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An expedient cyclization of polyfunctional (aryl)(pyrimidinyl)(pyranyl)methanes into spiro[furo[3,2-*c*]pyran-2,5'-pyrimidine] scaffold

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1. Experimental section

All melting points were measured with a Stuart SMP 30 melting point apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker AM-300 (300 and 75 MHz, respectively) at ambient temperature in DMSO-d_6 solutions. Chemical shift values are given in δ scale relative to Me_4Si. IR spectra were registered with a Bruker ALPHA-T FT-IR spectrometer in KBr pellets. Mass-spectra (EI = 70 eV) were obtained directly with a Finningan MAT INCOS 50 spectrometer.

Morpholin-4-ium 5-[(aryl)(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)methyl]-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-olates **1a-j** were obtained by earlier reported method [S1]. Melting points and ^{1}H-NMR spectra of earlier reported compounds **1a,d-j** were fully consistent with previously published data [S1].

Morpholin-4-ium 5-[(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)(2-methylphenyl)methyl]-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-olate (1b).

Yield 98%, mp: 125-126 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.06 (s, 3H, CH_3), 2.10 (s, 3H, CH_3), 3.07 (s, 6H, 2 CH_3), 3.12 (m, 4H 2CH_2), 3.76 (m, 4H 2CH_2), 5.81 (s, 1H, CH), 5.89 (s, 1H, CH), 6.87-7.01 (m, 3H, Ar), 7.02-7.11 (m, 1H, Ar), 8.69 (br s, 2H, NH_2^+), 14.59 (s, 1H, OH) ppm. ^{13}C NMR (75 MHz, DMSO-d_6): δ 18.9, 19.4, 27.4 (2C), 33.9, 42.9 (2C), 63.3 (3C), 88.2, 102.6, 103.7, 124.4, 124.6, 128.0, 129.8, 135.7, 142.2, 152.0, 158.4, 163.1, 165.6, 168.5 ppm. MS (*m/z* relative intensity %): 384 $[M\text{-}C_4H_{10}NO]^+$ (1), 269 (17), 258 (30), 243 (65), 213 (29), 186 (18), 156 (45), 115 (36), 29 (100). IR (KBr) ν = 3342, 3014, 2976, 2867, 2502, 2350, 1678, 1584, 1452, 1377, 1106 cm^{-1}. Anal. calcd for $C_{24}H_{29}N_3O_7$: C, 61.14; H, 6.20; N, 8.91 %. Found: C, 61.07; H, 6.15; N, 8.84 %.

Morpholin-4-ium 5-[(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)(3-methylphenyl)methyl]-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-olate (1c).

Yield 98%, mp: 175-176 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.11 (s, 3H, CH_3), 2.19 (s, 3H, CH_3), 2.98-3.21 (m, 10H, $2NCH_{2morph}$+$2CH_3$), 3.76 (m, 4H $2OCH_2$), 5.78 (s, 1H, CH), 6.02 (s, 1H, CH), 6.74-6.87 (m, 3H, Ar), 6.96-7.05 (m, 1H, Ar), 8.72 (br s, 2H, NH_2^+), 15.02 (s, 1H, OH) ppm. ^{13}C NMR (75 MHz, DMSO-d_6): δ 18.9, 19.4, 27.4 (2C), 33.9, 42.9 (2C), 63.3 (3C), 88.2, 102.6, 103.7, 124.4, 124.6, 128.0, 129.8, 135.7, 142.2, 152.0, 158.4, 163.1, 165.6, 168.5 ppm. MS (*m/z* relative intensity %): 384 [M-$C_4H_{10}NO$]$^+$ (23), 299 (2), 257 (40), 243 (37), 228 (55), 213 (100), 156 (64), 115 (64), 87 (39), 57 (68). IR (KBr) ν = 3272, 2983, 2805, 2731, 2470, 1679, 1597, 1456, 1301, 1105 cm^{-1}. Anal. calcd for $C_{24}H_{29}N_3O_7$: C, 61.14; H, 6.20; N, 8.91 %. Found: C, 61.10; H, 6.17; N, 8.85 %.

General procedure of oxidative cyclization of 5-[(aryl)(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)methyl]-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-olates (1a-j)

A mixture of morpholin-4-ium 5-[(aryl)(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)methyl]-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-olate **1a-j** (1 mmol), *N*-bromosuccinimide (0.21 g, 1.2 mmol) and sodium acetate (0.08 g, 1 mmol) was stirred in ethanol (10 ml) at room temperature for one hour. The target compounds were isolated by simple filtration, then dried on the filter for two hours.

1',3',6-Trimethyl-3-phenyl-2'*H*,3*H*,4*H*-spiro[furo[3,2-*c*]pyran-2,5'-pyrimidine]-2',4,4',6'(1'*H*,3'*H*)-tetraone (2a)

Yield 97%, mp: 248-250 °C (Lit. [S2] mp: 249-251 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.38 (s, 3H, CH_3), 2.57 (s, 3H, CH_3), 3.43 (s, 3H, CH_3), 4.88 (s, 1H, CH), 6.28 (s, 1H, CH), 6.99-7.13 (m, 2H, Ar), 7.30-7.40 (m, 3H, Ar) ppm.

3-(2-Methylphenyl)-1',3',6-trimethyl-2'*H*,3*H*,4*H*-spiro[furo[3,2-*c*]pyran-2,5'-pyrimidine]-2',4,4',6'(1'*H*,3'*H*)-tetraone (2b)

Yield 92%, mp: 282-283 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.25 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 2.61 (s, 3H, CH_3), 3.39 (s, 3H, CH_3), 5.25 (s, 1H, CH), 6.28 (s, 1H, CH), 6.95-7.02 (m, 1H, Ar), 7.09-7.25 (m, 3H, Ar) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 18.3, 19.9, 27.7, 28.7, 51.9, 90.5, 94.9, 99.5, 125.8, 128.2, 128.9, 130.2, 131.7, 136.1, 150.3, 158.9, 163.6, 165.9, 167.7, 171.7 ppm. MS (*m/z* relative intensity %): 382 [M$^+$] (16), 339 (50), 325 (9), 283 (4), 243 (12), 225 (2), 213 (3), 169 (6), 156 (9), 115 (34), 43 (100). IR (KBr) ν = 3434, 2997, 2949, 2531, 1738, 1693, 1588, 1452, 1263, 1190 cm^{-1}. Anal. calcd for $C_{20}H_{18}N_2O_6$: C, 62.82; H, 4.75; N, 7.33 %. Found: C, 62.74; H, 4.71; N, 7.28 %.

3-(3-Methylphenyl)-1',3',6-trimethyl-2'*H*,3*H*,4*H*-spiro[furo[3,2-*c*]pyran-2,5'-pyrimidine]-2',4,4',6'(1'*H*,3'*H*)-tetraone (2c)

Yield 94%, mp: 225-226 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.32 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 2.58 (s, 3H, CH_3), 3.44 (s, 3H, CH_3), 4.84 (s, 1H, CH), 6.28 (s, 1H, CH), 6.76-6.90 (m, 2H, Ar), 7.11-7.26 (m, 2H, Ar) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.7, 21.3, 28.4, 29.4, 59.0, 91.3, 95.5, 98.6, 125.5, 128.9, 129.0, 130.2, 132.3, 138.8, 149.9, 159.8, 163.6, 166.2, 167.7, 172.5 ppm. MS (*m/z* relative intensity %): 382 [M^+] (8), 339 (100), 282 (7), 267 (2), 225 (2), 213 (3), 169 (6), 156 (15), 115 (24). IR (KBr) ν = 3448, 3086, 2960, 2769, 2657, 2100, 1977, 1735, 1675, 1588, 1039 cm^{-1}. Anal. calcd for $C_{20}H_{18}N_2O_6$: C, 62.82; H, 4.75; N, 7.33 %. Found: C, 62.76; H, 4.73; N, 7.25 %.

3-(4-Methylphenyl)-1',3',6-trimethyl-2'*H*,3*H*,4*H*-spiro[furo[3,2-*c*]pyran-2,5'-pyrimidine]-2',4,4',6'(1'*H*,3'*H*)-tetraone (2d)

Yield 97%, mp: 290-292 °C (Lit. [S2] mp: 290-291 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.33 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 2.60 (s, 3H, CH_3), 3.43 (s, 3H, CH_3), 4.85 (s, 1H, CH), 6.27 (s, 1H, CH), 6.93 (d, J = 8.2 Hz, 2H, Ar), 7.14 (d, J = 8.2 Hz, 2H, Ar) ppm.

3-(4-Methoxyphenyl)-1',3',6-trimethyl-2'*H*,3*H*,4*H*-spiro[furo[3,2-*c*]pyran-2,5'-pyrimidine]-2',4,4',6'(1'*H*,3'*H*)-tetraone (2e)

Yield 96%, mp: 246-248 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.37 (s, 3H, CH_3), 2.65 (s, 3H, CH_3), 3.43 (s, 3H, CH_3), 3.79 (s, 3H, OCH_3), 4.84 (s, 1H, CH), 6.27 (s, 1H, CH), 6.85 (d, J = 8.5 Hz, 2H, Ar), 6.97 (d, J = 8.5 Hz, 2H, Ar) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.7, 28.5, 29.5, 55.4, 58.5, 91.2, 95.5, 98.8, 114.4 (2C), 124.9, 129.7 (2C), 149.9, 159.9, 160.4, 163.7, 166.3, 167.7, 172.3 ppm. MS (*m/z* relative intensity %): 398 [M^+] (10), 355 (100), 298 (3), 172 (5), 157 (3), 114 (2), 89 (1), 69 (3). IR (KBr) ν = 3435, 2963, 2842, 2533, 1733, 1691, 1584, 1448, 1255, 1173 cm^{-1}. Anal. calcd for $C_{20}H_{18}N_2O_7$: C, 60.30; H, 4.55; N, 7.03 %. Found: C, 60.23; H, 4.52; N, 6.97%.

