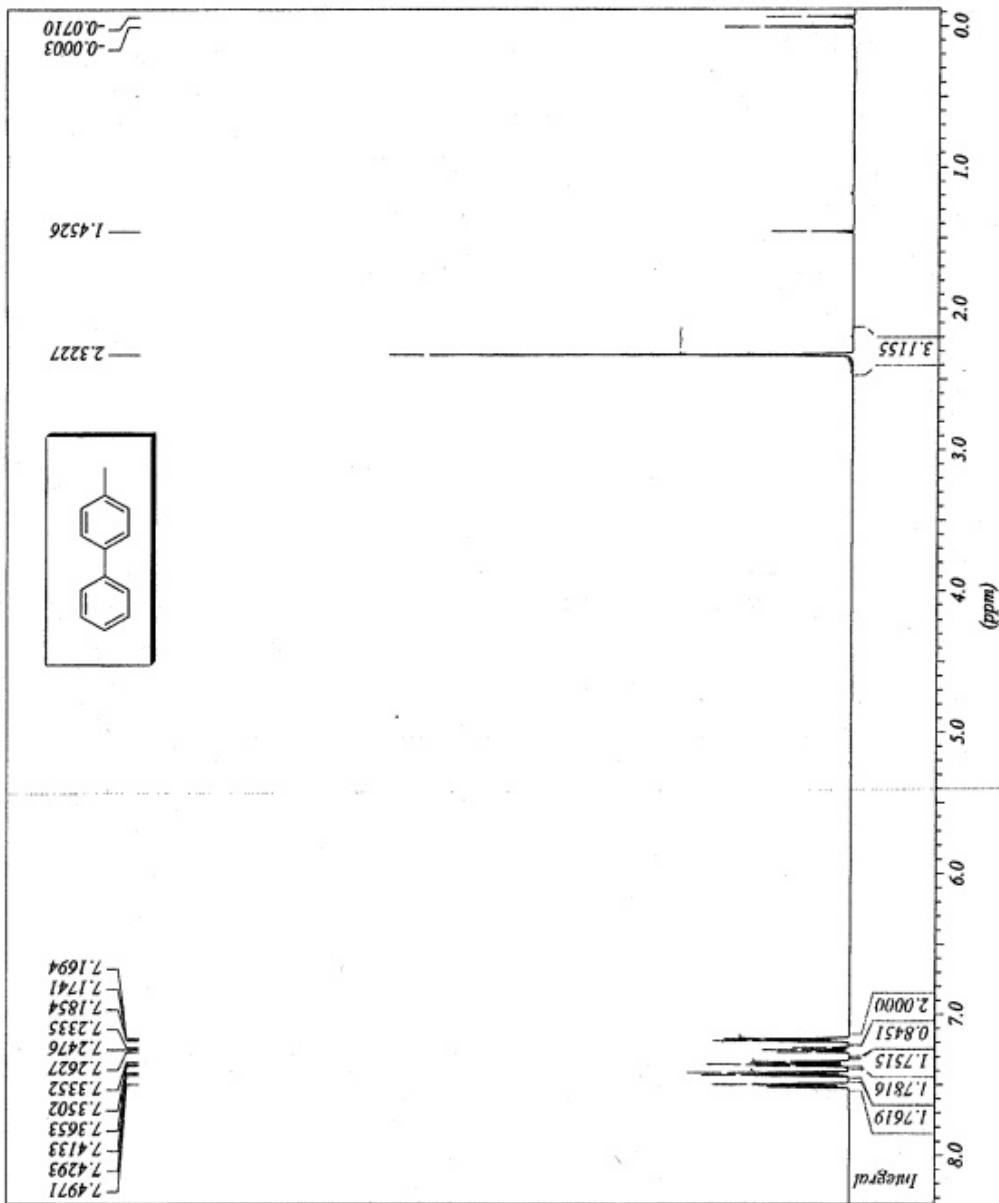
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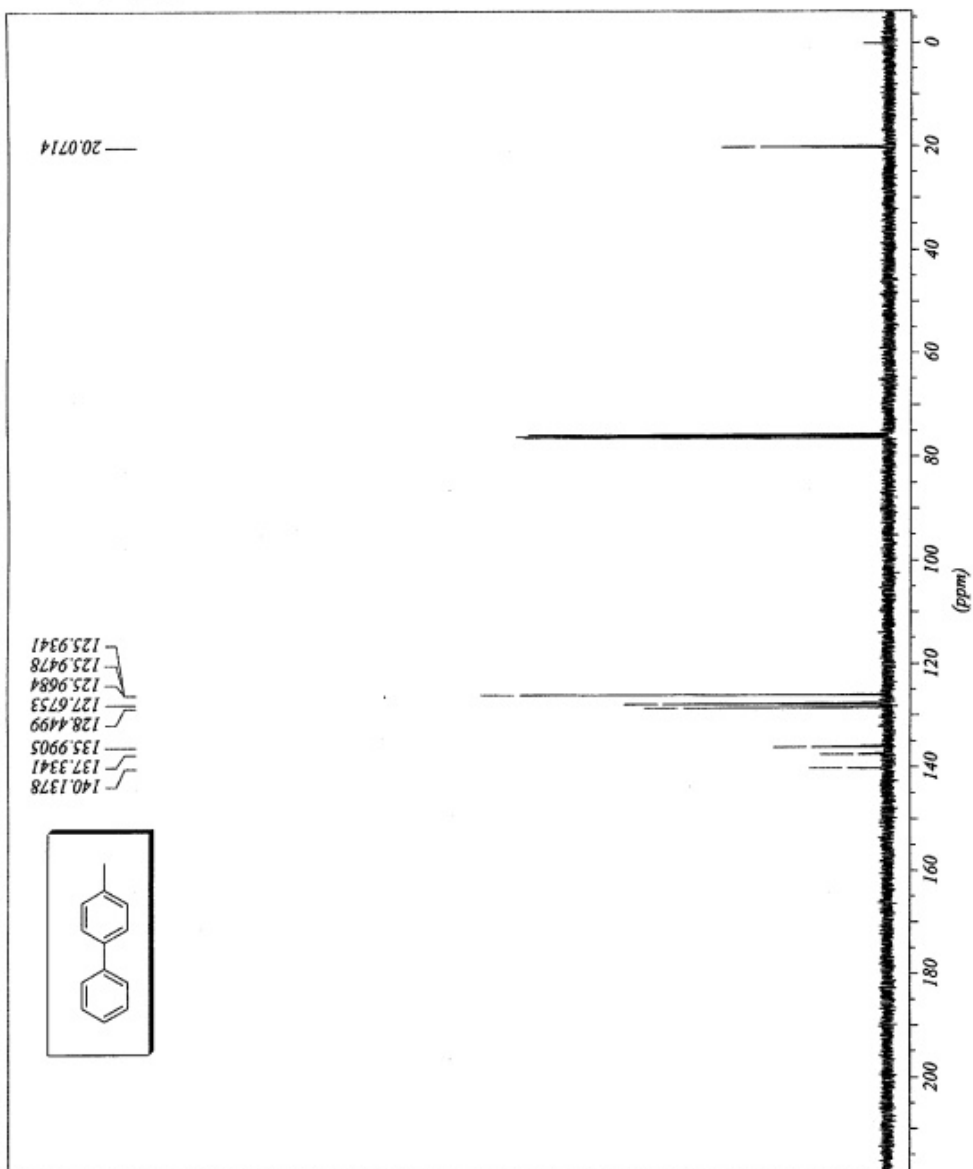
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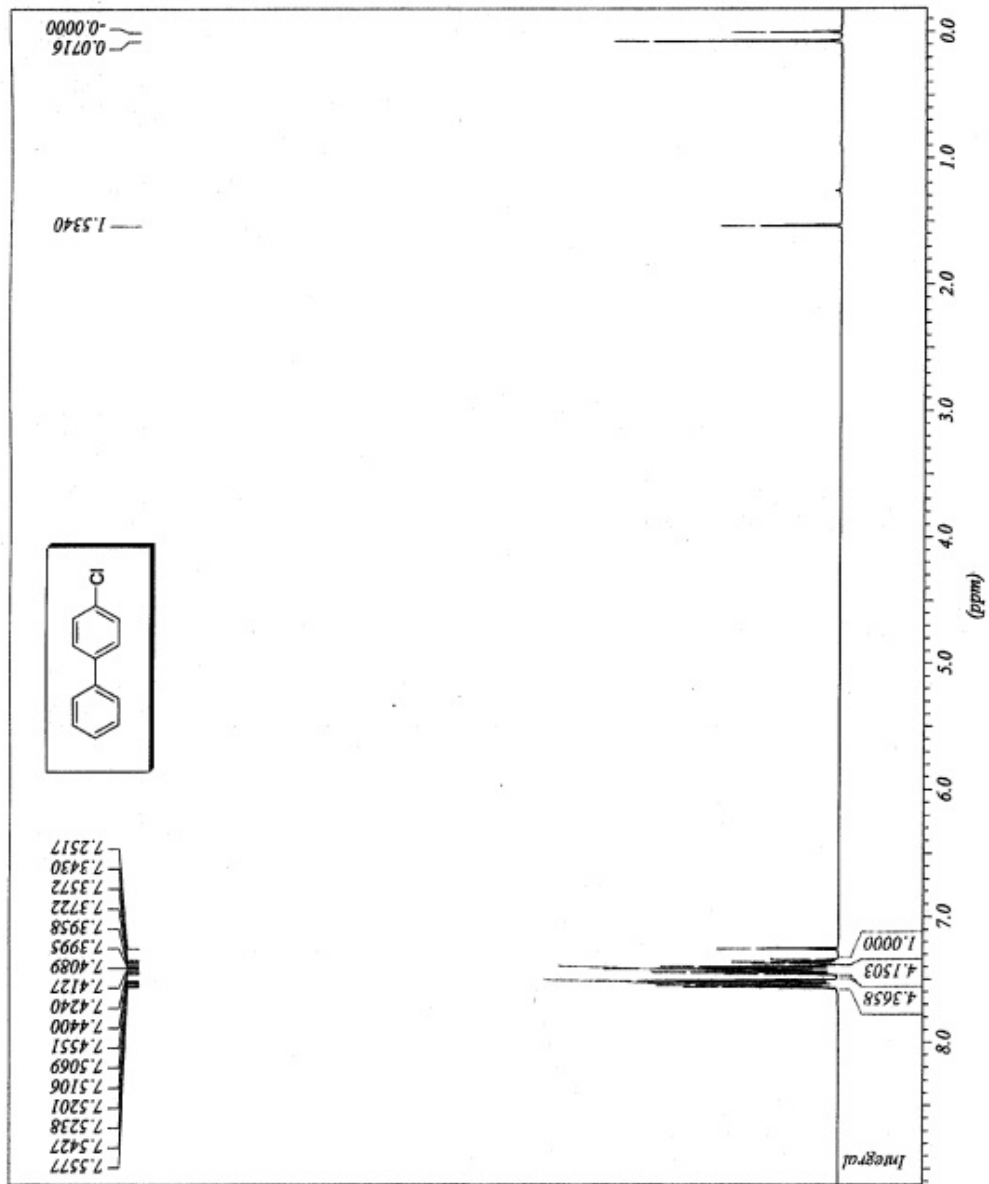
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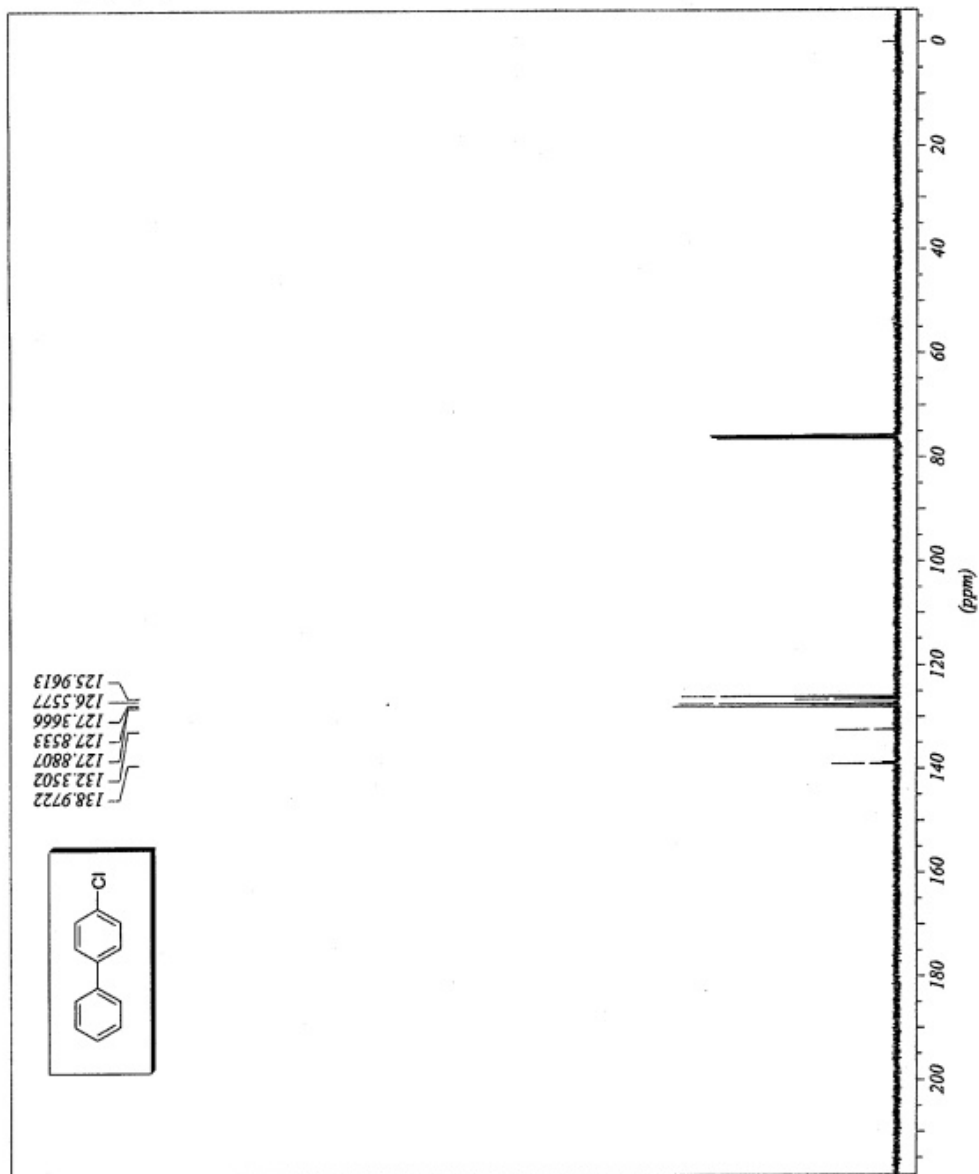
