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Catalyst-free visible-light-induced condensation to synthesize bis(indolyl)methanes and biological activity evaluation of them as potent human carboxylesterase 2 inhibitors

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Contents:

3,3'-(phenylmethylene)bis(2-methyl-1H-indole) (4a). Pale pink solid; mp = 262-263 °C (243-245 [lit 1]); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 10.72 (s, 2H), 7.27-7.18 (m, 7H), 6.91-6.87 (m, 2H), 6.81 (d, J = 7.9 Hz, 2H), 6.69-6.66 (m, 2H), 5.93 (s, 1H), 2.07 (s, 6H).

3,3'-(*o*-tolylmethylene)bis(2-methyl-1H-indole) (4b). Pale pink solid; mp = 263-265 °C (255 [lit 2]); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 10.69 (s, 2H), 7.21 (d, J = 8.0 Hz, 2H), 7.16-7.11 (m, 2H), 7.03 (d, J = 2.9 Hz, 2H), 6.89 (t, J = 7.5 Hz, 2H), 6.77 (d, J = 7.9 Hz, 2H), 6.66 (t, J = 7.5 Hz, 2H), 5.88 (s, 1H), 2.13 (s, 3H), 2.00 (s, 6H).

3,3'-(*m*-tolylmethylene)bis(2-methyl-1H-indole) (4c). Pale pink solid; mp = 260-262 °C (181-184 [lit 3]); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 10.70 (s, 2H), 7.21 (d, J = 7.9 Hz, 2H), 7.14-7.11 (m, 1H), 7.05-6.82 (m, 7H), 6.67 (t, J = 7.4 Hz, 2H), 5.88 (s, 1H), 2.21 (s, 3H), 2.05 (s, 6H).

3,3'-(*p*-tolylmethylene)bis(2-methyl-1H-indole) (4d). Pale pink solid; mp = 225-227 °C (175-176 [lit 1]); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 10.69 (s, 2H), 7.21 (d, J = 8.0 Hz, 2H), 7.08-7.04 (m, 4H), 6.90-6.87 (t, J = 7.5 Hz, 2H), 6.84-6.82 (d, J = 7.9 Hz, 2H), 6.69 (t, J = 7.9 Hz, 2H), 5.87 (s, 1H), 2.28 (s, 3H), 2.06 (s, 6H).

3,3'-((2-methoxyphenyl)methylene)bis(2-methyl-1H-indole) (4e). Pale pink solid; mp = 252-254 °C (240-242 [lit 4]); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 10.61 (s, 2H), 7.23-7.18 (m, 3H), 7.07 (dd, J = 7.6, 1.6 Hz, 1H), 7.00 (d, J = 7.6 Hz, 1H), 6.88-6.85 (m, 2H), 6.82-6.77 (m, 3H), 6.67-6.63 (m, 2H), 6.09 (s, 1H), 3.67 (s, 3H), 1.97 (s, 6H).

3,3'-((3-methoxyphenyl)methylene)bis(2-methyl-1H-indole) (4f). Pale pink solid; mp = 250-253 °C (237-239 [lit 5]); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 10.71 (s, 2H), 7.22-7.15 (m, 3H), 6.91-6.87 (m, 2H), 6.84 (d, J = 7.9 Hz, 2H), 6.80-6.74 (m, 3H), 6.70-6.67 (m, 2H), 5.89 (s, 1H), 3.63 (s, 3H), 2.07 (s, 6H).

3,3'-((4-methoxyphenyl)methylene)bis(2-methyl-1H-indole) (4g). Pale pink solid; mp = 217-220 °C (194-195 [lit 5]); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 10.68 (s, 2H), 7.20 (d, J = 8.0 Hz, 2H), 7.08 (d, J = 8.5 Hz, 2H), 6.90-6.81 (m, 6H), 6.69-6.66 (m, 2H), 5.85 (s, 1H), 3.72 (s, 3H), 2.06 (s, 6H).

3,3'-((2-chlorophenyl)methylene)bis(2-methyl-1H-indole) (4h). Pale pink solid; mp = 276-278 °C (233-234 [lit 4]); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 10.77 (s, 2H), 7.31 (d, J = 8.5 Hz, 2H), 7.24-7.18 (m, 4H), 6.92-6.89 (m, 2H), 6.82 (d, J = 7.9 Hz, 2H), 6.72-6.69 (m, 2H), 5.93 (s, 1H), 2.04 (s, 6H).

3,3'-((3-chlorophenyl)methylene)bis(2-methyl-1H-indole) (4i). Pale pink solid; mp = 280-283 °C (265-266 [lit 6]); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 10.79 (s, 2H), 7.31-7.15 (m, 6H), 6.91 (t, J = 7.5 Hz, 2H), 6.81 (d, J = 8.0 Hz, 2H), 6.71 (t, J = 7.5 Hz, 2H), 5.96 (s, 1H), 2.10 (s, 6H).

3,3'-((4-chlorophenyl)methylene)bis(2-methyl-1H-indole) (4j). Pale pink solid; mp = 249-251 °C (202-204 [lit 6]); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 10.76 (s, 2H), 7.31 (d, J = 7.1 Hz, 2H), 7.23-7.18 (m, 4H), 6.90 (t, J = 7.5 Hz, 2H), 6.81 (d, J = 7.9 Hz, 2H), 6.70 (t, J = 7.5 Hz, 2H), 5.92 (s, 1H), 2.08 (s, 6H).

3,3'-((2-bromophenyl)methylene)bis(2-methyl-1H-indole) (4k). Pale pink solid; mp = 250-253 °C (138-140 [lit 1]); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 10.75 (s, 2H), 7.61 (dd, J = 7.1, 0.9 Hz, 1H), 7.28-7.15 (m, 5H), 6.92-6.88 (m, 2H), 6.76 (d, J = 7.9 Hz, 2H), 6.70-6.67 (m, 2H), 6.03 (s, 1H), 2.00 (s, 6H).

3,3'-((3-bromophenyl)methylene)bis(2-methyl-1H-indole) (4l). Pale pink solid; mp = 226-228 °C (150-153 [lit 1]); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 10.79 (s, 2H), 7.41 (d, J = 7.5 Hz, 1H), 7.33 (s, 1H), 7.21-7.19 (m, 4H), 6.91 (t, J = 7.5 Hz, 2H), 6.81 (d, J = 7.9 Hz, 2H), 6.70 (t, J = 7.5 Hz, 2H), 5.95 (s, 1H), 2.09 (s, 6H).

