

## One-Pot, Three-Component Coupling Approach to the Synthesis of $\alpha$ -Iminocarboxamides

Hisashi Masui, Shinichiro Fuse, and Takashi Takahashi\*

Department of Applied Chemistry, Tokyo Institute of Technology, 2-12-1 Ookayama, Meguro-ku, Tokyo  
152-8552, Japan

ttak@apc.titech.ac.jp

General----- S1

General procedure and spectral data----- S2

$^1\text{H}$  and  $^{13}\text{C}$  NMR spectra for products-----S10

---

### General

NMR spectra were recorded on a JEOL Model EX-270 (270 MHz for  $^1\text{H}$ , 67.8 MHz for  $^{13}\text{C}$ ) or a JEOL Model ECP-400 (400 MHz for  $^1\text{H}$ , 100 MHz for  $^{13}\text{C}$ ) instrument in the indicated solvent. In  $^1\text{H}$  NMR spectra, chemical shifts (ppm) referenced to internal tetramethylsilane (0.00 ppm) in  $\text{CDCl}_3$ . In  $^{13}\text{C}$  NMR spectra, chemical shifts (ppm) referenced to  $\text{CDCl}_3$  (77.1 ppm). Multiplicities are reported by the following abbreviation: s; singlet, d; doublet, t; triplet, q; quartet, sep; septet, m; multiplet, br; broad, *J*; coupling constants in Hertz.

IR spectra were recorded on Perkin-Elmer Spectrum One FT-IR spectrometer. Only the strongest and/or structurally important peaks are reported as IR data given in  $\text{cm}^{-1}$ . All reactions were monitored by thin-layer chromatography carried out on 0.2 mm E. Merck silica gel plate (60F-254) with UV light (254 nm), visualized by *p*-anisaldehyde solution, ceric sulfate or 10% ethanolic phosphomolybdic acid. Merck silica gel was used for column chromatography. ESI-TOF Mass spectra were measured with Waters LCT Premier<sup>TM</sup> XE. HRMS (ESI-TOF) were calibrated leu-enkephalin. All reagents were purified by distillation or recrystallization. Tetrahydro-2-(3-bromopropoxy)-2*H*-pyran (**11**)<sup>1</sup> and all isocyanides **2**, **8**, and **10**<sup>2</sup> were prepared according to literature procedures.

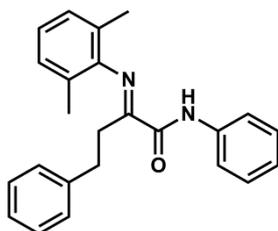
---

<sup>1</sup> Pinchuk, A. N.; Rampy, M. A.; Longino, M. A.; Skinner, R. W. S.; Gross, M. D.; Weichert, J. P.; Counsell, R. *E. J. Med. Chem.* **2006**, *49*, 2155.

<sup>2</sup> Obrecht, R.; Ugi, I. *Synthesis* **1985**, 400.

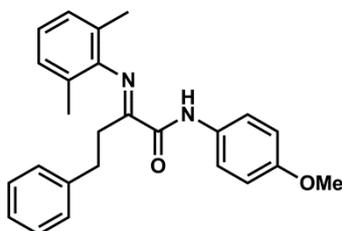
**General procedure for the preparation of  $\alpha$ -iminocarboxamide**

To a solution of **isocyanide** (2.00 equiv) and  $\text{SmI}_2$  (6.00 equiv) in THF and HMPA (16.0 equiv) was added **alkyl halide** (3.00 equiv) at  $-15\text{ }^\circ\text{C}$ . After being stirred at  $-15\text{ }^\circ\text{C}$  for 3 h, to the reaction mixture was added **isocyanate** (1.00 equiv) at  $-78\text{ }^\circ\text{C}$ . After being stirred at the same temperature for 5 min~12 h, the reaction mixture was quenched with water and diluted with hexane, filtered Florisil<sup>®</sup>, and concentrated *in vacuo*. The residue was purified by thin-layer chromatography (10% diethyl ether in hexane) to give  **$\alpha$ -iminocarboxamide**.

**2-(2,6-Dimethylphenylimino)-*N*,4-diphenylbutanamide (4a)**

According to the general procedure, 2,6-dimethylphenyl isocyanide (**2**) (32.8 mg, 0.250 mmol), HMPA (0.348 mL, 2.00 mmol),  $\text{SmI}_2$  (0.0933 M solution in THF, 8.04 mL, 0.750 mmol), phenethyl bromide (**1**) (50.7  $\mu\text{L}$ , 0.375 mmol) and phenyl isocyanate (**3**) (13.5  $\mu\text{L}$ , 0.125 mmol) was reacted. The residue was purified by thin-layer chromatography to give 2-(2,6-dimethylphenylimino)-*N*,4-diphenylbutanamide (**4a**) (51.3 mg, 0.143 mmol, quant) as a pale yellow solid.

mp  $84\text{ }^\circ\text{C}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.58 (br s, 1H), 7.74 (d,  $J = 7.7$  Hz, 2H), 7.40 (dd,  $J = 7.7, 7.7$  Hz, 2H), 7.23-7.11 (m, 4H), 7.07 (d,  $J = 7.7$  Hz, 2H), 7.04-6.97 (m, 3H), 2.81 (dd,  $J = 6.7, 9.2$  Hz, 2H), 2.70 (dd,  $J = 6.7, 9.2$  Hz, 2H), 1.96 (s, 6H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  166.2, 160.8, 145.9, 140.6, 137.3, 129.1, 128.5, 128.2, 128.1, 126.3, 125.1, 124.5, 124.3, 119.5, 32.4, 31.2, 18.0; IR (neat): 3337, 2923, 1691, 1649, 1601, 1529, 1445, 1378, 1175, 1091, 1065, 1030, 903  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) calcd for  $\text{C}_{24}\text{H}_{25}\text{N}_2\text{O}$   $[\text{M}+\text{H}]^+$  357.1967, found 357.1967.

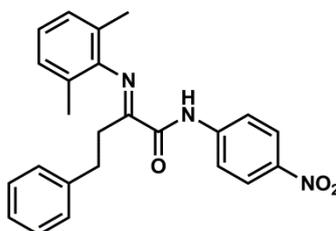
**2-(2,6-Dimethylphenylimino)-*N*-(4-methoxyphenyl)-4-phenylbutanamide (4b)**

According to the general procedure, 2,6-dimethylphenyl isocyanide (**2**) (32.8 mg, 0.250 mmol), HMPA (0.348 mL, 2.00 mmol),  $\text{SmI}_2$  (0.105 M solution in THF, 7.14 mL, 0.750 mmol), phenethyl bromide (**1**) (50.7  $\mu\text{L}$ , 0.375 mmol) and 4-methoxyphenyl isocyanate (**5**) (16.1  $\mu\text{L}$ , 0.125 mmol) was reacted. The residue was purified by thin-layer chromatography to give 2-(2,6-dimethylphenylimino)-*N*-(4-methoxyphenyl)-4-phenylbutanamide (**4b**) (50.4 mg, 0.130 mmol, quant)

as a yellow solid.

mp 137 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.47 (br s, 1H), 7.68-7.62 (m, 2H), 7.23-7.11 (m, 3H), 7.07 (d,  $J$  = 7.7 Hz, 2H), 7.03-6.96 (m, 3H), 6.95-6.90 (m, 2H), 3.81 (s, 3H), 2.80 (dd,  $J$  = 6.3, 9.6 Hz, 2H), 2.69 (dd,  $J$  = 6.3, 9.6 Hz, 2H), 1.96 (s, 6H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  166.3, 160.5, 156.5, 145.4, 140.6, 130.6, 128.4, 128.2, 128.1, 126.2, 125.1, 124.2, 121.0, 114.3, 55.4, 32.4, 31.3, 18.0; IR (neat): 3337, 2934, 1686, 1593, 1529, 1466, 1415, 1378, 1301, 1246, 1172, 1068, 1035, 908  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) calcd for  $\text{C}_{25}\text{H}_{27}\text{N}_2\text{O}_2$   $[\text{M}+\text{H}]^+$  387.2073, found 387.2075.

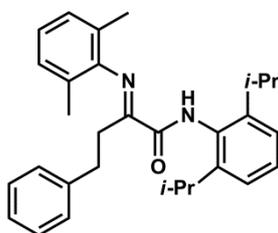
### 2-(2,6-Dimethylphenylimino)-*N*-(4-nitrophenyl)-4-phenylbutanamide (4c)



According to the general procedure, 2,6-dimethylphenyl isocyanide (**2**) (65.6 mg, 0.500 mmol), HMPA (0.696 mL, 4.00 mmol),  $\text{SmI}_2$  (0.100 M solution in THF, 15.0 mL, 1.50 mmol), phenethyl bromide (**1**) (101  $\mu\text{L}$ , 0.750 mmol) and 4-nitrophenyl isocyanate (**6**) (41.0 mg, 0.250 mmol) was reacted. The residue was purified by thin-layer chromatography to give 2-(2,6-dimethylphenylimino)-*N*-(4-nitrophenyl)-4-phenylbutanamide (**4c**) (85.8 mg, 0.214 mmol, 86%) as a yellow solid.

mp 137 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.93 (br s, 1H), 8.29 (d,  $J$  = 9.1 Hz, 2H), 7.91 (d,  $J$  = 9.1 Hz, 2H), 7.26-7.14 (m, 3H), 7.09 (d,  $J$  = 7.2 Hz, 3H), 7.05-7.01 (m, 2H), 7.02 (t,  $J$  = 7.2 Hz, 1H), 2.85-2.77 (m, 2H), 2.75-2.67 (m, 2H), 1.97 (s, 6H);  $^{13}\text{C}$  NMR (67.8 MHz,  $\text{CDCl}_3$ )  $\delta$  165.7, 161.1, 145.5, 143.78, 143.0, 140.2, 128.6, 128.3, 128.2, 126.4, 125.2, 125.0, 124.7, 119.1, 32.3, 31.1, 18.0; IR (neat): 3317, 2924, 1697, 1649, 1598, 1511, 1410, 1341, 1169, 1112, 906  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) calcd for  $\text{C}_{24}\text{H}_{24}\text{N}_3\text{O}_3$   $[\text{M}+\text{H}]^+$  402.1818, found 402.1824.

### *N*-(2,6-Diisopropylphenyl)-2-(2,6-dimethylphenylimino)-4-phenylbutanamide (4d)

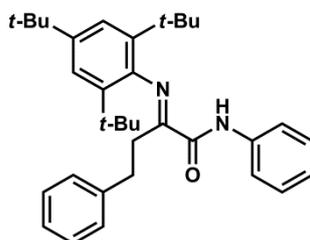


According to the general procedure, 2,6-dimethylphenyl isocyanide (**2**) (32.8 mg, 0.250 mmol), HMPA (0.348 mL, 2.00 mmol),  $\text{SmI}_2$  (0.100 M solution in THF, 7.50 mL, 0.750 mmol), phenethyl bromide (**1**) (50.7  $\mu\text{L}$ , 0.375 mmol) and 2,6-diisopropylphenyl isocyanate (**7**) (25.7  $\mu\text{L}$ , 0.125 mmol) was reacted. The residue was purified by thin-layer chromatography to give *N*-(2,6-diisopropylphenyl)-2-

(2,6-dimethylphenylimino)-4-phenylbutanamide (**4d**) (58.4 mg, 0.133 mmol, quant) as a pale yellow solid.

mp 124 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.99 (br s, 1H), 7.32 (dd,  $J = 6.7, 6.7$  Hz, 1H), 7.23-7.11 (m, 5H), 7.07 (d,  $J = 7.7$  Hz, 2H), 7.04-6.97 (m, 3H), 3.15 (sep,  $J = 6.8$  Hz, 2H), 2.85 (dd,  $J = 6.7, 8.7$  Hz, 2H), 2.73 (dd,  $J = 6.7, 8.7$  Hz, 2H), 1.95 (s, 6H), 1.26 (d,  $J = 6.8$  Hz, 12H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  166.0, 162.5, 146.1, 145.9, 140.5, 131.1, 128.4, 128.3, 128.1, 126.3, 125.2, 124.2, 123.5, 32.3, 31.3, 29.1, 23.5, 17.8; IR (neat): 3346, 2963, 1694, 1648, 1592, 1495, 1473, 1383, 1362, 1204, 1172, 1093, 1067, 940  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) calcd for  $\text{C}_{30}\text{H}_{37}\text{N}_2\text{O}$   $[\text{M}+\text{H}]^+$  441.2906, found 441.2905.

