

Supplementary Information

Aminonaphthoquinone Mannich Bases Derived from Lawsone and Their Copper(II) Complex Derivatives: Synthesis and Potential Cholinesterase Inhibitors as Identified by On-flow Assay

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Data of compounds 1-10

3-[N-(*n*-Butyl)4-fluoro-aminobenzyl]-2-hydroxy-1,4-naphthoquinone (1)

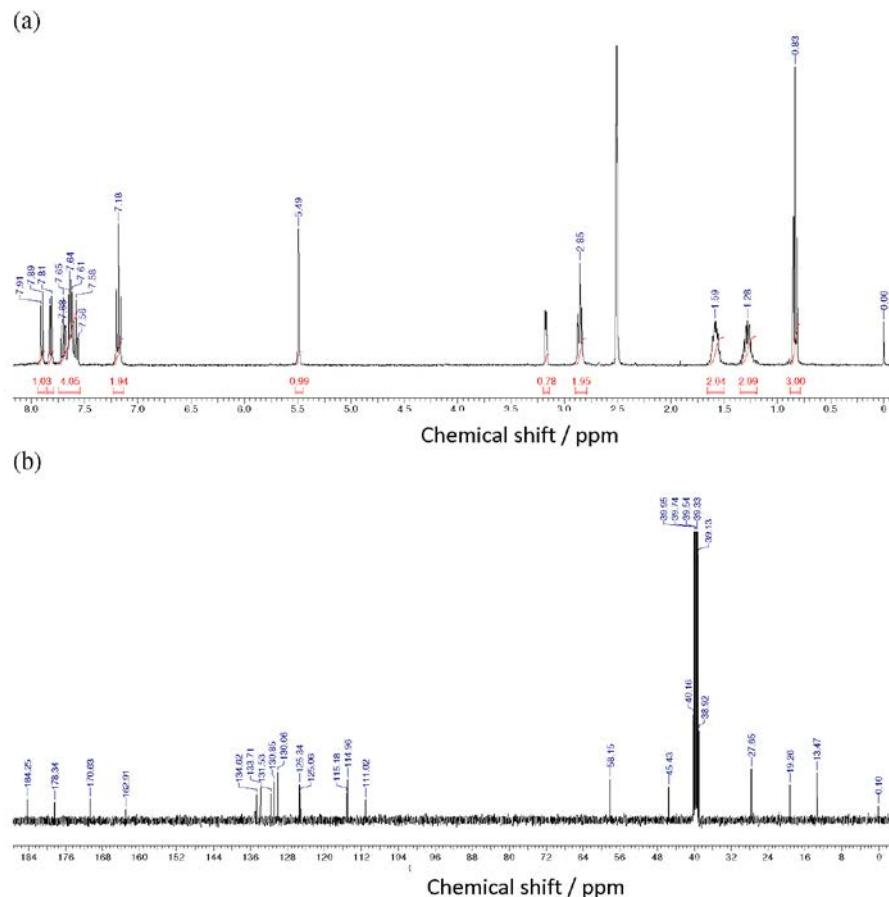


Figure S1. ¹H NMR spectrum (400 MHz, DMSO-*d*₆) (a); ¹³C NMR spectrum (100 MHz, DMSO-*d*₆) (b); IR (KBr) (c); UV-Vis (d); mass spectrum (e) of compound 1.

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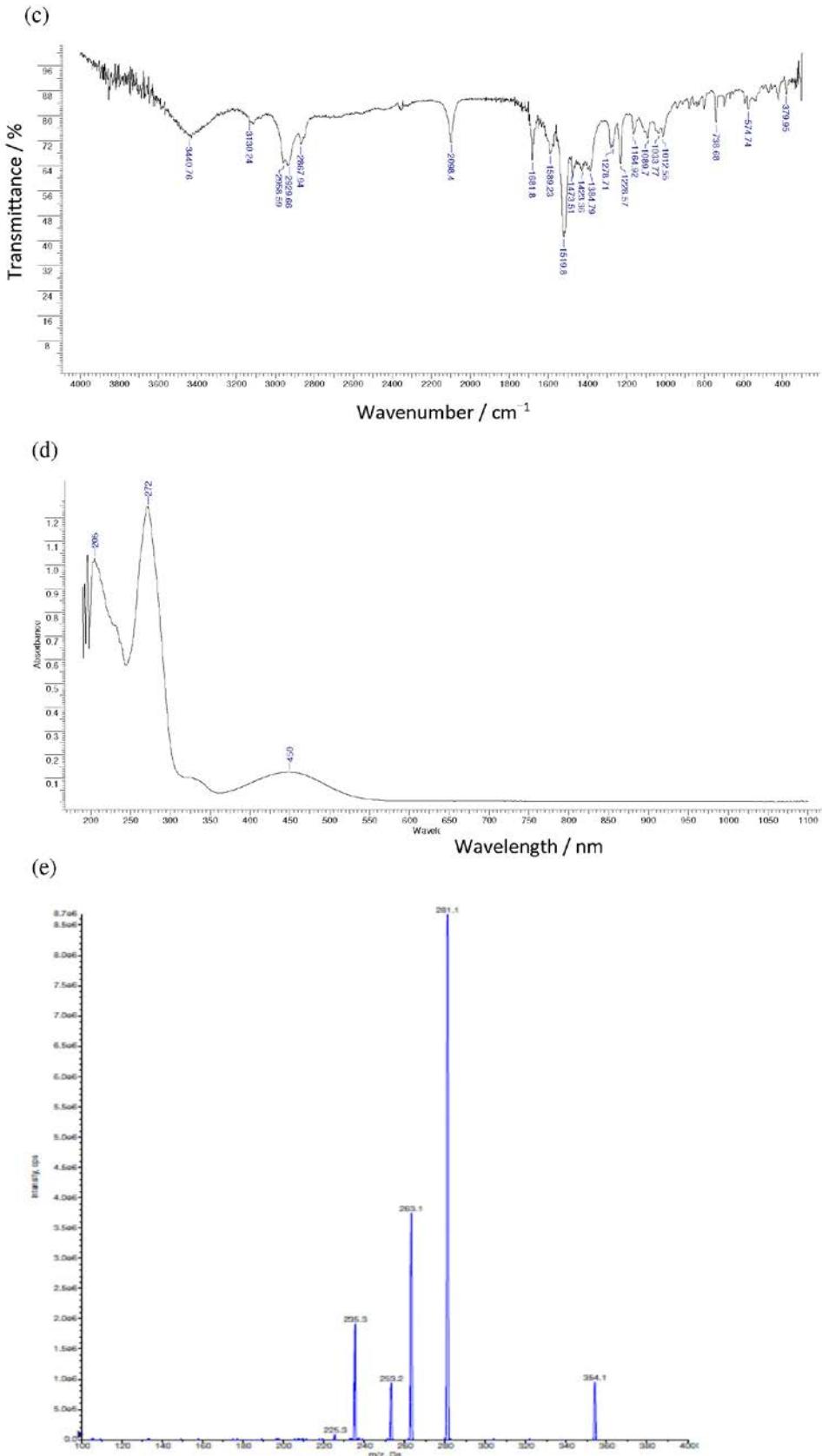


Figure S1. ^1H NMR spectrum (400 MHz, $\text{DMSO}-d_6$) (a); ^{13}C NMR spectrum (100 MHz, $\text{DMSO}-d_6$) (b); IR (KBr) (c); UV-Vis (d); mass spectrum (e) of compound **1** (cont.).

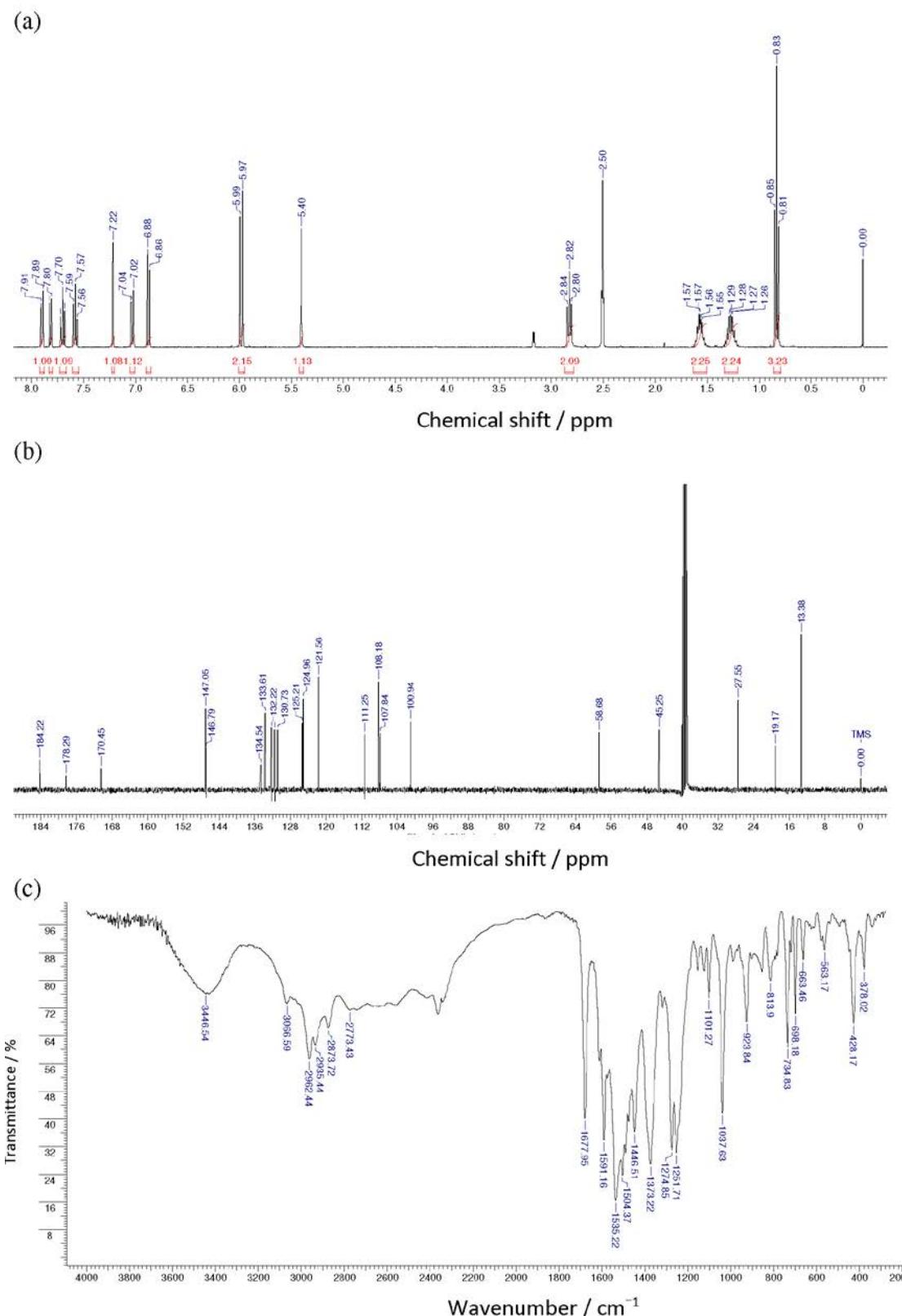
3-[*N*-(*n*-Butyl)aminopiperonyl]-2-hydroxy-1,4-naphthoquinone (**2**)

Figure S2. ^1H NMR spectrum (400 MHz, $\text{DMSO}-d_6$) (a); ^{13}C NMR spectrum (100 MHz, $\text{DMSO}-d_6$) (b); IR (KBr) (c); UV-Vis (d); mass spectrum (e) of compound **2**.

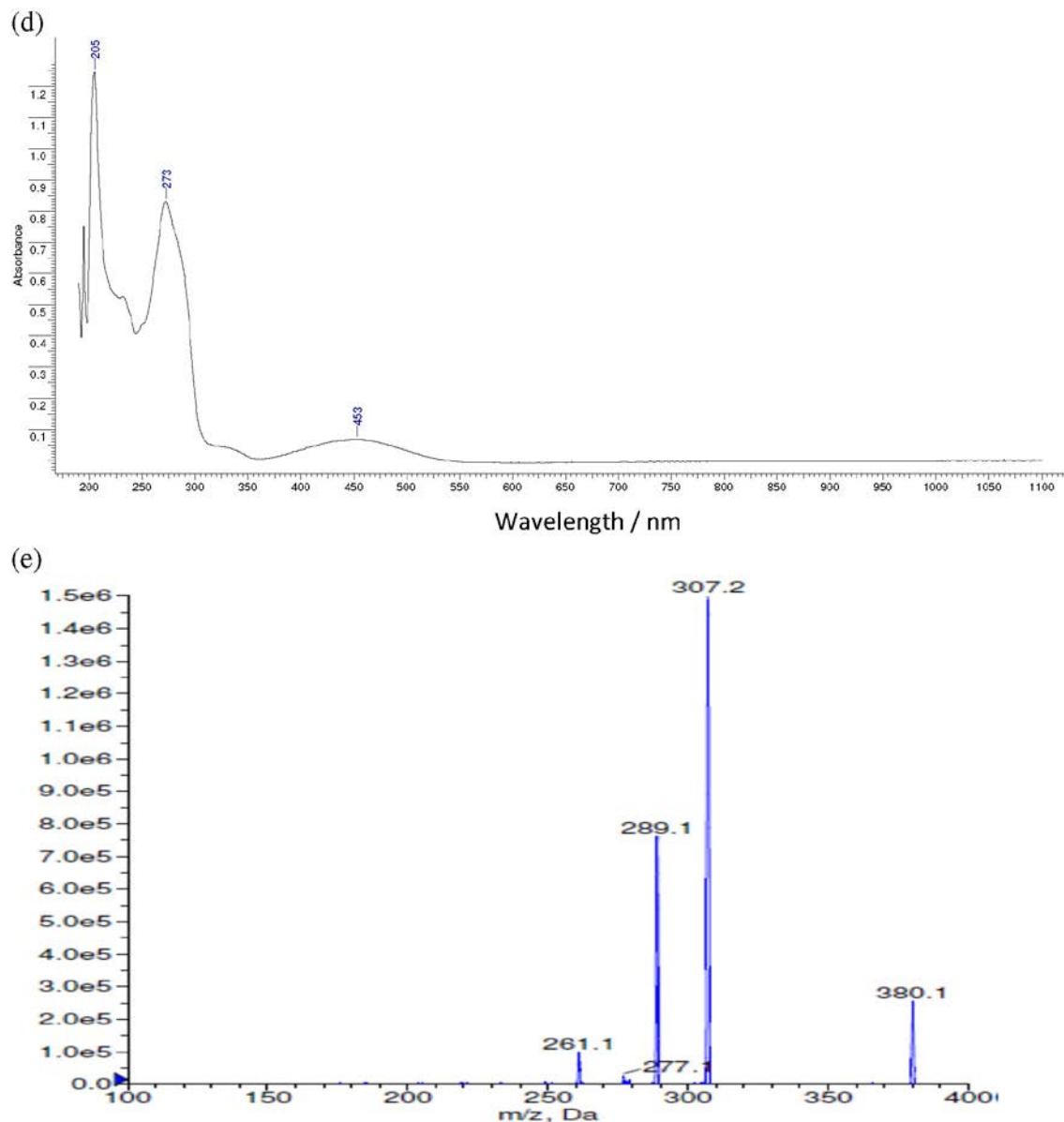


Figure S2. ^1H NMR spectrum (400 MHz, $\text{DMSO}-d_6$) (a); ^{13}C NMR spectrum (100 MHz, $\text{DMSO}-d_6$) (b); IR (KBr) (c); UV-Vis (d); mass spectrum (e) of compound 2 (cont.).

