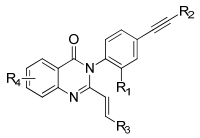
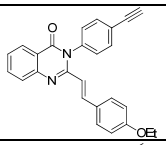
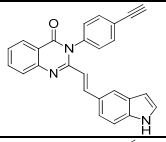
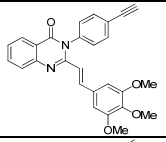
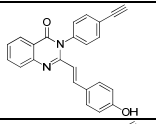
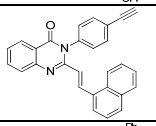
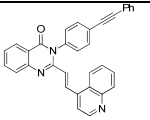
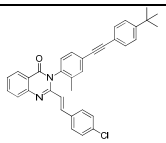
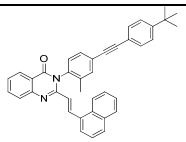
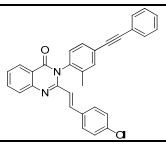
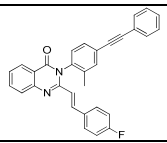
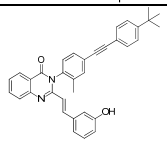
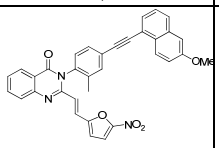
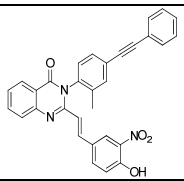
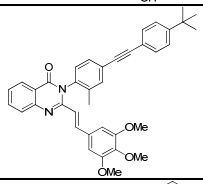
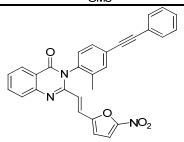
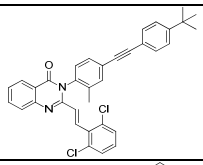
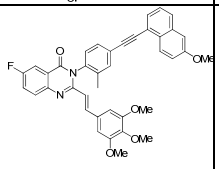
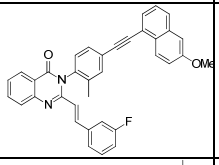
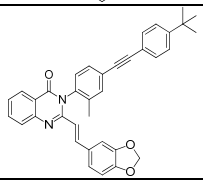
Table S1. Ethynyl Styryl Quinazolinone derivatives



Entry	Structure	Name	Differentiation	Apoptosis
16		(*E*)-2-(4-ethoxystyryl)-3-(4-ethynylphenyl)quinazolin-4(3*H*)-one	-	-
17		(*E*)-2-(2-(1*H*-indol-5-yl)vinyl)-3-(4-ethynylphenyl)quinazolin-4(3*H*)-one	-	-
18		*(E)*-3-(4-ethynylphenyl)-2-(3,4,5-trimethoxystyryl)quinazolin-4(3*H*)-one	-	-
19		(*E*)-3-(4-ethynylphenyl)-2-(4-hydroxystyryl)quinazolin-4(3*H*)-one	+	+
20		(*E*)-3-(4-ethynylphenyl)-2-(2-(naphthalen-1-yl)vinyl)quinazolin-4(3*H*)-one	-	-
21		(*E*)-3-(4-(phenylethynyl)phenyl)-2-(2-(quinolin-4-yl)vinyl)quinazolin-4(3*H*)-one	-	-
22		(*E*)-3-(4-((4-(tert-butyl)phenyl)ethynyl)-2-methylphenyl)-2-(4-chlorostyryl)quinazolin-4(3*H*)-one	-	-
23		(*E*)-3-(4-((4-(tert-butyl)phenyl)ethynyl)-2-methylphenyl)-2-(2-(naphthalen-1-yl)vinyl)quinazolin-4(3*H*)-one	-	-
24		(*E*)-2-(4-chlorostyryl)-3-(2-methyl-4-(phenylethynyl)phenyl)quinazolin-4(3*H*)-one	-	-