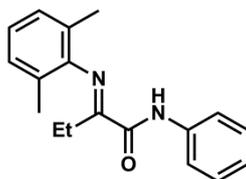
#### *N*,4-Diphenyl-2-(2,4,6-tri-*tert*-butylphenylimino)butanamide (**4e**)



According to the general procedure, 2,4,6-tri-*tert*-butylphenyl isocyanide (**8**) (67.9 mg, 0.250 mmol), HMPA (0.348 mL, 2.00 mmol),  $\text{SmI}_2$  (0.100 M solution in THF, 7.50 mL, 0.750 mmol), phenethyl bromide (**1**) (50.7  $\mu\text{L}$ , 0.375 mmol) and phenyl isocyanate (**3**) (13.5  $\mu\text{L}$ , 0.125 mmol) was reacted. The residue was purified by thin-layer chromatography to give *N*,4-diphenyl-2-(2,4,6-tri-*tert*-butylphenylimino)butanamide (**4e**) (49.0 mg, 0.0986 mmol, 79%) as a yellow solid.

mp 157 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.64 (br s, 1H), 7.75 (d,  $J = 7.7$  Hz, 2H), 7.41 (dd,  $J = 7.7, 7.7$  Hz, 2H), 7.32 (s, 2H), 7.23-7.10 (m, 4H), 6.99 (d,  $J = 7.2$  Hz, 2H), 2.80-2.74 (m, 2H), 2.52-2.47 (m, 2H), 1.34 (s, 18H), 1.33 (s, 9H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  166.1, 160.9, 145.3, 143.6, 141.4, 137.4, 137.0, 129.2, 128.4, 128.2, 126.0, 124.6, 122.2, 119.6, 36.1, 34.6, 33.3, 32.0, 31.6, 31.5; IR (neat): 3349, 2962, 1691, 1638, 1602, 1523, 1443, 1393, 1362, 1219, 1120, 1130, 879  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) calcd for  $\text{C}_{34}\text{H}_{45}\text{N}_2\text{O}$   $[\text{M}+\text{H}]^+$  497.3532, found 497.3536.

#### 2-(2,6-Dimethylphenylimino)-*N*-phenylbutanamide (**4f**)



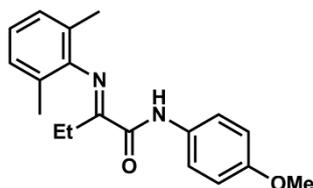
According to the general procedure, 2,6-dimethylphenyl isocyanide (**2**) (65.6 mg, 0.500 mmol), HMPA (0.696 mL, 4.00 mmol),  $\text{SmI}_2$  (0.100 M solution in THF, 15.0 mL, 1.50 mmol), ethyl bromide (**9**) (56.0  $\mu\text{L}$ , 0.750 mmol) and phenyl isocyanate (**3**) (27.1  $\mu\text{L}$ , 0.250 mmol) was reacted. The residue was purified by thin-layer chromatography to give 2-(2,6-dimethylphenylimino)-*N*-phenylbutanamide (**4f**) (56.2 mg, 0.200

## Supporting Information

mmol, 80%) as a pale yellow oil.

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  9.59 (br s, 1H), 7.72 (d,  $J = 7.9$  Hz, 2H), 7.38 (dd,  $J = 7.9, 7.9$  Hz, 2H), 7.15 (t,  $J = 7.9$  Hz, 1H), 7.11-7.06 (m, 2H), 7.03-6.92 (m, 1H), 2.42 (q,  $J = 7.6$  Hz, 2H), 2.04 (s, 6H), 1.04 (t,  $J = 7.6$  Hz, 3H);  $^{13}\text{C}$  NMR (67.8 MHz,  $\text{CDCl}_3$ )  $\delta$  168.1, 160.7, 146.2, 137.4, 129.1, 128.1, 125.0, 124.4, 124.1, 119.4, 22.2, 18.1, 10.8; IR (neat): 3336, 2939, 1692, 1650, 1601, 1527, 1444, 1379, 1314, 1144, 1093, 1035, 894  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) calcd for  $\text{C}_{18}\text{H}_{21}\text{N}_2\text{O}$   $[\text{M}+\text{H}]^+$  281.1654, found 281.1644.

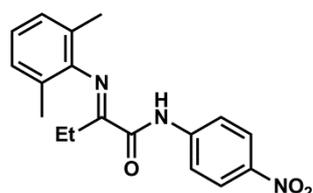
### 2-(2,6-Dimethylphenylimino)-*N*-(4-methoxyphenyl)butanamide (4g)



According to the general procedure, 2,6-dimethylphenyl isocyanide (**2**) (32.8 mg, 0.250 mmol), HMPA (0.348 mL, 2.00 mmol),  $\text{SmI}_2$  (0.100 M solution in THF, 7.50 mL, 0.750 mmol), ethyl bromide (**9**) (28.0  $\mu\text{L}$ , 0.375 mmol) and 4-methoxyphenyl isocyanate (**5**) (16.1  $\mu\text{L}$ , 0.125 mmol) was reacted. The residue was purified by thin-layer chromatography to give 2-(2,6-dimethylphenylimino)-*N*-(4-methoxyphenyl)butanamide (**4g**) (38.3 mg, 0.123 mmol, 99%) as a yellow oil.

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  9.49 (br s, 1H), 7.64 (d,  $J = 8.9$  Hz, 2H), 7.08 (d,  $J = 7.2$  Hz, 2H), 6.99 (dd,  $J = 7.2, 7.2$  Hz, 1H), 6.92 (d,  $J = 8.9$  Hz, 2H), 3.82 (s, 3H), 2.41 (q,  $J = 7.6$  Hz, 2H), 2.03 (s, 6H), 1.04 (t,  $J = 7.6$  Hz, 3H);  $^{13}\text{C}$  NMR (67.8 MHz,  $\text{CDCl}_3$ )  $\delta$  168.2, 160.4, 156.4, 146.2, 130.7, 128.1, 125.0, 124.0, 120.9, 114.3, 55.5, 22.2, 18.1, 10.8; IR (neat): 2939, 1649, 1593, 1527, 1465, 1379, 1108, 1037, 899  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) calcd for  $\text{C}_{19}\text{H}_{23}\text{N}_2\text{O}_2$   $[\text{M}+\text{H}]^+$  311.1760, found 311.1760.

### 2-(2,6-Dimethylphenylimino)-*N*-(4-nitrophenyl)butanamide (4h)



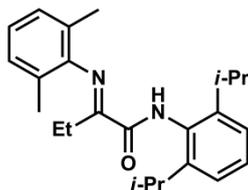
According to the general procedure, 2,6-dimethylphenyl isocyanide (**2**) (32.8 mg, 0.250 mmol), HMPA (0.348 mL, 2.00 mmol),  $\text{SmI}_2$  (0.100 M solution in THF, 7.50 mL, 0.750 mmol), ethyl bromide (**9**) (28.0  $\mu\text{L}$ , 0.375 mmol) and 4-nitrophenyl isocyanate (**6**) (20.5 mg, 0.125 mmol) was reacted. The residue was purified by thin-layer chromatography to give 2-(2,6-dimethylphenylimino)-*N*-(4-nitrophenyl)butanamide (**4h**) (26.7 mg, 0.0821 mmol, 66%) as a yellow solid.

mp 109  $^\circ\text{C}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.96 (br s, 1H), 8.28 (d,  $J = 9.2$  Hz, 2H), 7.90 (d,  $J = 9.2$  Hz, 2H),

## Supporting Information

7.11 (dd,  $J = 6.7, 6.7$  Hz, 2H), 7.02 (dd,  $J = 6.7, 8.3$  Hz, 1H), 2.43 (q,  $J = 7.7$  Hz, 2H), 2.04 (s, 6H), 1.06 (t,  $J = 7.7$  Hz, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  167.6, 161.0, 145.7, 143.7, 143.0, 128.2, 125.2, 124.9, 124.5, 119.0, 22.1, 18.1, 10.8; IR (neat): 3319, 2940, 1697, 1597, 1534, 1410, 1379, 1340, 1256, 1094, 1031, 968  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) calcd for  $\text{C}_{18}\text{H}_{20}\text{N}_3\text{O}_3$   $[\text{M}+\text{H}]^+$  326.1505, found 326.1515.

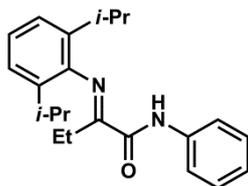
### *N*-(2,6-Diisopropylphenyl)-2-(2,6-dimethylphenylimino)butanamide (4i)



According to the general procedure, 2,6-dimethylphenyl isocyanide (**2**) (32.8 mg, 0.250 mmol), HMPA (0.348 mL, 2.00 mmol),  $\text{SmI}_2$  (0.100 M solution in THF, 7.50 mL, 0.750 mmol), ethyl bromide (**9**) (28.0  $\mu\text{L}$ , 0.375 mmol) and 2,6-diisopropylphenyl isocyanate **7** (25.7  $\mu\text{L}$ , 0.125 mmol) was reacted. The residue was purified by thin-layer chromatography to give *N*-(2,6-diisopropylphenyl)-2-(2,6-dimethylphenylimino) butanamide (**4i**) (46.8 mg, 0.128 mmol, quant) as a yellow solid.

mp 94  $^\circ\text{C}$ ;  $^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  9.00 (br s, 1H), 7.49-6.90 (m, 6H), 3.13 (septet,  $J = 6.9$  Hz, 2H), 2.43 (q,  $J = 7.6$  Hz, 2H), 2.08 (s, 6H), 1.25 (d,  $J = 6.9$  Hz, 12H), 1.04 (t,  $J = 7.6$  Hz, 3H);  $^{13}\text{C}$  NMR (67.8 MHz,  $\text{CDCl}_3$ )  $\delta$  168.2, 162.4, 146.4, 145.9, 131.2, 128.2, 128.1, 124.9, 124.0, 123.5, 29.1, 23.5, 22.4, 18.0, 10.7; IR (neat): 2964, 1694, 1652, 1593, 1496, 1382, 1363, 1146, 1094, 1061, 913  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) calcd for  $\text{C}_{24}\text{H}_{33}\text{N}_2\text{O}$   $[\text{M}+\text{H}]^+$  365.2593, found 365.2591.

### 2-(2,6-Diisopropylphenylimino)-*N*-phenylbutanamide (4j)

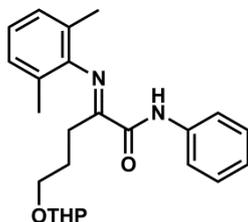


According to the general procedure, 2,6-diisopropylphenyl isocyanide (**2**) (31.2 mg, 0.167 mmol), HMPA (0.232 mL, 1.33 mmol),  $\text{SmI}_2$  (0.100 M solution in THF, 5.00 mL, 0.500 mmol), ethyl bromide (**9**) (18.7  $\mu\text{L}$ , 0.250 mmol) and phenyl isocyanate (**3**) (14.5  $\mu\text{L}$ , 0.133 mmol) was reacted. The residue was purified by thin-layer chromatography to give 2-(2,6-diisopropylphenylimino)-*N*-phenylbutanamide (**4j**) (12.7 mg, 37.7  $\mu\text{mol}$ , 57%) as a yellow oil.

$^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  9.54 (br s, 1H), 7.71 (d,  $J = 7.9$  Hz, 2H), 7.39 (dd,  $J = 7.9, 7.9$  Hz, 2H), 7.17-7.15 (m, 4H), 2.63 (septet,  $J = 6.9$  Hz, 2H), 2.44 (q,  $J = 7.6$  Hz, 2H), 1.20 (d,  $J = 6.9$  Hz, 6H), 1.14 (d,  $J = 6.9$  Hz, 6H), 1.08 (t,  $J = 7.6$  Hz, 3H);  $^{13}\text{C}$  NMR (67.8 MHz,  $\text{CDCl}_3$ )  $\delta$  167.7, 160.6, 143.6, 137.4, 135.5, 129.1, 124.8, 124.4, 123.1, 119.5, 28.3, 23.6, 22.6, 22.2, 10.5; IR (neat): 3339, 2964, 1693, 1648, 1602, 1527,

1443, 1362, 1327, 1188, 1143, 894  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) calcd for  $\text{C}_{22}\text{H}_{29}\text{N}_2\text{O}$   $[\text{M}+\text{H}]^+$  337.2280, found 337.2267.