3-(4-Chlorophenyl)-1',3',6-trimethyl-2'*H*,3*H*,4*H*-spiro[furo[3,2-*c*]pyran-2,5'-pyrimidine]-2',4,4',6'(1'*H*,3'*H*)-tetraone (2f)

Yield 92%, mp: 258-260 °C (Lit. [S2] mp: 258-260 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.38 (s, 3H, CH_3), 2.67 (s, 3H, CH_3), 3.43 (s, 3H, CH_3), 4.85 (s, 1H, CH), 6.28 (s, 1H, CH), 6.99 (d, J = 8.4 Hz, 2H, Ar), 7.32 (d, J = 8.4 Hz, 2H, Ar).

3-(3-Bromophenyl)-1',3',6-trimethyl-2'*H*,3*H*,4*H*-spiro[furo[3,2-*c*]pyran-2,5'-pyrimidine]-2',4,4',6'(1'*H*,3'*H*)-tetraone (2g)

Yield 93%, mp: 228-230 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.39 (s, 3H, CH_3), 2.68 (s, 3H, CH_3), 3.44 (s, 3H, CH_3), 4.82 (s, 1H, CH), 6.29 (s, 1H, CH), 6.99 (d, J = 7.8 Hz, 1H, Ar), 7.07 (s, 1H, Ar), 7.16-7.26 (m, 1H, Ar), 7.50 (d, J = 7.8 Hz, 1H, Ar) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.8, 28.6, 29,6, 58.2, 90.9, 95.5, 98.2, 123.1, 127.2, 130.5, 131.6, 132.7, 134.9, 149.7, 159.6, 163.3, 165.9, 168.2, 172.8 ppm. MS (*m/z* relative intensity %): 448 [M^+] Br^{81} (4), 446 [M^+] Br^{79} (5), 406 (8), 405 (100), 404 (19), 403 (97), 325 (20), 324 (83), 323 (12), 277

(7), 275 (2), 267 (6), 222 (9), 220 (8), 182 (2), 155 (1), 126 (12), 85 (11), 43 (37). IR (KBr) ν = 3435, 3108, 2959, 1724, 1689, 1592, 1447, 1380, 1261, 1034 cm^{-1}. Anal. calcd for $C_{19}H_{15}BrN_2O_6$: C, 51.03; H, 3.38; Br, 17.87; N, 6.26 %. Found: C, 50.95; H, 3.36; Br, 17.82; N, 6.19 %.

1',3',6-Trimethyl-3-(3-nitrophenyl)-2'*H*,3*H*,4*H*-spiro[furo[3,2-*c*]pyran-2,5'-pyrimidine]-2',4,4',6'(1'*H*,3'*H*)-tetraone (2h)

Yield 98%, mp: 257-258 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.39 (s, 3H, CH_3), 2.66 (s, 3H, CH_3), 3.47 (s, 3H, CH_3), 4.97 (s, 1H, CH), 6.33 (s, 1H, CH), 7.42 (d, J = 7.8 Hz, 1H, Ar), 7.56 (t, J = 7.8 Hz, 1H, Ar), 7.94 (s, 1H, Ar), 8.24 (d, J = 7.8 Hz, 1H, Ar) ppm. ^{13}C NMR (75 MHz, DMSO-d_6): δ 20.0, 27.7, 29,1, 54.0, 90.3, 95.1, 97.7, 123.2, 123.6, 129.9, 135.4, 136.5, 147.5, 150.0, 159.2, 163.4, 165.4, 168.5, 172.6 ppm. MS (*m/z* relative intensity %): 413 [M^+] (7), 396 (17), 371 (22), 370 (100), 354 (38), 353 (76), 323 (29), 282 (17), 187 (22), 141 (9), 126 (25), 85 (31), 43 (91). IR (KBr) ν = 3434, 3094, 2961, 2544, 1717, 1688, 1524, 1381, 1264, 1039 cm^{-1}. Anal. calcd for $C_{19}H_{15}N_3O_8$: C, 55.21; H, 3.66; N, 10.17 %. Found: C, 55.15; H, 3.62; N, 10.11 %.

Methyl 4-(1',3',6-trimethyl-2',4,4',6'-tetraoxo-1',3',4',6'-tetrahydro-2'*H*,3*H*,4*H*-spiro[furo[3,2-*c*]pyran-2,5'-pyrimidin]-3-yl)benzoate (2i)

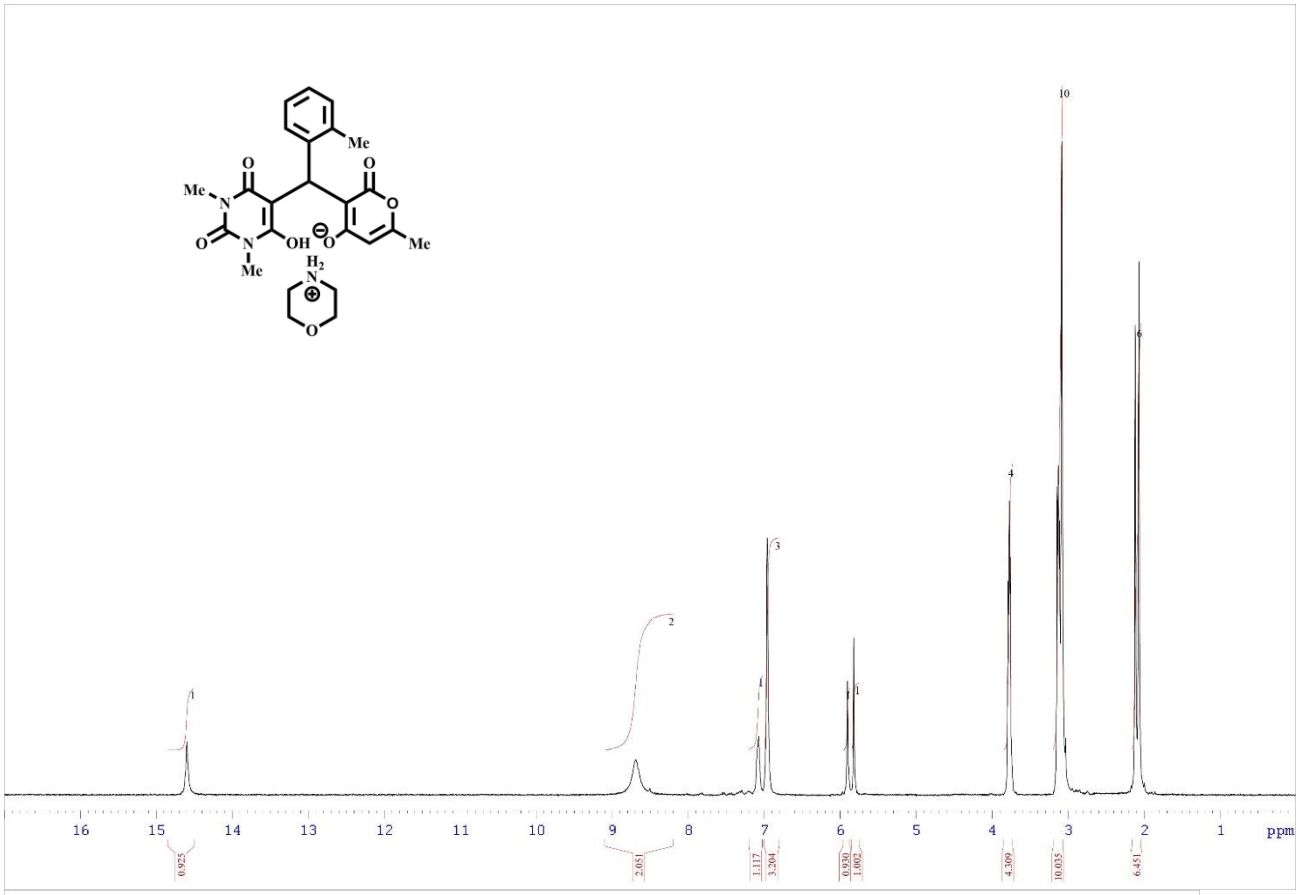
Yield 97%, mp: 274-276 °C (Lit. [S2] mp: 275-276 °C).. ^{1}H NMR (300 MHz, $CDCl_3$): 2.39 (s, 3H, CH_3), 2.39 (s, 3H, CH_3), 2.60 (s, 3H, CH_3), 3.45 (s, 3H, CH_3), 3.93 (s, 3H, CO_2Me), 4.92 (s, 1H, CH), 6.30 (s, 1H, CH), 7.14 (d, J = 8.4 Hz, 2H, Ar), 8.01 (d, J = 8.4 Hz, 2H, Ar).