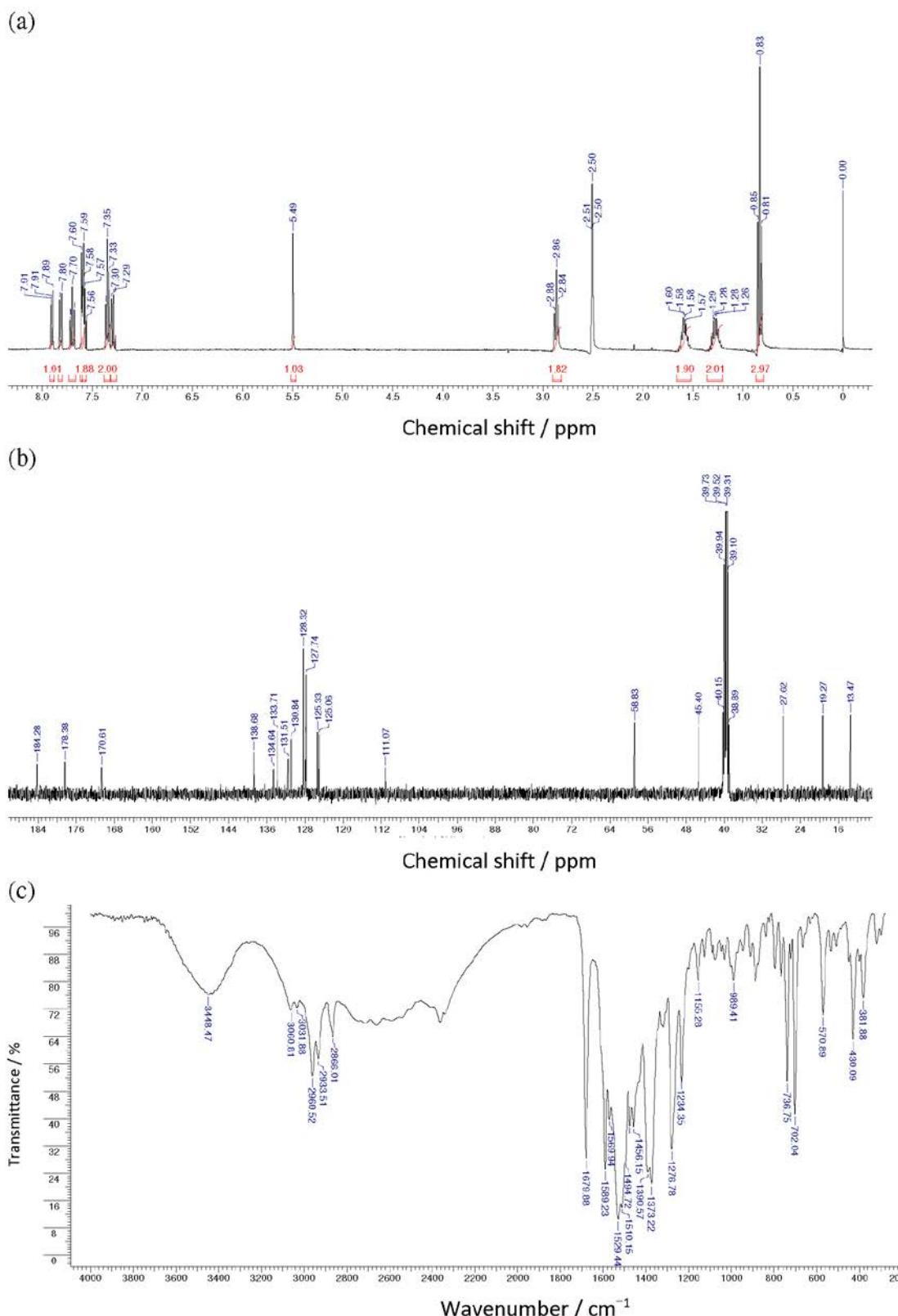
3-[*N*(*n*-Butyl)aminobenzyl]-2-hydroxy-1,4-naphthoquinone (**3**)

Figure S3. ^1H NMR spectrum (400 MHz, $\text{DMSO}-d_6$) (a); ^{13}C NMR spectrum (100 MHz, $\text{DMSO}-d_6$) (b); IR (KBr) (c); UV-Vis (d); mass spectrum (e) of compound **3**.

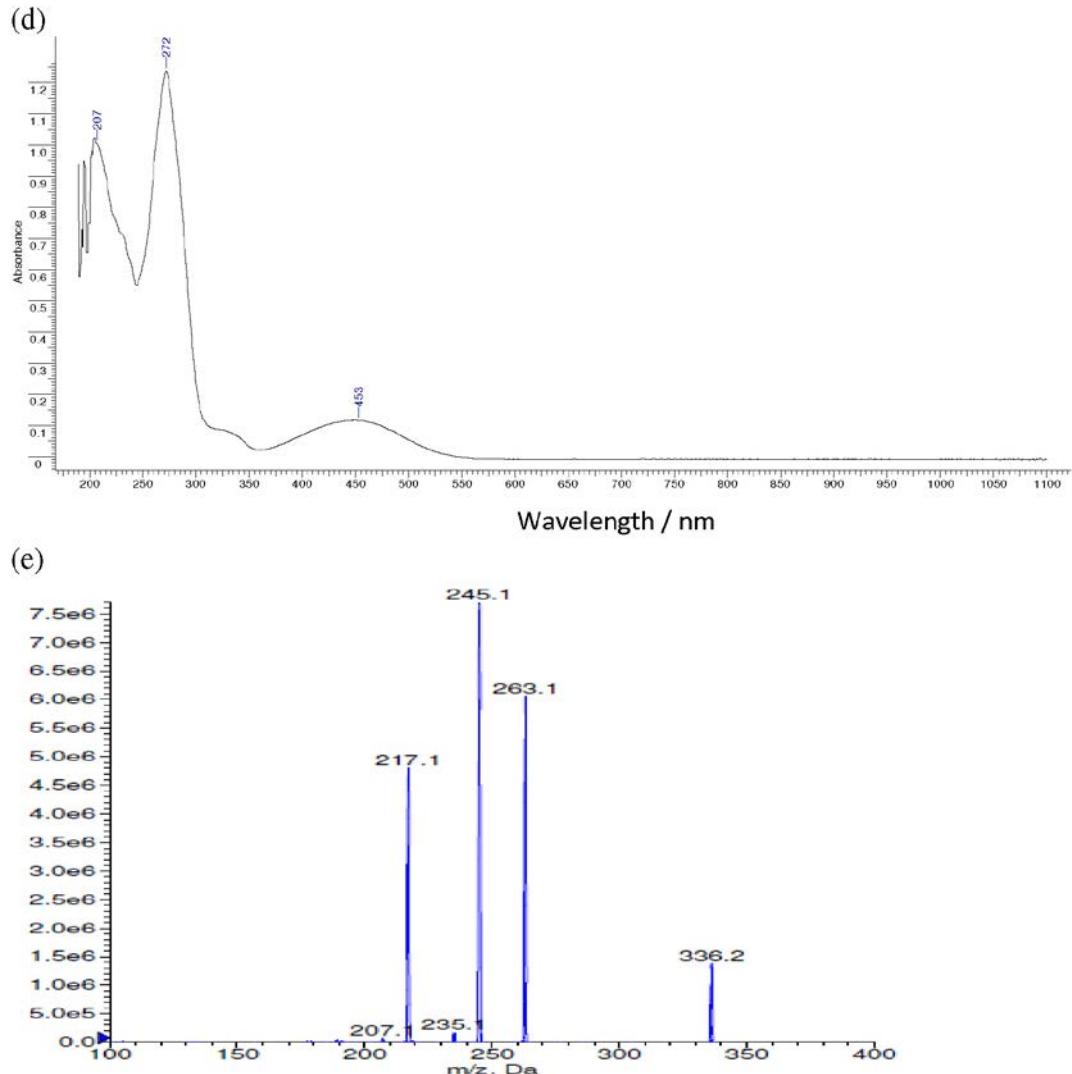


Figure S3. ^1H NMR spectrum (400 MHz, $\text{DMSO}-d_6$) (a); ^{13}C NMR spectrum (100 MHz, $\text{DMSO}-d_6$) (b); IR (KBr) (c); UV-Vis (d); mass spectrum (e) of compound 3 (cont.).

3-[*N*-(*n*-Octyl)4-fluoro-aminobenzyl]-2-hydroxy-1,4-naphthoquinone (4**)**

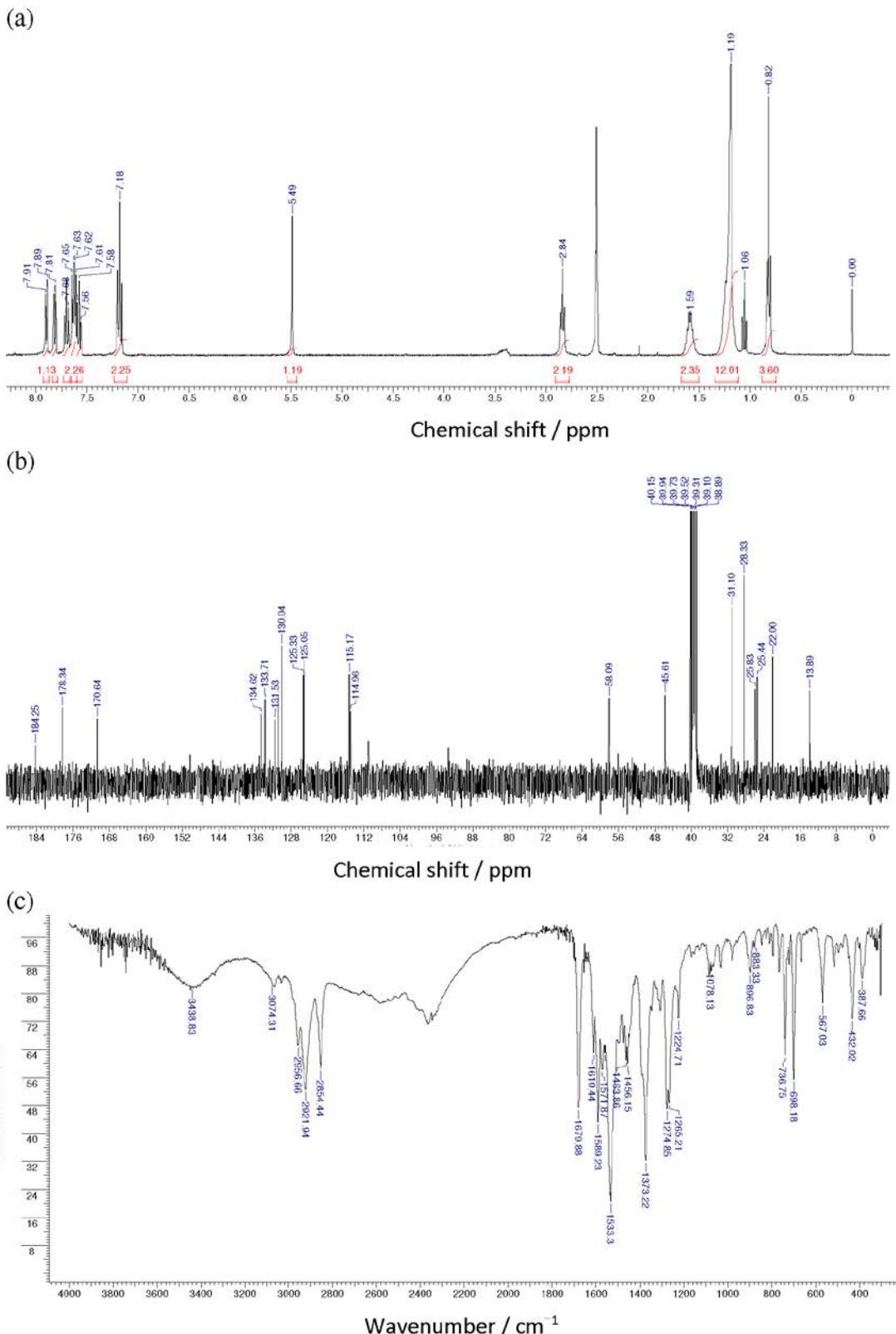


Figure S4. ^1H NMR spectrum (400 MHz, $\text{DMSO}-d_6$) (a); ^{13}C NMR spectrum (100 MHz, $\text{DMSO}-d_6$) (b); IR (KBr) (c); UV-Vis (d); mass spectrum (e) of compound **4**.

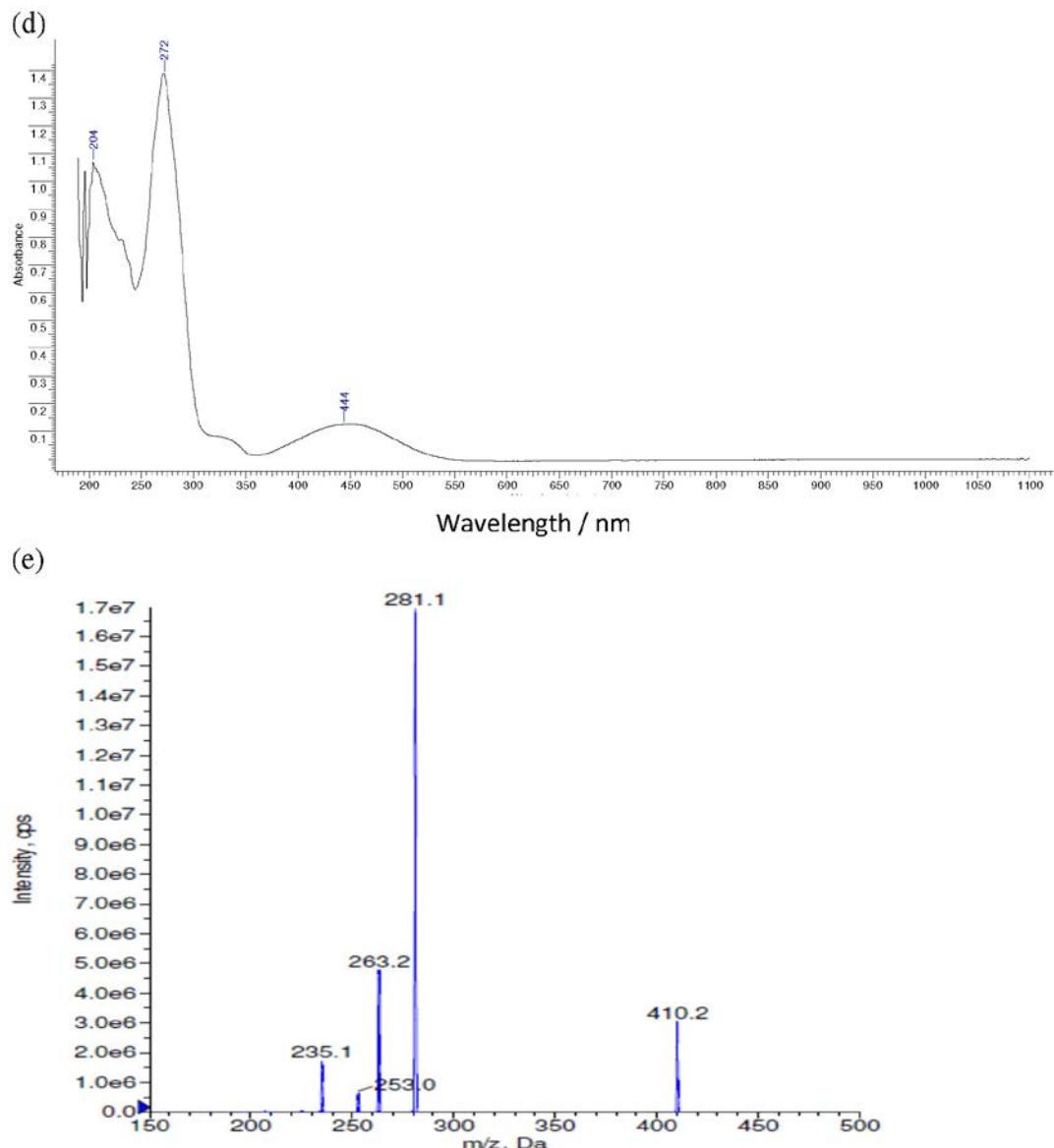


Figure S4. ^1H NMR spectrum (400 MHz, $\text{DMSO}-d_6$) (a); ^{13}C NMR spectrum (100 MHz, $\text{DMSO}-d_6$) (b); IR (KBr) (c); UV-Vis (d); mass spectrum (e) of compound 4 (cont.).