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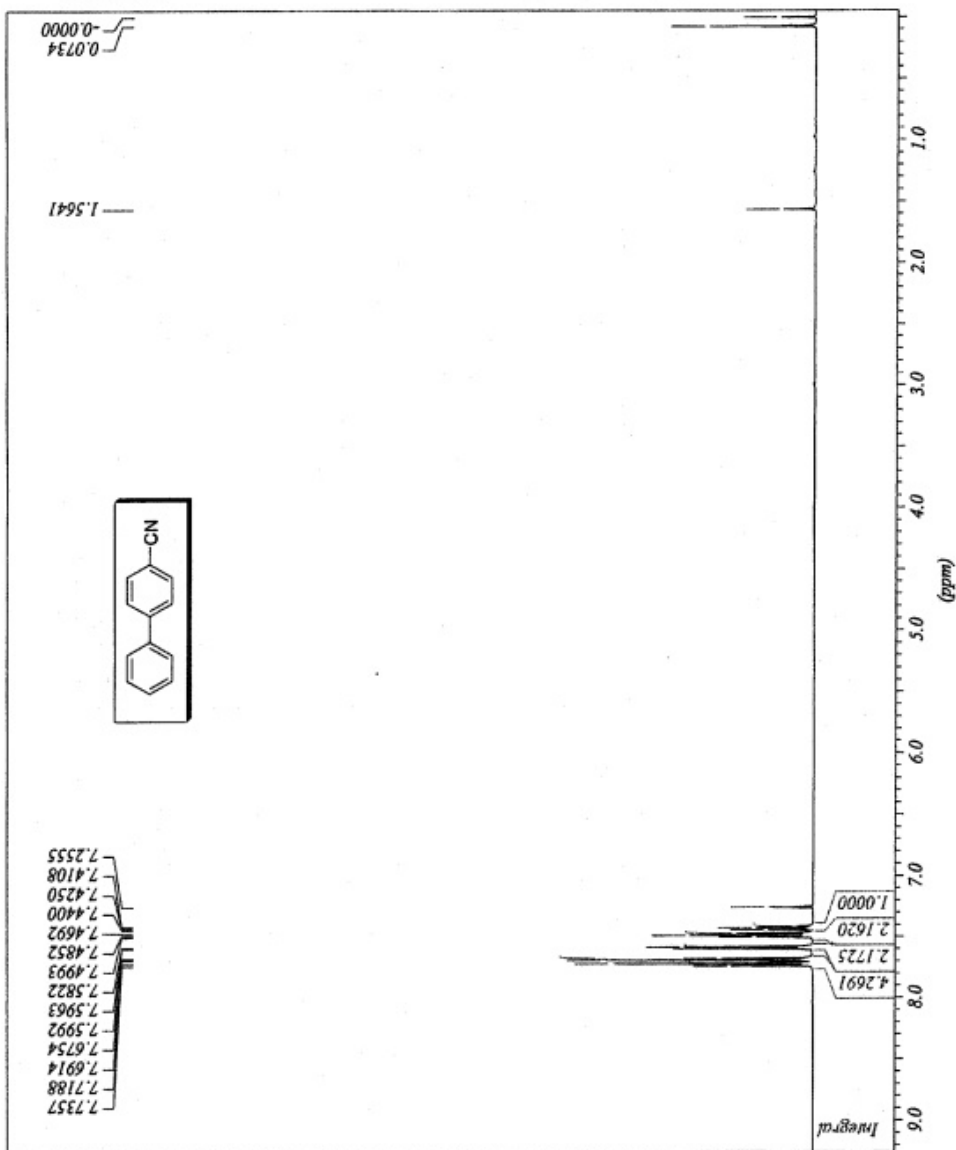
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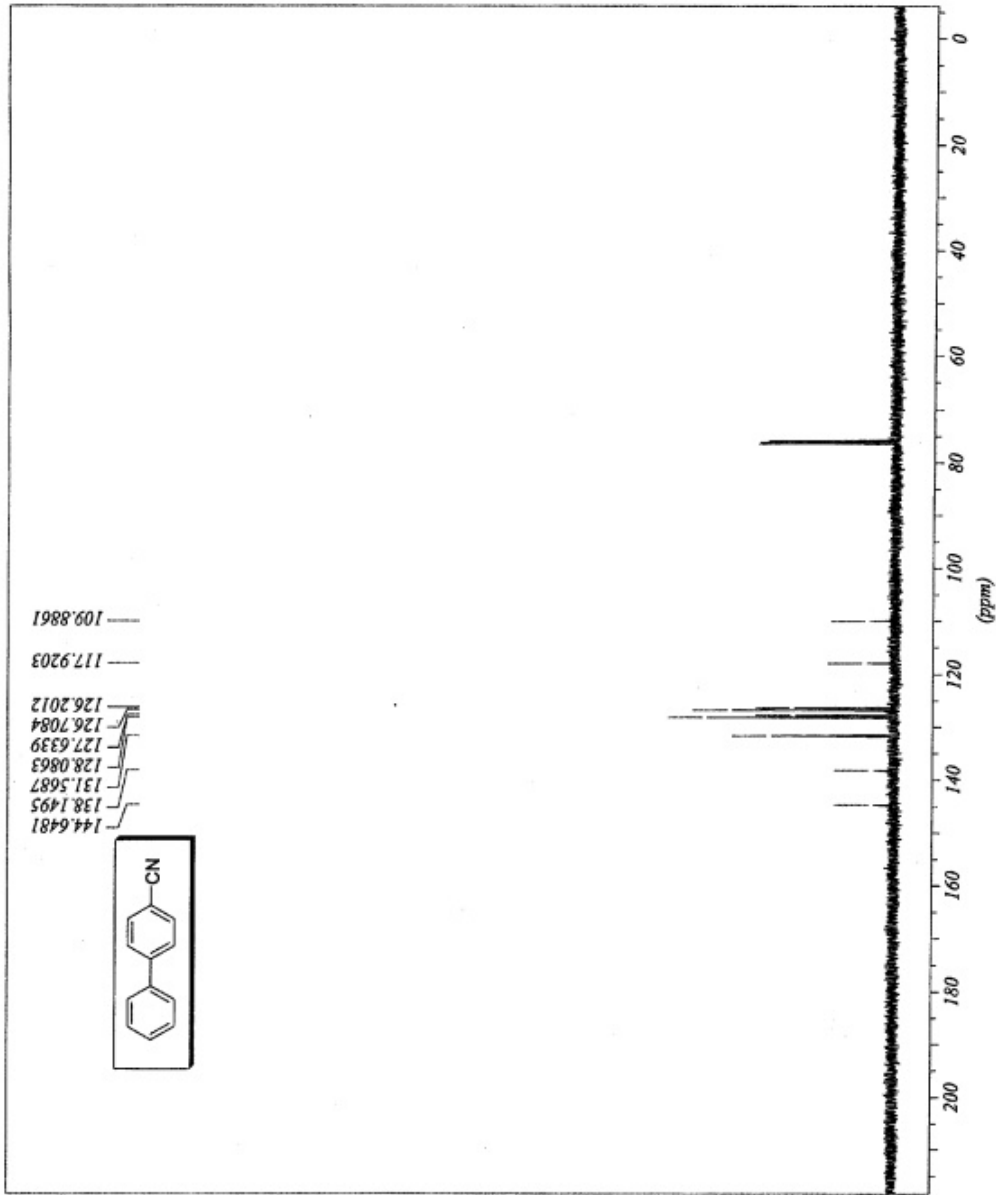
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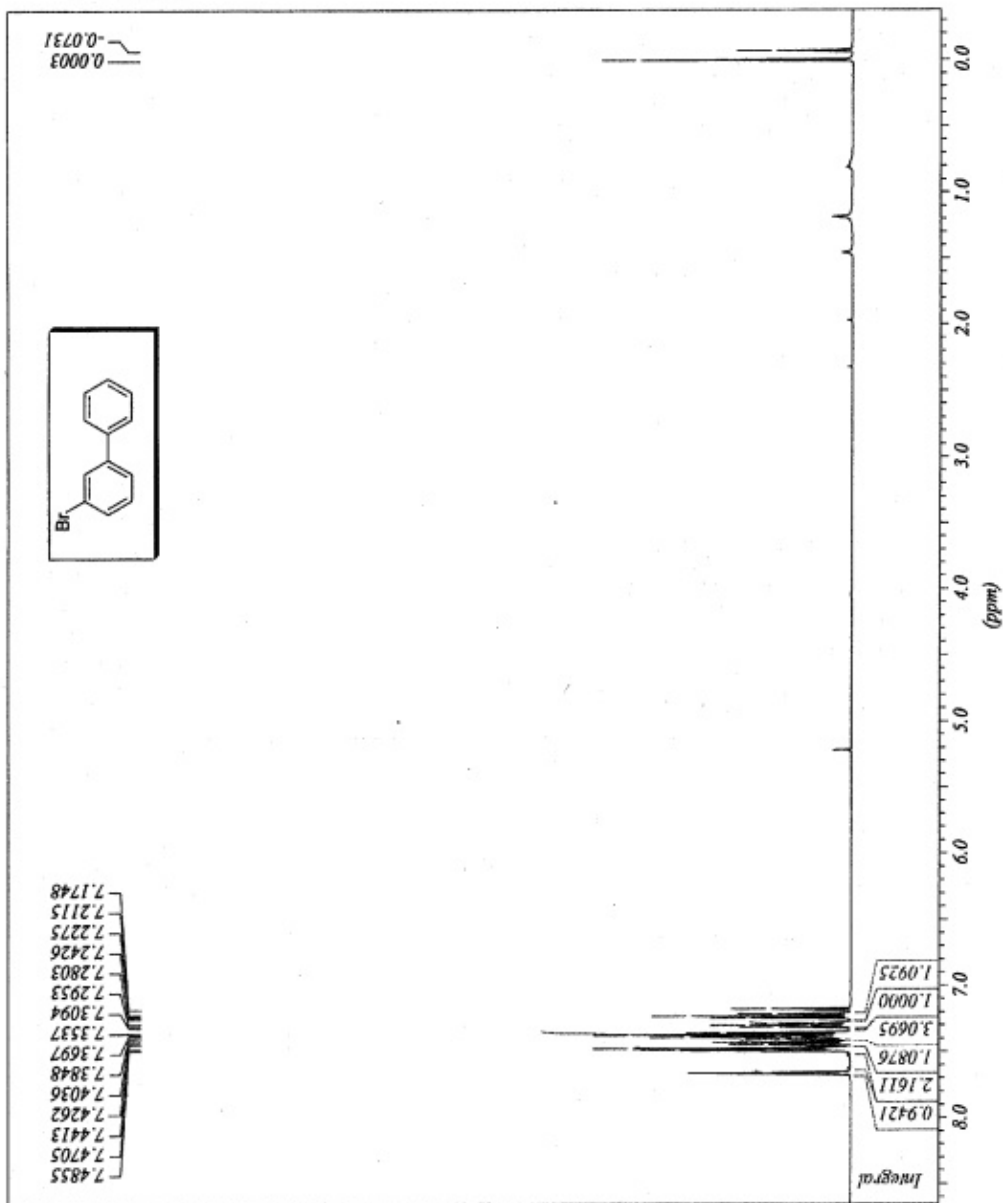
