Supplementary Material (ESI) for Chemical Communications

One-step synthesis of polysubstituted benzenes by multi-component cyclization of α-bromoacetate, malononitrile and aromatic aldehydes

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Supporting Information

Figures

Crystallographic data (**1a**: CCDC 663309; **1b**: CCDC 663310; **1c**: CCDC 663311; **1h** CCDC 663312. **D1**: CCDC 663313; **D2**: CCDC 663314. **F** CCDC 663315.) have been deposited vat the Cambridge Crystallographic Database Centre and is available on request from the Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (Fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www:http//www.ccdc.cam.ac.uk).

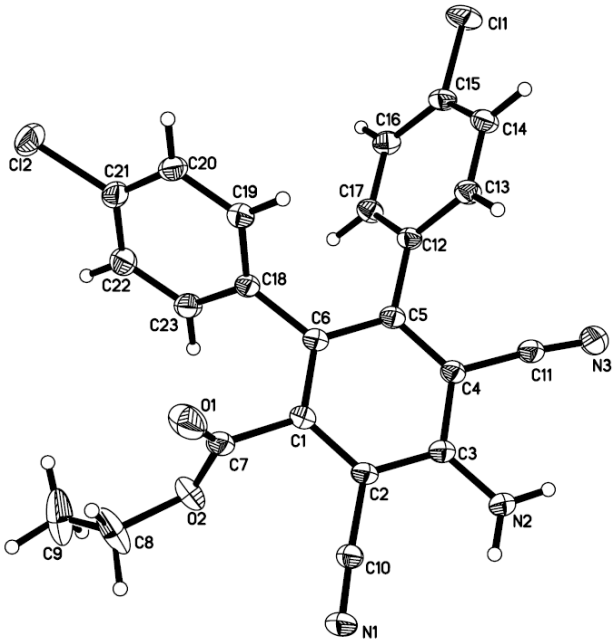


Figure 1 Molecular structure of **1c** in the crystal

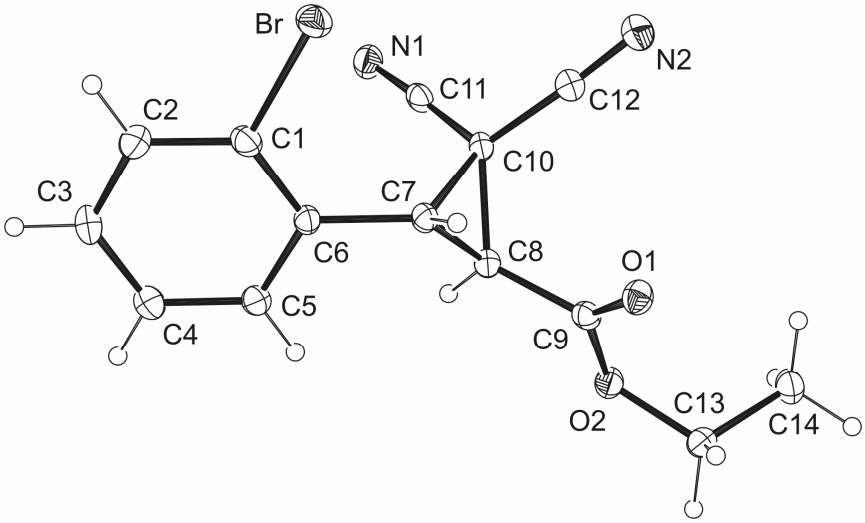


Figure 2 Molecular structure of cyclopropane derivative **D2** in the crystal

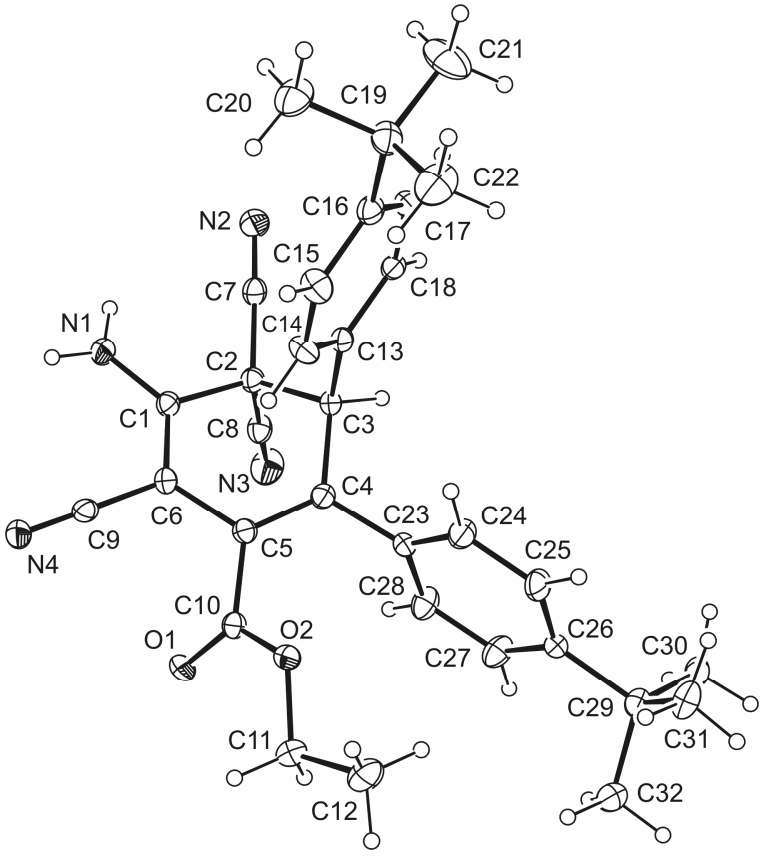


Figure 3 Molecular structure of intermediate **F** in the crystal

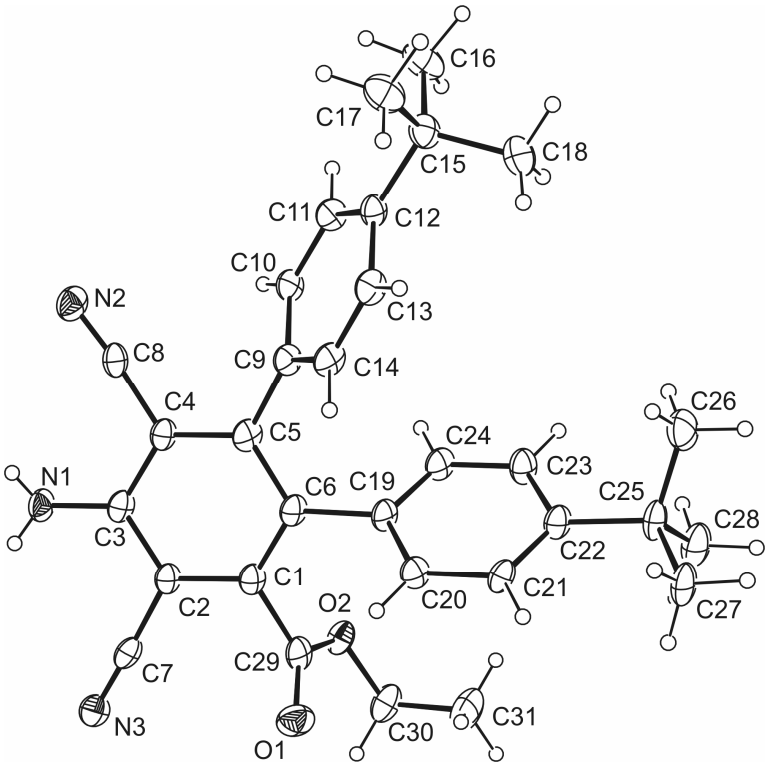
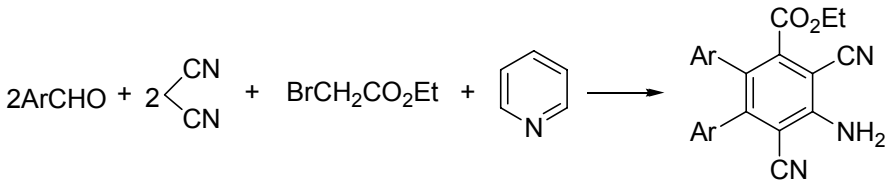
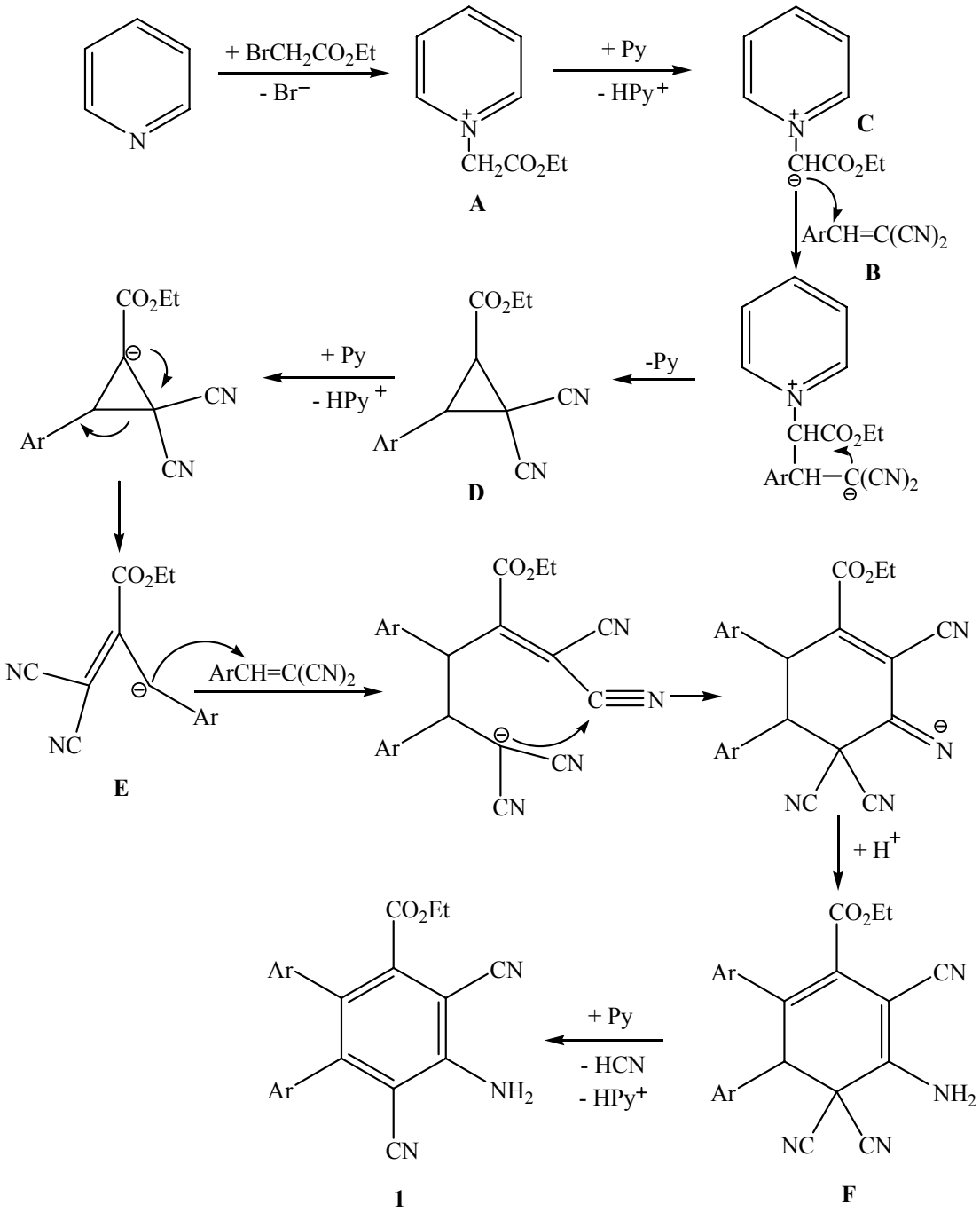


