Supporting Information

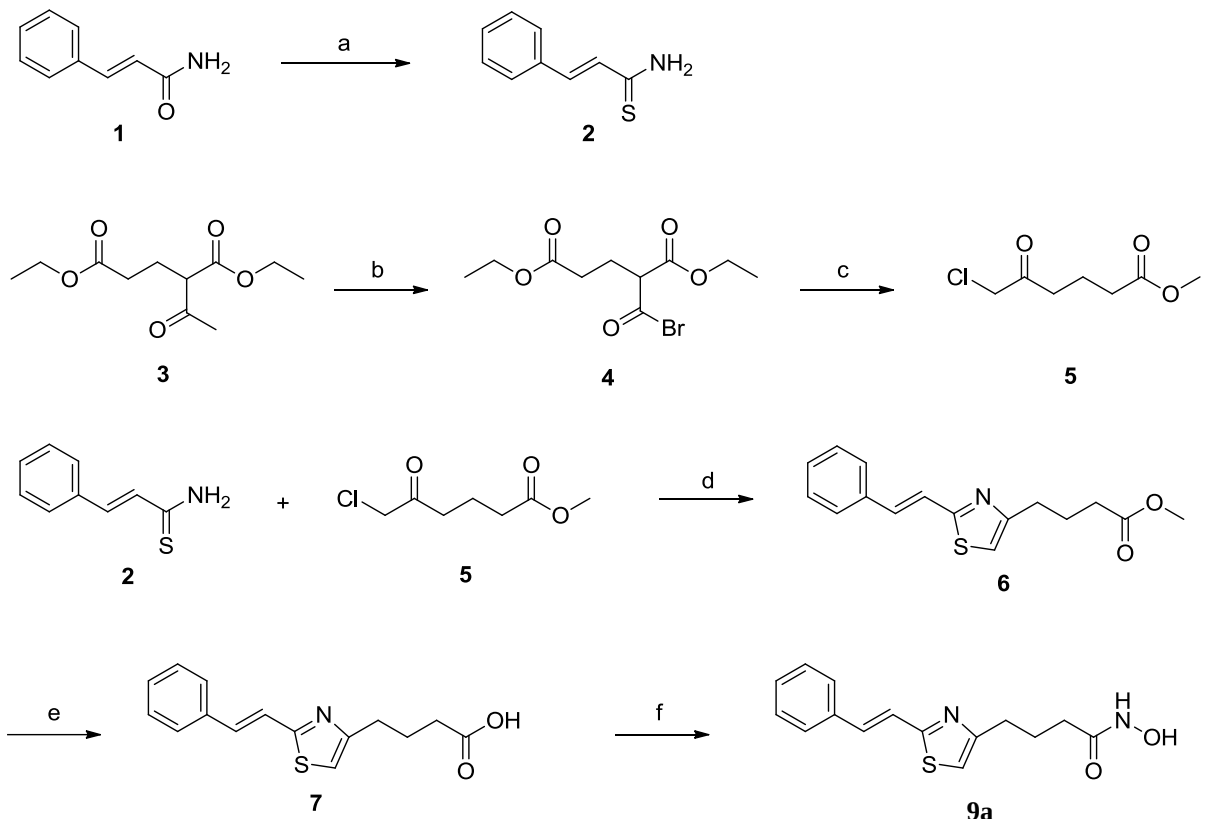

Figure S1

The synthetic routes of 9a. Reagents and conditions: (a) P_2S_5, THF, rt; (b) Br_2, Et_2O, 0℃ then to room temperature (RT); (c) 12N HCl, CH_3COOH, MeOH, 50℃ then to 70℃; (d) MeOH, reflux; (e) 1N-NaOH, MeOH, THF, RT; (f) EDCI, HOBt hydrate, $NH_2OH{\cdot}HCl$, TEA, CH_3CN, DMF, RT. (E)-3-phenylprop-2-enethioamide (2) was prepared from thiation of cinnamide (1) under Lawesson's reagent. Diethyl 2-acetylpentanedioate (3) was treated with bromine to afford acyl bromide, which was converted to methyl 6-chloro-5-oxohexanoate (5) using 12N HCl and acetic acid. Next, (E)-3-phenylprop-2-enethioamide (2) was coupled with methyl 6-chloro-5-oxohexanoate (5) to give (E)-methyl 4-(2-styrylthiazol-4-yl)butanoate (6). Treatment of (E)-methyl 4-(2-styrylthiazol-4-yl)butanoate (6) with $NH_2OH{\cdot}HCl$, EDCI, HOBt hydrate produced the compound 9a. Commercially available reagents were used without

additional purification, unless otherwise stated. All reactions were performed under an inert atmosphere of nitrogen or argon. Nuclear magnetic resonance spectra (^{1}H and ^{13}C NMR) were recorded on a Bruker Unity 300 MHz and Varian Unit 500 MHz spectrometer for CD_3OD solutions, and chemical shifts are reported as parts per million (ppm) relative to, respectively, residual CD_3OD δH (3.31 ppm) and CD_3OD δ_C (49.00 ppm) as internal standards. Resonance patterns are reported with the notations s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). Coupling constants (*J*) are reported in hertz (Hz). Thin layer chromatography was carried out using plates coated with Kieselgel 60F254 (Merck). For flash column chromatography, E. Merck Kieselgel 60 (230-400 mesh) was used.