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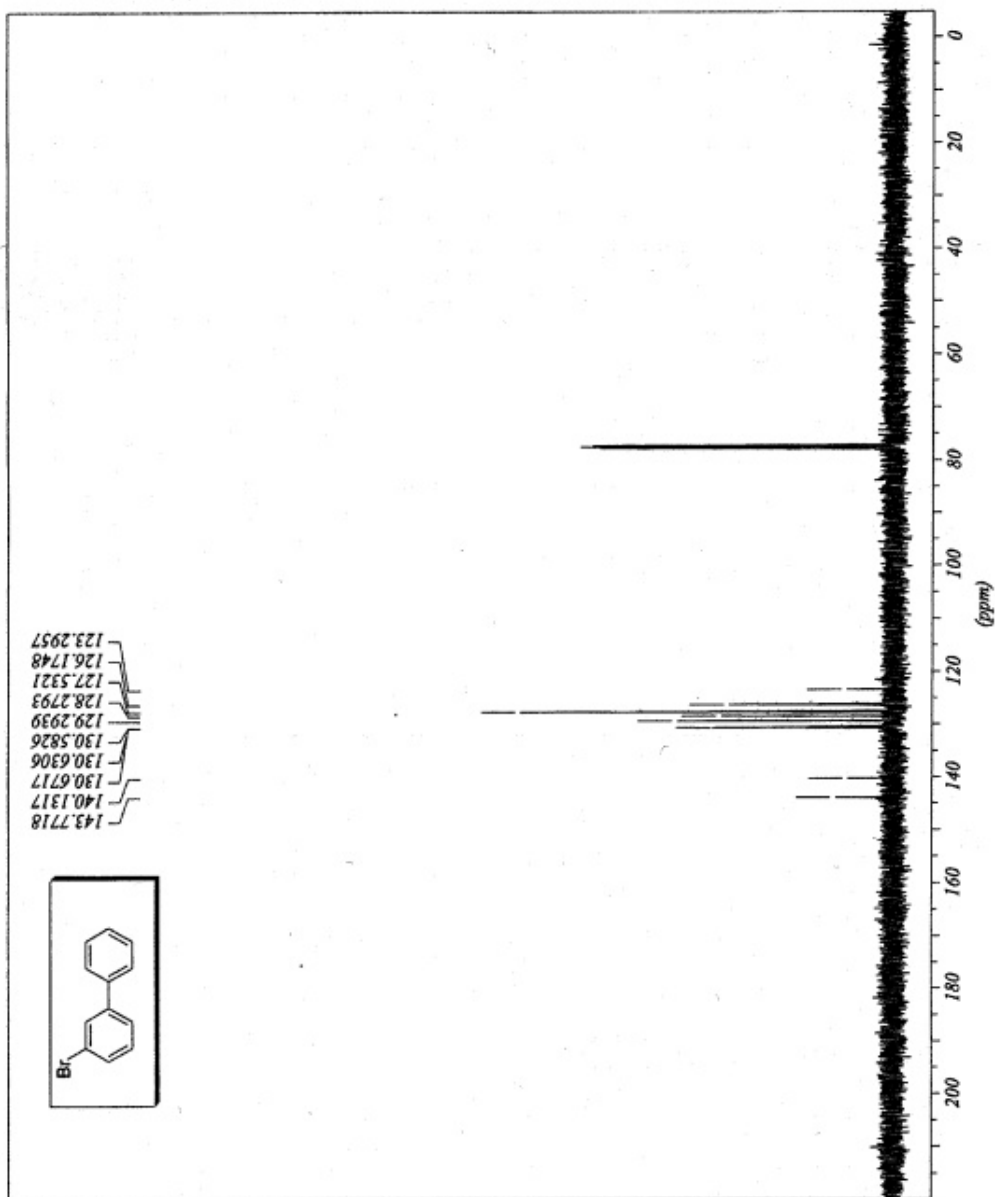


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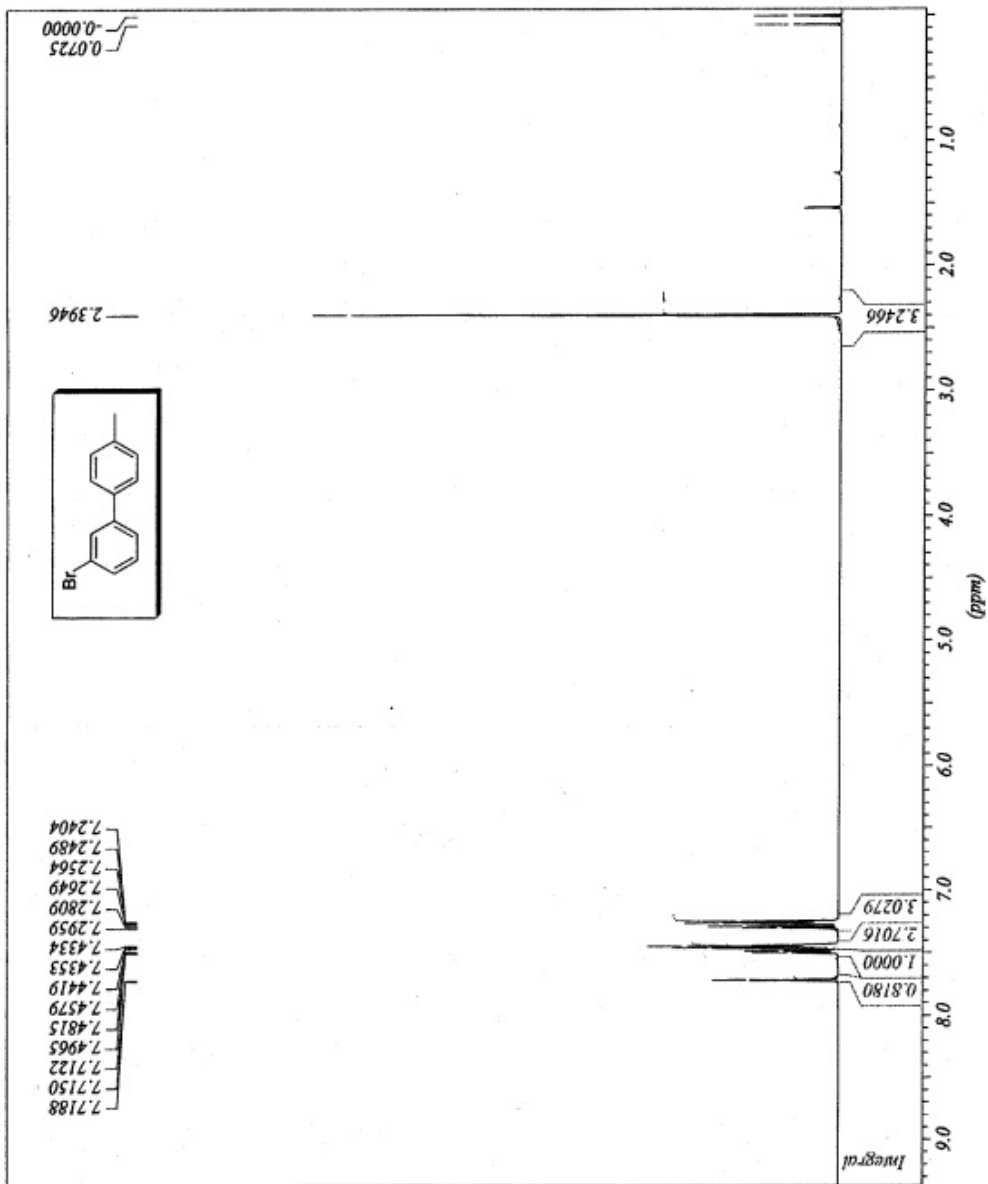




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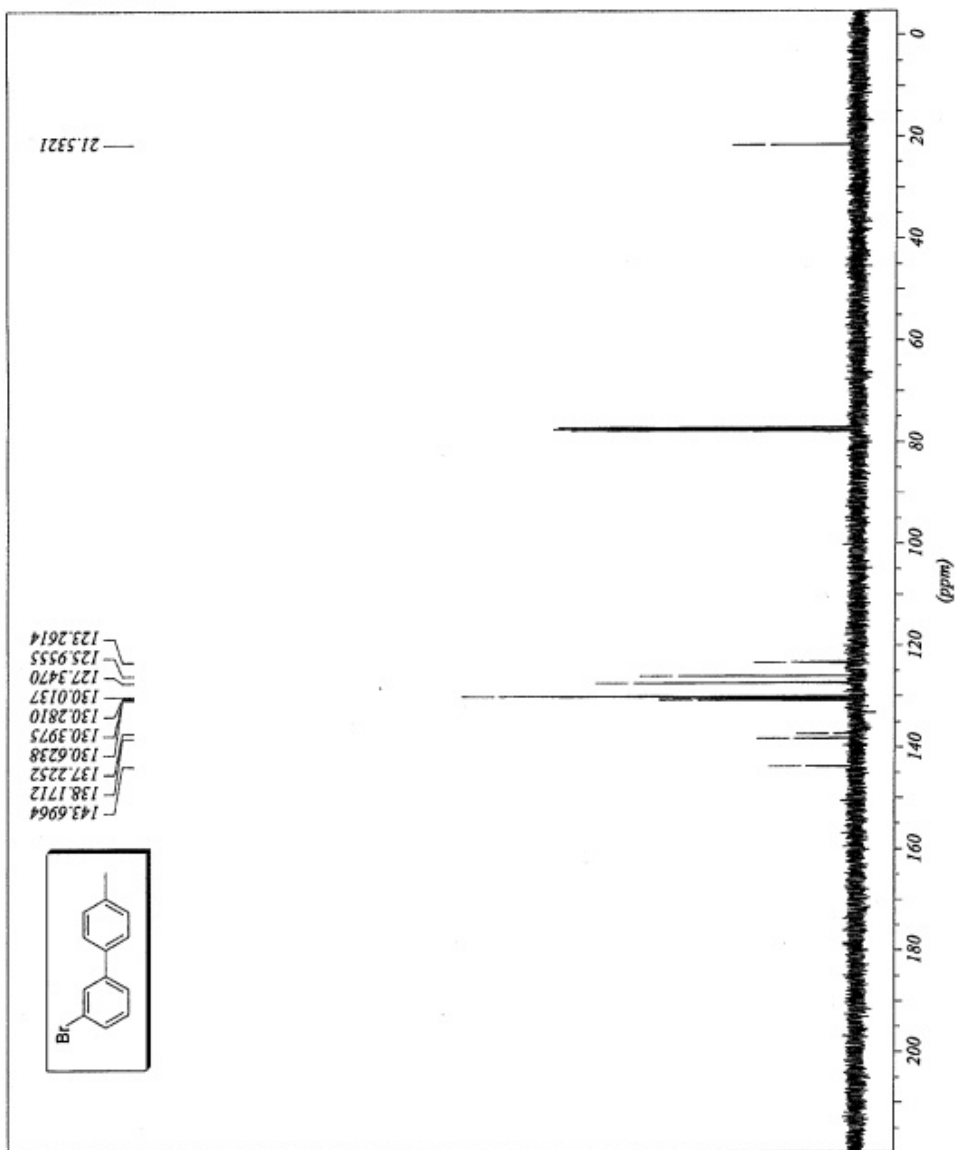