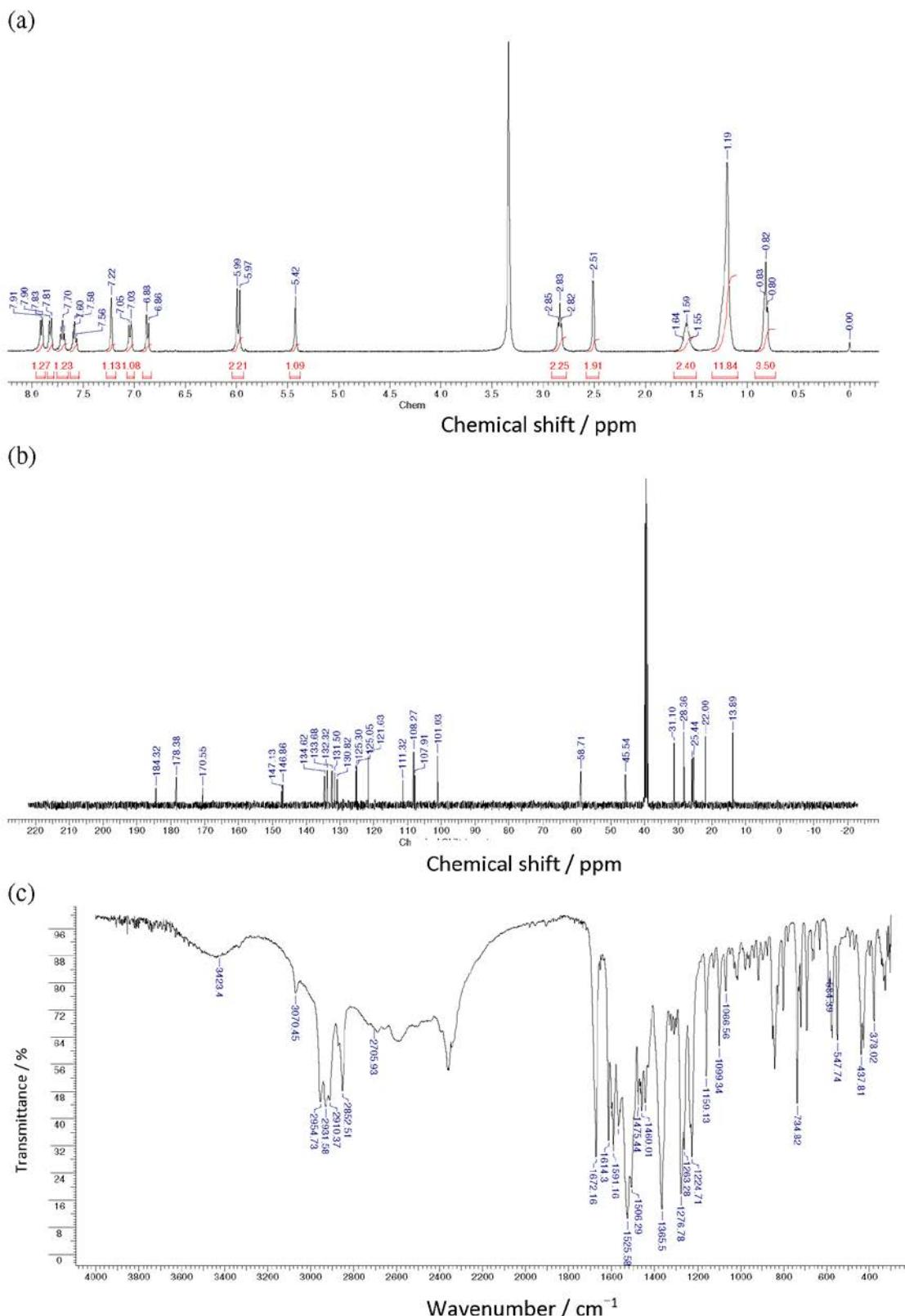
3-[*N*(*n*-Octyl)aminopiperonyl]-2-hydroxy-1,4-naphthoquinone (**5**)

Figure S5. ^1H NMR spectrum (400 MHz, DMSO- d_6) (a); ^{13}C NMR spectrum (100 MHz, DMSO- d_6) (b); IR (KBr) (c); UV-Vis (d); mass spectrum (e) of compound **5**.

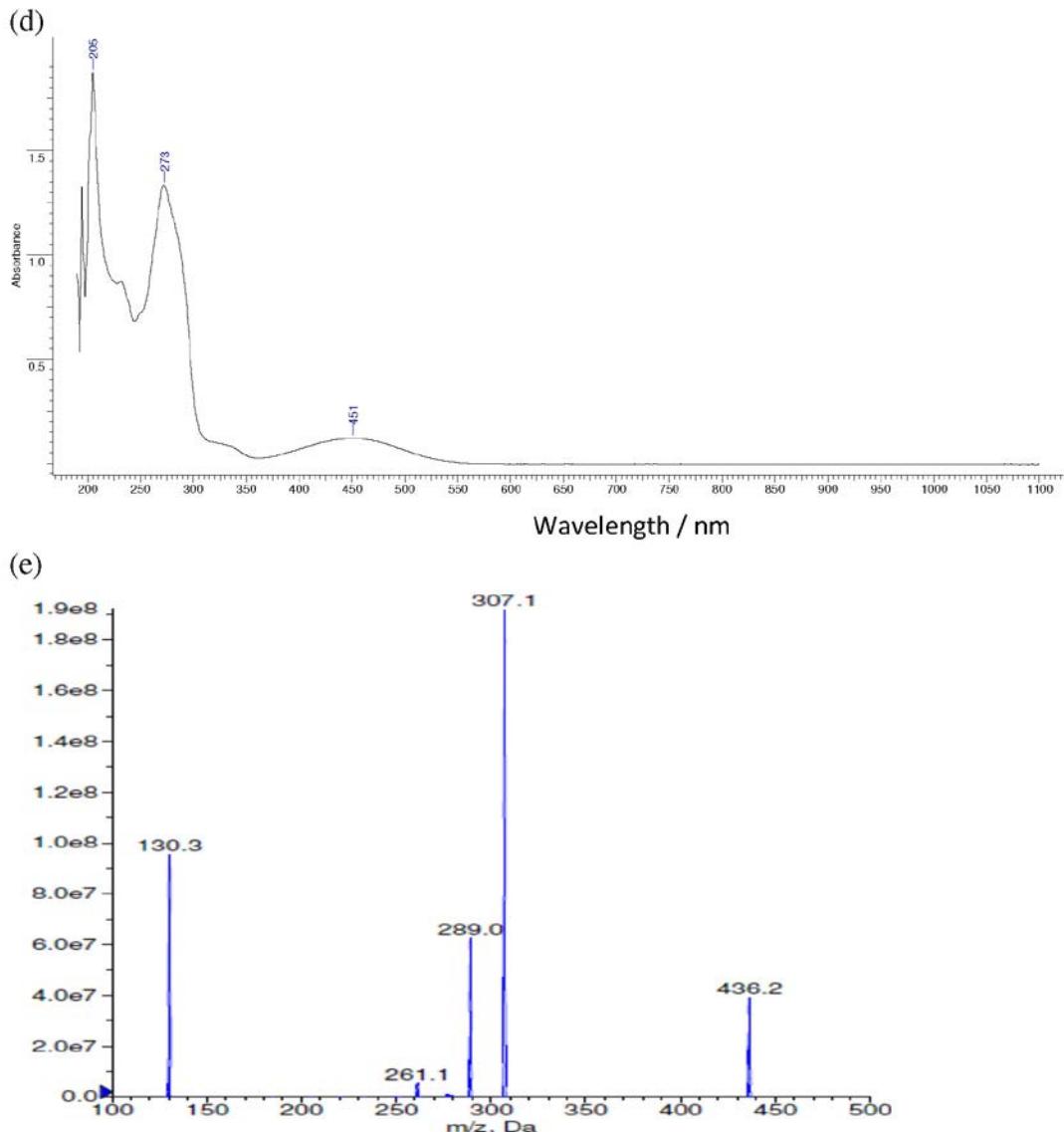


Figure S5. ^1H NMR spectrum (400 MHz, $\text{DMSO}-d_6$) (a); ^{13}C NMR spectrum (100 MHz, $\text{DMSO}-d_6$) (b); IR (KBr) (c); UV-Vis (d); mass spectrum (e) of compound 5 (cont.).

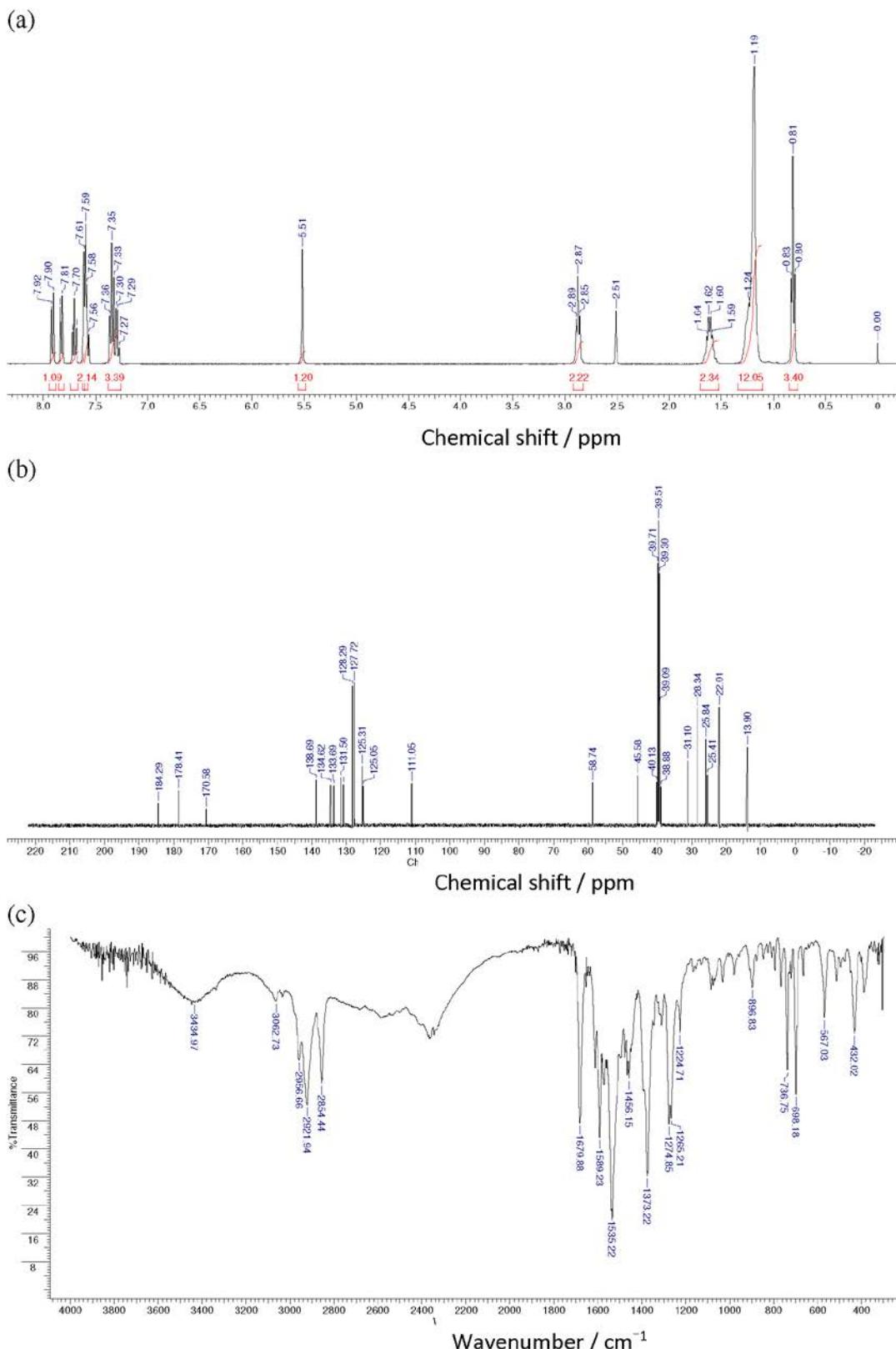
3-[*N*(*n*-Octyl)aminobenzyl]-2-hydroxy-1,4-naphthoquinone (6**)**

Figure S6. ^1H NMR spectrum (400 MHz, $\text{DMSO}-d_6$) (a); ^{13}C NMR spectrum (100 MHz, $\text{DMSO}-d_6$) (b); IR (KBr) (c); UV-Vis (d); mass spectrum (e) of compound **6**.