Figure 4 Molecular structure of **1h** in the crystal



Scheme 1 One-pot four-component reaction affording polysubstituted benzene derivatives

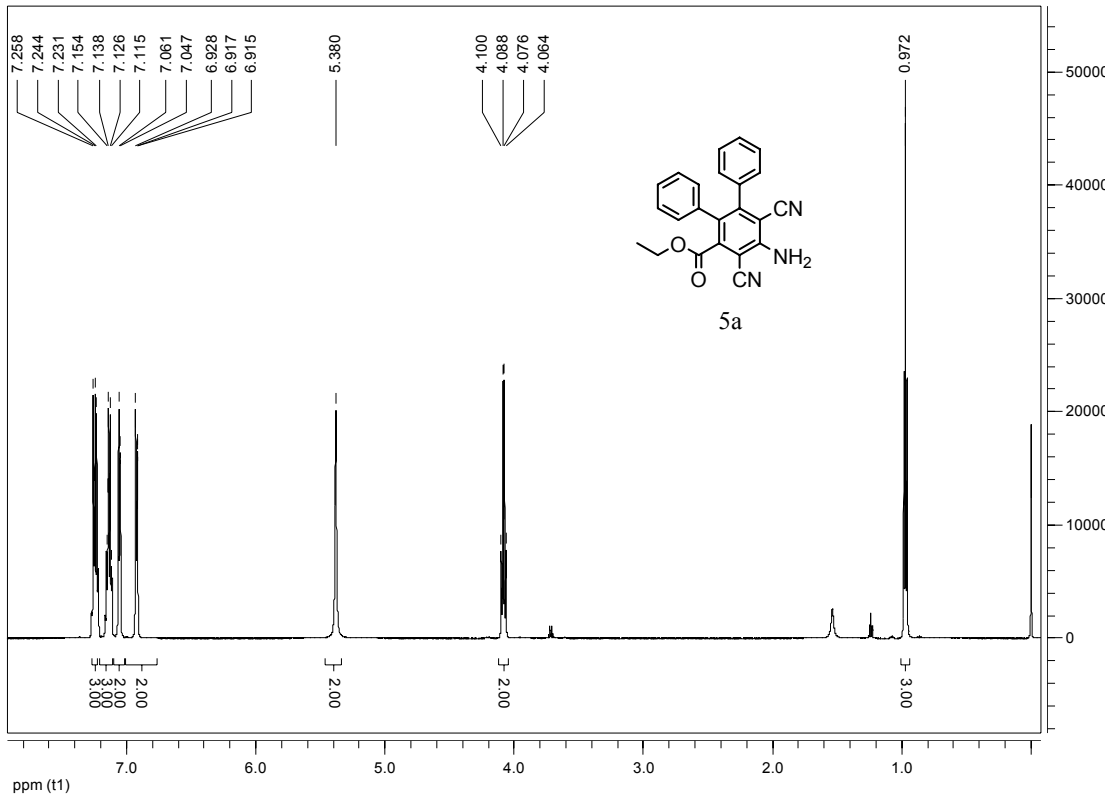


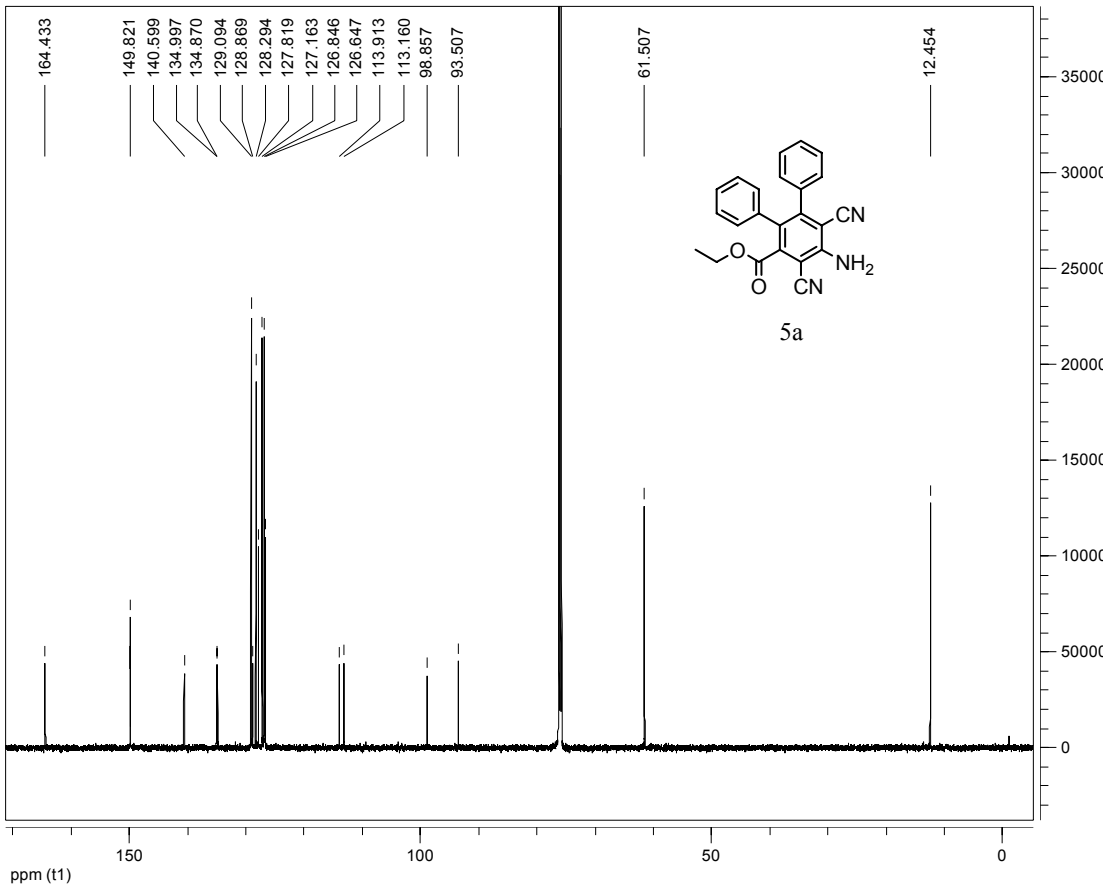
Scheme 2 Proposed mechanism for the formation of polysubstituted benzenes **1**

General procedure for the synthesis of polysubstituted Benzenes

A mixture of pyridine (20.0mmol, 1.58g), ethyl α-bromoacetate (4.0mmol, 0.668g), aromatic aldehyde (4.0mmol, 0.562g) and malononitrile (4.0mmol, 0.264g) in acetonitrile (20mL) was refluxed for 12 hours. The solvent was removed by evaporation and the residue was titrated with ethanol (10mL) to give the crude product, which is recrystallized in ethanol to give light yellow solid

1a： mp151~152□. ^{1}H NMR ($CDCl_3$, 600 MHz) δ(ppm) 7.273 (m, J = 8.4Hz, 3H, C_6H_5), 7.132 (m, J = 7.2 Hz, 3H, C_6H_5), 7.054 (d, J = 8.4 Hz, 2H, C_6H_5), 6.921 (d, J = 8.4 Hz, 2H, C_6H_5), 5.380 (s, 2H, NH_2), 4.082 (q, J = 7.2 Hz, 2H, CH_2), 0.972 (t, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 600 MHz) δ(ppm) 147.81, 147.48, 146.97, 131.34, 131.14, 128.82, 127.86, 127.24, 126.55, 124.80, 124.52, 124.23, 109.93, 38.44, 34.54, 34.13, 27.43, 27.05, 19.78; IR(KBr) ν 3432, 3355, 3254, 2220, 1727, 1648, 1565, 1568, 1454, 1374, 1267, 1231, 1034, 754, 703; Found: C,75.15; H,4.47; N,11.39. $C_{23}H_{17}N_3O_2$ requires C,75.19; H,4.66; N,11.44. The structure of **1a** was further proved by X-ray crystallographic analysis (Figure 1).