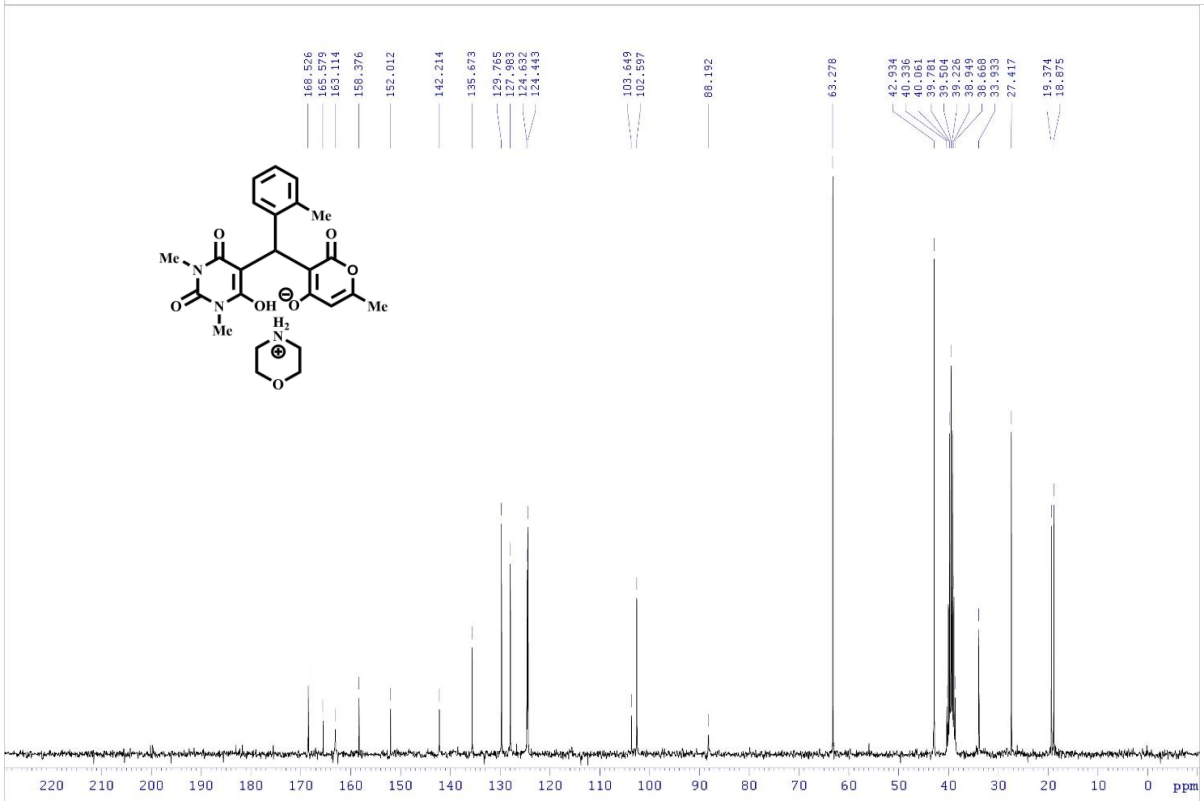
1',3',6-Trimethyl-3-(4-trifluoromethylphenyl)-2'*H*,3*H*,4*H*-spiro[furo[3,2-*c*]pyran-2,5'-pyrimidine]-2',4,4',6'(1'*H*,3'*H*)-tetraone (2j)

Yield 93%, mp: 282-284 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.40 (s, 3H, CH_3), 2.60 (s, 3H, CH_3), 3.45 (s, 3H, CH_3), 4.93 (s, 1H, CH), 6.30 (s, 1H, CH), 7.20 (d, J = 8.2 Hz, 2H, Ar), 7.62 (d, J = 8.2 Hz, 2H, Ar) ppm. ^{13}C NMR (75 MHz, DMSO-d_6): δ 19.9, 27.5, 29.0, 54.6, 90.5, 95.0, 97.8, 124.0 (q, J = 268.3 Hz), 125.0 (q, J = 3.6 Hz, 2C), 129.1 (q, J = 32.7 Hz, 2C), 129.6, 138.8, 150.0, 159.1, 163.3, 165.6, 168.2, 172.4 ppm. MS (*m/z* relative intensity %): 436 [M^+] (3), 394 (20), 393 (100), 336 (3), 280 (1), 267 (3), 210 (9), 175 (3), 85 (7). IR (KBr) ν = 3451, 2968, 2733,1733, 1696, 1591, 1444, 1333, 1165, 1114, 1109 cm^{-1}. Anal. calcd for $C_{20}H_{15}F_3N_2O_6$: C, 55.05; H, 3.46; F, 13.06; N, 6.42 %. Found: C, 54.98; H, 3.44; F, 13.01; N, 6.37 %.

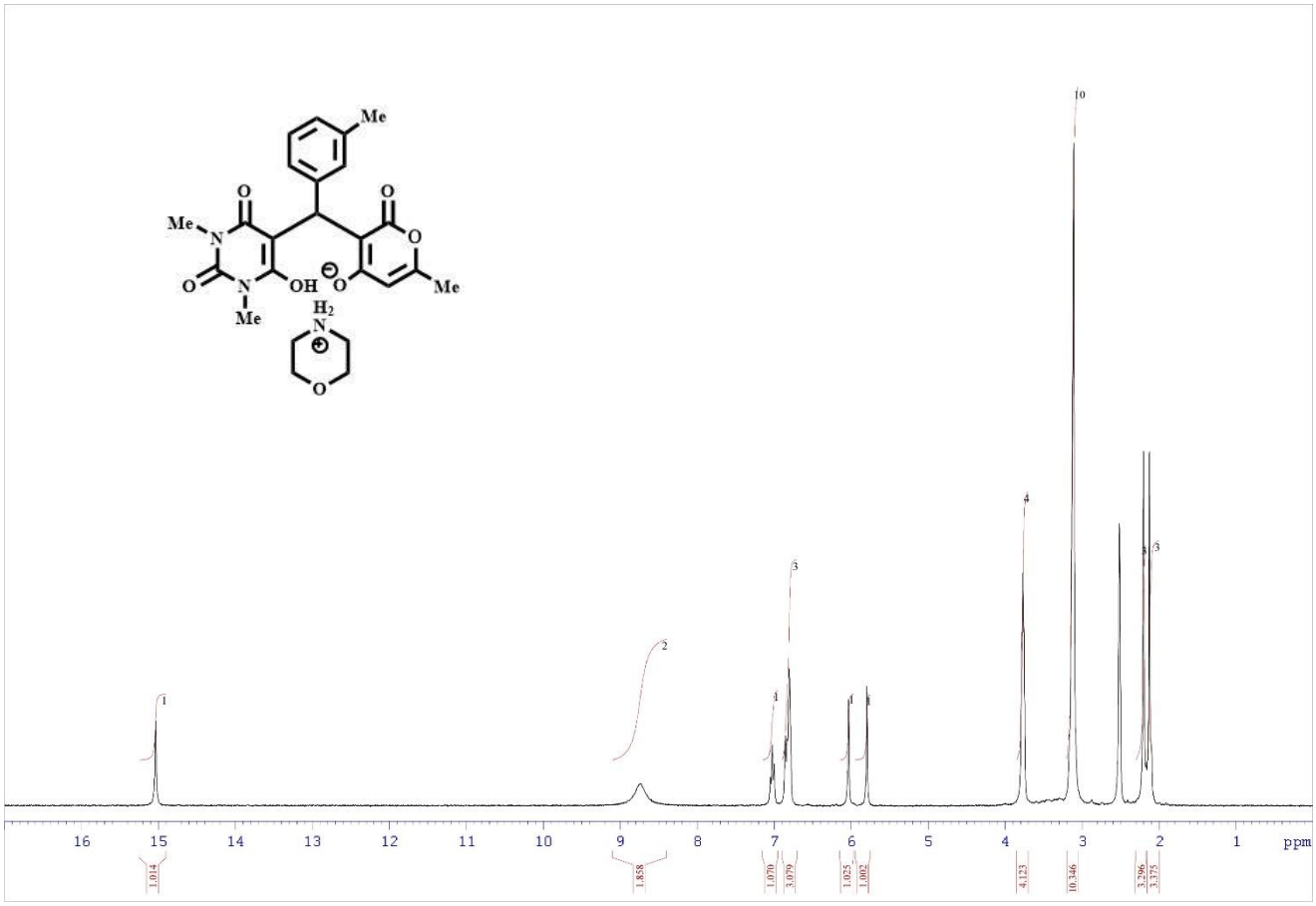
2. ^{1}H and ^{13}C NMR spectra for new compounds 1b,c,h and 2b,c,e,g,h,j

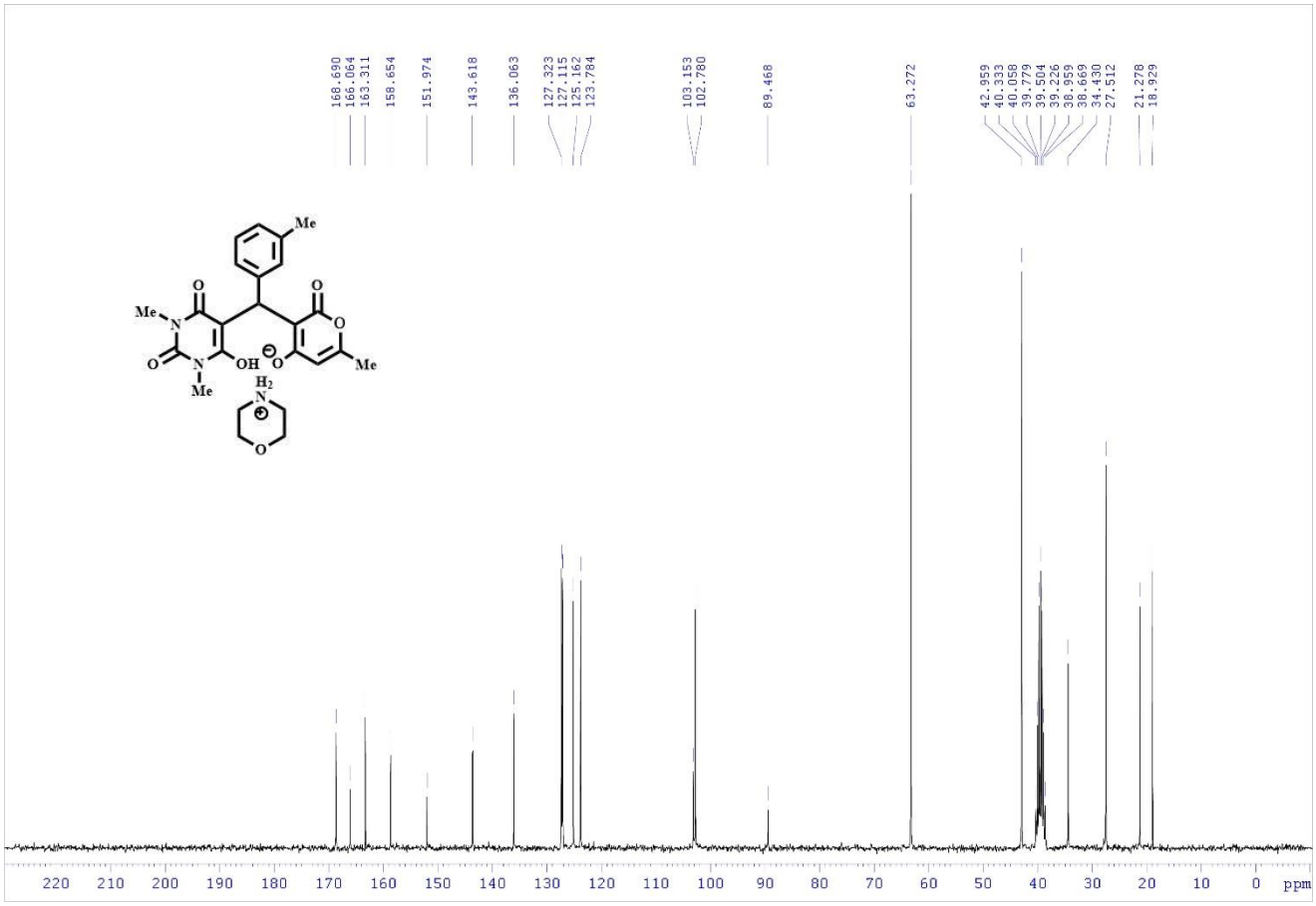
Morpholin-4-ium 5-[(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)(2-methylphenyl)methyl]-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-olate (1b).