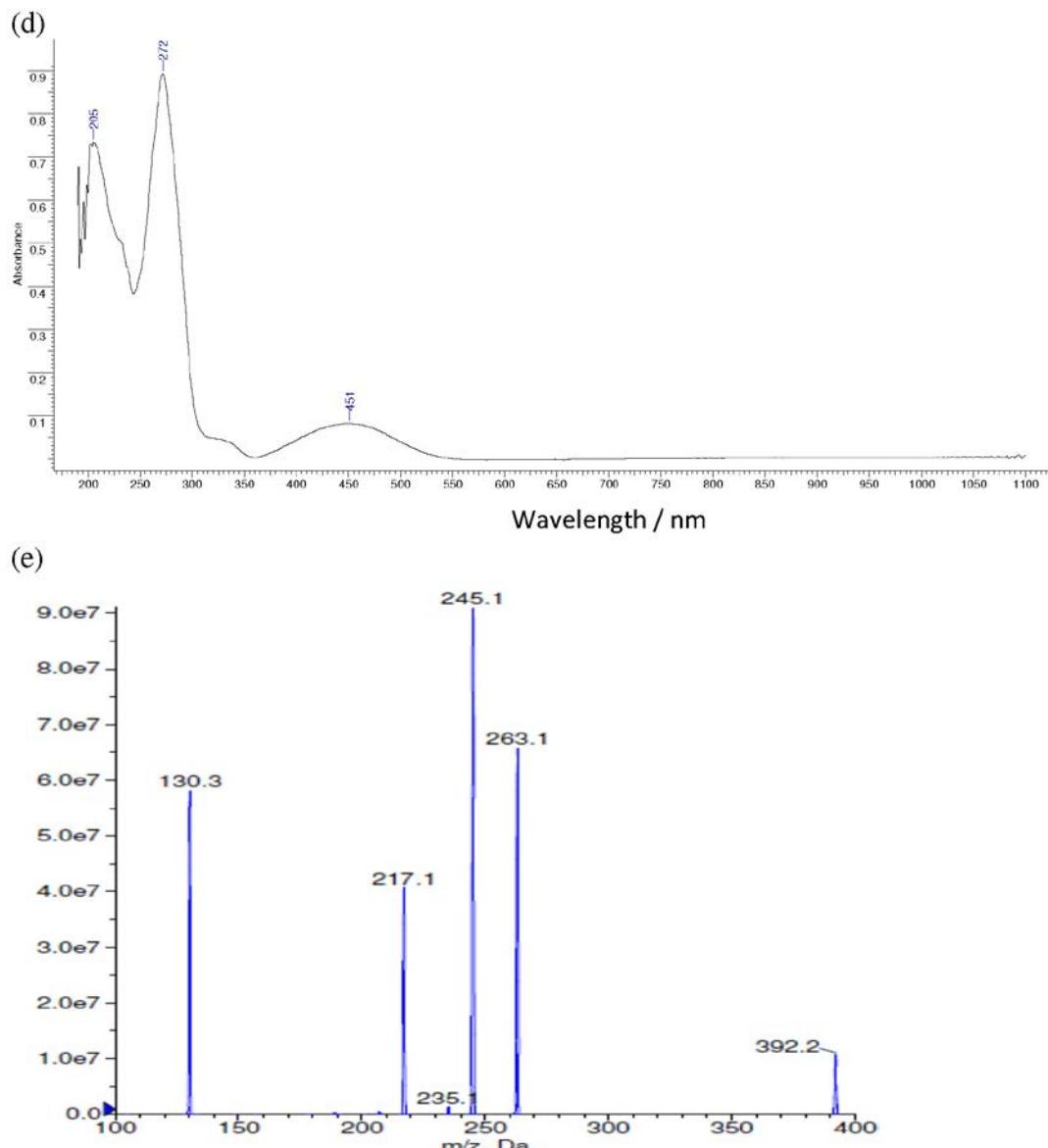


Figure S6. ^1H NMR spectrum (400 MHz, $\text{DMSO}-d_6$) (a); ^{13}C NMR spectrum (100 MHz, $\text{DMSO}-d_6$) (b); IR (KBr) (c); UV-Vis (d); mass spectrum (e) of compound **6** (cont.).

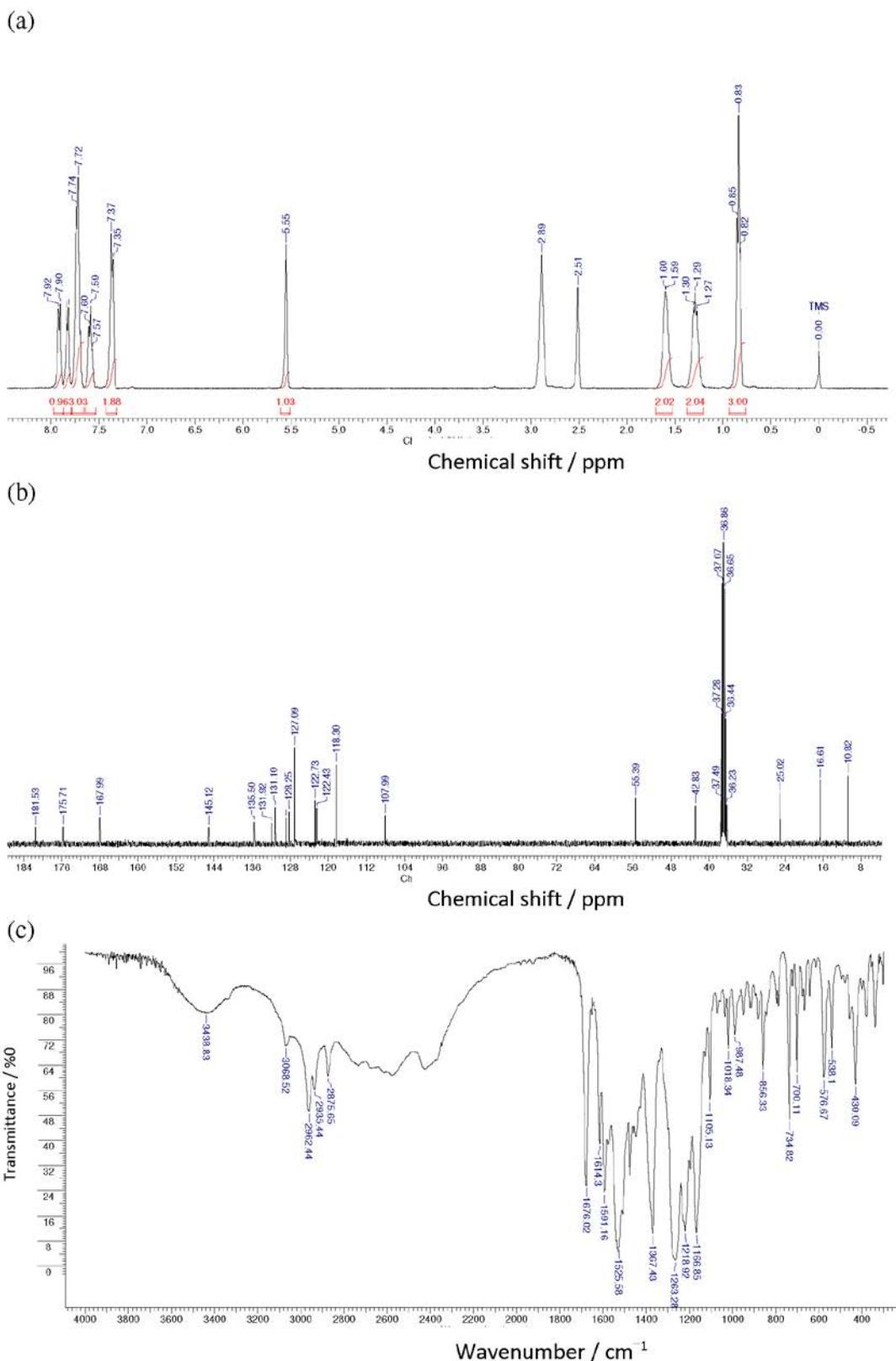
3-[*N*-(*n*-Butyl)4-trifluoromethyl-aminobenzyl]-2-hydroxy-1,4-naphthoquinone (**7**)

Figure S7. ^1H NMR spectrum (400 MHz, $\text{DMSO}-d_6$) (a); ^{13}C NMR spectrum (100 MHz, $\text{DMSO}-d_6$) (b); IR (KBr) (c); UV-Vis (d); mass spectrum (e) of compound **7**.

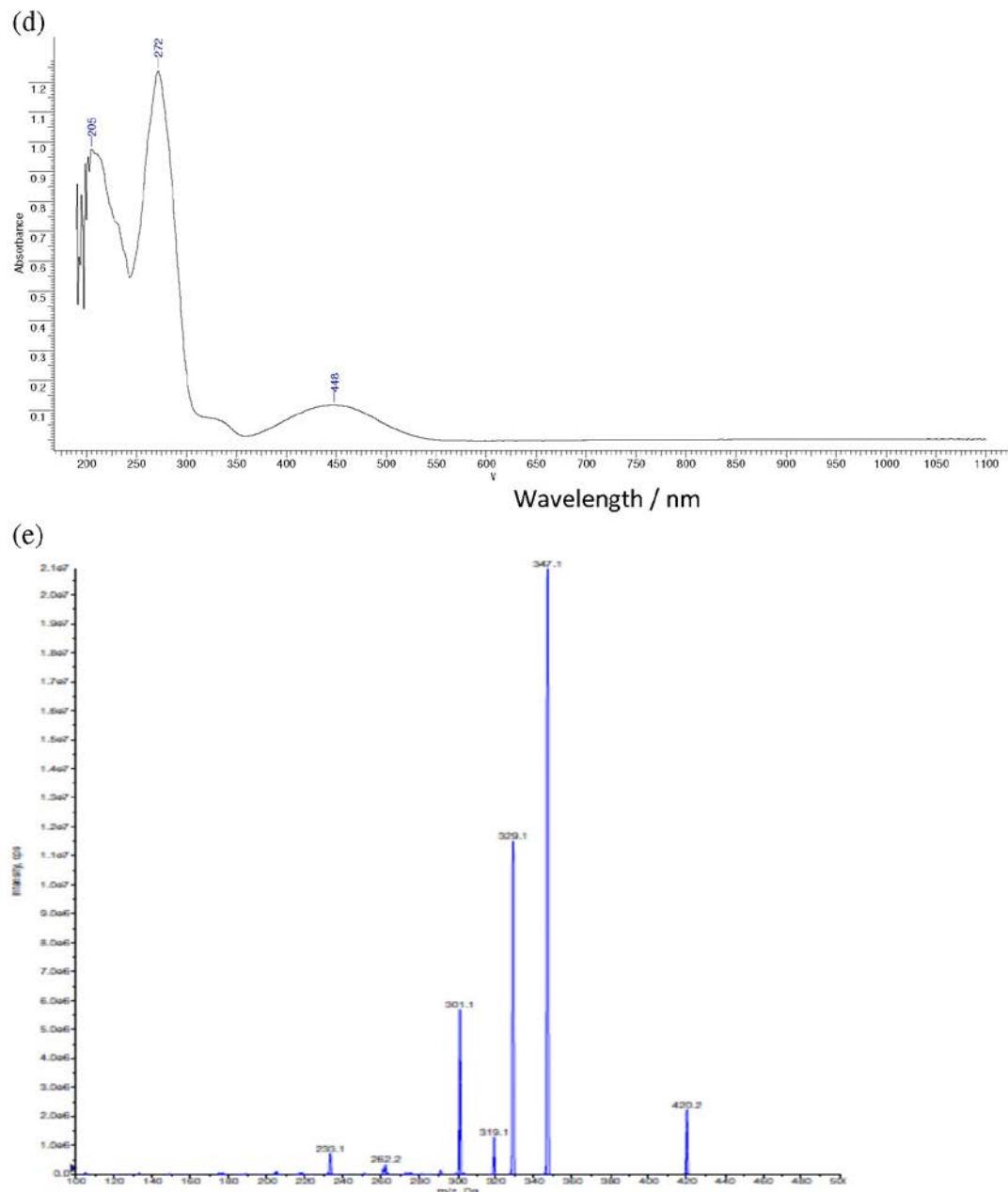


Figure S7. ^1H NMR spectrum (400 MHz, $\text{DMSO}-d_6$) (a); ^{13}C NMR spectrum (100 MHz, $\text{DMSO}-d_6$) (b); IR (KBr) (c); UV-Vis (d); mass spectrum (e) of compound 7 (cont.).

3-[*N*(*n*-Octyl)4-trifluoromethyl-aminobenzyl]-2-hydroxy-1,4-naphthoquinone (8**)**

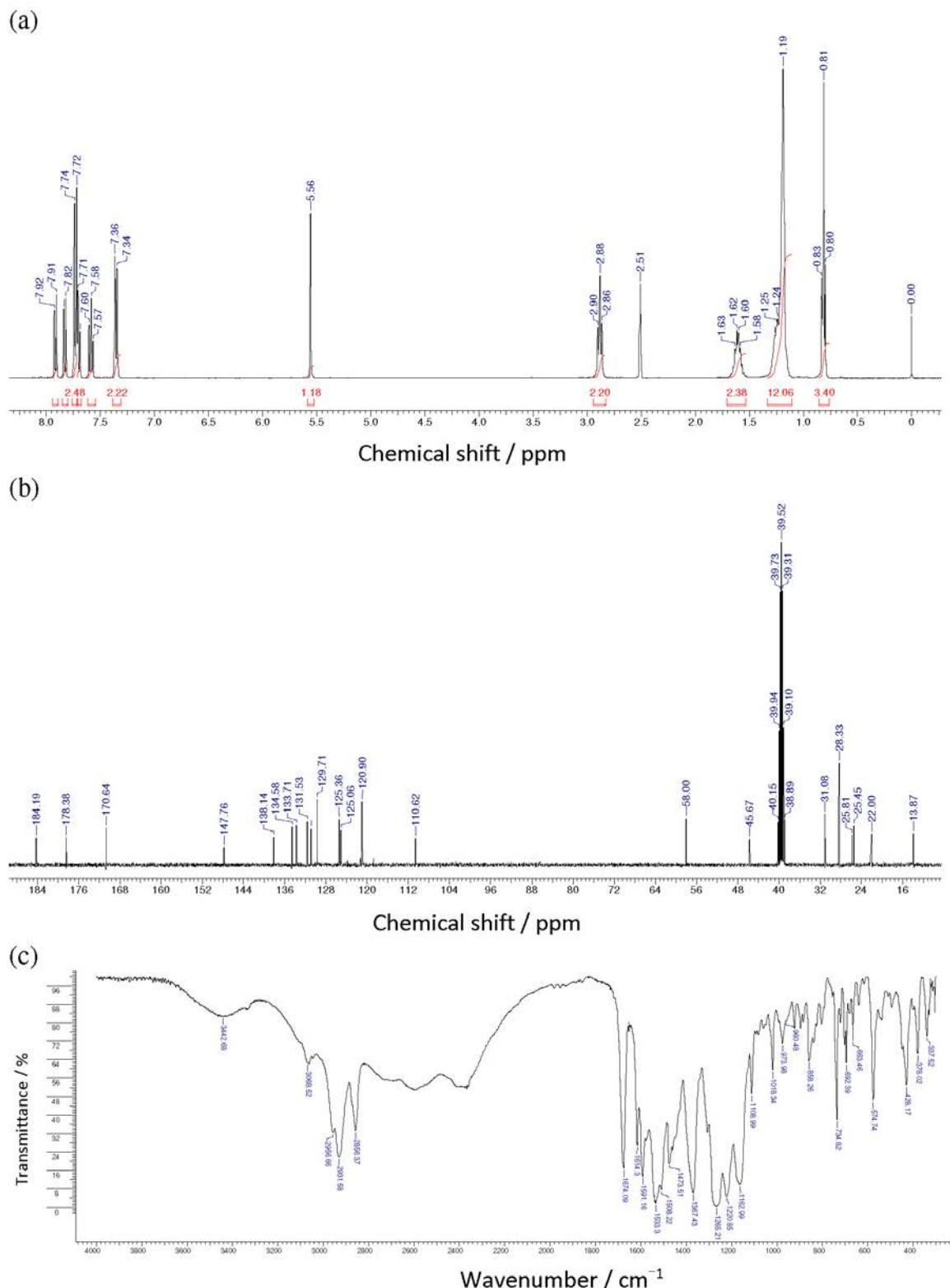


Figure S8. ^1H NMR spectrum (400 MHz, $\text{DMSO}-d_6$) (a); ^{13}C NMR spectrum (100 MHz, $\text{DMSO}-d_6$) (b); IR (KBr) (c); UV-Vis (d); mass spectrum (e) of compound **8**.