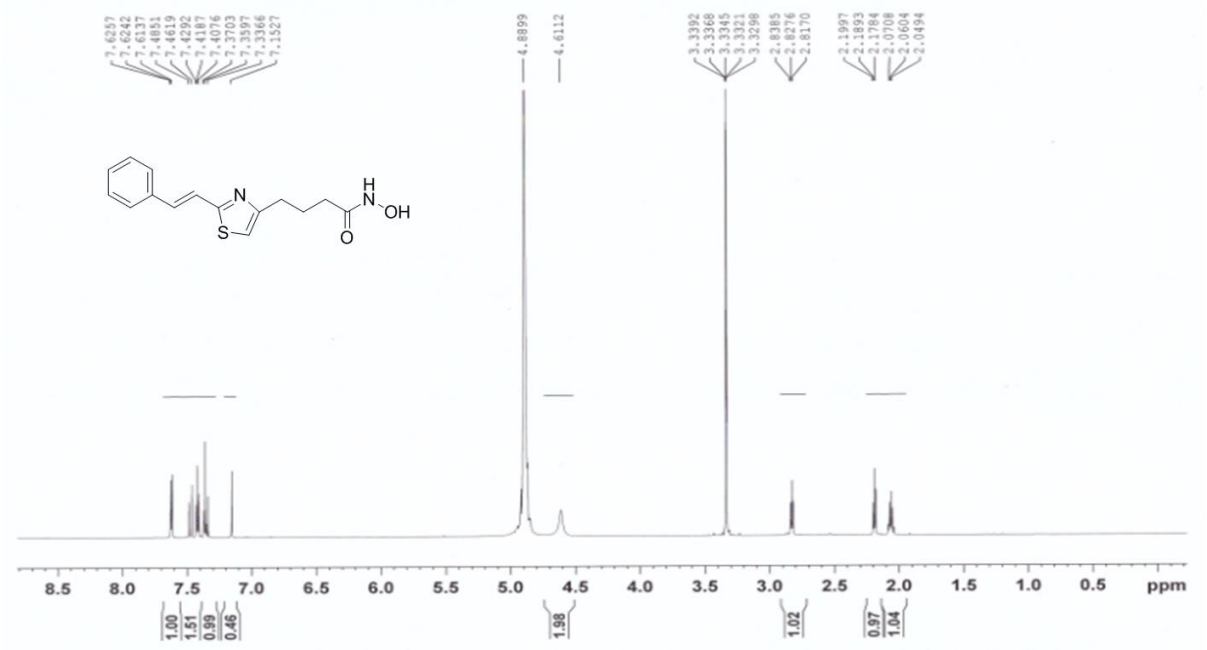

Figure S2

^{1}H NMR spectrum of 9a. ^{1}H NMR (500MHz, CD_3OD): δ 7.62 (d, *J* = 5.6 Hz, 2H), 7.48-7.33 (m, *J* = 5H), 7.15 (s, 1H), 2.83-2.81 (t, *J* = 10 Hz, 2H), 2.19-2.17 (t, *J* = 10 Hz, 2H), 2.07-2.05 (t, *J* = 10 Hz, 2H)