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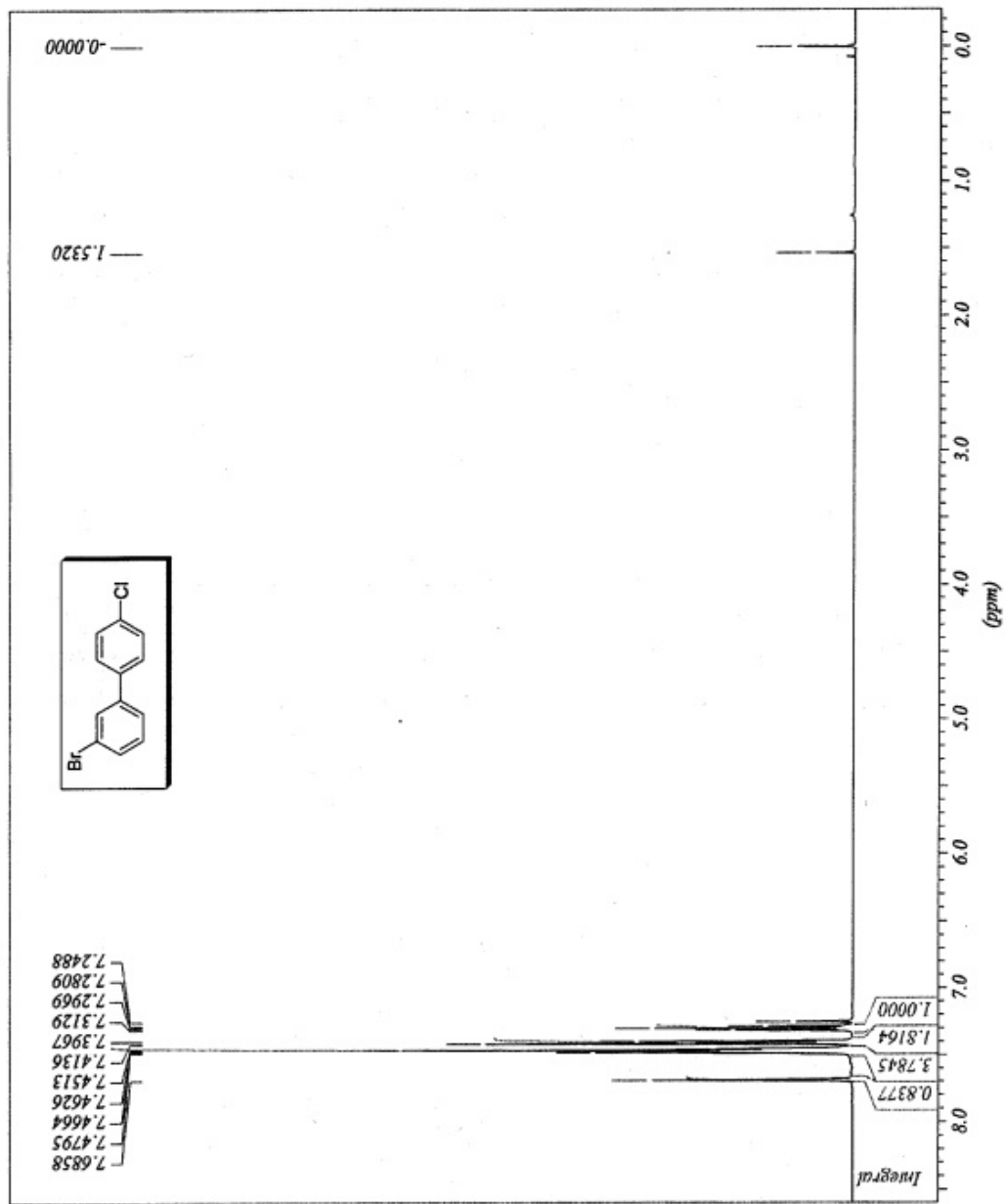
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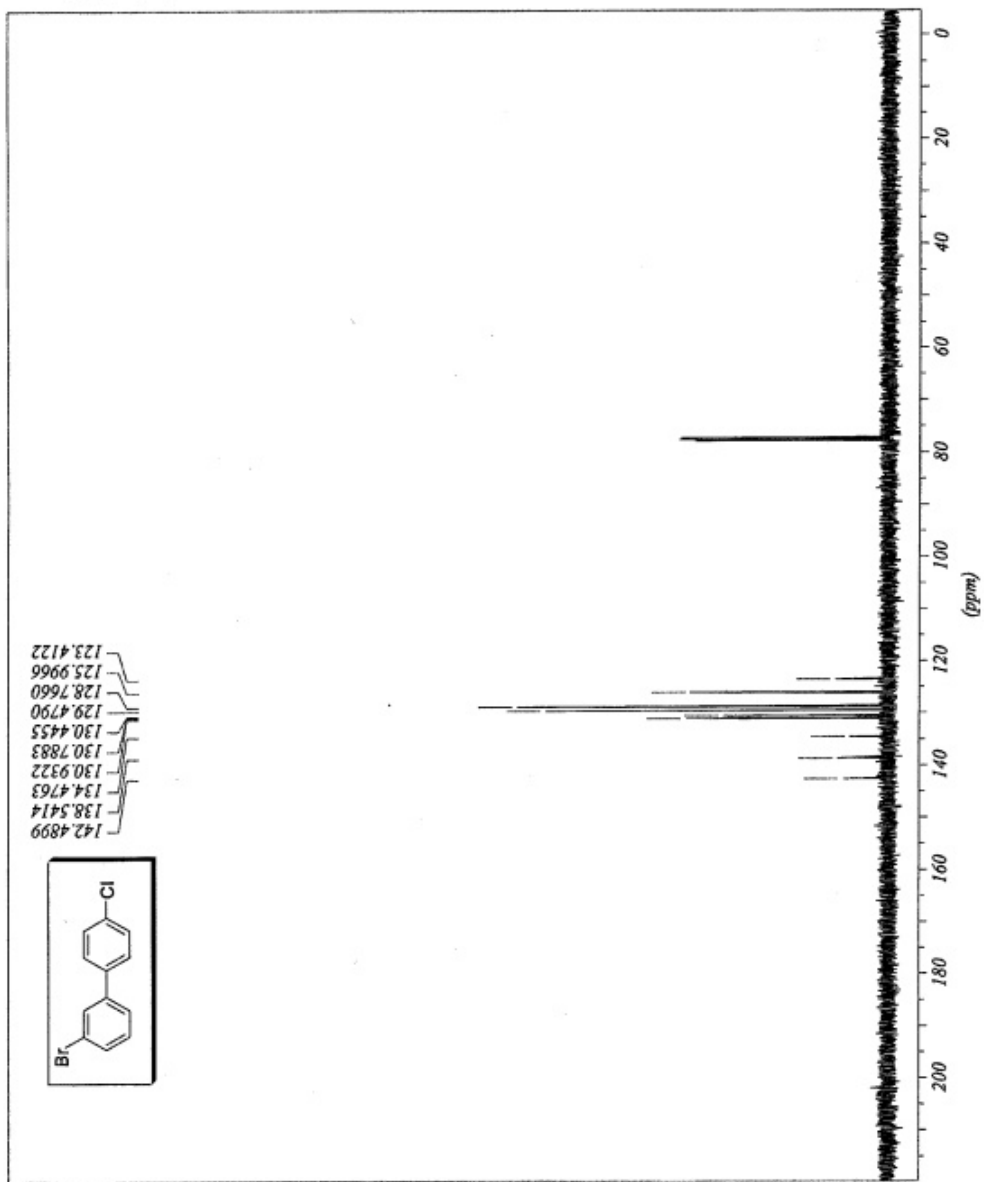
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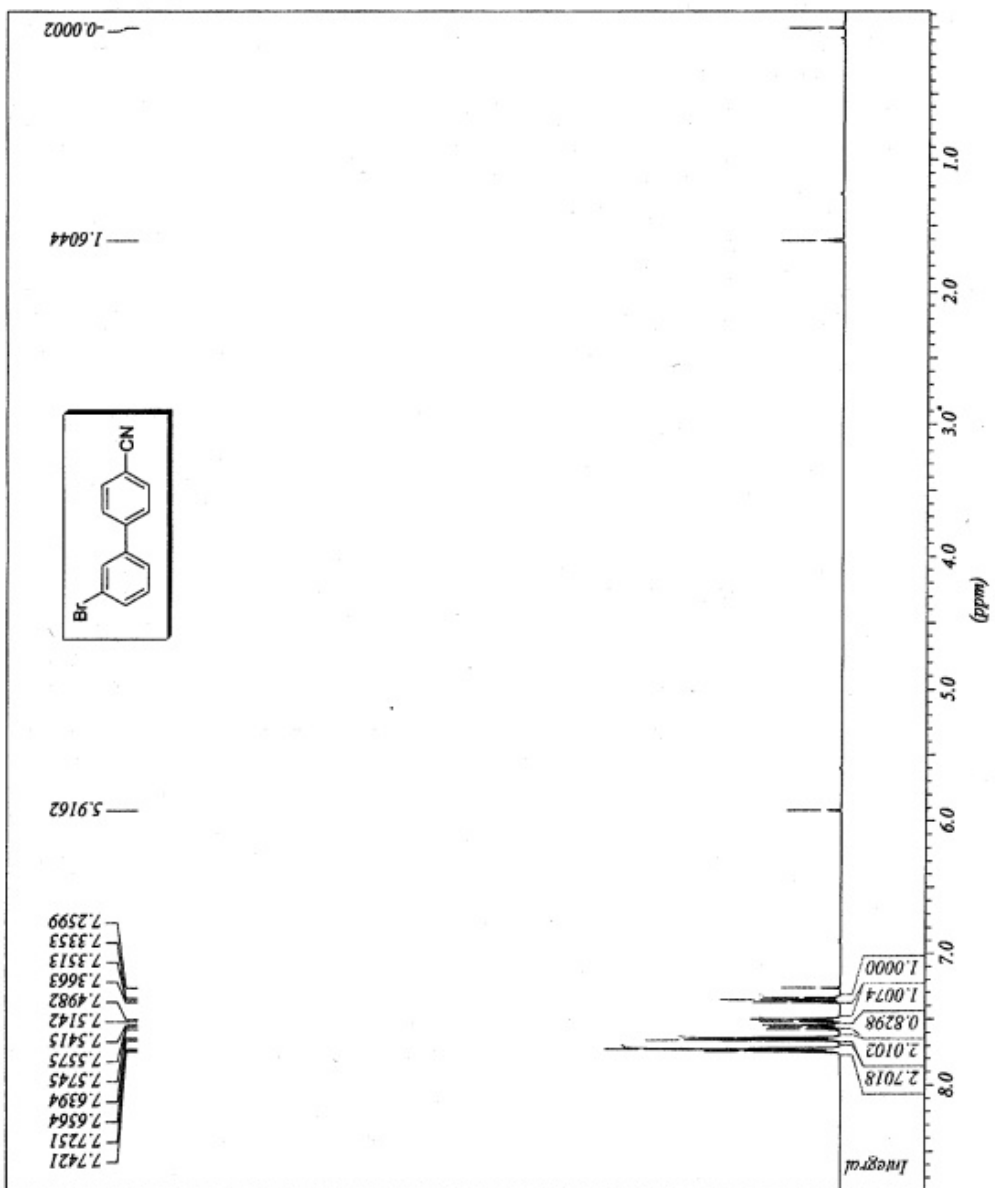