25		(*E*)-2-(4-fluorostyryl)-3-(2-methyl-4-(phenylethynyl)phenyl)quinazolin-4(3*H*)-one	-	-
26		(*E*)-3-(4-((4-(tert-butyl)phenyl)ethynyl)-2-methylphenyl)-2-(3-hydroxystyryl)quinazolin-4(3*H*)-one	-	-
27		(*E*)-3-(4-((6-methoxynaphthalen-1-yl)ethynyl)-2-methylphenyl)-2-(2-(5-nitrofuran-2-yl)vinyl)quinazolin-4(3*H*)-one	-	-
28		(*E*)-2-(4-hydroxy-3-nitrostyryl)-3-(2-methyl-4-(phenylethynyl)phenyl)quinazolin-4(3*H*)-one	-	-
29		(*E*)-3-(4-((4-(tert-butyl)phenyl)ethynyl)-2-methylphenyl)-2-(3,4,5-trimethoxystyryl)quinazolin-4(3*H*)-one	-	-
30		(*E*)-3-(2-methyl-4-(phenylethynyl)phenyl)-2-(2-(5-nitrofuran-2-yl)vinyl)quinazolin-4(3*H*)-one	-	-
31		(*E*)-3-(4-((4-(tert-butyl)phenyl)ethynyl)-2-methylphenyl)-2-(2,6-dichlorostyryl)quinazolin-4(3*H*)-one	-	-
32		(*E*)-6-fluoro-3-(4-((6-methoxynaphthalen-1-yl)ethynyl)-2-methylphenyl)-2-(3,4,5-trimethoxystyryl)quinazolin-4(3*H*)-one	-	-
33		(*E*)-2-(3-fluorostyryl)-3-(4-((6-methoxynaphthalen-1-yl)ethynyl)-2-methylphenyl)quinazolin-4(3*H*)-one	-	-
34		(*E*)-2-(2-(benzo[d][1,3]dioxol-5-yl)vinyl)-3-(4-((4-(tert-butyl)phenyl)ethynyl)-2-methylphenyl)quinazolin-4(3*H*)-one	-	-

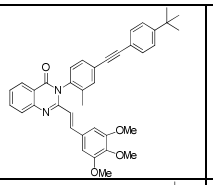
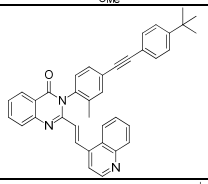
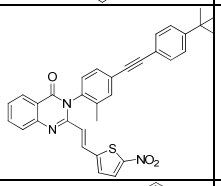
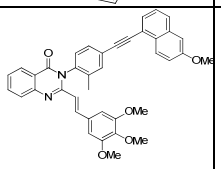
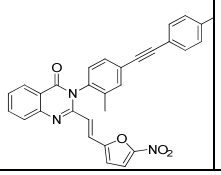
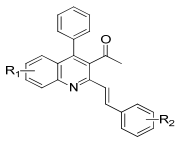
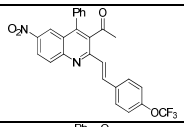
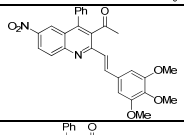
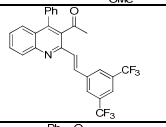
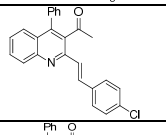
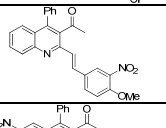
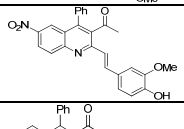
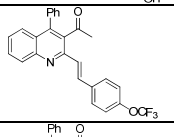
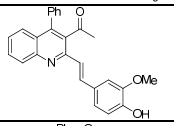
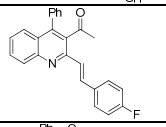
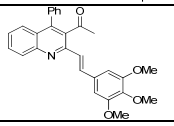
35		(*E*)-3-(4-((4-(tert-butyl)phenyl)ethynyl)-2-methylphenyl)-2-(3,4,5-trimethoxystyryl)quinazolin-4(3*H*)-one	-	-
36		(*E*)-3-(4-((4-(tert-butyl)phenyl)ethynyl)-2-methylphenyl)-2-(2-(quinolin-4-yl)vinyl)quinazolin-4(3*H*)-one	-	-
37		(*E*)-3-(4-((4-(tert-butyl)phenyl)ethynyl)-2-methylphenyl)-2-(2-(5-nitrothiophen-2-yl)vinyl)quinazolin-4(3*H*)-one	-	-
38		(*E*)-3-(4-((6-methoxynaphthalen-1-yl)ethynyl)-2-methylphenyl)-2-(3,4,5-trimethoxystyryl)quinazolin-4(3*H*)-one	-	-
39		(*E*)-3-(4-((4-(tert-butyl)phenyl)ethynyl)-2-methylphenyl)-2-(2-(5-nitrofuran-2-yl)vinyl)quinazolin-4(3*H*)-one	+	+