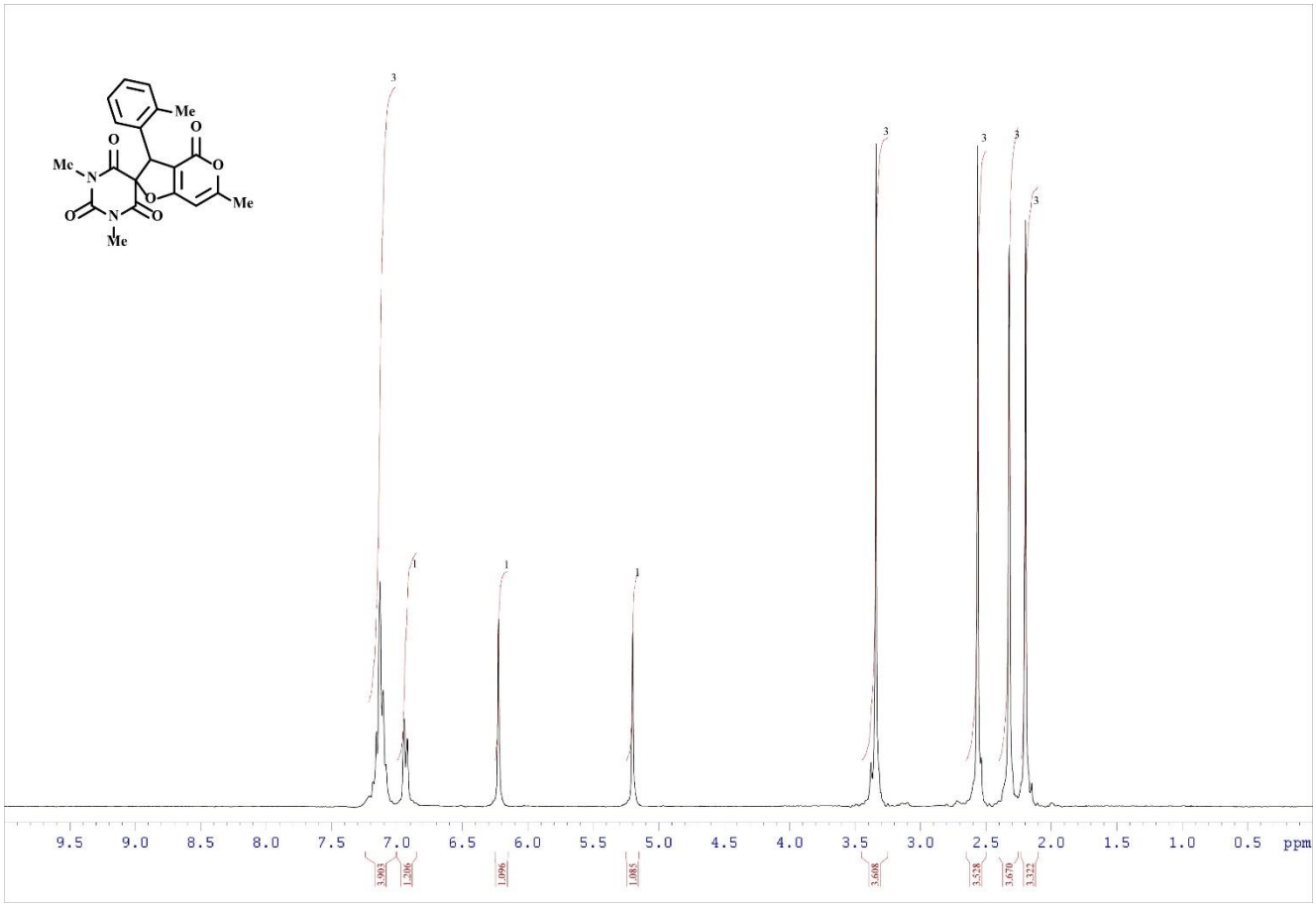


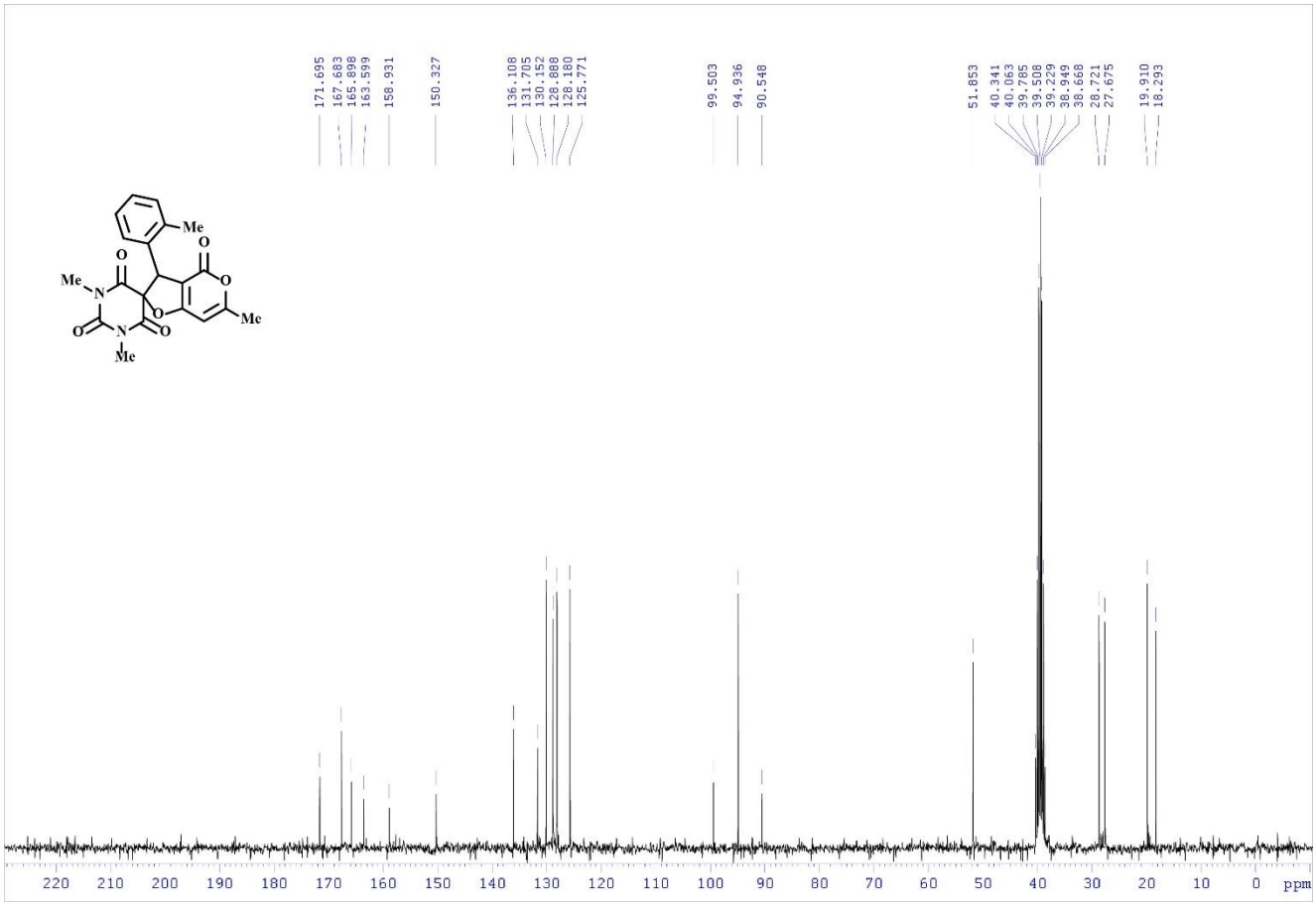
Morpholin-4-ium 5-[(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)(3-methylphenyl)methyl]-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-olate (1c).



