

Synthesis, *in vitro*, and *in silico* anti-inflammatory screening of orthocetamol azo derivatives

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Appendices

A1: Data characterization of 1-19.

(E)-N-(2-hydroxy-5-(phenyldiazenyl)phenyl)acetamide (1)

Pale yellowish-brown powder; 40.94% yield: m.p: 189-190 °C; $\nu_{\max}$ (ATR, cm^{-1}) 3374 (NH), 3062 (OH), 1641 (C=O), 1587 (Ar-C), 1421 (N=N), 1276 (C-N), 1094 (C-O). ¹H NMR (500 MHz, DMSO- d_6 , ppm) δ_{H} : 10.78 (1H, s, NH), 9.36 (1H, s, OH), 8.48 (1H, s), 7.81 (2H, d, J = 9.00 Hz), 7.60 (1H, d, J = 8.50 Hz), 7.56 (2H, t, J = 7.25 Hz), 7.50 (1H, t, J = 7.25 Hz), 7.04 (1H, d, J = 8.50 Hz), 2.14 (3H, s). ¹³C NMR (125 MHz, DMSO- d_6) δ_{C} : 169.6, 152.6, 151.6, 145.4, 131.1, 129.8, 127.7, 122.6, 121.8, 115.9, 115.6, 24.3.

(E)-N-(5-((2-fluorophenyl)diazenyl)-2-hydroxyphenyl)acetamide (2)

Yellowish orange powder; 53.98% yield: m.p: 178-179 °C; $\nu_{\max}$ (ATR, cm^{-1}) 3408 (NH), 3033 (OH), 1652 (C=O), 1429 (N=N), 1287 (C-N), 1095 (C-O). ¹H NMR (500 MHz, DMSO- d_6 , ppm) δ_{H} : 10.93 (1H, s, NH), 9.38 (1H, s, OH), 8.50 (1H, s), 7.69–7.61 (2H, m), 7.53 (1H, s), 7.45 (1H, t, J = 9.5 Hz), 7.31 (1H, t, J = 7.2 Hz), 7.07 (1H, d, J = 8.40 Hz), 2.14 (3H, s). ¹³C NMR (125 MHz, DMSO- d_6) δ_{C} : 169.7, 160.4, 158.4, 152.2, 145.7, 140.5, 140.5, 132.9, 132.8, 127.8, 125.4, 122.3, 118.0, 117.7, 117.6, 116.0, 115.8, 24.3.

(E)-N-(5-((3-fluorophenyl)diazenyl)-2-hydroxyphenyl)acetamidephenol (3)

Pale yellowish-brown powder; 38.61% yield: m.p: 201-202 °C; $\nu_{\max}$ (ATR, cm^{-1}) 3265 (NH), 3079 (OH), 1587 (C=O), 1424 (N=N), 1276 (C-N), 1098 (C-O). ¹H NMR (500 MHz, DMSO- d_6 , ppm) δ_{H} : 10.95 (1H, s, NH), 9.36 (1H, s, OH), 8.51 (1H, d, J = 8.0 Hz), 7.71 (2H, t, J = 8.9 Hz), 7.62 (2H, d, J = 6.3 Hz), 7.58–7.54 (1H, m), 7.35 (1H, d, J = 8.6 Hz), 7.07 (1H, t, J = 9.5 Hz), 2.15 (3H, s). ¹³C NMR (125 MHz, DMSO- d_6) δ_{C} : 169.6, 164.2, 162.3, 154.3, 152.2, 145.2, 131.7, 131.6, 127.8, 122.4, 120.4, 117.7, 117.5, 115.9, 115.7, 107.8, 107.6, 24.3.

(E)-N-(5-((4-fluorophenyl)diazenyl)-2-hydroxyphenyl)acetamide (4)

Brown powder; 72.46 % yield: m.p: 197-198 °C; $\nu_{\max}$ (ATR, cm^{-1}) 3395 (NH), 3057 (OH), 1652 (C=O), 1587 (Ar-C), 1420 (N=N), 1276 (C-N), 1090 (C-O). ¹H-NMR (500 MHz, DMSO- d_6) δ_{H} : 10.81 (1H, s, NH), 9.35 (1H, s, OH), 8.47 (1H, d, J = 1.7 Hz), 7.89–7.86 (2H, m), 7.58 (1H, dd, J = 8.6, 2.3 Hz), 7.38 (2H, td, J = 8.7, 2.5 Hz), 7.04 (1H, d, J = 8.6 Hz), 2.14 (3H, s). ¹³C NMR (125 MHz, DMSO- d_6) δ_{C} : 169.6, 164.7, 162.8, 151.7, 149.3, 145.2, 127.7, 124.9, 124.8, 121.8, 117.0, 116.9, 116.7, 115.9, 115.6, 24.3.

(E)-N-(5-((2-chlorophenyl)diazenyl)-2-hydroxyphenyl)acetamide (5)

Orange powder; 40.1 % yield: m.p: 211-212 °C; $\nu_{\max}$ (ATR, cm^{-1}) 3405 (NH), 3066 (OH), 1662 (C=O), 1588 (Ar-C), 1458 (N=N), 1286 (C-N), 1097 (C-O). ¹H-NMR (500 MHz, DMSO- d_6) δ_{H} : 10.97 (1H, s, OH), 9.38 (1H, s, NH), 8.52 (1H, s), 7.66–7.60 (3H, m), 7.46 (2H, td, J = 14.9, 7.4

Hz), 7.07 (1H, d, J = 8.6 Hz), 2.14 (3H, s). ^{13}C NMR (125 MHz, DMSO- d_6) δ_{C} : 169.7, 152.4, 148.6, 145.7, 133.7, 132.2, 131.1, 128.5, 127.8, 122.3, 118.1, 116.3, 116.0, 24.3

(E)-N-(5-((3-chlorophenyl)diazenyl)-2-hydroxyphenyl)acetamide (6)

Orange powder; 37.14 % yield: m.p: 223-224°C; ν_{max} (ATR, cm^{-1}) 3256 (NH), 3073 (OH), 1613 (C=O), 1584 (Ar-C), 1423 (N=N), 1278 (C-N), 1099 (C-O). ^1H -NMR (500 MHz, DMSO- d_6) δ_{H} : 10.96 (1H, s, OH), 9.35 (1H, s, NH), 8.49 (1H, s), 7.79 (2H, t, J = 7.2 Hz), 7.63–7.54 (3H, m), 7.06 (1H, d, J = 8.6 Hz), 2.14 (3H, s). NMR (125 MHz, DMSO- d_6) δ_{C} : 169.6, 153.7, 152.3, 145.2, 134.6, 131.7, 130.5, 127.8, 122.7, 122.5, 121.0, 115.9, 115.6, 24.3.

(E)-N-(5-((4-chlorophenyl)diazenyl)-2-hydroxyphenyl)acetamide (7)

Yellow powder; 80.6 % yield: m.p: 242-243 °C; ν_{max} (ATR, cm^{-1}) 3333 (NH), 3035 (OH), 1650 (C=O), 1586 (Ar-C), 1387 (N=N), 1265 (C-N), 1089 (C-O). ^1H -NMR (500 MHz, DMSO- d_6) δ_{H} : 10.87 (1H, s, OH), 9.35 (1H, s, NH), 8.49 (s, 1H), 7.83 (2H, d, J = 8.6 Hz), 7.62-7.59 (m, 3H), 7.05 (1H, d, J = 8.6 Hz). ^{13}C NMR (125 MHz, DMSO- d_6) δ_{C} : 169.1, 151.4, 150.7, 144.7, 134.9, 129.4, 127.2, 123.8, 121.6, 115.4, 115.1, 23.8.

(E)-N-(5-((2-bromophenyl)diazenyl)-2-hydroxyphenyl)acetamide (8)

Orange powder; 54.8 % yield: m.p: 205-206°C; ν_{max} (ATR, cm^{-1}) 3393 (NH), 3060 (OH), 1657 (C=O), 1586 (Ar-C), 1456 (N=N), 1284 (C-N), 1095 (C-O). ^1H -NMR (500 MHz, DMSO- d_6) δ_{H} : 10.92 (1H, s, OH), 9.37 (1H, s, NH), 8.52 (s, 1H), 7.83 (1H, d, J = 7.4 Hz,), 7.63 (1H, d, J = 10.9 Hz), 7.59 (1H, d, J = 8.0 Hz), 7.49 (1H, t, J = 7.4 Hz), 7.42-7.40 (1H, m), 7.07 (1H, d, J = 8.6 Hz), 2.14 (3H, s). ^{13}C NMR (125 MHz, DMSO- d_6) δ_{C} : 169.7, 152.37, 149.61, 145.65, 134.13, 132.39, 129.14, 127.82, 124.36, 122.03, 118.28, 116.64, 116.05, 24.32.

(E)-N-(5-((3-bromophenyl)diazenyl)-2-hydroxyphenyl)acetamide (9)

Brown powder; 48.7 % yield: m.p: 215-216°C; ν_{max} (ATR, cm^{-1}) 3372 (NH), 3062 (OH), 1661 (C=O), 1586 (Ar-C), 1456 (N=N), 1284 (C-N), 1095 (C-O). ^1H -NMR (500 MHz, DMSO- d_6) δ_{H} : 10.92 (1H, s, OH), 9.37 (1H, s, NH), 8.52 (s, 1H), 7.83 (1H, d, J = 7.4 Hz,), 7.63 (1H, d, J = 10.9 Hz), 7.59 (1H, d, J = 8.0 Hz), 7.49 (1H, t, J = 7.4 Hz), 7.42-7.40 (1H, m), 7.07 (1H, d, J = 8.6 Hz), 2.14 (3H, s). ^{13}C NMR (125 MHz, DMSO- d_6) δ_{C} : 169.6, 153.8, 152.3, 145.2, 133.4, 132.0, 127.8, 123.7, 123.2, 123.0, 122.5, 115.9, 115.6, 24.4.

(E)-N-(5-((4-bromophenyl)diazenyl)-2-hydroxyphenyl)acetamide (10)

Brownish orange powder; 62.8 % yield: m.p: 216-217°C; ν_{max} (ATR, cm^{-1}) 3391 (NH), 3072 (OH), 1645 (C=O), 1586 (Ar-C), 1457 (N=N), 1275 (C-N), 1099 (C-O). ^1H -NMR (500 MHz, CDCl_3) δ_{H} : 9.09 (1H, s, OH), 8.27 (1H, s, NH), 7.91 (s, 1H), 7.82 (2H, d, J = 8.6 Hz), 7.77 (2H, d, J = 8.6 Hz), 7.70 (1H, d, J = 8.6 Hz), 7.65 (1H, d, J = 8.6 Hz, 1H), 2.29 (3H, s). ^{13}C NMR (125 MHz, CDCl_3) δ_{C} : 168.6, 151.3, 148.0, 146.8, 145.8, 135.6, 133.0, 132.4, 128.9, 125.3, 124.5, 123.5, 116.3, 25.0.

(E)-N-(2-hydroxy-5-((2-iodophenyl)diazenyl)phenyl)acetamide (11)

Yellowish orange powder; 70.9 % yield: m.p: 223-224°C; ν_{max} (ATR, cm^{-1}) 3389 (NH), 3053 (OH), 1657 (C=O), 1588 (Ar-C), 1457 (N=N), 1281 (C-N), 1097 (C-O). ^1H -NMR (500 MHz, DMSO- d_6) δ_{H} : 10.91 (1H, s, OH), 9.37 (1H, s, NH), 8.54 (1H, s), 8.06 (1H, d, J = 8.6 Hz), 7.63 (1H, dd, J = 8.6, 2.3 Hz), 7.53-7.48 (2H, m), 7.26-7.22 (1H, m), 7.07 (1H, d, J = 8.6 Hz), 2.14 (3H, s). ^{13}C NMR (125 MHz, DMSO- d_6) δ_{C} : 169.6, 152.3, 151.5, 145.4, 140.2, 132.6, 129.8, 127.8, 121.7, 117.6, 117.1, 116.0, 102.2, 24.3.

(E)-N-(2-hydroxy-5-((3-iodophenyl)diazenyl)phenyl)acetamide (12)

Yellowish brown powder; 50.3 % yield: m.p: 212-213 °C; $\nu_{\max}$ (ATR, cm^{-1}) 3376 (NH), 3059 (OH), 1644 (C=O), 1589 (Ar-C), 1421 (N=N), 1277 (C-N), 1093 (C-O). $^1\text{H-NMR}$ (500 MHz, DMSO-d_6) δ_{H} : 10.91 (1H, s, OH), 9.35 (1H, s, NH), 8.49 (1H, s), 8.08 (1H, s), 7.85 (2H, d, $J = 7.6$ Hz), 7.62 (1H, d, $J = 7.6$ Hz), 7.37 (1H, t, $J = 7.6$ Hz), 7.05 (1H, d, $J = 8.6$ Hz), 2.14 (3H, s). $^{13}\text{C NMR}$ (125 MHz, DMSO-d_6) δ_{C} : 169.6, 153.6, 152.2, 145.2, 139.3, 132.0, 129.6, 127.8, 123.6, 122.5, 115.9, 115.6, 95.9, 24.4.

(E)-N-(2-hydroxy-5-((4-iodophenyl)diazenyl)phenyl)acetamide (13)

Brown powder; 64.1 % yield: m.p: 219-220 °C; $\nu_{\max}$ (ATR, cm^{-1}) 3313 (NH), 3096 (OH), 1643 (C=O), 1590 (Ar-C), 1423 (N=N), 1277 (C-N), 1096 (C-O). $^1\text{H-NMR}$ (500 MHz, DMSO-d_6) δ_{H} : 10.86 (1H, s, OH), 9.34 (1H, s, NH), 8.48 (1H, s), 7.92 (2H, d, $J = 8.6$ Hz), 7.59 (3H, d, $J = 6.9$ Hz), 7.04 (1H, d, $J = 8.6$ Hz), 2.13 (3H, s). $^{13}\text{C NMR}$ (125 MHz, DMSO-d_6) δ_{C} : 169.6, 152.0, 145.3, 138.9, 138.8, 127.8, 124.7, 124.6, 122.1, 115.9, 115.7, 98.0, 24.4.

(E)-N-(2-hydroxy-5-(o-tolyldiazenyl)phenyl)acetamide (14)

Brown powder; 46.9 % yield: m.p: 189-190 °C; $\nu_{\max}$ (ATR, cm^{-1}) 3380 (NH), 3036 (OH), 1646 (C=O), 1594 (Ar-C), 1426 (N=N), 1276 (C-N), 1091 (C-O). $^1\text{H-NMR}$ (500 MHz, DMSO-d_6) δ_{H} : 10.74 (1H, s, OH), 9.36 (1H, s, NH), 8.49 (1H, s), 7.59 (1H, dd, $J = 8.6, 2.3$ Hz), 7.51 (1H, d, $J = 8.0$ Hz), 7.38 (2H, d, $J = 5.2$ Hz), 7.30-7.27 (1H, m), 7.05 (1H, d, $J = 8.6$ Hz), 2.63 (3H, s), 2.14 (3H, s). $^{13}\text{C NMR}$ (125 MHz, DMSO-d_6) δ_{C} : 169.7, 151.5, 150.6, 146.0, 137.3, 131.8, 130.9, 127.7, 127.1, 121.4, 116.1, 116.0, 115.5, 24.3, 17.6.

(E)-N-(2-hydroxy-5-(m-tolyldiazenyl)phenyl)acetamide (15)

Yellow powder; 31.3 % yield: m.p: 219-220 °C; $\nu_{\max}$ (ATR, cm^{-1}) 3263 (NH), 3086 (OH), 1610 (C=O), 1585 (Ar-C), 1482 (N=N), 1277 (C-N), 1096 (C-O). $^1\text{H-NMR}$ (500 MHz, DMSO-d_6) δ_{H} : 10.76 (1H, s, OH), 9.34 (1H, s, NH), 8.47 (1H, s), 7.63 (1H, s), 7.60 (2H, d, $J = 8.6$ Hz), 7.43 (1H, d, $J = 15.5$ Hz), 7.31 (1H, d, $J = 6.9$ Hz), 7.04 (1H, d, $J = 8.6$ Hz), 2.40 (3H, s), 2.14 (3H, s). $^{13}\text{C NMR}$ (125 MHz, DMSO-d_6) δ_{C} : 169.6, 152.7, 151.6, 145.5, 139.3, 131.7, 129.7, 127.7, 122.7, 121.7, 120.3, 115.9, 115.7, 24.4, 21.4.

(E)-N-(2-hydroxy-5-(p-tolyldiazenyl)phenyl)acetamide (16)

Yellow powder; 65.6 % yield: m.p: 236-237 °C; $\nu_{\max}$ (ATR, cm^{-1}) 3409 (NH), 3030 (OH), 1658 (C=O), 1591 (Ar-C), 1423 (N=N), 1283 (C-N), 1096 (C-O). $^1\text{H-NMR}$ (500 MHz, DMSO-d_6) δ_{H} : 10.73 (1H, s, OH), 9.34 (1H, s, NH), 8.45 (1H, s), 7.73 (2H, d, $J = 8.0$ Hz), 7.57 (1H, d, $J = 8.6$ Hz), 7.36 (2H, d, $J = 6.3$ Hz), 7.04 (1H, d, $J = 5.7$ Hz), 2.38 (3H, s), 2.08 (3H, s). $^{13}\text{C NMR}$ (125 MHz, DMSO-d_6) δ_{C} : 207.0, 169.6, 151.4, 150.7, 145.4, 141.1, 130.4, 127.7, 122.7, 121.6, 115.9, 115.6, 24.3, 21.5.

(E)-N-(2-hydroxy-5-((2-methoxyphenyl)diazenyl)phenyl)acetamide (17)

Brownish-orange powder; 95.1 % yield: m.p: 196-197 °C; $\nu_{\max}$ (ATR, cm^{-1}) 3356 (NH), 2937 (OH), 1656 (C=O), 1588 (Ar-C), 1485 (N=N), 1278 (C-N), 1095 (C-O). $^1\text{H-NMR}$ (500 MHz, DMSO-d_6) δ_{H} : 9.39 (1H, s, OH), 8.38 (1H, s, NH), 7.55 (1H, d, $J = 8.6$ Hz), 7.46 (2H, q, $J = 7.6$ Hz), 7.22 (1H, d, $J = 8.6$ Hz), 7.05-6.99 (2H, m), 3.93 (3H, s), 2.14 (3H, s). $^{13}\text{C NMR}$ (125 MHz, DMSO-d_6) δ_{C} : 169.2, 156.2, 151.0, 145.5, 141.7, 131.9, 127.1, 121.3, 120.6, 116.3, 115.5, 115.4, 113.3, 56.0, 23.8.

(E)-N-(2-hydroxy-5-((3-methoxyphenyl)diazenyl)phenyl)acetamide (18)

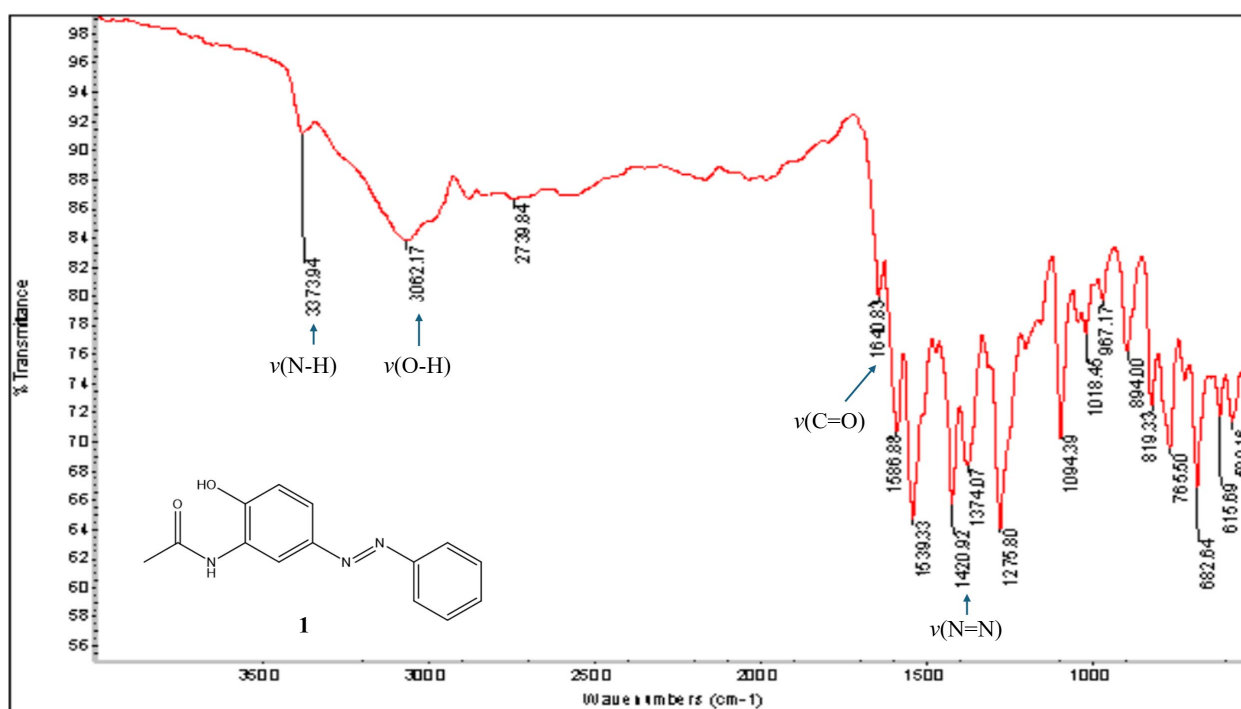
Brownish-orange powder; 62.3 % yield: m.p: 171-172 °C; $\nu_{\max}$ (ATR, cm^{-1}) 3262 (NH), 3073 (OH), 1679 (C=O), 1587 (Ar-C), 1482 (N=N), 1278 (C-N), 1100 (C-O). $^1\text{H-NMR}$ (500 MHz, DMSO-d_6) δ_{H} : 9.39 (1H, s, OH), 8.38 (1H, s, NH), 7.55 (1H, d, $J = 8.6$ Hz), 7.46 (2H, q, $J = 7.6$ Hz), 7.22 (1H, d, $J = 8.6$ Hz), 7.05-6.99 (2H, m), 3.93 (3H, s), 2.14 (3H, s). $^{13}\text{C NMR}$ (125 MHz,

DMSO-d₆) δ_C : 168.2, 159.2, 152.5, 150.4, 143.9, 129.3, 126.3, 120.5, 116.0, 114.9, 114.5, 114.4, 104.8, 54.5, 23.0.