Table S2. Quinolinone derivatives



Entry	Structure	Name	Differentiation	Apoptosis
40		(*E*)-1-(6-nitro-4-phenyl-2-(4-(trifluoromethoxy)styryl)quinolin-3-yl)ethanone	-	-
41		(*E*)-1-(6-nitro-4-phenyl-2-(3,4,5-trimethoxystyryl)quinolin-3-yl)ethanone	-	-
42		(*E*)-1-(2-(3,5-bis(trifluoromethyl)styryl)-4-phenylquinolin-3-yl)ethanone	-	-
43		(*E*)-1-(2-(4-chlorostyryl)-4-phenylquinolin-3-yl)ethanone	-	-
44		(*E*)-1-(2-(4-methoxy-3-nitrostyryl)-4-phenylquinolin-3-yl)ethanone	-	-
45		(*E*)-1-(2-(4-hydroxy-3-methoxystyryl)-6-nitro-4-phenylquinolin-3-yl)ethanone	-	-
46		(*E*)-1-(4-phenyl-2-(4-(trifluoromethoxy)styryl)quinolin-3-yl)ethanone	-	-
47		(*E*)-1-(2-(4-hydroxy-3-methoxystyryl)-4-phenylquinolin-3-yl)ethanone	-	-
48		(*E*)-1-(2-(4-fluorostyryl)-4-phenylquinolin-3-yl)ethanone	-	-
49		(*E*)-1-(4-phenyl-2-(3,4,5-trimethoxystyryl)quinolin-3-yl)ethanone	-	-

Materials and Methods

Reagents: All *trans* retinoic acid (ATRA) was purchased from Sigma-Aldrich (R2625 St Louis, MO). Compounds **1** to **15** were synthesized at Cancer Science Institute of Singapore. Compounds **16** to **49** were obtained from Indian Institute of Chemical Technology and the synthesis of the compounds were reported earlier.[15] Stock solutions for the compounds were dissolved in DMSO and stored at -20 °C. These compounds were diluted in fresh complete medium before experiment, and the final concentration of DMSO was 0.1 %. Human G-SCF was purchased from Miltenyl Biotec (130-096-345, Bergisch Gladbach, Germany). Human G-CSF was prepared in 0.1 % bovine serum albumin / PBS, and stored at -20 °C.

Cells: HL-60 (CCL-240) cells were purchased from American Type Culture Collection (ATCC, Manassas, VA). These cell lines were maintained in RPMI1640 with 10 % fetal bovine serum at 37 °C with 5 % CO_2.

Morphological analysis and Nitro Blue Tetrazolium Reduction Assay: HL-60 cells were treated with 0.1 % DMSO, 10 μM of **1**, 3 μM of **2**, **5**, **6**, **39** for 7 days and stained with Wright-Giemsa. Maximum cell concentrations were adjusted lower than 100,000 /mL. These treated HL-60 cells were incubated with 1.0 mg/mL nitroblue tetrazolium/PBS, 0.36 μM Phorbol-12-myristate-13-acetate (PMA) at 37 °C for 30-40 minutes and stained with safranin O. Morphological differentiation and apoptosis were evaluated as – (0-5%), + (5-30%), ++ (30-60%), and +++ (more than 60%).