3,3'-((4-bromophenyl)methylene)bis(2-methyl-1H-indole) (4m). Pale pink solid; mp = 252-254 °C (145-148 [lit 1]); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 10.77 (s, 2H), 7.44 (d, J = 8.3 Hz, 2H), 7.23 (d, J = 8.0 Hz, 2H), 7.13 (d, J = 8.4 Hz, 2H), 6.90 (t, J = 7.5 Hz, 2H), 6.82 (d, J = 7.9 Hz, 2H), 6.70 (t, J = 7.5 Hz, 2H), 5.91 (s, 1H), 2.08 (s, 6H).

3,3'-((2-nitrophenyl)methylene)bis(2-methyl-1H-indole) (4n). Yellow solid; mp = 258-261 °C (248-249 [lit 4]); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 10.85 (s, 2H), 8.16 (d, J = 8.8 Hz, 2H), 7.43 (d, J = 8.6 Hz, 2H), 7.25 (d, J = 8.0 Hz, 2H), 6.92 (t, J = 7.5 Hz, 2H), 6.81 (d, J = 7.9 Hz, 2H), 6.71 (t, J = 7.9 Hz, 2H), 6.08 (s, 1H), 2.10 (s, 6H).

3,3'-((3-nitrophenyl)methylene)bis(2-methyl-1H-indole) (4o). Yellow solid; mp = 283-286 °C (278-280 [lit6]); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 10.75 (s, 2H), 8.10 (d, J = 7.9 Hz, 1H), 8.00 (s, 1H), 7.65 (d, J = 7.7 Hz, 1H), 7.57 (t, J = 7.9 Hz, 1H), 7.25 (d, J = 8.0 Hz, 2H), 6.92 (t, J = 8.0 Hz, 2H), 6.80 (d, J = 7.9 Hz, 2H), 6.71 (t, J = 8.0 Hz, 2H), 5.96 (s, 1H), 2.10 (s, 6H).

3,3'-((4-nitrophenyl)methylene)bis(2-methyl-1H-indole) (4p). Yellow solid; mp = 271-272 °C (240-242 [lit 1]); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 10.82 (s, 2H), 7.83 (dd, J = 7.9, 1.2 Hz, 1H), 7.57 (td, J = 7.6, 1.2 Hz, 1H), 7.51-7.48 (m, 1H), 7.27 (d, J = 7.6 Hz, 1H), 7.22 (d, J = 8.0 Hz, 2H), 6.93-6.89 (m, 2H), 6.74-6.68 (m, 4H), 6.58 (s, 1H), 2.03 (s, 6H).

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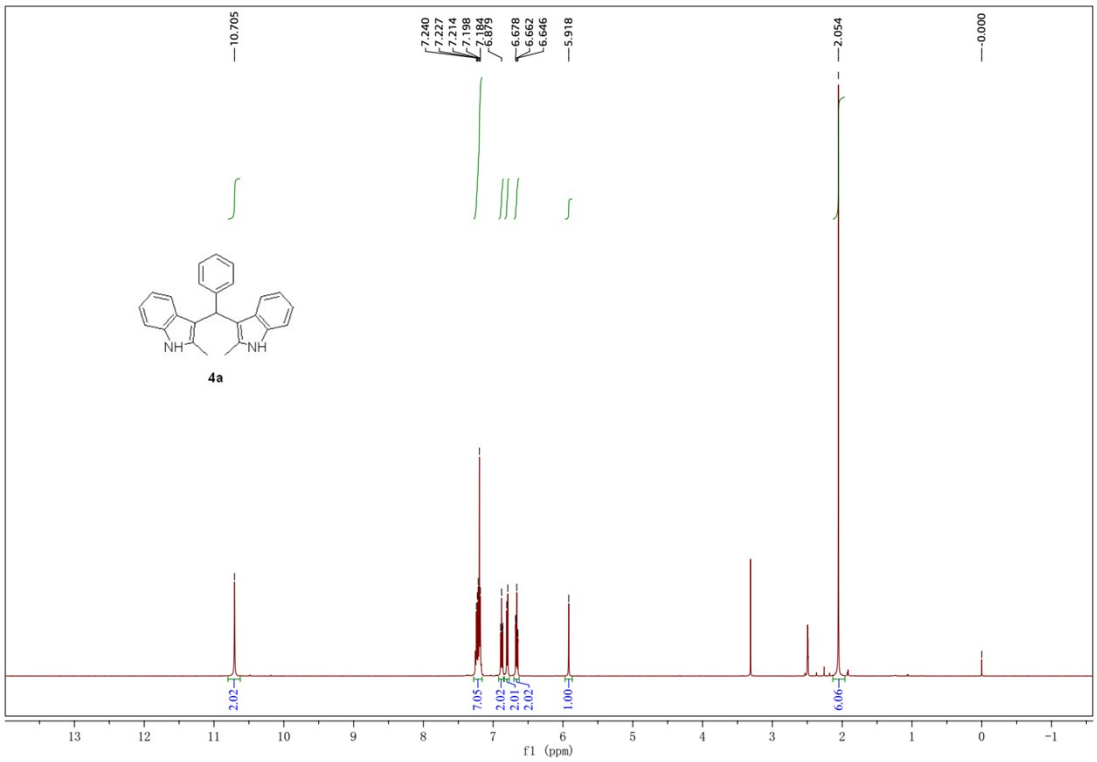
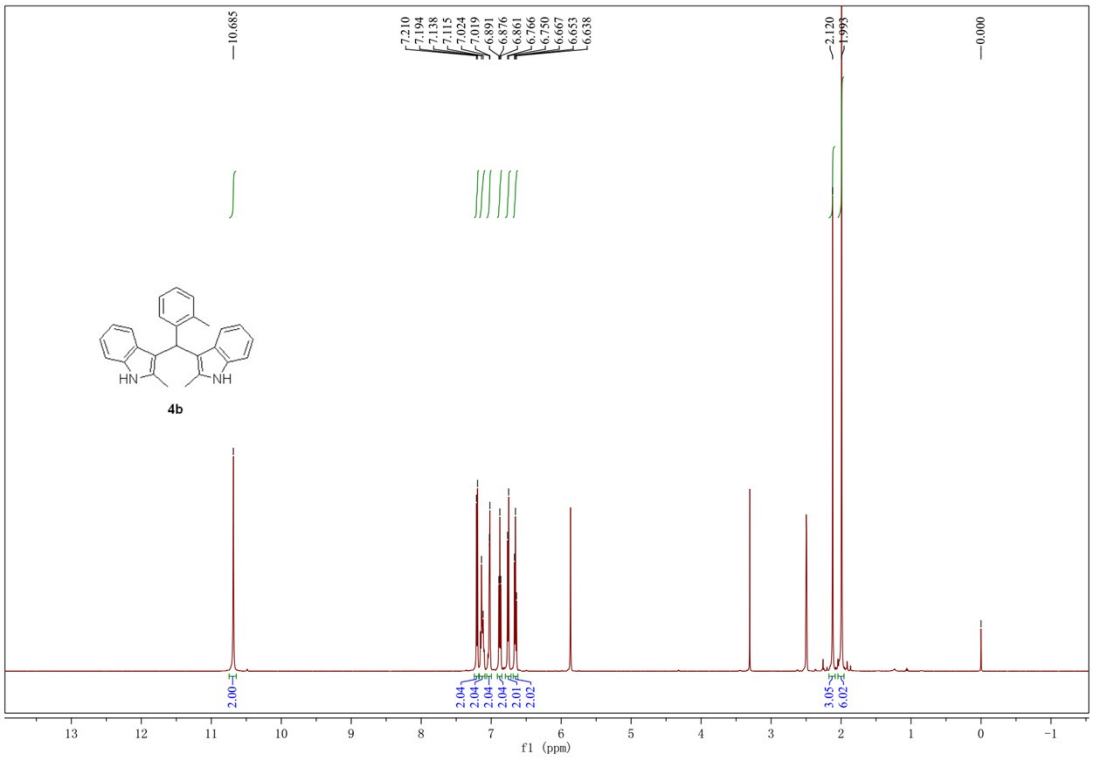
2. NMR spectra of 4a-4p