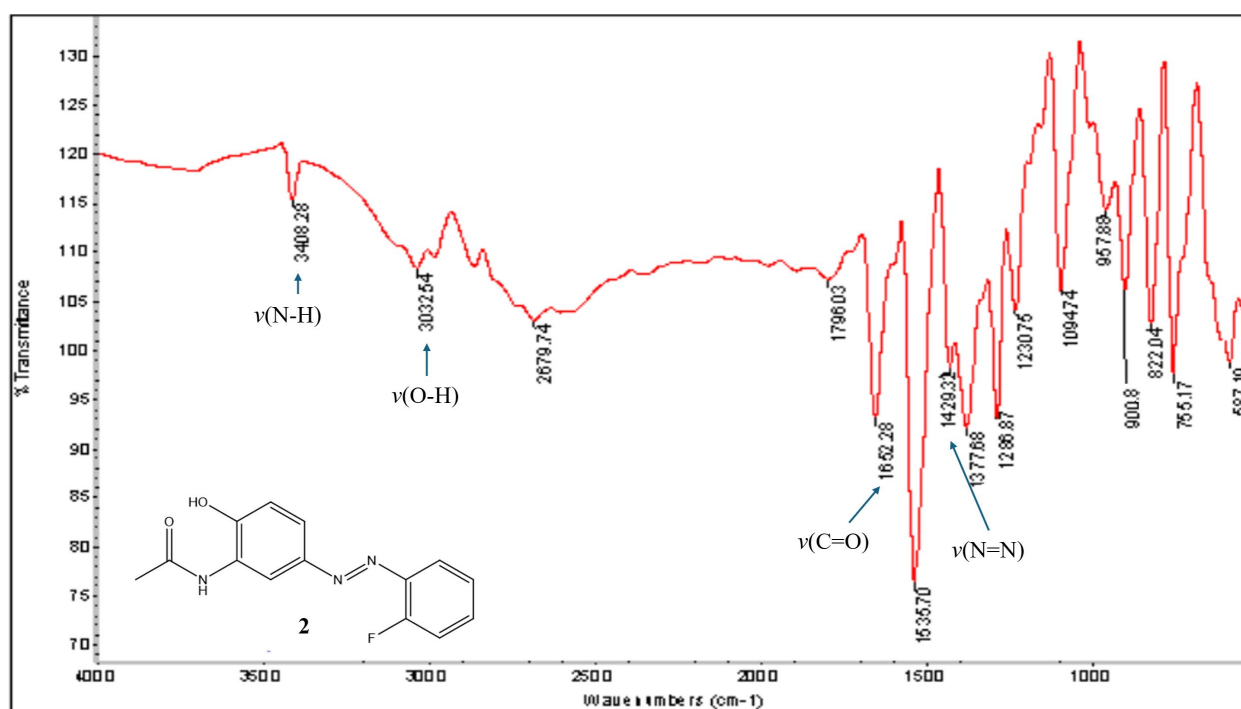
(E)-N-(2-hydroxy-5-((4-methoxyphenyl)diazenyl)phenyl)acetamide (19)

Yellow powder; 81.6 % yield; m.p: 206-207 °C; $\nu_{\max}$ (ATR, cm⁻¹) 3268 (NH), 3076 (OH), 1593 (C=O), 1548 (Ar-C), 1416 (N=N), 1239 (C-N), 1095 (C-O). ¹H-NMR (500 MHz, DMSO-d₆) δ_H : 10.67 (1H, s, OH), 9.35 (1H, s, NH), 8.41 (1H, s), 7.81 (2H, d, J = 9.2 Hz), 7.53 (1H, d, J = 8.6 Hz), 7.09 (2H, d, J = 9.2 Hz), 7.02 (1H, d, J = 8.6 Hz), 3.84 (3H, s), 2.14 (3H, s). ¹³C NMR (125 MHz, DMSO-d₆) δ_C : 169.1, 161.3, 150.5, 146.3, 144.9, 127.1, 124.0, 120.7, 115.4, 115.0, 114.5, 55.6, 23.8.

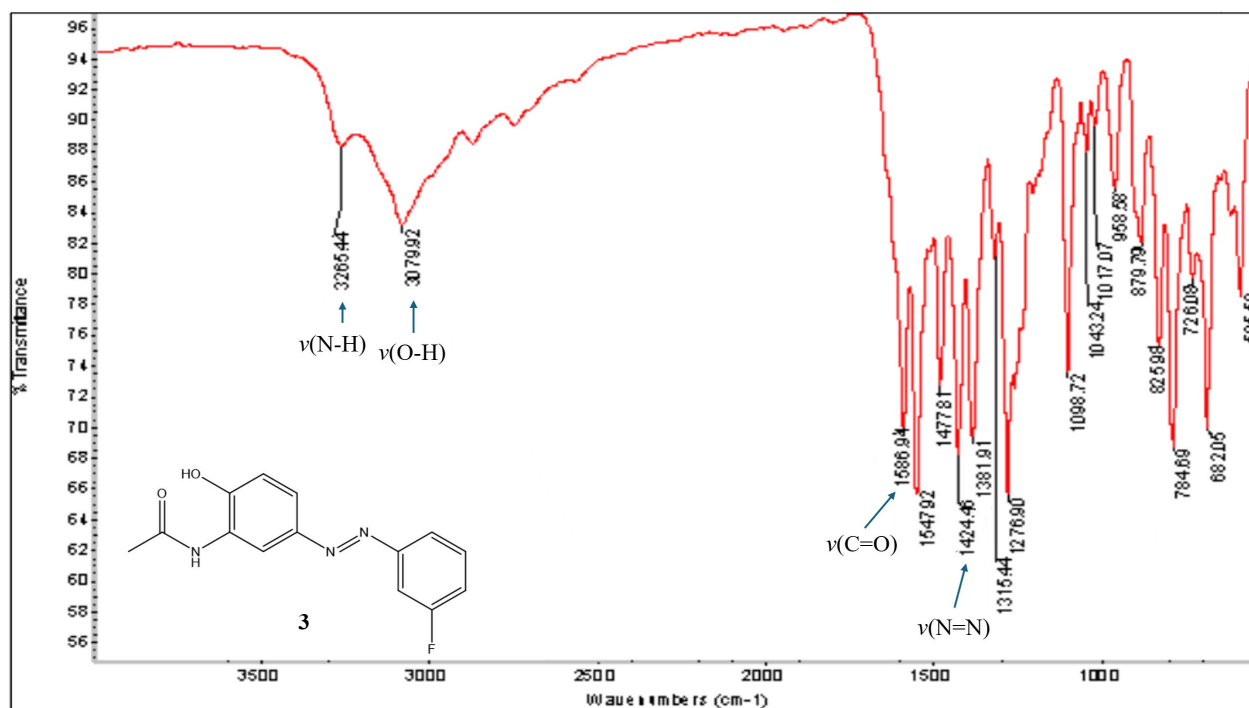
A2: FTIR spectra of orthocetamol azo 1-19.



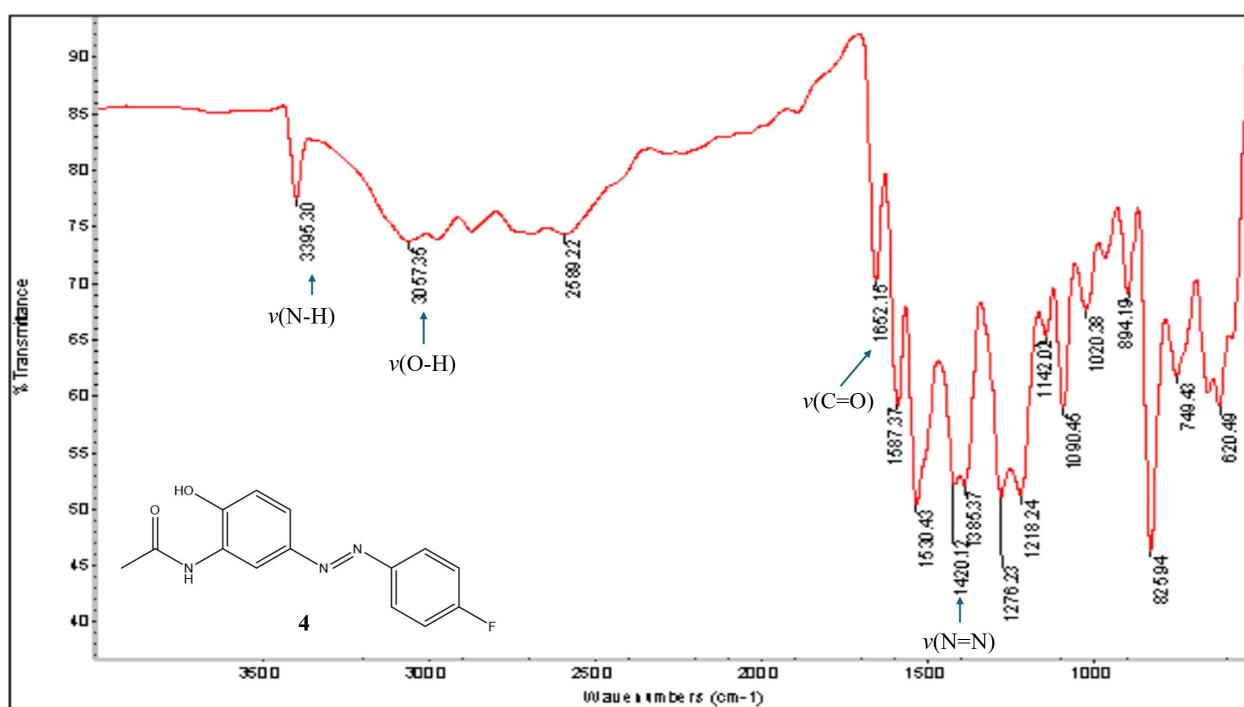
1(H)



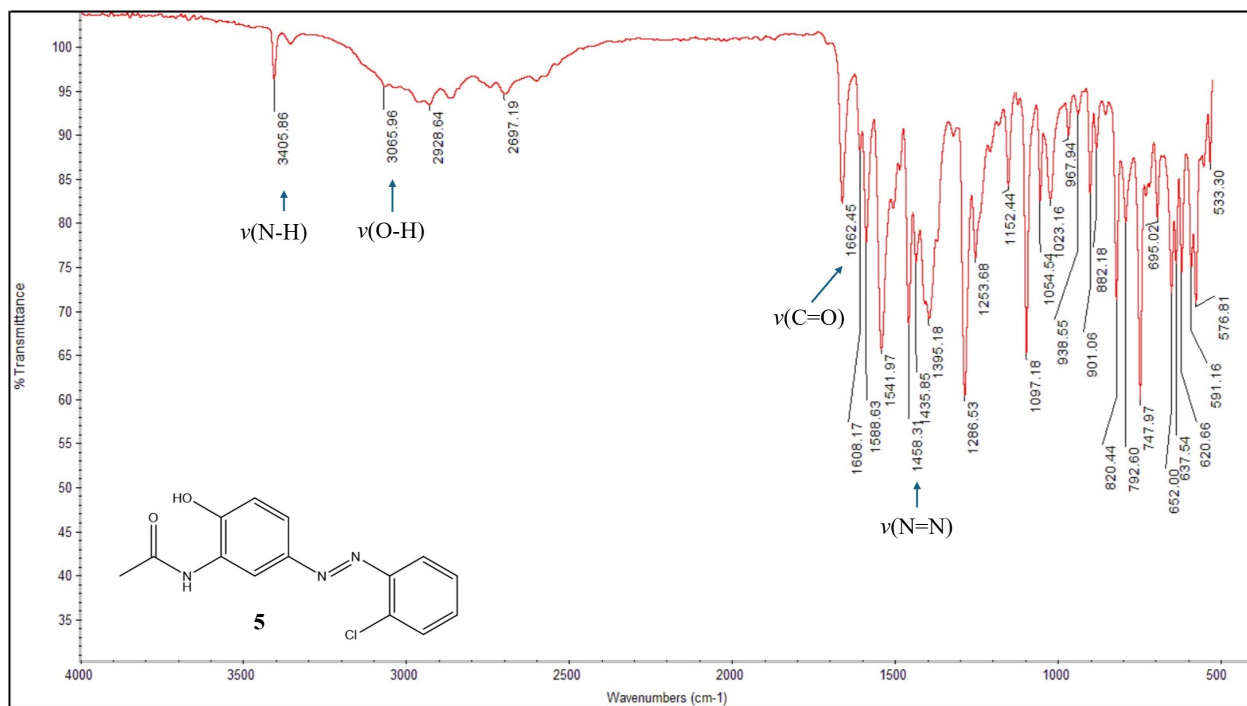
2 (o-F)



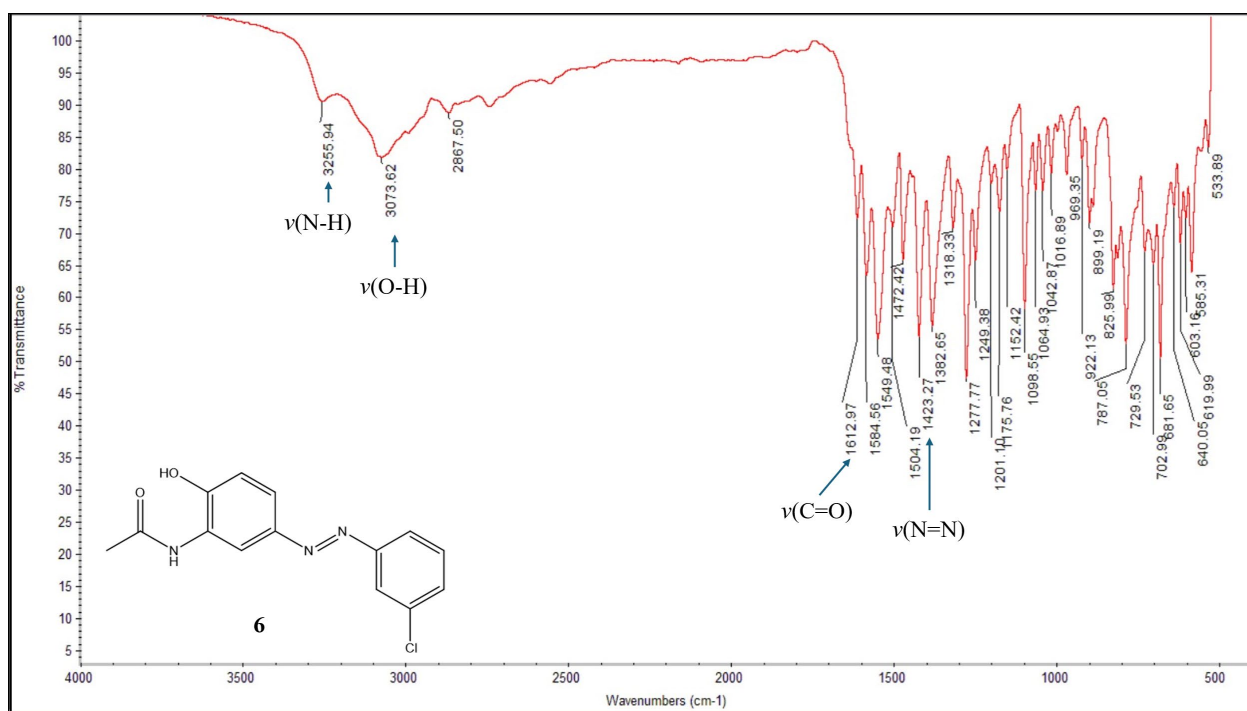
3 (*m*-F)



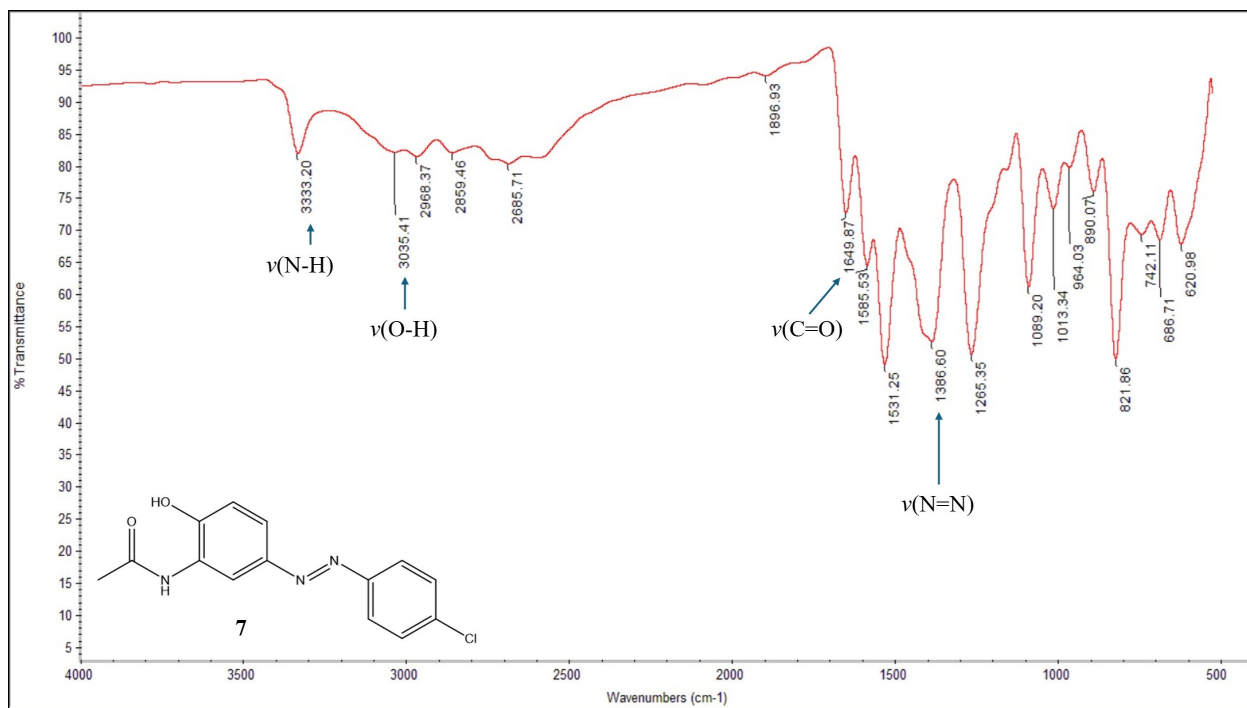
4 (*p*-F)



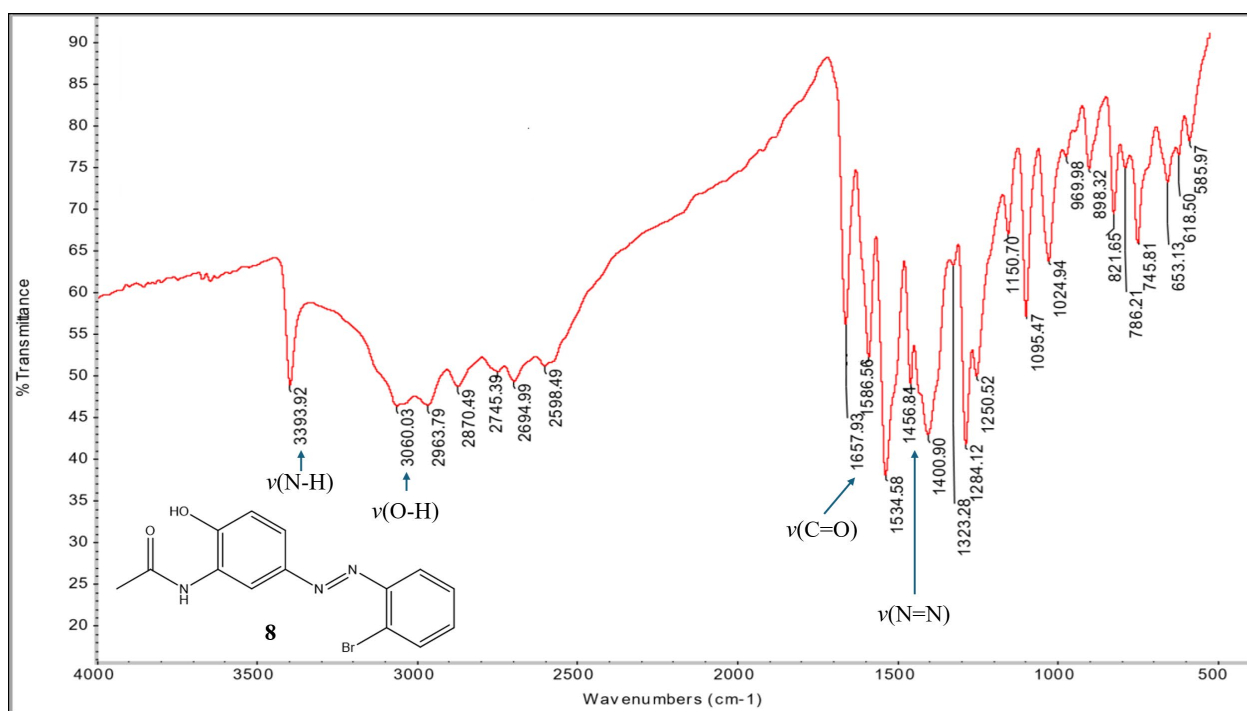
5 (*o*-Cl)



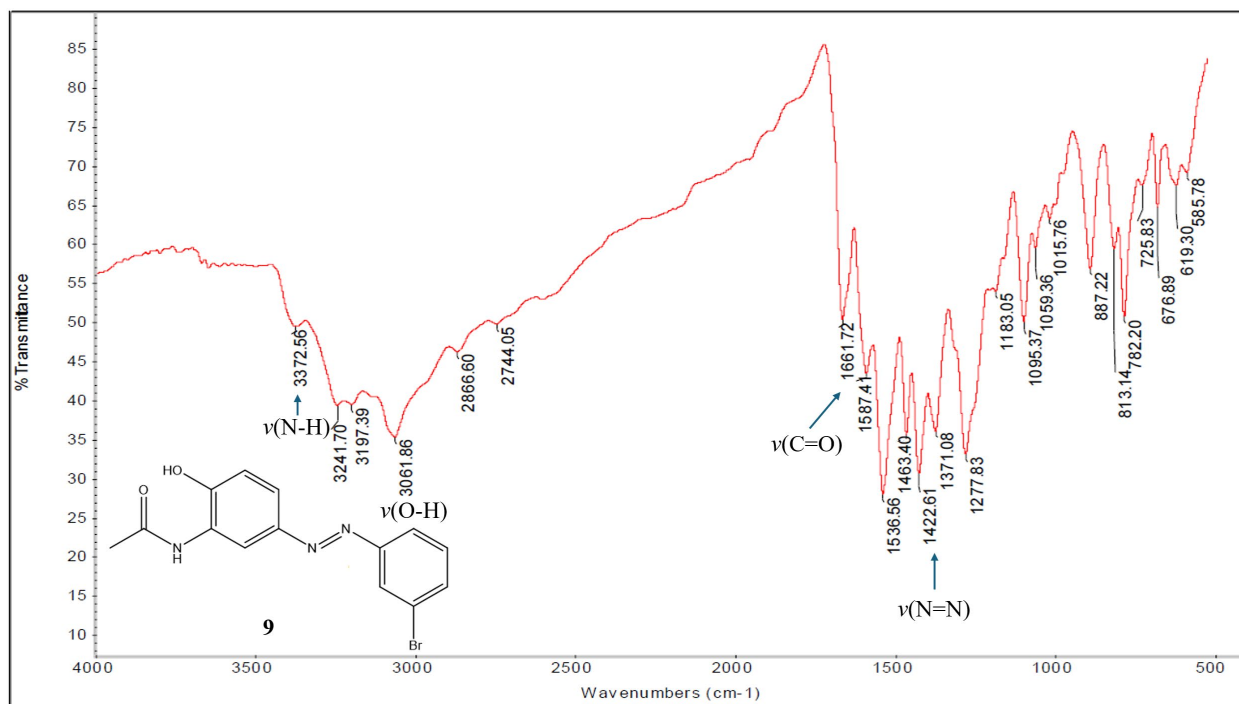
6 (*m*-Cl)



