

Supporting information

Bronsted acidic surfactant $[HDMM]^+ [HSO_4]^-$: A Green microreactor assembly for stereoselective synthesis of novel thiazolyl-pyrazole-chromen-2-one in water

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A) General:

Various substituted acetoacetyl coumarins were synthesized from salicylaldehyde and 4-hydroxy-6-methyl pyrone. Dialkyl acetylene dicarboxylates (Sigma Aldrich) and thiosemicarbazide (Alfa Aesar) were used as received. Melting points (M.P) were determined in open capillary and are uncorrected. IR spectra were recorded on ATR-IR-4600 spectrometer. NMR spectra were recorded on Bruker AMX-400 spectrometer (400 MHz ^1H NMR and 100 MHz for ^{13}C NMR) in DMSO-d₆ employing TMS as an internal standard and δ values are expressed in ppm. HRMS spectra were recorded on JEOL GC MATE-II HR Mass spectrometer from IIT Madras.

B) Typical procedure:

Synthesis of surfactant $[\text{HDMM}]^+ [\text{HSO}_4]^-$:

A solution of 4-methyl morpholine (5 g, 0.058 mol) and 1- bromohexadecane (17.69 g, 0.058 mol) in acetone (40 mL) was refluxed at 60 °C for 12-24 h. The white precipitate was filtered after cooling and washed with diethyl ether yielded 4-hexadecyl-4-methyl morpholin-4- ium bromide $[\text{HDMM}]^+ [\text{Br}]^-$ in 96 % yield.

The anion exchange was performed by adding equimolar quantity of sulfuric acid (H_2SO_4) at 80 °C in dry toluene for 24 h and the final product $[\text{HDMM}]^+ [\text{HSO}_4]^-$ was obtained as a waxy solid after separating two phases. The product was washed with ethyl acetate to get pure product.

Synthesis of thiazolyl-pyrazole-chromen-2-one:

In a 50 mL round bottom flask, acetoacetyl coumarin, (1 mmol), thiosemicarbazide (1 mmol) and $[\text{HDMM}]^+ [\text{HSO}_4]^-$ surfactant (20 mol %) in water (5 mL) was stirred at room temperature for 1-2 h to afford chromeno pyrazole carbothioamide intermediate. Then dialkyl acetylene dicarboxylate (1 mmol) was added in the resulting reaction mixture and stirred at room temperature for time specified in **Table 2**. The progress of reaction was monitored by TLC. After completion of the reaction, reaction mixture was filtered and washed with water. The product was recrystallized in ethanol to furnish corresponding pure thiazolyl-pyrazole- chromen-2-one. These synthesized products were characterized by IR, $^1\text{H}, ^{13}\text{C}$ NMR and Mass analysis.

Spectral data of synthesized novel Bronsted acid surfactant catalyst 4-hexadecyl-4-methylmorpholin-4-i um hydrogen sulphate, [HDMM]⁺[HSO₄]⁻

Brownish waxy solid; IR (**Fig. 1**): 3411, 2918, 2851, 1686, 1642, 1466, 1365, 1174, 1124, 1042, 889, 760, 720, 653 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) (**Fig. 2**): δ 0.86-0.89 (t, 3H), 1.25 (s, 26H), 1.77 (s, 2H), 3.44 (s, 3H), 3.56-3.61 (m, 2H), 3.67-3.76 (m, 4H), 4.01-4.05 (m, 2H), 4.12-4.17 (m, 2H), 8.47 (br s, 1H); ¹³C NMR (100 MHz, CDCl₃) (**Fig. 3**): δ 14.34, 22.17, 22.92, 26.60, 29.58, 29.61, 29.79, 29.87, 29.93, 29.99, 32.17, 47.86, 60.06, 65.71 ppm.

Spectral data of thiazolyl-pyrazole-chromen-2-one derivatives

Entry 4a, Table 2: methyl (E)-2-(2-(3-methyl-5-(2-oxo-2H-chromen-3-yl)-1H-pyrazol-1-yl)-4-oxothiazol-5(4H)-ylidene)

Orange solid; Obs. m.p. 280–282 °C. IR (**Fig. 4**): 3158, 3086, 2899, 2778, 2396, 1725, 1605, 1521, 1444, 1333, 1195, 1118, 1082, 1015, 938, 866, 799, 754, 694, 650, 584 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆) (**Fig. 5**): δ 2.26 (s, 3H, -CH₃), 3.79 (s, 3H, -OCH₃), 6.69 (s, 1H, pyrazole-CH), 6.73 (s, 1H, vinyl -CH), 7.37-7.45 (m, Ar-2H), 7.66-7.70 (dd, Ar-1H, J = 7.2 Hz, 1.6 Hz), 7.97-7.99 (d, Ar-1H, J = 7.6 Hz), 8.76 (s, 1H, coumarin -CH) ppm; ¹³C NMR (100 MHz, DMSO-d₆) (**Fig. 6**): δ 15.89, 52.50, 100.42, 114.81, 116.15, 118.59, 118.77, 124.81, 126.10, 129.20, 140.70, 141.77, 146.06, 153.05, 153.24, 161.09, 163.91, 166.12, 170.89 ppm; HRMS (**Fig. 7**): Mass calculated for [C₁₉H₁₃N₃O₅S]: 395.39 (M⁺); Obs. Mass: 395.38 (M⁺).

Entry 4b, Table 2 : ethyl (E)-2-(2-(3-methyl-5-(2-oxo-2H-chromen-3-yl)-1H-pyrazol-1-yl)-4-oxothiazol-5(4H)-ylidene)acetate

Orange solid; Obs. m.p. 290 °C; IR (**Fig. 8**): 3162, 3079, 1725, 1601, 1441, 1335, 1193, 1122, 1010, 755, 696 cm⁻¹; ¹H NMR, (400 MHz, DMSO-d₆) (**Fig. 9**): δ 1.27-1.30 (t, 3H), 2.26 (s, 3H, -CH₃), 4.24-4.29 (q, 2H, -OCH₂), 6.68 (s, 1H, pyrazole -CH), 6.75 (s, 1H, vinyl-CH), 7.36-7.49 (m, Ar-2H), 7.66-7.68 (d, Ar-1H, J = 8.4 Hz), 7.96-7.98 (d, Ar-1H, J = 7.6 Hz), 8.77 (s, 1H, coumarin -CH) ppm; ¹³C NMR (100 MHz, DMSO-d₆) (**Fig. 10**): δ 14.02, 17.35, 56.75, 105.35, 113.56, 116.14, 119.71, 122.61, 124.33, 125.39, 128.38,

136.23, 140.96, 142.75, 146.94, 150.80, 153.80, 156.35, 161.83, 167.76, 170.41 ppm; HRMS (**Fig. 11**): Mass calculated for [C₂₀H₁₅N₃O₅S]: 409.42 (M⁺) ; Obs. Mass: 409.41 (M⁺).

Entry 4c, Table 2: methyl (E)-2-(2-(5-(6-methoxy-2-oxo-2H-chromen-3-yl)-3-methyl-1*H*-pyrazol-1-yl)-4-oxothiazol-5(4*H*)- ylidene)acetate

Red solid; Obs. m.p. 284 °C; IR (**Fig. 12**): 3161, 3073, 1713, 1603, 1525, 1505, 1428, 1379, 1332, 1288, 1196, 1122, 1023, 940, 902, 862, 810, 766, 705, 615, 592 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆) (**Fig. 13**): δ 2.26 (s, 3H, -CH₃), 3.31 (s, 3H, -OCH₃), 3.81 (s, 3H, -OCH₃), 6.72 (s, 1H, pyrazole - CH), 6.74 (s, 1H, vinyl -CH), 7.25-7.29 (m, Ar-1H), 7.33-7.40 (m, Ar-1H), 7.58-7.58 (d, Ar-1H, J = 3.2 Hz), 8.13 (s, 1H, coumarin - CH) ppm ; ¹³C NMR (100 MHz, DMSO-d₆) (**Fig. 14**): δ 15.91, 52.54, 56.39, 105.23, 114.83, 117.35, 123.80, 124.35, 125.71, 127.80, 135.38, 140.02, 145.96, 149.33, 150.78, 154.61, 157.33, 161.35, 166.14, 167.76 ppm; HRMS (**Fig. 15**): Mass calculated for [C₂₀H₁₅N₃O₆S] :425.42 (M⁺) ; Obs. Mass: 425.41 (M⁺).

Entry 4d, Table 2 : ethyl (E)-2-(2-(5-(6-methoxy-2-oxo-2*H*- chromen-3-yl)-3-methyl-1*H*-pyrazol-1-yl)-4-oxothiazol-5(4*H*)- ylidene)acetate

Red solid; Obs. m.p. 292 °C; IR (**Fig. 16**): 3162, 3073, 1707, 1595, 1506, 1430, 1323, 1193, 1122, 1027, 826, 814, 708, 619 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆) (**Fig. 17**): δ 1.26-1.30 (t, 3H), 2.26 (s, 3H, -CH₃), 3.81 (s, 3H, -OCH₃), 4.23-4.28 (q, 2H, -OCH₂), 6.71 (s, 1H, pyrazole -CH), 6.71 (s, 1H, vinyl -CH), 7.25-7.29 (m, Ar-1H), 7.37- 7.39 (m, Ar-1H), 7.56-7.57 (d, Ar-1H, J = 3.2 Hz), 8.72 (s, 1H, coumarin -CH) ppm; ¹³C NMR (100 MHz, DMSO-d₆) (**Fig. 18**): δ 14.94, 18.76, 54.91, 58.41, 105.56, 115.35, 116.14, 119.71, 122.61, 124.33, 125.39, 128.38, 136.23, 140.96, 142.75, 146.02, 148.80, 153.80, 158.35, 160.83, 165.35, 168.75 ppm; HRMS (**Fig. 19**): Mass calculated for [C₂₁H₁₇N₃O₆S]: 439.45 (M⁺) ; Obs. Mass: 439.43 (M⁺).

Entry 4e, Table 2 : methyl (E)-2-(2-(3-methyl-5-(6-nitro-2-oxo-2*H*- chromen-3-yl)-1*H*-pyrazol-1-yl)-4-oxothiazol-5(4*H*)- ylidene)acetate

Orange solid; Obs. m.p. 298 °C; IR (**Fig. 20**): 3101, 3077, 2358, 1836, 1742, 1700, 1617, 1525, 1468, 1335, 1243, 1196, 1101, 1017, 923, 819, 737, 605, 592 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆) (**Fig. 21**): δ 2.27 (s, 3H, -CH₃), 3.80 (s, 3H, -OCH₃), 6.68 (s, 1H, pyrazole -CH), 6.74 (s, 1H, vinyl -CH), 7.64-7.66 (d, Ar-1H, J = 8.8 Hz), 8.43-8.46 (dd, Ar-1H, J = 1.6 Hz, 9.2 Hz), 8.75 (s, 1H, coumarin -CH), 8.880- 8.889 (d, Ar-1H, J = 3.6 Hz)

ppm; ^{13}C NMR (100 MHz, DMSO-d₆) (**Fig. 22**): δ 14.89, 53.50, 101.42, 115.81, 116.15, 117.59, 118.77, 125.81, 126.10, 128.20, 140.70, 141.77, 147.06, 153.95, 154.24, 162.09, 164.91, 167.12, 169.89 ppm; HRMS (**Fig. 23**): Mass calculated for [C₁₉H₁₂N₄O₇S]: 440.39 (M⁺) ; Obs. Mass: 440.38 (M⁺)

Entry 4f, Table 2: ethyl (E)-2-(2-(3-methyl-5-(6-nitro-2-oxo-2H-chromen-3-yl)-1H-pyrazol-1-yl)-4-oxothiazol-5(4H)-ylidene)acetate

Orange solid; Obs. m.p. >300 °C; IR (**Fig. 24**): 3158, 3124, 2265, 1730, 1701, 1658, 1519, 1486, 1368, 1268, 1181, 1130, 1065, 923, 802, 737, 605 cm⁻¹; ^1H NMR (400 MHz, DMSO-d₆) (**Fig. 25**): δ 1.26-1.30 (t, 3H, -CH₂CH₃), 2.28 (s, 3H, -CH₃), 4.24- 4.29 (q, 2H, -CH₂), 6.68 (s, 1H, pyrazole - CH), 6.69 (s, 1H, vinyl -CH), 7.62-7.64 (d, Ar-1H, *J* = 9.2 Hz), 8.21-8.24 (dd, Ar-1H, *J* = 3.2 Hz, 9.2 Hz), 8.75 (s, 1H, coumarin - CH), 8.98-8.99 (d, Ar-1H, *J* = 3.2 Hz); ^{13}C NMR (100 MHz, DMSO-d₆): (δ ppm) : Due to insufficient solubility we are unable to scan its ^{13}C NMR; HRMS (**Fig. 26**): Mass calculated for [C₂₀H₁₄N₄O₇S]: 454.41 (M⁺) ; Obs. Mass: 454.40 (M⁺).

Entry 4g, Table 2 : methyl (E)-2-(2-(5-(6-bromo-2-oxo-2H-chromen-3-yl)-3-methyl-1H-pyrazol-1-yl)-4-oxothiazol-5(4H)- ylidene)acetate

Orange solid; Obs. m.p. 300 °C; IR (**Fig. 27**): 3270, 3060, 1923, 1836, 1780, 1731, 1698, 1595, 1551, 1512, 1470, 1403, 1328, 1285, 1240, 1189, 1114, 1067, 1013, 930, 877, 803, 673, 593 cm⁻¹; ^1H NMR (400 MHz, DMSO-d₆) (**Fig. 28**): δ 2.26 (s, 3H, -CH₃), 3.80 (s, 3H, -OCH₃), 6.69 (s, 1H, pyrazole -CH), 6.74 (s, 1H, vinyl -CH), 7.40-7.42 (d, Ar-1H, *J* = 9.2 Hz), 7.80-7.83 (dd, Ar-1H, *J* = 2.4 Hz, 8.8 Hz), 8.23-8.24 (d, Ar-1H, *J* = 2 Hz), 8.74 (s, 1H, coumarin -CH) ppm; ^{13}C NMR (100 MHz, DMSO-d₆): (δ ppm): Due to insufficient solubility we are unable to scan its ^{13}C NMR; HRMS (**Fig. 29**): Mass calculated for [C₁₉H₁₂BrN₃O₅S]: 474.29 (M⁺) ; Obs. Mass: 474.28 (M⁺).