^{1}H NMR spectra of 4a



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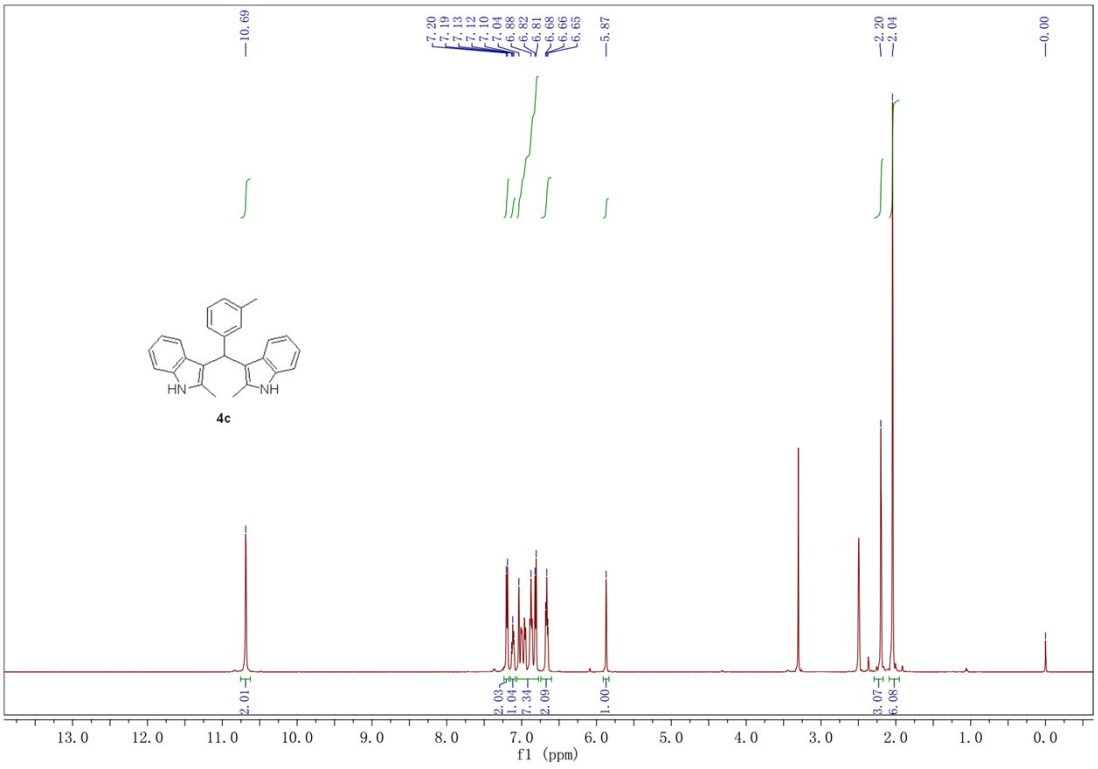

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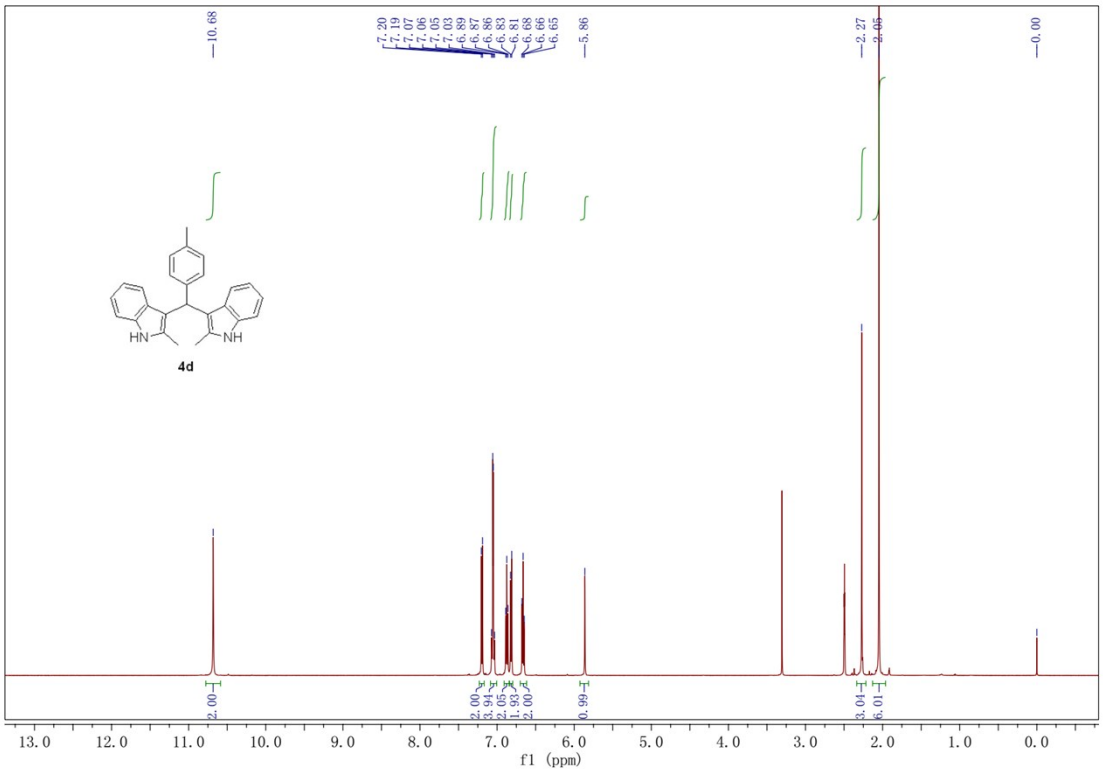

