SUPPLEMENTARY MATERIAL TO

# Synthesis and biological evaluation of (3-aryl-1,2-oxazol-5-yl)methyl 6-fluoro-4-oxo-4H-chromene-2-carboxylates as antioxidant and antimicrobial agents

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## ANALYTICAL AND SPECTRAL DATA OF THE SYNTHESIZED COMPOUNDS

### *Spectral data*

*ethyl 6-fluoro-4-oxo-4H-chromene-2-carboxylate* (**2**): Yellow solid; M.P: 208-210 $^{o}$C: ESI-MS (m/z): 237.0 (M+H).

*6-fluoro-4-oxo-4H-chromene-2-carboxylic acid* (**3**): Yellow solid; M.P: 255-257 $^{o}$C. ESI-MS (m/z): 209.0 (M+H).

*prop-2-yn-1-yl 6-fluoro-4-oxo- 4H-chromene-2-carboxylate* (**4**): Off white solid; M.P: 112-114 $^{o}$C; IR (KBr, $cm^{-1}$): $\nu_{max}$ 3051 (C-H, Ar), 2121 (alkyne), 1741(C=O, ester), 1654 (C=O, chromene), 1220, 1128 (C-O-C); $^{1}$H-NMR (400 MHz, $CDCl_3$): δ 7.83 (d, 1H, *J* = 4Hz, Ar-H), 7.64 (dd, 1H, *J* = 4Hz, 4Hz, Ar-H), 7.46-7.51 (m, 1H, Ar-H), 7.15 (s, 1H, chromene-CH), 5.00 (s, 2H, O-$CH_2$), 2.61 (s, 1H, alkyne); ESI-MS (*m/z*): 247.0 (M+H).

*[3-(4-methoxyphenyl)-1,2-oxazol-5-yl]methyl6-fluoro-4-oxo-4H-chromene-2-carboxylate* (**$C_1$**): Light brown solid; M.P: 142-144 $^{o}$C; IR (KBr, $cm^{-1}$): $\nu_{max}$ 3061 (C-H, Ar), 1740 (C=O, ester), 1657 (C=O, chromene), 1608 (C=N), 1220, 1130 (C-O-C); $^{1}$H-NMR (400 MHz, $CDCl_3$): δ 7.80-7.86 (m, 1H, Ar-H ), 7.61-7.65 (m, 1H, Ar-H), 7.46-7.50 (m, 1H, Ar-H ), 7.37 ( d, 2H, J = 8Hz,

Ar-H ), 7.15 (s, 1H, chromene-CH), 7.12 (d, 2H, J = 8Hz, Ar-H ), 6.82 (s, 1H, Isoxazole-CH), 5.62 (s, 2H, O-$CH_2$), 3.82 (s, 3H, O-$CH_3$); $^{13}$C-NMR (100 MHz, $CDCl_3$): δ 178.6, 168.7, 162.3, 162.1, 161.5, 160.6, 159.8, 153.0, 128.5, 124.6, 122.1, 121.4, 120.6, 118.6, 114.7, 109.8, 100.1, 61.9, 58.8, Anal. calcd. for $C_{21}H_{14}FNO_6$: C, 63.80; H, 3.57; N, 3.54. Found: C, 63.88; H, 3.50; N, 3.57; ESI-MS (m/z): 396.0 (M+H).

*[3-(pyridin-3-yl)-1, 2-oxazol-5-yl]methyl 6-fluoro-4-oxo-4H-chromene-2-carboxylate* (**$C_2$**): White solid. M.P: 152-154 ºC; IR (KBr, $cm^{-1}$): $\nu_{max}$ 3062 (C-H, Ar), 1735 (C=O, ester), 1656 (C=O, chromene), 1609 (C=N), 1231, 1128 (C-O-C); $^1$H-NMR (400 MHz, $CDCl_3$): δ 9.06 (s, 1H, Ar-H), 8.03- 8.10 (m, 1H), 7.82-7.86 (m, 1H), 7.69-7.74 (m, 2H), 7.61-7.66 (m, 1H), 7.45-7.48 (m, 1H), 7.17 (s, 1H, chromene-CH), 6.83 (s, 1H, Isoxazole-CH), 5.58 (s, 2H, O-$CH_2$); $^{13}$C-NMR (100 MHz, $CDCl_3$): δ 178.6, 163.5, 162.3, 162.1, 161.6, 159.2, 153.0, 148.1, 147.8, 134.5, 133.5, 124.7, 124.5 , 122.1, 121.6, 119.1, 110.2, 100.1, 58.9; Anal. calcd for $C_{19}H_{11}FN_2O_5$: C, 62.30; H, 3.03; N, 7.65. Found: C, 62.28; H, 3.00; N, 7.64; ESI-MS (*m/z*): 367.0 (M+H).