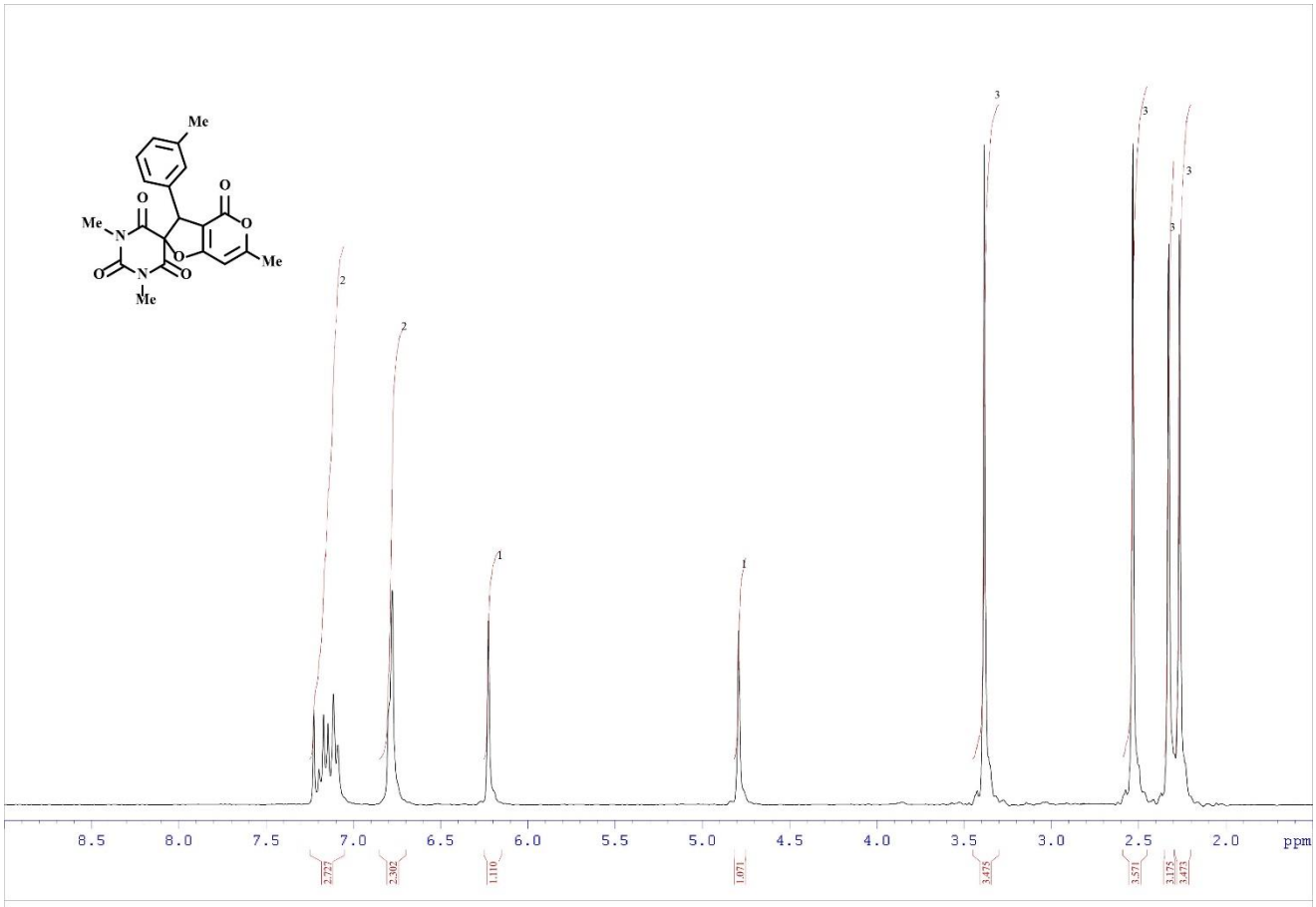


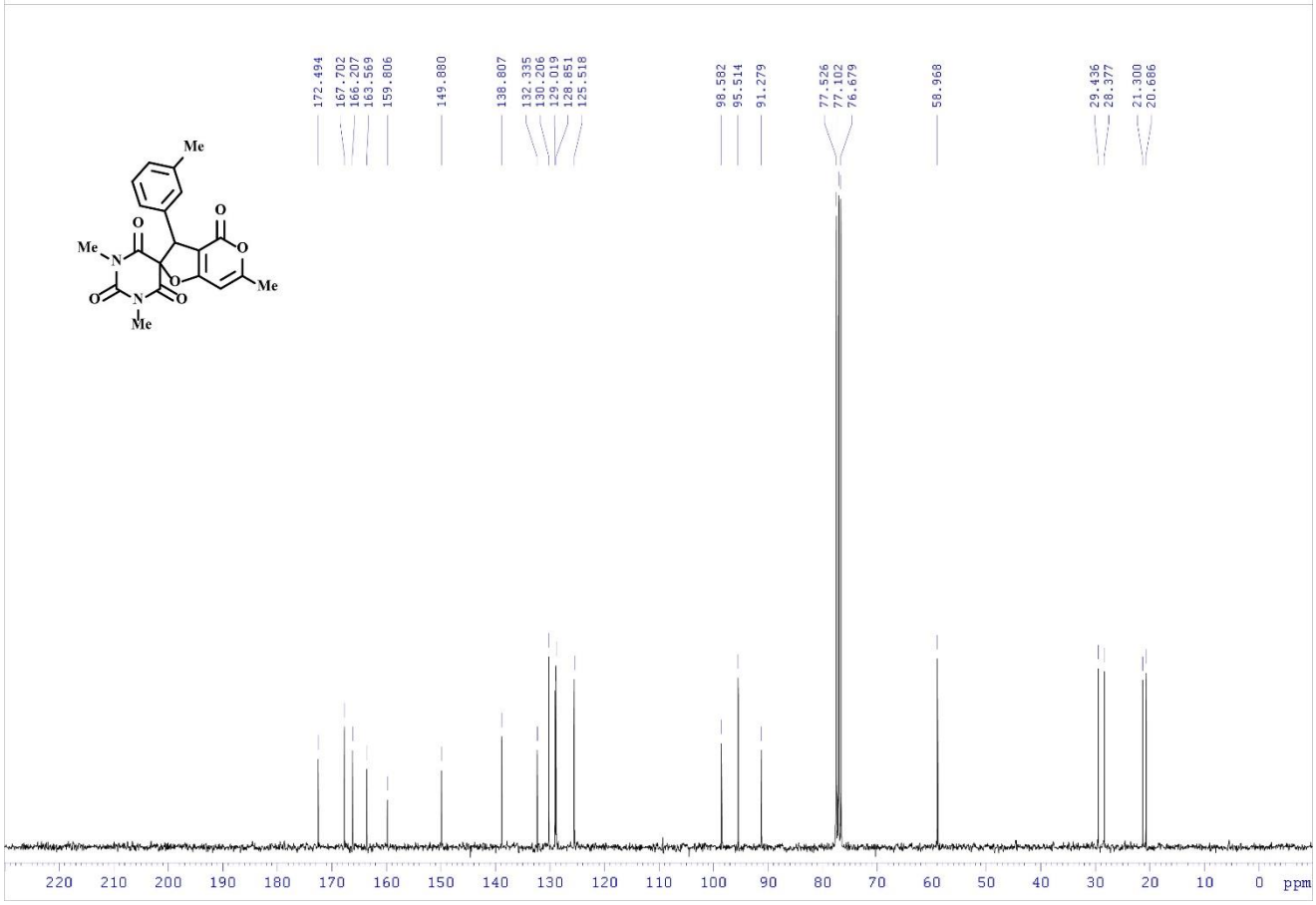
3-(2-Methylphenyl)-1',3',6-trimethyl-2'*H*,3*H*,4*H*-spiro[furo[3,2-*c*]pyran-2,5'-pyrimidine]-2',4,4',6'(1'*H*,3'*H*)-tetraone (2b).