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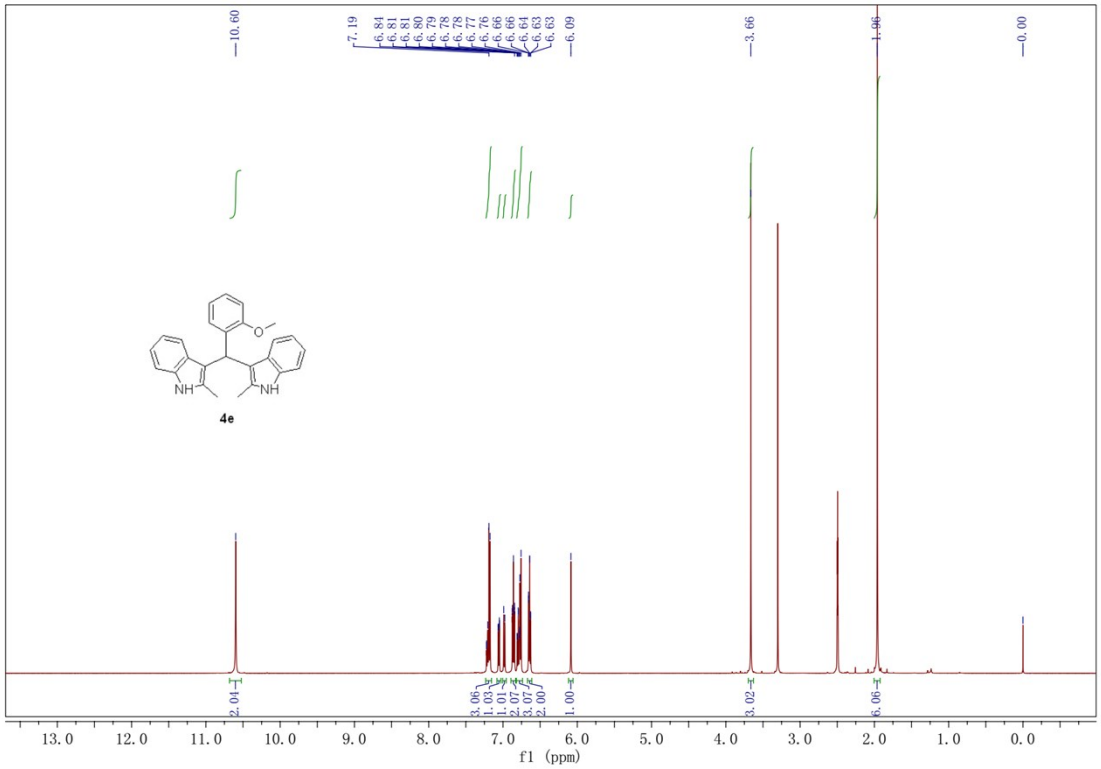

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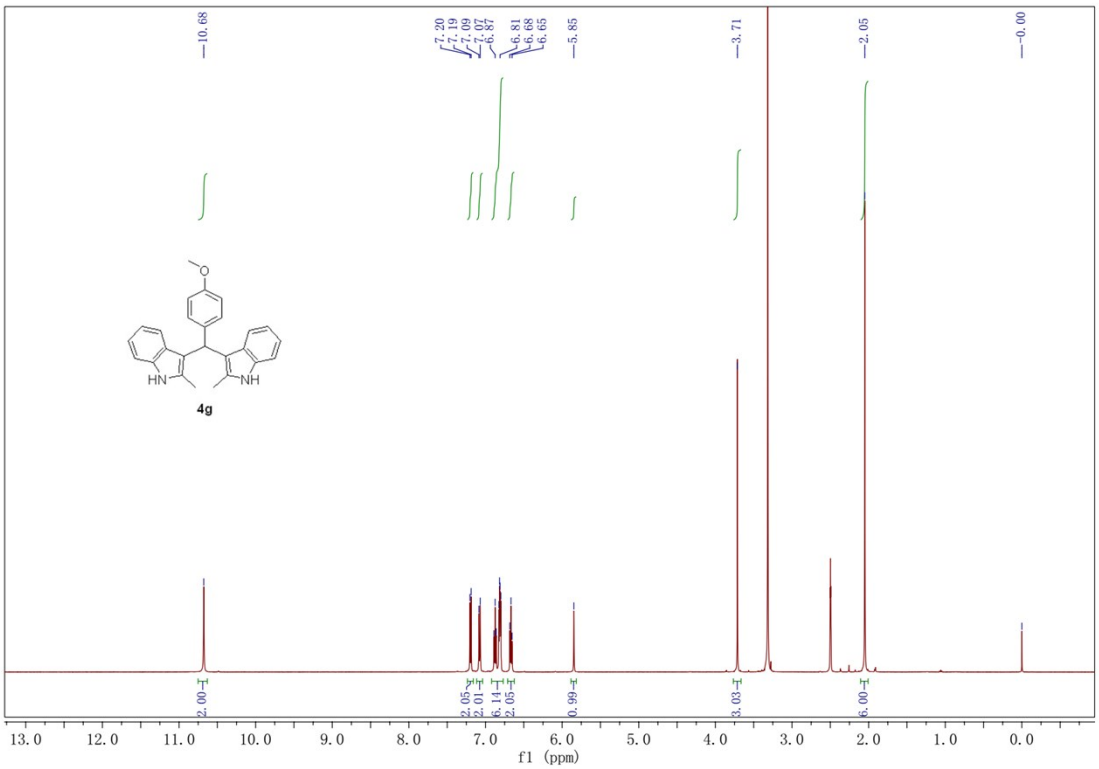
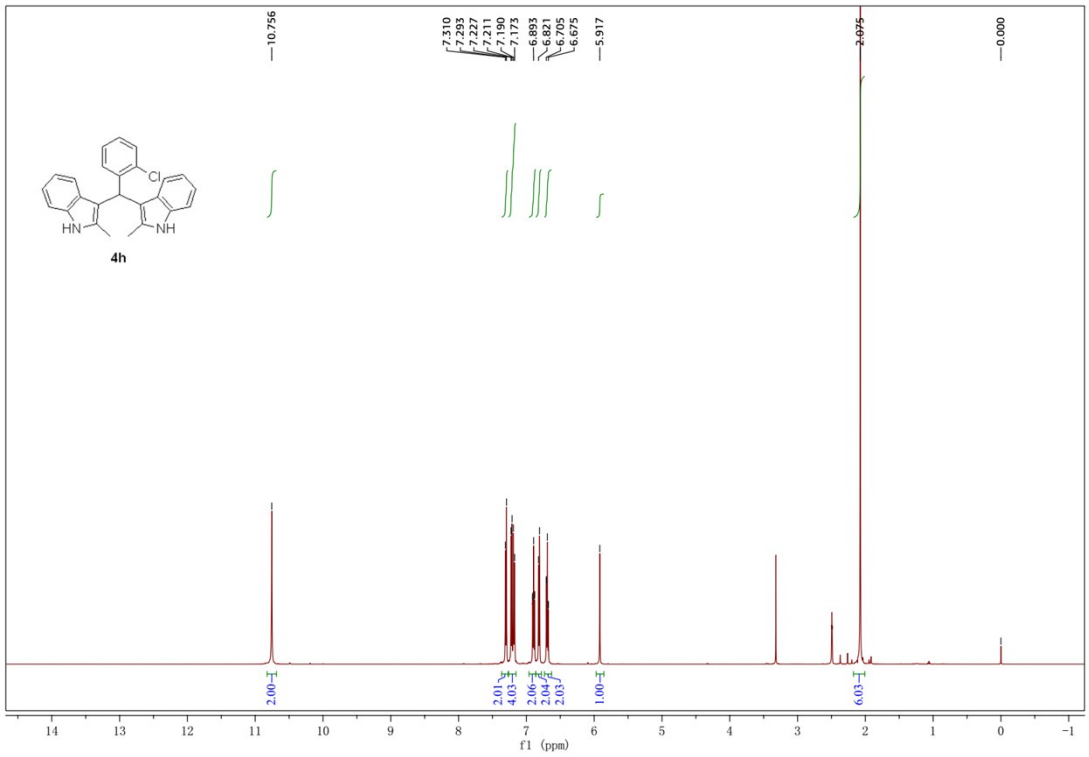