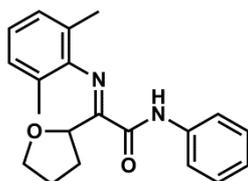
**2-(2,6-Dimethylphenylimino)-*N*-phenyl-5-((tetrahydro-2*H*-pyran-2-yl)oxy)pentanamide (4k)**



According to the general procedure, 2,6-dimethylphenyl isocyanide (**2**) (32.8 mg, 0.250 mmol), HMPA (0.348 mL, 2.00 mmol),  $\text{SmI}_2$  (0.100 M solution in THF, 7.50 mL, 0.750 mmol), 2-(3-bromopropoxy)tetrahydro-2*H*-pyran (**11**) (83.7 mg, 0.375 mmol) and phenyl isocyanate (**3**) (13.5  $\mu\text{L}$ , 0.125 mmol) was reacted. The residue was purified by thin-layer chromatography to give 2-(2,6-dimethylphenylimino)-*N*-phenyl-5-((tetrahydro-2*H*-pyran-2-yl)oxy)pentanamide (**4k**) (40.2 mg, 0.102 mmol, 82%) as a pale yellow oil.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.69 (br s, 1H), 7.11 (d,  $J = 7.7$  Hz, 2H), 7.37 (dd,  $J = 7.7, 7.7$  Hz, 2H), 7.14 (t,  $J = 7.7$  Hz, 1H), 7.06 (d,  $J = 7.7$  Hz, 2H), 6.98 (t,  $J = 7.7$  Hz, 1H), 4.44 (m, 1H), 3.75-3.60 (m, 2H), 3.46-3.32 (m, 2H), 2.57-2.42 (m, 2H), 2.06 (s, 3H), 2.03 (s, 3H), 1.79-1.61 (m, 3H), 1.59-1.34 (m, 5H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  166.9, 160.9, 146.0, 137.4, 129.1, 128.1, 125.2, 124.9, 124.3, 124.1, 119.4, 98.2, 66.6, 62.0, 30.4, 26.5, 25.9, 25.4, 19.2, 18.1, 18.0; IR (neat): 3337, 2942, 1692, 1648, 1601, 1527, 1444, 1353, 1259, 1121, 1079, 1033, 986  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) calcd for  $\text{C}_{24}\text{H}_{31}\text{N}_2\text{O}_3$   $[\text{M}+\text{H}]^+$  395.2335, found 395.2339.

**2-(2,6-Dimethylphenylimino)-*N*-phenyl-2-(tetrahydrofuran-2-yl)acetamide (4l)**

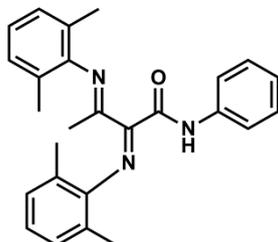


According to the general procedure, 2,6-dimethylphenyl isocyanide (**2**) (1.99 mg, 1.51 mmol), HMPA (2.09 mL, 12.0 mmol),  $\text{SmI}_2$  (0.100 M solution in THF, 45.0 mL, 4.50 mmol), iodobenzene (**12**) (0.140 mL, 2.25 mmol) and phenyl isocyanate (**3**) (0.130 mL, 1.20 mmol) was reacted. The residue was purified by column chromatography to give 2-(2,6-dimethylphenylimino)-*N*-phenyl-2-(tetrahydrofuran-2-yl)acetamide (**4l**) (194 mg, 0.602 mmol, 50%) as a yellow solid.

mp 115  $^\circ\text{C}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.42 (br s, 1H), 7.67 (d,  $J = 7.7$  Hz, 2H), 7.35 (dd,  $J = 7.7, 7.7$  Hz, 2H), 7.13 (t,  $J = 7.7$  Hz, 1H), 7.04 (d,  $J = 7.7$  Hz, 2H), 6.95 (t,  $J = 7.7$  Hz, 1H), 4.54 (t,  $J = 8.2$  Hz, 1H), 3.93-3.85 (m, 1H), 3.81-3.75 (m, 1H), 2.42-2.32 (m, 1H), 2.28-1.99 (m, 2H), 2.09 (s, 3H), 2.02 (s, 3H), 1.86-1.74 (m, 1H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  165.3, 160.1, 145.9, 137.3, 129.0, 127.8, 127.7, 125.0,

124.4, 123.8, 123.6, 119.6, 75.8, 69.6, 30.2, 26.7, 18.3, 18.1; IR (neat): 1634, 1523, 1443, 1170, 1090, 1009  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) calcd for  $\text{C}_{20}\text{H}_{23}\text{N}_2\text{O}_2$   $[\text{M}+\text{H}]^+$  323.1760, found 323.1744.

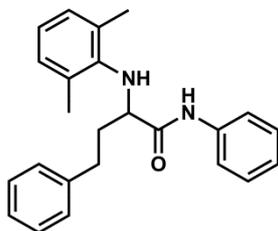
### 2,3-Bis(2,6-dimethylphenylimino)-*N*-phenylbutanamide (4m)



To a solution of 2,6-dimethylphenyl isocyanide (**2**) (98.4 mg, 0.750 mmol, 6.00 equiv),  $\text{SmI}_2$  (0.100 M solution in THF, 7.50 mL, 0.750 mmol, 6.00 equiv), and HMPA (0.348 mL, 2.00 mmol, 16.0 equiv) was added iodo methane (23.3  $\mu\text{L}$ , 0.375 mmol 3.00 equiv) at  $-15^\circ\text{C}$ . After being stirred at  $-15^\circ\text{C}$  for 4 h, to the reaction mixture was added phenyl isocyanate (**3**) (13.5  $\mu\text{L}$ , 0.125 mmol, 1.00 equiv). After being stirred at the same temperature for 30 min, the reaction mixture was quenched with water and diluted with hexane, filtered Florisil<sup>®</sup>, and concentrated *in vacuo*. The residue was purified by thin-layer chromatography (10% diethyl ether in hexane) to give 2,3-bis(2,6-dimethylphenylimino)-*N*-phenylbutanamide (**4m**) (26.6 mg, 0.0669 mmol, 54%) as an orange solid.

mp  $124^\circ\text{C}$ ;  $^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  9.47 (br s, 1H), 7.74 (d,  $J = 7.6$  Hz, 2H), 7.40 (dd,  $J = 7.6, 7.6$  Hz, 2H), 7.17 (t,  $J = 7.6$  Hz, 1H), 7.05-6.83 (m, 6H), 2.17 (s, 6H), 1.77 (s, 3H), 1.63 (s, 6H);  $^{13}\text{C}$  NMR (67.8 MHz,  $\text{CDCl}_3$ )  $\delta$  165.2, 161.3, 159.9, 147.0, 145.8, 137.0, 129.2, 128.0, 127.8, 125.7, 125.3, 124.8, 124.5, 123.4, 119.7, 19.2, 18.5, 17.2; IR (neat): 3021, 2921, 1693, 1652, 1596, 1531, 1445, 1358, 1091, 890  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) calcd for  $\text{C}_{26}\text{H}_{28}\text{N}_3\text{O}$   $[\text{M}+\text{H}]^+$  398.2232, found 398.2229.

### 2-(2,6-Dimethylphenylamino)-*N*,4-diphenylbutanamide (4n)

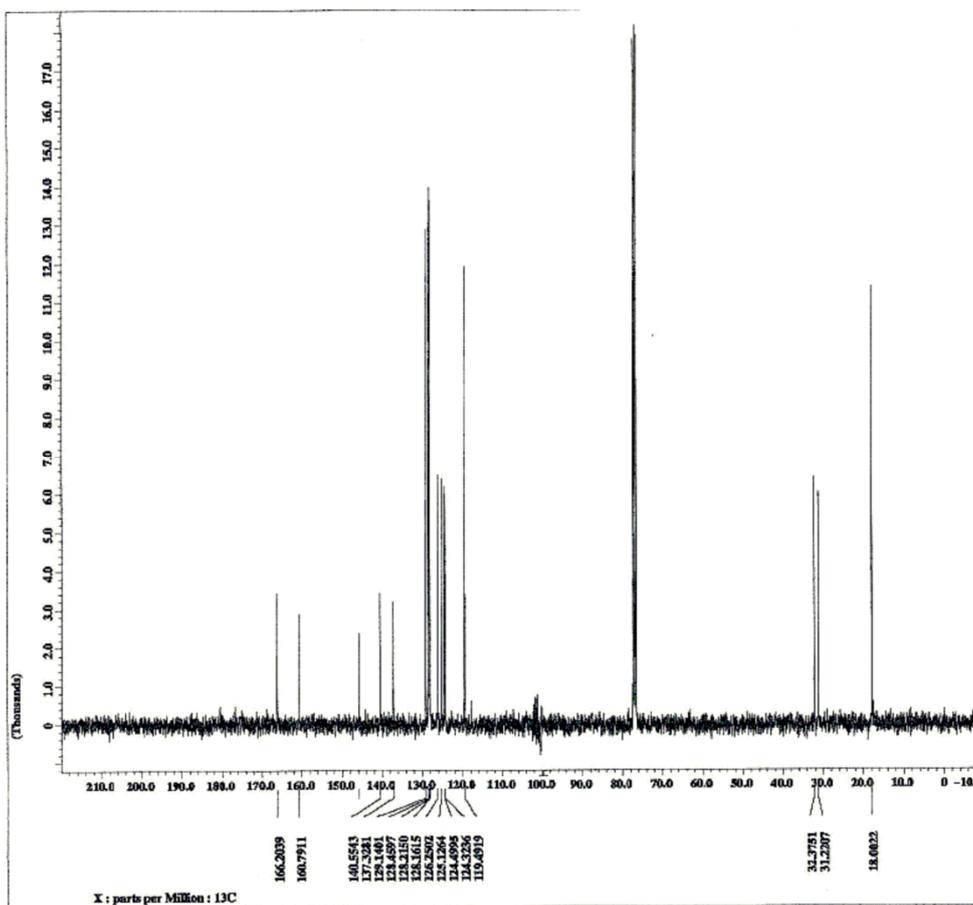
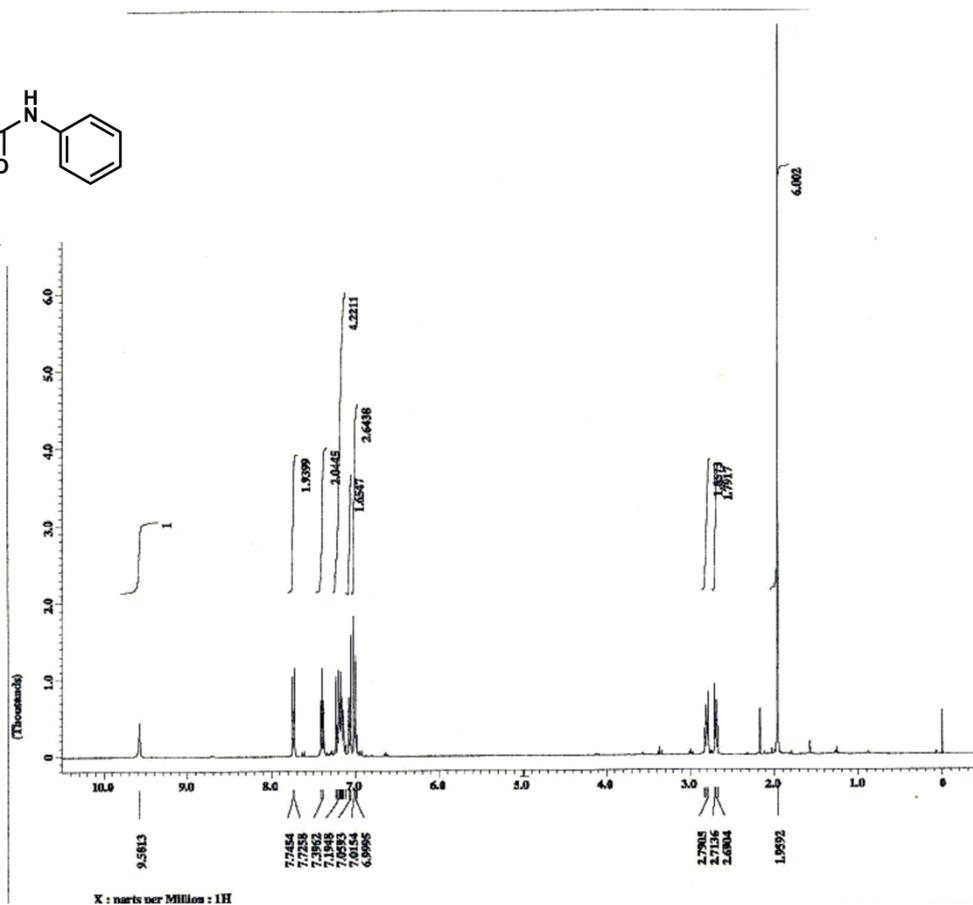
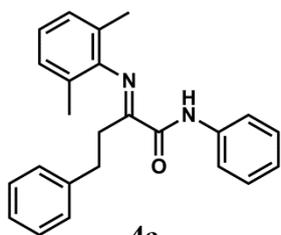