(3-(2-(trifluoromethyl)phenyl)isoxazol-5-yl)methyl 6-fluoro-4-oxo-4H-chromene-2-carboxylate (**$C_3$**): Off white solid. M.P: 148-150 ºC; IR (KBr, $cm^{-1}$): $\nu_{max}$ 3058 (C-H, Ar), 1739 (C=O, ester), 1655 (C=O, chromene), 1609 (C=N), 1232, 1129 (C-O-C); $^1$H-NMR (400 MHz, $CDCl_3$): δ 7.80-7.90 (m, 2H), 7.46-7.66 (m, 5H), 7.12 (s, 1H, chromene-CH), 6.82 (s, 1H, Isoxazole-CH), 5.62 (s, 2H, O-$CH_2$); $^{13}$C-NMR (100 MHz, $CDCl_3$): δ 178.6, 168.8, 162.4, 162.1, 161.5, 159.8, 153.0, 133.1, 130.6, 129.2, 128.9, 127.3, 127.3, 126.4, 125.5, 124.6, 122.1, 121.4, 118.9, 110.2, 100.1,

58.8; Anal. calcd. for $C_{21}H_{11}F_4NO_5$: C, 58.21; H, 2.56; N, 3.23. Found: C, 58.11; H, 2.52; N, 3.22; ESI-MS (m/z): 434.0 (M+H).

*[3-(4-nitrophenyl)-1,2-oxazol-5-yl]methyl 6-fluoro-4-oxo-4H-chromene-2-carboxylate* (**$C_4$**): Pale Yellow solid. M.P: 198-200 $^oC$; IR (KBr, $cm^{-1}$): $\nu_{max}$ 3076 (C-H, Ar), 1736 (C=O, ester), 1653 (C=O, chromene), 1609 (C=N), 1234, 1135 (C-O-C); $^1$H-NMR (400 MHz, $CDCl_3$): δ 8.45 (d, 2H, J = 8.4 Hz, Ar-H ), 8.02 (d, 2H, J = 8.4 Hz, Ar-H ), δ 7.81-7.84 (m, 1H, Ar-H), 7.60-7.63 (m, 1H, Ar-H), 7.45-7.50 (m, 1H, Ar-H), 7.14 (s, 1H, chromene-CH), 6.81 (s, 1H, Isoxazole-CH), 5.65 (s, 2H, O-$CH_2$); $^{13}$C-NMR (100 MHz, $CDCl_3$): δ 178.6, 170.1, , 162.5, 161.5, 160.8, 159.8, 153.0, 148.2, 134.9, 126.8, 124.7, 124.6, 122.1, 121.4, 118.6, 109.8, 100.1, 58.8; Anal. calcd. for $C_{20}H_{11}FN_2O_7$: C, 58.54; H, 2.70; N, 6.83. Found: C, 58.46; H, 2.75; N, 6.75; ESI-MS (*m/z*): 411.0 (M+H).