^{1}H NMR spectra of 4f

^{1}H NMR spectra of 4g



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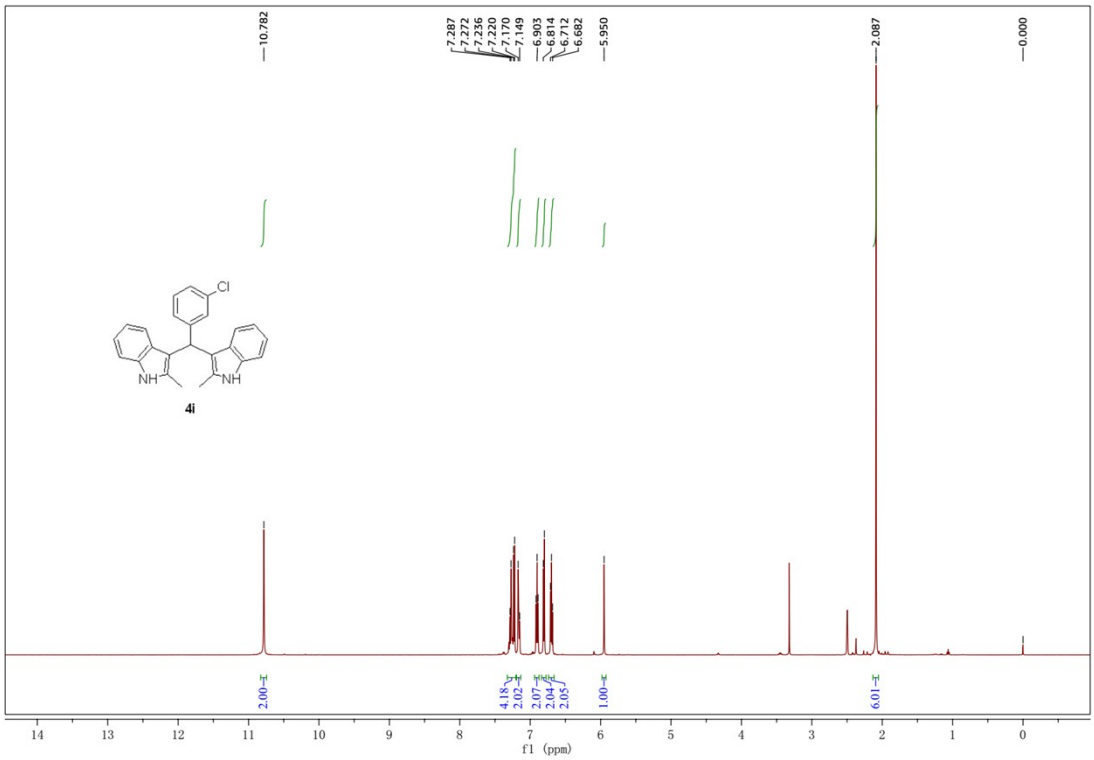
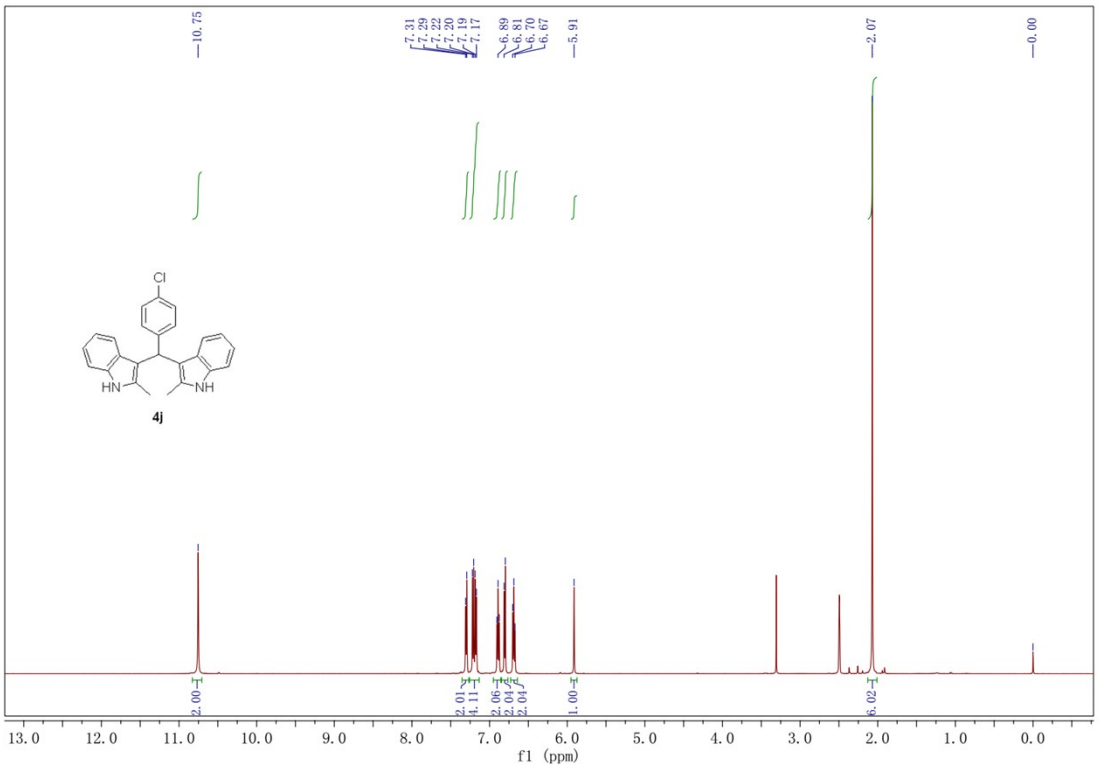
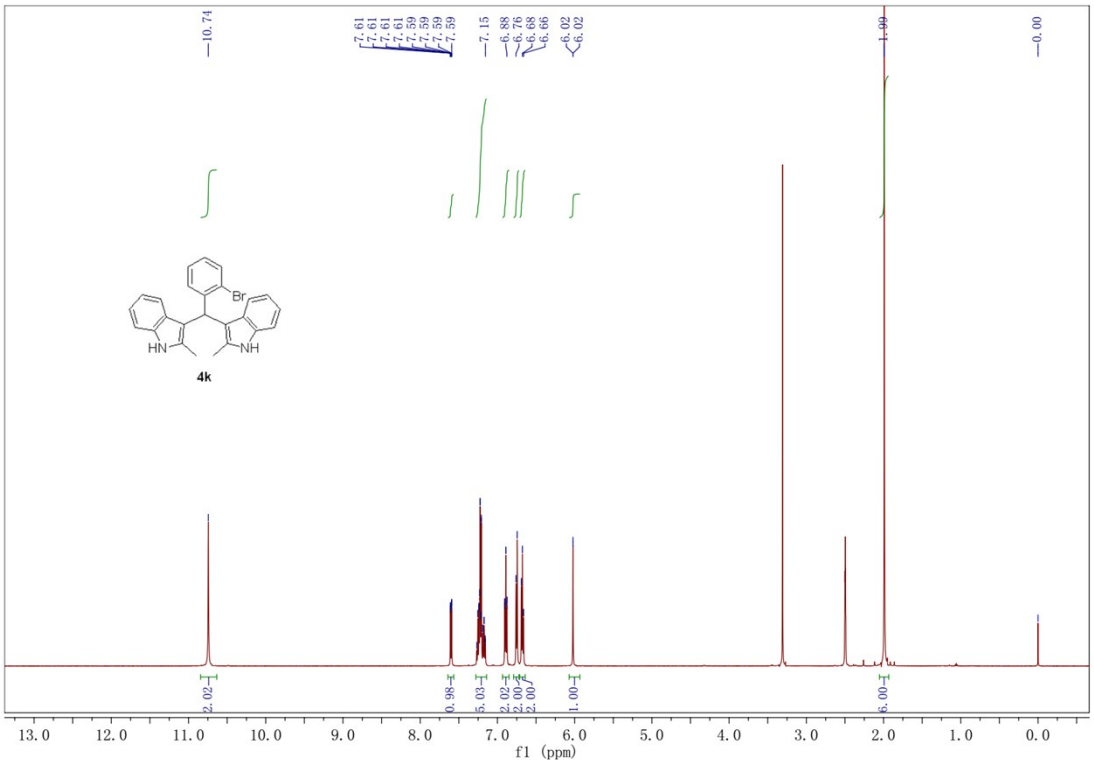