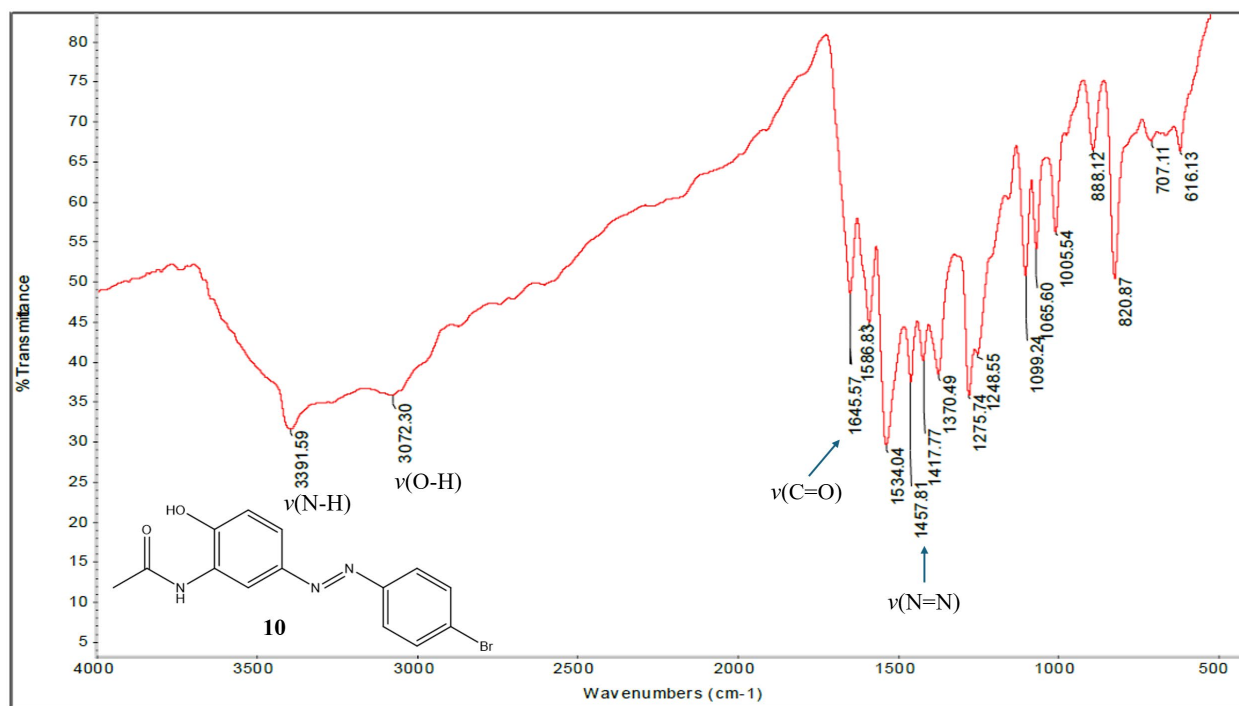
7 (*p*-Cl)



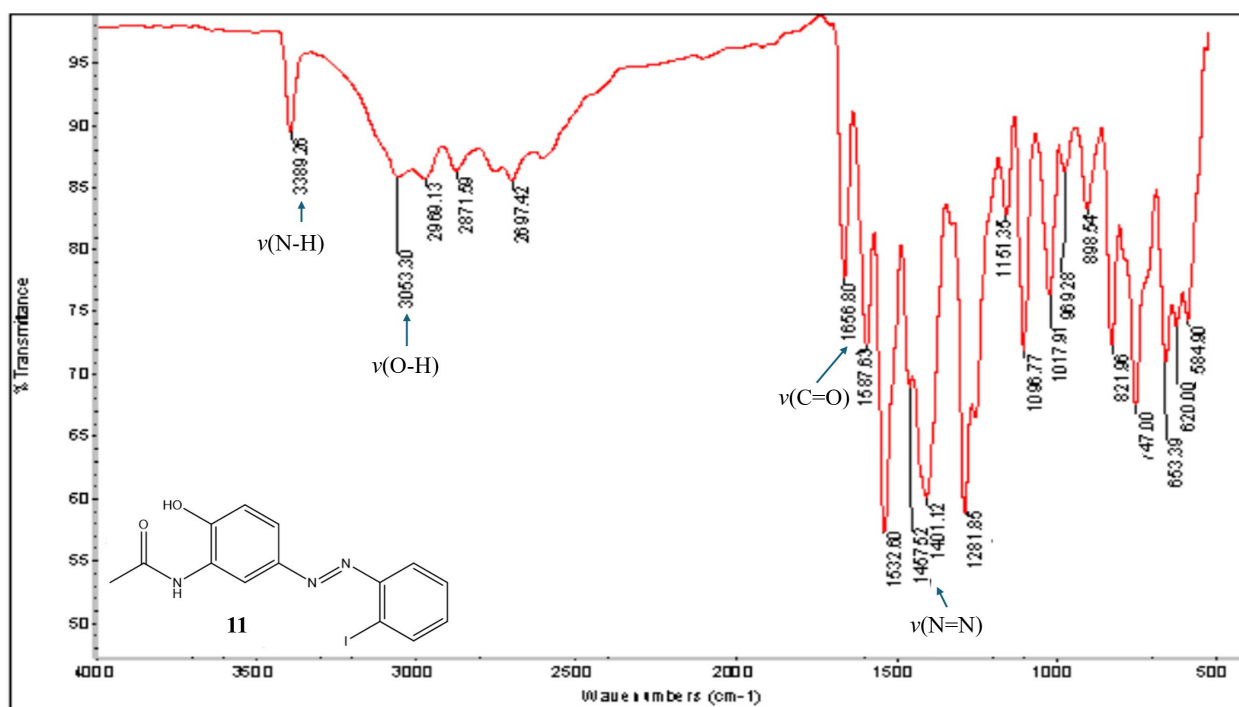
8 (*o*-Br)



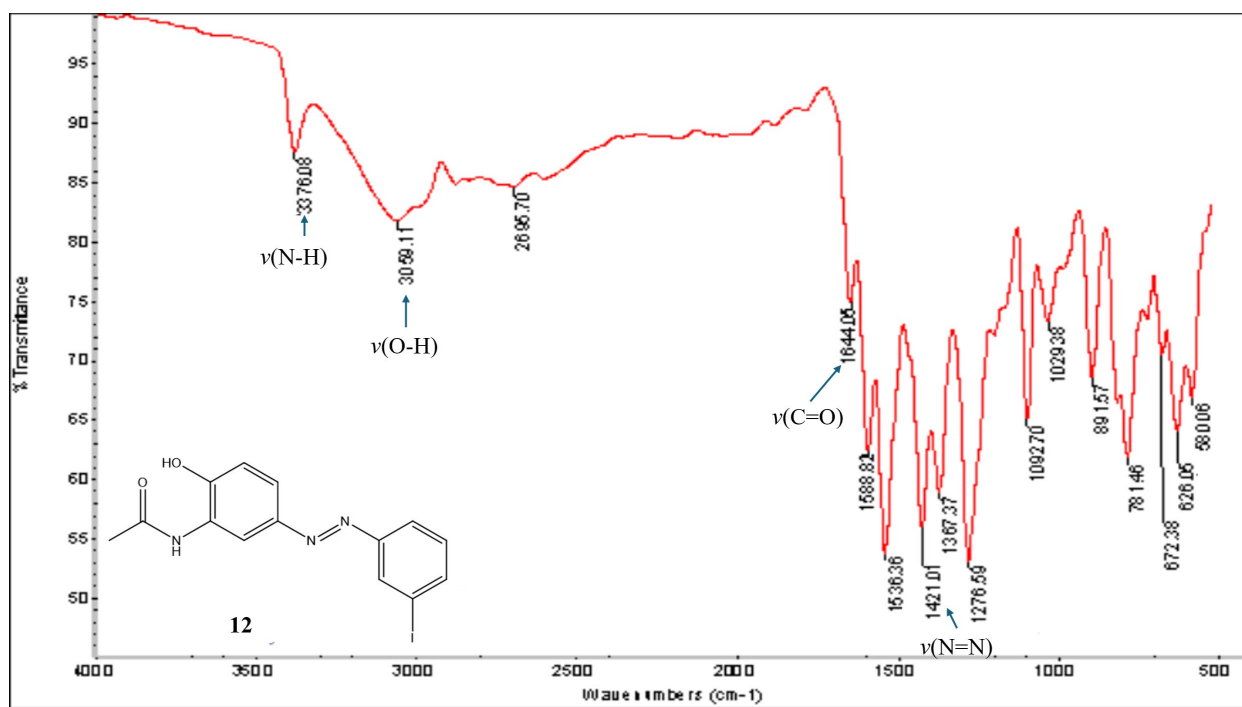
9 (*m*-Br)



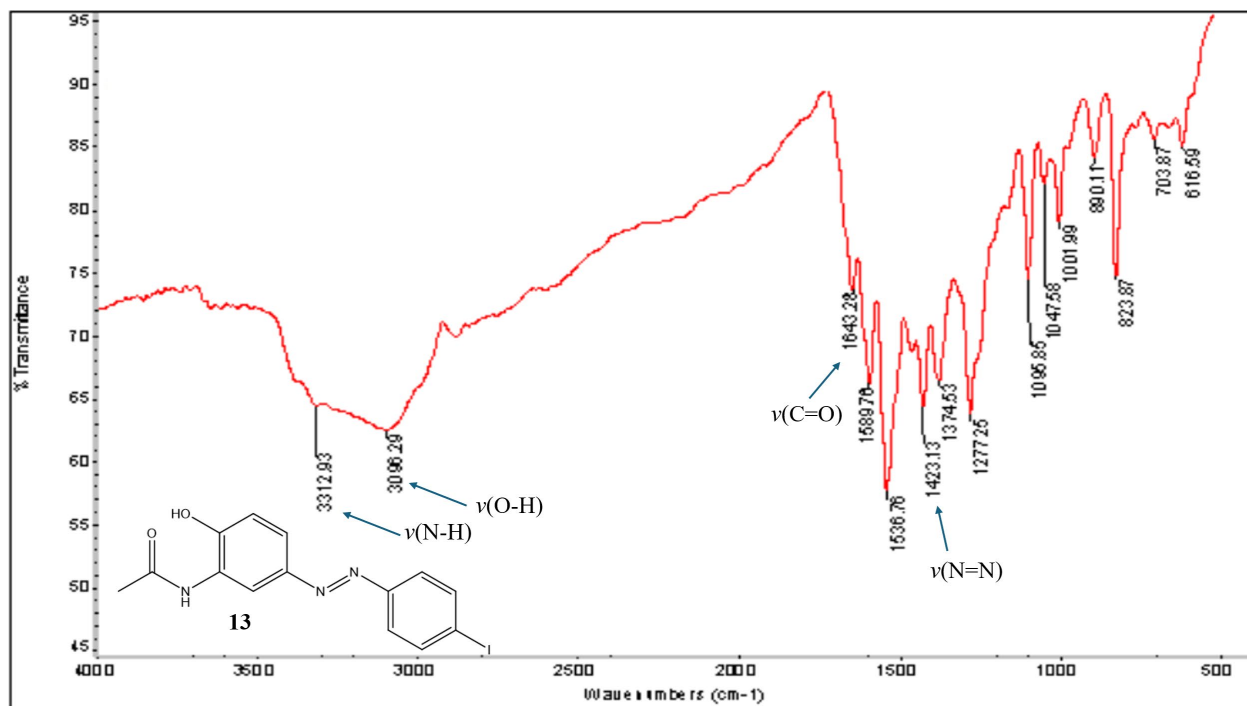
10 (*p*-Br)



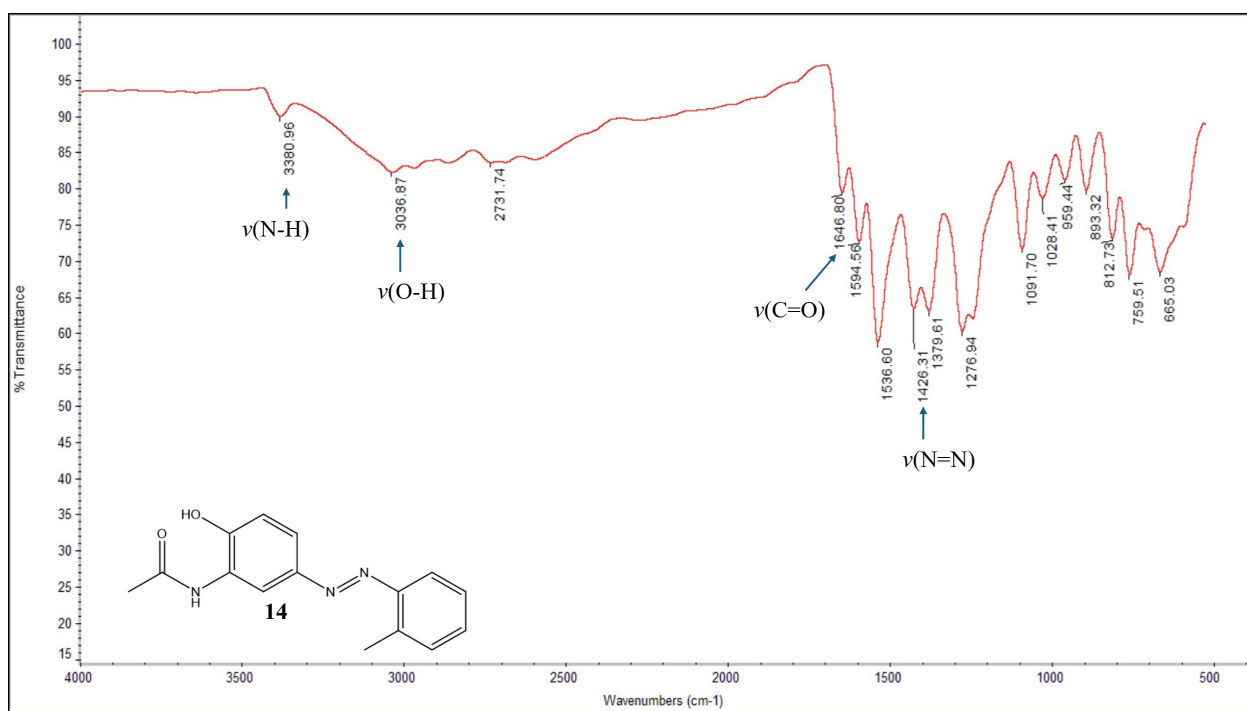
11(o-I)



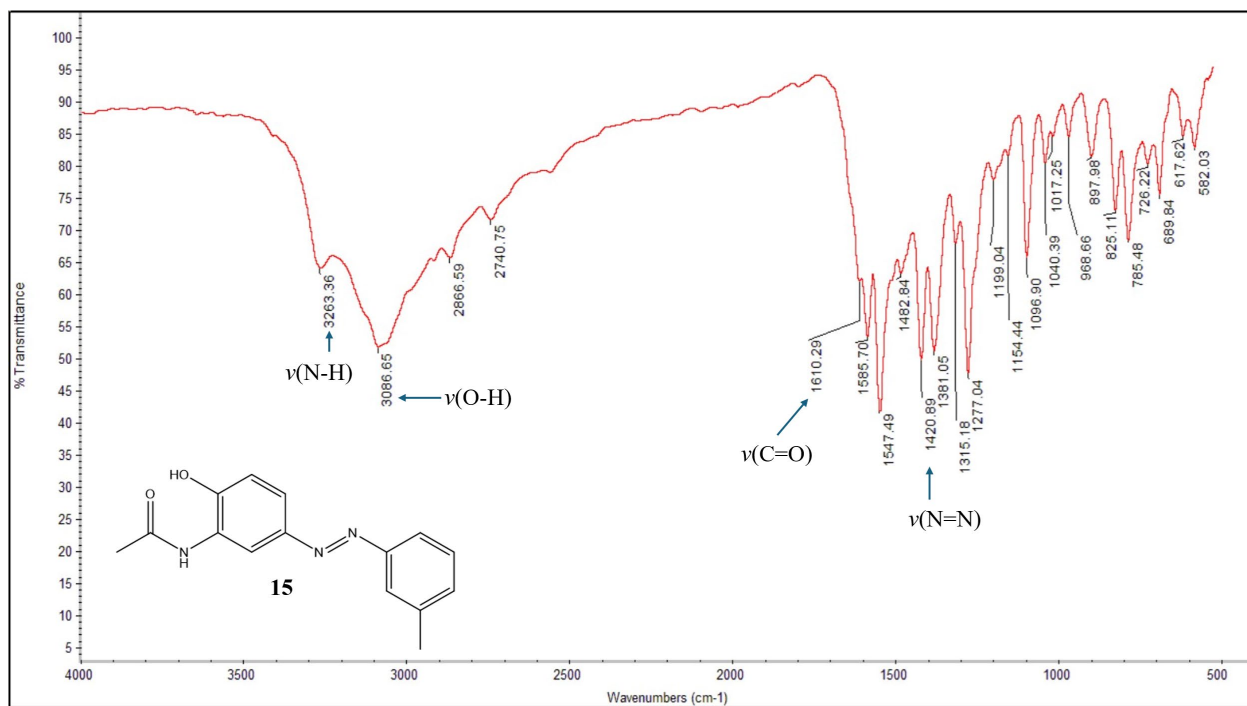
12(m-I)



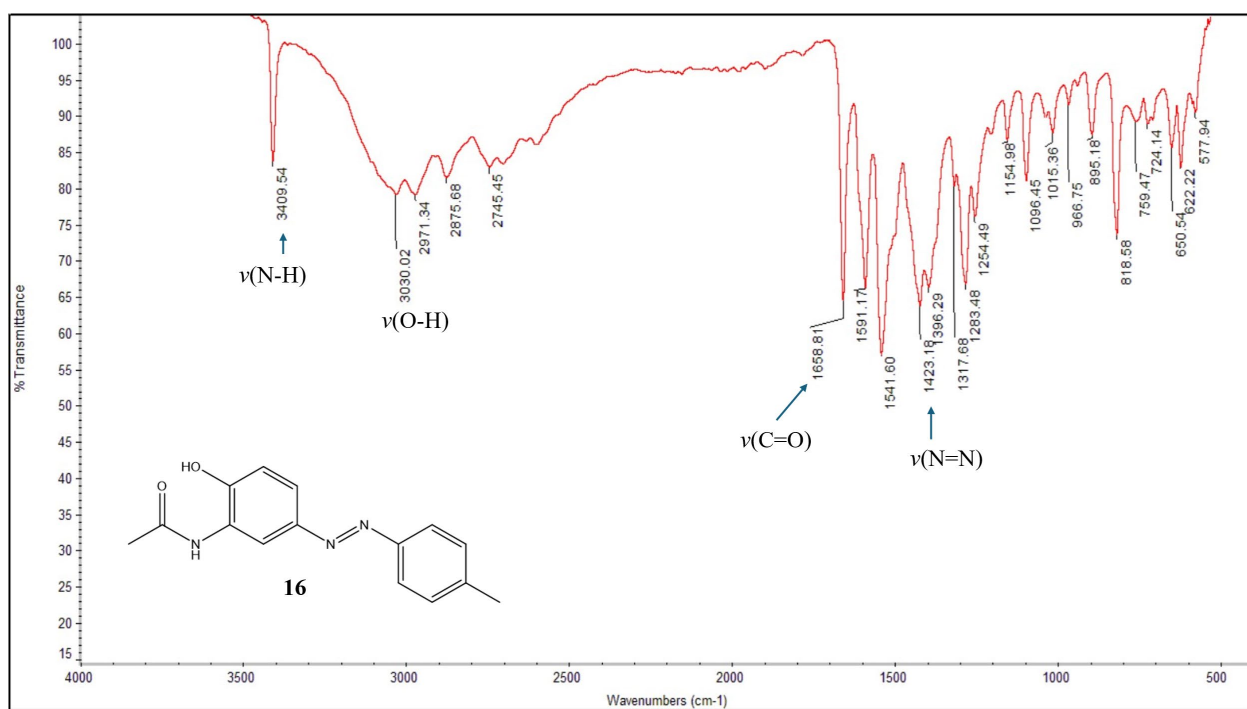
13 (*p*-I)



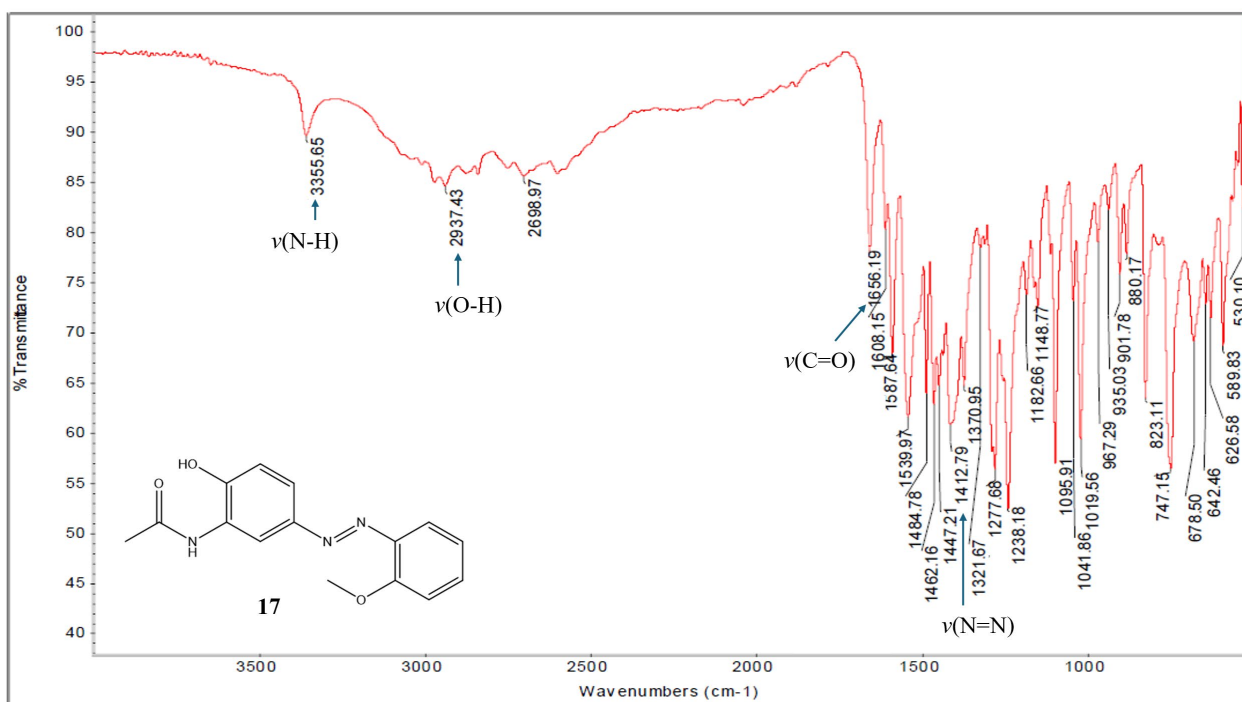
14 (*o*-CH₃)