*(3-(4-butylphenyl)isoxazol-5-yl)methyl 6-fluoro-4-oxo-4H-chromene-2-carboxylate* (**$C_5$**): Off white solid. M.P: 188-190 $^oC$; IR (KBr, $cm^{-1}$): $\nu_{max}$ 3068 (C-H, Ar), 1737 (C=O, ester), 1655 (C=O, chromene), 1608 (C=N), 1230, 1129 (C-O-C); $^1$H-NMR (400 MHz, $CDCl_3$): δ 7.80-7.86 (m, 1H, Ar-H), 7.60-7.66 (m, 3H, Ar-H), 7.44-7.49 (m, 1H, Ar-H), 7.35 (d, 2H, *J* = 8.0 Hz, Ar-H), 7.13 (s, 1H, chromene-CH), 6.82 (s, 1H, Isoxazole-CH), 5.62 (s, 2H, O-$CH_2$), 2.68 (t, 2H, *J* = 8.0 Hz, Ar-$CH_2$), 1.60-1.67 (m, 2H, -$CH_2$), 1.33-1.42 (m, 2H, -$CH_2$ ), 0.94 (t, 3H, *J* = 8.0 Hz, -$CH_3$); $^{13}$C-NMR (100 MHz, $CDCl_3$): δ 178.5, 168.1 162.0, 162.3, 161.4, 160.0, 153.2, 142.8, 130.5, 125.8, 125.6, 124.5, 122.1, 121.5, 118.7, 110.1, 100.1,, 58.8, 36.1, 34.0, 22.4, 14.2 :Anal. calcd. for $C_{24}H_{20}FNO_5$ : C, 68.40; H, 4.78; N, 3.32; Found: C, 68.30; H, 4.69; N, 3.30; ESI-MS (*m/z*): 422.1 (M+H).

*[3-(2-hydroxyphenyl)-1,2-oxazol-5-yl]methyl 6-fluoro-4-oxo-4H-chromene-2-carboxylate* (**$C_6$**): Off white solid. M.P: 171-173 $^oC$; IR (KBr, $cm^{-1}$): $\nu_{max}$ 3335 (-OH), 3074 (C-H, Ar), 1736 (C=O, ester) , 1657 (C=O, chromene), 1605 (C=N), 1225, 1125 (C-O-C); $^1$H-NMR (400 MHz, $CDCl_3$): δ 9.30 (s, 1H, -OH ), 7.81-7.87 (m, 1H, Ar-H), 7.61-7.67 (m, 1H, Ar-H), 7.46-7.54 (m, 2H, Ar-H), 7.34-7.41 (m, 1H, Ar-H), 7.17 (s, 1H, chromene-CH), 7.07-7.13 (m, 1H, Ar-H), 6.97-7.03 (m, 1H, Ar-H), 6.83 (s, 1H, Isoxazole-C<u>H</u>), 5.58 (s, 2H, O-$CH_2$); $^{13}$C-NMR (100 MHz, $CDCl_3$): δ in ppm: 178.5, 164.3, 161.8, 162.2, 161.5, 159.8, 156.1, 153.0, 131.9, 130.2, 124.7, 122.3, 122.1, 121.5, 120.2, 118.7, 117.0, 109.9, 100.2, 58.8; Anal. calcd. for $C_{20}H_{12}FNO_6$: C, 63.00 ; H, 3.17; N, 3.67. Found: C, 63.06; H, 3.11; N, 3.59; ESI-MS (m/z): 382.1 (M+H).

*[3-(3-chlorophenyl)isoxazol-5-yl]methyl 6-fluoro-4-oxo-4H-chromene-2-carboxylate* (**$C_7$**): Off white solid. M.P: 152-154 $^oC$; IR (KBr, $cm^{-1}$): $\nu_{max}$ 3085 (C-H, Ar), 1739 (C=O, ester), 1652 (C=O, chromene), 1606 (C=N), 1228, 1123 (C-O-C); $^1$H-NMR (400 MHz, $CDCl_3$): δ 7.80-7.83 (m, 2H, Ar-<u>H</u>), 7.60-7.67 (m, 3H, Ar-<u>H</u>), 7.46-7.49 (m, 2H, Ar-<u>H</u>), 7.13 (s, 1H, chromene-C<u>H</u>), 6.80 (s, 1H, Isoxazole-C<u>H</u>), 5.58 (s, 2H, O-C<u>$H_2$</u>); $^{13}$C-NMR (100 MHz, $CDCl_3$): δ in ppm: 178.6, 165.9, 162.3, 162.2, 161.6, 159.9, 153.1, 135.6, 134.9, 134.6, 129.9, 129.6,129.0, 125.8, 124.5, 122.1, 121.5, 118.7, 109.9, 100.1, 58.8; Anal. calcd. for $C_{20}H_{11}ClFNO_5$ : C, 60.09; H, 2.77; N, 3.50. Found: C, 60.01; H, 2.72; N, 3.45; ESI-MS (m/z): 400.0 (M+H).