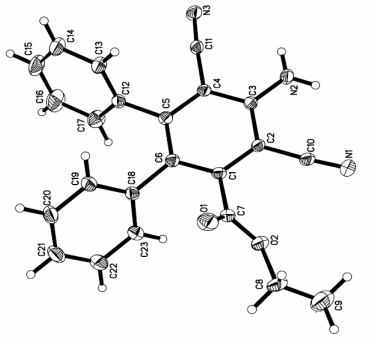
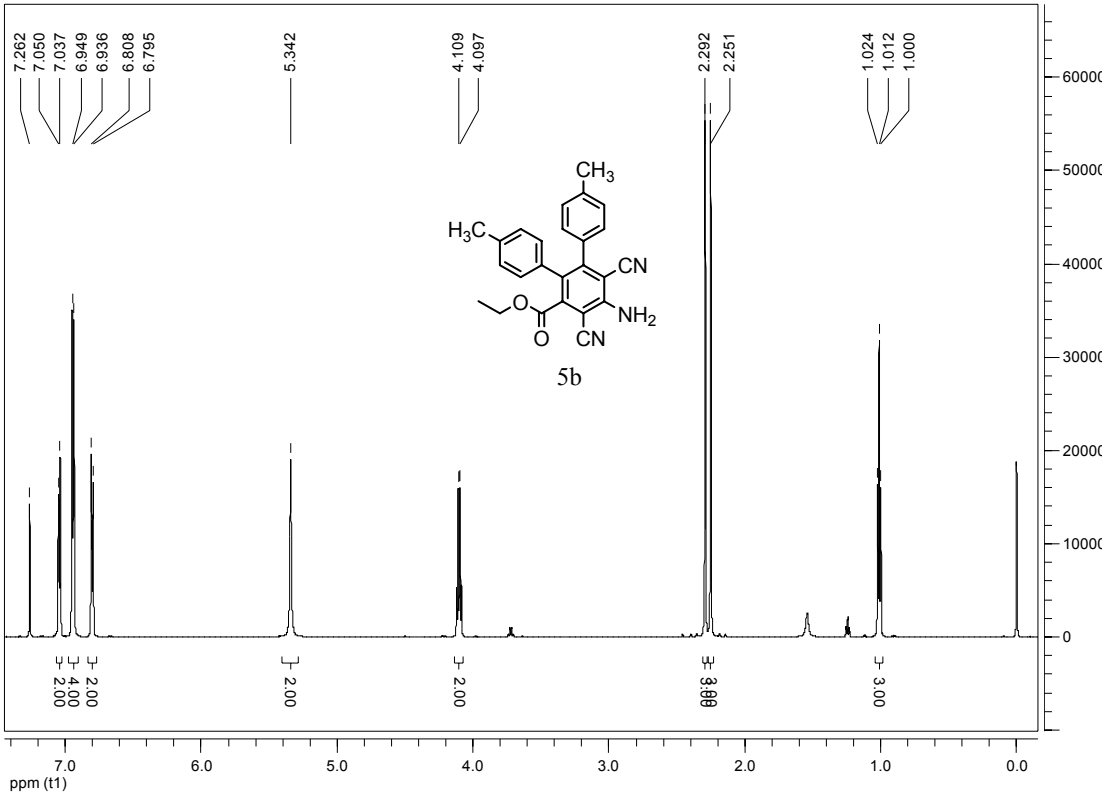
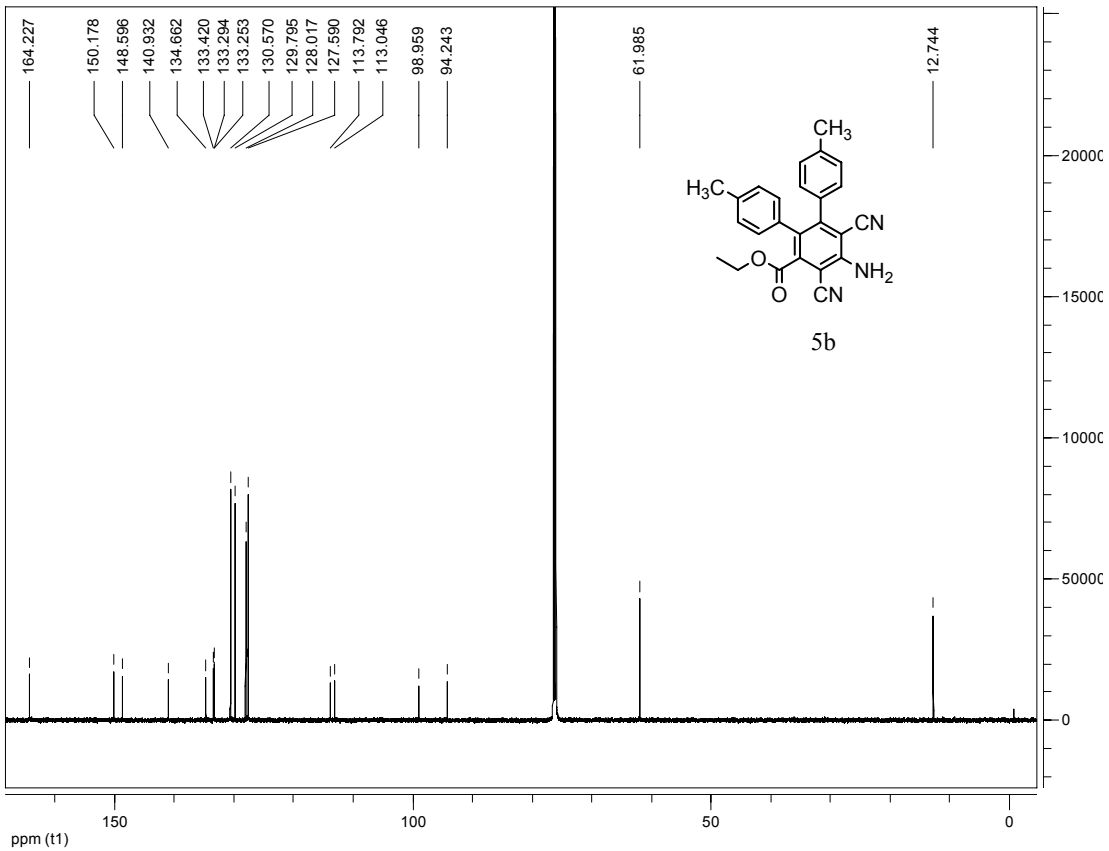


Figure 1 X-ray crystallographic structure of **1a**

1b mp190~191□. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.049 (d, *J* = 7.8 Hz, 2H, *p*-$CH_3C_6H_4$), 6.942 (d, *J* = 7.8 Hz, 4H, *p*-$CH_3C_6H_4$), 6.801 (d, *J* = 7.8 Hz, 2H, *p*-$CH_3C_6H_4$) 5.342 (s, 2H, NH_2), 4.103 (q, *J* = 7.2 Hz, 2H, CH_2), 2.292 (s, 3H, CH_3), 2.251 (s, 3H, CH_3), 0.972 (t, *J* = 7.2 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 600 MHz) δ(ppm) 164.23, 150.18, 148.60, 140.93, 134.66, 133.42, 133.29, 133.25, 130.57, 129.80, 128.02, 127.59, 113.79, 113.04, 96.97, 94.24, 61.57, 12.74; IR(KBr) ν 3467,

3356, 3256, 2225, 1741, 1640, 1588, 1560, 1449, 1376, 1266, 1232, 1031, 795, 762; Found: C,76.12; H,5.11; N,10.60. $C_{25}H_{21}N_3O_2$ requires C,75.93; H,5.35; N,10.63. The structure of 5b was further proved by X-ray crystallographic analysis (Figure 2).





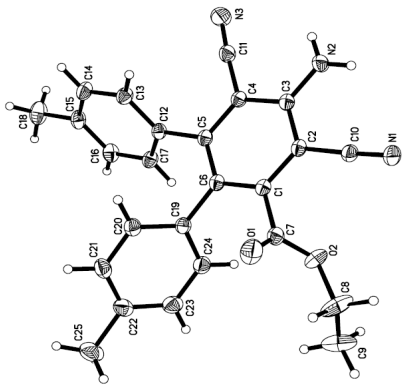
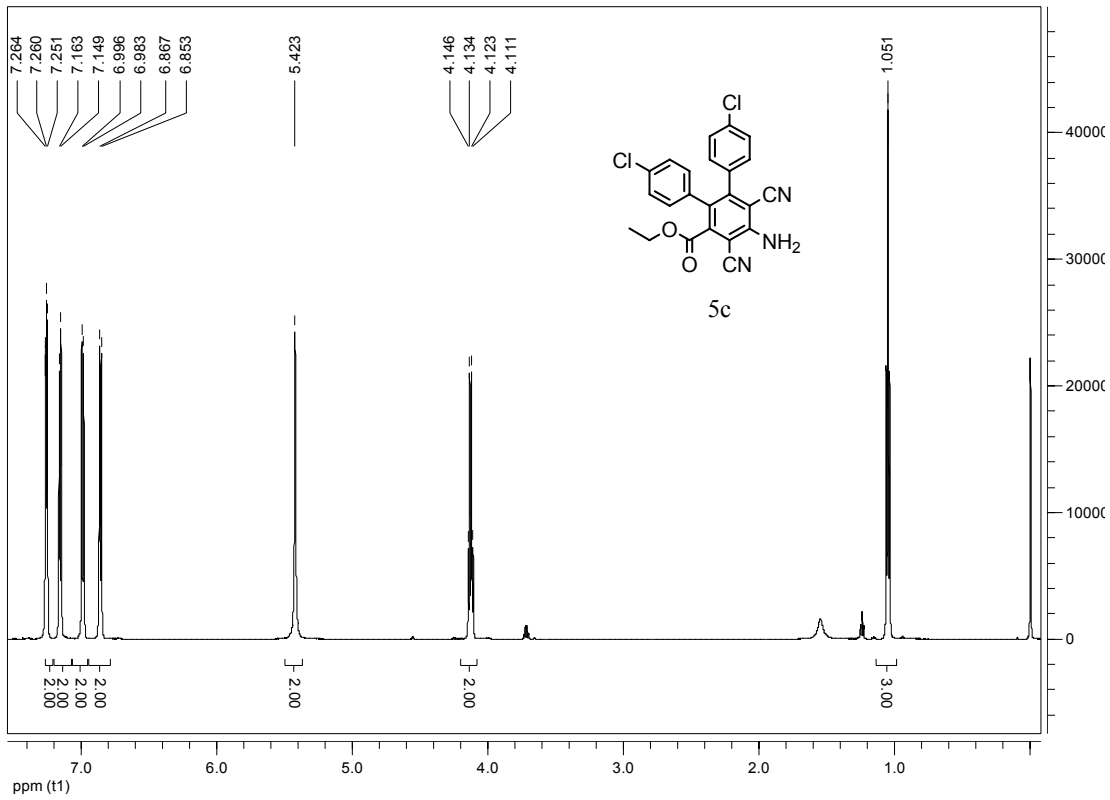
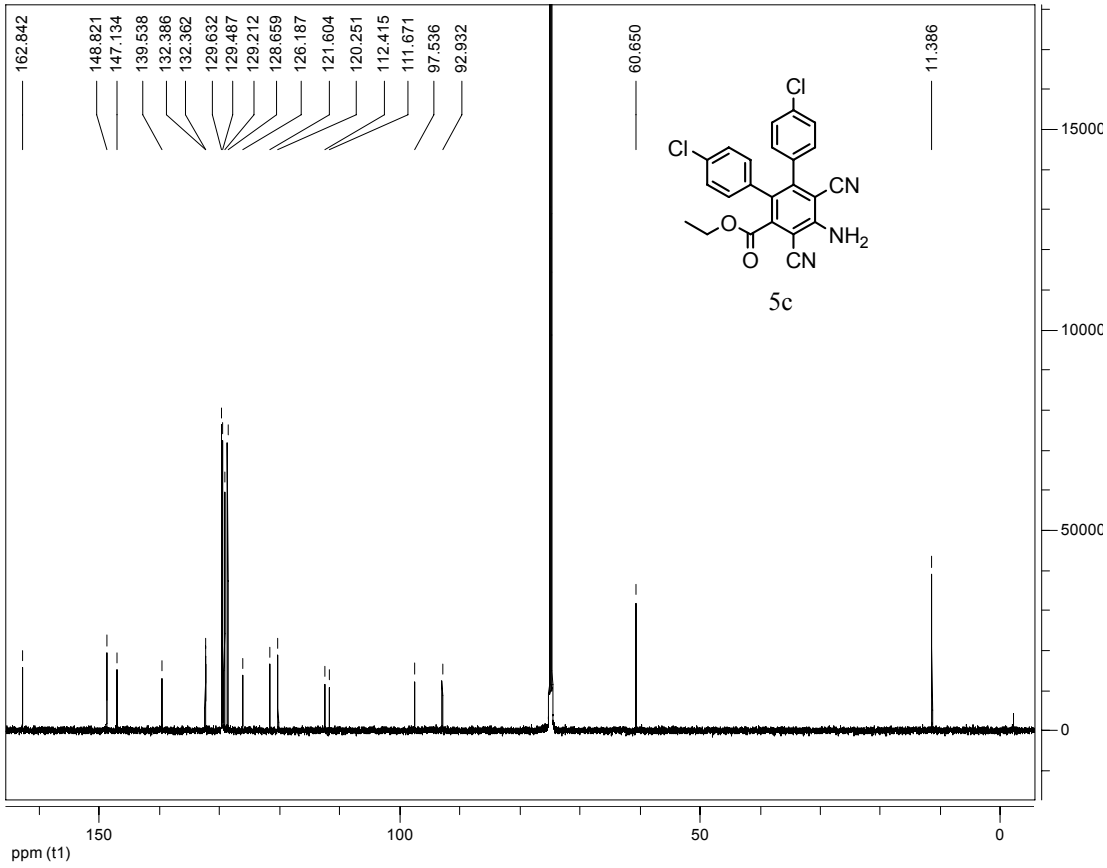


Figure 2 X-ray crystallographic structure of **1b**

1c mp231~232□. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.257 (d, J = 7.8 Hz, 2H, p-ClC_6H_4), 7.156 (d, J = 8.4 Hz, 2H, p-ClC_6H_4), 6.990 (d, J = 7.8 Hz, 2H, p-ClC_6H_4), 6.860 (d, J = 8.4 Hz, 2H, p-ClC_6H_4), 5.423 (s, 2H, NH_2), 4.129 (q, J = 7.2 Hz, 2H, CH_2), 1.051 (t, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 600 MHz) δ(ppm) 162.84, 148.82, 147.13, 139.53, 132.40, 132.36, 129.63, 129.49, 129.21, 126.67, 125.19,

121.60, 120.25, 112.42, 111.67, 97.54, 92.93, 60.66, 11.37; IR(KBr) ν 3469, 3351, 3244, 2221, 1743, 1642, 1557, 1493, 1447, 1375, 1276, 1218, 1016, 789, 743;Found: C,63.09; H,3.22; N,9.54. $C_{23}H_{15}Cl_2N_3O_2$ requires C,63.32; H,3.47; N,9.63. The structure of 5c was further proved by X-ray crystallographic analysis (Figure 3).