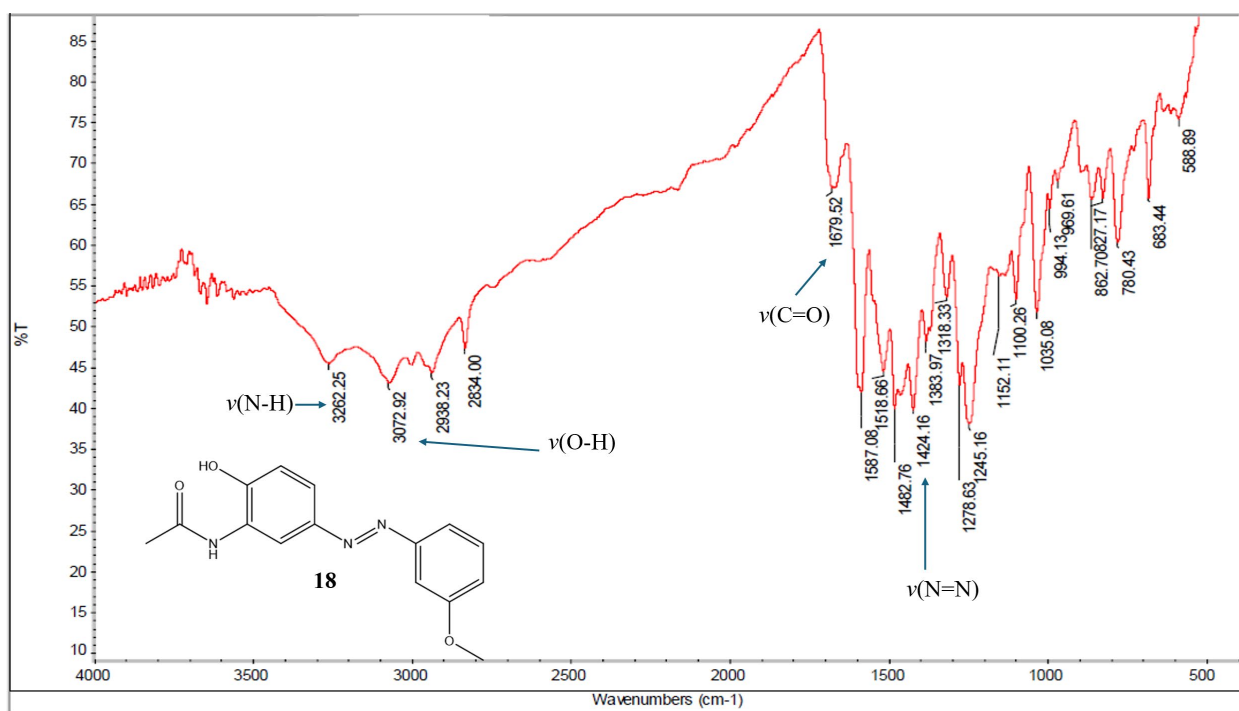
15 (*m*-CH₃)



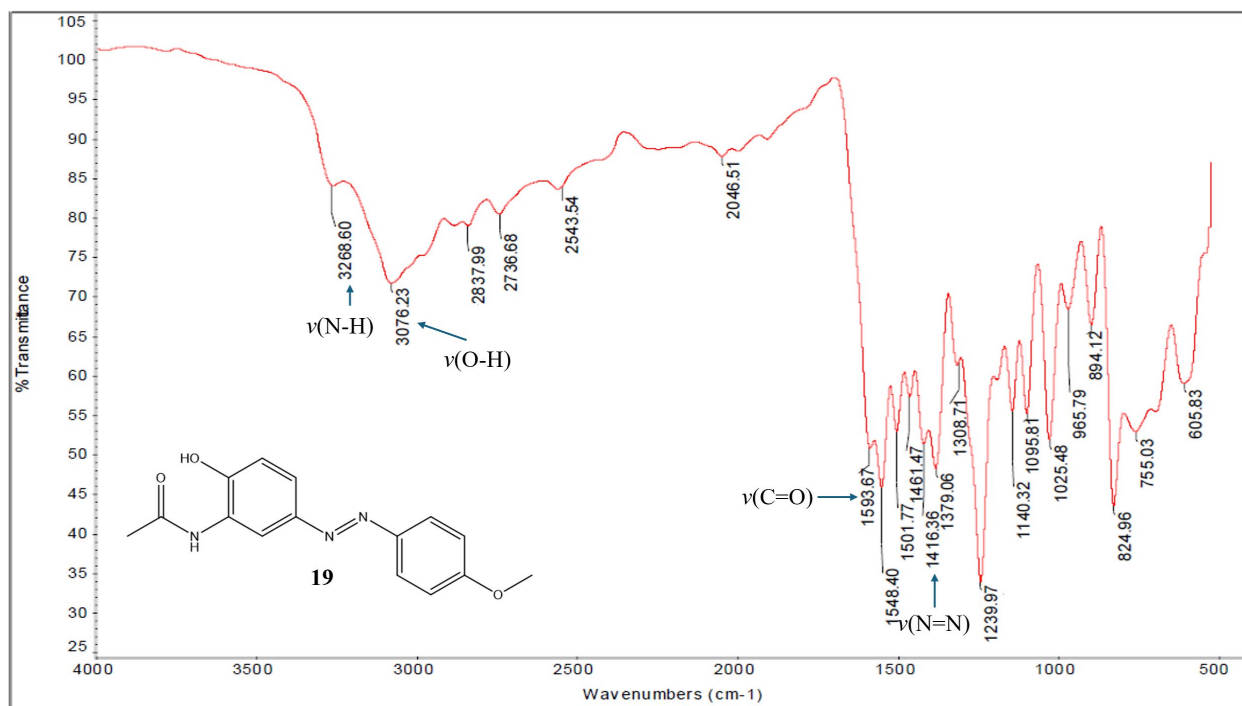
16 (*p*-CH₃)



17 (*o*-OCH₃)



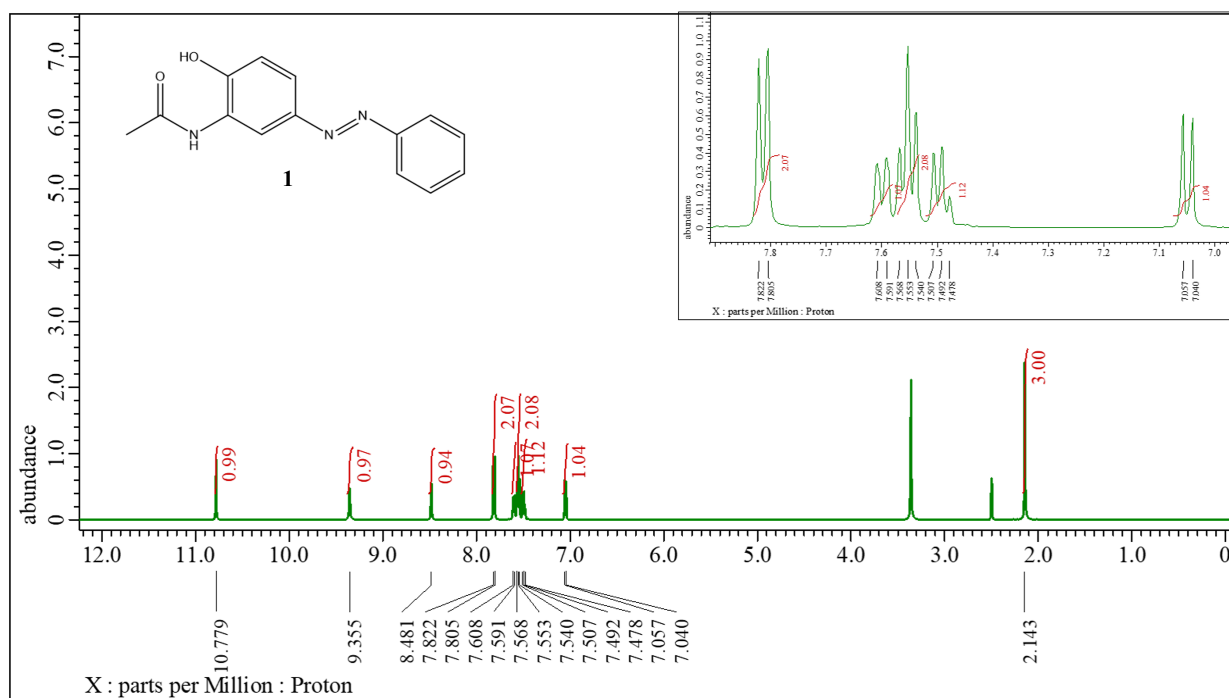
18 (*m*-OCH₃)



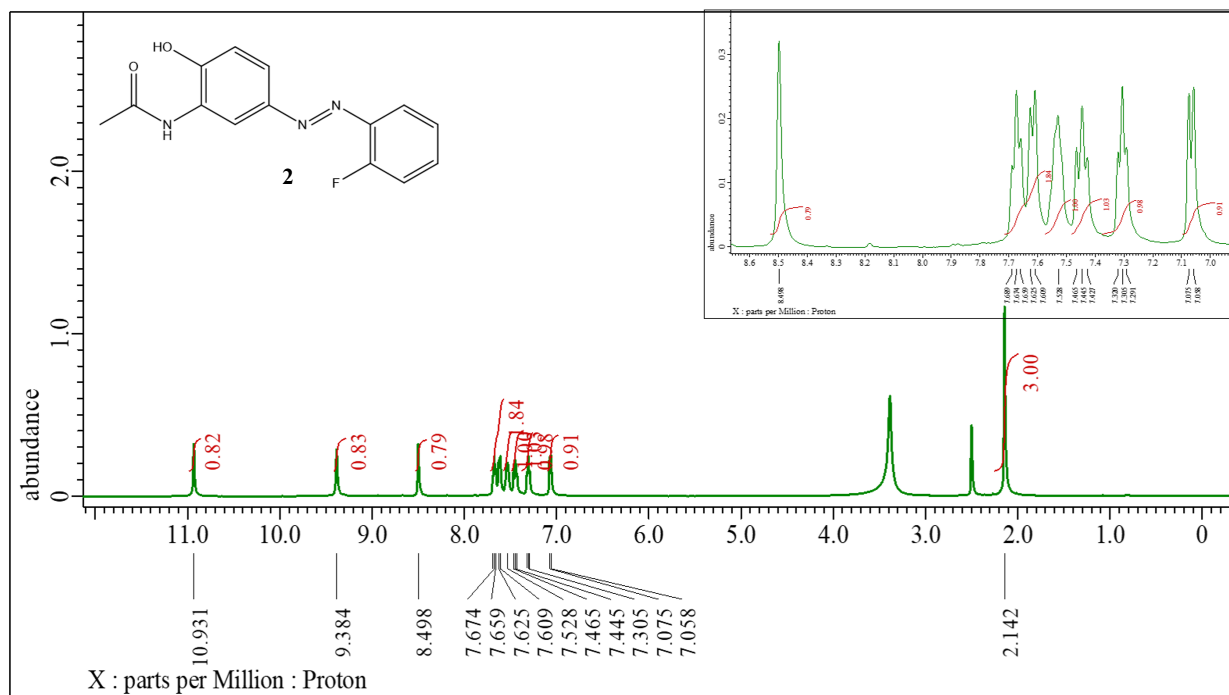
19 (*p*-OCH₃)

A3: ^1H NMR data characterization of 1-19.

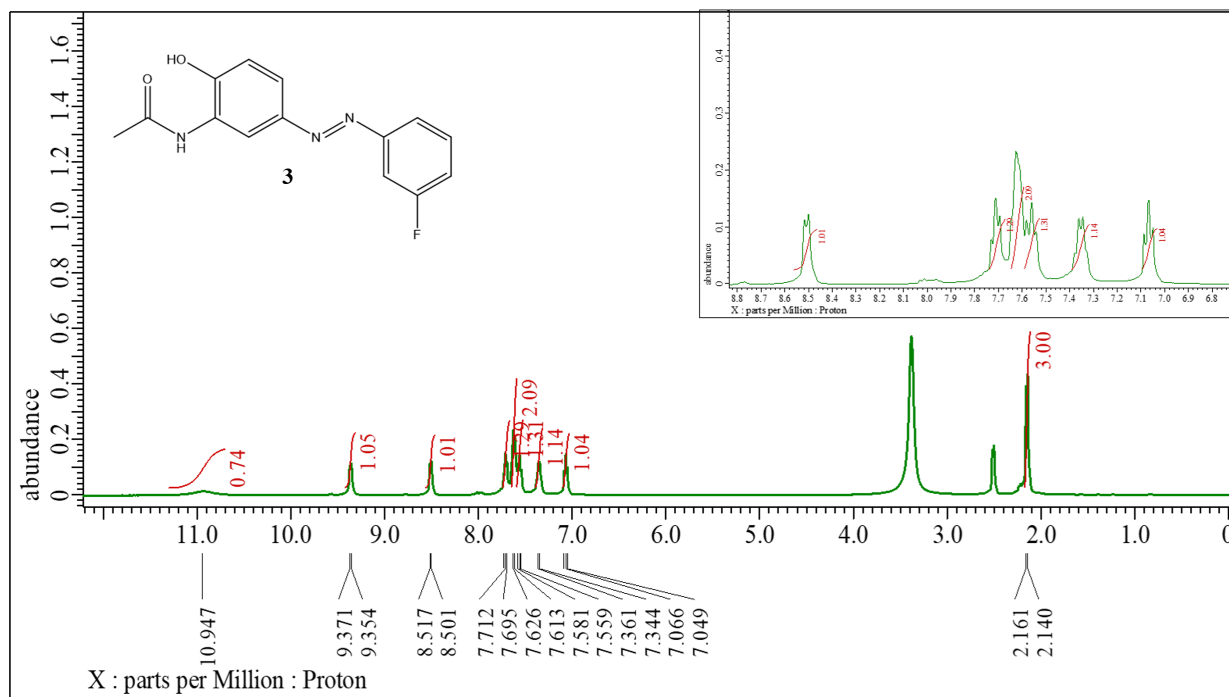
Figure A2: ^1H NMR spectra of orthocetamol azo 1-19.



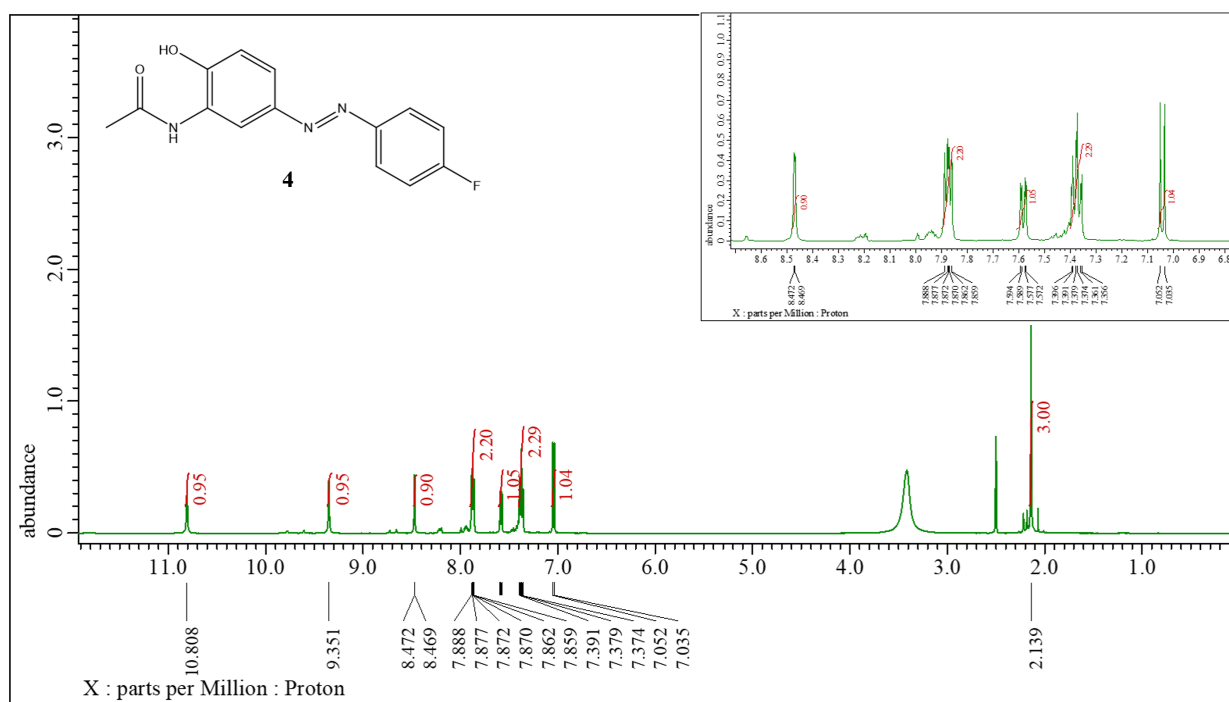
1(H)



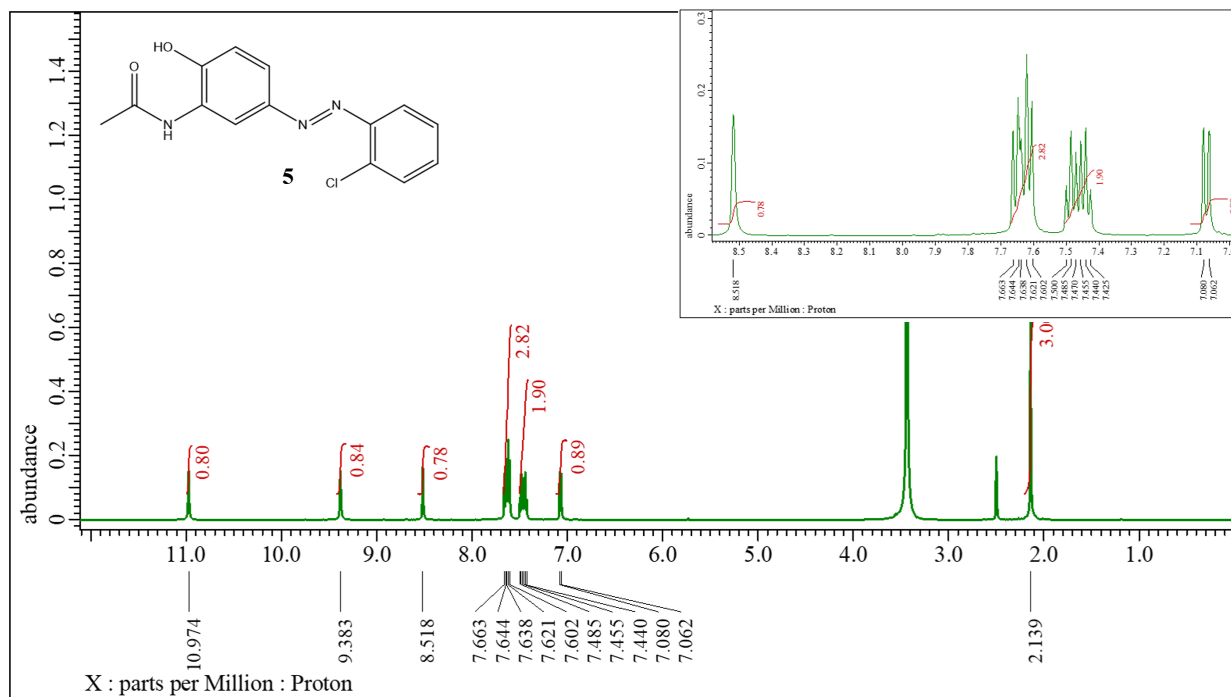
2 (o-F)



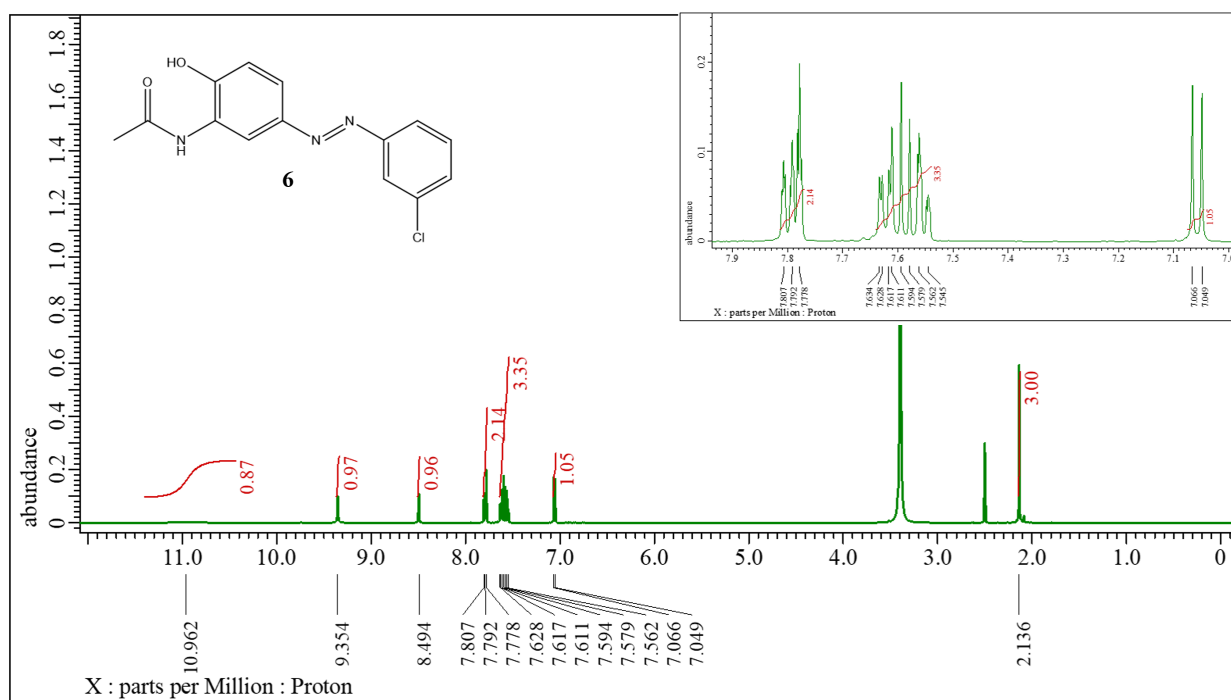
3 (*m*-F)