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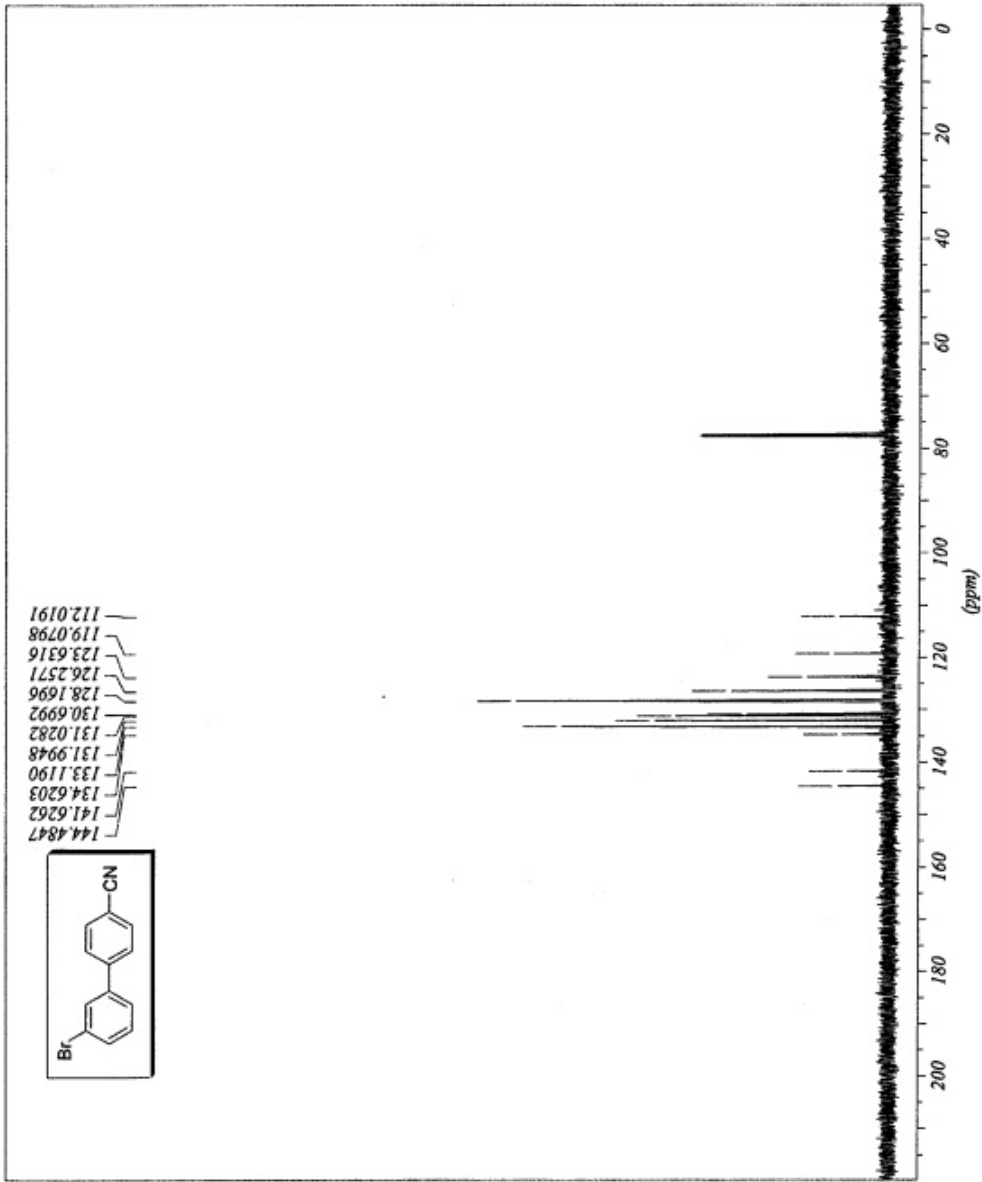


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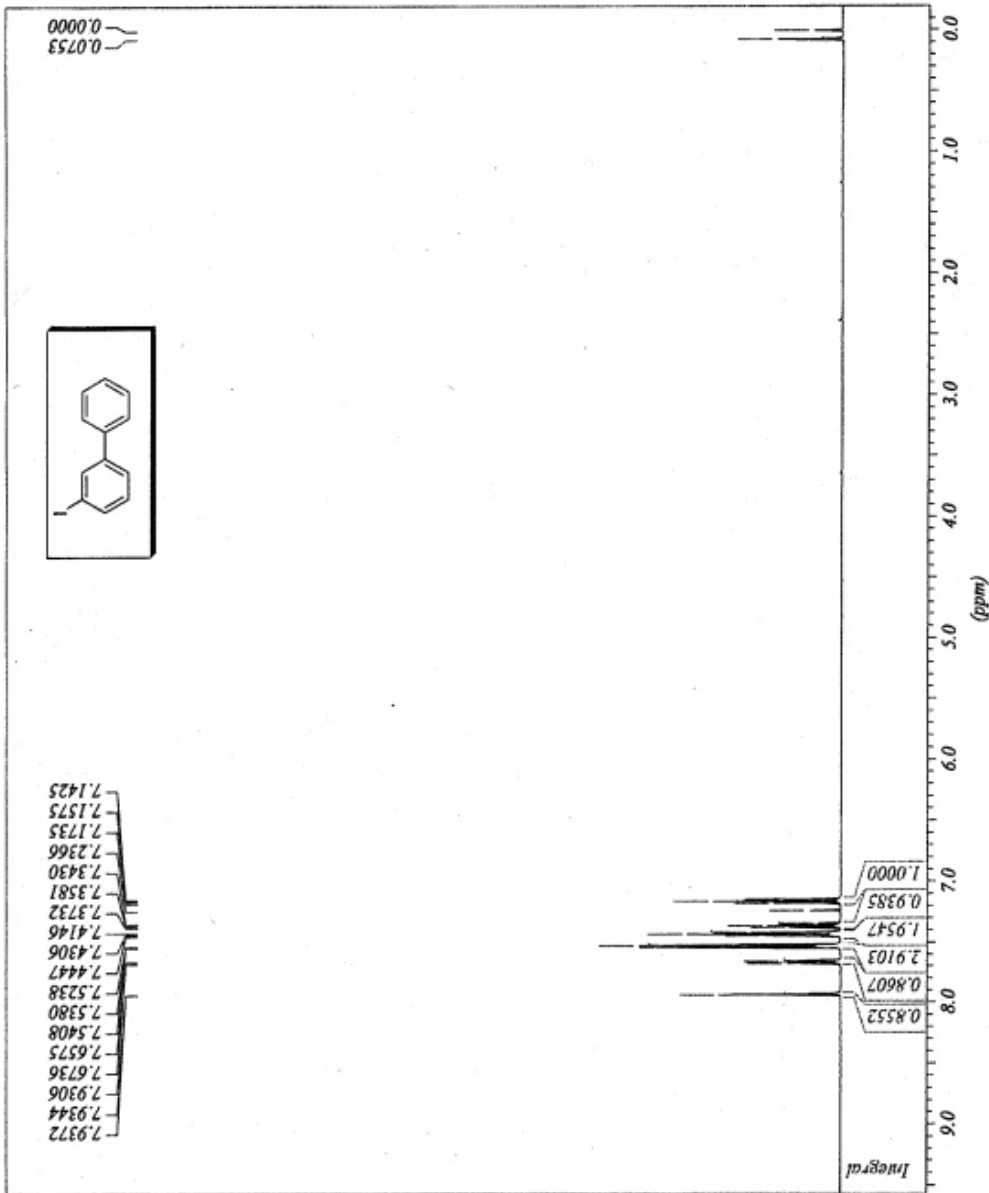
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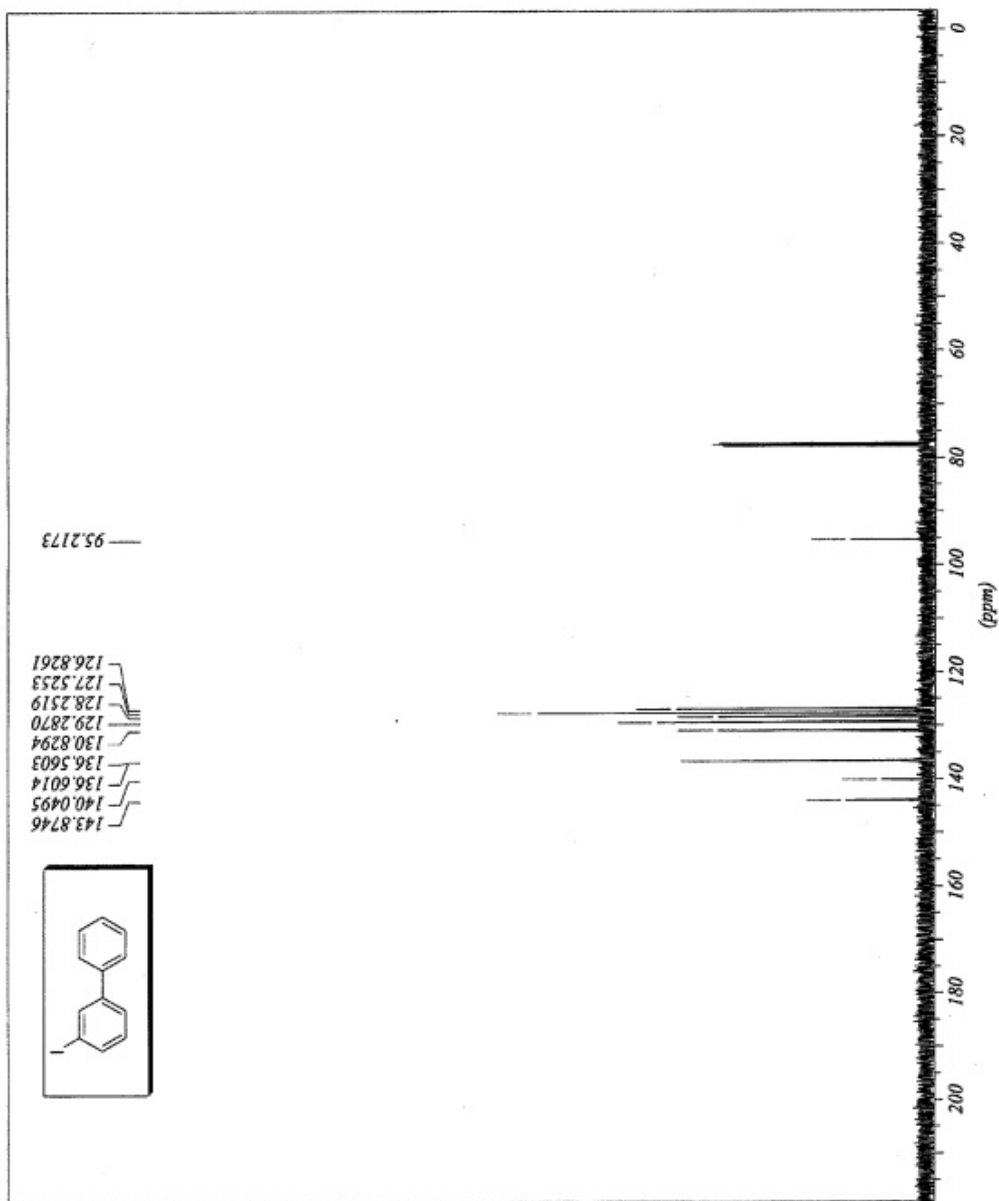