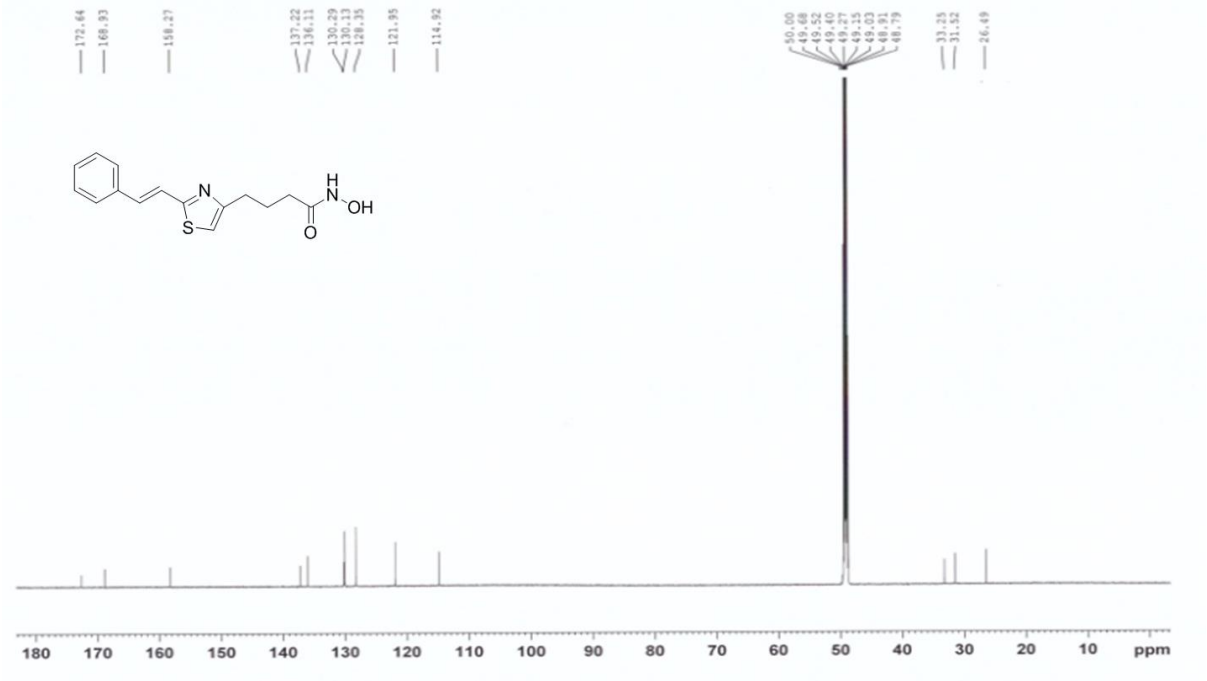

Figure S3

^{13}C NMR spectrum of 9a. ^{13}C NMR (125MHz, CD_3OD): δ 172.64, 168.93, 158.27, 137.22, 136.11, 130.29, 130.13, 128.35, 121.95, 114.92, 33.25, 31.52, 26.49

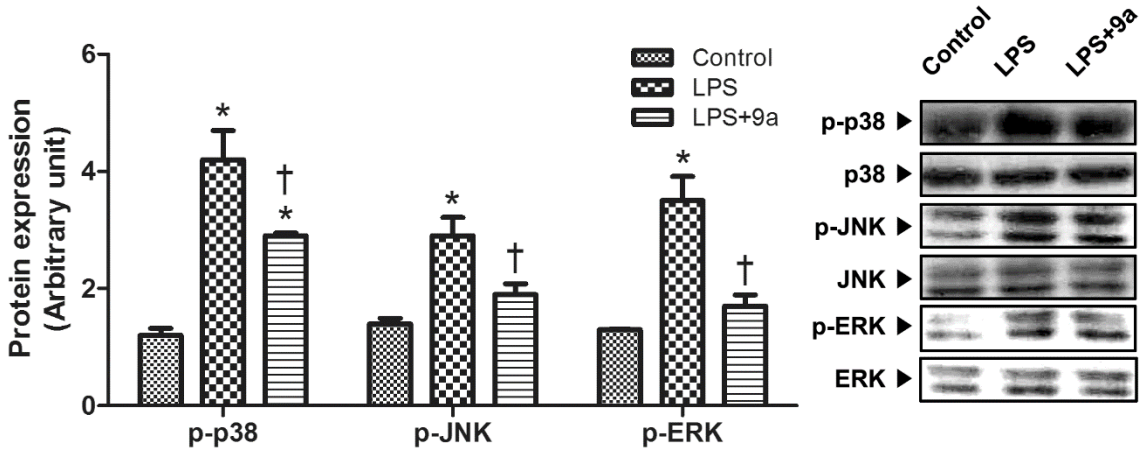

Figure S4

Effect of 9a on phosphorylation of MAPK in LPS-stimulated Kupffer cells. Kupffer cells were isolated from SD rats (male; 160-180 g) by differential centrifugation using Percoll. After the liver was digested with collagenase-contained buffer, the suspension was filtered through cell strainer and cell fraction was obtained by centrifugation. The Kupffer cells fraction was collected, centrifuged at 1700 rpm for 5 min and suspended again in RPMI 1640 media. The Kupffer cells were incubated with 12.5 μM 9a 1 h before LPS treatment (10 $ng \cdot mL^{-1}$). The cell were harvested 24 h after LPS treatment. Phosphorylation of p38, JNK and ERK significantly increased to 3.5-, 2.1- and 2.7-fold than those of control group. The results are presented as mean ± SEM of independent experiments. Significantly different ($^{*}P<0.05$) from control. Significantly different ($^{\dagger}P<0.05$) from LPS.