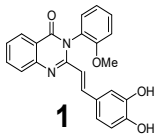
Flow cytometry: HL-60 cells treated with 0.1 % DMSO, 10 μM of **1**, 3 μM of **2**, **5**, **6**, **39** with or without 60 ng/mL human G-CSF for 7 days were stained with APC anti-

mouse/human CD11b Antibody, Biolegend (101211, San Diego, CA) and analyzed by LSRII flow (BD Biosciences, Franklin Lakes, NJ). We used FlowJo (FLOWJO, LLC, Ashland, OR) to analyze data.

Quantitative Real-time PCR (QT-PCR): Total RNA was isolated from HL-60 cells using RNeasy Mini Kit (Qiagen, Valencia, CA). Complementary DNA was synthesized using SuperScript II (Thermo Fisher Scientific, Waltham, MA). The mRNA levels of genes were measured by QT-PCR using Rotor Gene 6000 sequence detection system (Qiagen, Valencia, CA) with iTaq Universal SYBR Green Supermix (BIO-RAD, Hercules, CA). The expression levels of the glyceraldehyde 3-phosohate dehydrogenase (GAPDH) were used for normalization. Reactions were performed in technical triplicates. The primers for qPCR, human C/EBPα sense 5'- TGTGCCTTGGAAATGCAAAC -3', antisense 5'- CGGGAAGGAGGCAGGAAA -3', human C/EBPε sense 5'- GCGTTCTCAAGGCCCCTT -3', antisense 5'- GGGAGGGCGCCTTCAG -3', human GAPDH sense 5'- CCACATCGCTCAGACACCAT -3', antisense 5'- CCAGGCGCCCAATACG -3'.

Statistical analysis: Differences between the experimental groups were tested with Student's t-test. P-values of less than 0.05 were considered statistically significant.

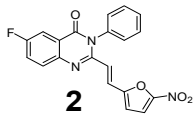
Spectral data of compound **1**:



1

^{1}H NMR (DMSO-d$_6$, 400 MHz): 9.25 (brs, 1H), 8.81 (brs, 1H), 8.57 (d, 1H, *J* = 8.0 Hz), 8.30 (m, 3H), 7.91 (m, 2H), 7.62 (m, 3H), 7.17 (m, 3H), 6.52 (d, 1H, *J* = 16 Hz, *trans* double bond), 4.12 (s, 3H). ^{13}C NMR (DMSO-d$_6$, 100 MHz): 160.96, 154.41, 152.40, 147.22, 146.69, 144.76, 140.87, 134.00, 130.51, 129.24, 126.65, 126.33, 126.06, 125.50, 124.85, 120.70, 119.84, 115.22, 114.60, 113.79, 111.82, 55.0. HPLC: tR = 13.8 min (96% purity); LCMS (ESI): *m/z* for $C_{23}H_{19}N_2O_4^+$ 387 ([M+H]$^+$, found).

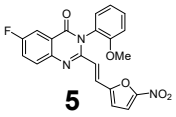
Spectral data of compound **2**:



2

^{1}H NMR (DMSO-d$_6$, 400 MHz): 7.97 (dd, 1H, *J* = 4, 8.0 Hz), 7.83 (m, 2H), 7.64 (m, 3H), 7.57 (dt, 1H, *J* = 4, 8 Hz), 7.32 (m, 3H), 6.67 (d, 1H, *J* = 4.0 Hz), 6.61 (d, 1H, *J* = 16 Hz, *trans* double bond). ^{13}C NMR (DMSO-d$_6$, 100 MHz): 169.6, 160.7, 156.9, 152.3, 150.9, 149.3, 145.7, 140.9, 133.0, 131.1, 130.8, 128.1, 124.9, 122.0, 119.0, 115.6, 113.1, 112.7. HPLC: tR = 18.7 min (98% purity); LCMS (ESI): *m/z* for $C_{20}H_{13}FN_3O_4^+$ 378 ([M+H]$^+$, found).