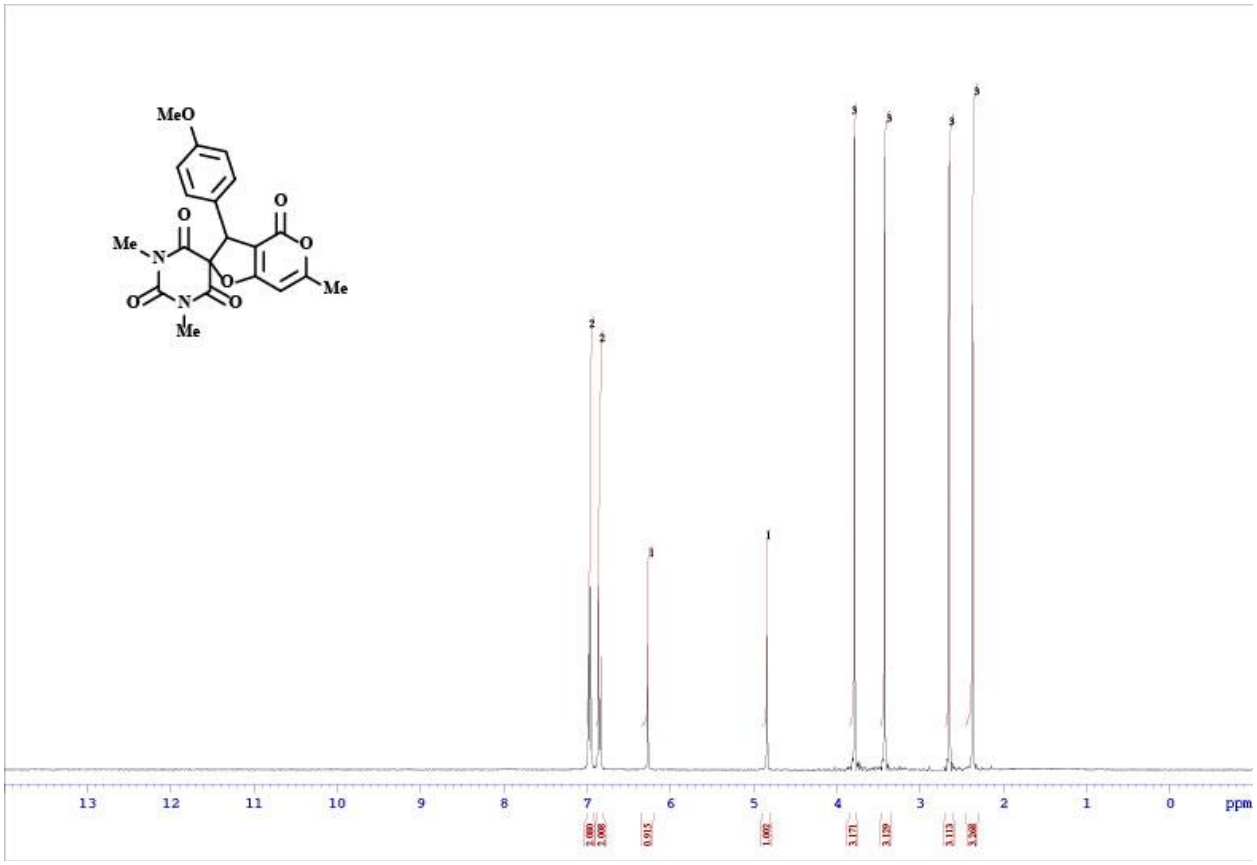


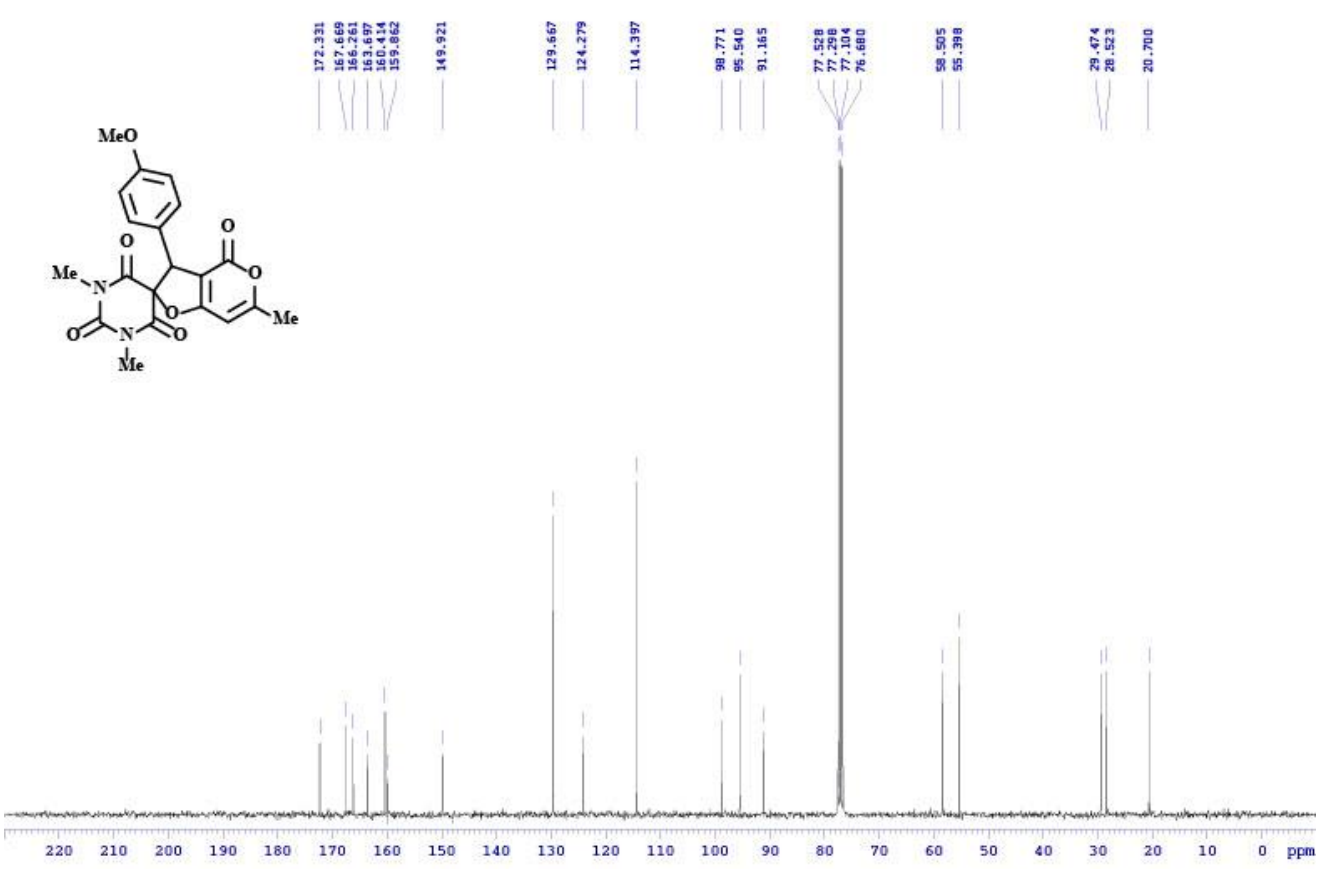
3-(3-Methylphenyl)-1',3',6-trimethyl-2'*H*,3*H*,4*H*-spiro[furo[3,2-*c*]pyran-2,5'-pyrimidine]-2',4,4',6'(1'*H*,3'*H*)-tetraone (2c).