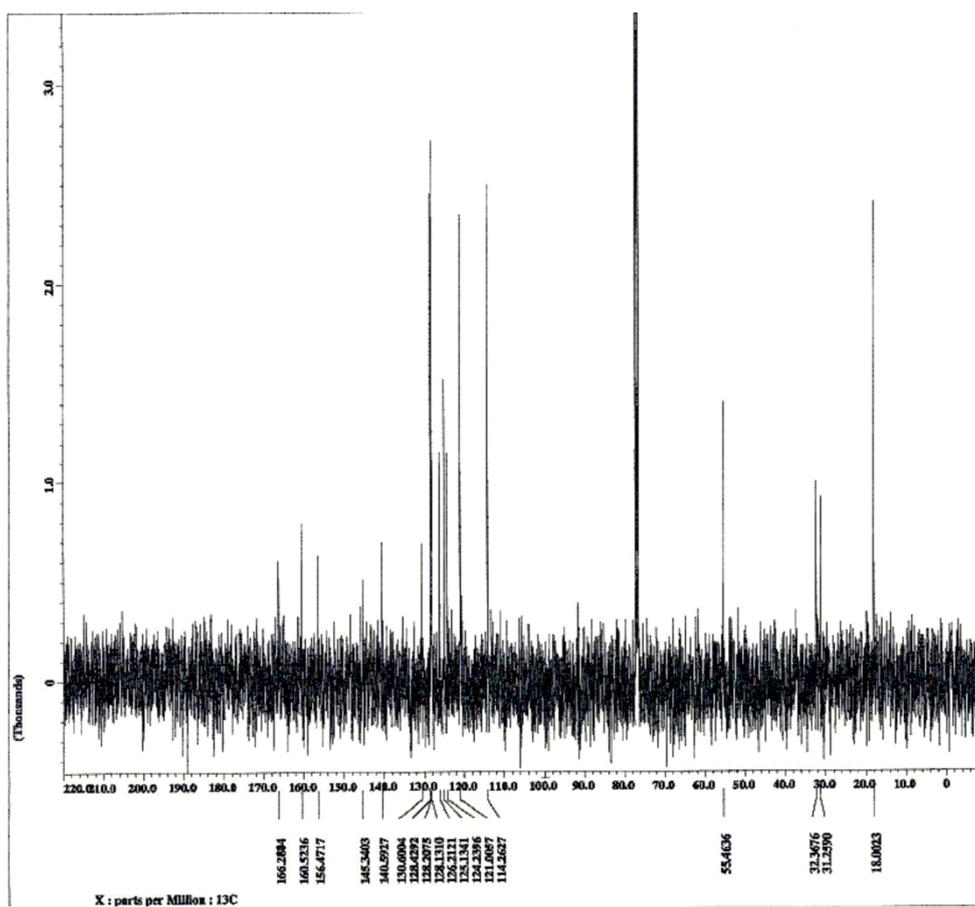
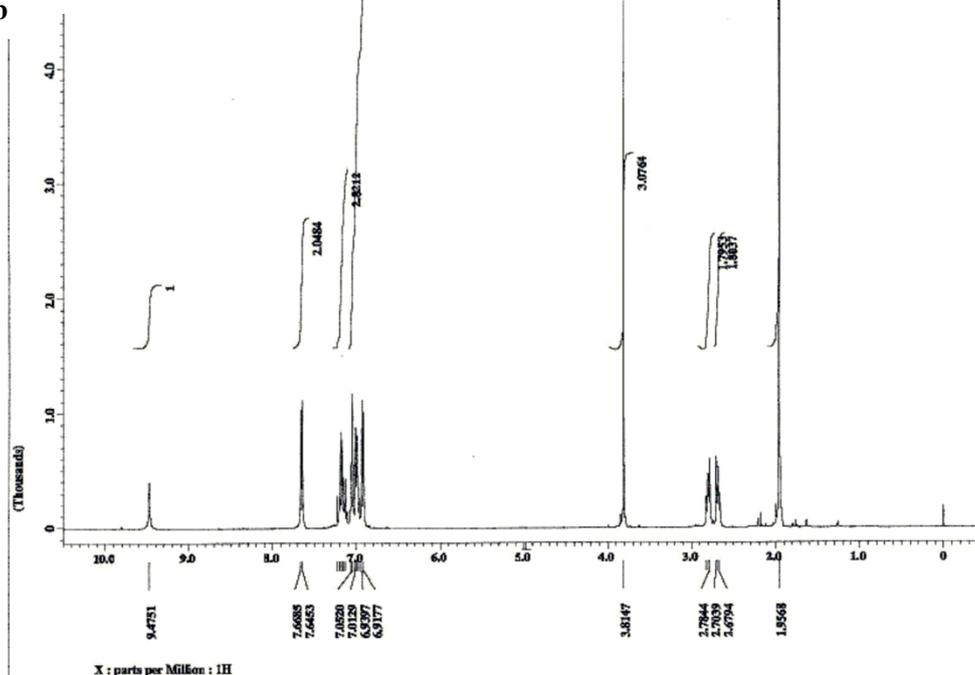
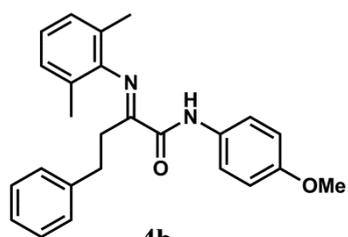
To a solution of 2,6-dimethylphenyl isocyanide (**2**) (32.8 mg, 0.250 mmol, 2.00 equiv),  $\text{SmI}_2$  (0.105 M solution in THF, 9.52 mL, 1.00 mmol, 8.00 equiv), and HMPA (0.348 mL, 2.00 mmol, 16.0 equiv) was added phenethyl bromide (**1**) (50.7  $\mu\text{L}$ , 0.375 mmol 3.00 equiv) at  $-15^\circ\text{C}$ . After being stirred at  $-15^\circ\text{C}$  for 3 h, to the reaction mixture was added phenyl isocyanate (**3**) (13.5  $\mu\text{L}$ , 0.125 mmol, 1.00 equiv). After being stirred at the same temperature for 30 min, the reaction mixture was quenched with water and diluted with hexane, filtered Florisil<sup>®</sup>, and concentrated *in vacuo*. The residue was purified by thin-layer chromatography (10% diethyl ether in hexane) to give 2-(2,6-dimethylphenylamino)-*N*,4-diphenylbutanamide (**4n**) (45.9 mg,

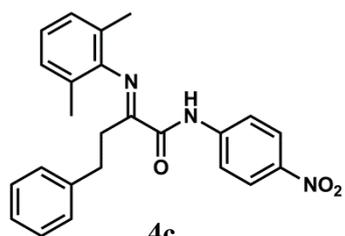
*Supporting Information*

0.128 mmol, quant) as a yellow solid.

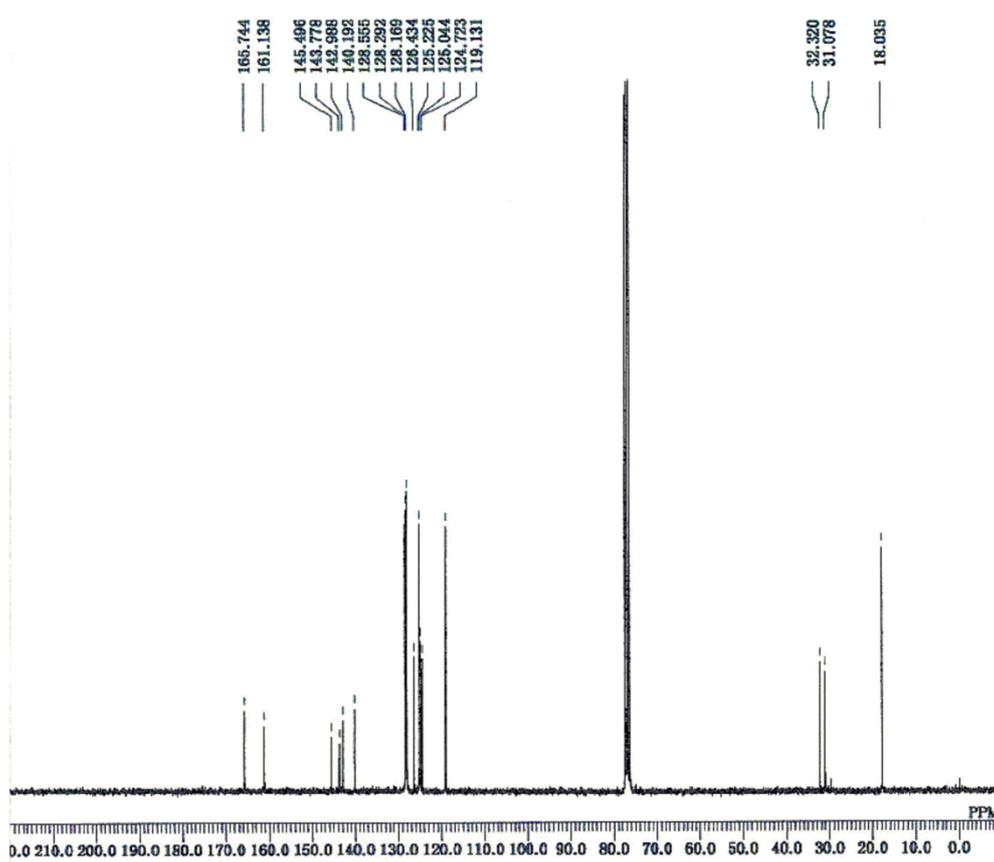
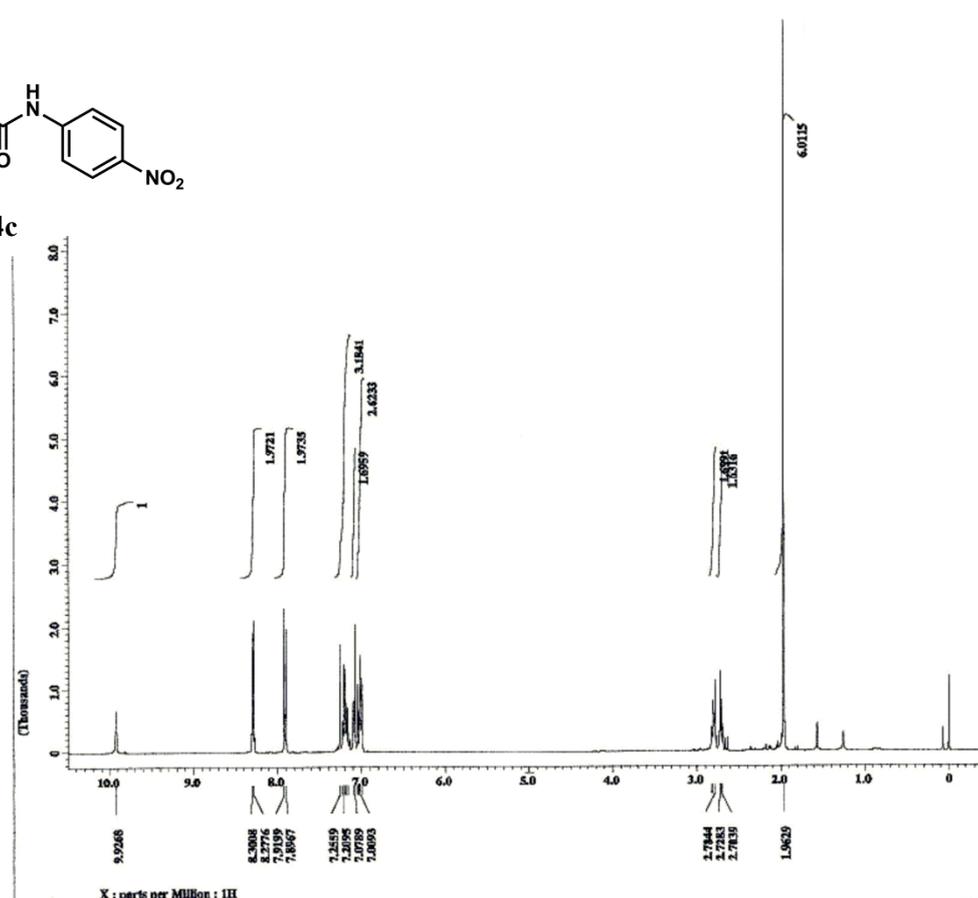
mp 136 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.96 (br s, 1H), 7.58 (d, *J* = 7.7 Hz, 2H), 7.35 (dd, *J* = 7.7, 7.7 Hz, 2H), 7.29-7.22 (m, 3H), 7.21-7.08 (m, 4H), 7.01 (d, *J* = 7.7 Hz, 2H), 6.86 (dd, *J* = 7.7, 7.7 Hz, 1H), 3.75-3.67 (m, 2H), 2.78-2.74 (m, 2H), 2.41-2.30 (m, 1H), 2.27 (s, 6H), 2.23-2.18 (m, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 171.8, 144.6, 140.7, 137.5, 129.5, 129.1, 128.5, 128.4, 128.0, 126.2, 124.4, 122.3, 119.6, 62.0, 36.0, 31.9, 19.0; IR (neat): 3310, 2925, 1655, 1600, 1523, 1475, 1443, 1310, 1102, 1030 cm<sup>-1</sup>; HRMS (ESI-TOF) calcd for C<sub>24</sub>H<sub>27</sub>N<sub>2</sub>O [M+H]<sup>+</sup> 359.2123, found 359.2122.