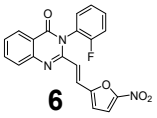
Spectral data of compound **5**:



5

^{1}H NMR (DMSO-d$_6$, 400 MHz): 7.98 (dd, 1H, *J* = 4, 8.0 Hz), 7.82 (m, 2H), 7.60 (m, 2H), 7.30 (d, 1H, *J* = 4 Hz), 7.26 (m, 1H), 7.20 (m, 2H), 6.67 (d, 1H, *J* = 4 Hz), 6.63 (d, 1H, *J* = 16 Hz, *trans* double bond), 3.80 (s, 3H). ^{13}C NMR (DMSO-d$_6$, 100 MHz): 162.7, 160.2, 159.9, 154.7, 152.7, 152.3, 151.5, 132.1, 129.5, 128.5, 127.5, 124.0, 123.7, 122.1, 121.7, 120.9, 116.4, 113.2, 112.7, 112.5, 56.0. HPLC: tR = 18.9 min (97% purity); LCMS (ESI): *m/z* for $C_{21}H_{15}FN_3O_5^+$ 408 ([M+H]$^+$, found).

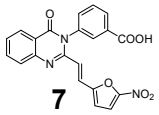
Spectral data of compound **6**:



6

^{1}H NMR (DMSO-d$_6$, 400 MHz): 8.34 (dd, 1H, *J* = 4, 8.0 Hz), 7.86 (m, 3H), 7.62 (m, 1H), 7.56 (dt, 1H, *J* = 4, 8 Hz), 7.43 (m, 3H), 7.31 (d, 1H, *J* = 4.0 Hz), 6.70 (d, 1H, *J* = 4 Hz), 6.65 (d, 1H, *J* = 16 Hz, *trans* double bond). ^{13}C NMR (DMSO-d$_6$, 100 MHz): 160.46, 158.60, 156.12, 152.65, 151.74, 149.82, 146.94, 135.37, 132.22, 131.15, 127.46, 126.60, 125.79, 125.24, 123.83, 121.82, 120.30, 117.36, 116.87, 114.69. HPLC: tR = 18.6 min (98% purity); LCMS (ESI): *m/z* for C20H13N3O4$^+$ 378 ([M+H]$^+$, found).

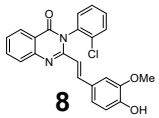
Spectral data of compound **7**:



7

^{1}H NMR (DMSO-d$_6$, 400 MHz): d 8.17 (dt, 2H, *J* = 4, 8.0 Hz), 7.92 (brs, 1H), 7.78 (m, 5H), 7.51 (m, 2H), 7.33 (m, 1H), 6.77 (m, 1H), 6.42 (d, 1H, *J* = 16 Hz, *trans* double bond). ^{13}C NMR (DMSO-d$_6$, 100 MHz): 166.23, 161.03, 152.65, 151.31, 149.32, 146.57, 136.01, 134.34, 132.63, 132.29, 130.16, 129.54, 129.40, 127.04, 126.84, 126.35, 124.35, 122.78, 120.36, 114.88, 113.22. HPLC: tR = 15.6 min (99% purity); LCMS (ESI): *m/z* for $C_{21}H_{14}N_3O_6^+$ 404 ([M+H]$^+$, found).

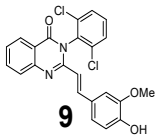
Spectral data of compound **8**:



8

^{1}H NMR (DMSO-d$_6$, 400 MHz): 8.62 (d, 1H, *J* = 4 Hz), 8.07 (dd, 1H, *J* = 4, 8.0 Hz), 7.99 (dt, 1H, *J* = 16 Hz, *trans* double bond), 7.65 (m, 6H), 6.86 (m, 3H), 6.10 (d, 1H, *J* = 16 Hz, *trans* double bond), 5.83 (s, 1H), 3.85 (s, 3H). ^{13}C NMR (DMSO-d$_6$, 100 MHz): 160.14, 152.24, 147.75, 146.61, 143.53, 141.62, 136.00, 134.64, 133.11, 130.95, 130.80, 130.45, 129.78, 129.02, 128.32, 127.74, 122.18, 121.82, 115.89, 114.83, 110.38, 90.56. HPLC: tR = 20.7 min (94% purity); LCMS (ESI): *m/z* for $C_{23}H_{18}ClN_2O_3^+$ 405 ([M+H]$^+$, found).