Entry 4h, Table 2 : methyl (E)-2-(2-(5-(6-chloro-2-oxo-2H-chromen-3-yl)-3methyl-1H-pyrazol-1-yl)-4-oxothiazol-5(4H)-ylidene)acetate

Orange solid; Obs. m.p. 286 °C; IR (**Fig. 30**): 3066, 1781, 1734, 1696, 1596, 1551, 1524, 1469, 1415, 1328, 1285, 1239, 1189, 1119, 1073, 1013, 931, 875, 803, 774, 701, 677, 616 cm⁻¹; ^1H NMR (400 MHz, DMSO-d₆) (**Fig. 31**): δ 2.23 (s, 3H, -CH₃), 3.76 (s, 3H, -OCH₃), 6.64 (s, 1H, pyrazol -CH), 6.70 (s, 1H, vinyl -CH), 7.40-7.42 (d, Ar-1H, *J* = 9.2 Hz), 7.56-7.58 (dd, Ar-1H, *J* = 2.4 Hz, 8.8 Hz), 8.06-8.07 (d, Ar-1H, *J* = 1.6 Hz), 8.70 (s, 1H, coumarin -CH) ppm; ^{13}C NMR (100 MHz, DMSO-d₆): (δ ppm): Due to insufficient

solubility we are unable to scan its ^{13}C NMR; HRMS (**Fig. 32**): Mass calculated for $[\text{C}_{19}\text{H}_{12}\text{ClN}_3\text{O}_5\text{S}]$: 429.83 (M^+); Obs. Mass: 429.82 (M^+).

Entry 4i, Table 2 : methyl (*E*)-2-(2-(5-(6-bromo-8-methoxy-2-oxo-2*H*-chromen-3-yl)-3-methyl-1*H*-pyrazol-1-yl)-4-oxothiazol-5(4*H*)- ylidene)acetate

Orange solid; Obs. m.p. 278 °C; IR (**Fig. 33**): 2973, 2784, 1719, 1636, 1497, 1444, 1325, 1252, 1096, 1036, 930, 813, 733, 616 cm^{-1} ; ^1H NMR (400 MHz, DMSO-d₆) (**Fig. 34**): δ 2.25 (s, 3H, -CH₃), 3.80 (s, 3H, -OCH₃), 3.94 (s, 3H, -OCH₃), 6.69 (s, 1H, pyrazol -CH), 6.73 (s, 1H, vinyl -CH), 7.48-7.48 (d, Ar-1H, J = 2Hz), 7.77-7.78 (d, Ar-1H, J = 1.6 Hz), 8.69 (s, 1H, coumarin -CH) ppm; ^{13}C NMR (100 MHz, DMSO-d₆) (**Fig. 35**): δ 15.60, 56.86, 57.80, 105.96, 120.18, 121.53, 121.72, 123.39, 123.62, 125.82, 125.99, 139.93, 141.81, 151.30, 157.37, 159.83, 163.01, 169.19, 170.31 ppm; HRMS (**Fig. 36**): Mass calculated for $[\text{C}_{20}\text{H}_{14}\text{BrN}_3\text{O}_6\text{S}]$: 504.31 (M^+) ; Obs. Mass: 504.30 (M^+).

Entry 4j, Table 2 : methyl (*E*)-2-(2-(3-methyl-5-(2-oxo-2*H*-benzo[g]chromen-3-yl)-1*H*-pyrazol-1-yl)-4-oxothiazol-5(4*H*)- ylidene)acetate

Orange solid; Obs. m.p. >300 °C; IR (**Fig. 37**): 2965, 2772, 1766, 1709, 1641, 1589, 1491, 1443, 1408, 1309, 1247, 1072, 1039, 968, 833, 787, 755, 733, 694, 628 cm^{-1} ; ^1H NMR (400 MHz, DMSO-d₆) (**Fig. 38**): δ 2.29 (s, 3H, -CH₃), 3.82 (s, 3H, -OCH₃), 6.73 (s, 1H, pyrazol -CH), 6.76 (s, 1H, vinyl -CH), 7.59-7.67 (m, Ar-2H), 7.75- 7.79 (m, Ar-1H), 8.06-8.08 (d, Ar-1H, J = 8 Hz), 8.10-8.29 (m, Ar-1H), 8.58-8.66 (m, Ar-1H), 9.30 (s, 1H, coumarin -CH) ppm; ^{13}C NMR (100 MHz, DMSO-d₆) (**Fig. 39**): δ 15.89, 52.06, 100.42, 114.81, 115.80, 115.98, 116.15, 118.59, 118.77, 124.82, 126.10, 129.20, 129.79, 132.29, 140.71, 141.77, 142.72, 146.05, 153.06, 153.24, 161.09, 163.91, 166.12, 170.89 ppm; HRMS (**Fig. 40**): Mass calculated for $[\text{C}_{23}\text{H}_{15}\text{N}_3\text{O}_5\text{S}]$: 445.45 (M^+); Obs. Mass: 445.44 (M^+).

IR, ^1H and ^{13}C NMR spectra of synthesized novel Bronsted acidic surfactant catalyst, 4-hexadecyl-4-methylmorpholin-4- ium hydrogen sulphate, $[\text{HDMM}]^+$ $[\text{HSO}_4]^-$.

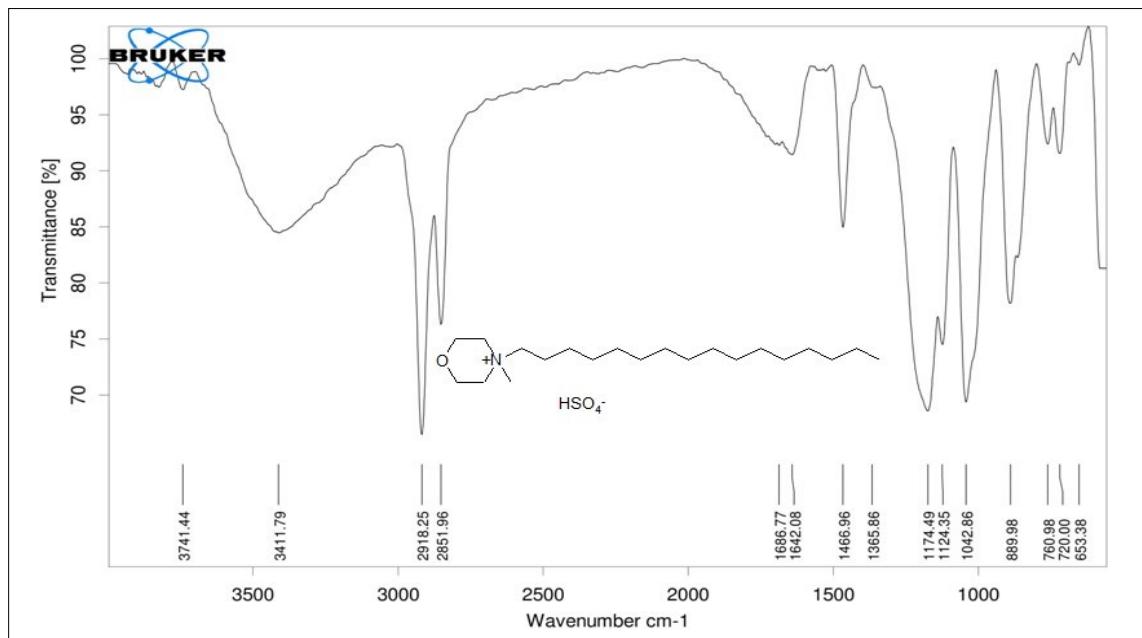


Fig. 1

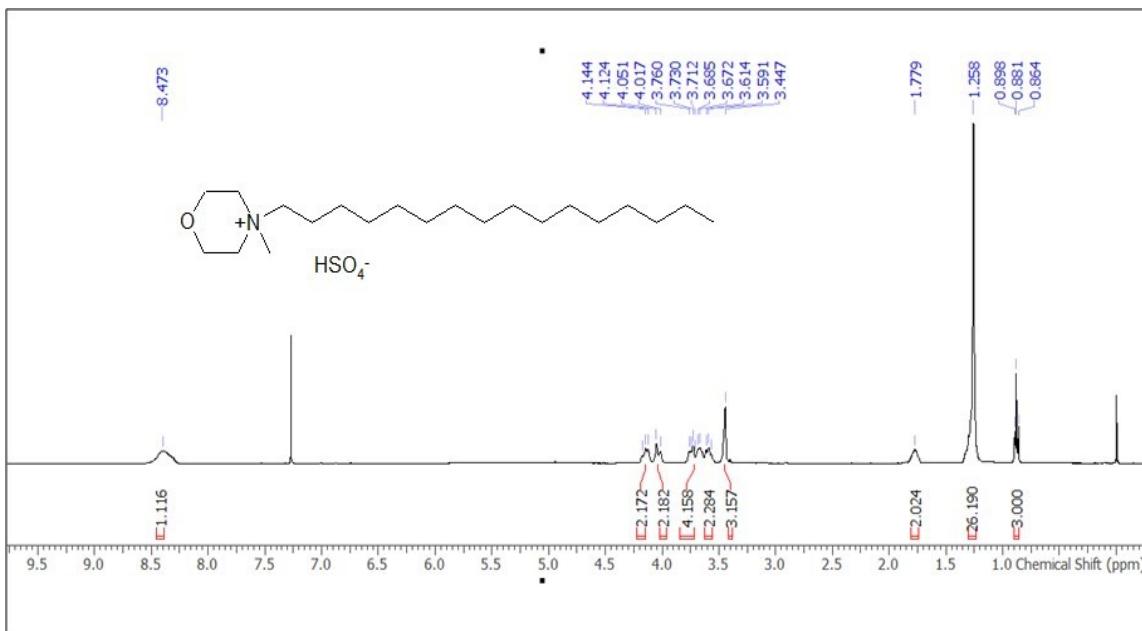


Fig. 2

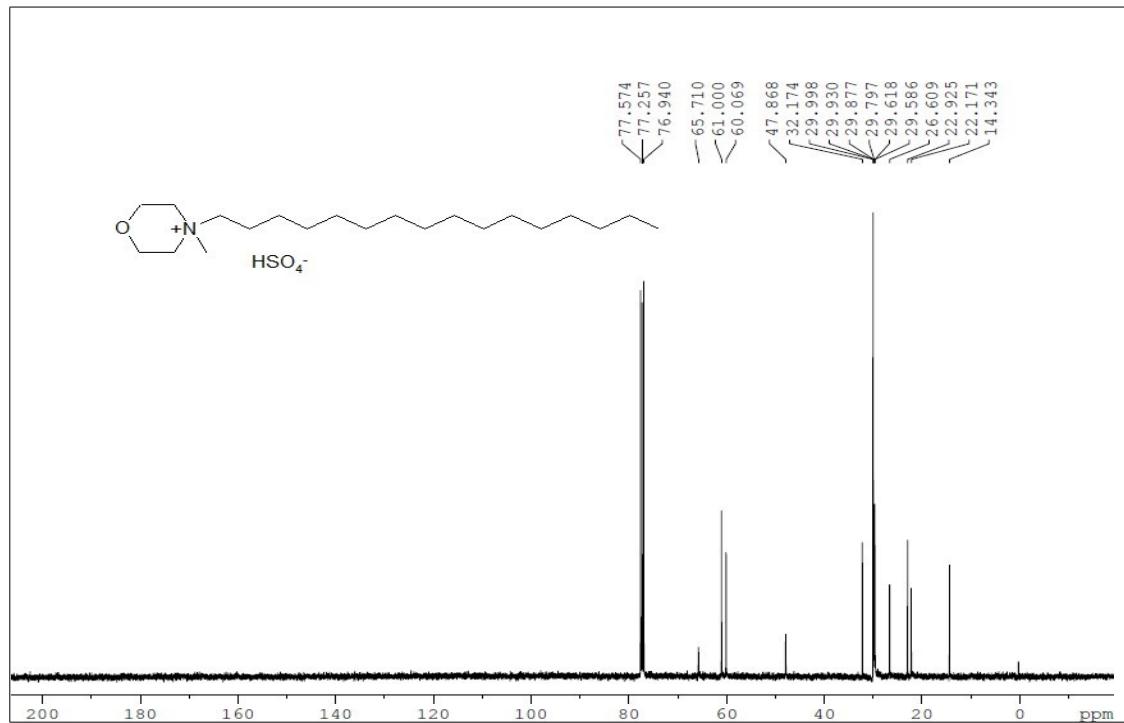


Fig. 3

IR, ^1H , ^{13}C and Mass spectra of synthesized thiazolyl-pyrazole chromen-2-one derivatives

Entry 4a, Table 3:

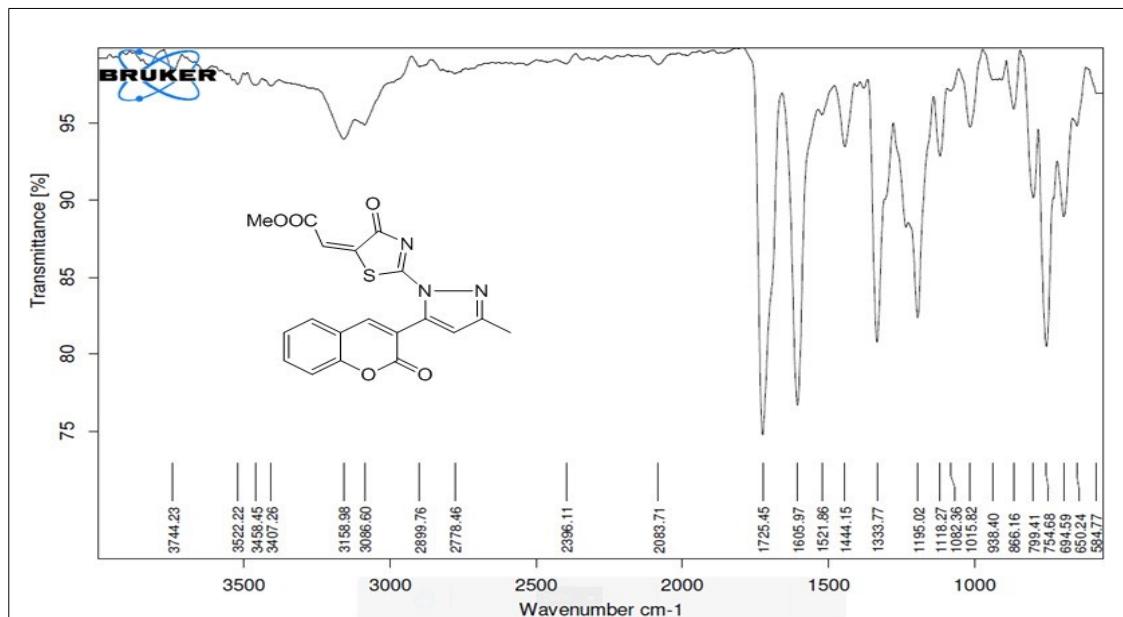


Fig. 4

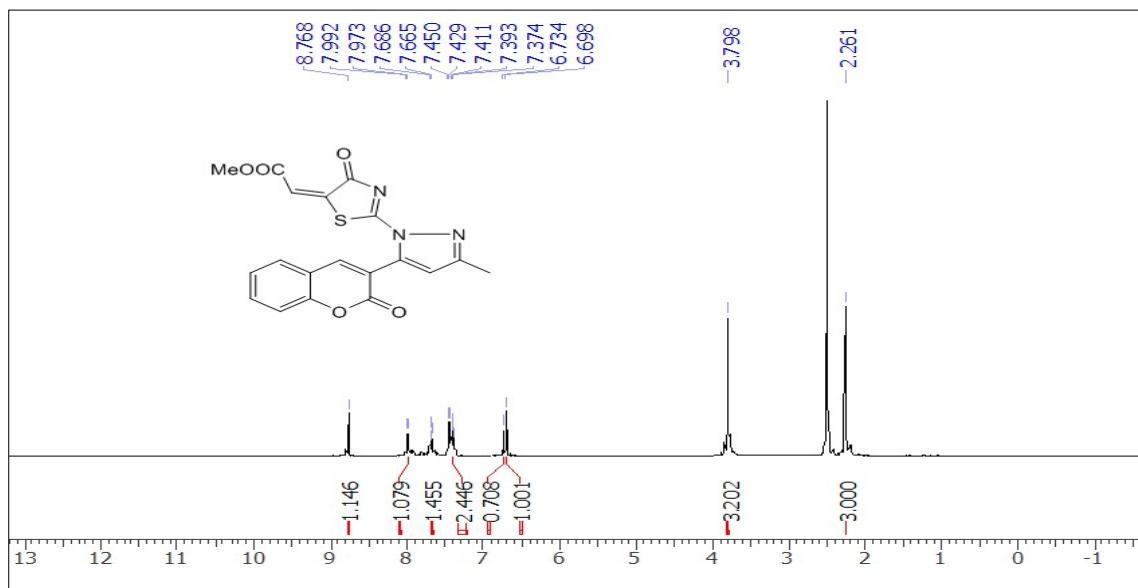


Fig. 5

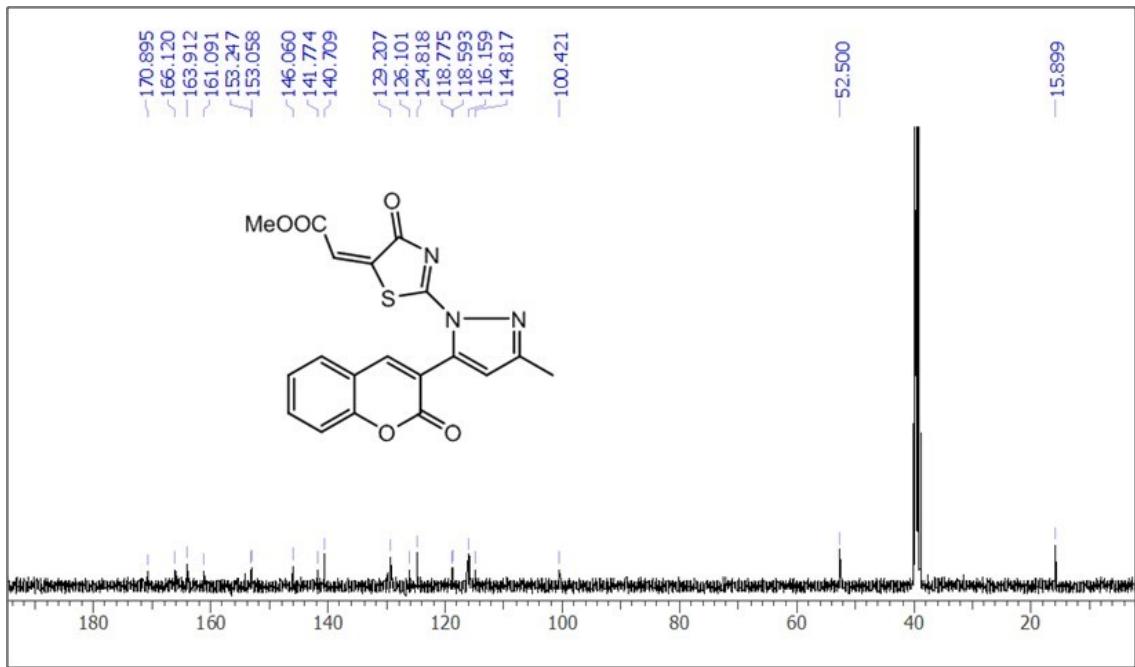


Fig. 6

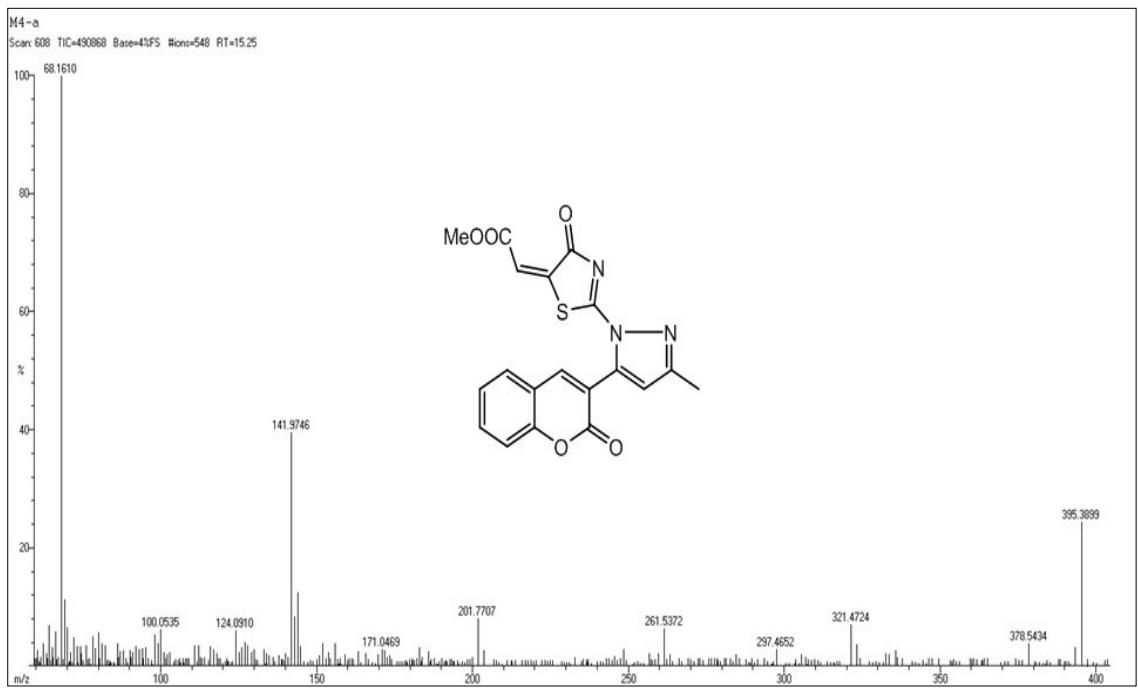


Fig. 7

Entry 4b, Table 3:

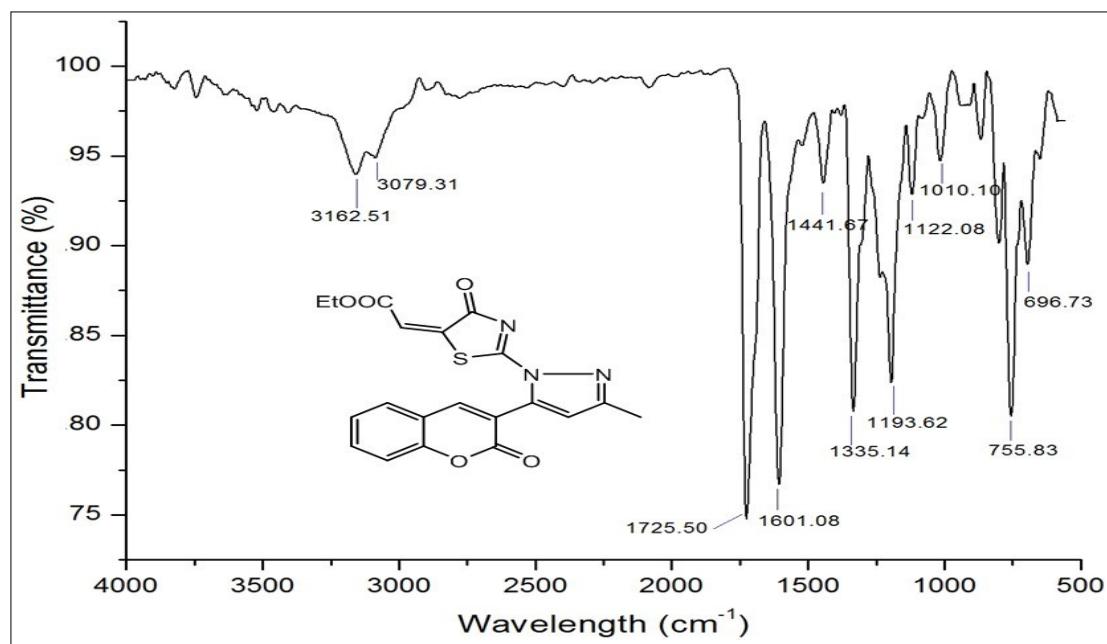


Fig. 8

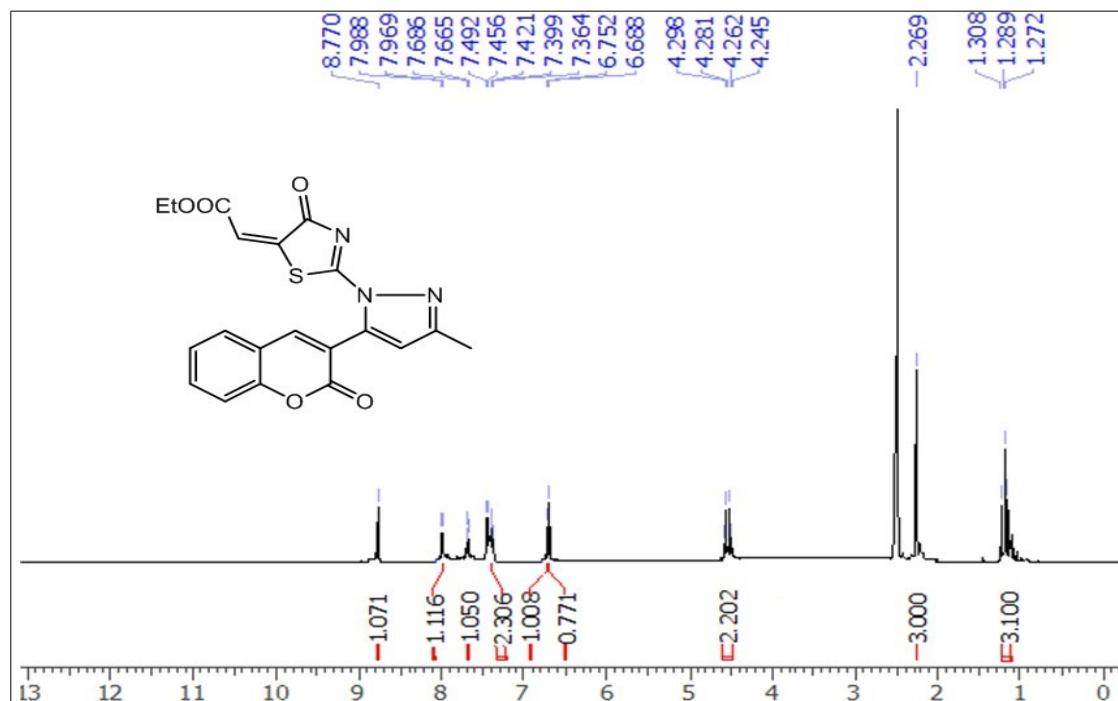


Fig. 9

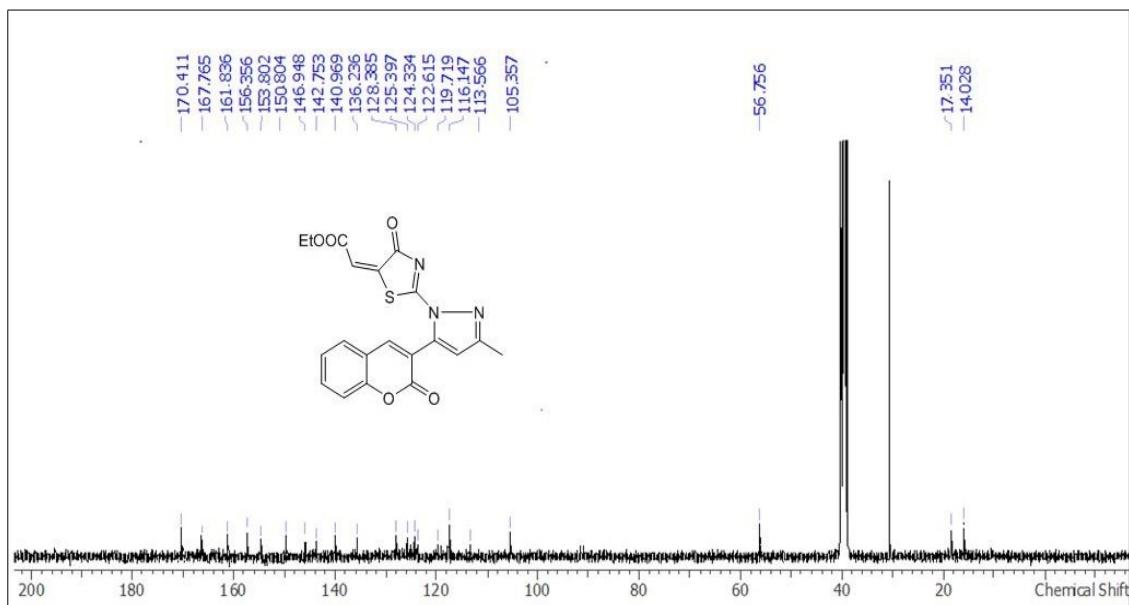


Fig. 10

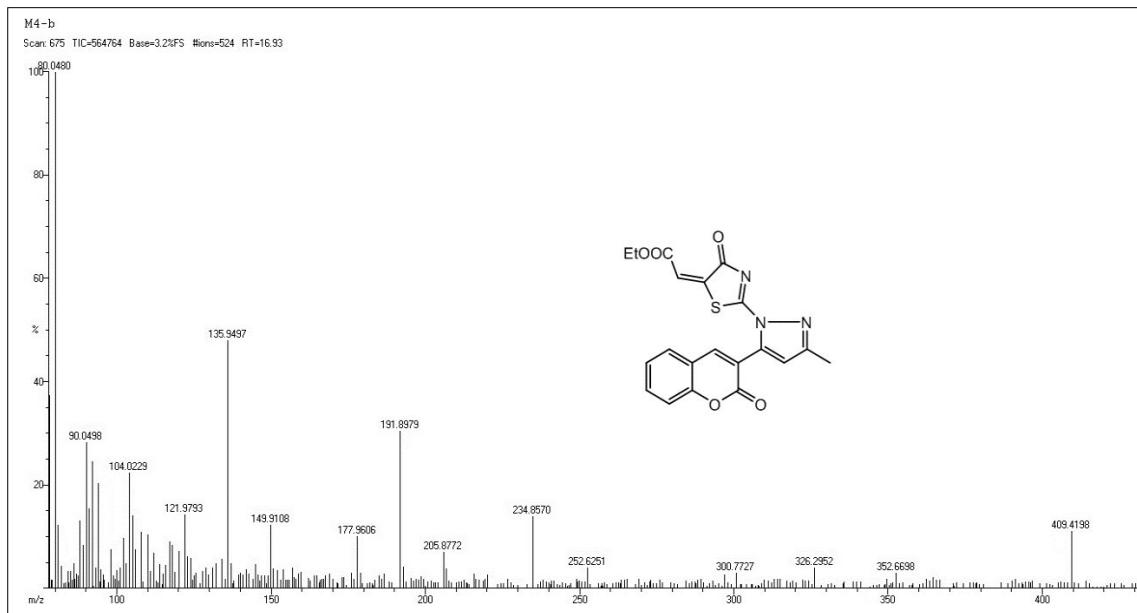


Fig. 11

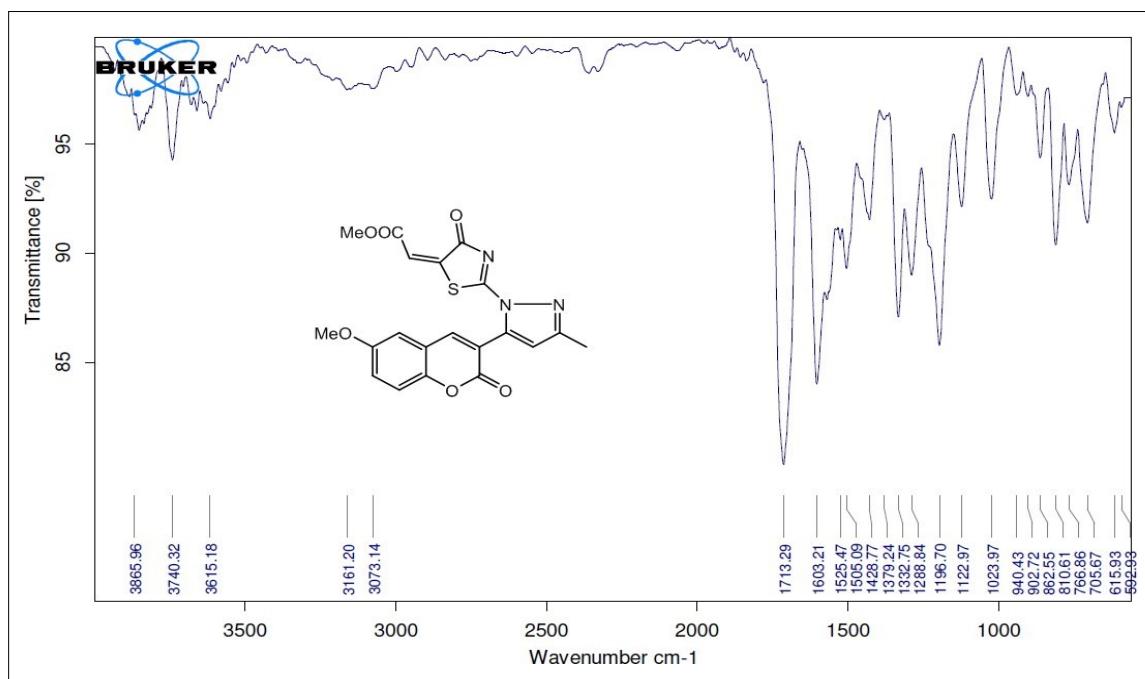


Fig. 12

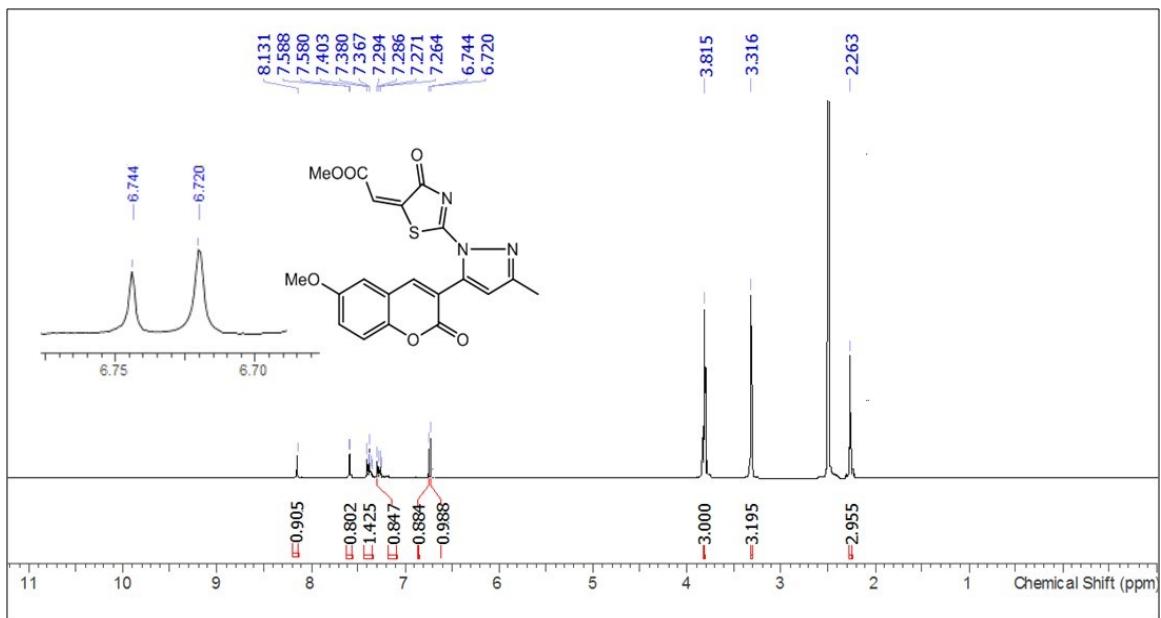


Fig. 13

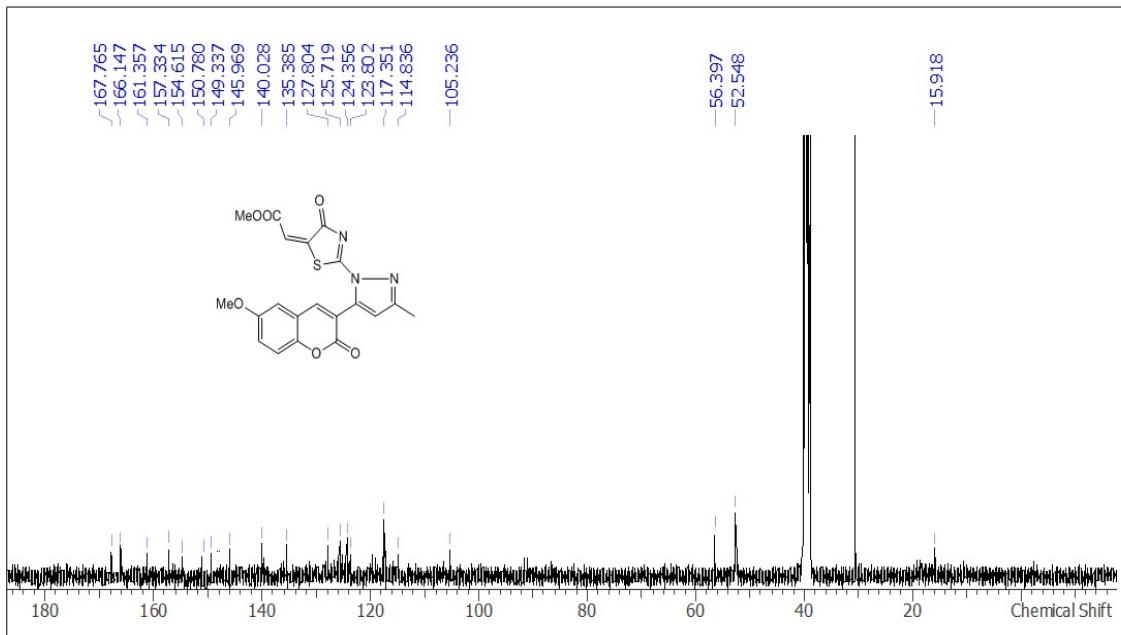


Fig. 14

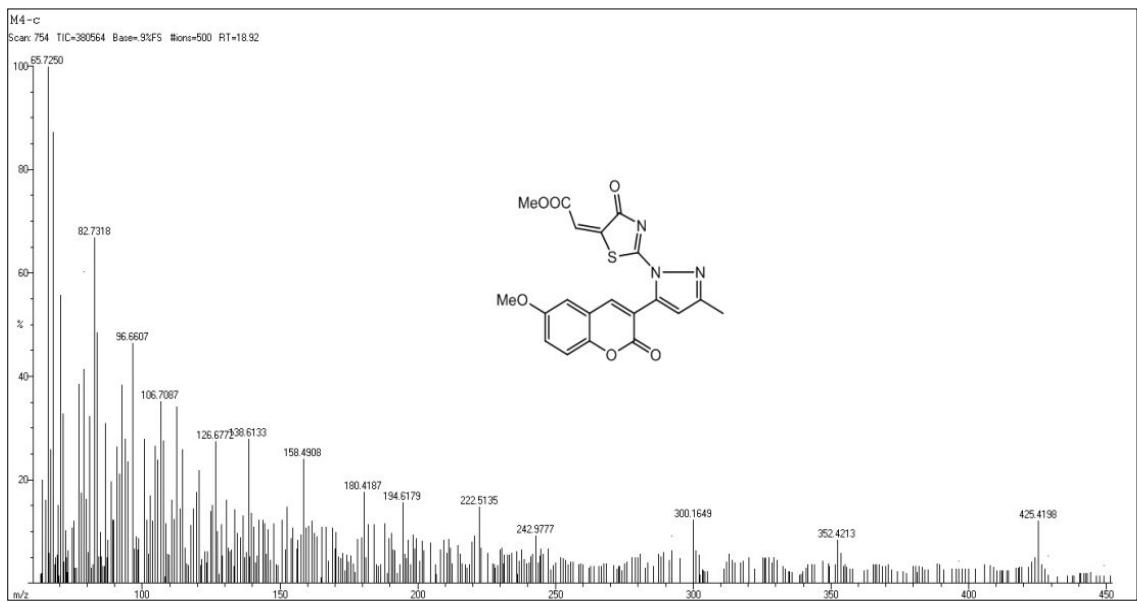


Fig. 15

Entry 4d, Table 3:

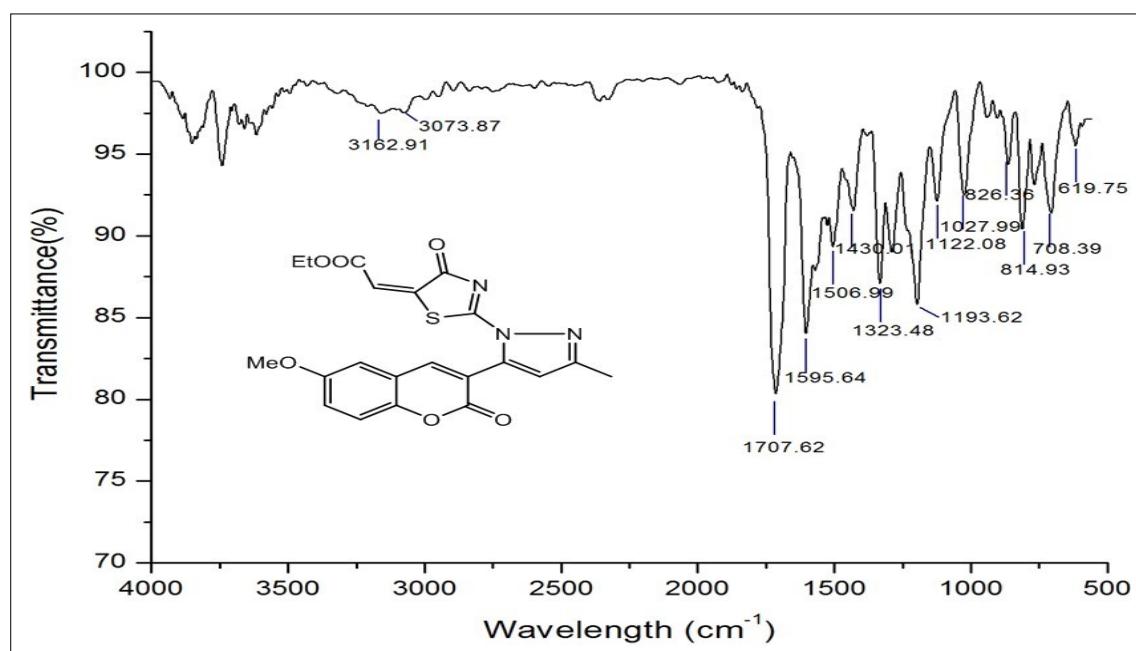


Fig. 16

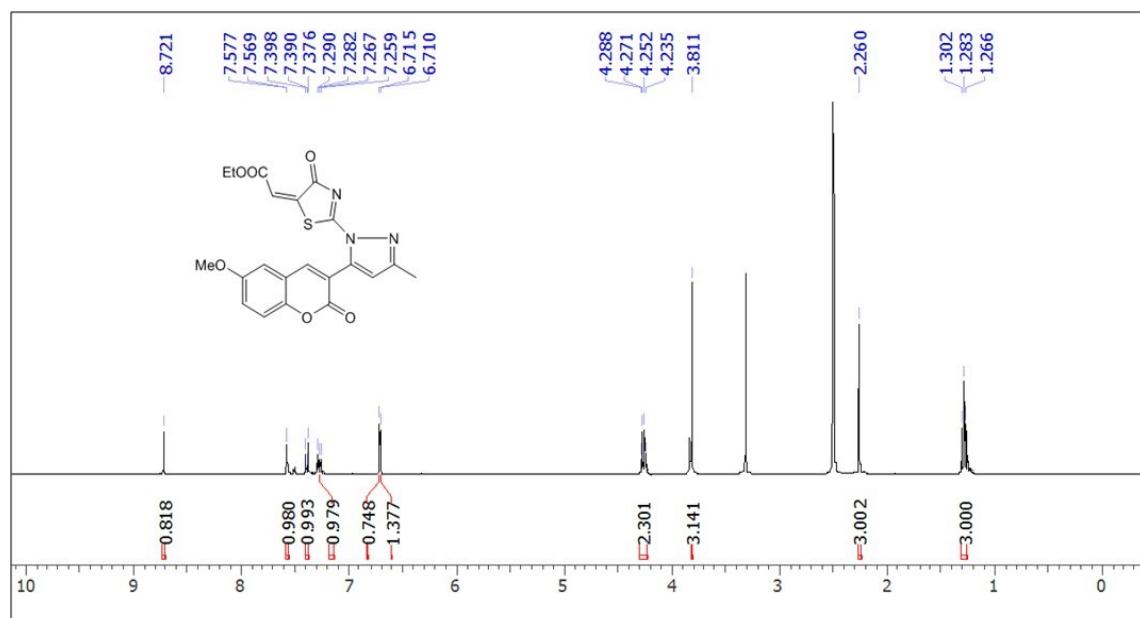


Fig. 17

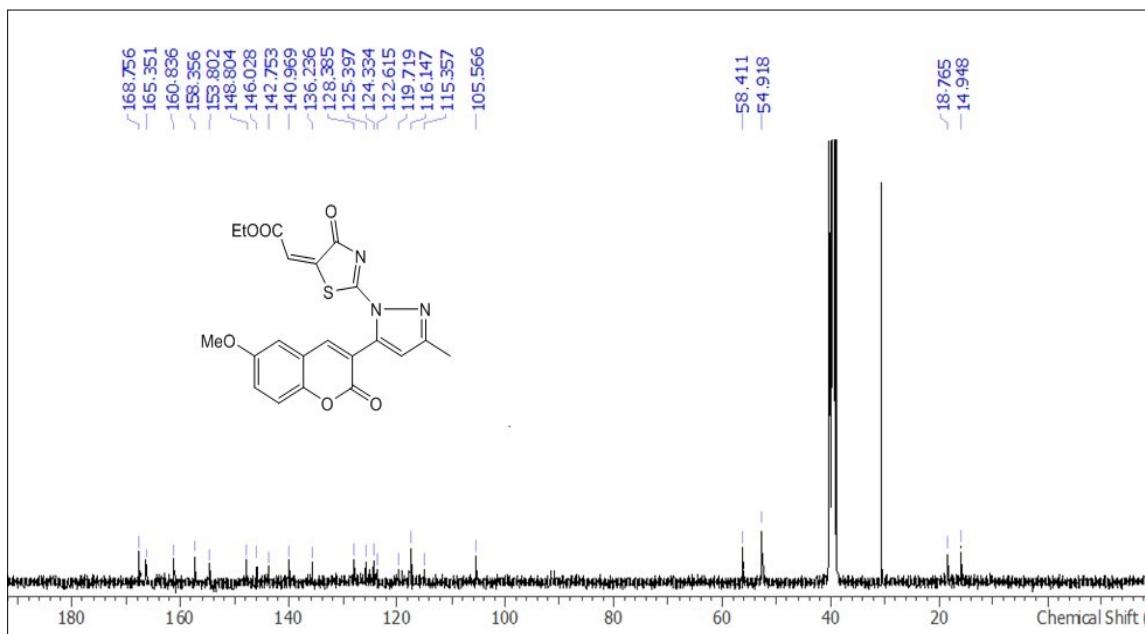


Fig. 18

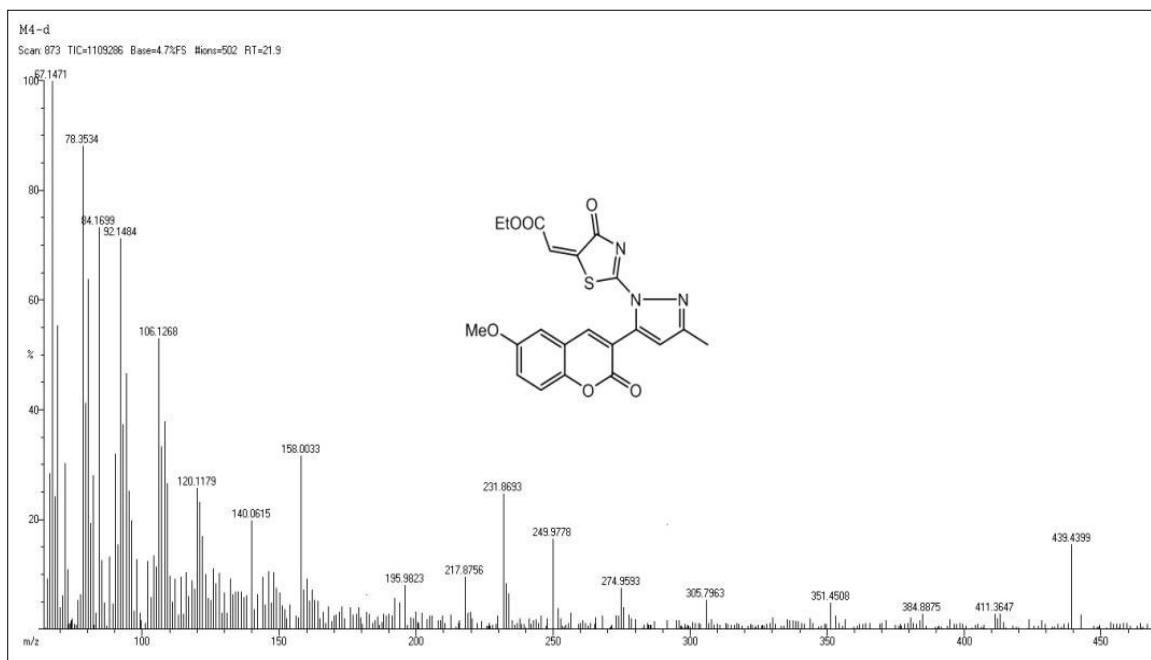


Fig. 19

Entry 4e, Table 3:

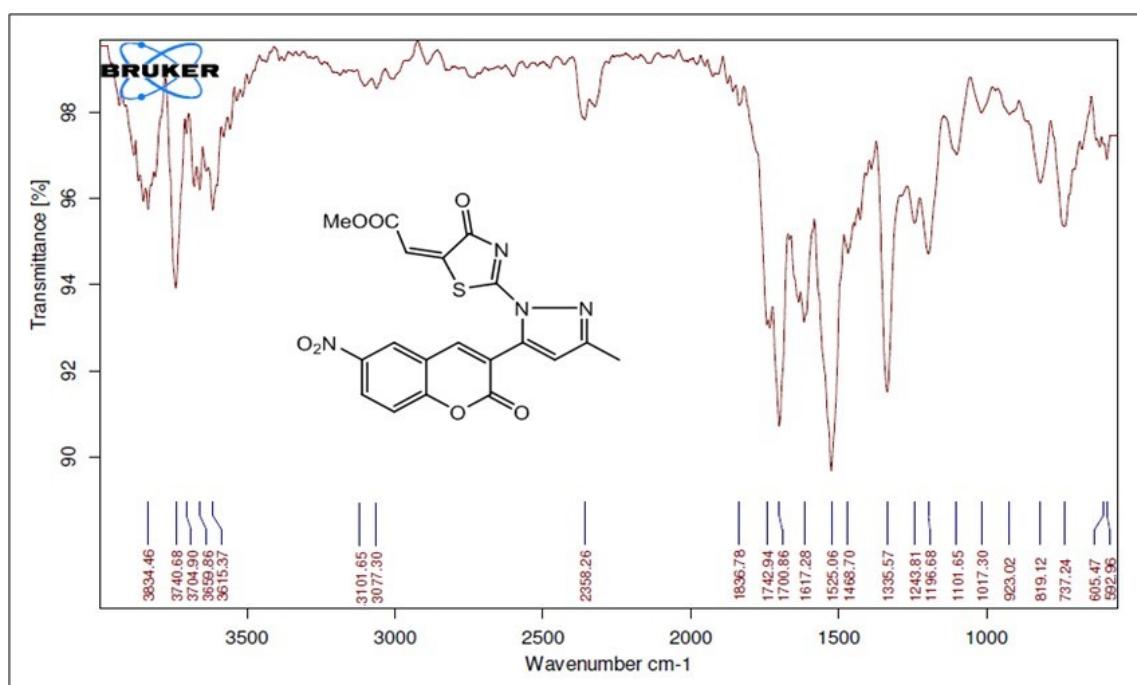


Fig. 20

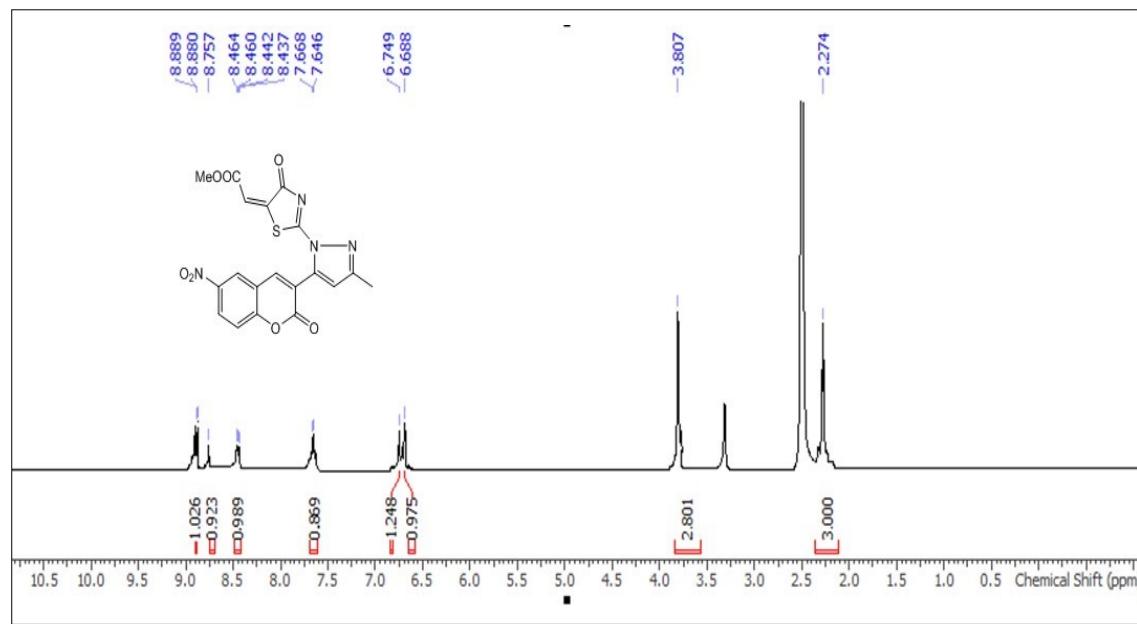


Fig. 21

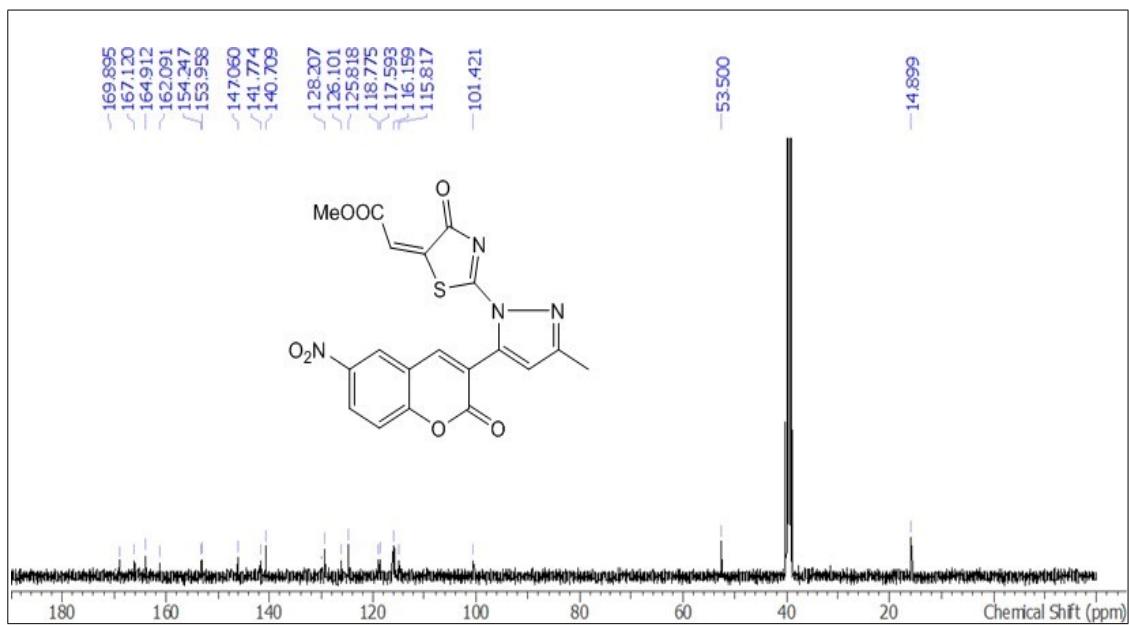


Fig. 22

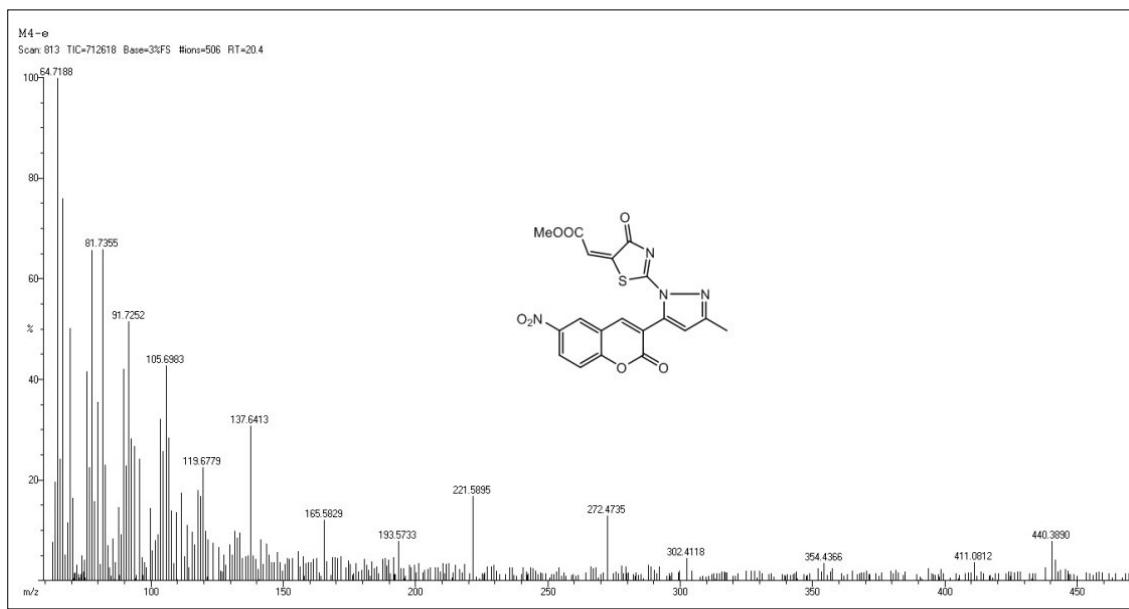


Fig. 23

Entry 4f, Table 3:

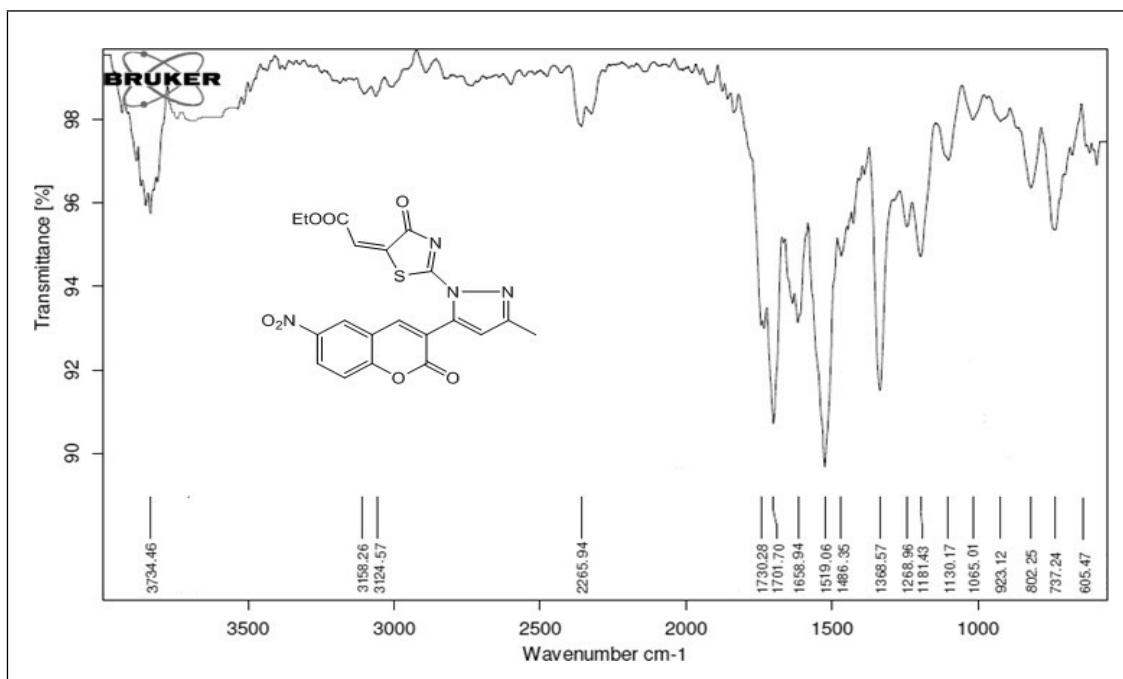


Fig. 24

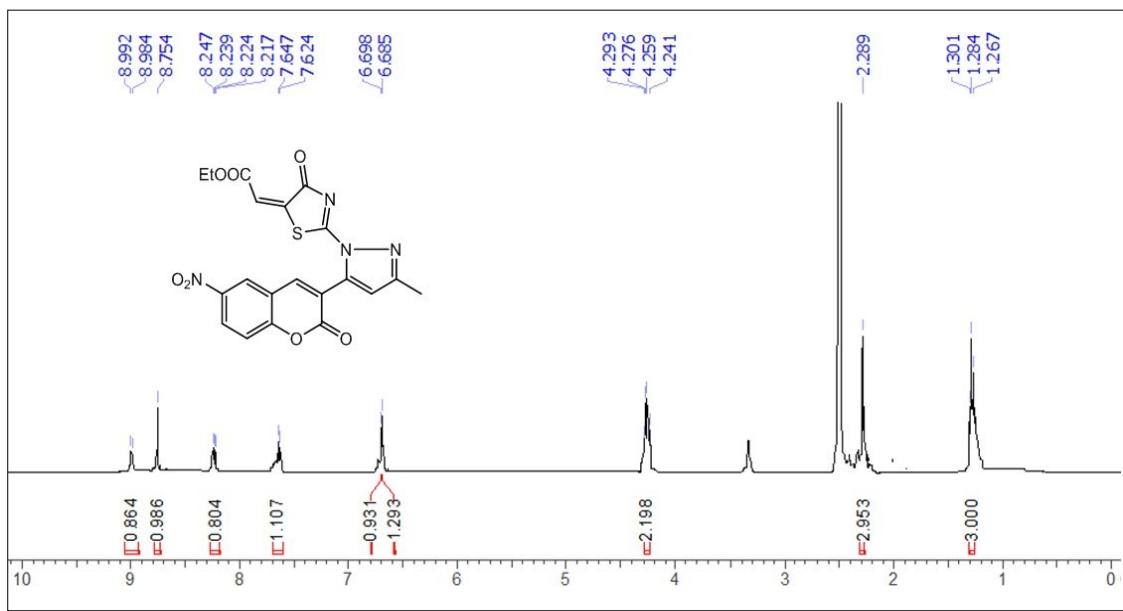


Fig. 25

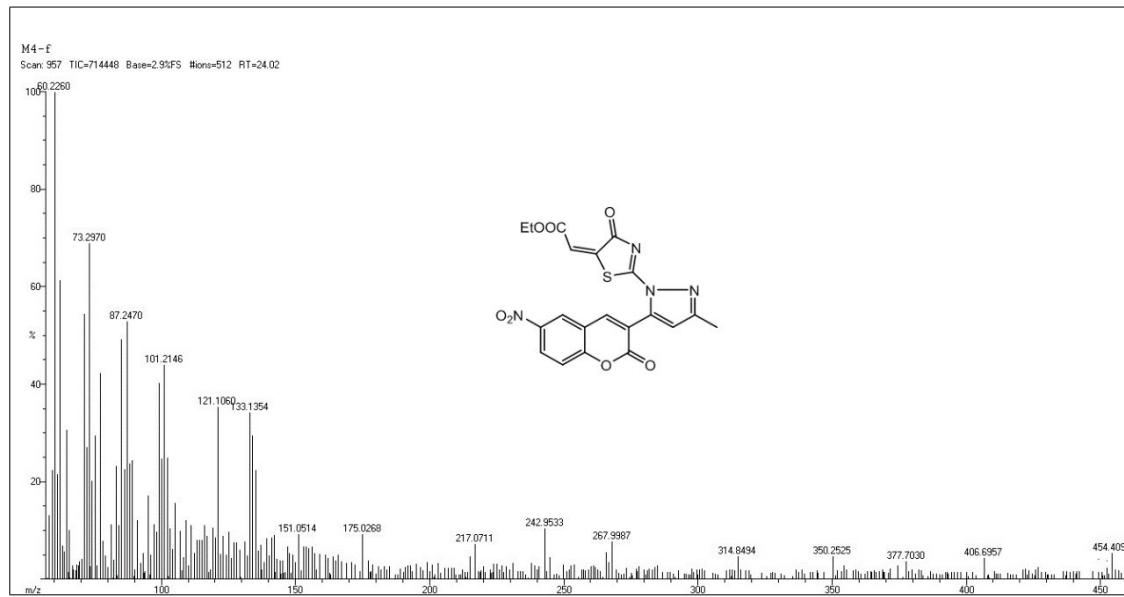


Fig. 26

Entry 4g, Table 3:

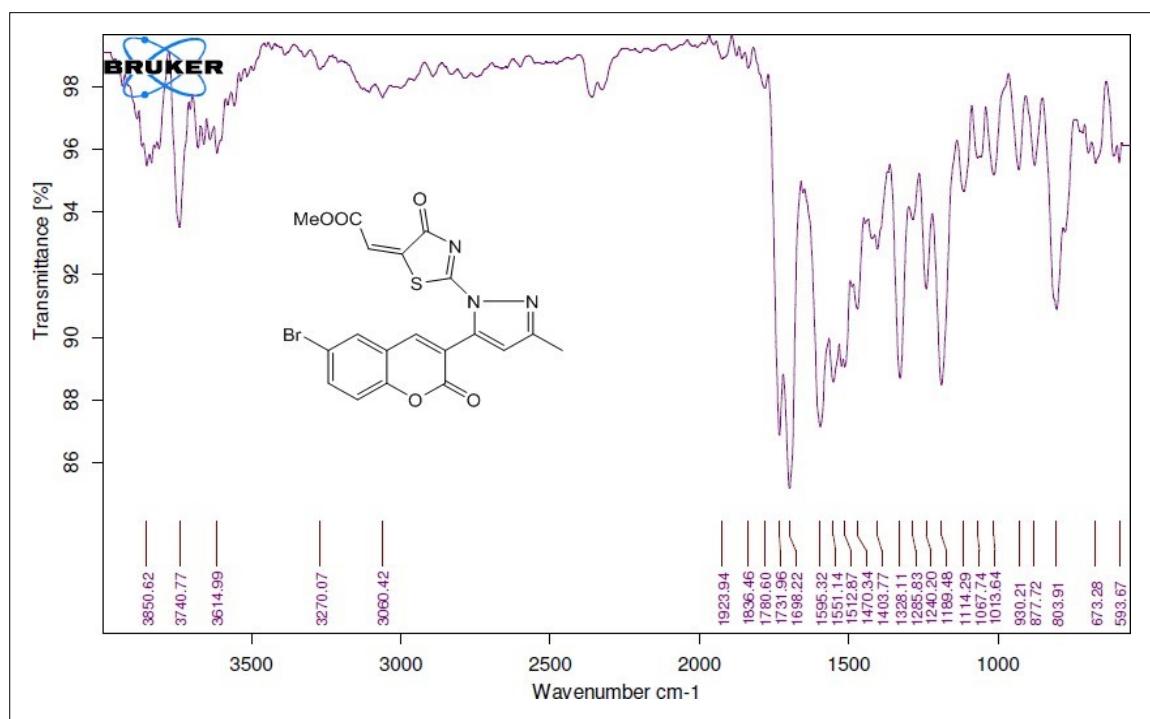


Fig. 27

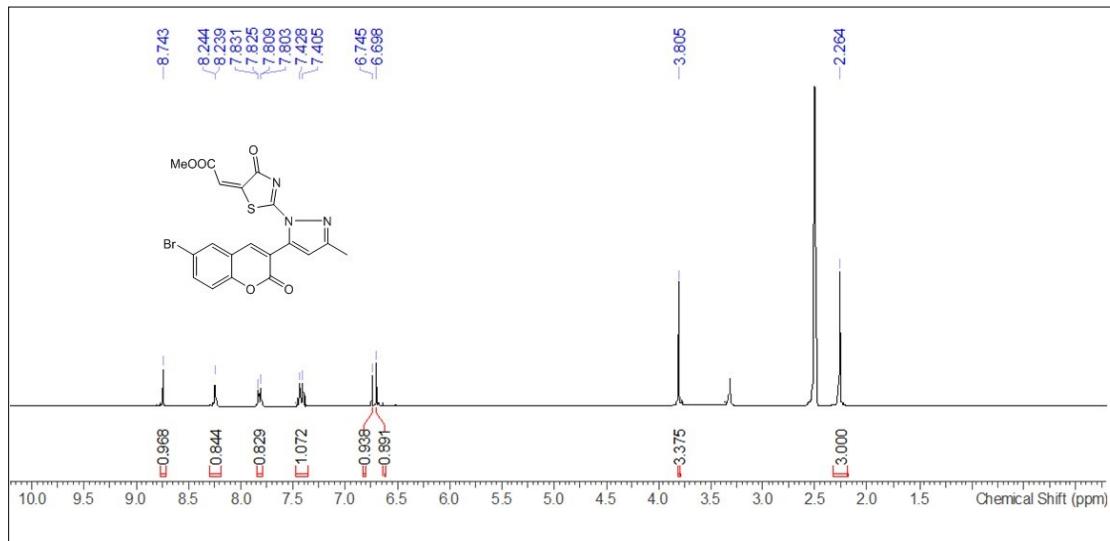


Fig. 28

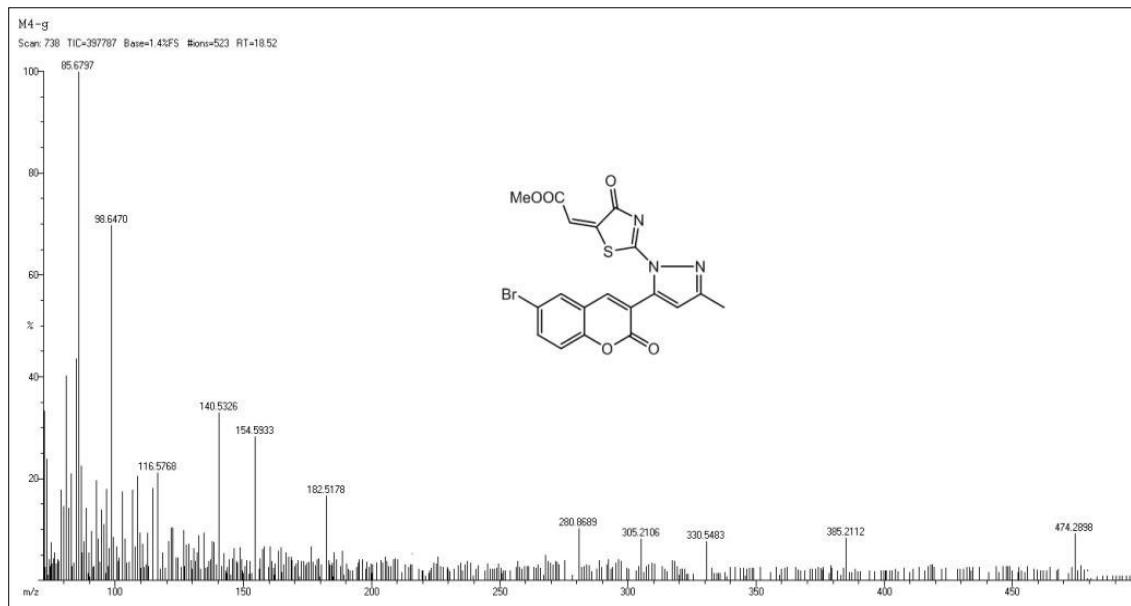


Fig. 29

Entry 4h, Table 3:

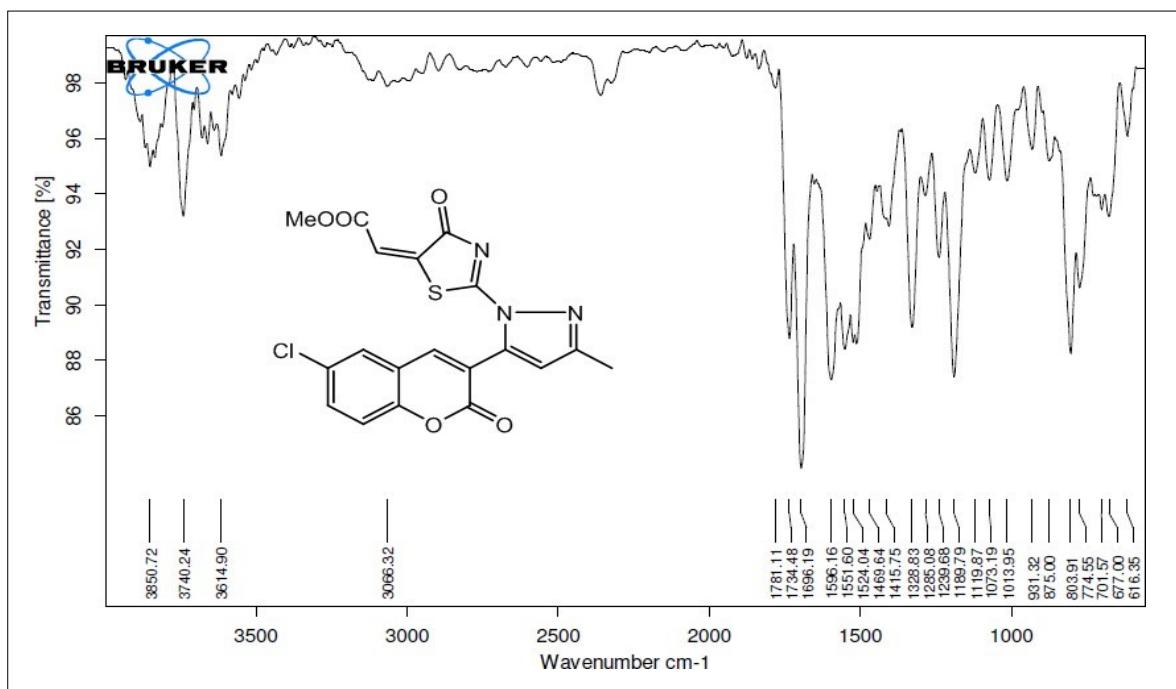


Fig. 30

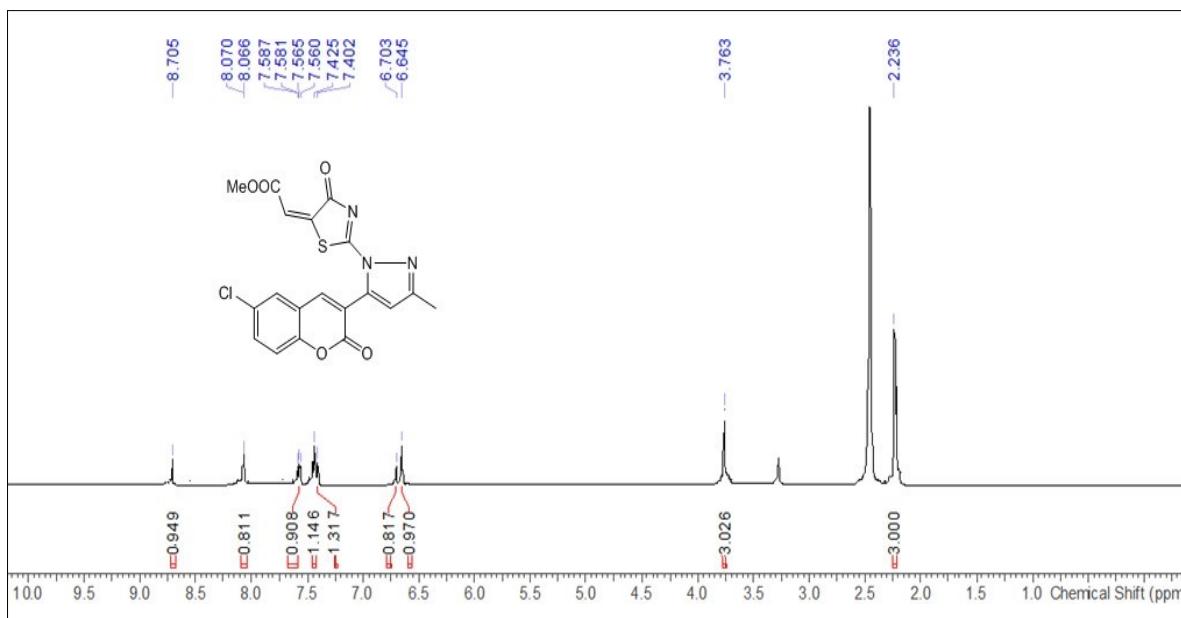


Fig. 31

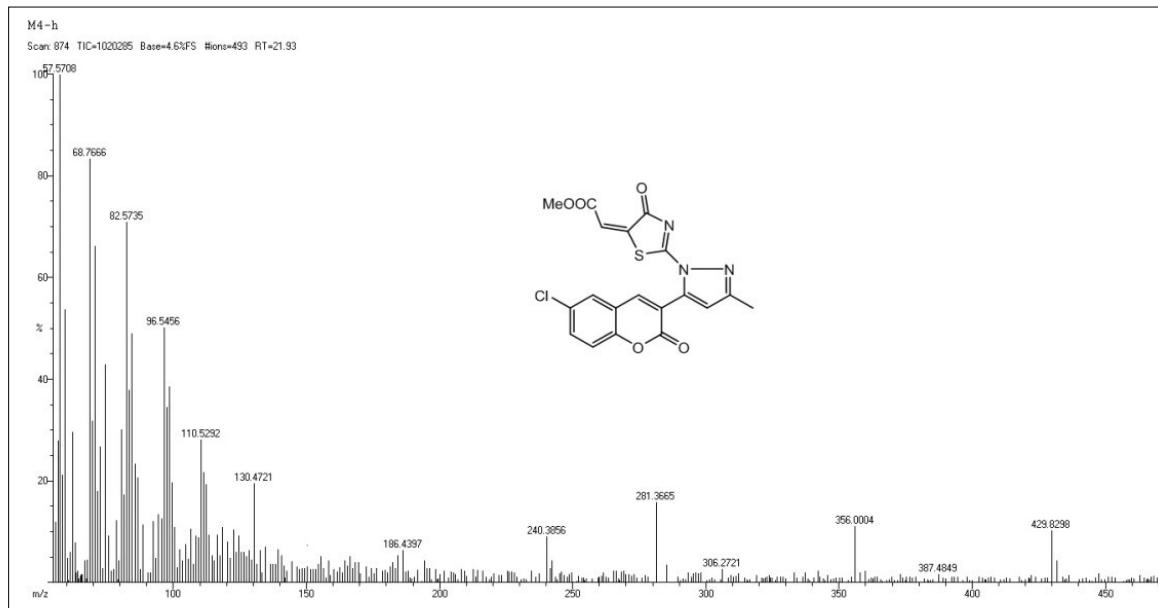


Fig. 32

Entry 4i, Table 3:

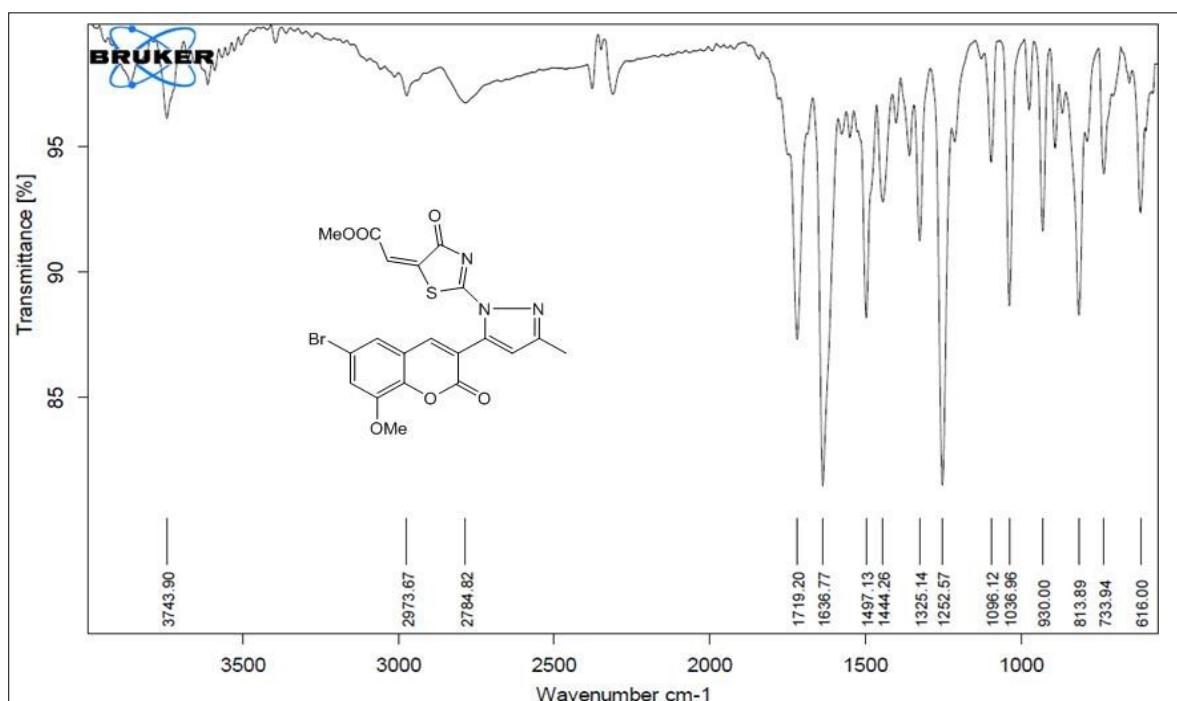


Fig. 33

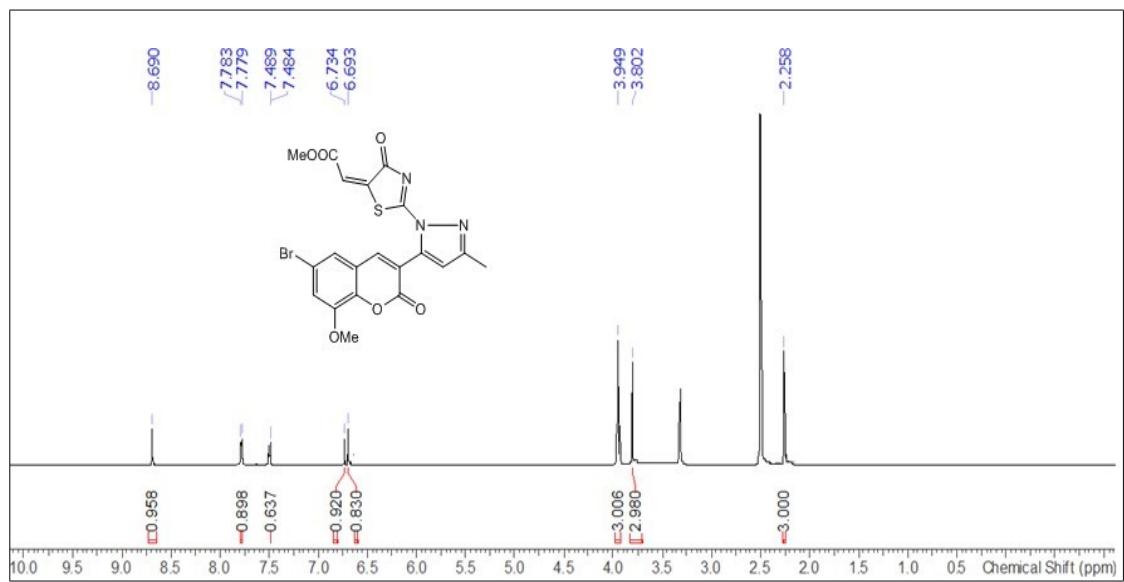


Fig. 34

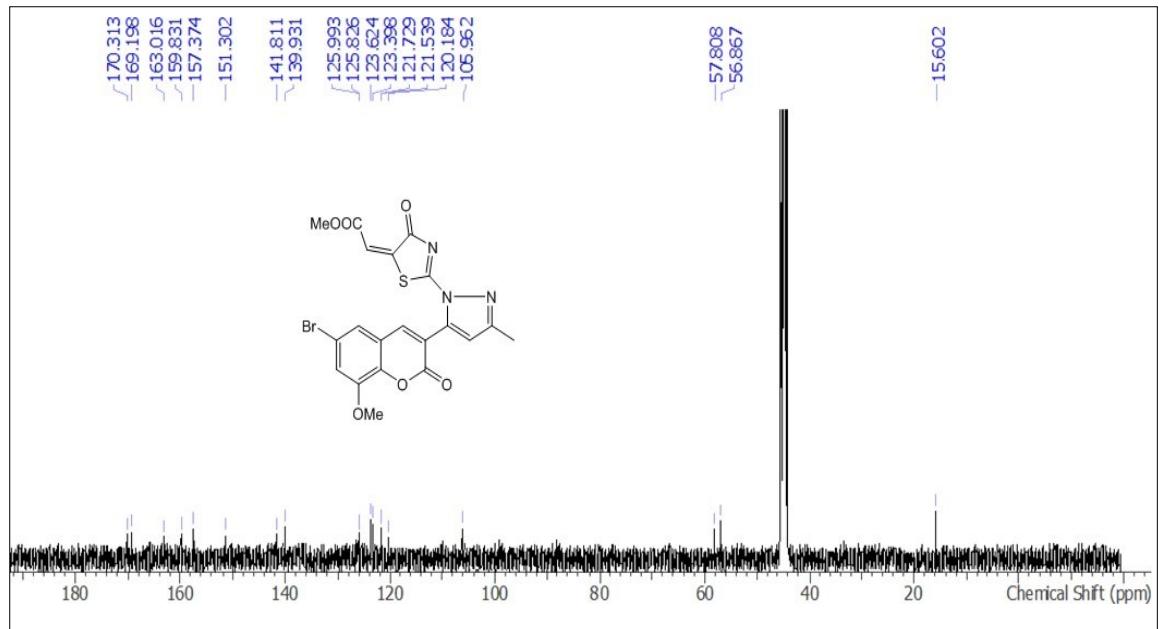


Fig. 35

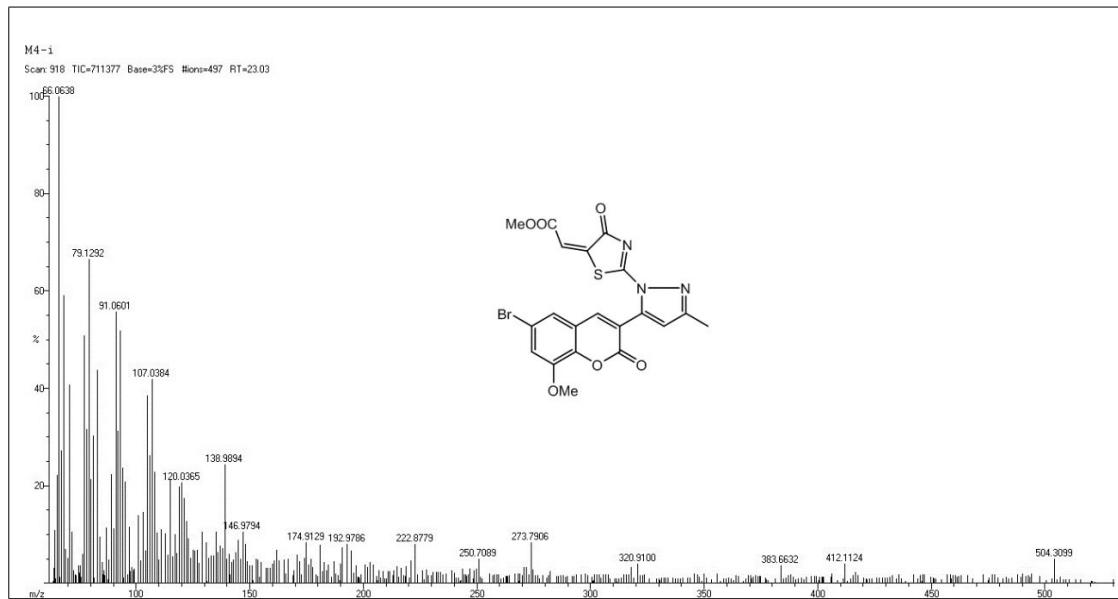


Fig. 36

Entry 4j, Table 3:

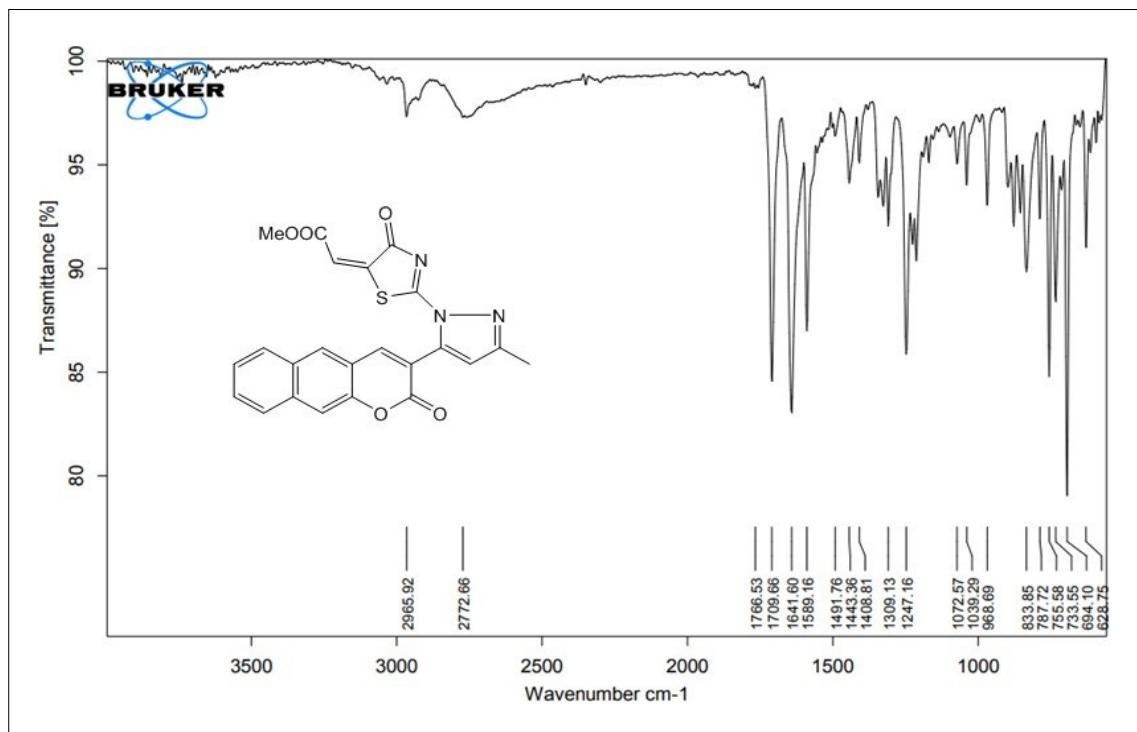


Fig. 37

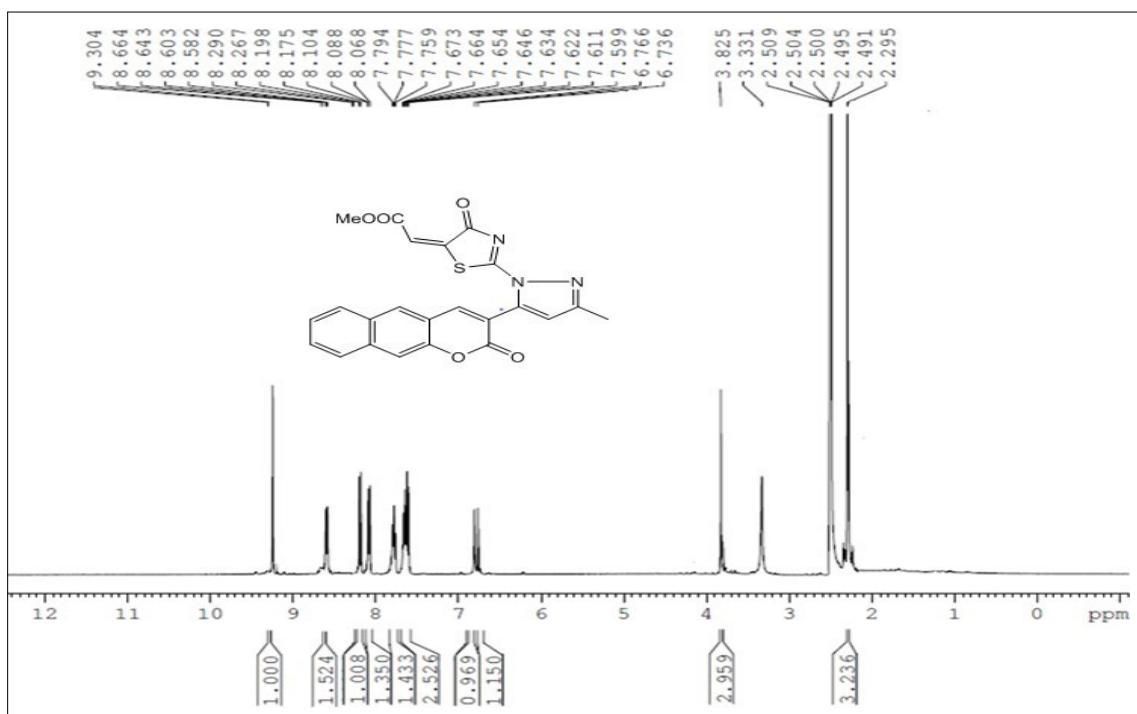


Fig. 38

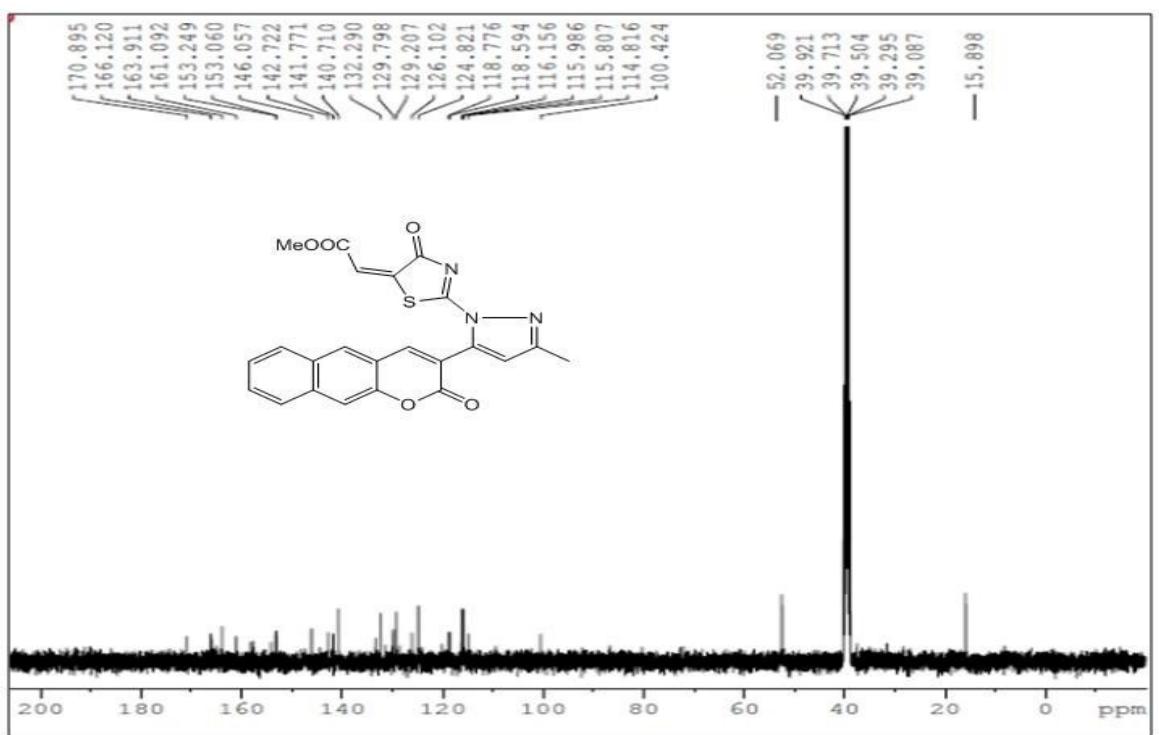


Fig. 39

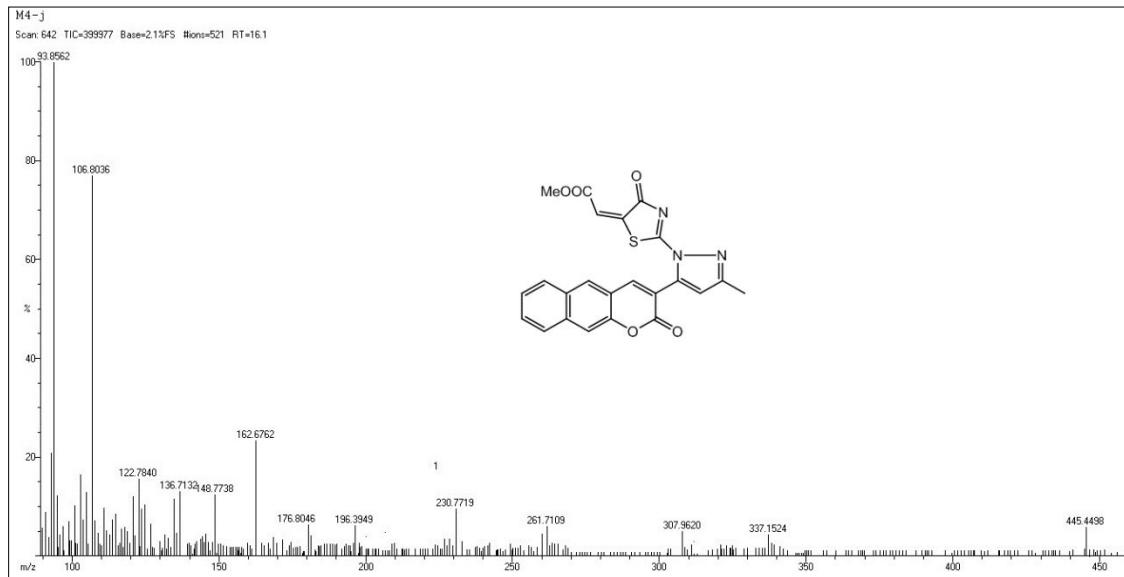


Fig. 40