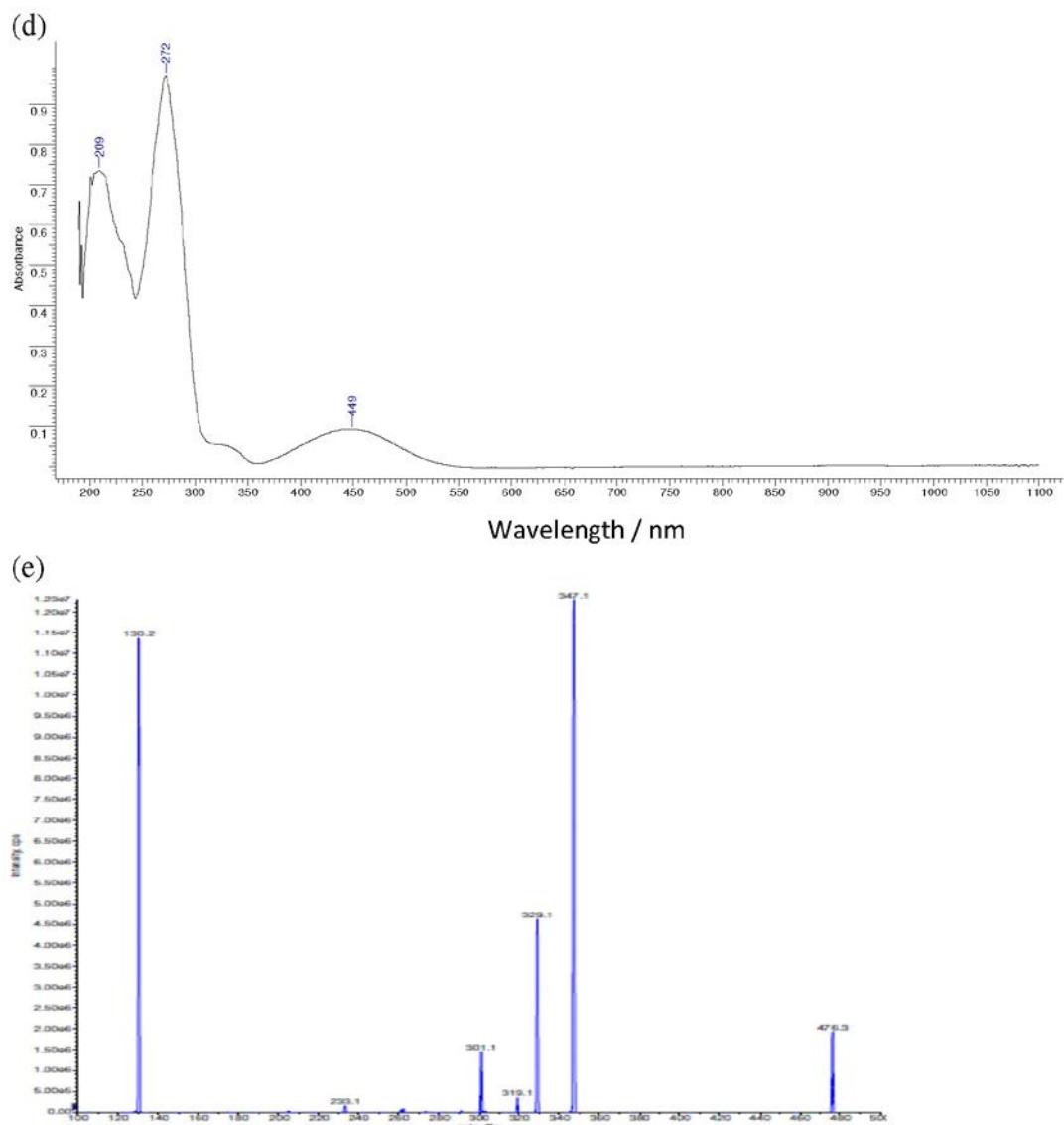


Figure S8. ^1H NMR spectrum (400 MHz, $\text{DMSO}-d_6$) (a); ^{13}C NMR spectrum (100 MHz, $\text{DMSO}-d_6$) (b); IR (KBr) (c); UV-Vis (d); mass spectrum (e) of compound **8** (cont.).

3-[*N*(*n*-Butyl)4-chloro-aminobenzyl]-2-hydroxy-1,4-naphthoquinone (9**)**

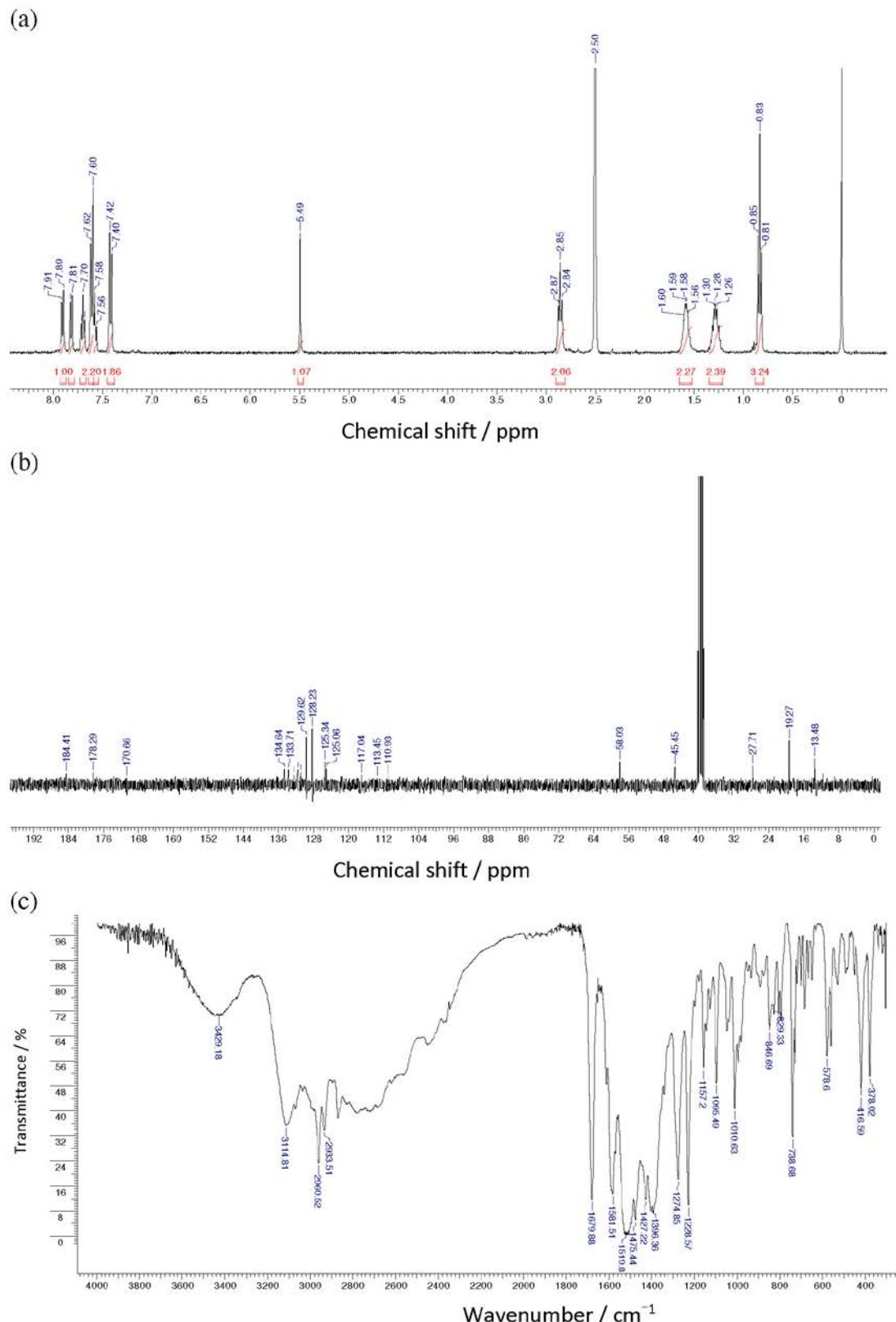


Figure S9. ^1H NMR spectrum (400 MHz, $\text{DMSO}-d_6$) (a); ^{13}C NMR spectrum (100 MHz, $\text{DMSO}-d_6$) (b); IR (KBr) (c); UV-Vis (d); mass spectrum (e) of compound **9**.

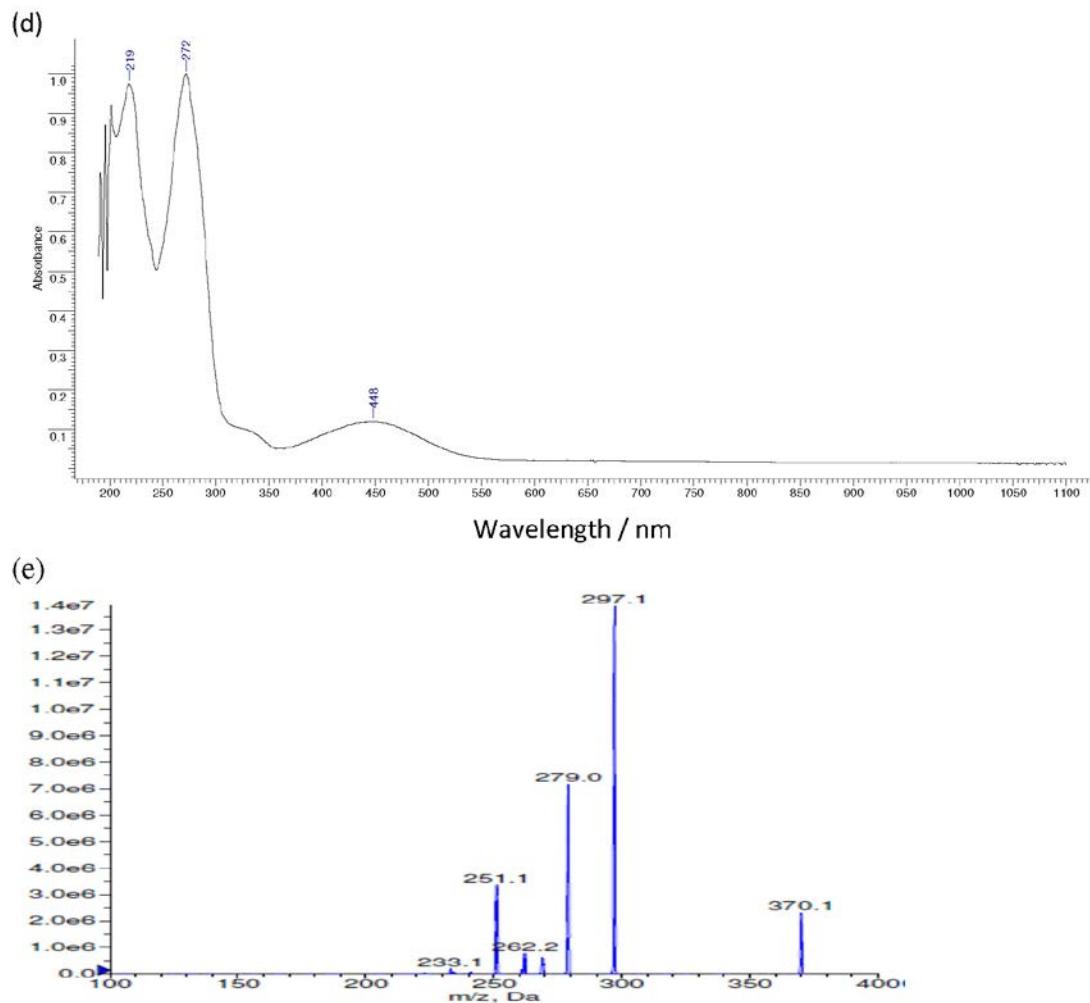


Figure S9. ^1H NMR spectrum (400 MHz, $\text{DMSO}-d_6$) (a); ^{13}C NMR spectrum (100 MHz, $\text{DMSO}-d_6$) (b); IR (KBr) (c); UV-Vis (d); mass spectrum (e) of compound **9** (cont.).

3-[*N*-(*n*-Octyl)4-chloro-aminobenzyl]-2-hydroxy-1,4-naphthoquinone (10**)**

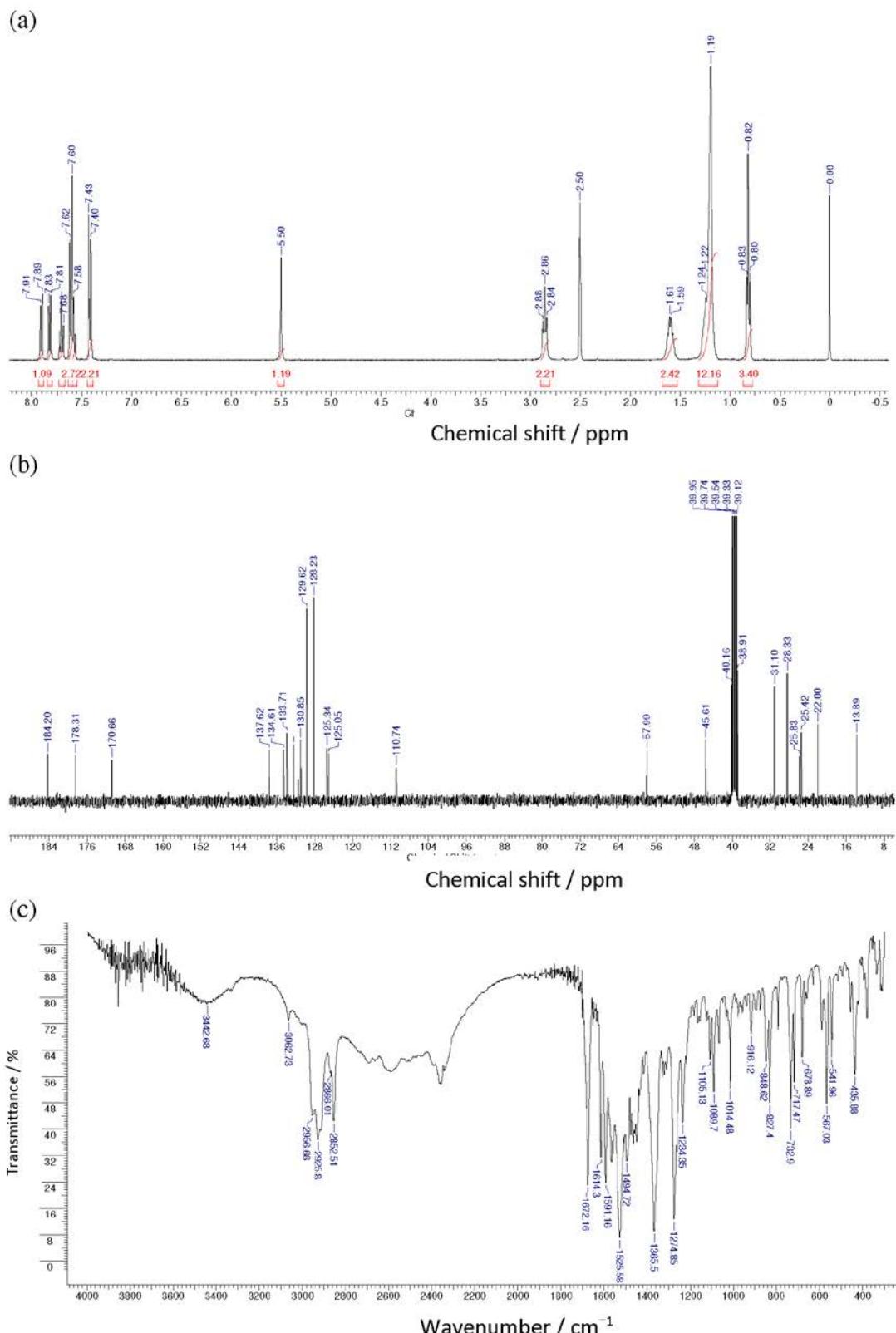


Figure S10. ^1H NMR spectrum (400 MHz, $\text{DMSO}-d_6$) (a); ^{13}C NMR spectrum (100 MHz, $\text{DMSO}-d_6$) (b); IR (KBr) (c); UV-Vis (d); mass spectrum (e) of compound **10**.