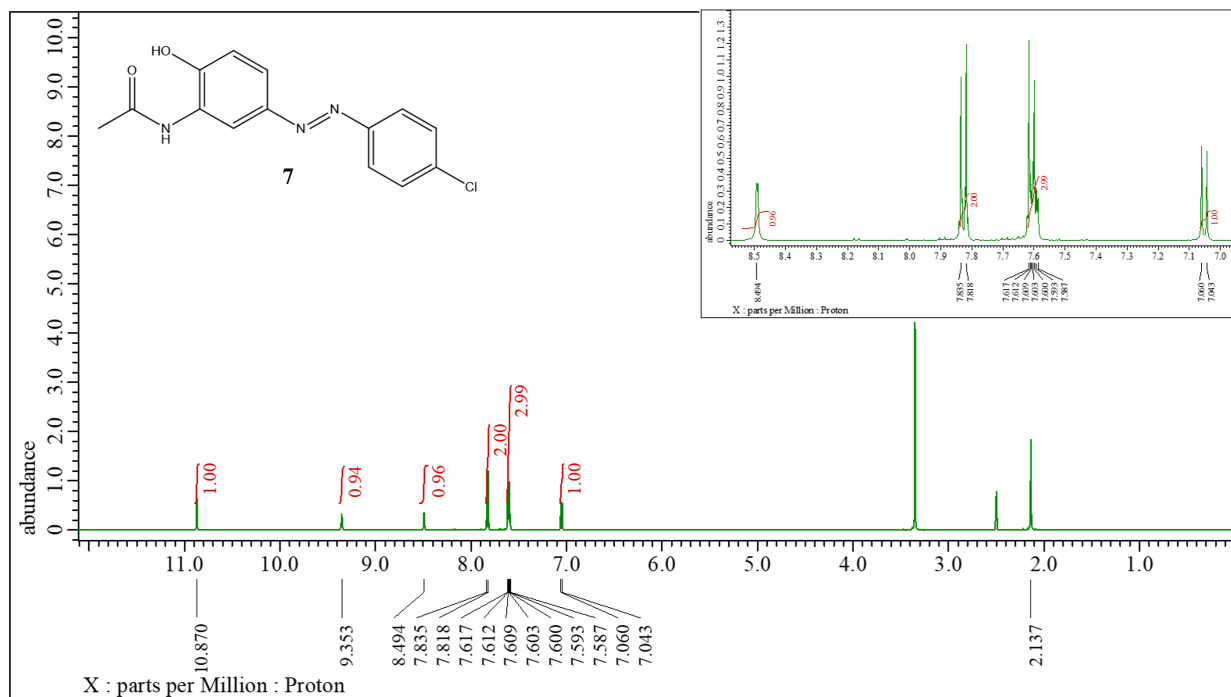
4 (*p*-F)



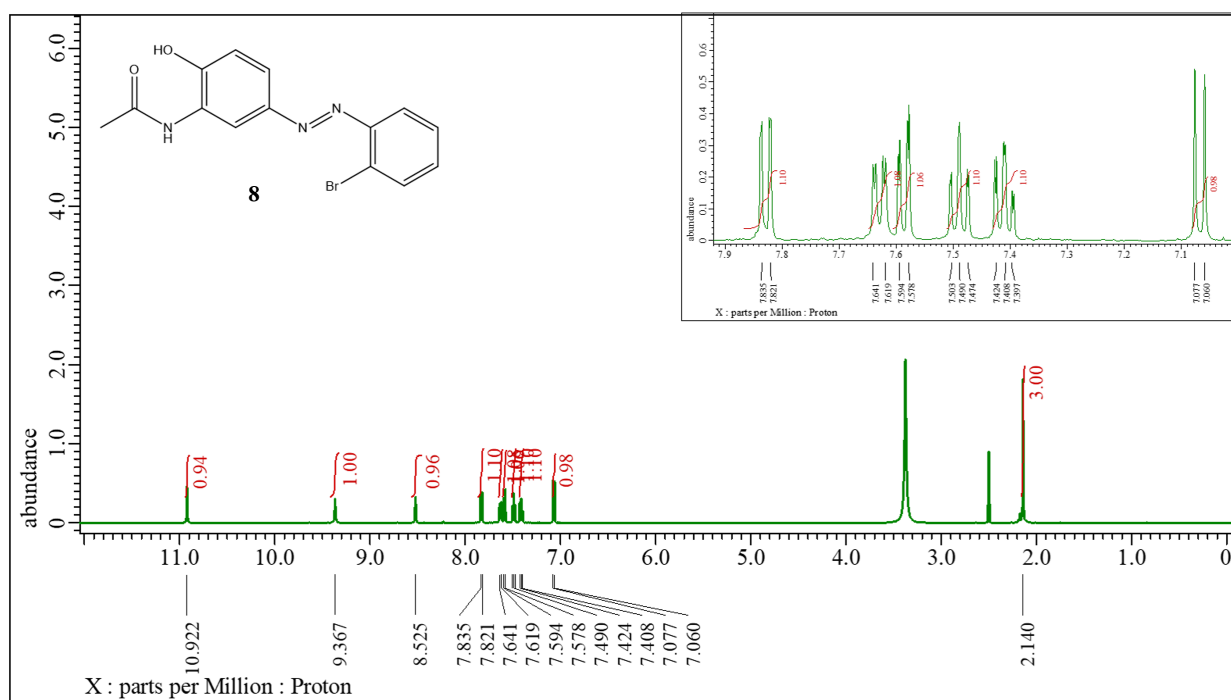
5 (*o*-Cl)



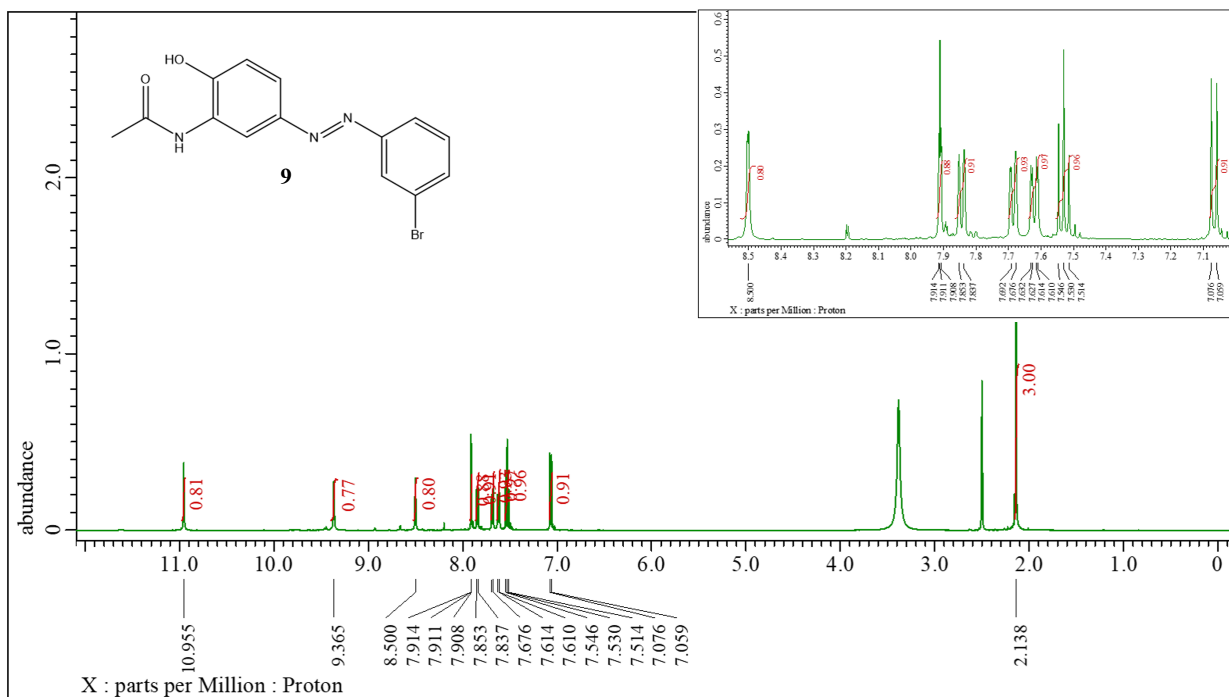
6 (*m*-Cl)



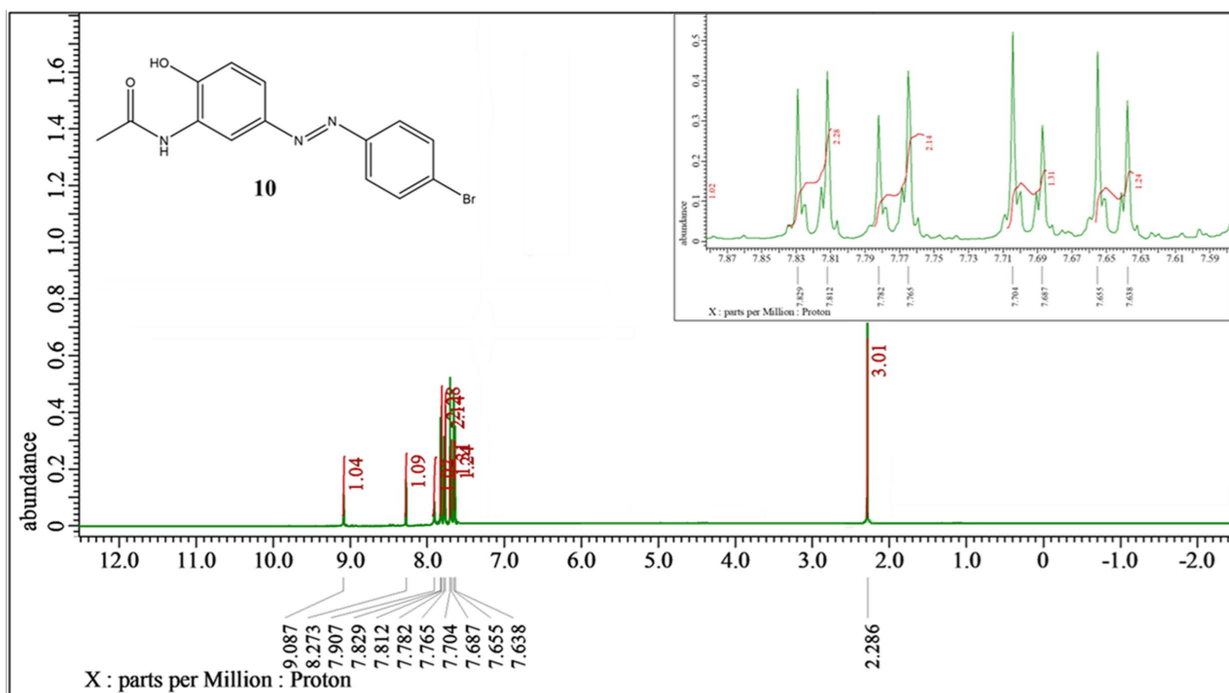
7 (*p*-Cl)



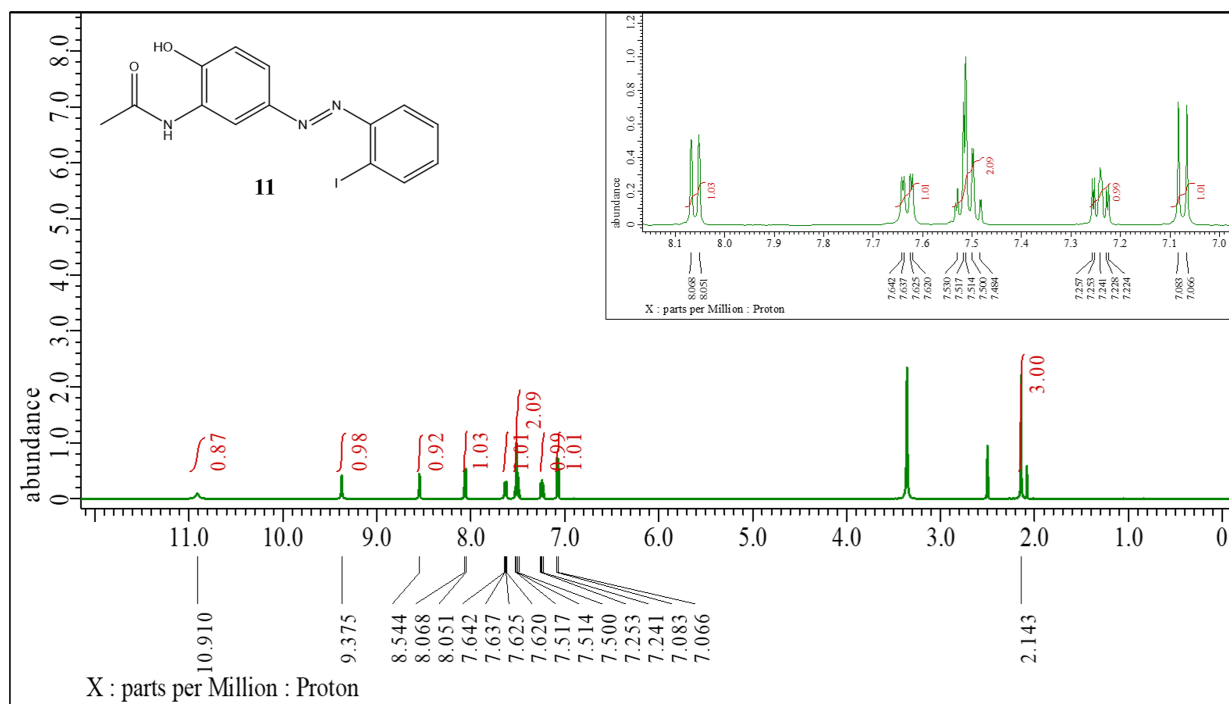
8 (*o*-Br)



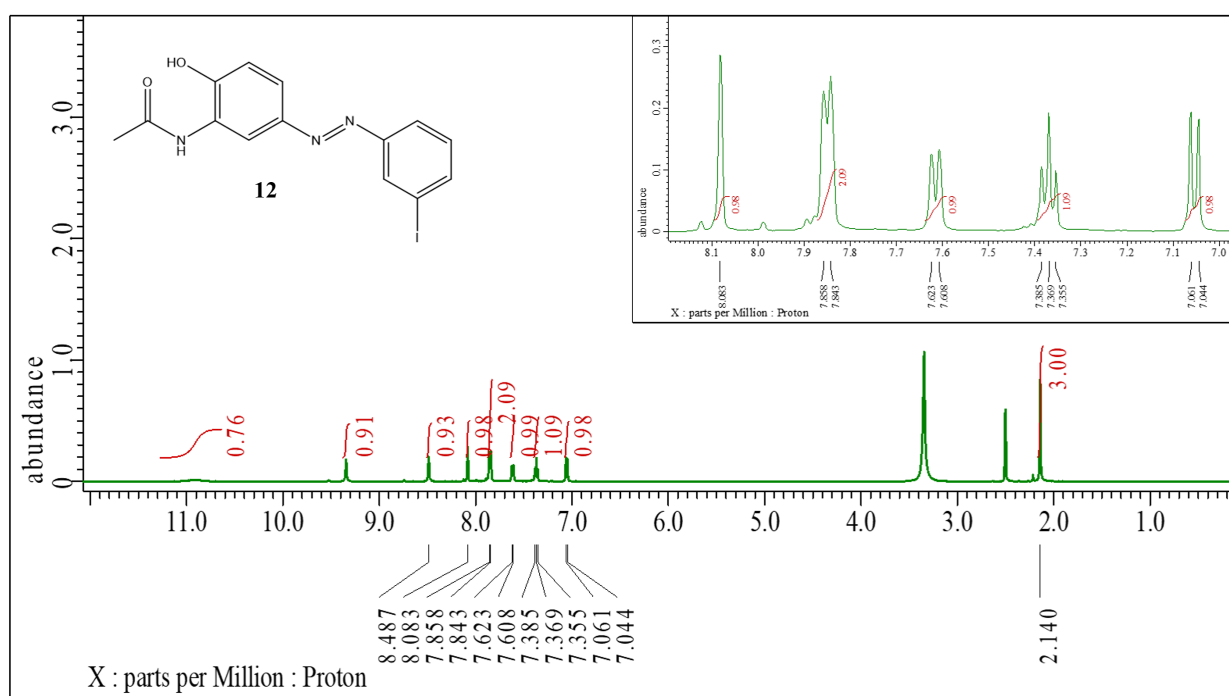
9 (m-Br)



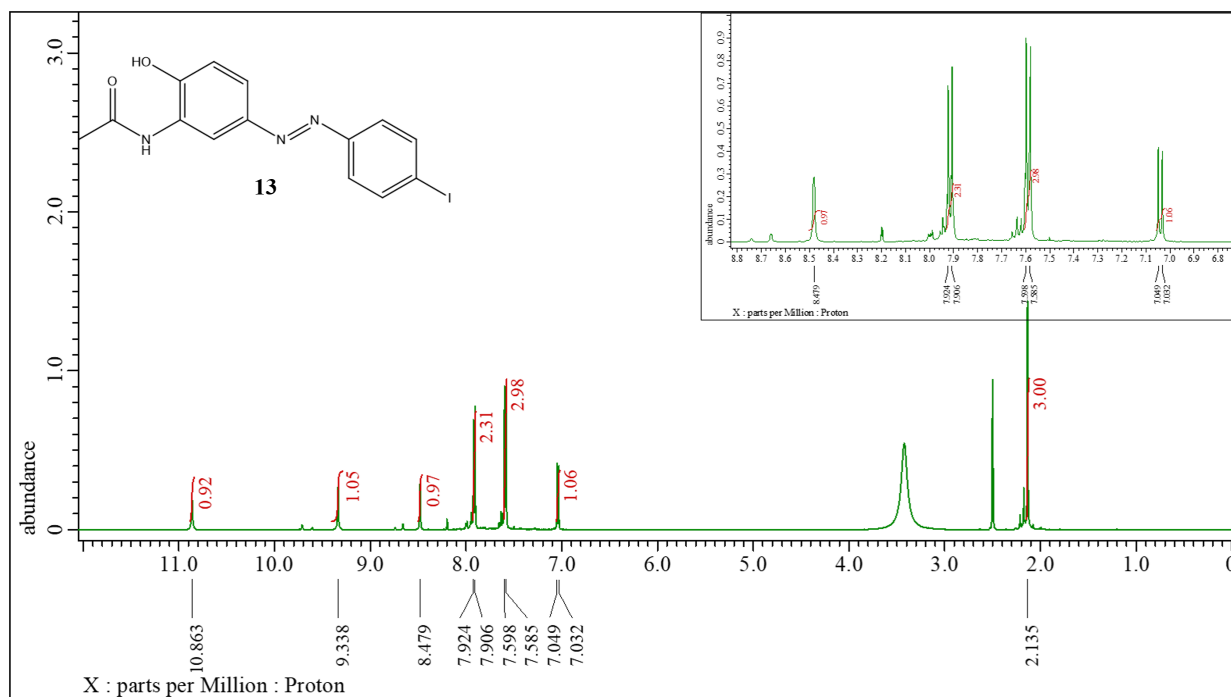
10(p-Br)



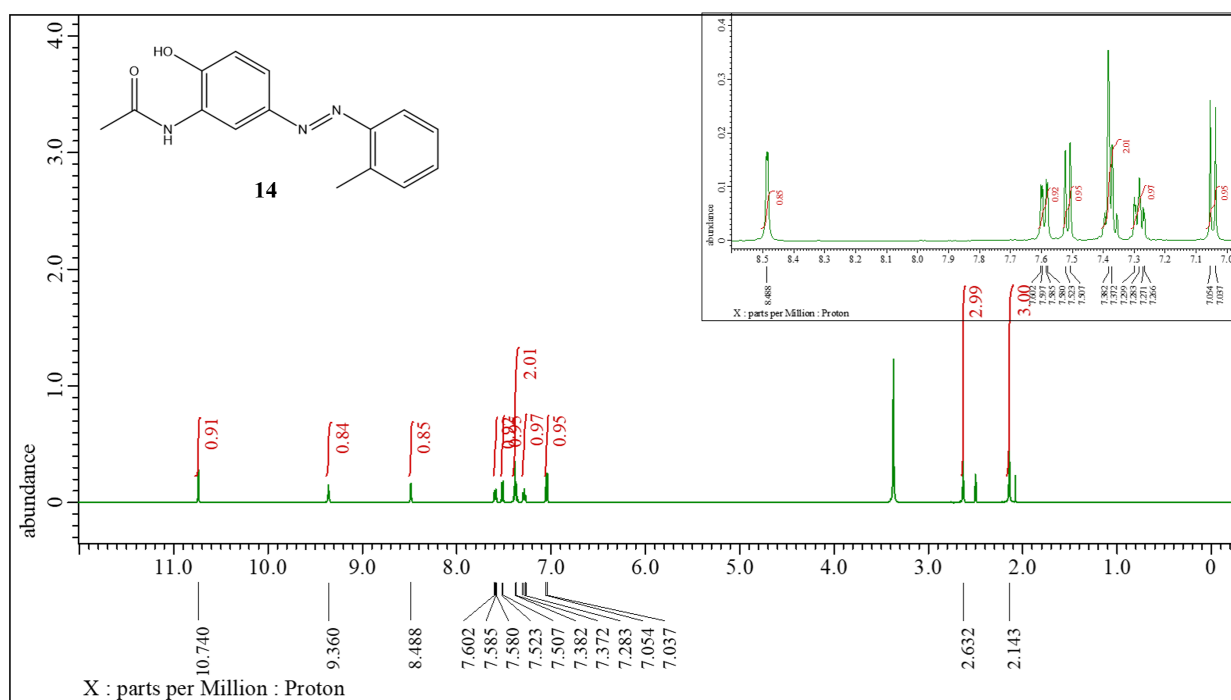
11(o-I)



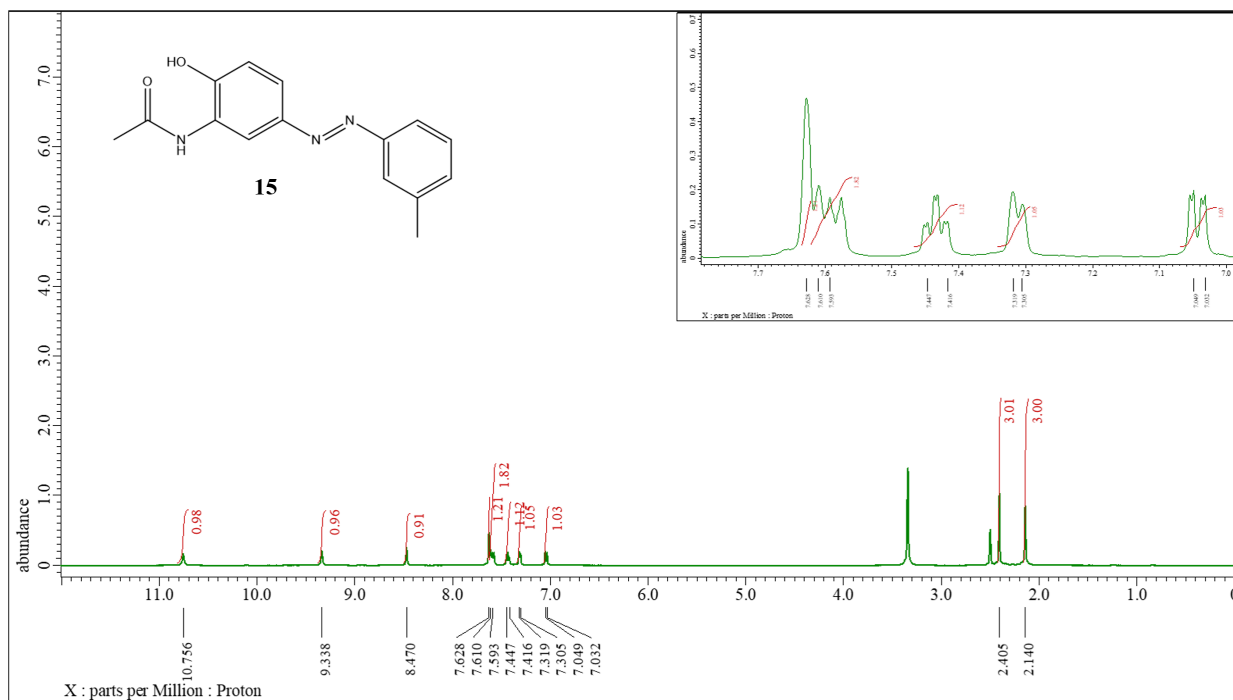
12(m-I)