*[3-(4-chlorophenyl)isoxazol-5-yl]methyl 6-fluoro-4-oxo-4H-chromene-2-carboxylate* (**$C_8$**): Pale yellow solid. M.P: 163-165 $^oC$; IR (KBr, $cm^{-1}$): $\nu_{max}$ 3069 (C-H, Ar), 1735 (C=O, ester), 1657 (C=O, chromene), 1605 (C=N), 1234, 1127 (C-O-C); $^1$H-NMR (400 MHz, $CDCl_3$): δ 7.70-7.79 (m, 1H, Ar-<u>H</u>), 7.60-7.68 (m, 1H, Ar-<u>H</u>), 7.52 (d, 2H, J = 8 Hz, Ar-<u>H</u>), 7.40-7.49 (m, 1H, Ar-<u>H</u>),

7.20 (d, 2H, J = 8 Hz, Ar-H), 7.12 (s, 1H, chromene-CH), 6.80 (s, 1H, Isoxazole-CH), 5.62 (s, 2H, O-$CH_2$); $^{13}$C-NMR (100 MHz, $CDCl_3$):δ 178.6, 167.5, 163.6, 162.1, 161.5, 159.8, 153.0, 135.3, 129.8, 127.4,128.3, 124.5, 122.1, 121.6, 121.5, 118.7, 109.9, 100.1, 58.8; Anal. calcd. for $C_{20}H_{11}ClFNO_5$: C, 60.09; H, 2.77; N, 3.50. Found: C, 60.01; H, 2.71; N, 3.48; ESI-MS (m/z): 400.0 (M+H).

*[3-(4-bromophenyl)-1,2-oxazol-5-yl]methyl 6-fluoro-4-oxo-4H-chromene-2-carboxylate* (**$C_9$**): Pale yellow solid. M.P: 178-180 $^oC$; IR (KBr, $cm^{-1}$): $\nu_{max}$ 3089 (C-H, Ar), 1730 (C=O, ester), 1653 (C=O, chromene), 1606 (C=N), 1238, 1123 (C-O-C); $^1$H-NMR (400 MHz, $CDCl_3$):δ 7.83 (d, 2H, *J* = 8.8 Hz, Ar-CH), 7.60-7.68 (m, 1H, Ar-CH), 7.44-7.51(m, 2H, Ar-H), 7.33 (d, 2H, *J* =8.8 Hz, Ar-H), 7.13 (s, 1H, chromene-CH), 6.81 (s, 1H, Isoxazole-CH), 5.62 (s, 2H, O-$CH_2$); $^{13}$C-NMR (100 MHz, $CDCl_3$): δ 178.6, 166.1, 163.6, 162.1, 161.6, 159.9, 153.1, 132.3, 128.6, 127.1, 124.5, 122.9, 122.2, 121.5, 118.7, 109.9, 100.2, 58.8; Anal. calcd. for $C_{20}H_{11}BrFNO_5$: C, 54.08; H, 2.50; N, 3.15. Found: C, 54.02; H, 2.48; N, 3.11; ESI-MS (m/z): 444.9 (M+2H).