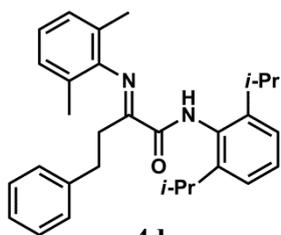




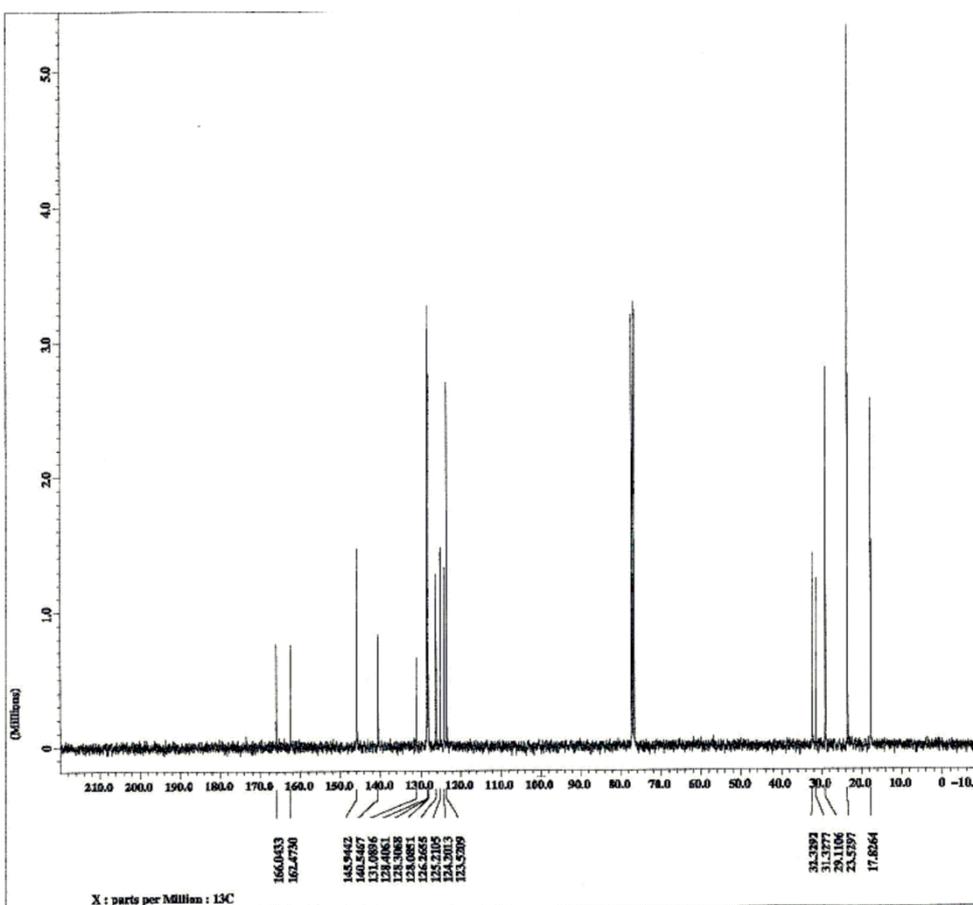
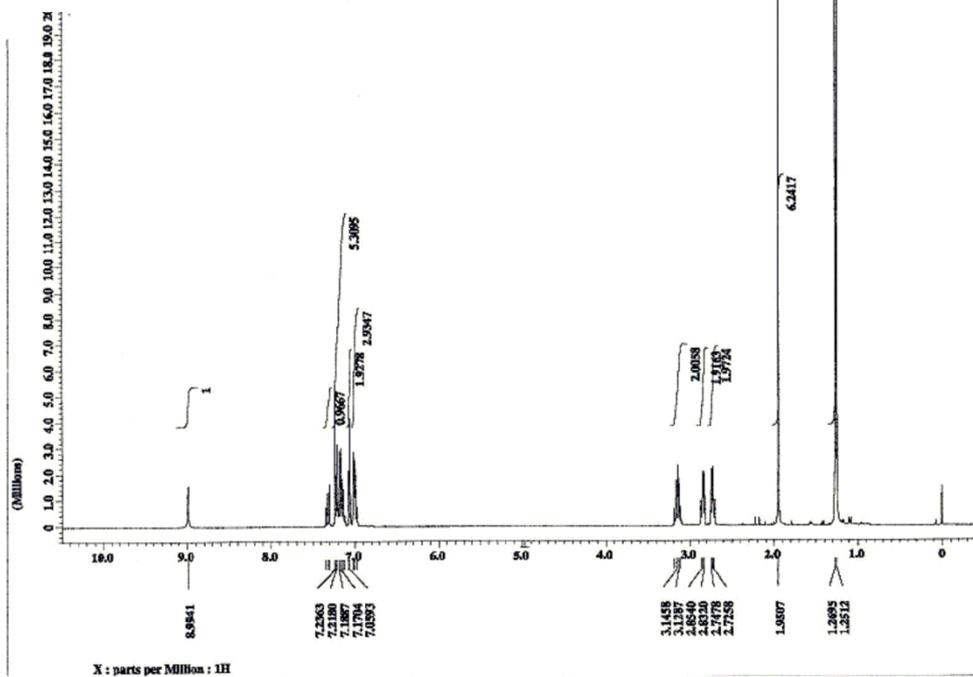


4c

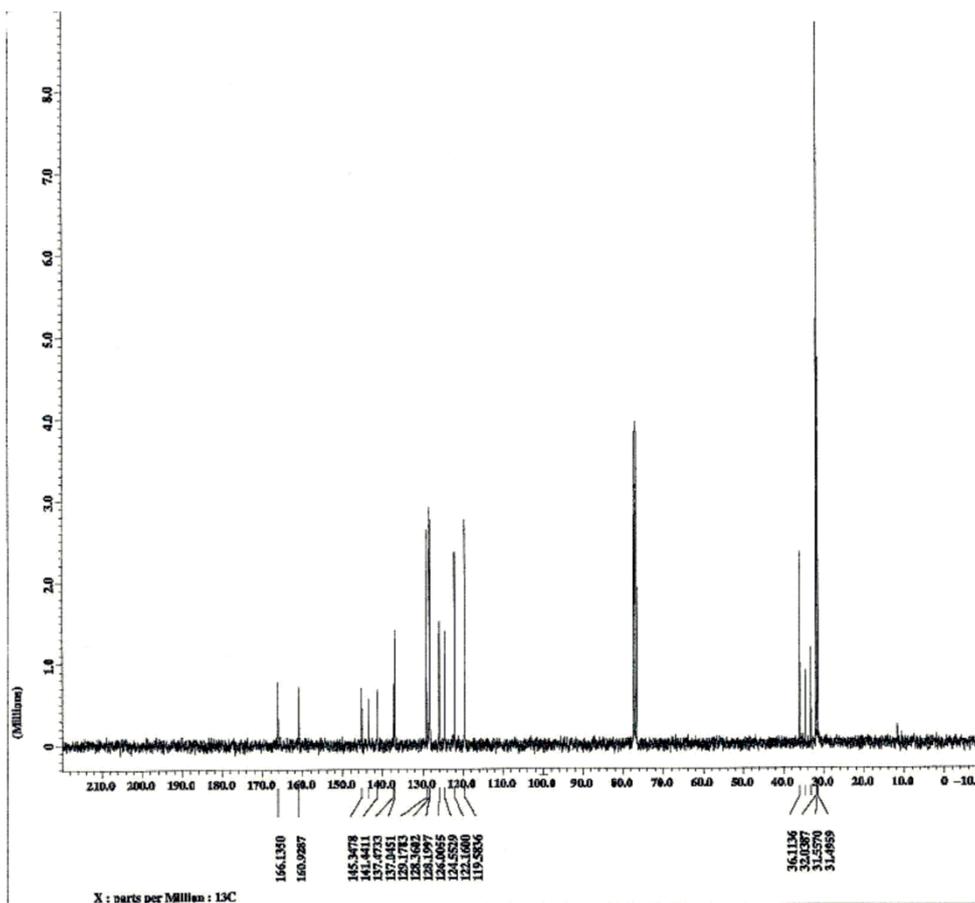
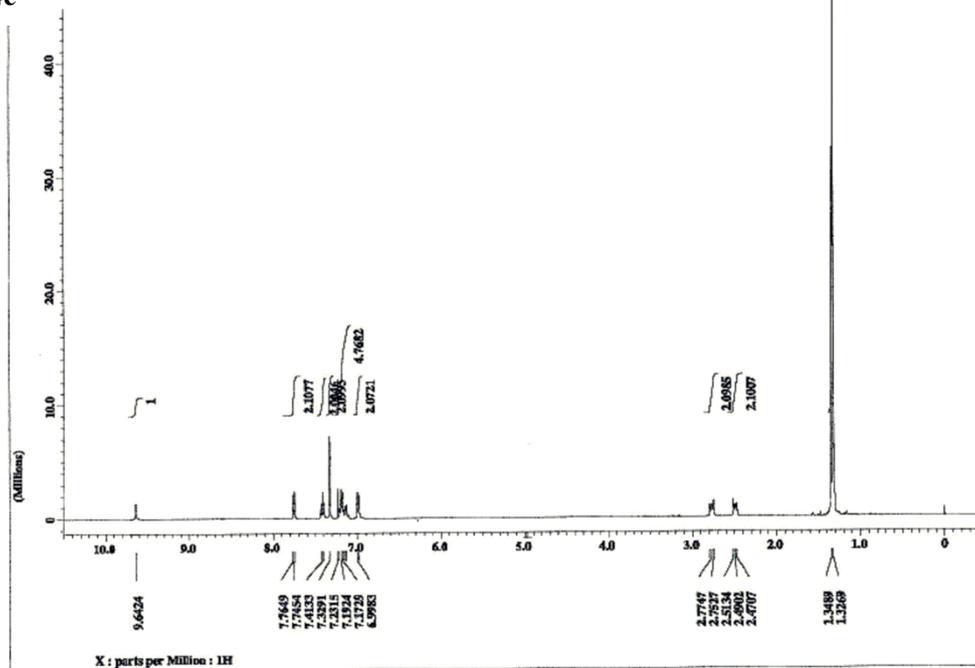
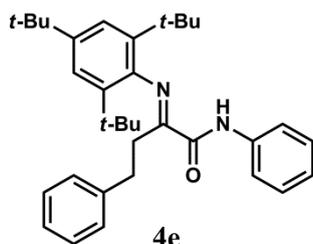