^{1}H NMR spectra of 4i



^{1}H NMR spectra of 4j



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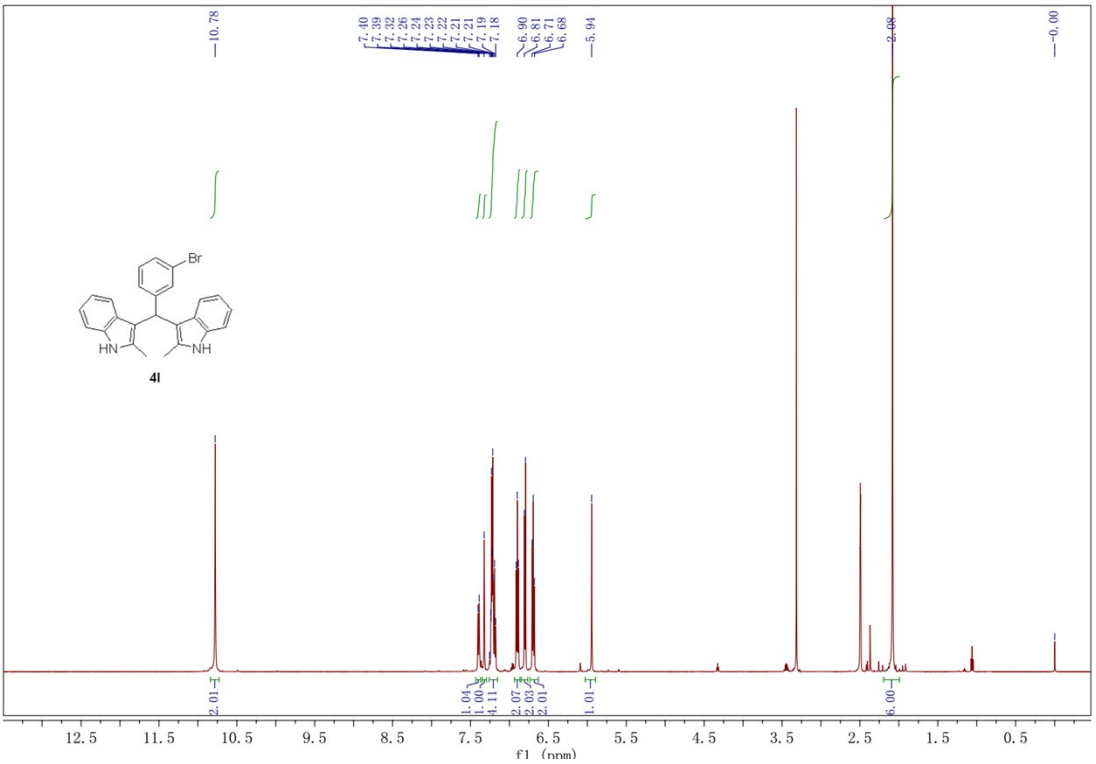