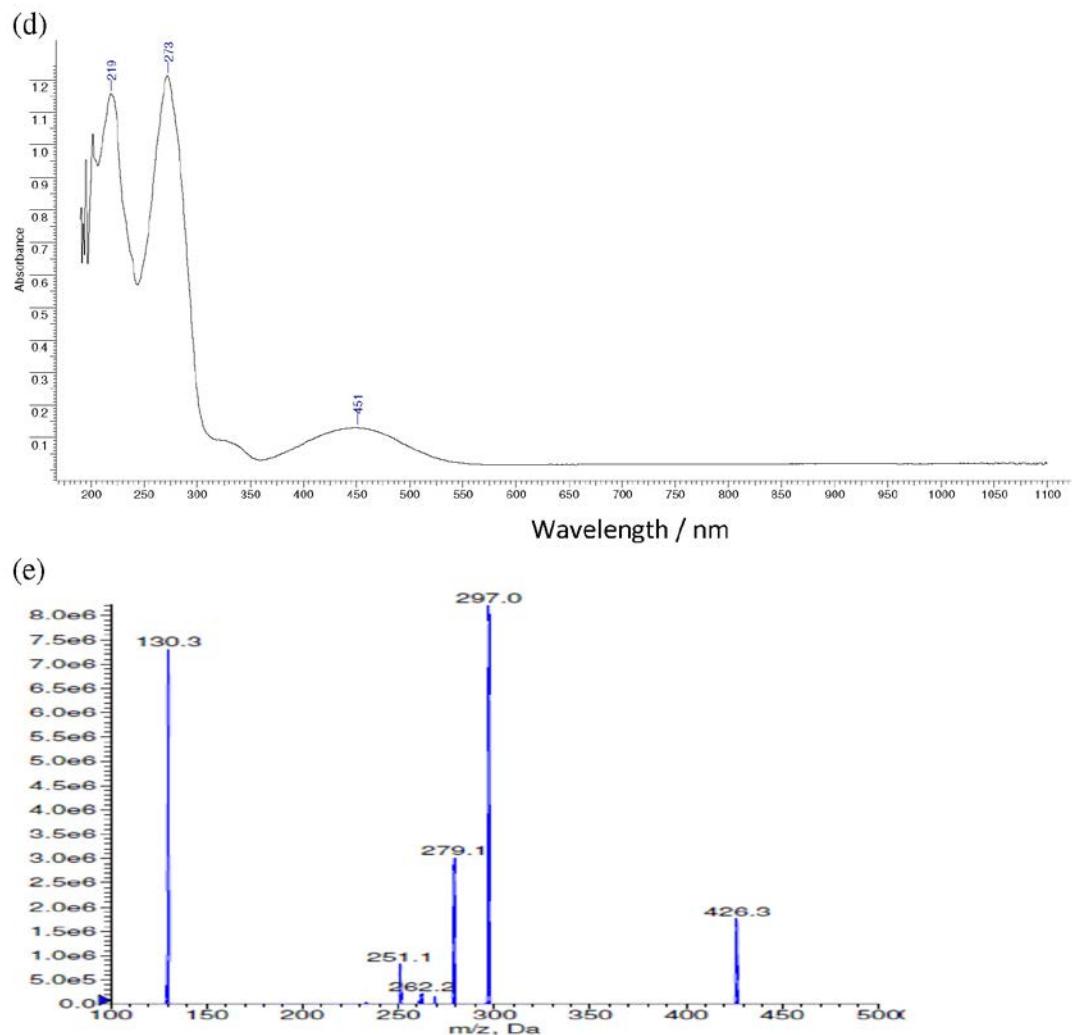


Figure S10. ^1H NMR spectrum (400 MHz, $\text{DMSO}-d_6$) (a); ^{13}C NMR spectrum (100 MHz, $\text{DMSO}-d_6$) (b); IR (KBr) (c); UV-Vis (d); mass spectrum (e) of compound **10** (cont.).

Data of compounds 11-20

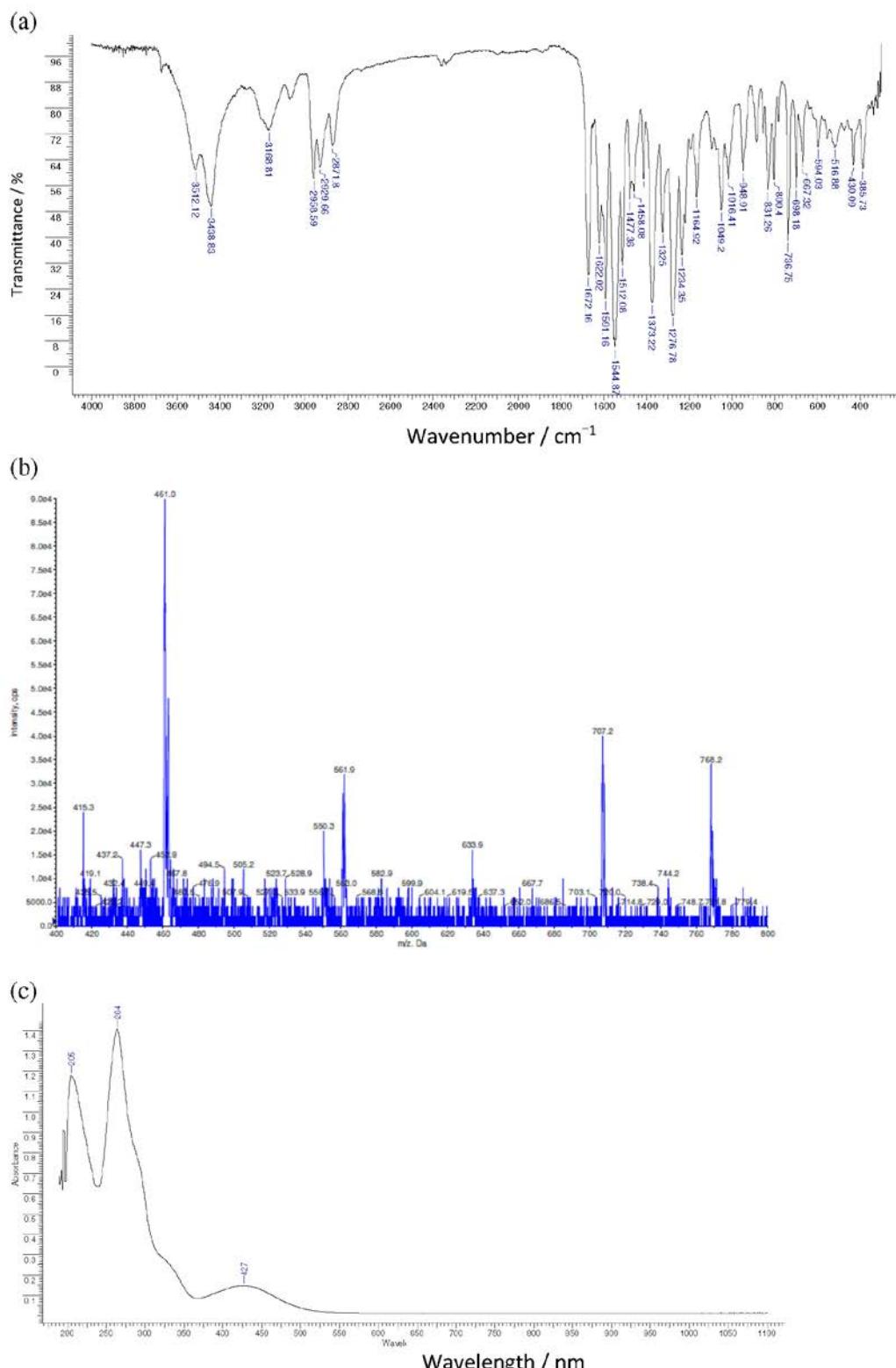
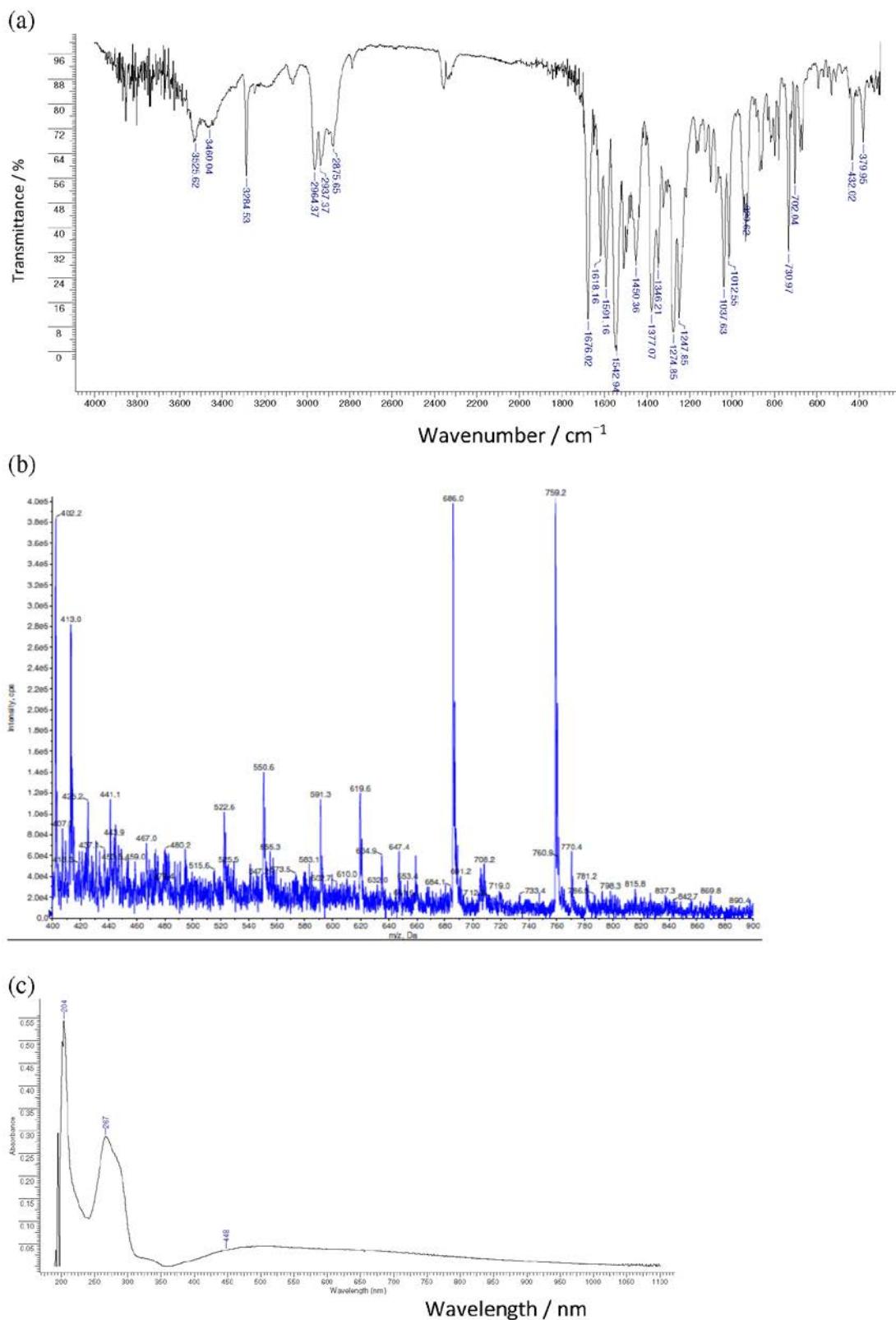
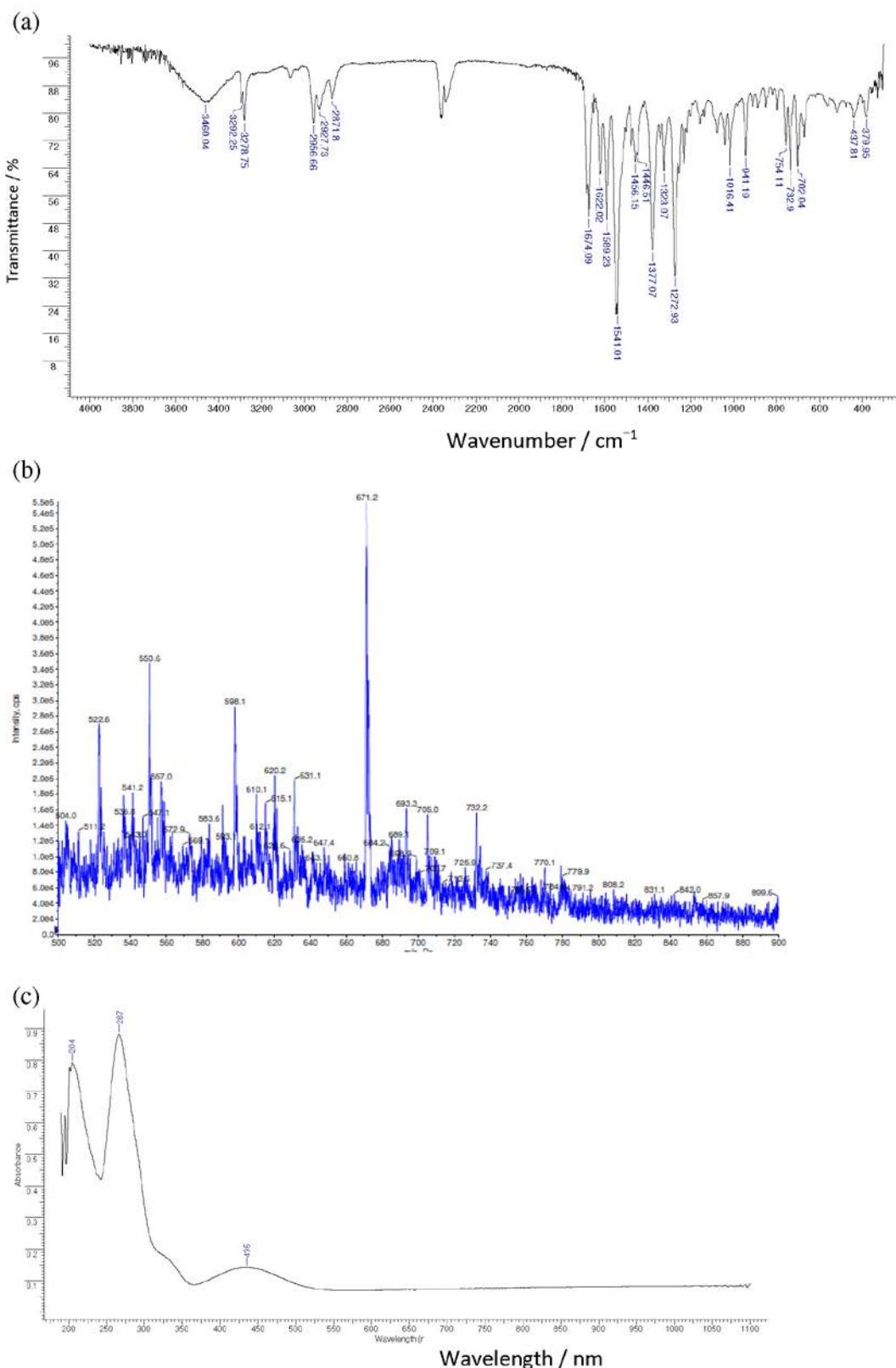
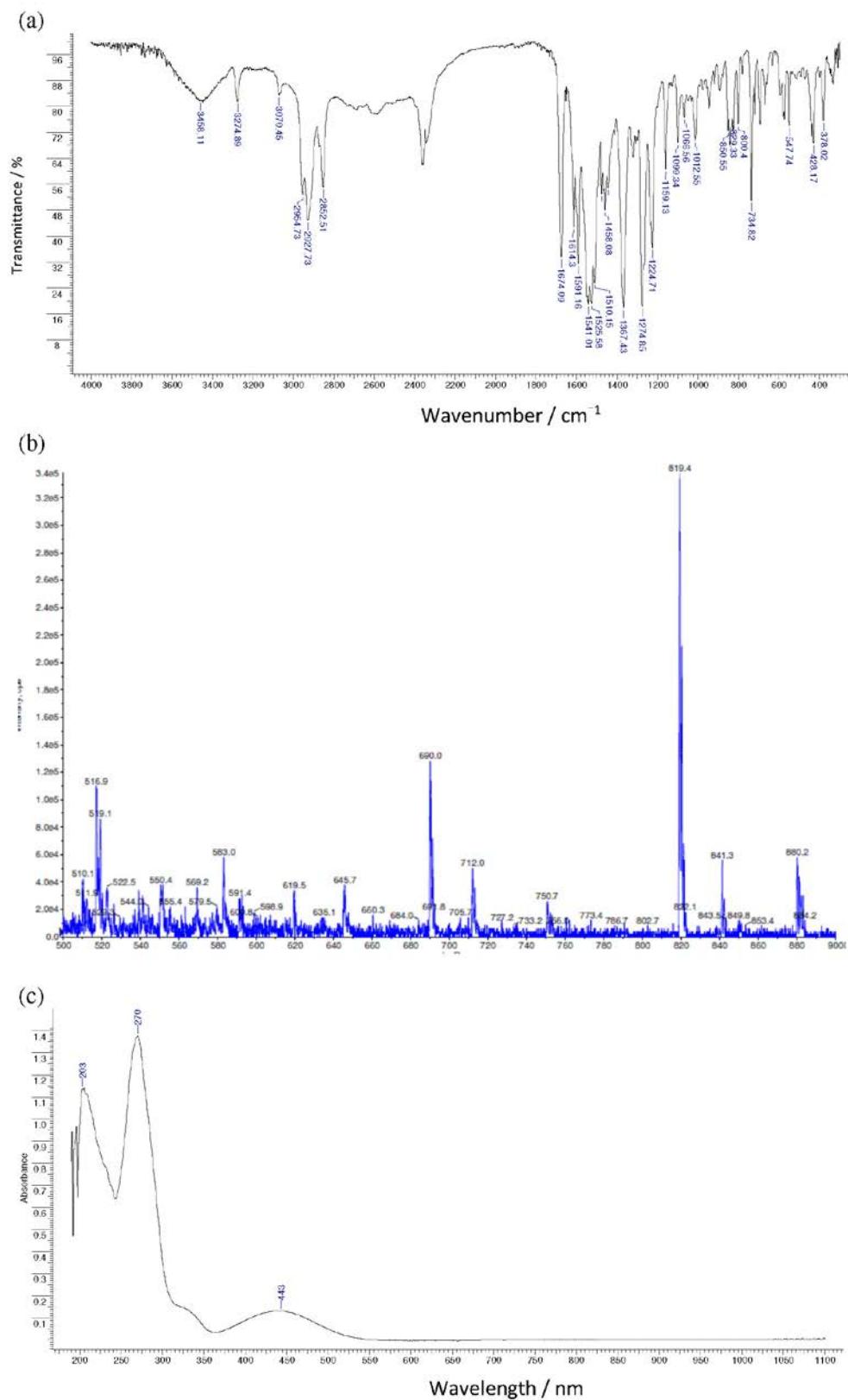
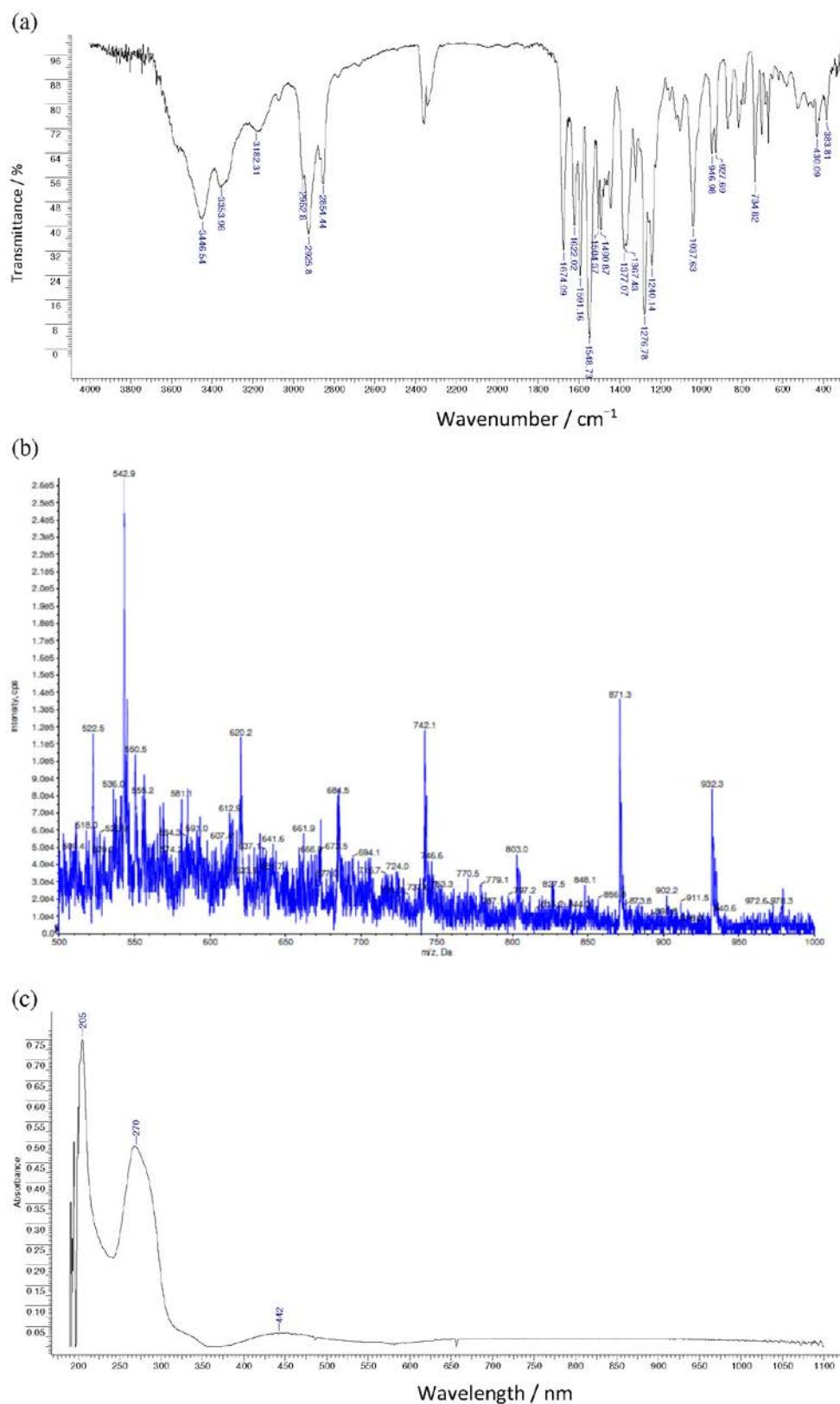
Cu(3-[*N*-(*n*-Butyl)4-fluoro-aminobenzyl]-2-hydroxy-1,4-naphthoquinone)₂ (**11**)