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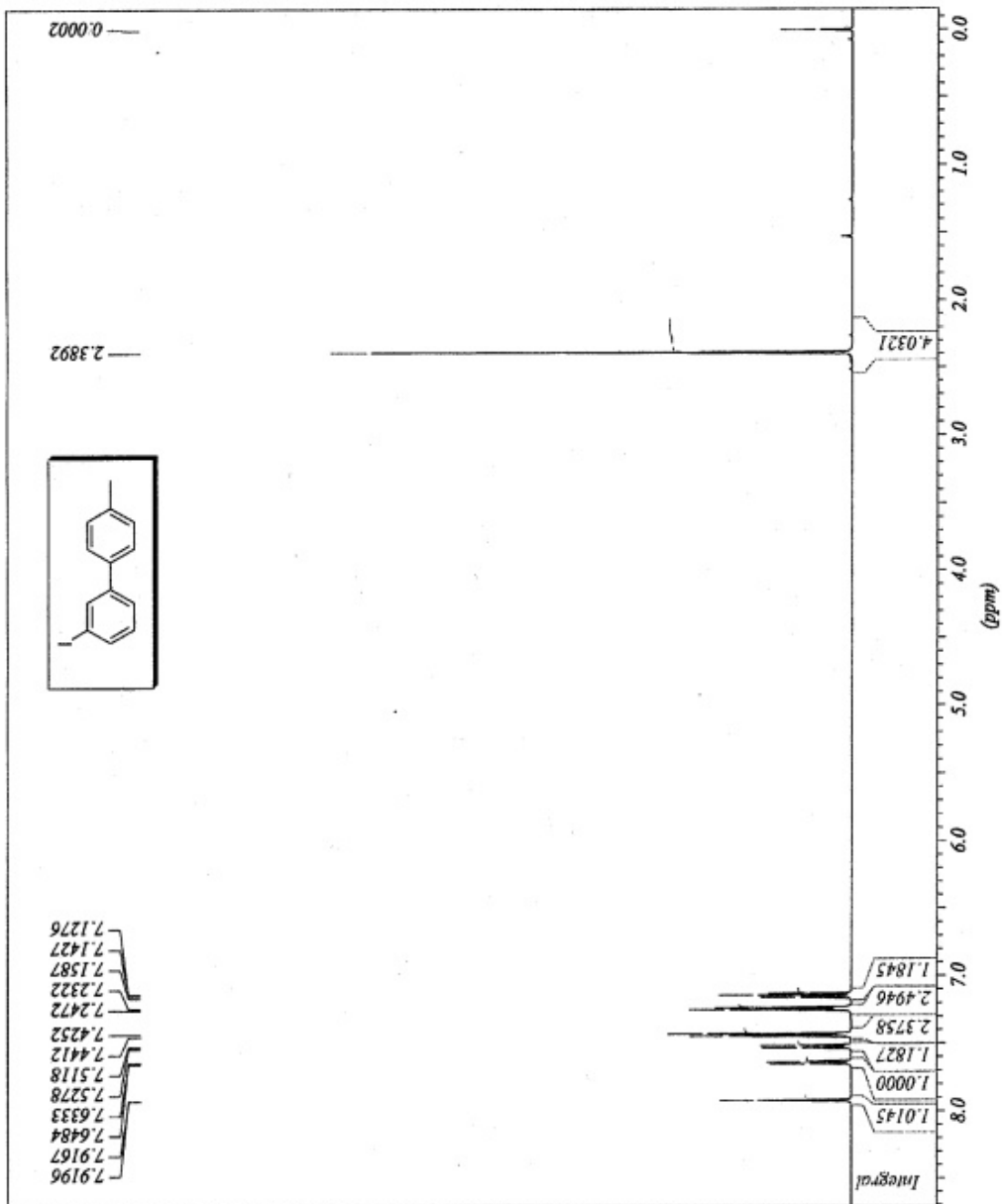
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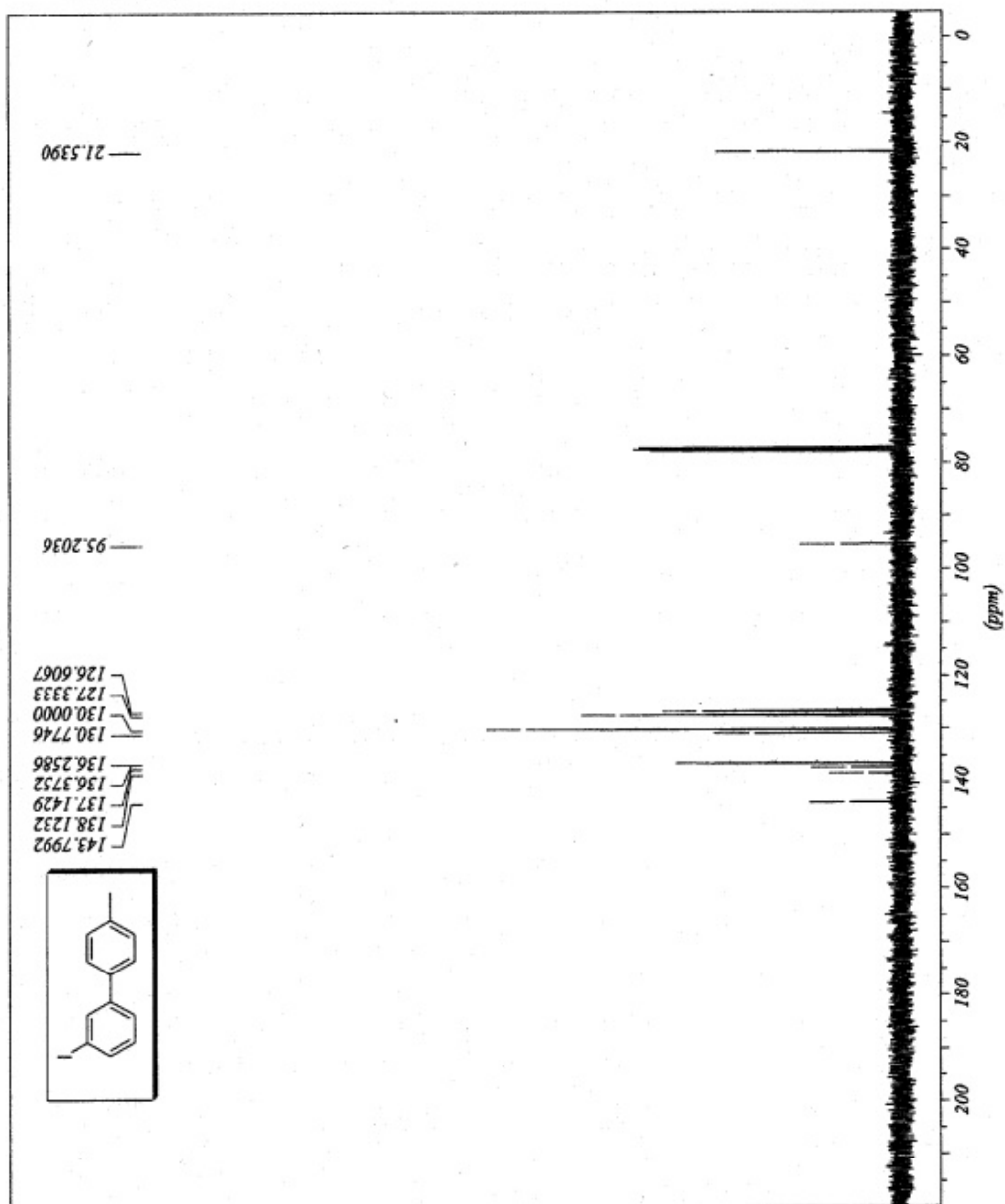
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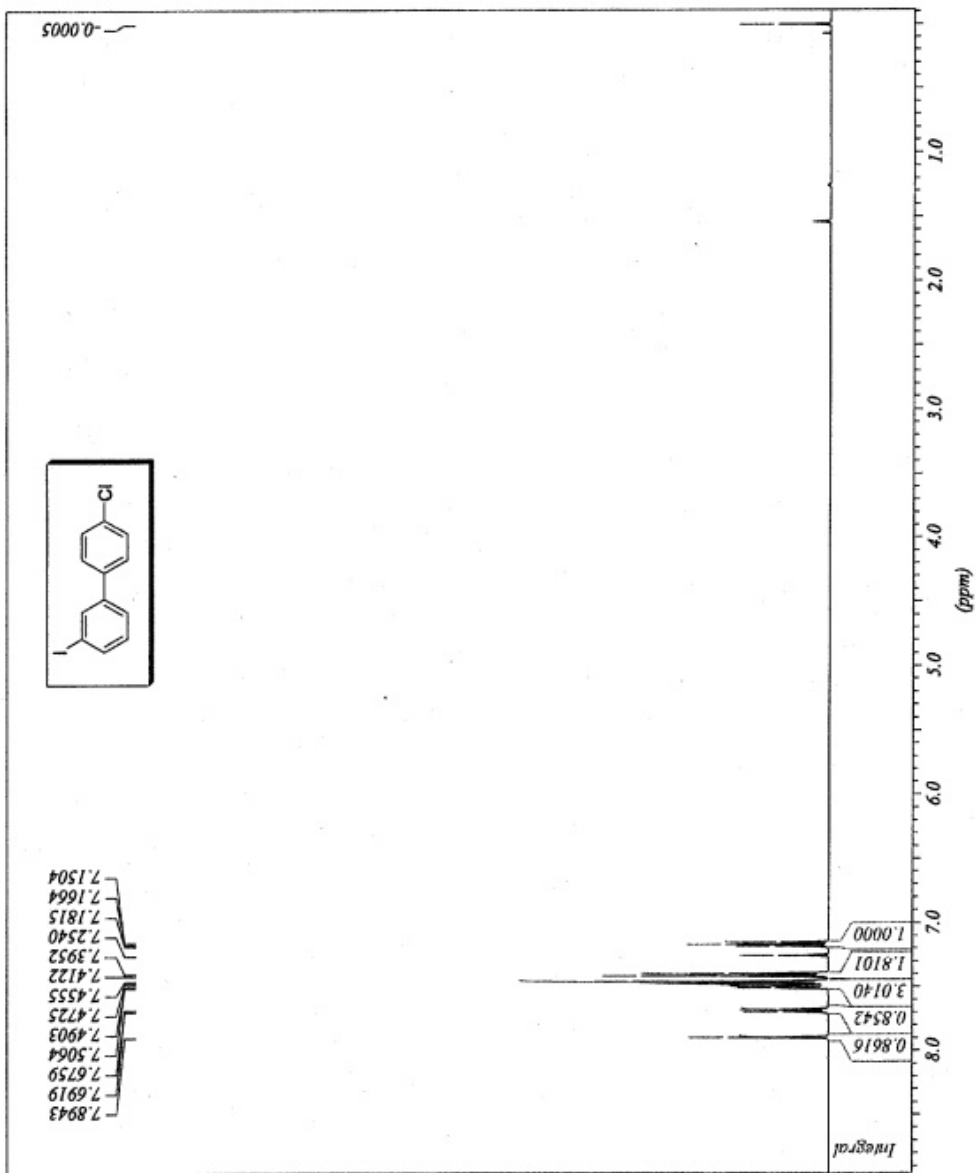