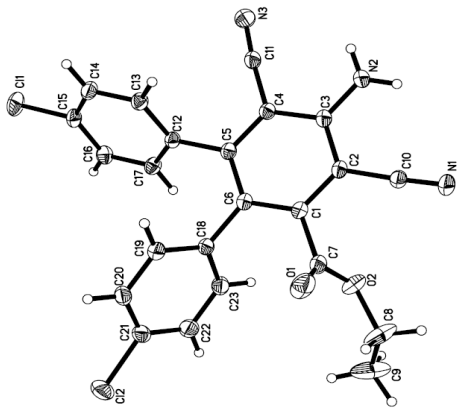
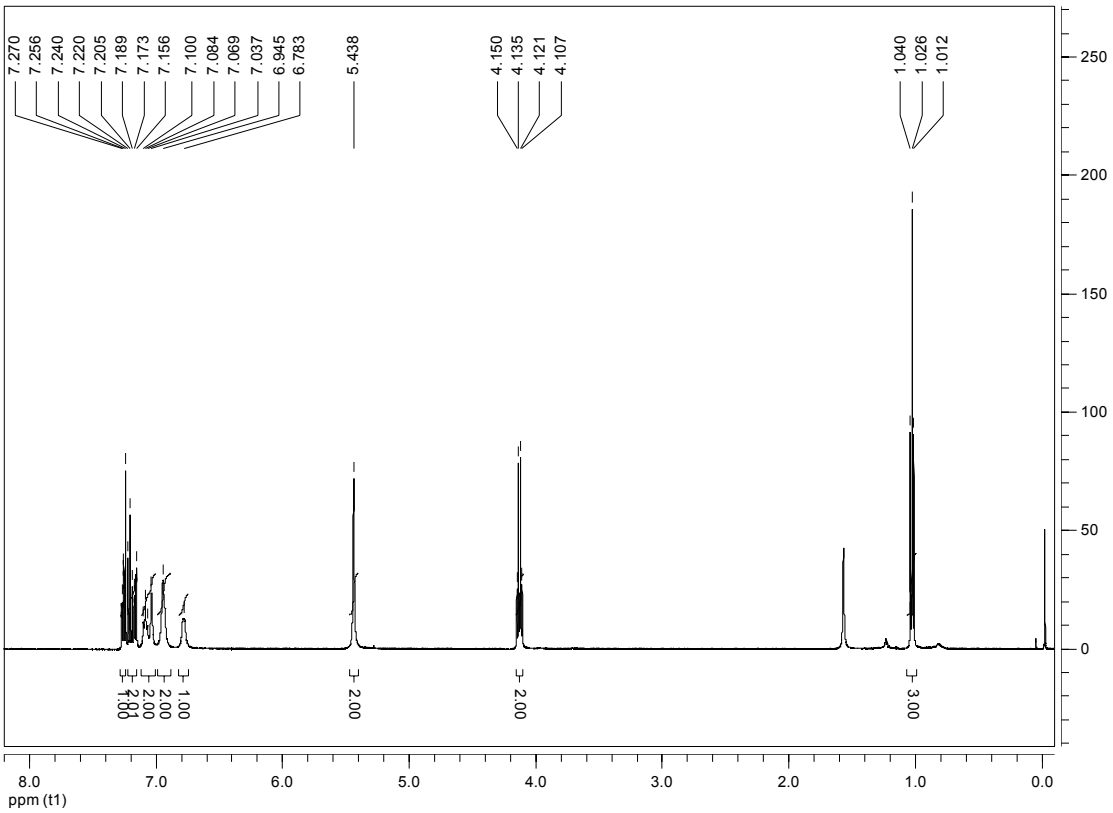


Figure 3 X-ray crystallographic structure of **1c**

1d mp201~202℃. ^{1}H NMR (600MHz, $CDCl_3$) δ(ppm) 7.27~7.25 (m, 1H, m-ClC_6H_4), 7.22~7.16 (m, 2H, m-ClC_6H_4), 7.10~7.04 (m, 2H, m-ClC_6H_4), 6.95 (s, 2H, m-ClC_6H_4), 6.78 (s, 1H, m-ClC_6H_4), 5.44 (s, 2H, NH_2), 4.13 (q, J = 8.4Hz, 2H, CH_2), 1.03 (t, J = 8.4Hz, 3H, CH_3). ^{13}C NMR (600MHz, $CDCl_3$) δ(ppm) 150.9, 148.9, 137.1, 137.1, 134.4, 134.4, 129.9, 129.7, 129.3, 129.2, 128.3, 128.2, 127.4, 114.4, 113.8,