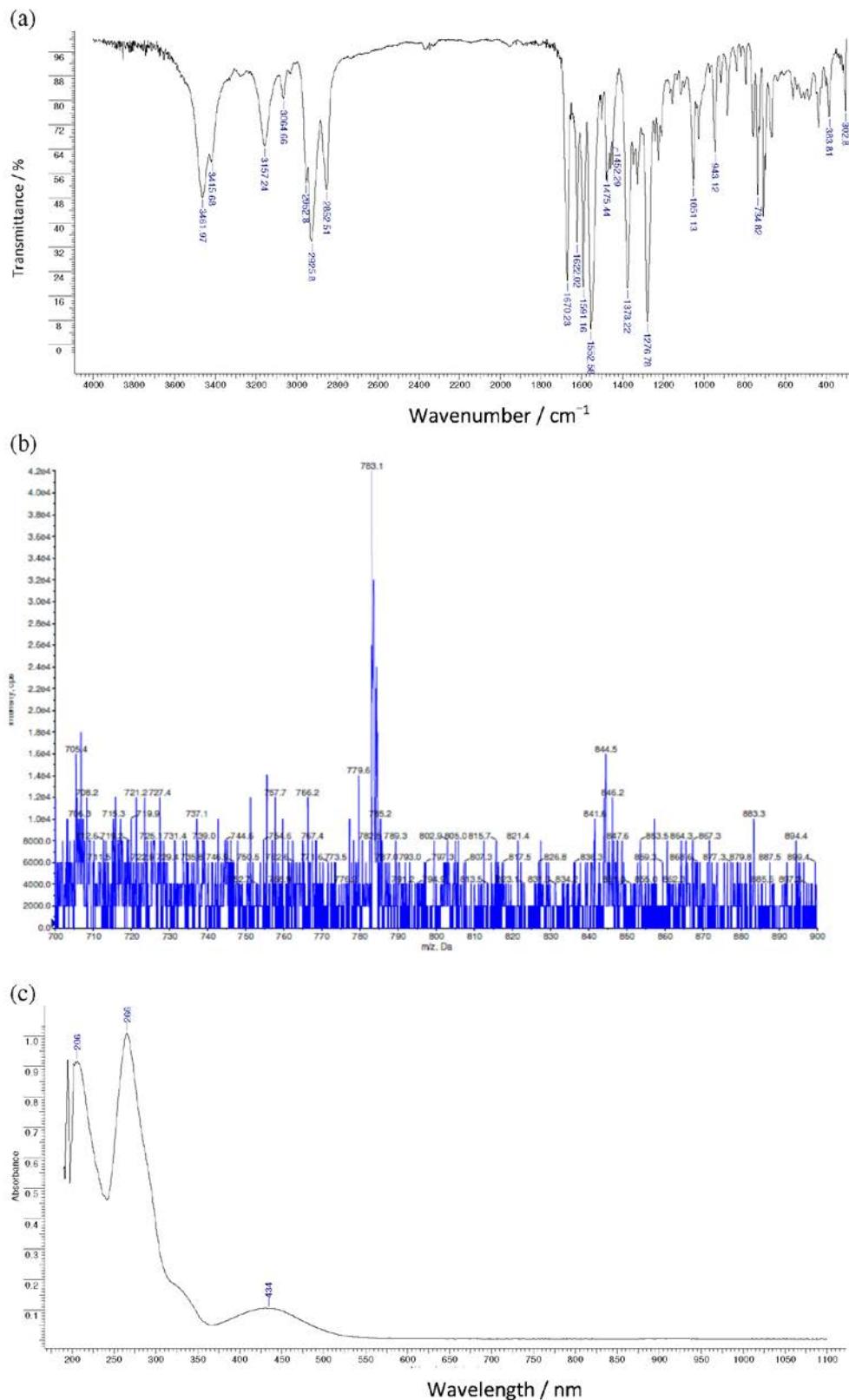
Figure S11. IR (KBr) (a); mass spectrum (b); UV-Vis (c) of compound 11.

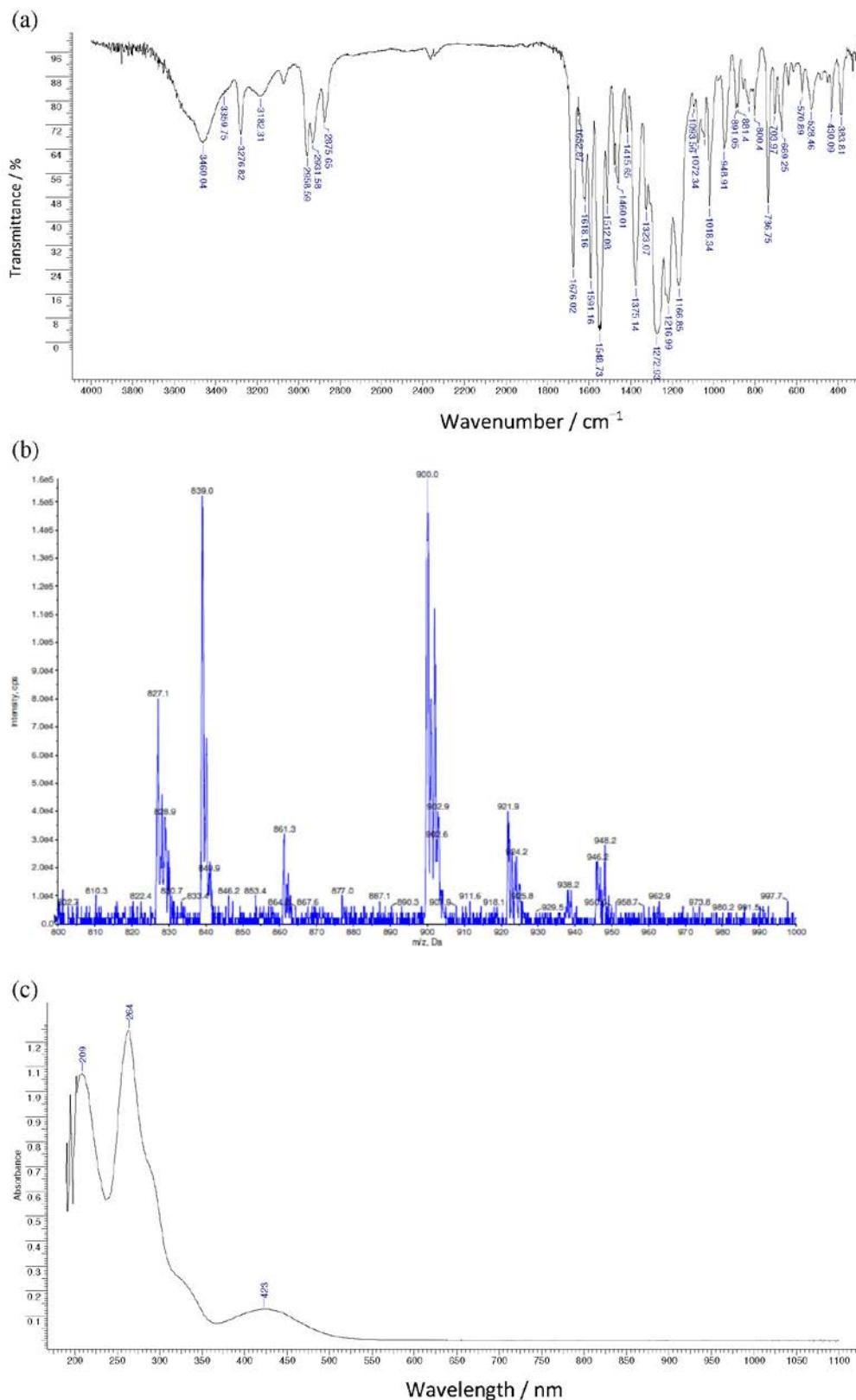
Cu(3-[*N*-(*n*-Butyl)aminopiperonyl]-2-hydroxy-1,4-naphthoquinone)₂ (12**)****Figure S12.** IR (KBr) (a); mass spectrum (b); UV-Vis (c) of compound **12**.