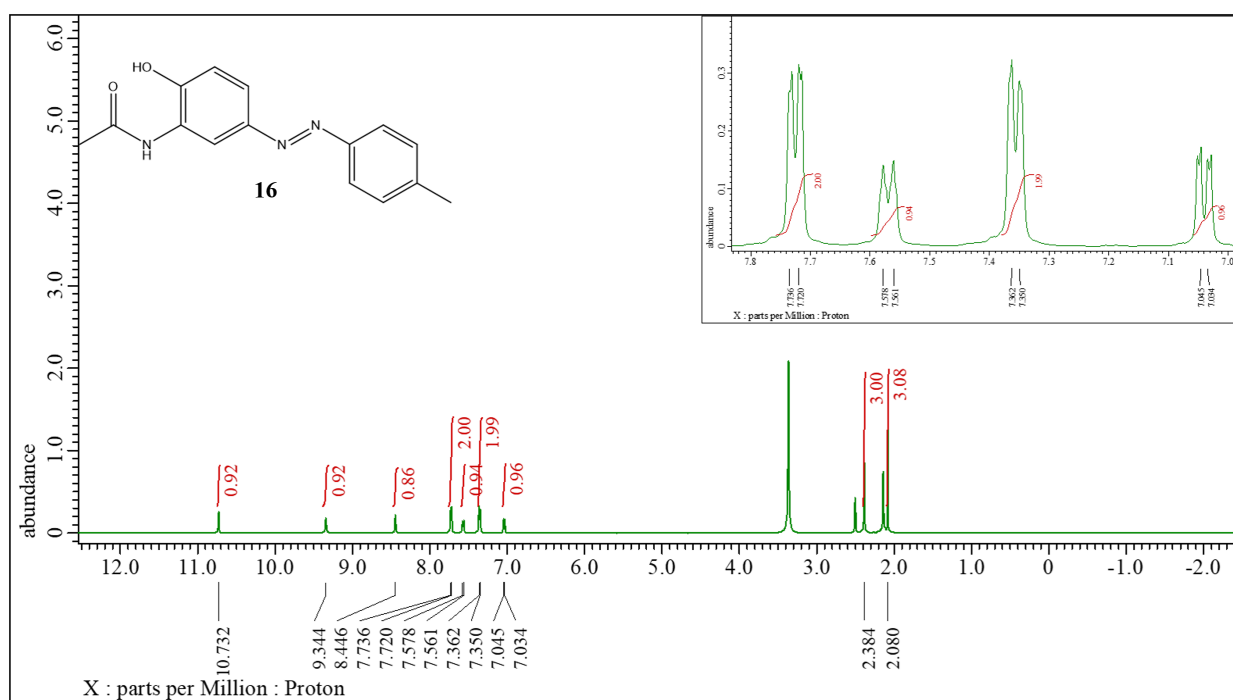
13 (*p*-I)



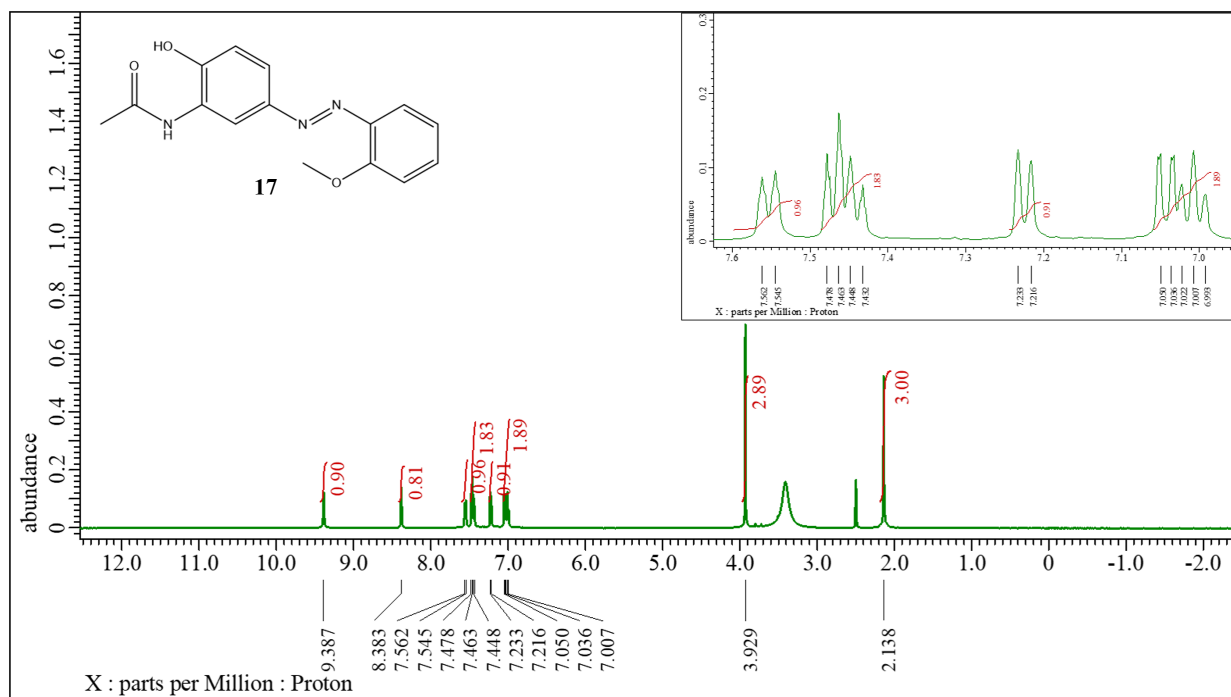
14 (*o*-CH₃)



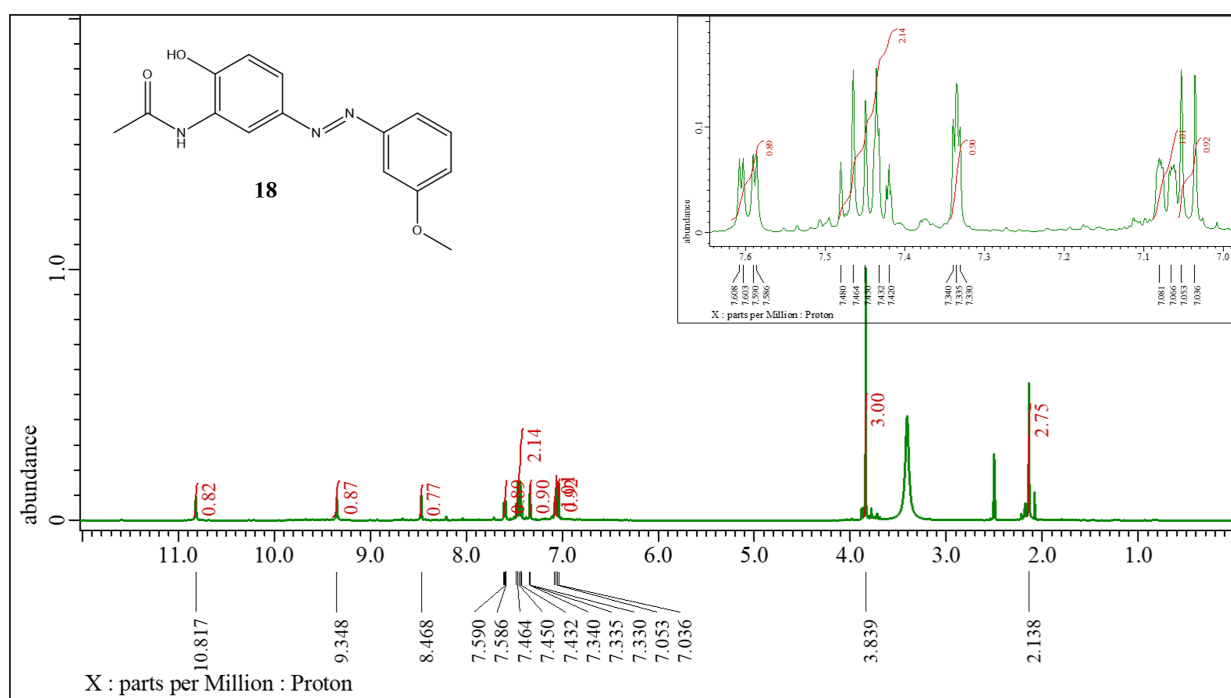
15 (*m*-CH₃)



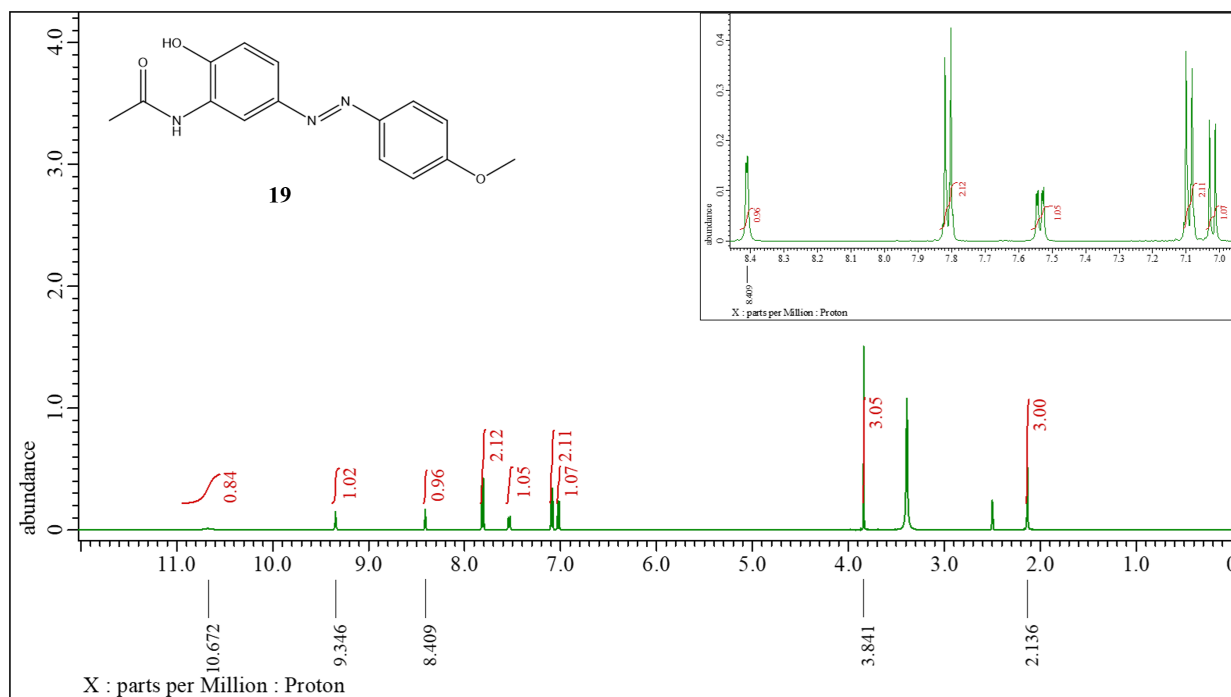
16 (*p*-CH₃)



17 (*o*-OCH₃)



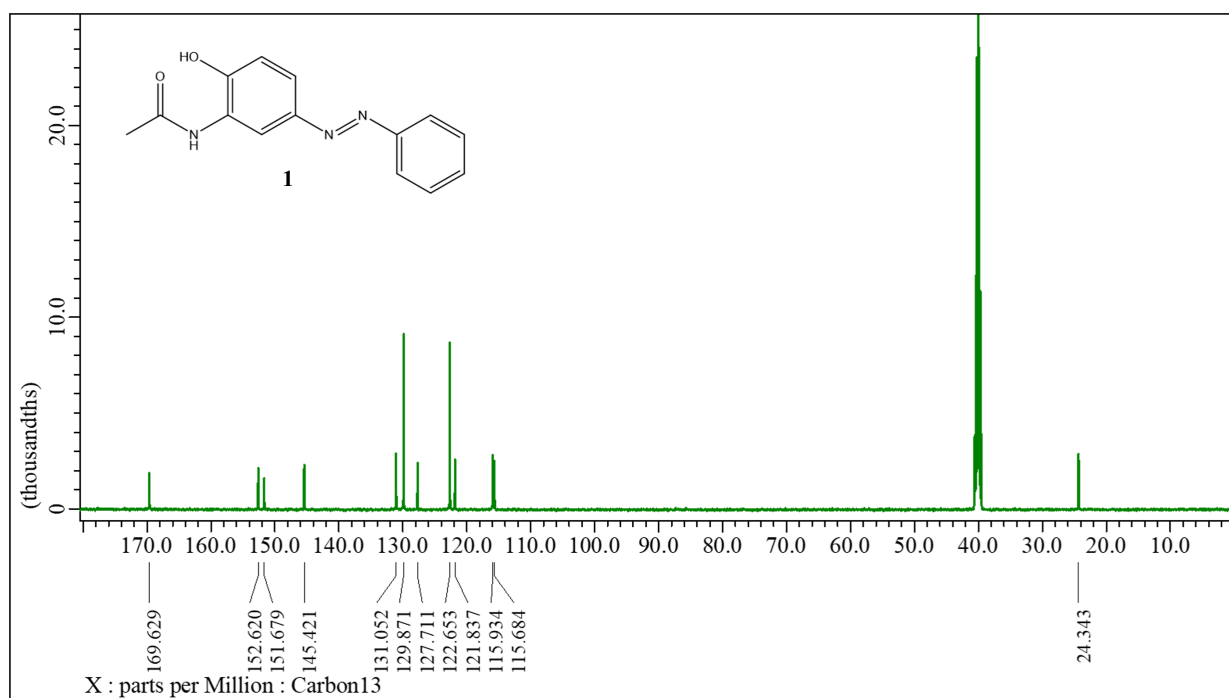
18 (*m*-OCH₃)



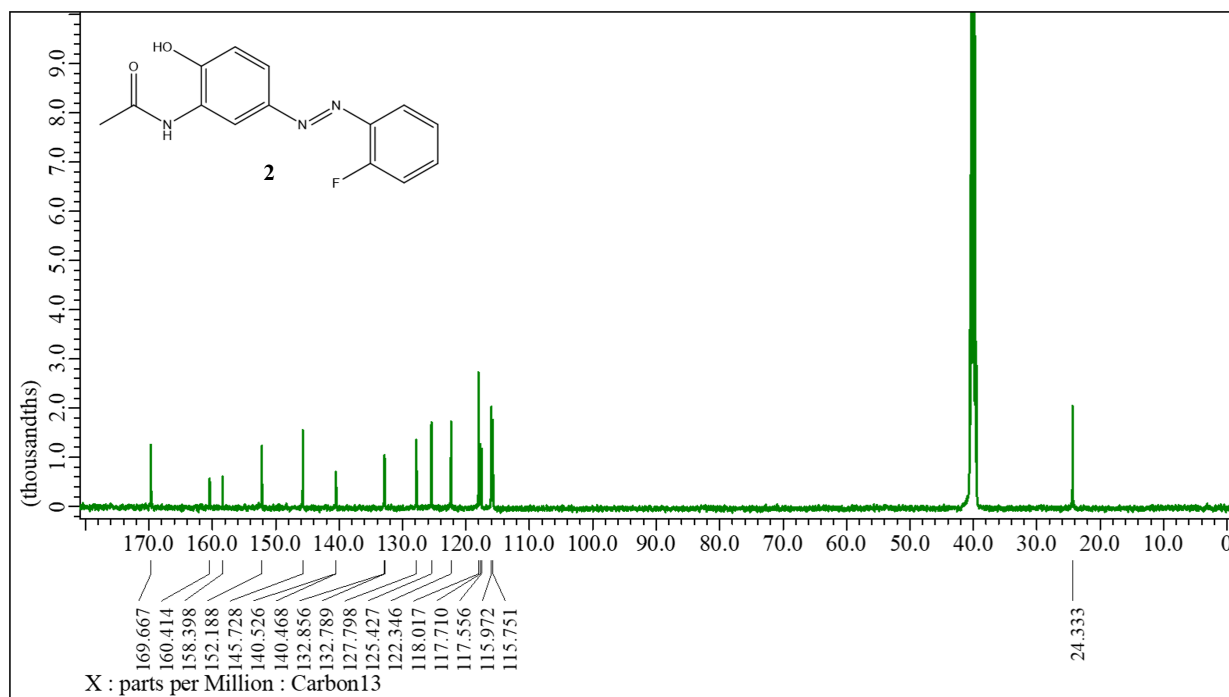
19 (*p*-OCH₃)

A4: ^{13}C NMR data characterization of 1-19.

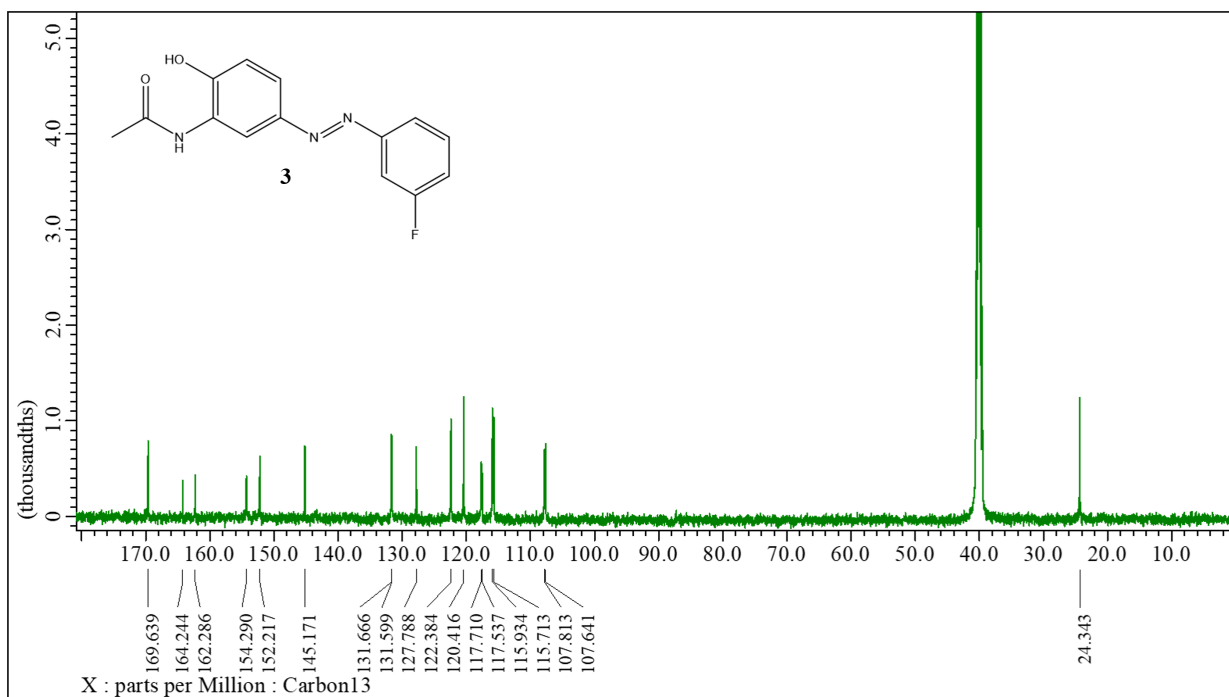
Figure A3: ^{13}C NMR spectra of orthocetamol azo 1-19.