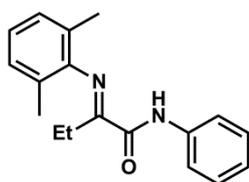
4d



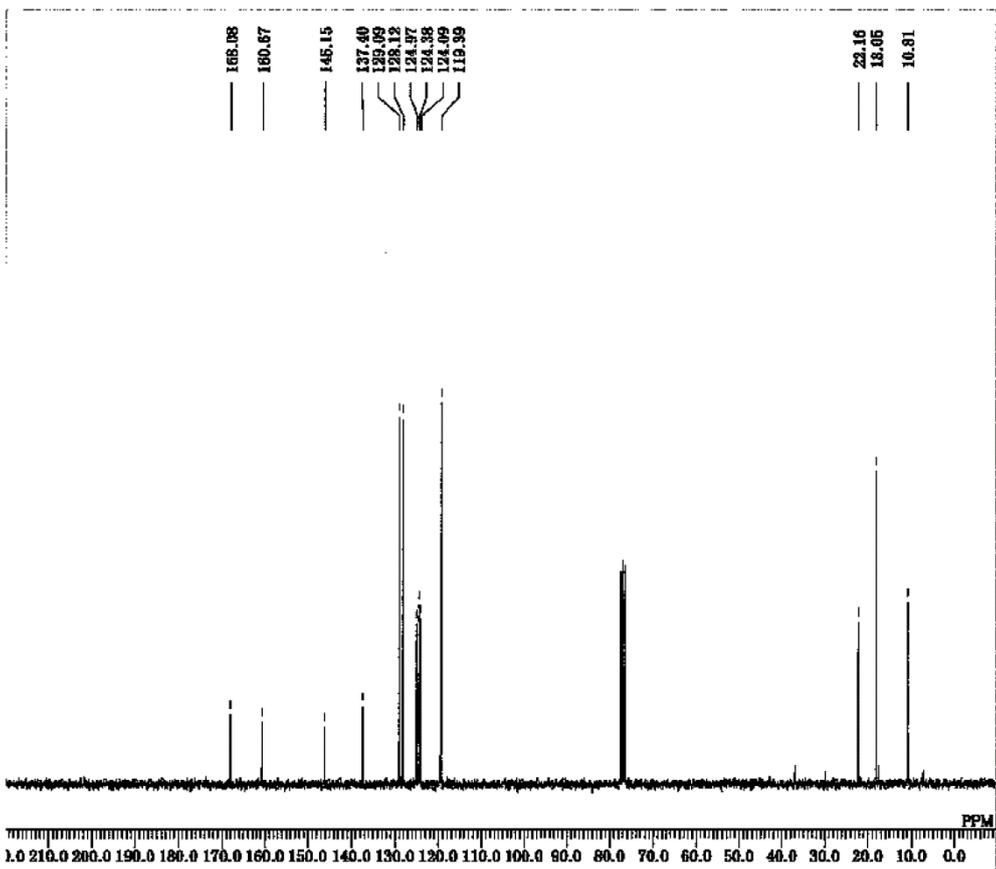
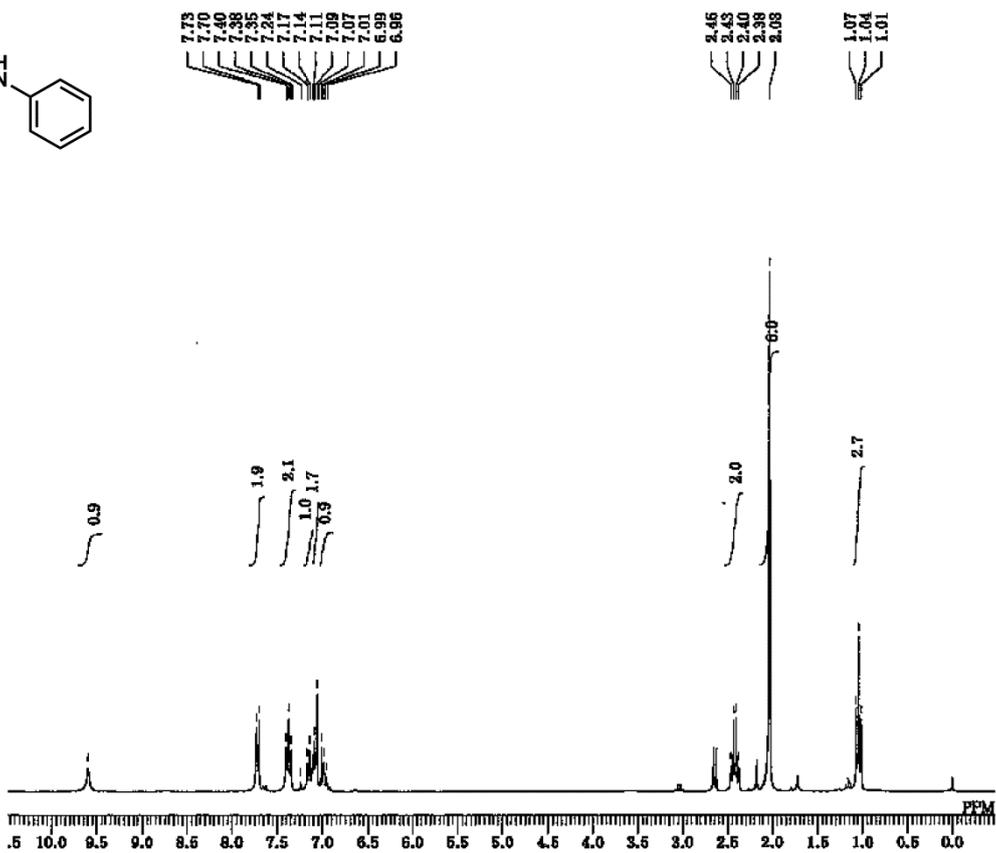
Supporting Information

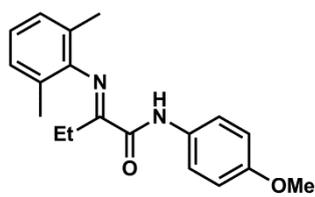


Supporting Information

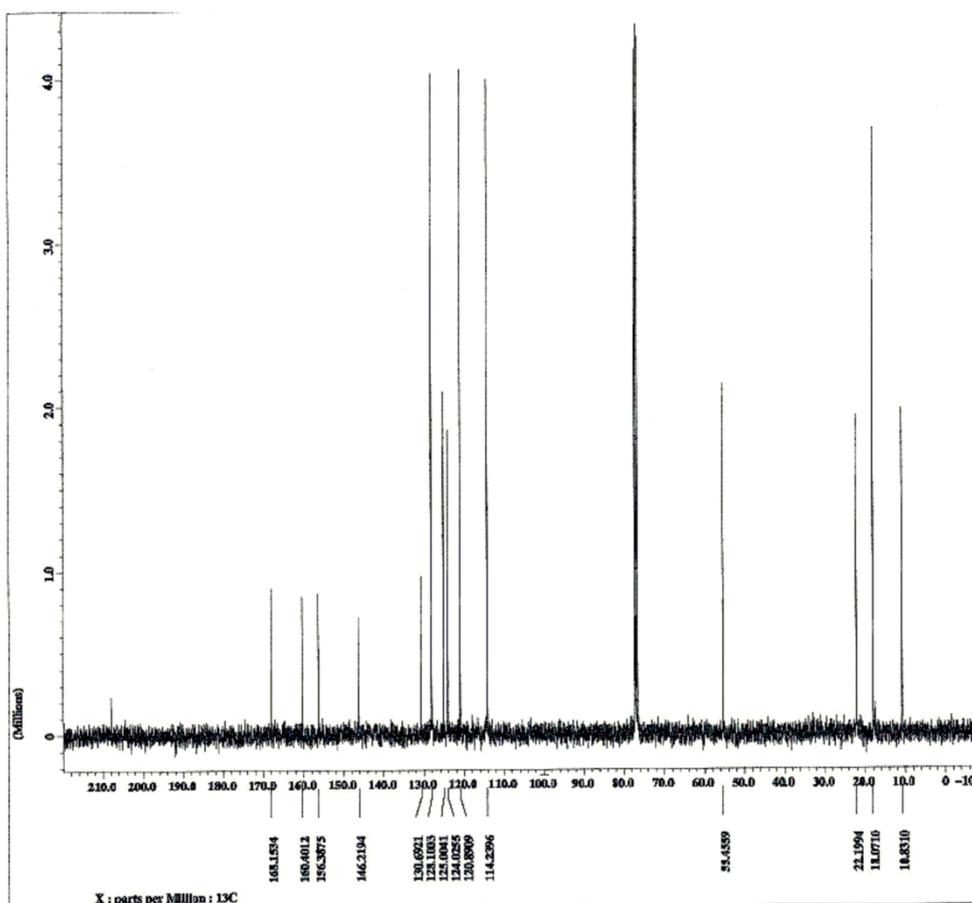
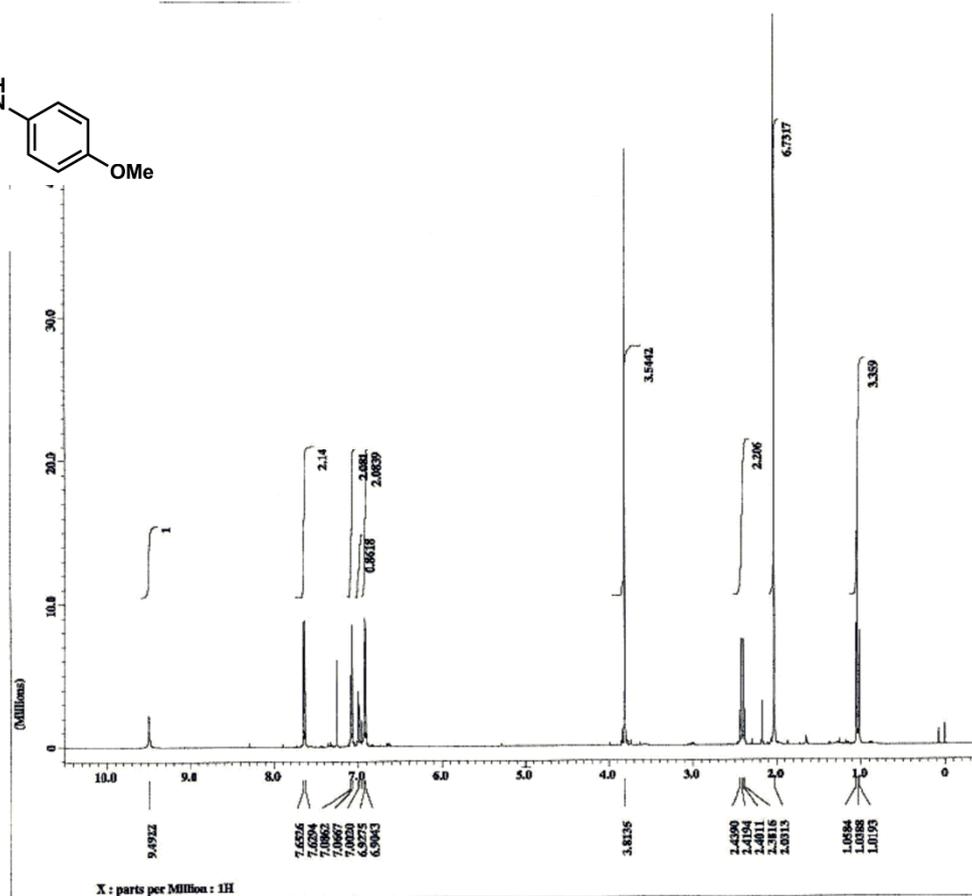


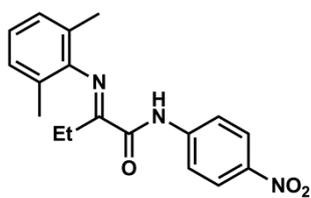
4f



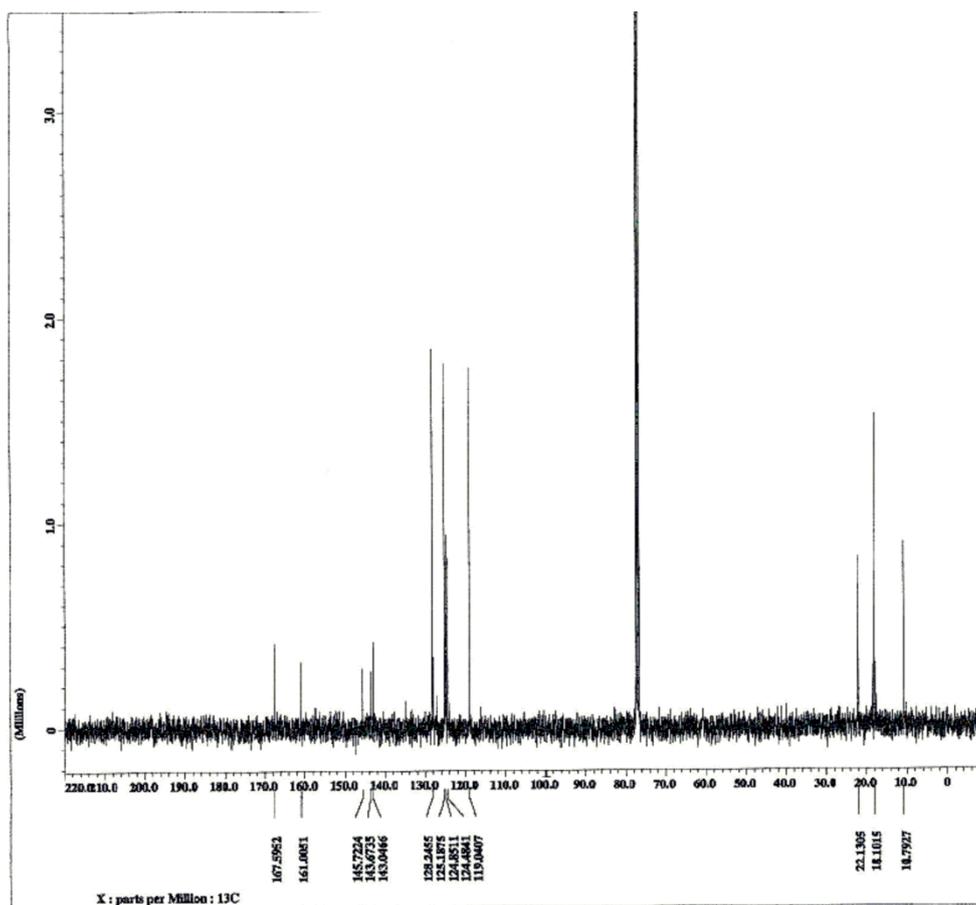
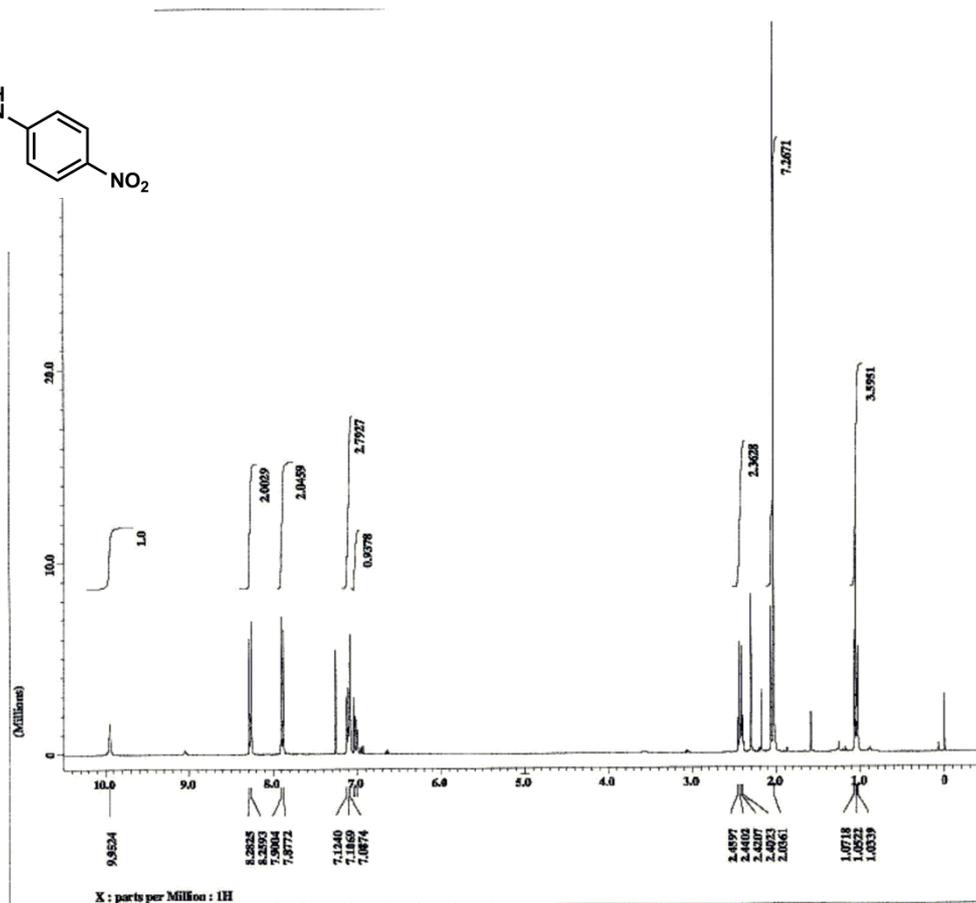