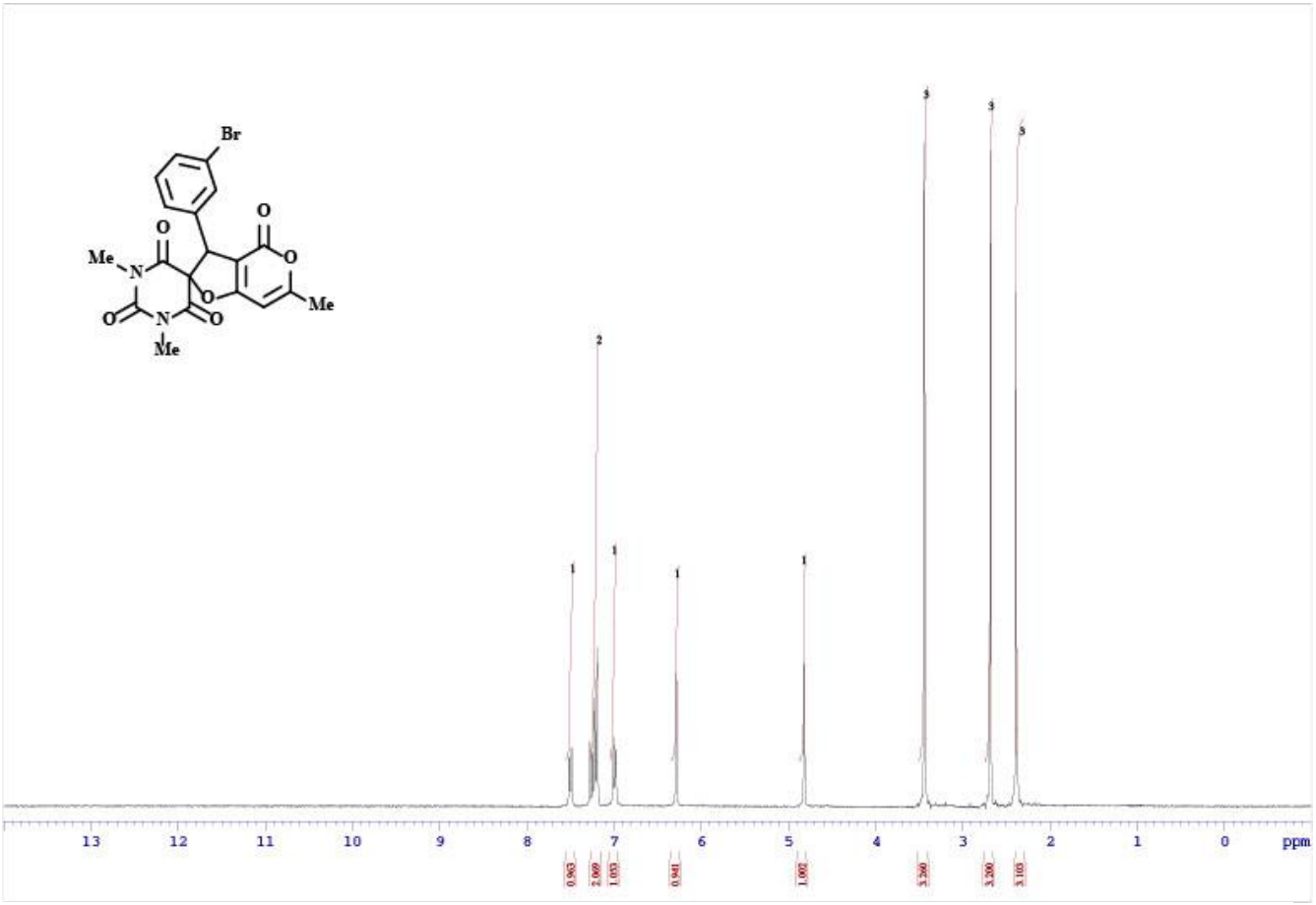


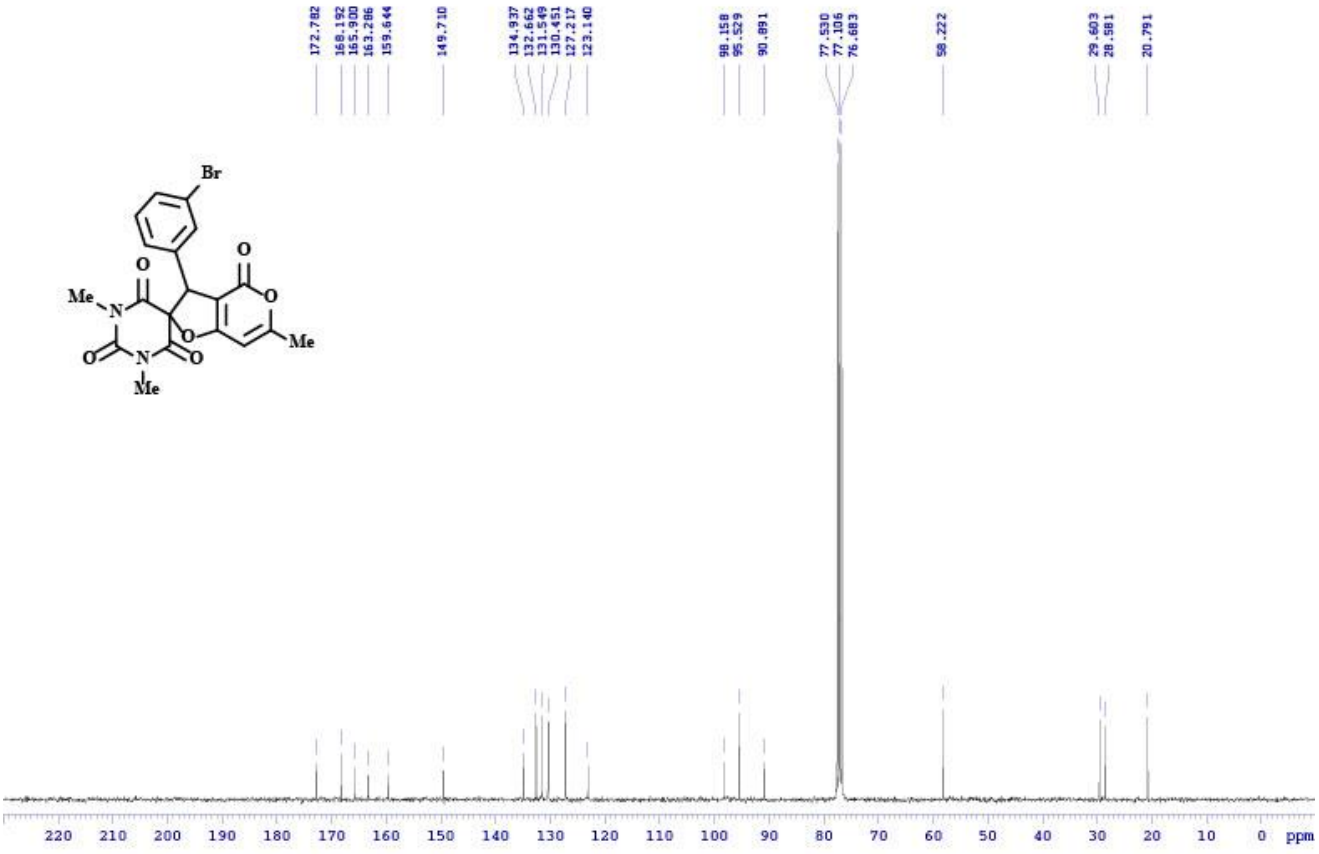
3-(4-Methoxyphenyl)-1',3',6-trimethyl-2'*H*,3*H*,4*H*-spiro[furo[3,2-*c*]pyran-2,5'-pyrimidine]-2',4,4',6'(1'*H*,3'*H*)-tetraone (2e).



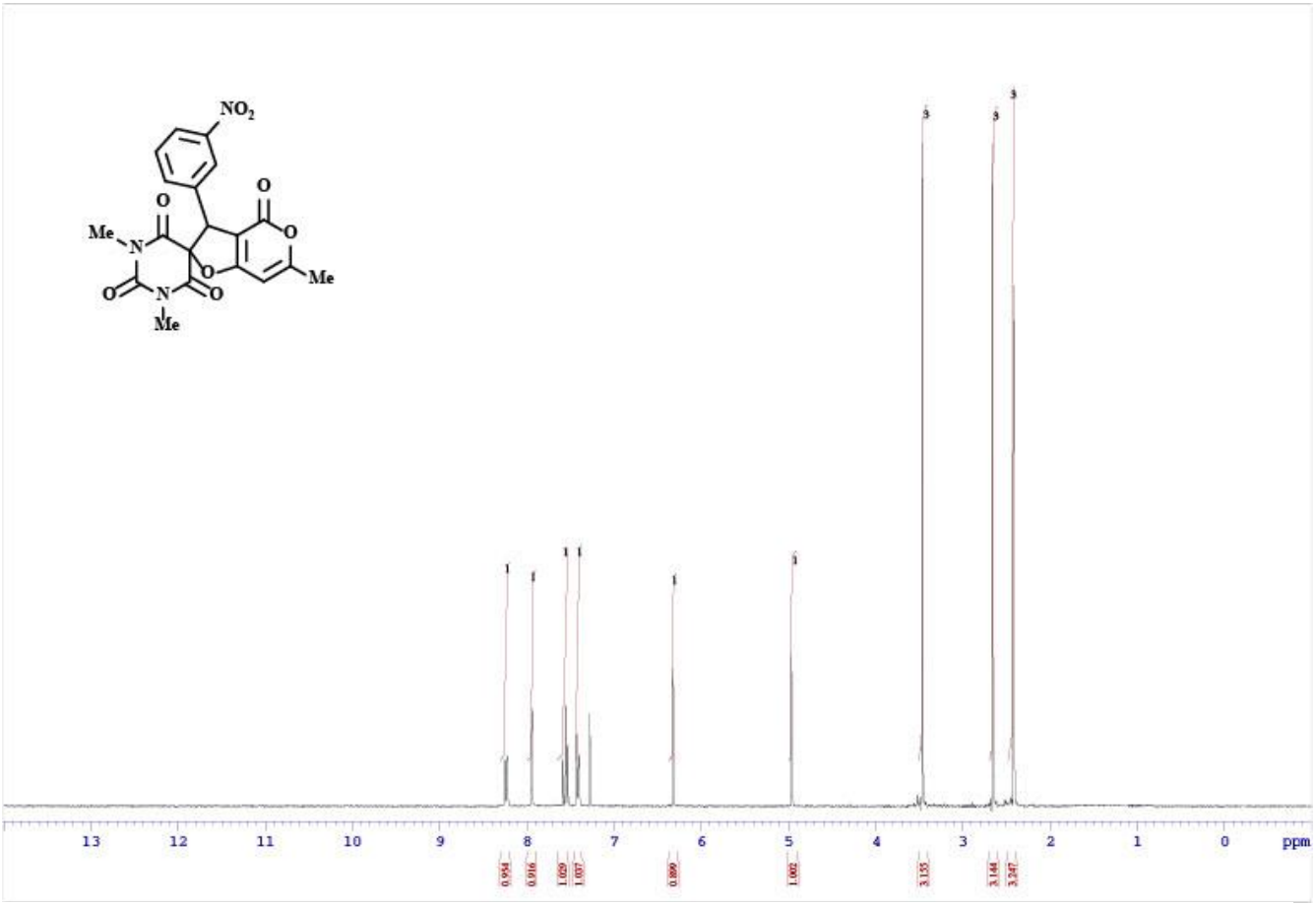


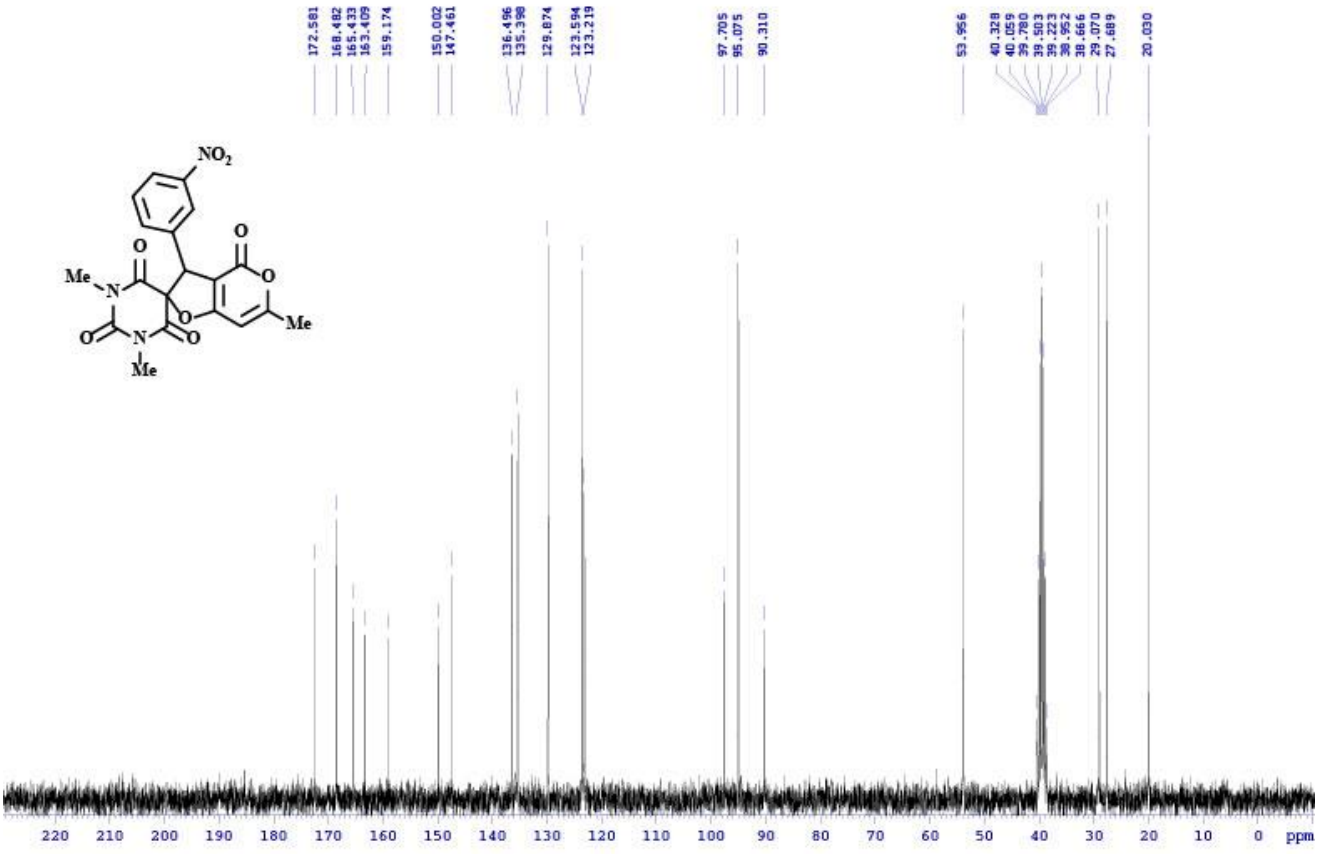
3-(3-Bromophenyl)-1',3',6-trimethyl-2'*H*,3*H*,4*H*-spiro[furo[3,2-*c*]pyran-2,5'-pyrimidine]-2',4,4',6'(1'*H*,3'*H*)-tetraone (2g).