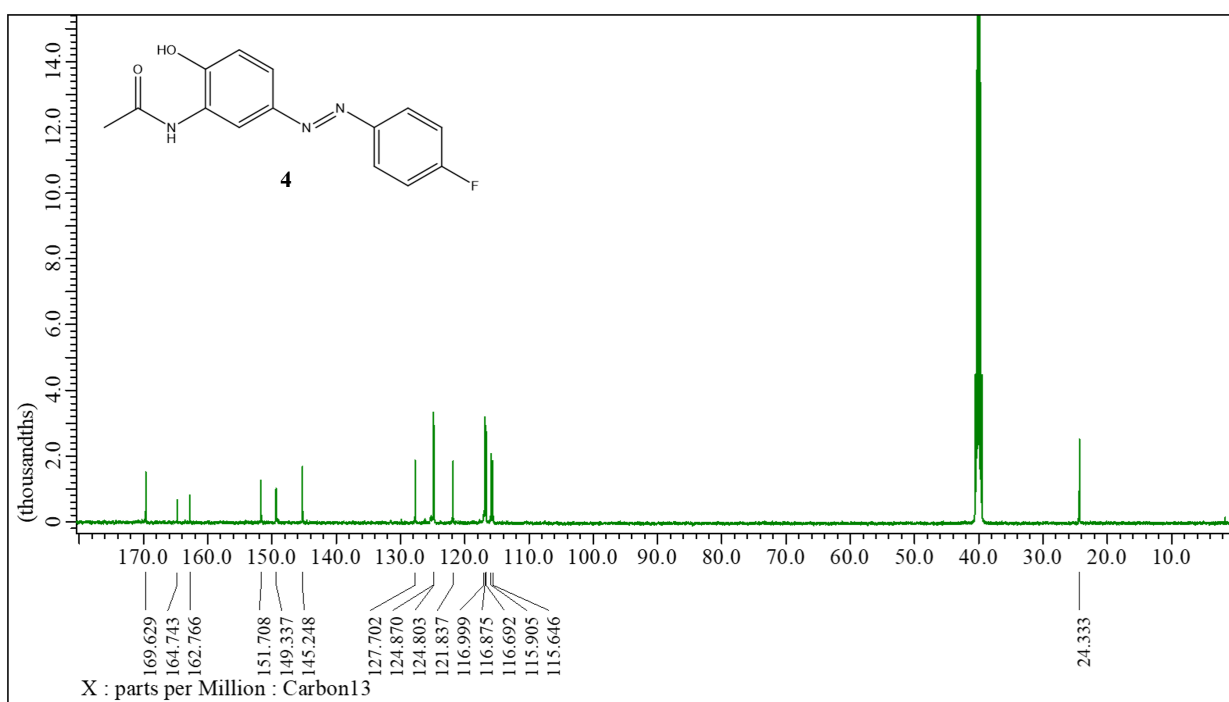
1(H)



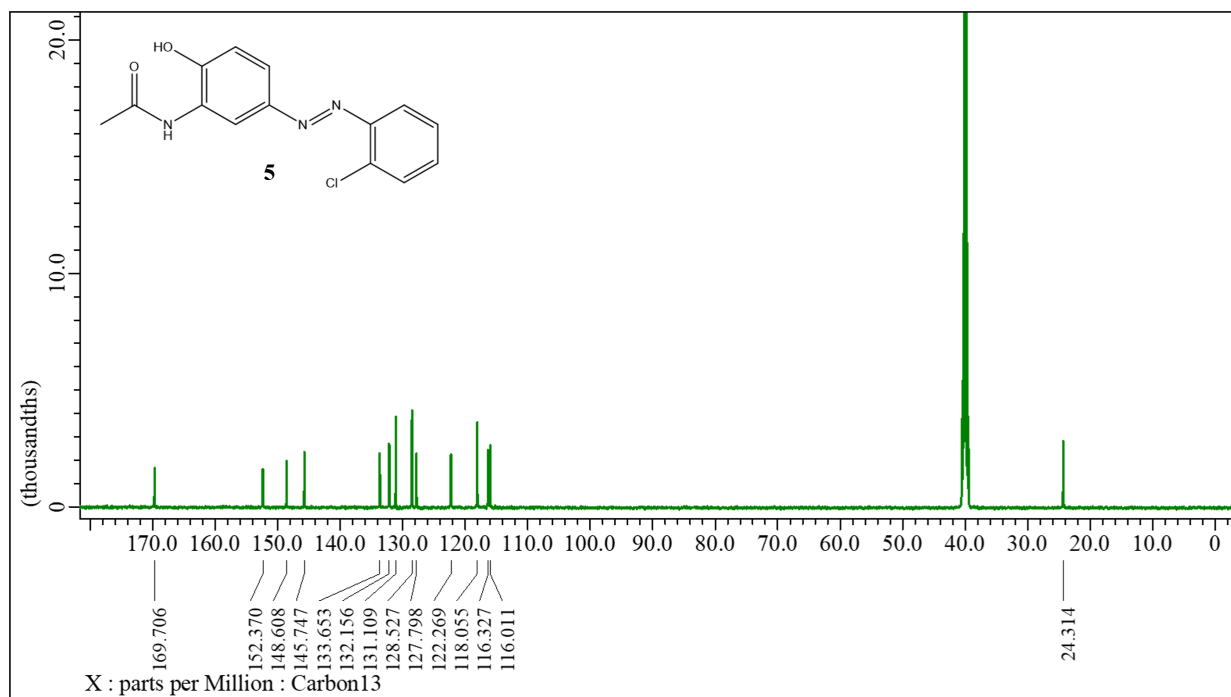
2 (o-F)



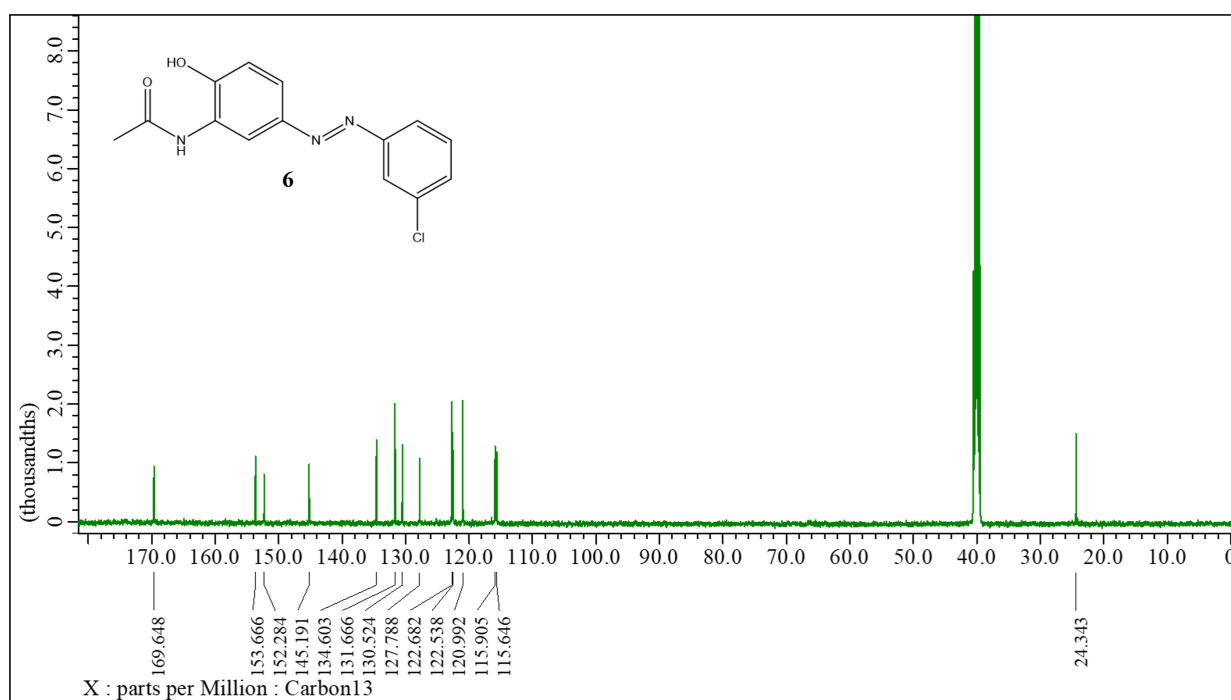
3 (*m*-F)



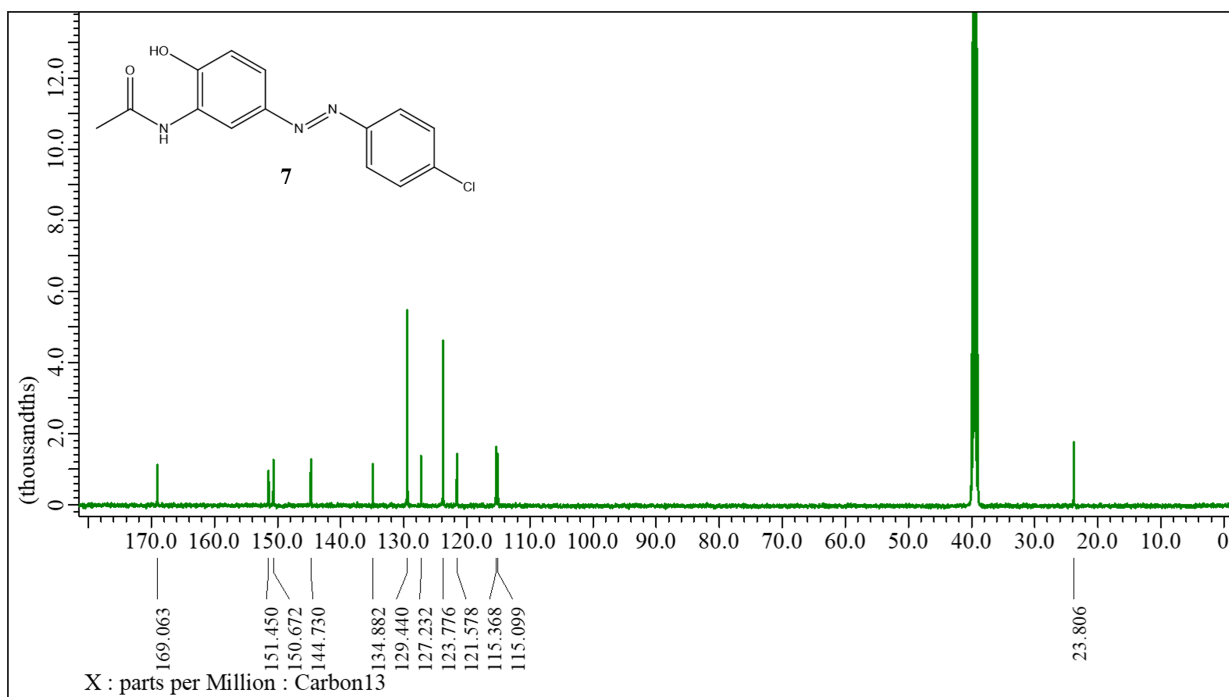
4 (*p*-F)



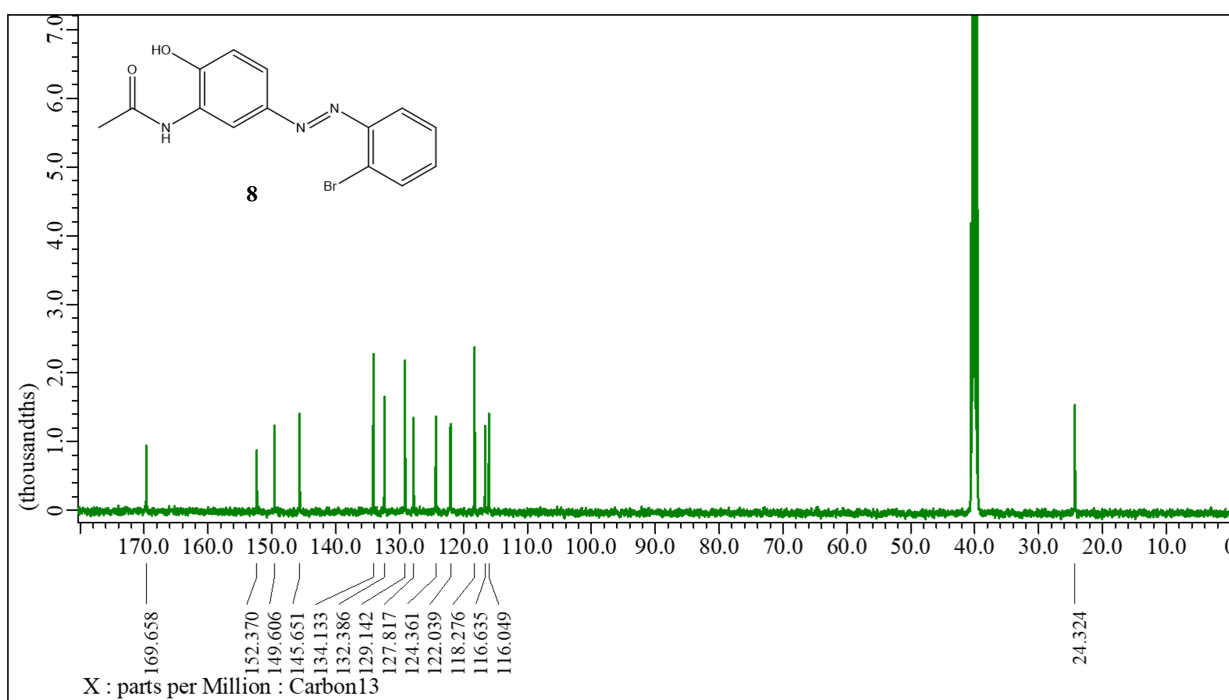
5 (*o*-Cl)



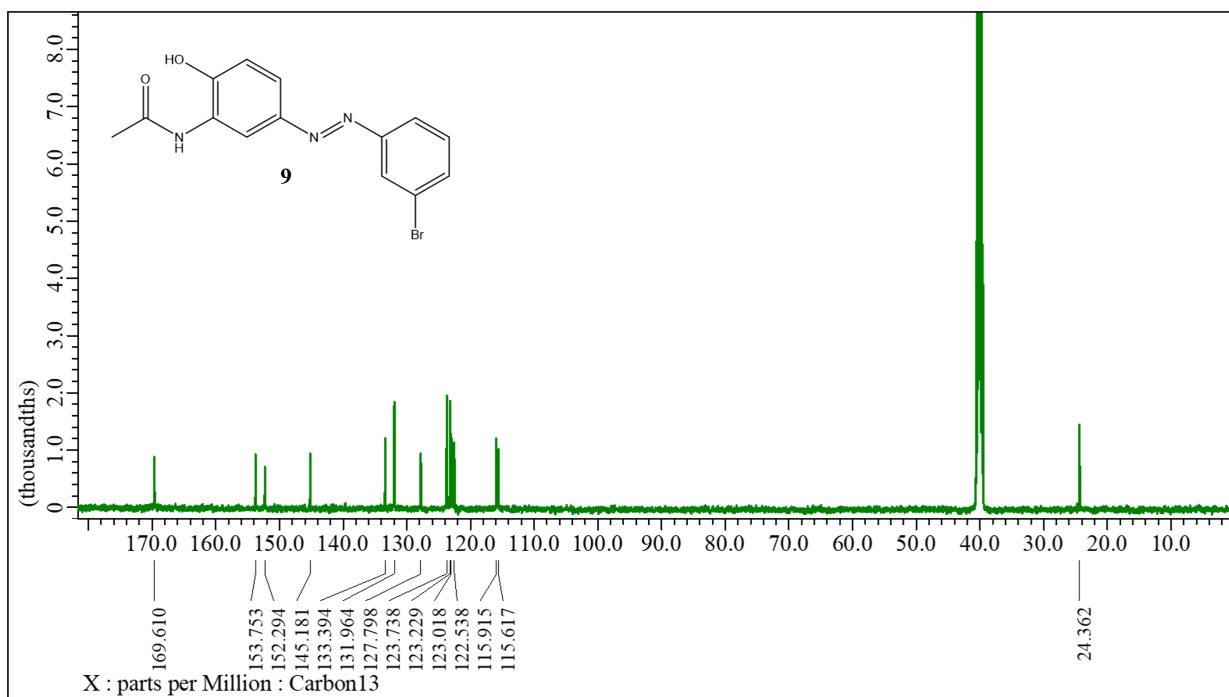
6 (*m*-Cl)



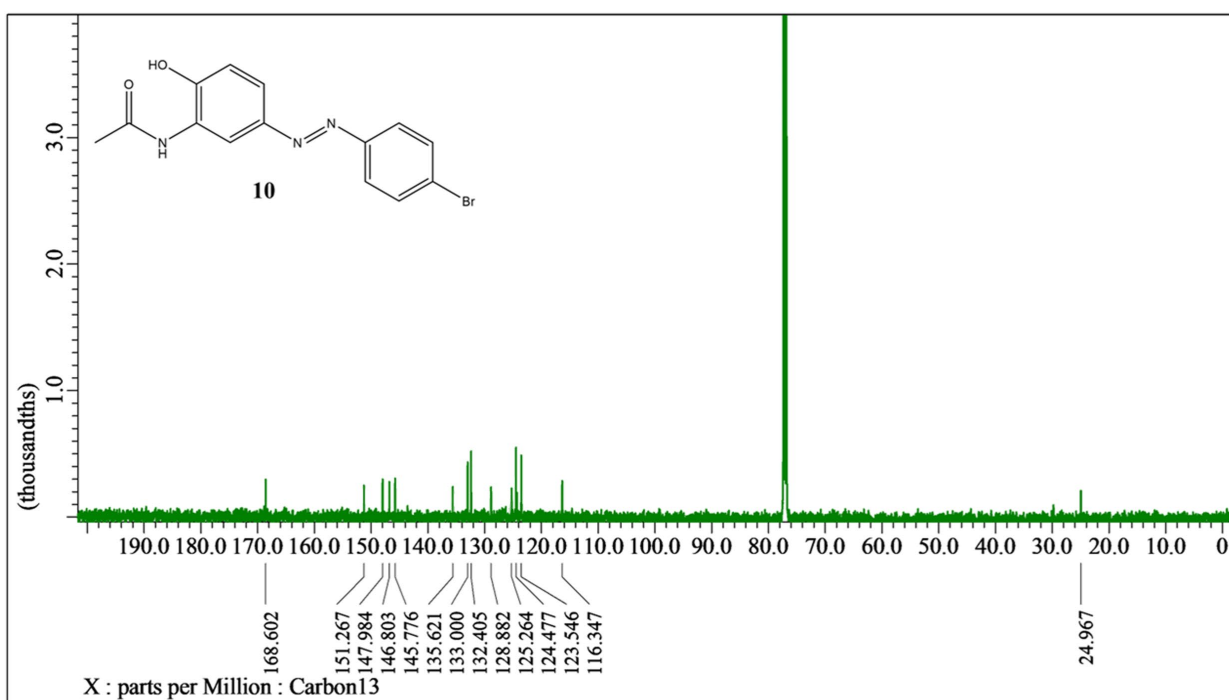
7 (*p*-Cl)



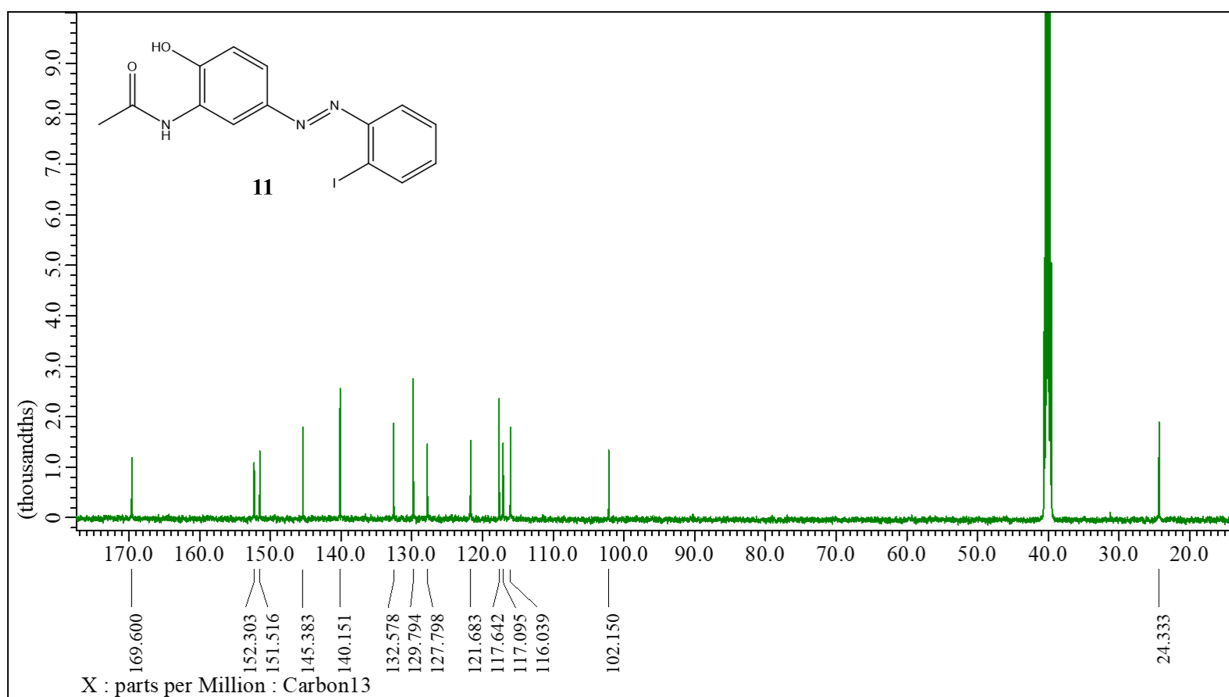
8 (*o*-Br)



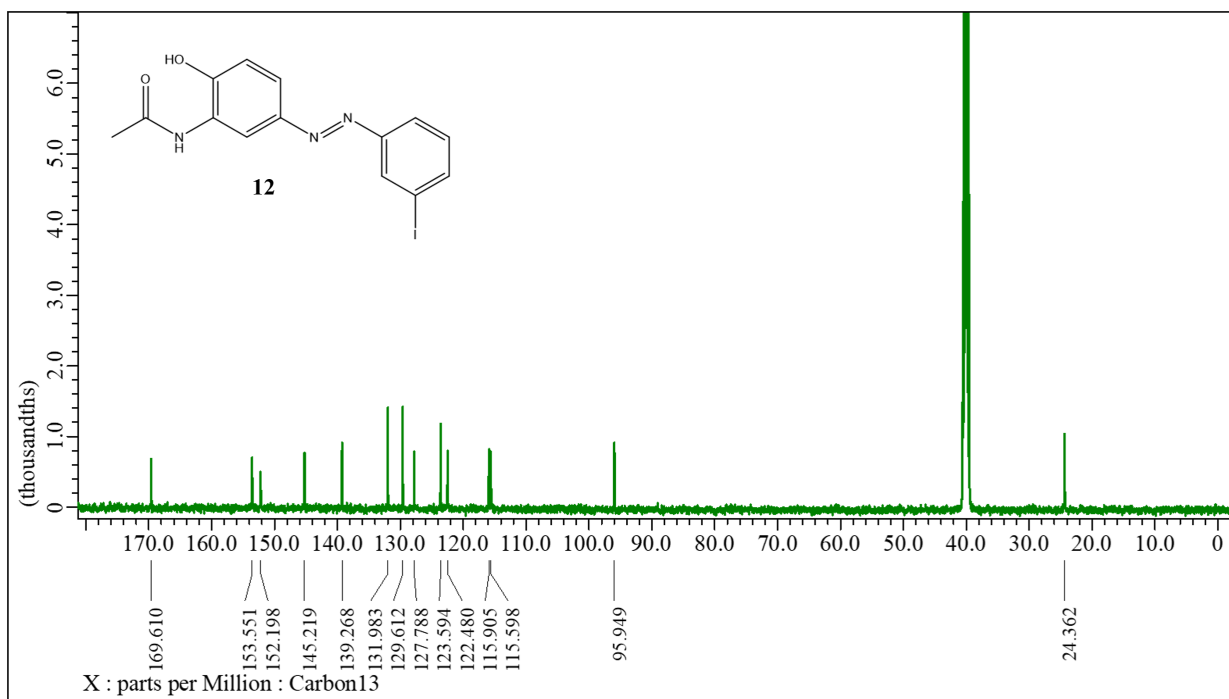
9 (*m*-Br)