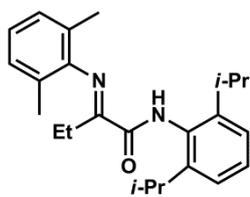
4g



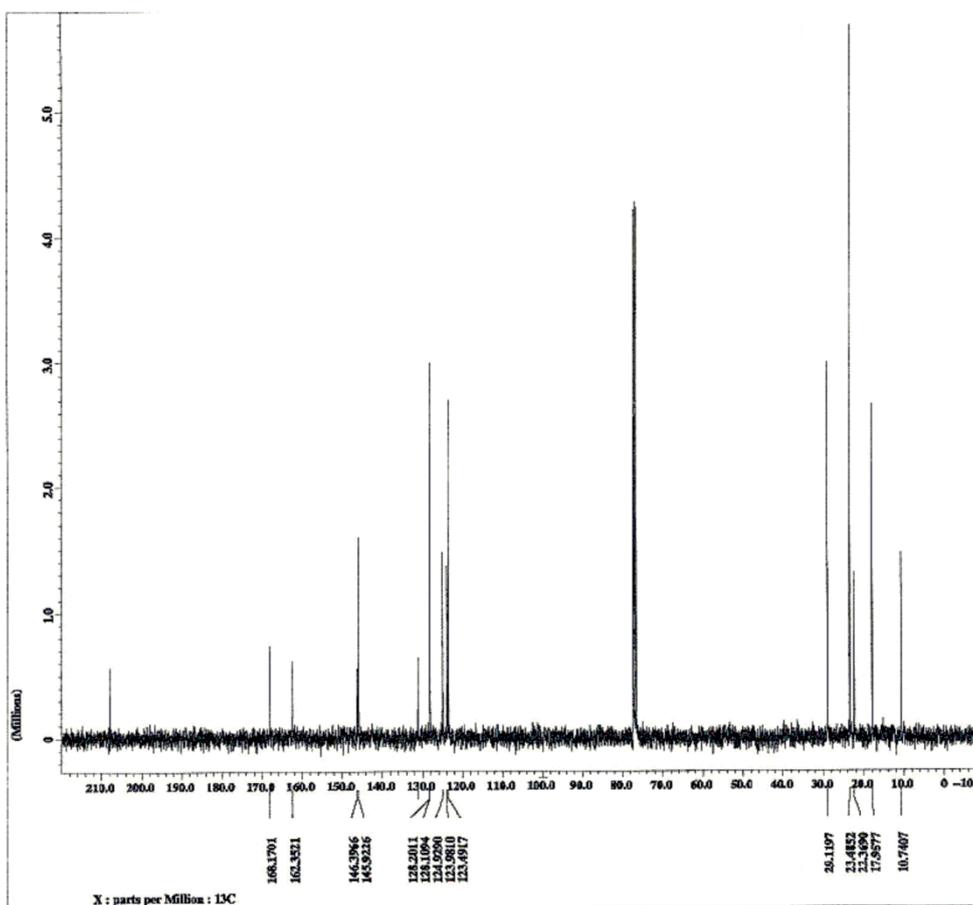
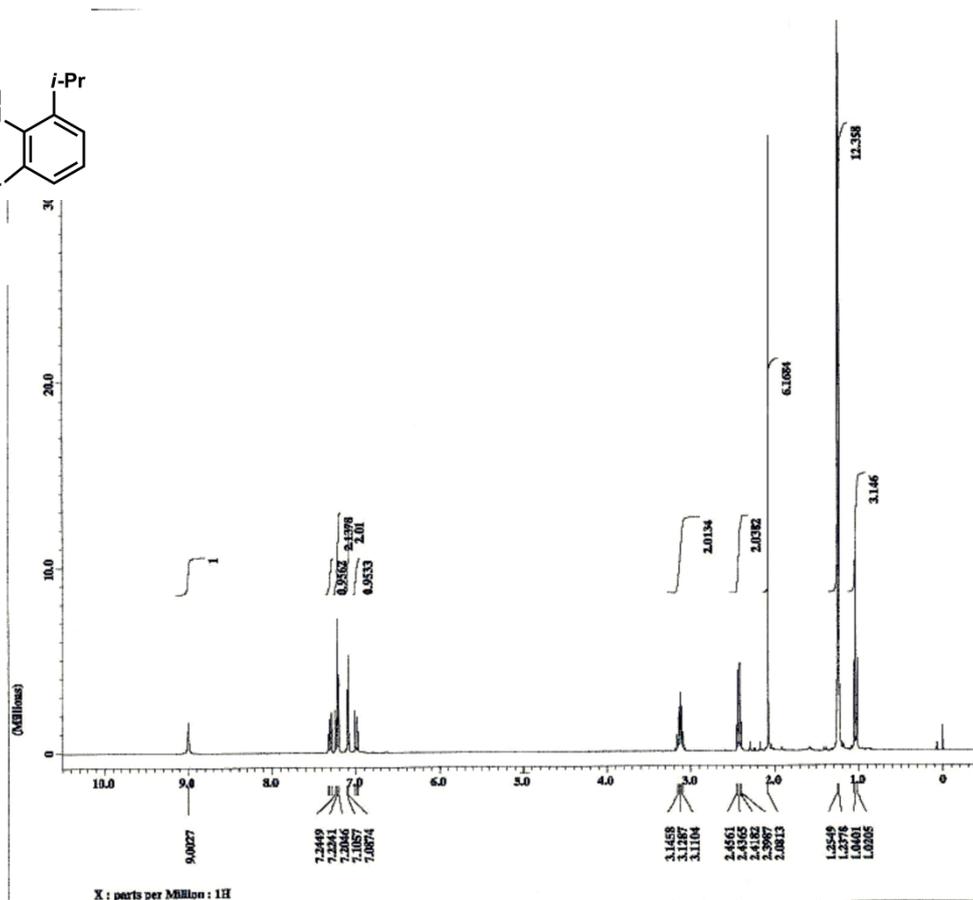


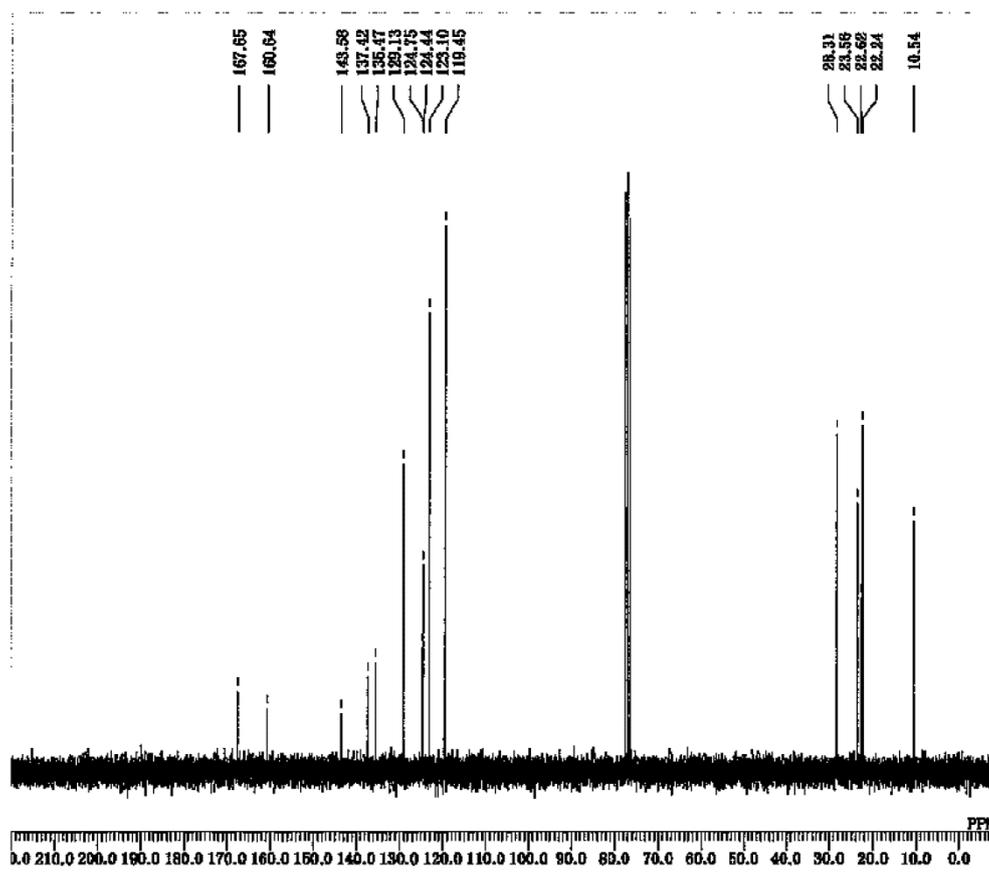
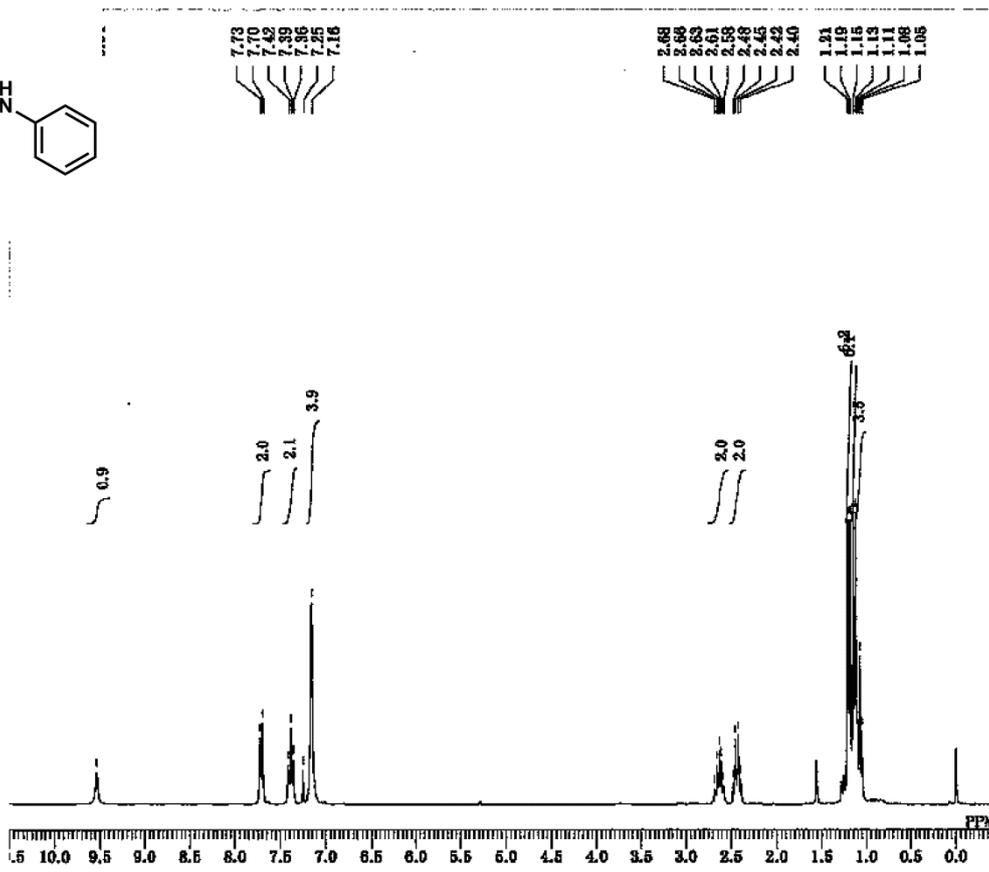
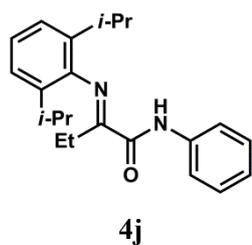
4h