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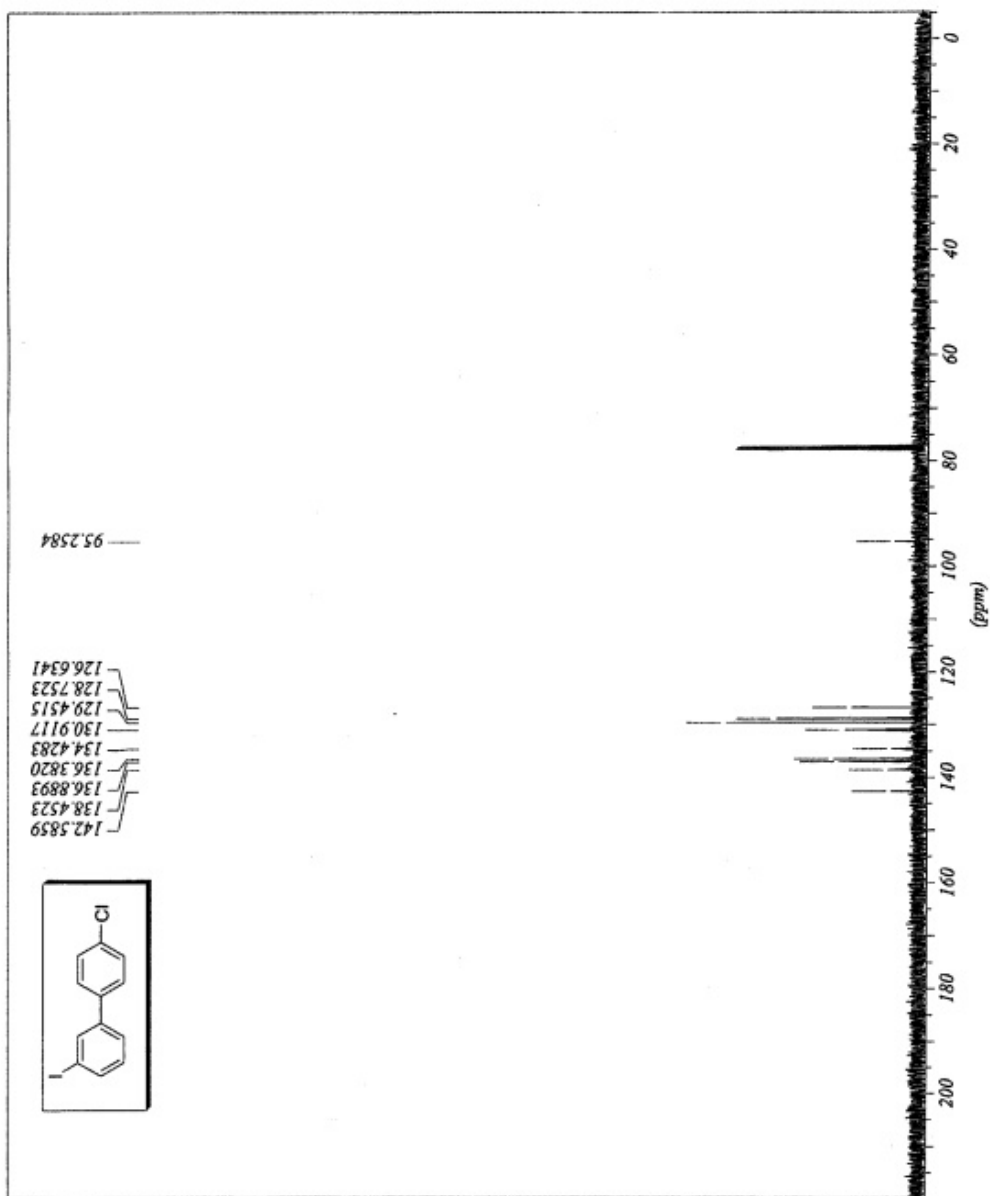


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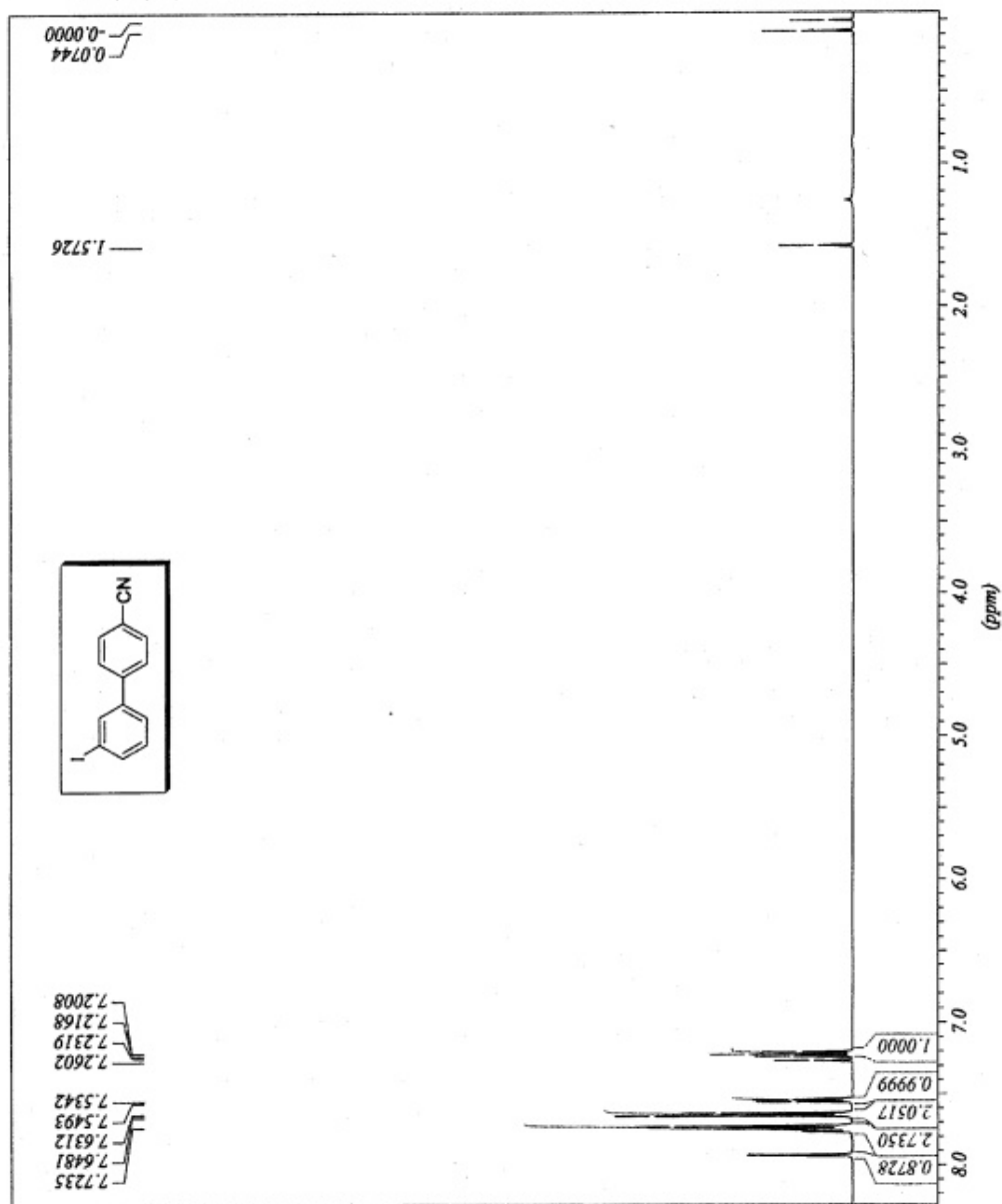
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LAKRA 642 58 44 --