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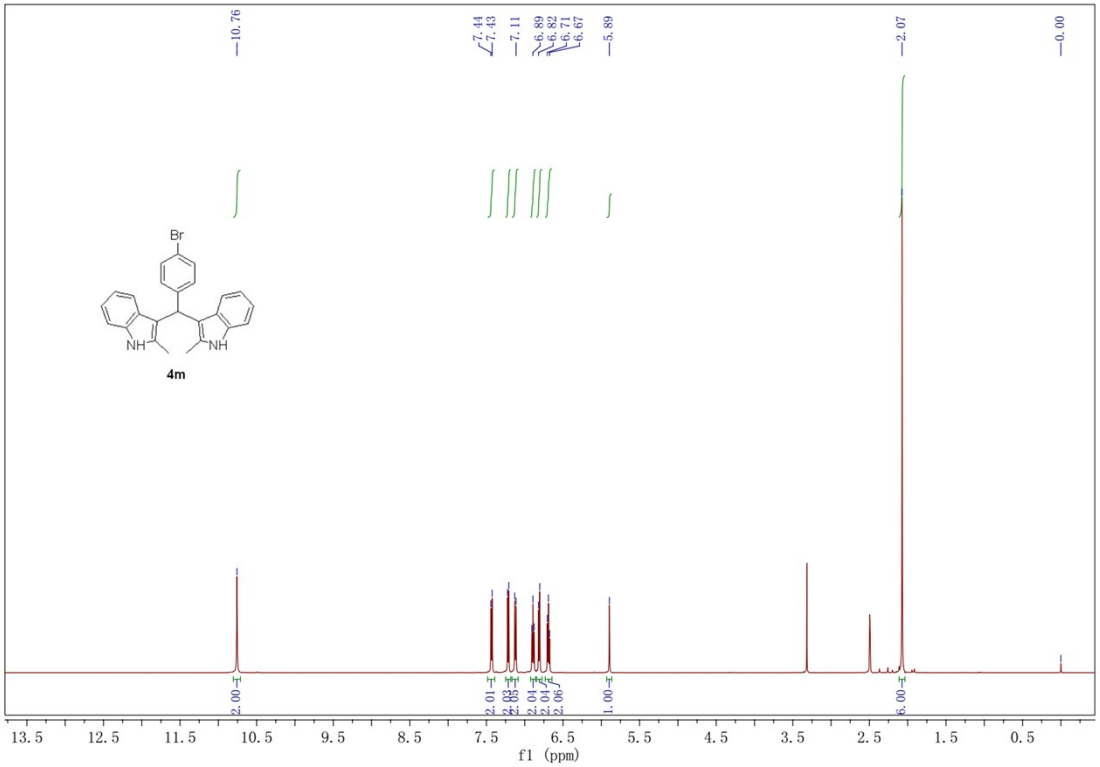