*(3-(2,3-dimethylphenyl)isoxazol-5-yl)methyl 6-fluoro-4-oxo-4H-chromene-2-carboxylate* (**$C_{10}$**): Off white solid. M.P: 165-167 $^oC$; IR (KBr, $cm^{-1}$): $\nu_{max}$ 3059 (C-H, Ar), 1737 (C=O, ester), 1655 (C=O, chromene), 1608 (C=N), 1230, 1127 (C-O-C); $^1$H-NMR (400 MHz, $CDCl_3$): δ 7.90-7.94 (m, 1H, Ar-H), 7.80-7.84 (m, 1H, Ar-H), 7.58-7.62 (m, 2H, Ar-H), 7.42-7.49 (m, 1H, Ar-H), 7.33-7.36 (m, 1H, Ar-H), 7.13 (s, 1H, chromene-CH), 6.82 (s, 1H, Isoxazole-CH), 5.62 (s, 2H, O-$CH_2$), 2.49 (s, 3H, Ar-$CH_3$), 2.35 (s, 3H, Ar-$CH_3$); $^{13}$C-NMR (100 MHz, $CDCl_3$): δ 178.7,164.3, 162.4, 162.3, 161.4, 159.9, 153.2, 138.2, 130.8, 130.1, 127.0, 126.3, 126.0, 124.5, 122.1, 121.5, 120.3, 118.9, 109.9, 100.0, 58.8, 20.1, 16.4, :Anal. calcd. for

$C_{22}H_{16}FNO_5$: C, 67.17; H, 4.10; N, 3.56. Found: C, 67.10, H, 4.05; N, 3.50; ESI-MS (m/z): 394.1 (M+H).

*(3-(3,5-dimethylphenyl)isoxazol-5-yl)methyl 6-fluoro-4-oxo-4H-chromene-2-carboxylate* (**$C_{11}$**): Pale Yellow solid. M.P: 176-178 $^oC$; IR (KBr, $cm^{-1}$): $\nu_{max}$ 3088 (C-H, Ar), 1737 (C=O, ester), 1655 (C=O, chromene), 1605 (C=N), 1230, 1132 (C-O-C); $^1$H-NMR (400 MHz, $CDCl_3$): δ 7.80-7.86 (m, 1H, Ar-H), 7.60-7.66 (m, 1H, Ar-H), 7.44-7.49 (m, 1H, Ar-H), 7.35 (s, 2H, Ar-H), 7.14 (s, 1H, chromene-CH), 7.09 (s, 1H, Ar-H), 6.81 (s, 1H, Isoxazole-CH), 5.62 (s, 2H, O-$CH_2$), 2.41 (s, 6H, 2xAr-$CH_3$));$^{13}$C-NMR (100 MHz, $CDCl_3$): δ 178.8, 166.3, 162.5, 162.3, 161.4, 160.0, 153.1, 139.2, 133.2, 131.0, 127.8, 124.5, 122.1, 121.5, 119.0, 109.9, 100.1, 58.8, 21.3: Anal. calcd. for $C_{20}H_{16}FNO_5$: C, 67.17; H, 4.10; N, 3.56. Found: C, 67.11; H, 4.02; N, 3.50; ESI-MS (m/z): 394.1 (M+H).

*[3-(naphthalen-1-yl)isoxazol-5-yl]methyl 6-fluoro-4-oxo-4H-chromene-2-carboxylate* (**$C_{12}$**): Pale red solid. M.P: 190-192 $^oC$; IR (KBr, $cm^{-1}$): $\nu_{max}$ 3069 (C-H, Ar), 1733 (C=O, ester), 1655 (C=O, chromene), 1605 (C=N), 1227, 1132 (C-O-C); $^1$H-NMR (400 MHz, $CDCl_3$): δ 7.85-7.97 (m, 1H, Ar-H), 7.70-7.78 (m, 1H, Ar-H), 7.50-7.65 (m, 3H, Ar-H), 7.32-7.42 (m, 3H, Ar-H), 7.12-7.30 (m, 3H, Ar-H), 6.80 (s, 1H, Isoxazole-CH), 5.64 (s, 2H, O-$CH_2$); $^{13}$C-NMR (100 MHz, $CDCl_3$):178.7, 164.5, 162.5, 162.2, 161.4, 159.9, 153.2, 140.8, 134.2, 133.4, 128.8, 128.5, 127.7, 126.8, 126.6, 125.3, 124.5, 122.8, 122.1, 121.6, 118.8, 109.9, 99.9, 58.8; Anal. calcd. for $C_{24}H_{14}FNO_5$: C, 69.40; H, 3.40; N, 3.37. Found: C, 69.35; H, 3.42; N, 3.31; ESI-MS (m/z): 416.1 (M+H).