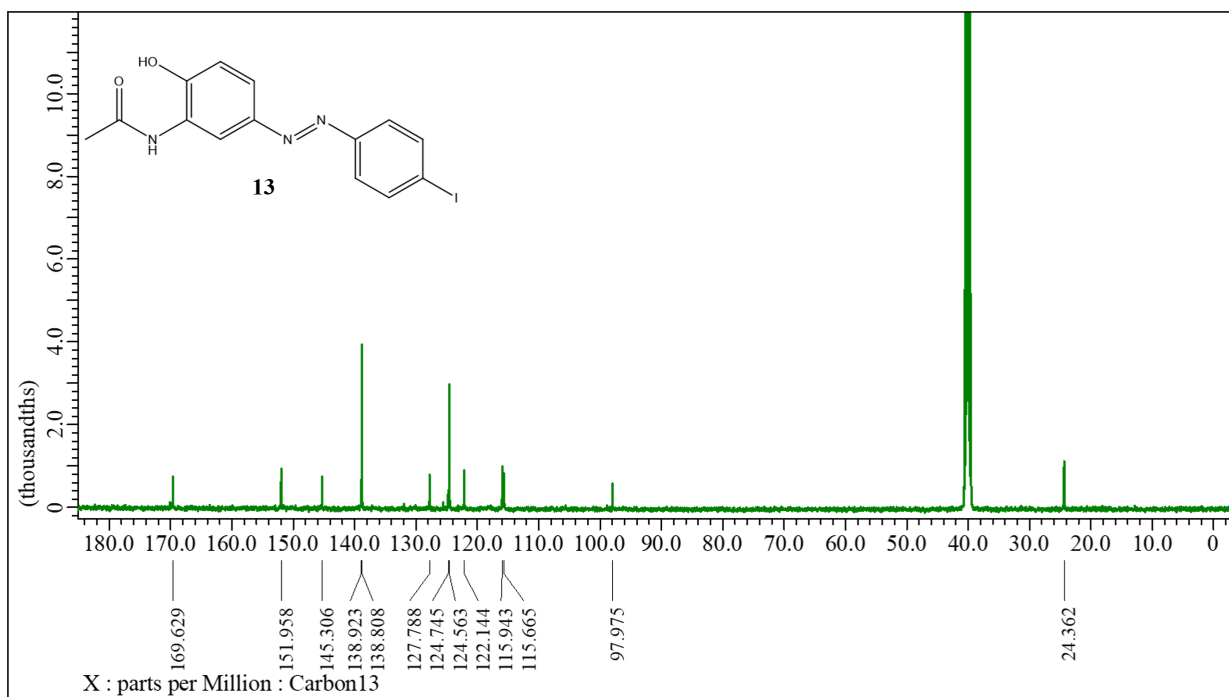
10 (*p*-Br)



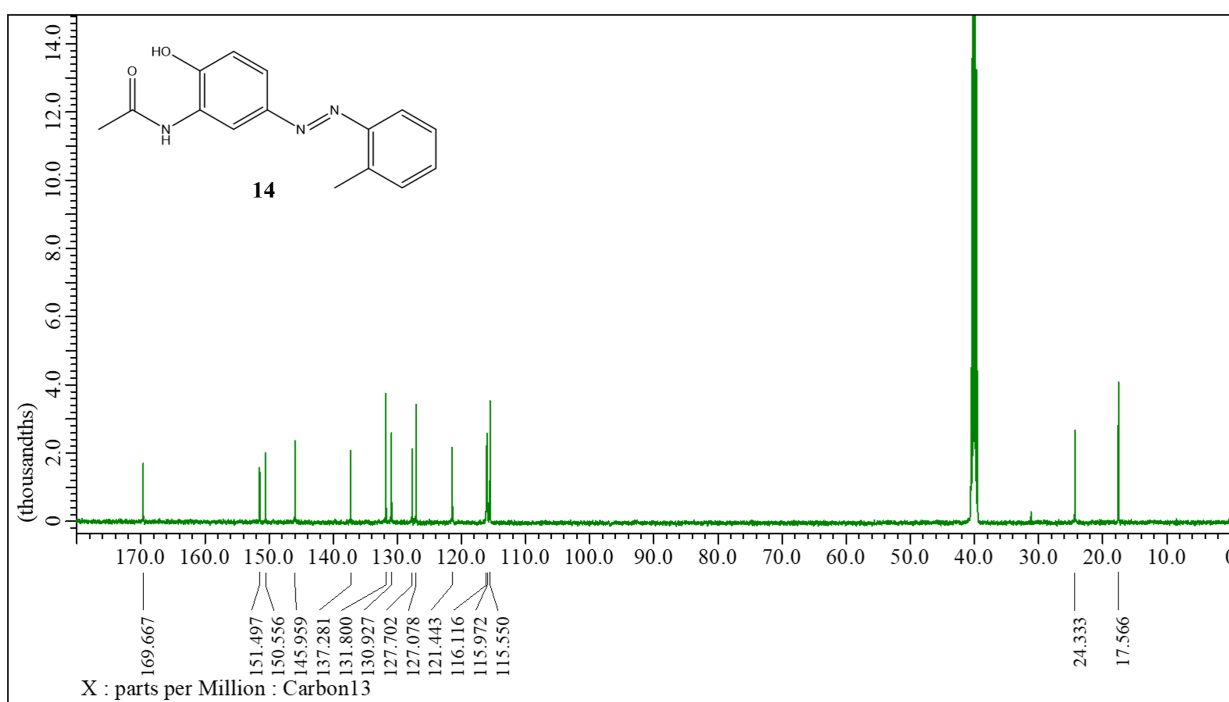
11(*o*-I)



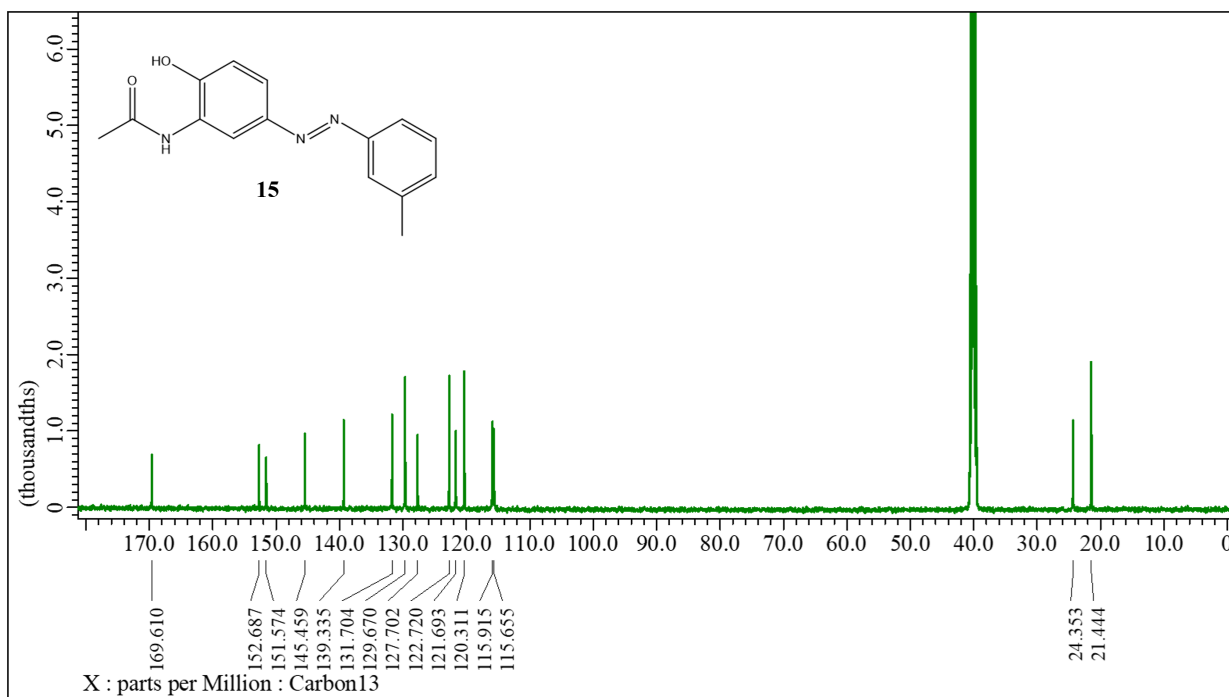
12(*m*-I)



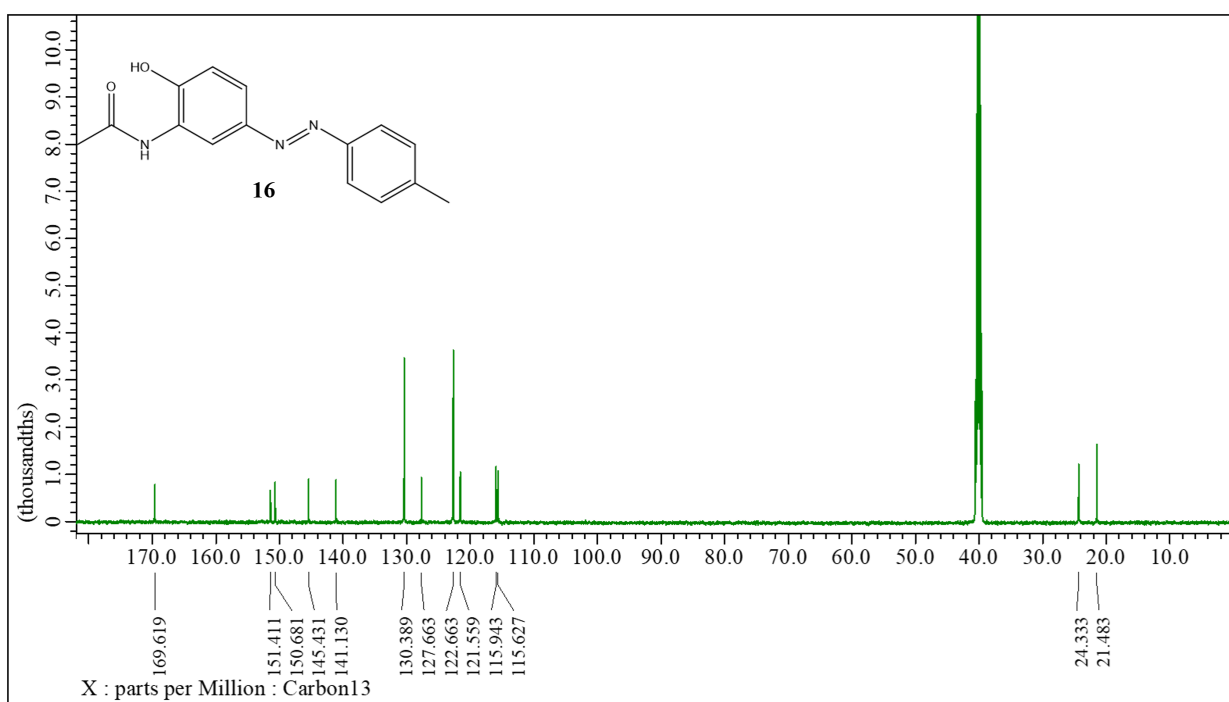
13 (*p*-I)



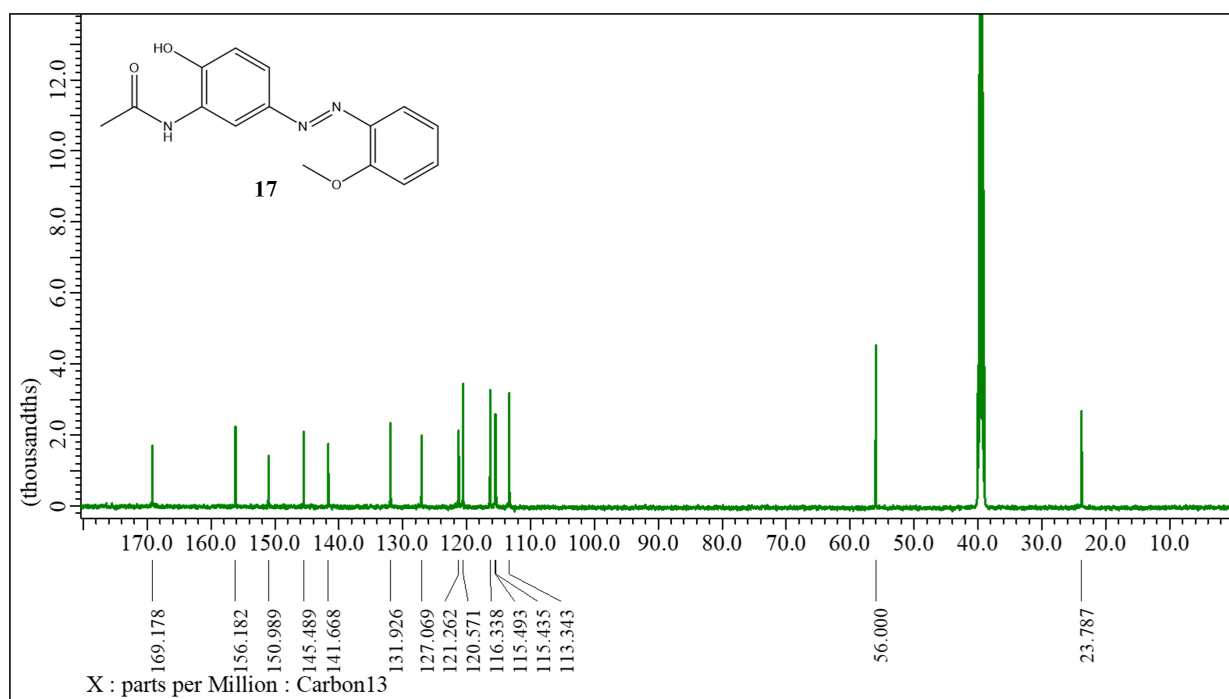
14 (*o*-CH₃)



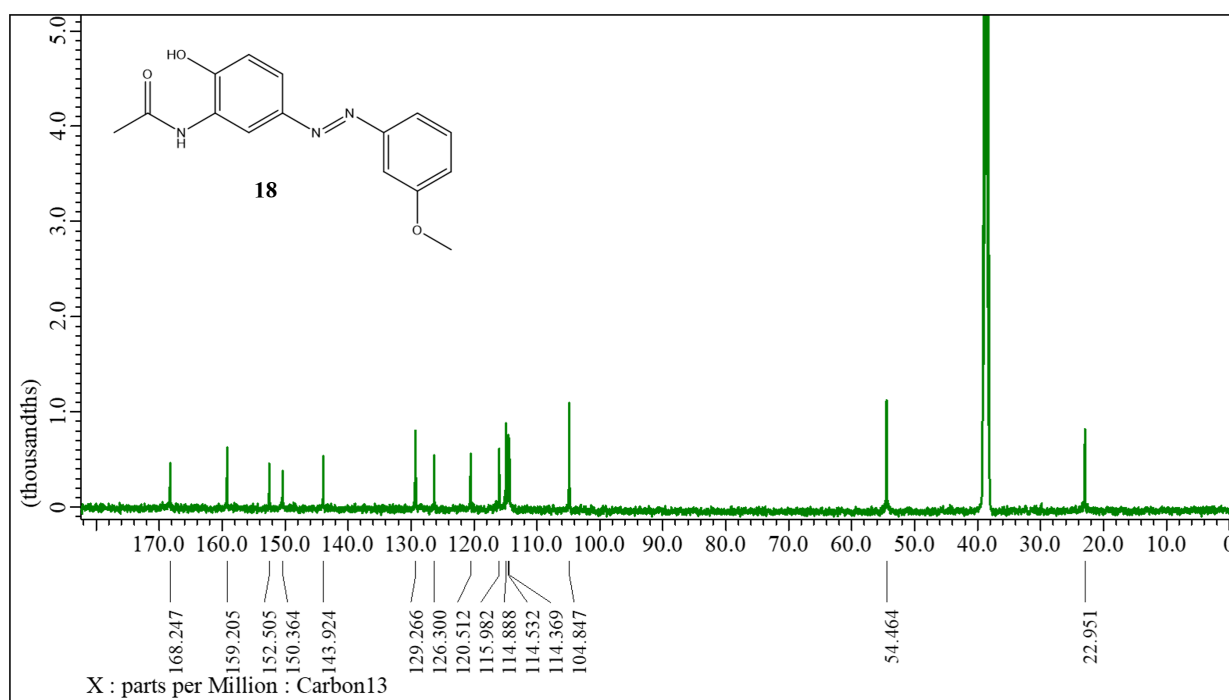
15 (*m*-CH₃)



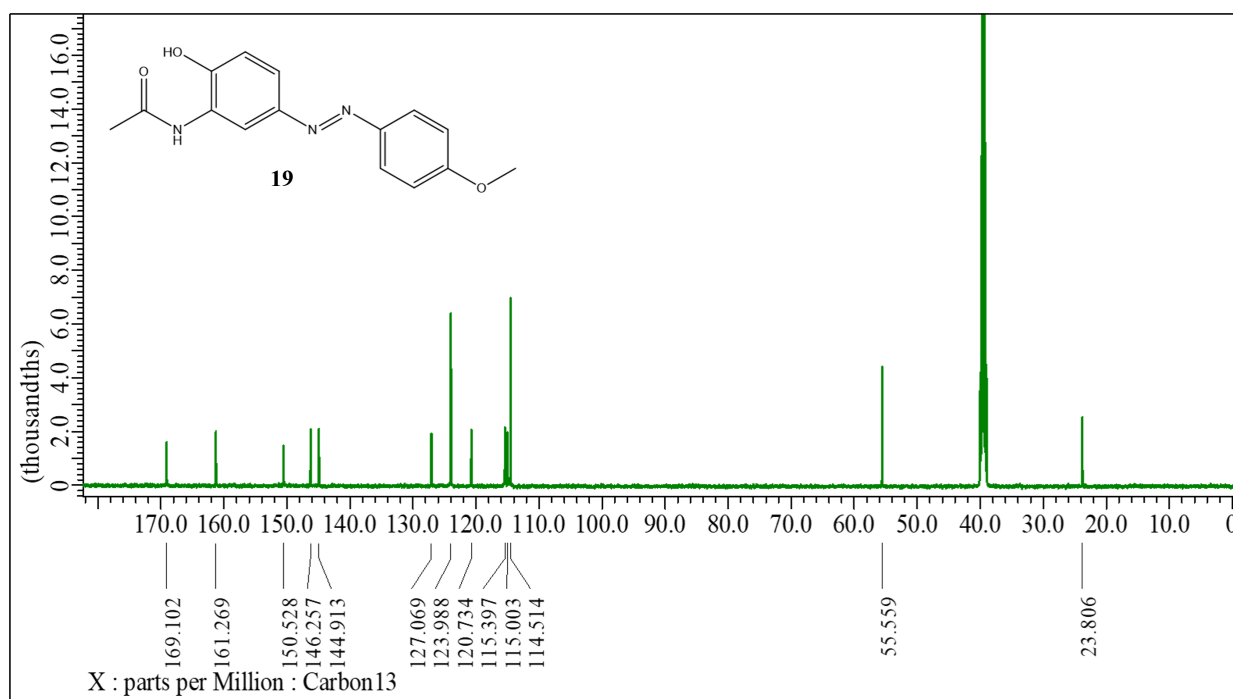
16 (*p*-CH₃)



17 (*o*-OCH₃)



18 (*m*-OCH₃)



19 (*p*-OCH₃)

B1: Druglikeness properties of orthocetamol azo 1-19.**Table 3** Druglikeness (SwissADME) of orthocetamol-azo (**1-19**) derivatives.

Compound	MW g mol ⁻¹	Rotatable bonds	H-bond donors	H-bond acceptors	Log P _{o/w}	TPSA (Å ²)
1 (H)	255.27	4	2	4	2.65	74.05
2 (o-F)	273.26	4	2	5	2.94	74.05
3 (m-F)	273.26	4	2	5	2.95	74.05
4 (p-F)	273.26	4	2	5	2.98	74.05
5 (o-Cl)	289.72	4	2	4	3.15	74.05
6 (m-Cl)	289.72	4	2	4	3.16	74.05
7 (p-Cl)	289.72	4	2	4	3.20	74.05
8 (o-Br)	334.17	4	2	4	3.24	74.05
9 (m-Br)	334.17	4	2	4	3.28	74.05
10 (p-Br)	334.17	4	2	4	3.29	74.05
11 (o-I)	381.17	4	2	4	3.28	74.05
12 (m-I)	381.17	4	2	4	3.32	74.05
13 (p-I)	381.17	4	2	4	3.33	74.05
14 (o-Me)	269.30	4	2	4	2.98	74.05
15 (m-Me)	269.30	4	2	4	2.99	74.05
16 (p-Me)	269.30	4	2	4	2.99	74.05
17 (o-MeO)	285.30	5	2	5	2.64	83.28
18 (m-MeO)	285.30	5	2	5	2.66	83.28
19 (p-MeO)	285.30	4	2	4	2.99	83.28
Dexamethasone	392.46	2	3	6	2.15	94.83
Sulfasalazine	398.39	6	3	8	2.22	149.69

*Note: **MW** = molecular weight; **H-Bond** = hydrogen bond; **log P_{o/w}** = octanal/water partition coefficient; **TPSA** = topology polar surface area.

Table 4 ADMET properties of **1-19** using pkCMS

Compound	Absorption			Distribution	Metabolism					Excretion		Toxicity
	CaCO2 permeability	Intestinal absorption	Skin Permeability	BBB Permeability	CYP1 A2	CYP2 C19	CYP2 C9	CYP2 D6	CYP3 A4	Clearance	Half-life	AMES Mutagenesis
1 (H)	0.806	87.34	-2.652	-0.15	Yes	Yes	Yes	No	No	1.03	High	Toxic
2 (o-F)	0.804	86.58	-2.701	-0.38	Yes	Yes	Yes	No	No	0.76	High	Toxic
3 (m-F)	0.836	87.43	-2.754	-0.40	Yes	Yes	Yes	No	No	1.05	High	Toxic
4 (p-F)	0.804	86.58	-2.701	-0.38	Yes	Yes	Yes	No	No	1.08	High	Toxic
5 (o-Cl)	0.671	88.27	-2.916	-0.44	Yes	Yes	Yes	No	No	0.72	High	Safe
6 (m-Cl)	0.652	87.81	-2.914	-0.44	Yes	Yes	Yes	No	No	0.87	High	Safe
7 (p-Cl)	0.663	87.73	-2.912	-0.45	Yes	Yes	Yes	No	No	0.90	High	Safe
8 (o-Br)	0.662	88.21	-2.912	-0.45	Yes	Yes	Yes	No	No	0.88	High	Safe
9 (m-Br)	0.644	87.75	-2.909	-0.45	Yes	Yes	Yes	No	No	0.90	High	Safe
10 (p-Br)	0.655	87.66	-2.908	-0.45	Yes	Yes	Yes	No	No	0.92	High	Safe
11 (o-I)	0.561	86.78	-2.622	-0.51	Yes	Yes	Yes	No	No	0.75	High	Safe
12 (m-I)	0.542	86.31	-2.641	-0.51	Yes	Yes	Yes	No	No	0.85	High	Safe
13 (p-I)	0.553	86.22	-2.641	-0.51	Yes	Yes	Yes	No	No	0.86	High	Safe
14 (o-Me)	0.72	89.73	-2.933	-0.26	Yes	Yes	Yes	No	No	0.80	High	Safe
15 (m-Me)	0.702	89.27	-2.93	-0.27	Yes	Yes	Yes	No	No	1.09	High	Safe
16 (p-Me)	0.713	89.19	-2.929	-0.27	Yes	Yes	Yes	No	No	1.09	High	Safe
17 (o-MeO)	0.889	90.66	-3.049	-0.45	Yes	Yes	Yes	No	No	1.32	High	Toxic
18 (m-MeO)	0.881	90.11	-3.092	-0.48	Yes	Yes	No	No	No	1.38	High	Toxic
19 (p-MeO)	0.916	90.10	-2.43	-1.59	Yes	Yes	Yes	No	No	1.39	High	Toxic
Dexamethasone	1.068	80.486	-4.123	-0.85	No	No	No	No	No	1.34	Low	Safe
Sulfasalazine	-0.709	64.51	-2.733	-1.76	No	No	Yes	No	No	-0.018	High	Toxic