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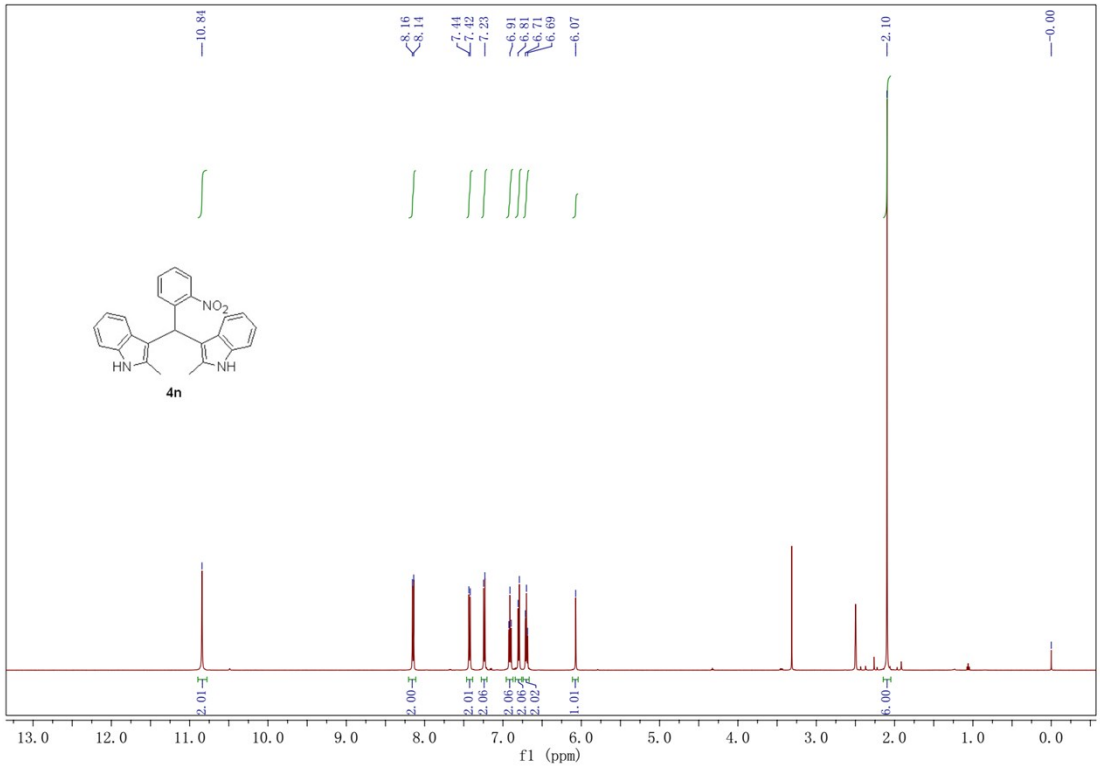
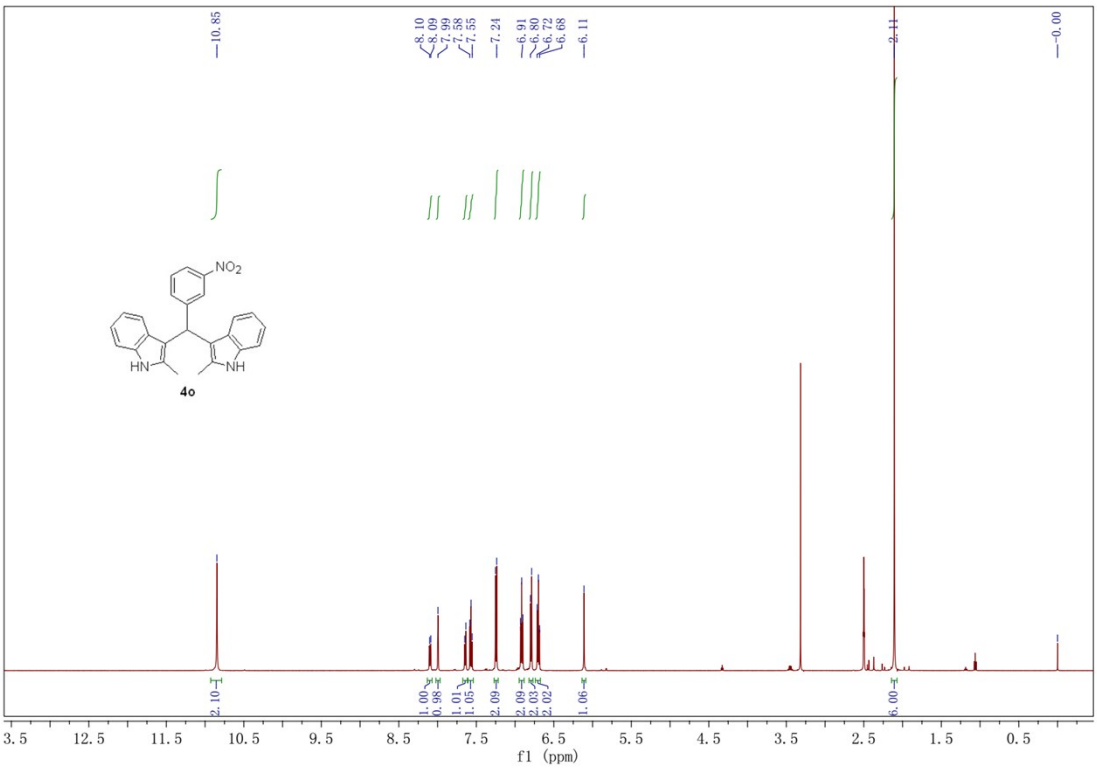
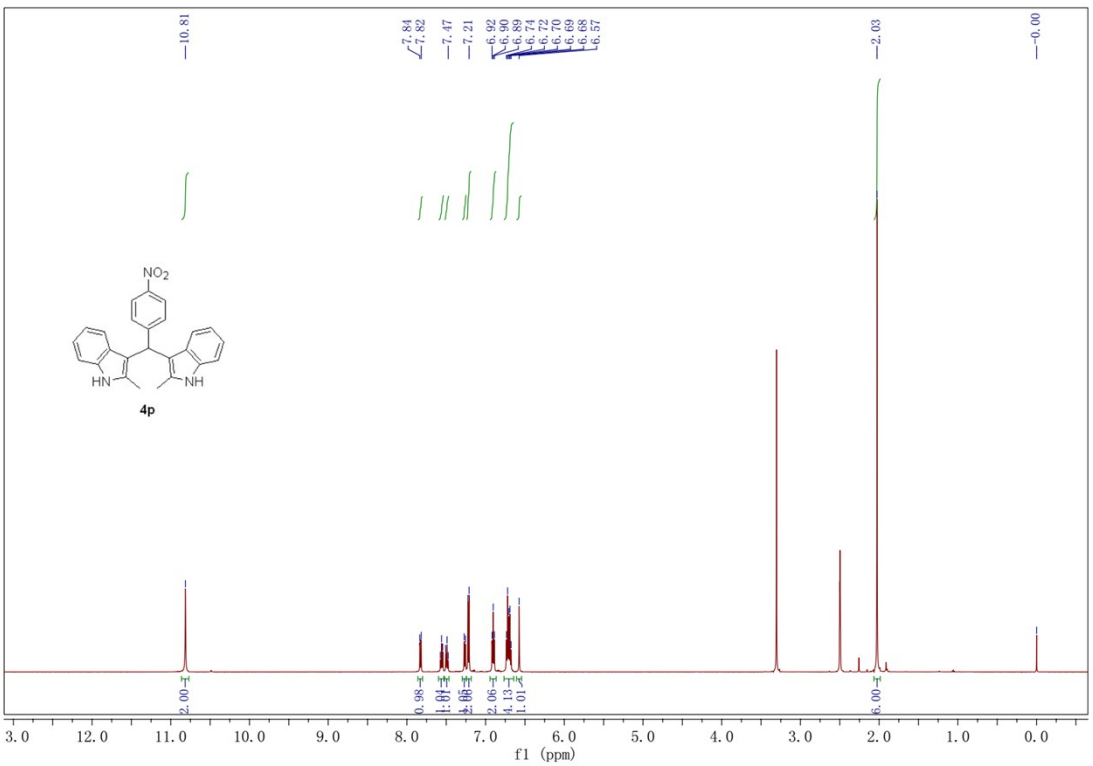


^{1}H NMR spectra of 4n

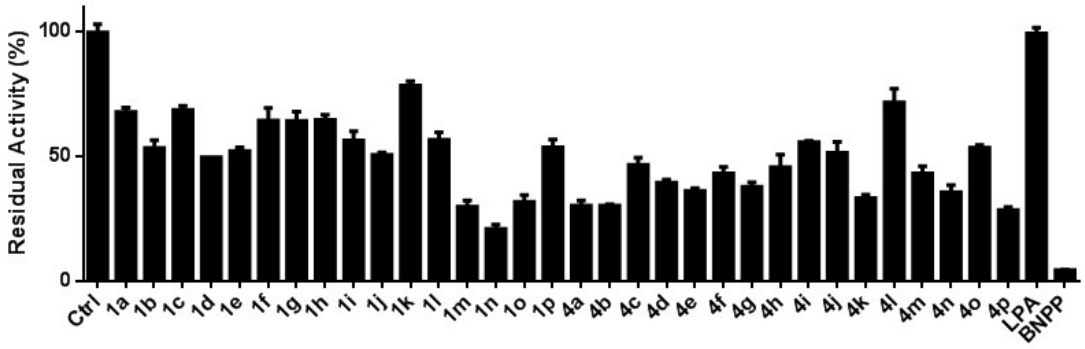


^{1}H NMR spectra of 4o



^{1}H NMR spectra of 4p

3. The inhibitory effects of indole derivatives on CES1



SI Fig. 1 The inhibitory effects of all indole derivatives (10 μM, final concentration) on the catalytic activities of CES1-mediated DME hydrolysis.