99.6, 62.8, 16.5.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7.220
7.205
7.189
7.173
7.156
7.100
7.084
7.069
7.037
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6.783
5.438
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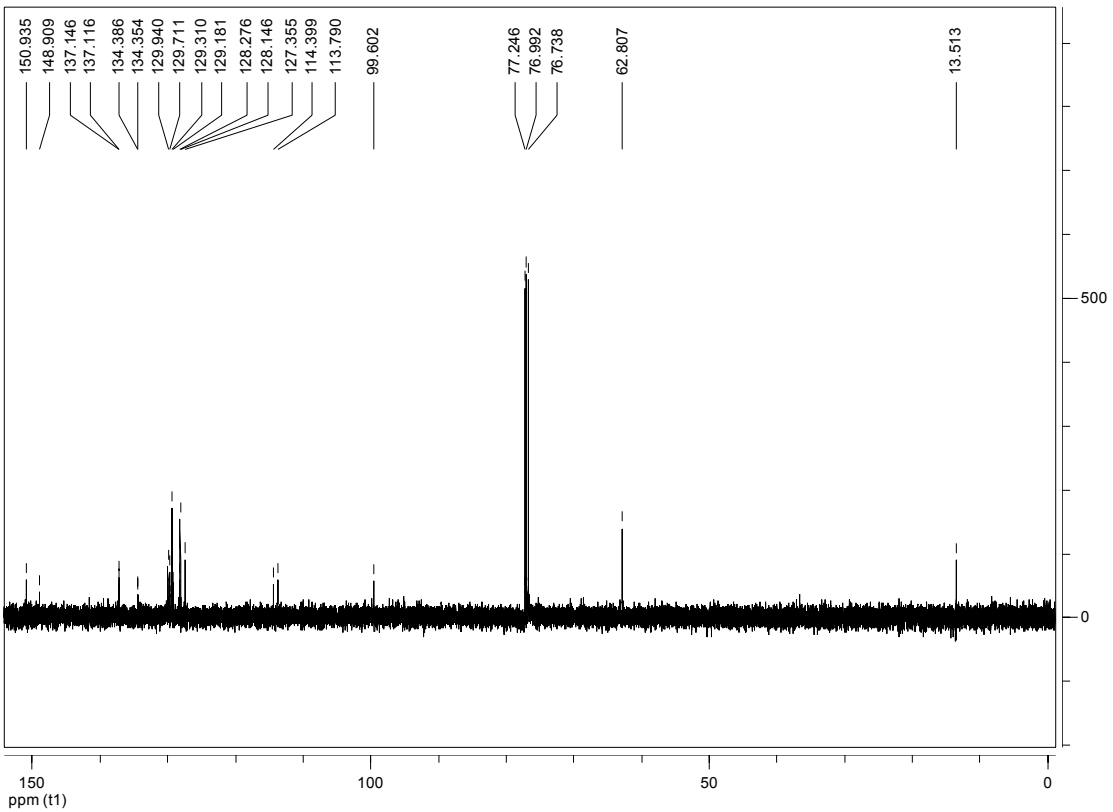
1.00
2.00
2.00
3.00
ppm (t1)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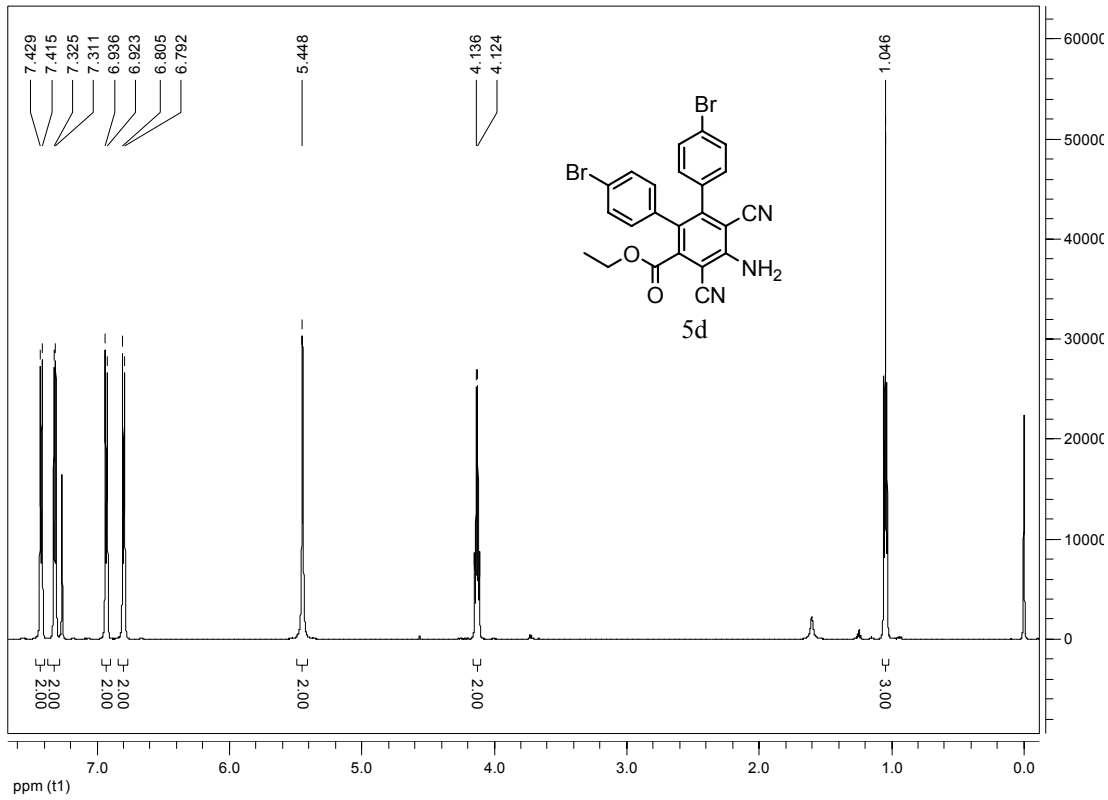
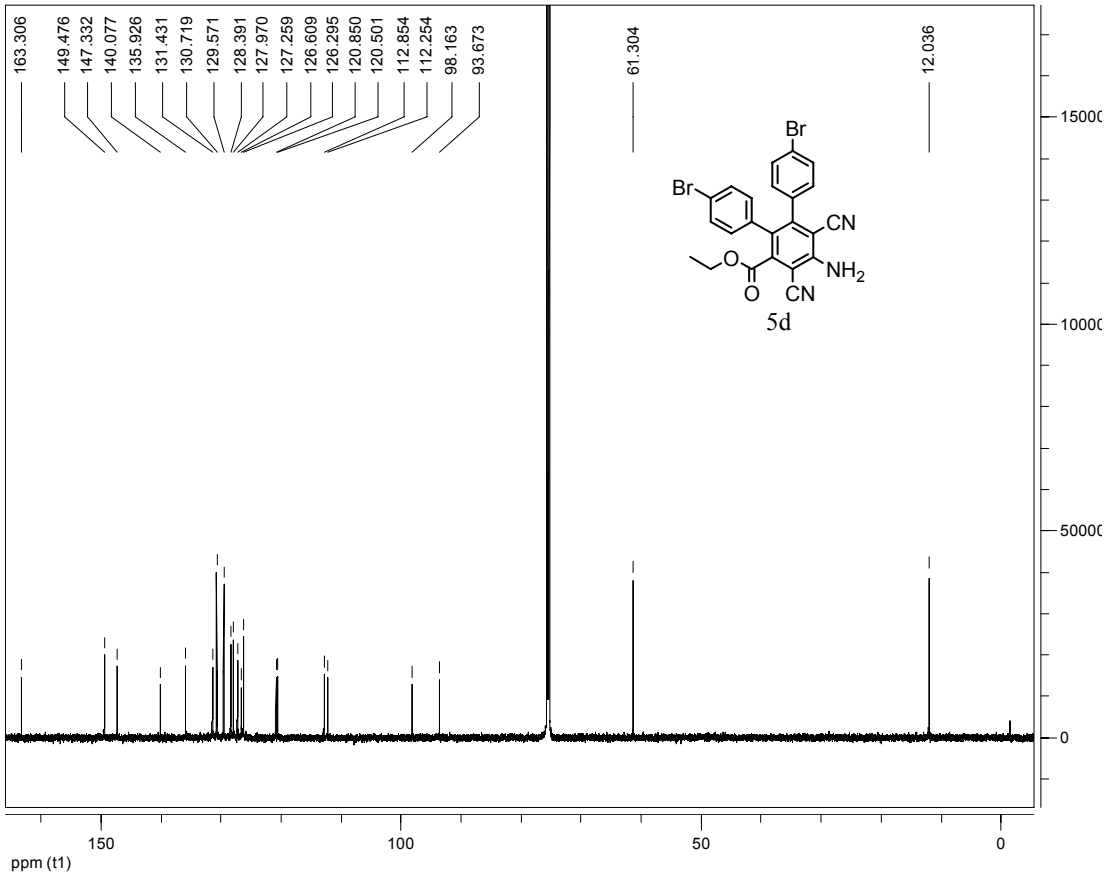
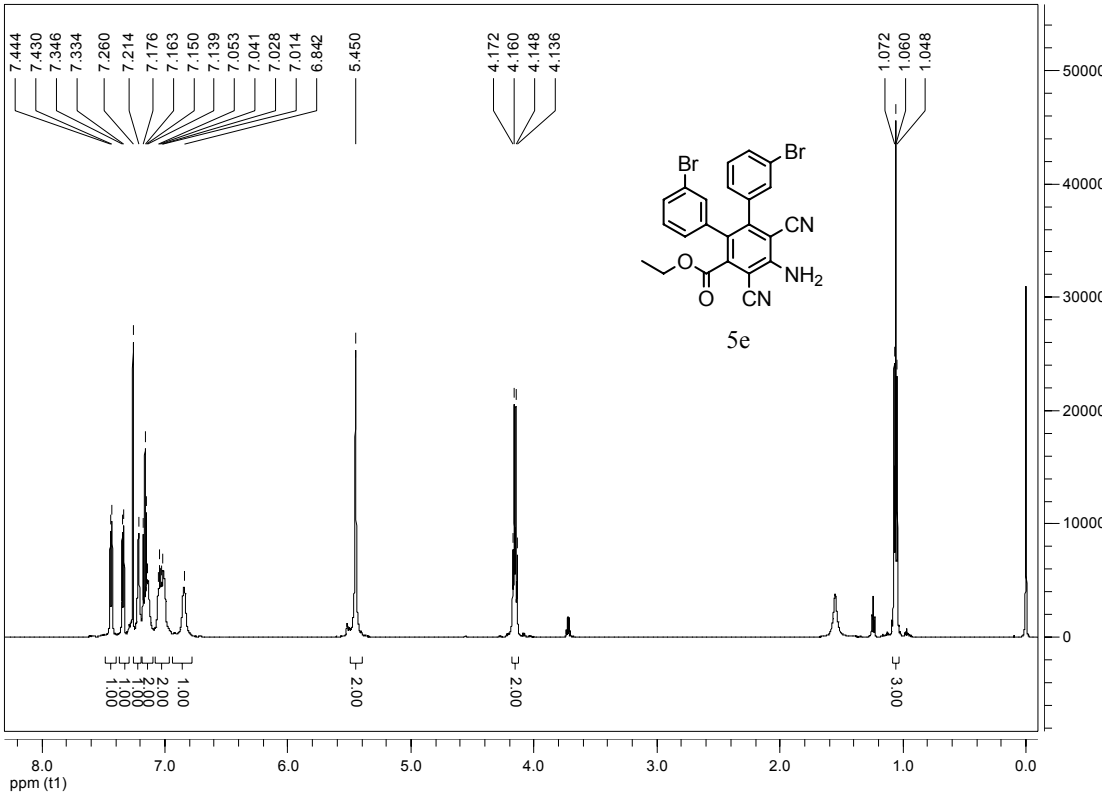
127.355
114.399
113.790
99.602
77.246
76.992
76.738
62.807
13.513
ppm (t1)

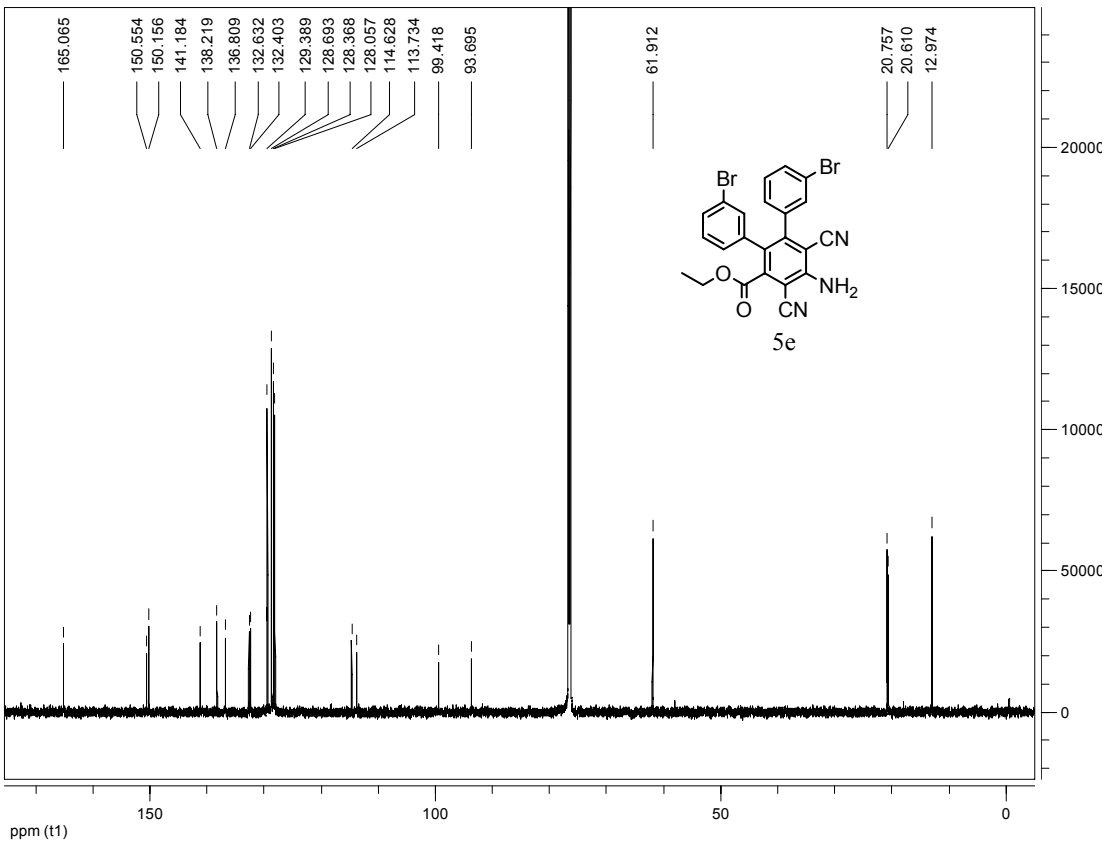
1e mp252~253□. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.419 (d, *J* = 8.4 Hz, 2H, *p*-BrC_6H_4), 7.315 (d, *J* = 8.4 Hz, 2H, *p*-BrC_6H_4), 6.926 (d, *J* = 8.4 Hz, 2H, *p*-BrC_6H_4), 6.797 (d, *J* = 8.4 Hz, 2H, *p*-BrC_6H_4), 5.423 (s, 2H, NH_2), 4.129 (q, *J* = 7.2 Hz, 2H, CH_2), 1.052 (t, *J* = 7.2 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 600 MHz) δ(ppm) 163.31, 149.48, 147.33, 140.08, 135.93, 131.43, 130.72, 129.57, 128.39, 127.97, 127.26, 125.61, 125.30, 120.85, 120.50, 112.85, 112.25, 96.16, 93.67, 61.30, 12.03; IR(KBr) ν 3469, 3352, 3243, 2221, 1742, 1639, 1558, 1445, 1376, 1305, 1262, 1219, 1025, 785, 734;Found: C,52.49; H,2.68; N,7.87. $C_{23}H_{15}Br_2N_3O_2$ requires C,52.60; H,2.88; N,8.00.