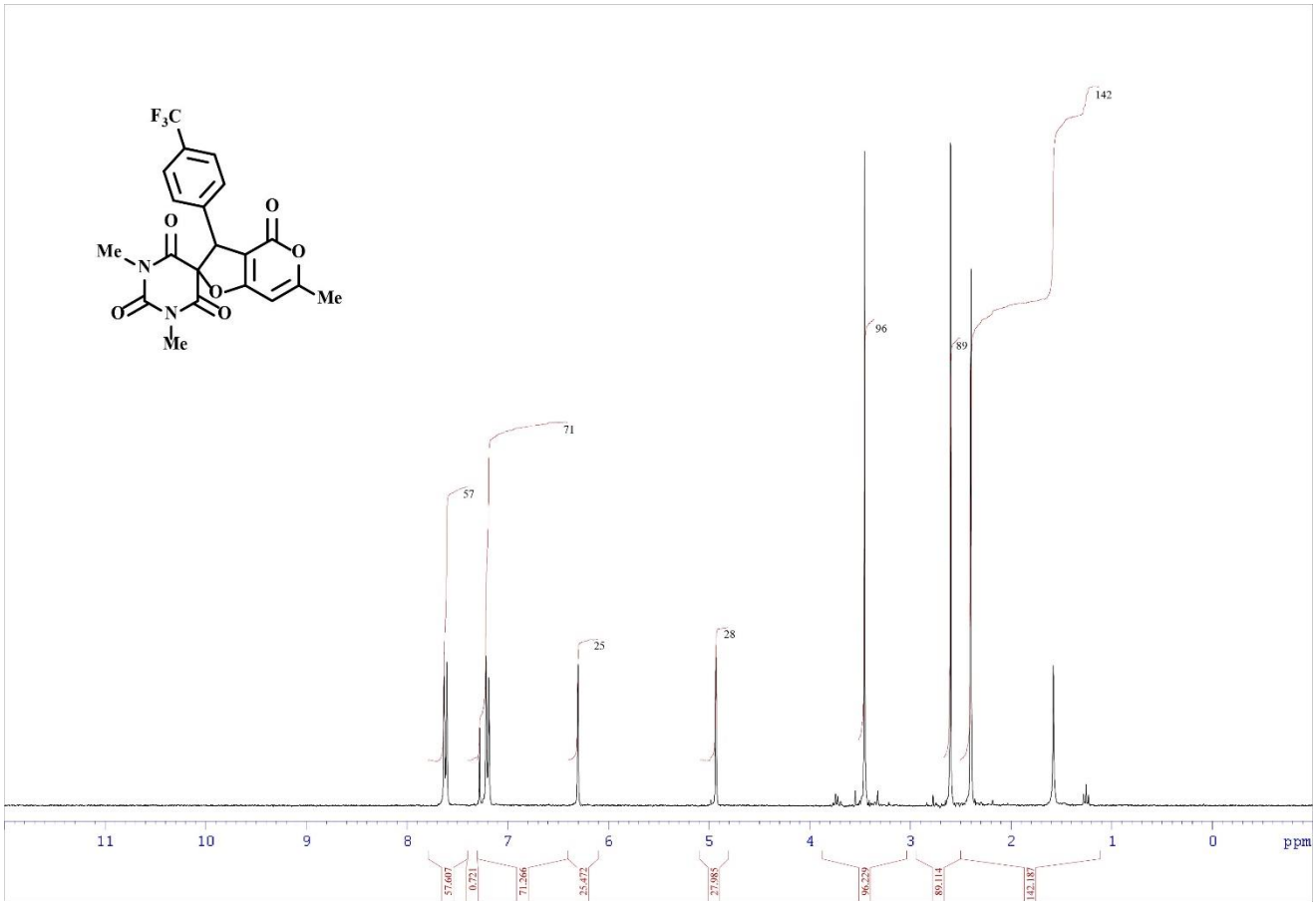


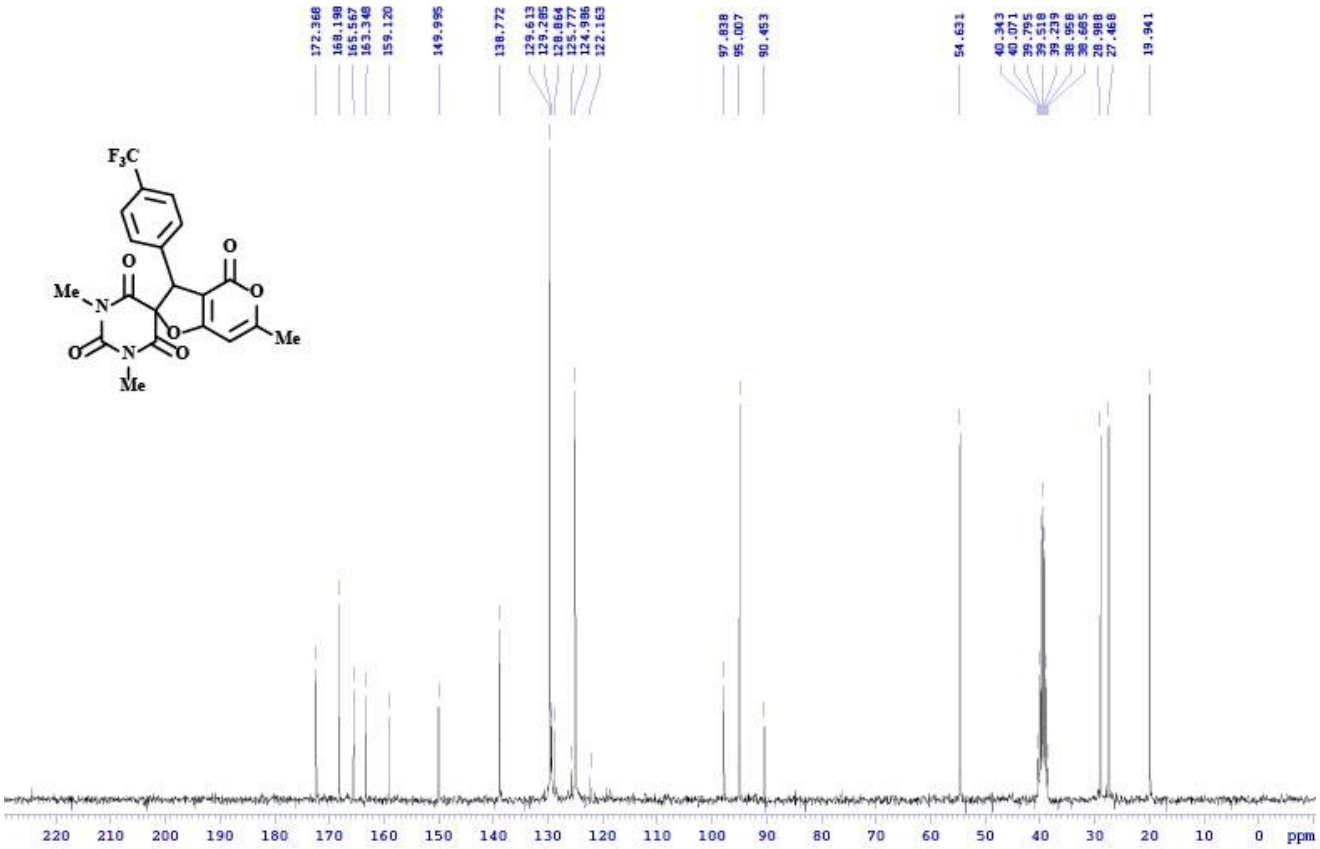
1',3',6-Trimethyl-3-(3-nitrophenyl)-2'*H*,3*H*,4*H*-spiro[furo[3,2-*c*]pyran-2,5'-pyrimidine]-2',4,4',6'(1'*H*,3'*H*)-tetraone (2h).





1',3',6-Trimethyl-3-(4-trifluoromethylphenyl)-2'*H*,3*H*,4*H*-spiro[furo[3,2-*c*]pyran-2,5'-pyrimidine]-2',4,4',6'(1'*H*,3'*H*)-tetraone (2j).





References

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