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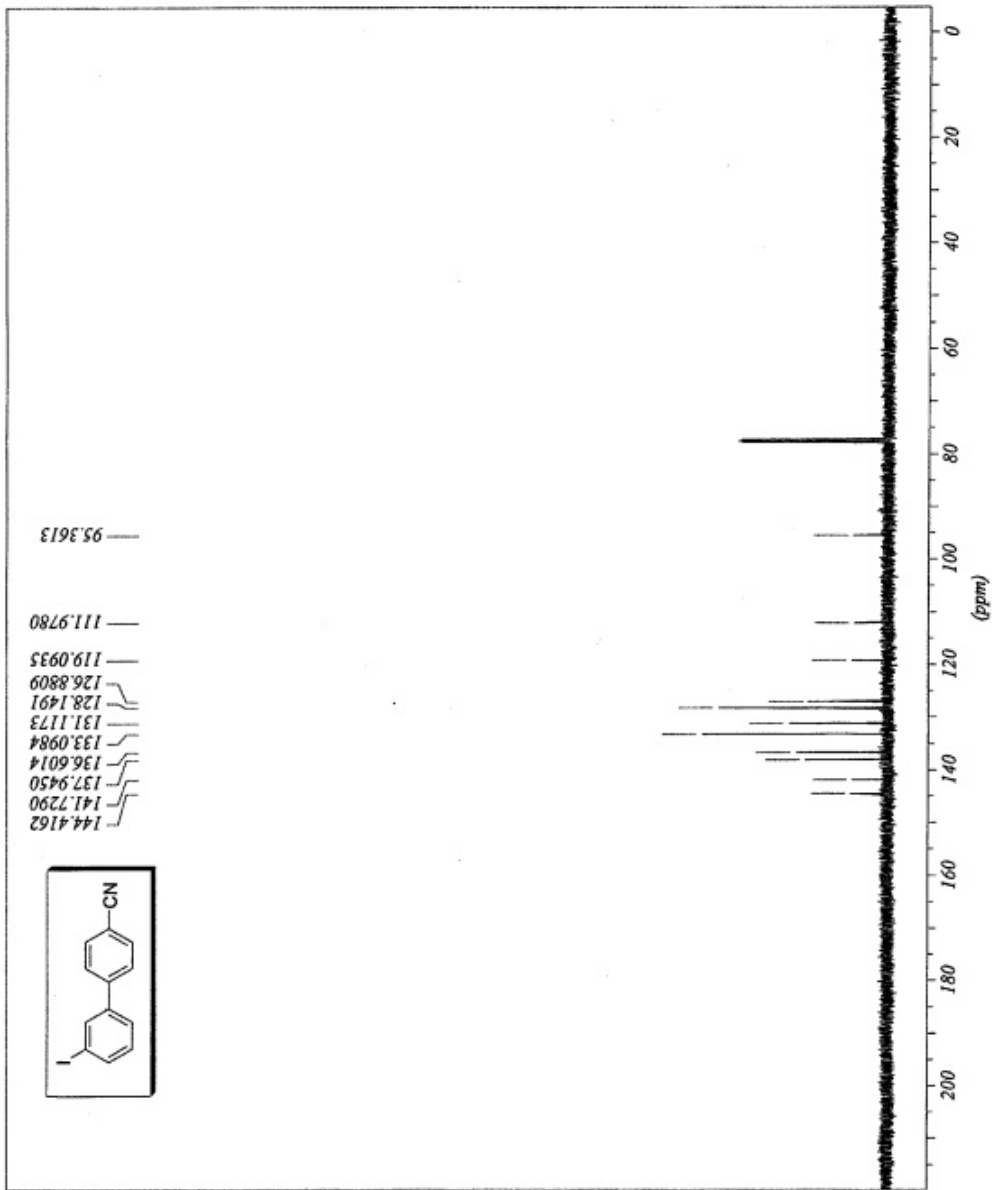


LKRA 642 66 A --



*** Current Data Parameters ***
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EXPNO : 711
PROCNO : 1

LXRJ 642 66 .1 . .



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