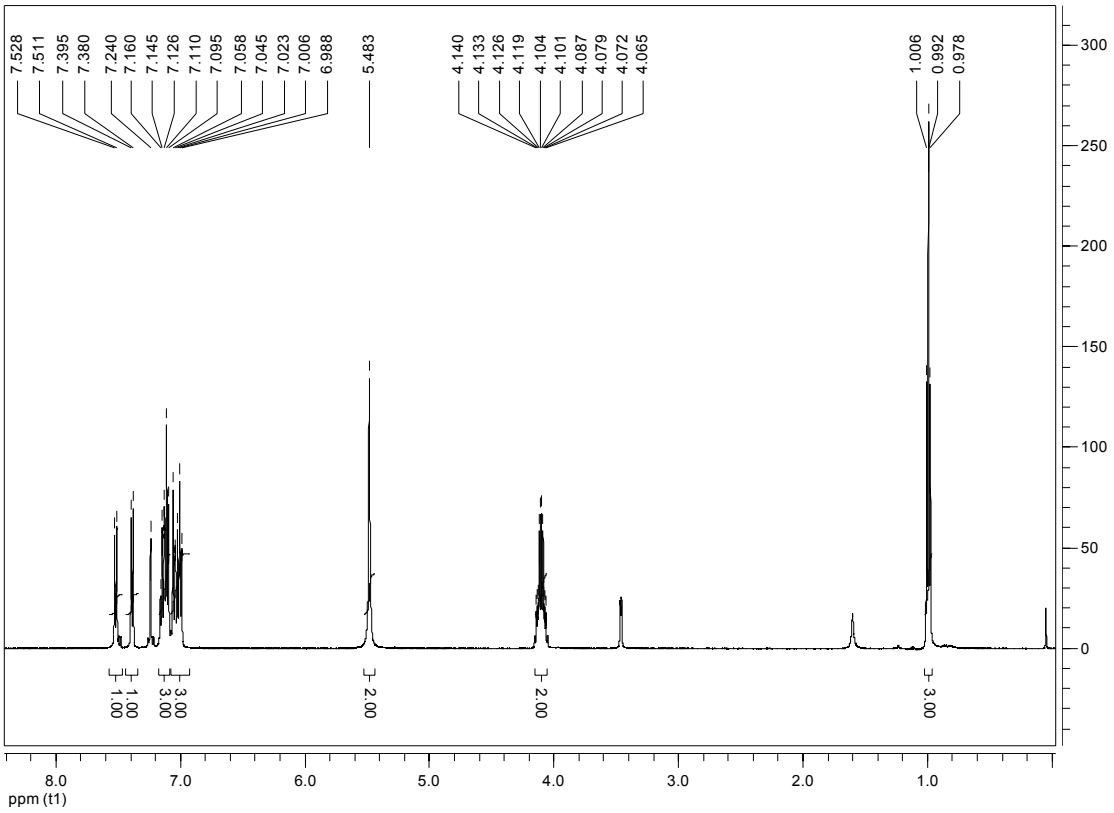
1f mp187~188□. ^{1}H NMR (CDCl3, 600 MHz) δ 7.437 (d, J = 8.4 Hz, 1H, m-BrC6H4), 7.340 (d, J = 7.2 Hz, 1H, m-BrC6H4), 7.214 (s, 1H, m-BrC6H4), 7.163 (q, J = 7.8 Hz, 2H, m-BrC6H4), 7.028 (q, J = 7.8 Hz, 2H, m-BrC6H4), 6.846 (s, 1H, m-BrC6H4), 5.450 (s, 2H, NH2),4.154(q, J = 7.2 Hz, 2H, CH2), 1.060 (t, J = 7.2 Hz, 3H, CH3); ^{13}C NMR (CDCl3, 600 MHz) δ(ppm) 165.05, 150.55, 150.15, 141.18, 138.22, 136.81, 132.53, 132.40, 129.40, 126.69, 126.36, 126.06, 114.63, 113.73, 99.42, 93.70, 61.91, 20.75, 20.61, 12.97; IR(KBr) ν 3464, 3348, 3238, 2223, 1728, 1636, 1563, 1448, 1384, 1275, 1232, 1029, 775, 682; Found: C,52.47; H,2.68; N,7.87. $C_{23}H_{15}Br_2N_3O_2$ requires C,52.60; H,2.88; N,8.00.

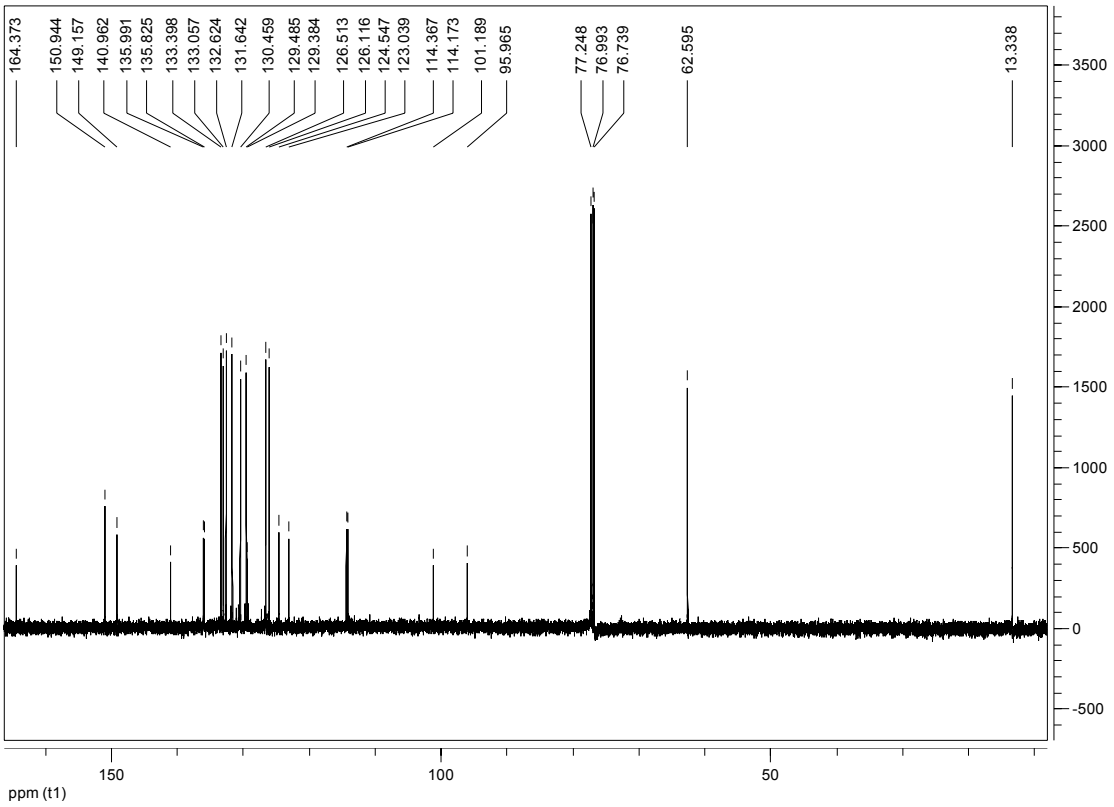




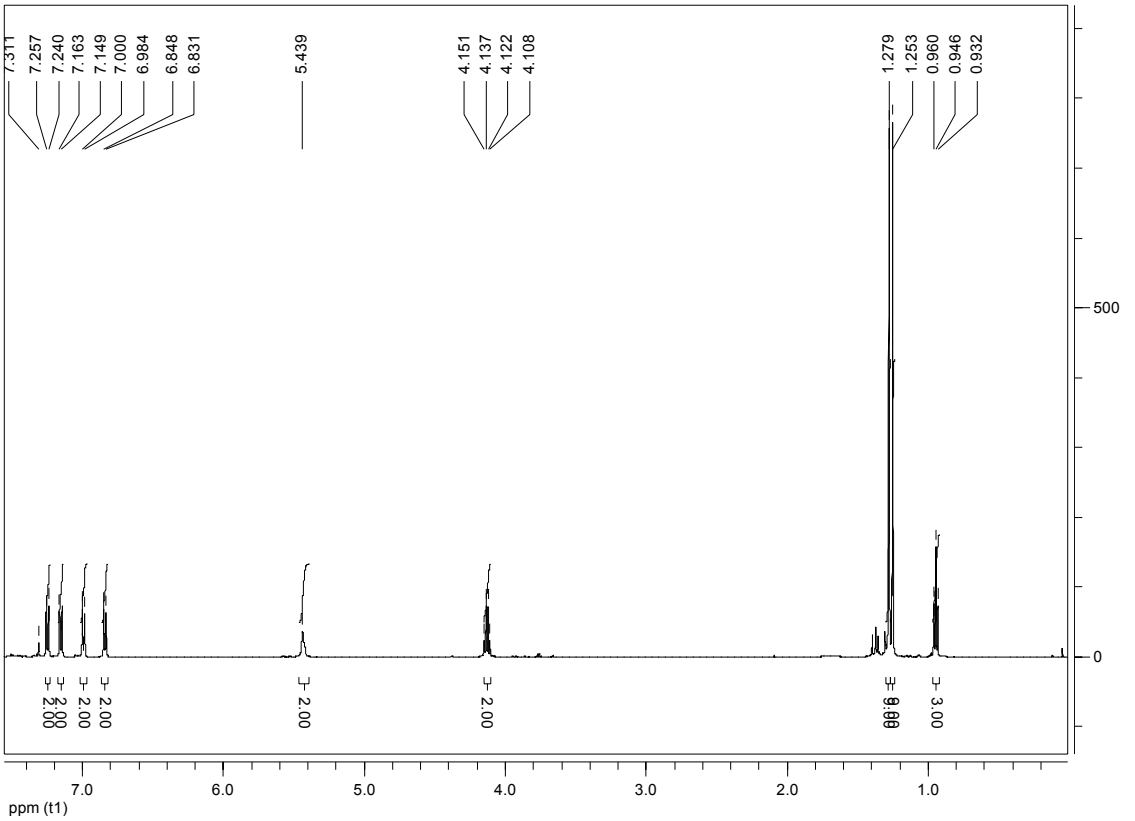
1g mp171~172℃. ^{1}H NMR (600MHz, $CDCl_3$) δ(ppm) 7.52 (d, J = 9.6Hz, 1H, *o*-BrC_6H_4), 7.39 (d, J = 8.4Hz, 1H, *o*-BrC_6H_4), 7.16~7.10 (m, 3H, *o*-BrC_6H_4),