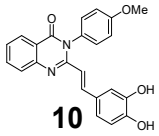
Spectral data of compound **9**:



9

^{1}H NMR (DMSO-d$_6$, 400 MHz): d 8.34 (d, 1H, *J* = 8.0 Hz), 8.08 (brs, 1H), 7.85 (m, 2H), 7.59 (m, 4H), 6.93 (m, 3H), 6.09 (d, 1H, *J* = 16 Hz, *trans* double bond), 5.80 (s, 1H), 3.88 (s, 3H). ^{13}C NMR (DMSO-d$_6$, 100 MHz): 166.8, 146.8, 146.0, 144.5, 136.2, 135.1, 134.8, 131.8, 131.7, 129.6, 129.3, 128.9, 128.1, 127.7, 127.5, 122.7, 121.8, 121.2, 119.2, 115.1, 30.9. HPLC: tR = 18.6 min (92% purity); LCMS (ESI): *m/z* for $C_{23}H_{17}Cl_2N_2O_3^+$ 440 ([M+H]$^+$, found).

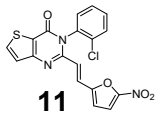
Spectral data of compound **10**:



10

^{1}H NMR (DMSO-d$_6$, 400 MHz): 9.35 (brs, 1H), 8.90 (brs, 1H), 8.56 (d, 1H, *J* = 8.0 Hz), 8.41 (m, 5H), 7.70 (d, 2H, *J* = 8 Hz), 7.46 (d, 2H, *J* = 8 Hz), 7.20 (m, 2H), 6.54 (d, 1H, *J* = 16 Hz, *trans* double bond), 4.27 (s, 3H). ^{13}C NMR (DMSO-d$_6$, 100 MHz): 160.5, 158.7, 152.2, 147.3, 144.8, 144.4, 141.3, 133.6, 128.5, 127.9, 125.7, 125.6, 125.2, 124.6, 120.6, 118.9, 114.7, 113.9, 113.4, 113.2. HPLC: tR = 13.7 min (97% purity); LCMS (ESI): *m/z* for $C_{23}H_{19}N_2O_4^+$ 387 ([M+H]$^+$, found).

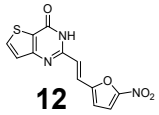
Spectral data of compound **11**:



11

^{1}H NMR (DMSO-d$_6$, 400 MHz): d 7.90 (d, 1H, *J* = 8.0 Hz), 7.81 (d, 1H, *J* = 16 Hz, *trans* double bond), 7.70 (dd, 1H, *J* = 4, 8 Hz), 7.57 (m, 2H), 7.44 (m, 2H), 7.30 (d, 1H, *J* = 4 Hz), 6.68 (d, 1H, *J* = 4 Hz), 6.51 (d, 1H, *J* = 16 Hz, *trans* double bond). ^{13}C NMR (DMSO-d$_6$, 100 MHz): 189.7, 181.0, 170.0, 165.5, 162.3, 138.0, 135.8, 131.8, 131.3, 131.1, 130.3, 128.7, 127.2, 123.7, 122.3, 121.2, 116.0, 113.2. HPLC: tR = 18.0 min (95.8 % purity); LCMS (ESI): *m/z* for $C_{18}H_{11}ClN_3O_4S^+$ 400 ([M+H]$^+$, found).