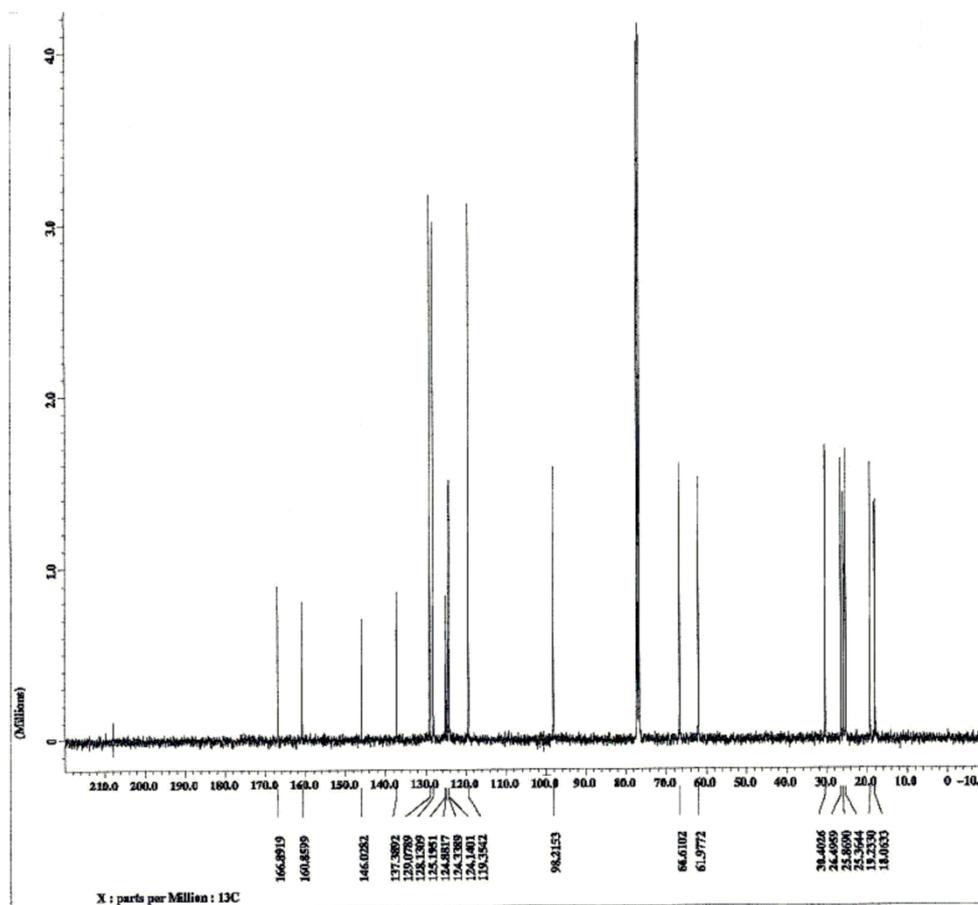
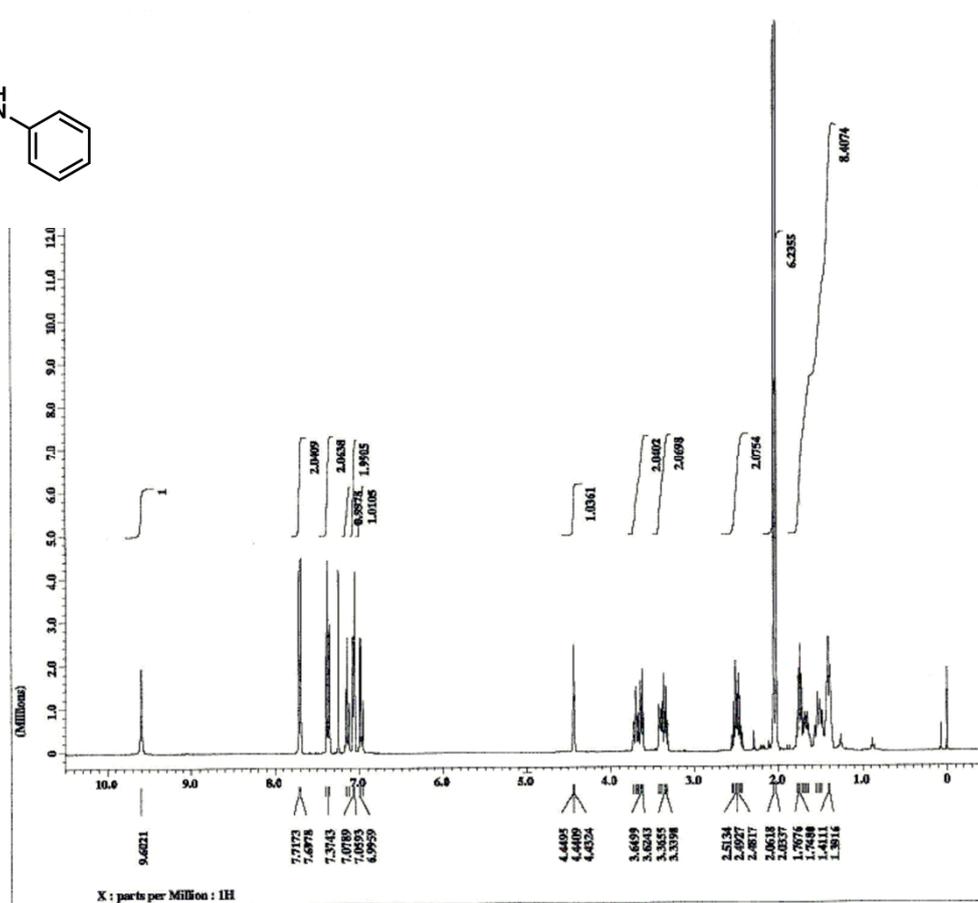
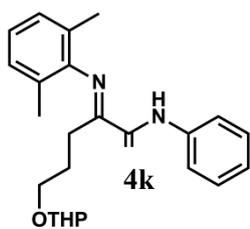


4i

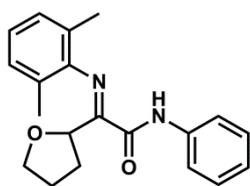




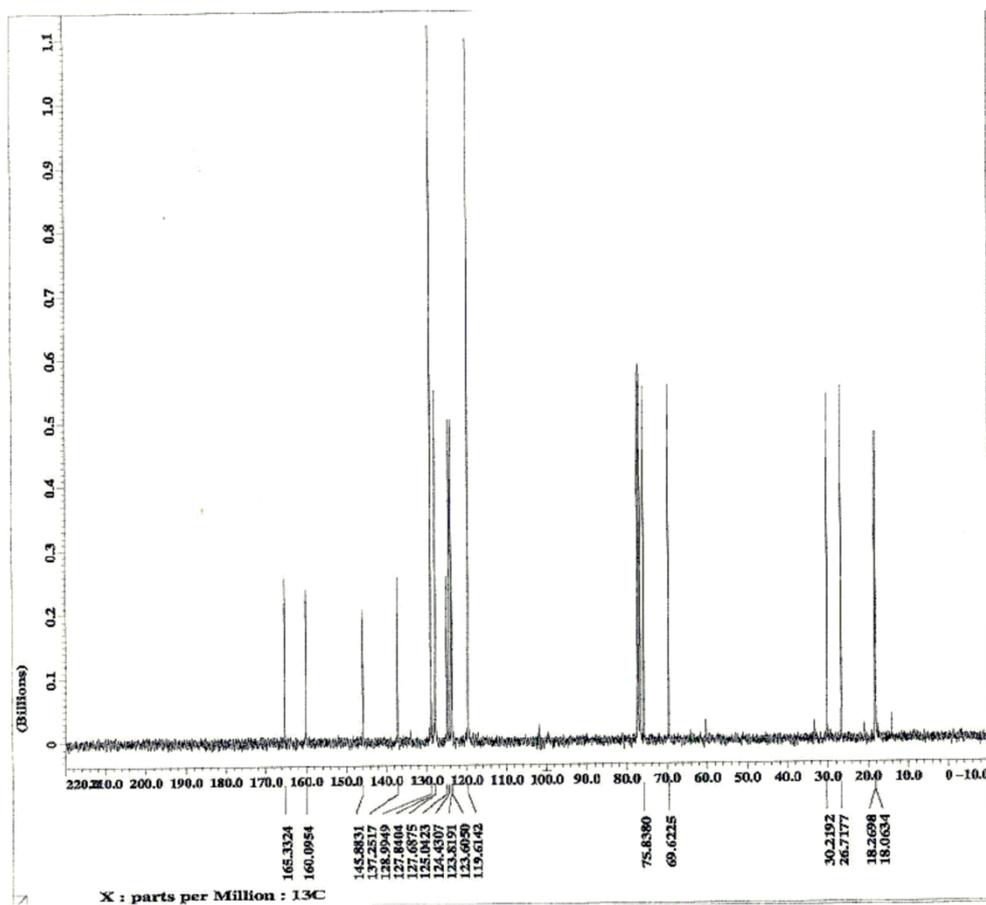
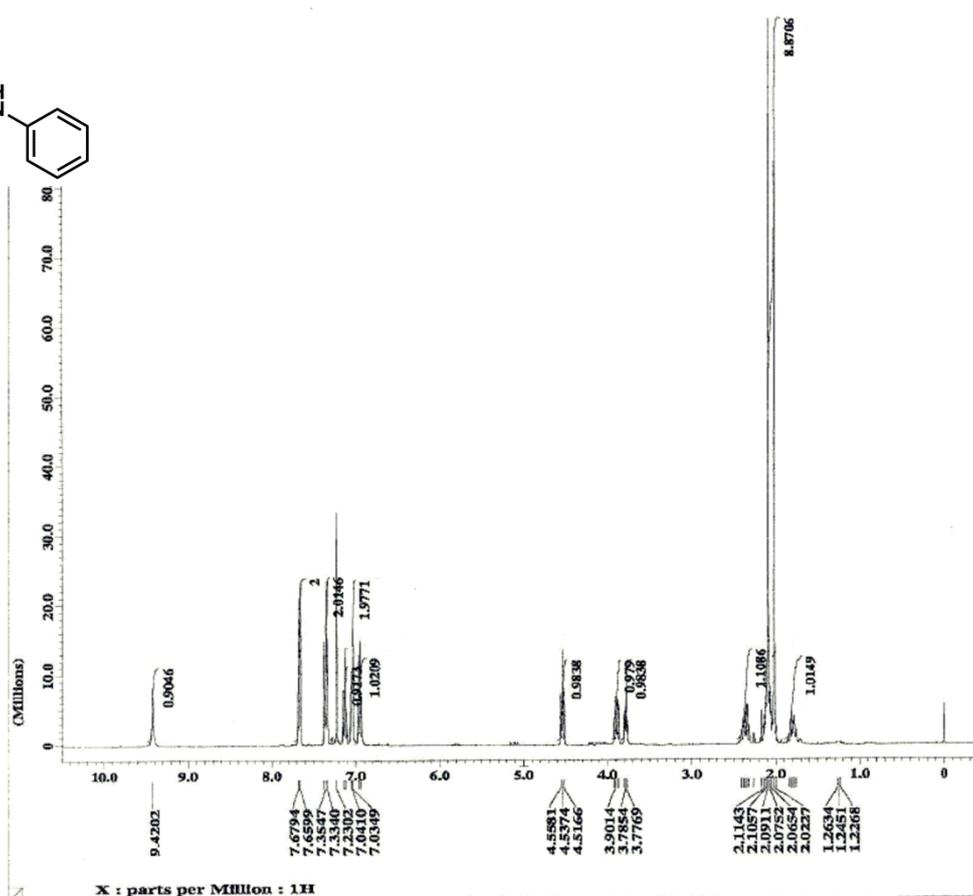
Supporting Information



Supporting Information



4I



Supporting Information