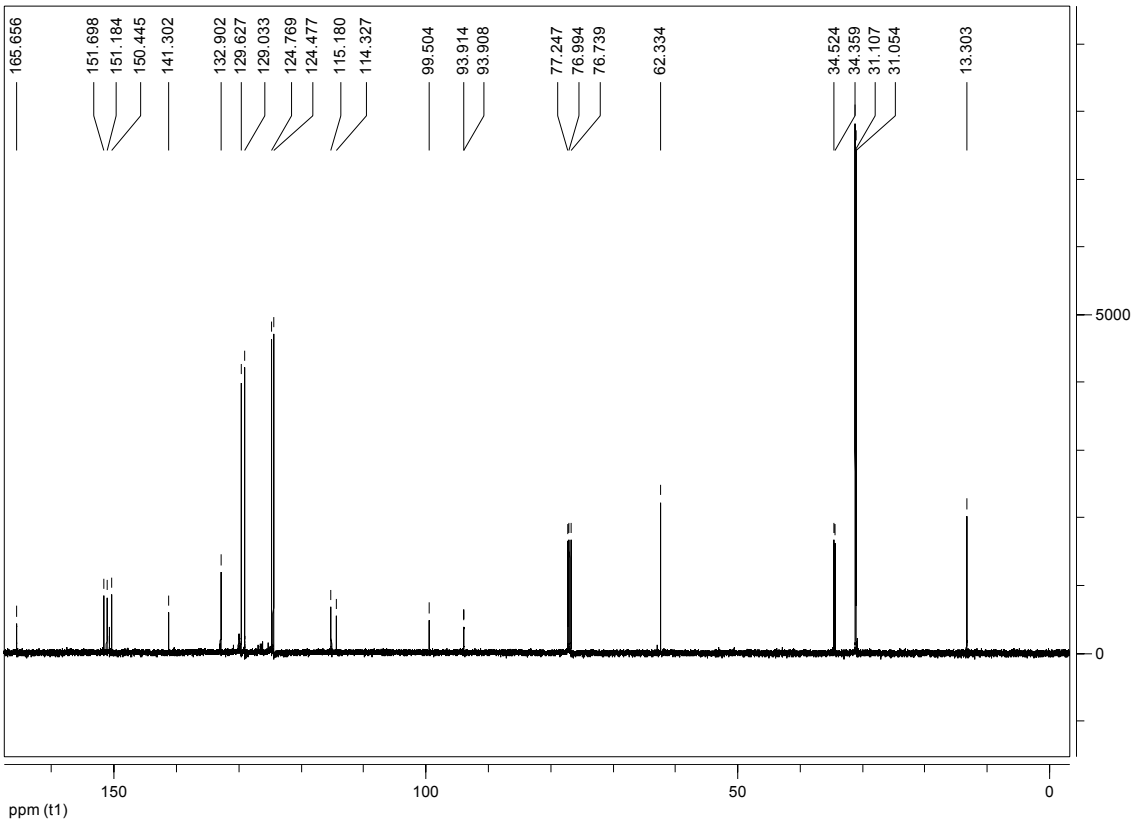
7.06~6.99 (m, 3H, *o*-BrC_6H_4), 5.48 (s, 2H, NH_2), 4.10 (q, J = 8.4Hz, 2H, CH_2), 0.99 (t, J = 8.4Hz, 3H, CH_3).^{13}CNMR (600MHz,$CDCl_3$) δ(ppm) 164.4, 150.9, 149.2, 140.9, 136.0, 135.8, 133.4, 133.1, 132.6, 131.6, 130.5, 129.5, 129.4, 126.5, 126.1, 124.5, 123.0, 114.4, 114.2, 101.2, 95.9, 62.6, 13.3 . C23H15Br2N3O2 (Mw= 525.19, M^+ = 525.95)





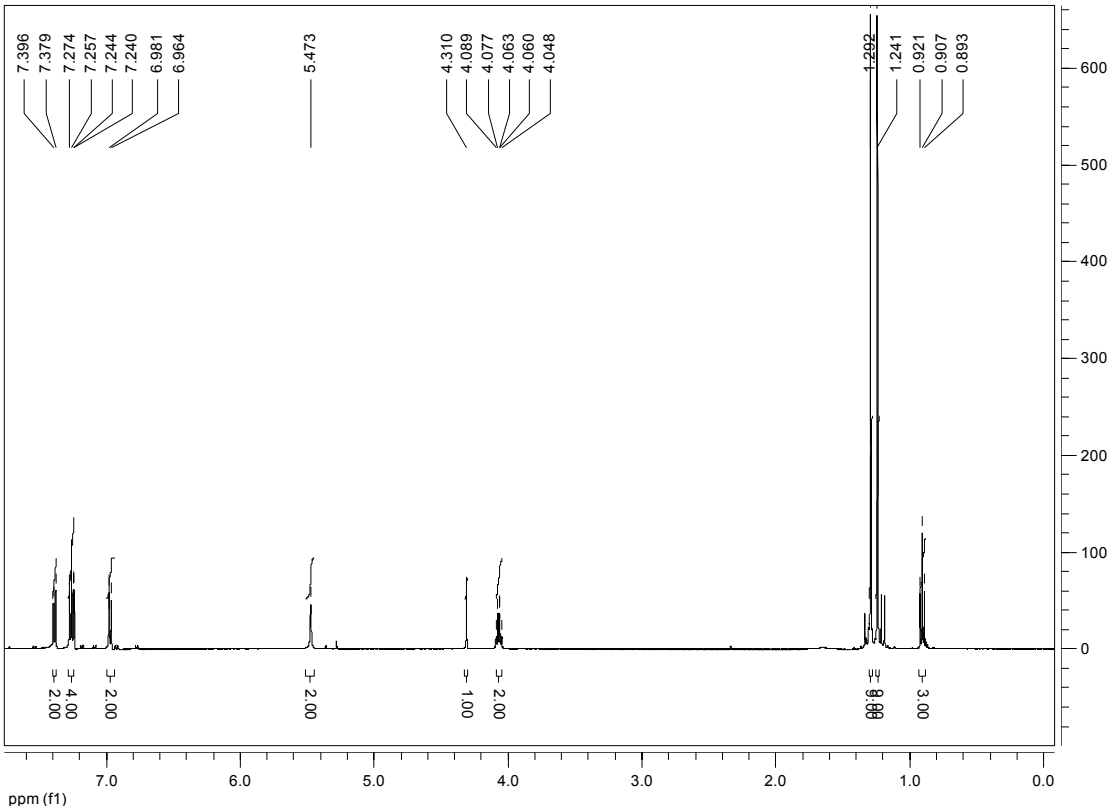
1h mp187-188℃. ^{1}H NMR (600MHz, $CDCl_3$) δ(ppm) 7.25 (d, *J* = 9.6Hz, 2H, *p*-$(CH_3)_3CC_6H_4$), 7.16 (d, *J* = 8.4Hz, 2H, *p*-$(CH_3)_3CC_6H_4$), 6.99 (d, *J* = 9.6Hz, 2H, *p*-$(CH_3)_3CC_6H_4$), 6.84 (d, *J* = 9.6Hz, 2H, *p*-$(CH_3)_3CC_6H_4$), 5.44 (s, 2H, NH_2), 4.13 (q, *J* = 8.4Hz, 2H, CH_2), 1.28 (s, 9H, $(CH_3)_3C$), 1.25 (s, 9H, $(CH_3)_3C$), 0.95 (t, *J* = 8.4Hz, 3H, CH_3). ^{13}C NMR (600MHz, $CDCl_3$) δ(ppm) 165.7, 151.7, 151.2, 150.5, 141.3, 132.9, 129.6, 129.0, 124.3, 124.5, 115.2, 114.3, 99.5, 93.9, 62.3, 34.5, 34.4, 31.1, 31.1, 13.3. $C_{31}H_{33}N_3O_2$ (Mw = 479.26, M^+ = 479.61)

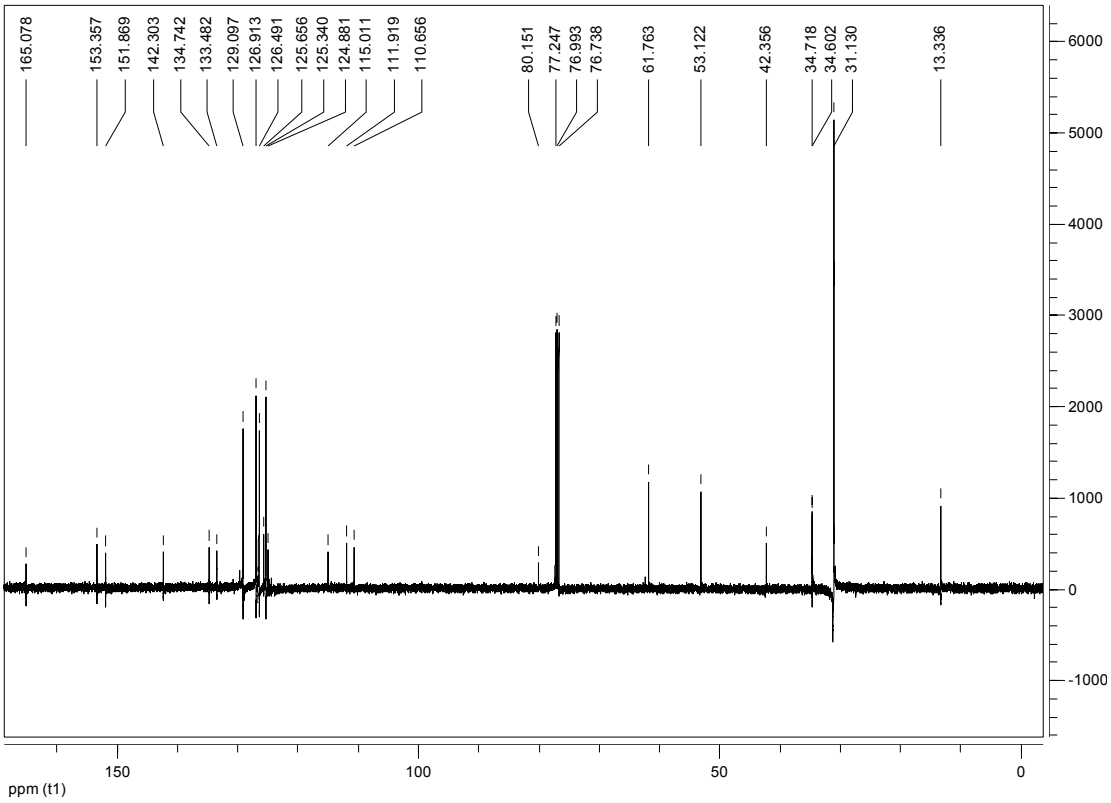




F （Ar = *p*-$(CH_3)_3CC_6H_4$） Yield: 22%; Mp: 180-182. ^{1}H NMR (600MHz, $CDCl_3$) δ(ppm) 7.39 (d, *J* = 9.6Hz, 2H, *p*-$(CH_3)_3CC_6H_4$), 7.26 (t, *J* = 8.4Hz, 4H, *p*-$(CH_3)_3CC_6H_4$), 6.97

(d, J = 9.6Hz, 2H, p-$(CH_3)_3CC_6H_4$), 5.47 (s, 2H, NH_2), 4.31 (s, 1H, CH), 4.07 (q, J = 7.2Hz, 2H, CH_2), 1.29 (s, 9H, $(CH_3)_3C$), 1.24 (s, 9H, $(CH_3)_3C$), 0.91 (t, J = 8.4Hz, 3H, CH_3). ^{13}C NMR (600MHz, $CDCl_3$) δ(ppm) 165.1, 153.4, 151.9, 142.3, 134.7, 133.5, 129.1, 126.9, 126.5, 125.7, 125.3, 124.9, 115.0, 111.9, 110.7, 80.2, 61.8, 53.1, 42.4, 34.7, 31.1, 13.3.$C_{32}H_{34}N_4O_2$ (Mw = 506.65, M^+ = 507.27)