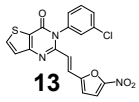
Spectral data of compound **12**:



12

^{1}H NMR (DMSO-d$_6$, 400 MHz): 7.98 (s, 1H), 7.97 (d, 1H, *J* = 4.0 Hz), 7.80 (d, 1H, *J* = 16 Hz, *trans* double bond), 7.55 (d, 1H, *J* = 4.0 Hz), 7.29 (d, 1H, *J* = 4.0 Hz), 7.18 (d, 1H, *J* = 16 Hz, *trans* double bond), 7.01 (d, 1H, *J* = 4.0 Hz). ^{13}C NMR (DMSO-d$_6$, 100 MHz): 156.5, 156.2, 151.9, 150.2, 133.1, 130.7, 123.5, 123.0, 121.7, 120.5, 113.9, 112.7. HPLC: tR = 13.4 min (95.6 % purity); LCMS (ESI): *m/z* for $C_{12}H_8N_3O_4S^+$ 290 ([M+H]$^+$, found).

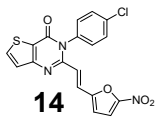
Spectral data of compound **13**:



13

^{1}H NMR (DMSO-d$_6$, 400 MHz): d 7.89 (d, 1H, *J* = 4.0 Hz), 7.77 (d, 1H, *J* = 16 Hz, *trans* double bond), 7.60 (m, 2H), 7.41 (d, 1H, *J* = 4.0 Hz), 7.35 (m, 1H), 7.32 (d, 1H, *J* = 4.0 Hz), 7.2 (dt, 1H, *J* = 4.0, 9.0 Hz), 6.89 (d, 1H, *J* = 4.0 Hz), 6.60 (d, 1H, *J* = 16 Hz, *trans* double bond). ^{13}C NMR (DMSO-d$_6$, 100 MHz): 157.44, 155.85, 152.88, 151.45, 136.85, 135.47, 135.18, 130.86, 130.07, 128.87, 126.83, 125.08, 124.42, 123.02, 122.03, 114.83, 113.14. HPLC: tR = 18.1 min (97.7 % purity); LCMS (ESI): *m/z* for $C_{18}H_{11}ClN_3O_4S^+$ 400 ([M+H]$^+$, found).

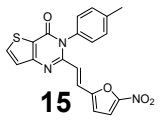
Spectral data of compound **14**:



14

^{1}H NMR (DMSO-d$_6$, 400 MHz): d 7.89 (d, 1H, *J* = 8.0 Hz), 7.76 (d, 1H, *J* = 16 Hz, *trans* double bond), 7.61 (d, 2H, *J* = 8.0 Hz), 7.41 (d, 1H, *J* = 8.0 Hz), 7.32 (d, 1H, *J* = 4.0 Hz), 7.28 (d, 2H, *J* = 8.0 Hz), 6.89 (d, 1H, *J* = 4.0 Hz), 6.62 (d, 1H, *J* = 16 Hz, *trans* double bond). ^{13}C NMR (DMSO-d$_6$, 100 MHz): 172.4, 166.2, 156.2, 153.1, 151.8, 148.1, 136.1, 135.3, 134.4, 130.5, 130.0, 125.3, 124.4, 123.5, 114.7, 113.2. HPLC: tR = 14.5 min (95.4% purity); LCMS (ESI): *m/z* for $C_{18}H_{11}ClN_3O_4S^+$ 400 ([M+H]$^+$, found).

Spectral data of compound **15**:



15

^{1}H NMR (DMSO-d$_6$, 400 MHz): d 7.86 (d, 1H, *J* = 4.0 Hz), 7.74 (d, 1H, *J* = 16 Hz, *trans* double bond), 7.42 (m, 3H), 7.30 (d, 1H, *J* = 4.0 Hz), 7.19 (d, 2H, *J* = 8.0 Hz), 6.66 (m, 2H), 2.5 (s, 3H). ^{13}C NMR (DMSO-d$_6$, 100 MHz): 156.1, 154.6, 151.8, 150.6, 137.9, 133.9, 132.0, 128.9, 126.9, 126.3, 123.7, 122.6, 122.1, 120.4, 114.1, 112.6, 19.6. HPLC: tR = 17.9 min (95% purity); LCMS (ESI): *m/z* for $C_{19}H_{14}N_3O_4S^+$ 380 ($[M+H]^+$, found).