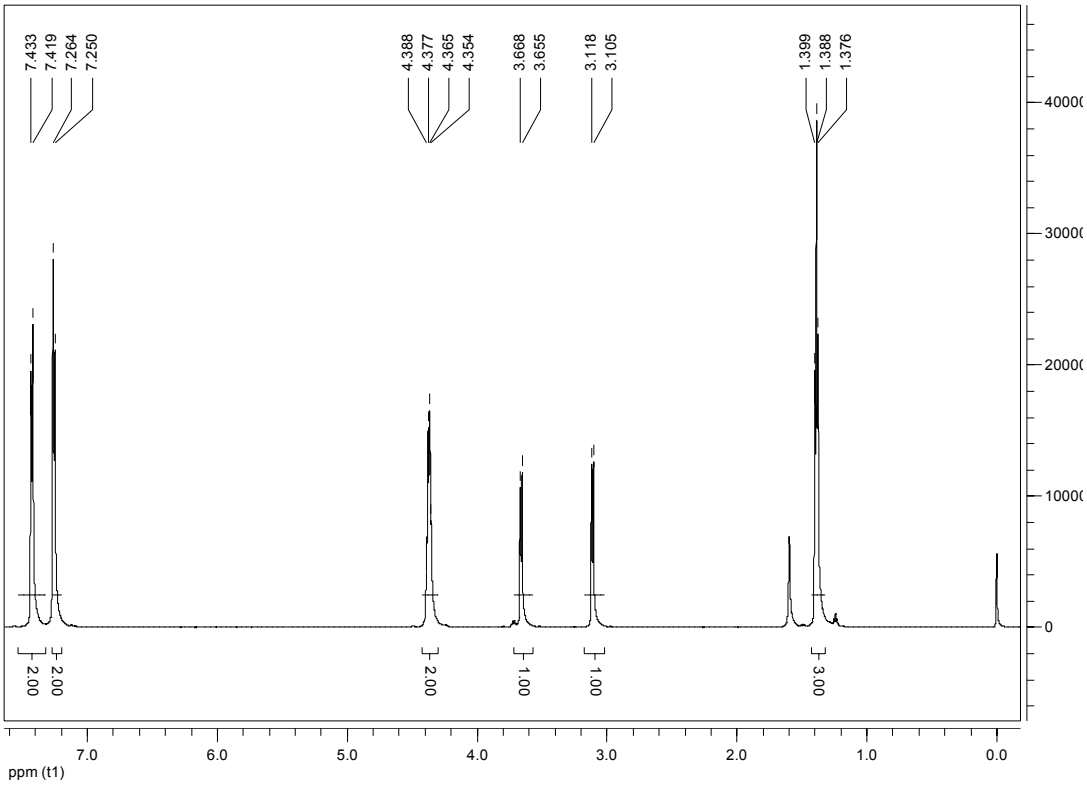




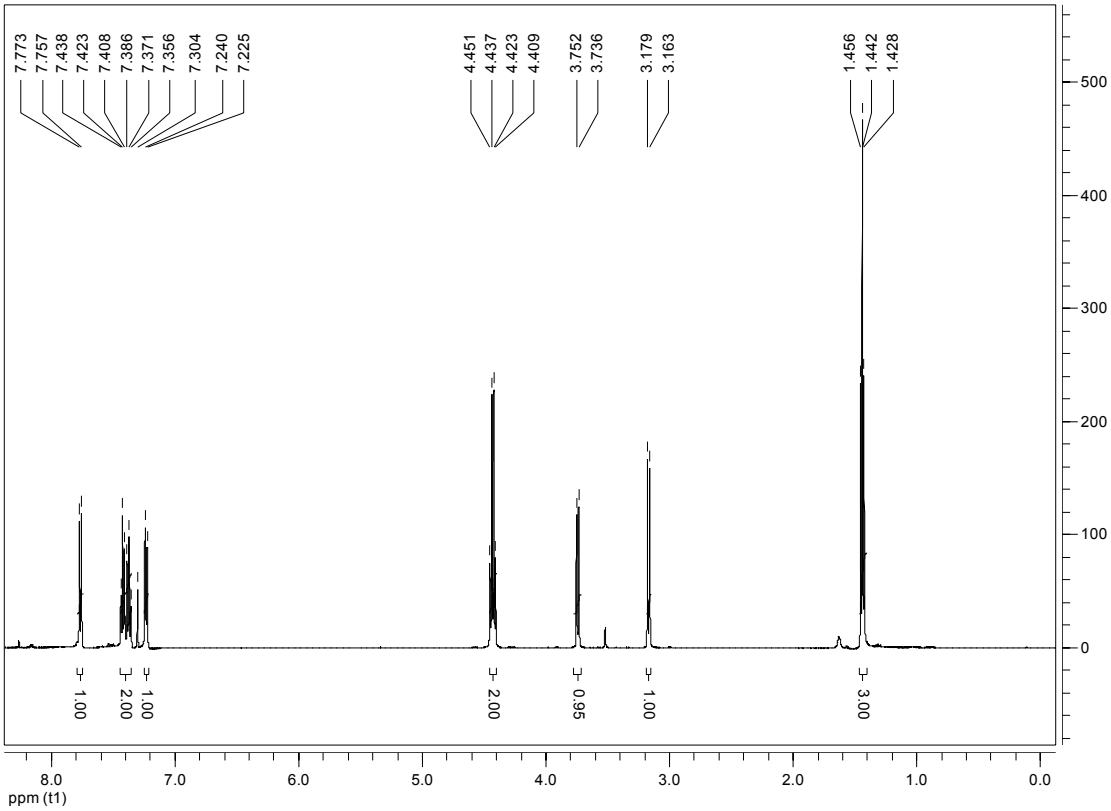
General procedure for the synthesis of cyclopropane derivatives

A mixture of pyridine (20.0mmol, 1.58g), ethyl α-bromoacetate (5.0mmol, 0.835g), aromatic aldehyde (5.0mmol), malononitrile (5.mmol, 0.330g) and triethylamine (1.0mL) in acetonitrile (20mL) was refluxed for 12 hours. The solvent was removed by evaporation and the residue was titrated with ethanol (10mL) to give the crude product, which is recrystallized in ethanol to give light yellow solid **D**

D1 (Ar = *p*-ClC_6H_4): yield 84.8%，mp: 175~176□。^{1}H NMR (600MHz, $CDCl_3$) δ (ppm) 7.43 (d, *J* = 8.4Hz, 2H, C_6H_4), 7.26 (d, *J* = 8.4Hz, 2H, C_6H_4), 4.71 (q, *J* = 7.2Hz, 2H, CH_2), 3.66 (d, *J* = 7.2Hz,1H, CH), 3.11 (d, *J* = 7.2Hz, 1H, CH), 1.39 (t, *J* = 7.2Hz,3H, CH_3).



D2 (Ar = *o*-BrC_6H_4): yield: 75.2% mp: 191-193□. ^{1}H NMR (600MHz, $CDCl_3$) δ(ppm) 7.77 (d, *J* = 9.6Hz, 1H, *o*-BrC_6H_4), 7.44~7.36 (m, 2H, *o*-BrC_6H_4), 7.23 (d, *J* = 8.4Hz, 1H, *o*-BrC_6H_4), 4.43 (q, *J* = 8.4Hz, 2H, CH_2), 3.74 (d, *J* = 7.2Hz, 1H, CH), 3.17 (d, *J* = 9.6Hz, 1H, CH), 1.44 (t, *J* = 8.4Hz, 3H, CH_3). ^{13}C NMR (600MHz, $CDCl_3$) δ(ppm) 164.5, 133.5, 133.5, 131.3, 131.3, 129.6, 129.6, 129.3, 129.3, 127.9, 127.9, 126.2, 126.207, 111.5, 111.3, 63.4, 39.2, 34.5, 14.0. C14H11BrN2O2 (M+ 318.93, 320.93)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7.423
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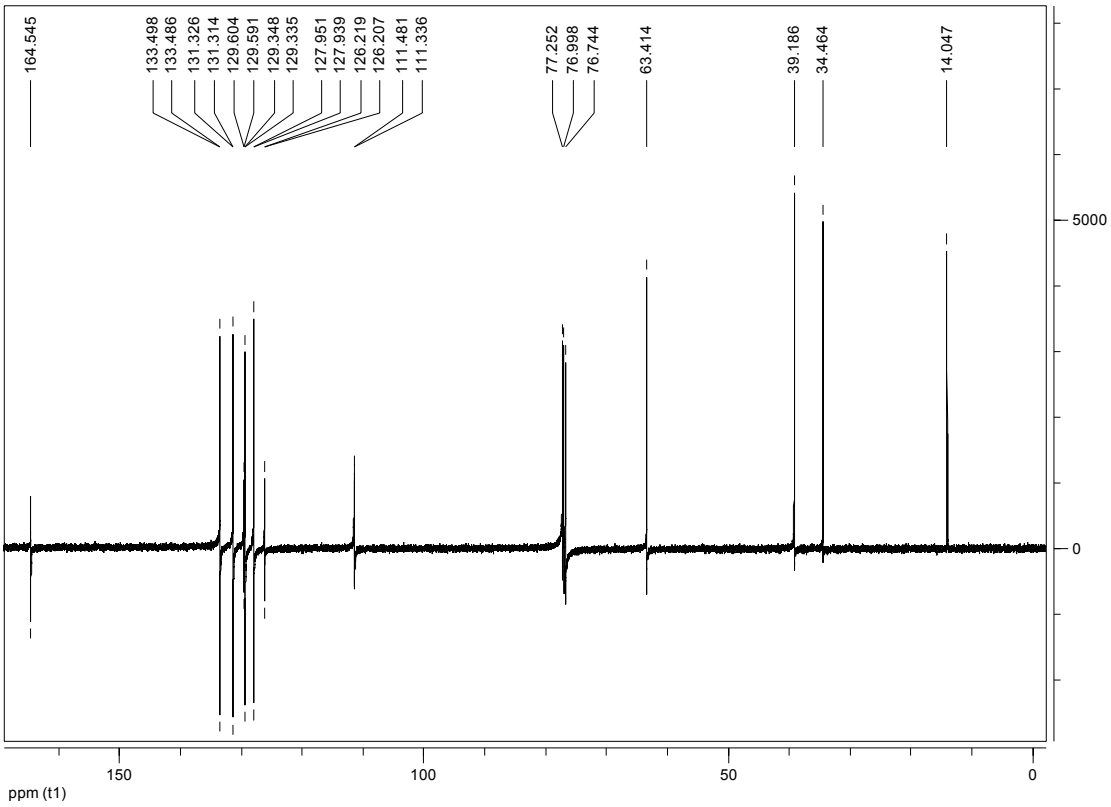
7.386
7.371
7.356
7.304
7.240
7.225
4.451
4.437
4.423
4.409
3.752
3.736
3.179
3.163
1.456
1.442
1.428
1.00
2.00
1.00
2.00
0.95
1.00
3.00
500
400
300
200
100
0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


164.545
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133.486
131.326
131.314
129.604
129.591
129.348
129.335
127.951
127.939
126.219
126.207
111.481
111.336
77.252
76.998
76.744
63.414
39.186
34.464
14.047
5000
0
150
100
50
0
ppm (t1)