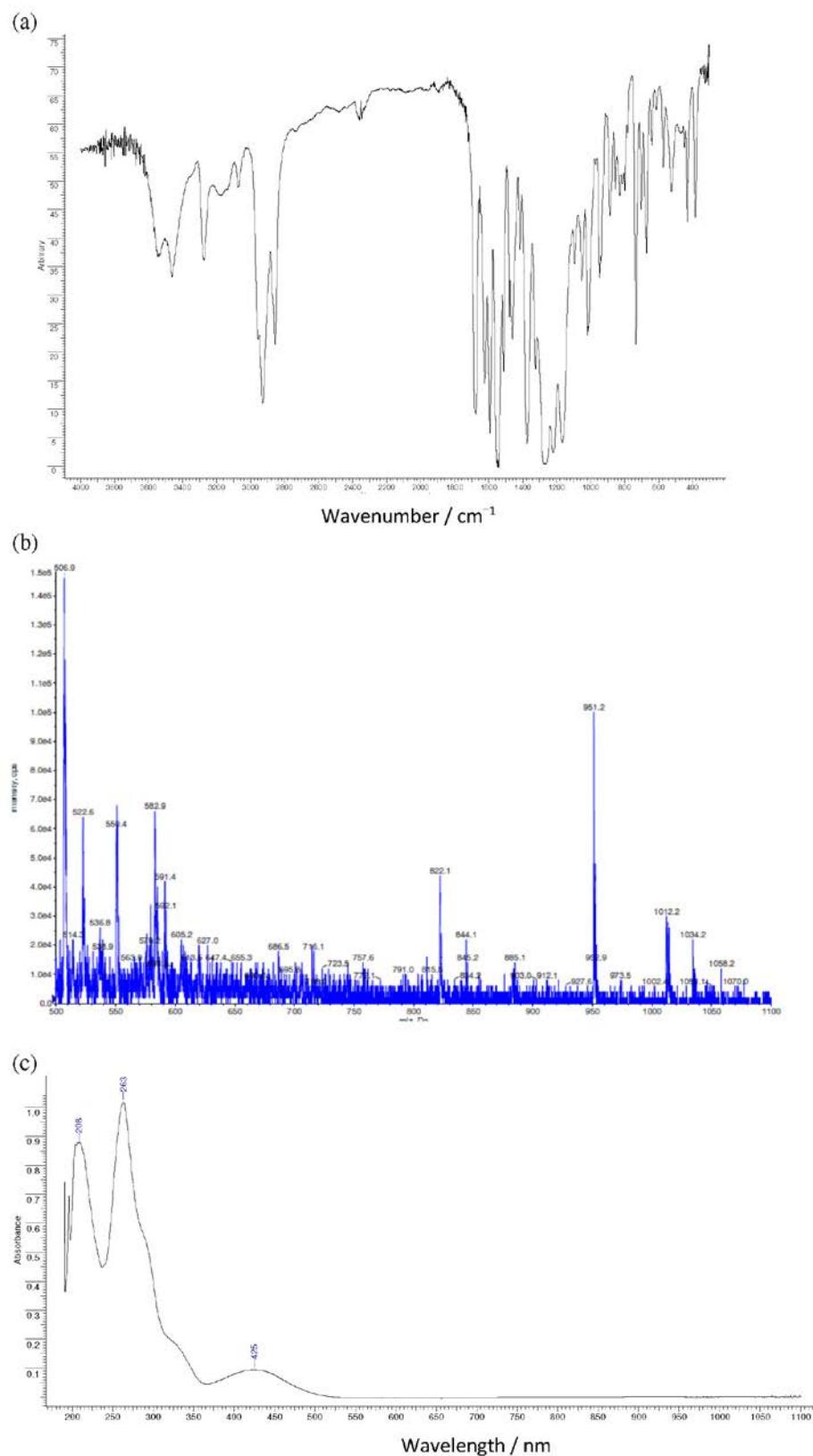
Cu(3-[*N*(*n*-Butyl)aminobenzyl]-2-hydroxy-1,4-naphthoquinone)₂ (13**)****Figure S13.** IR (KBr) (a); mass spectrum (b); UV-Vis (c) of compound **13**.

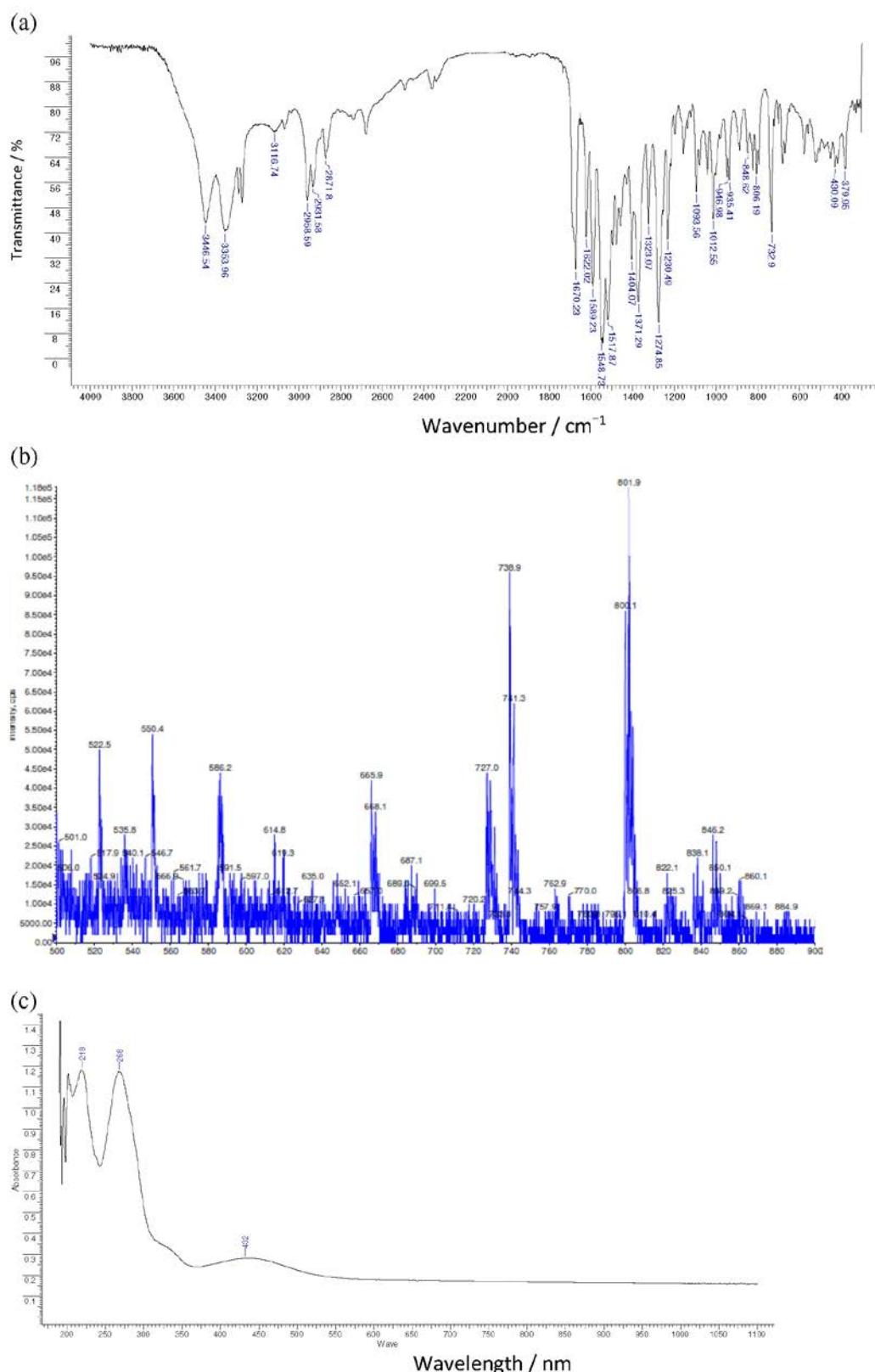
Cu(3-[*N*-(*n*-Octyl)4-fluoro-aminobenzyl]-2-hydroxy-1,4-naphthoquinone)₂ (14**)****Figure S14.** IR (KBr) (a); mass spectrum (b); UV-Vis (c) of compound **14**.

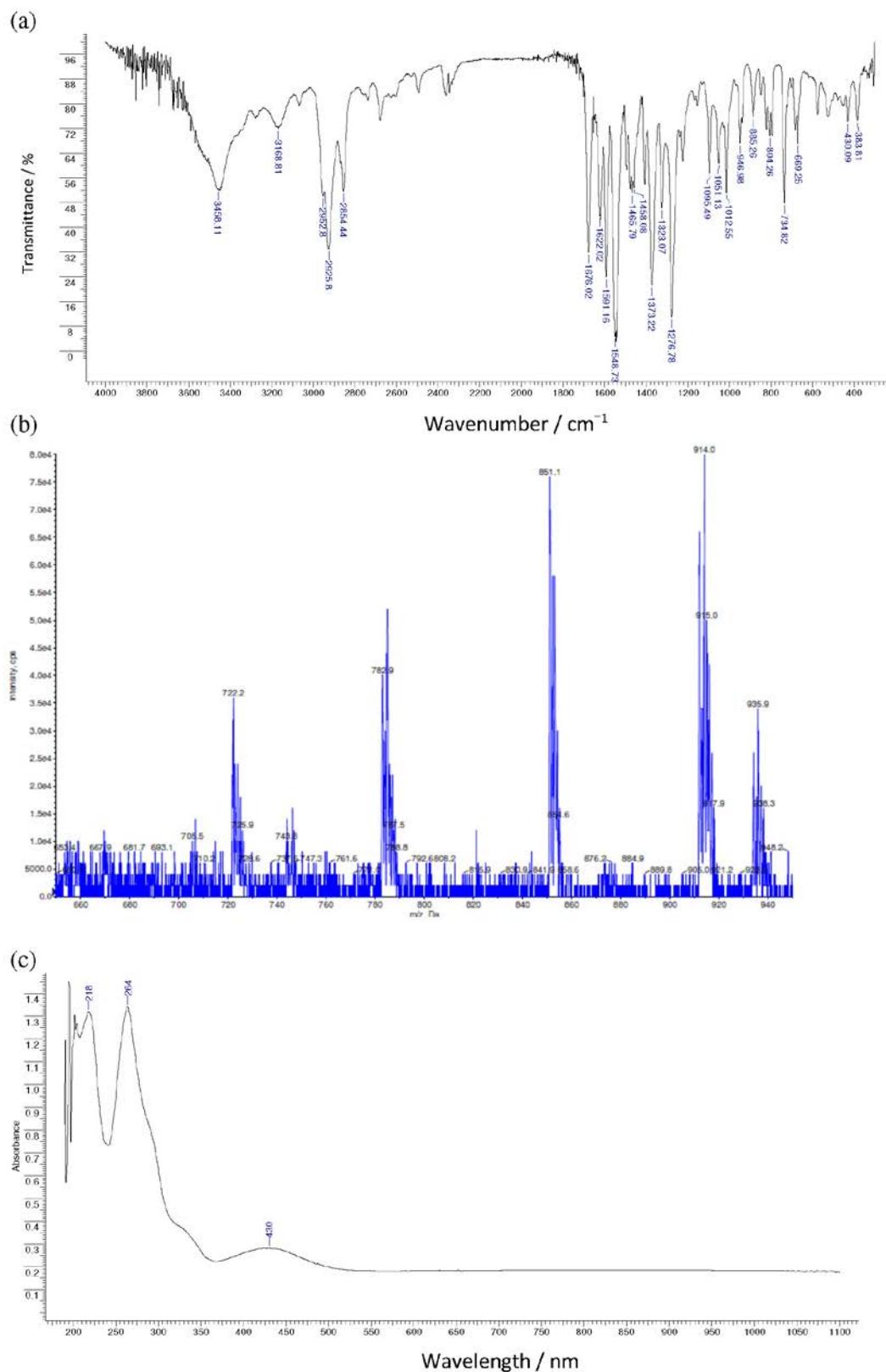
Cu(3-[*N*(*n*-Octyl)aminopiperonyl]-2-hydroxy-1,4-naphthoquinone)₂ (15**)****Figure S15.** IR (KBr) (a); mass spectrum (b); UV-Vis (c) of compound **15**.

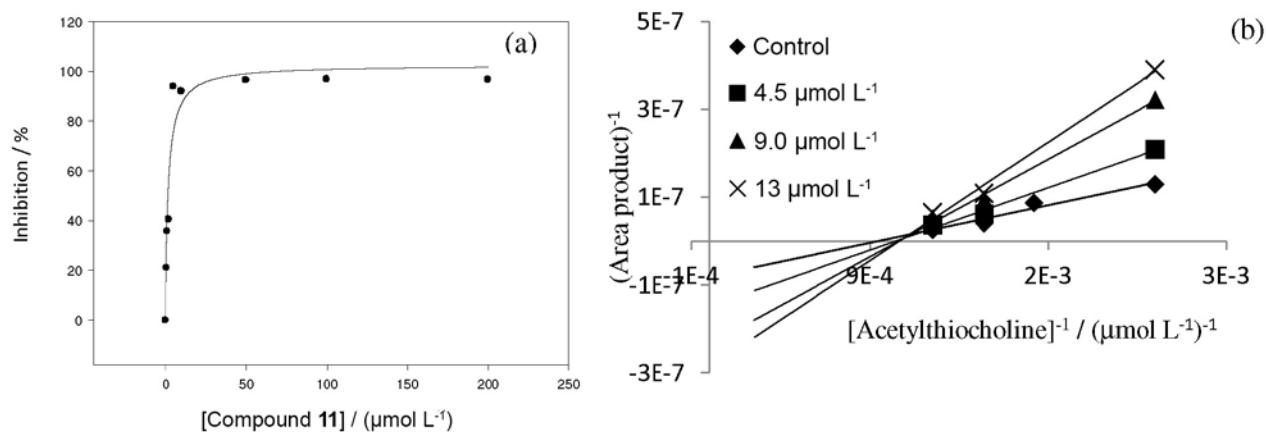
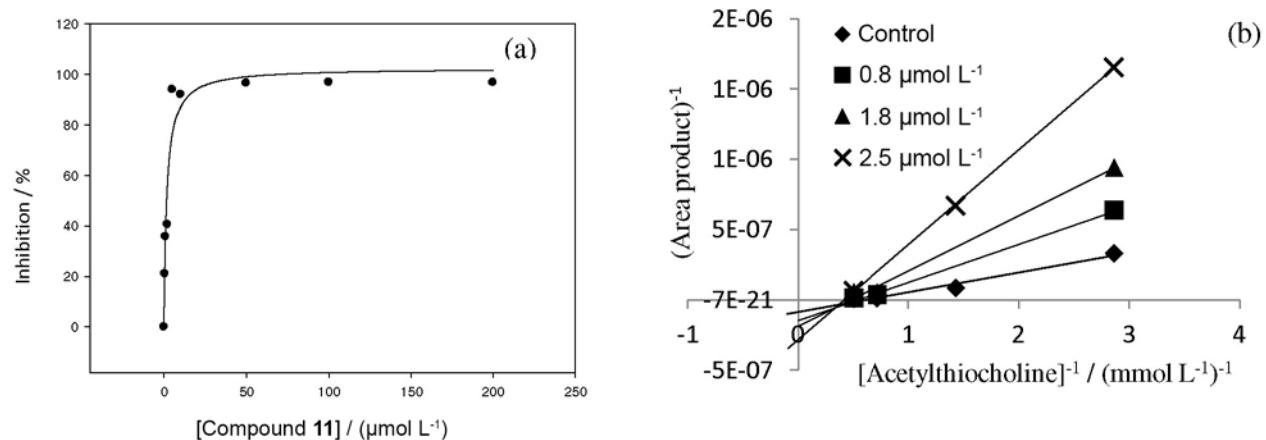
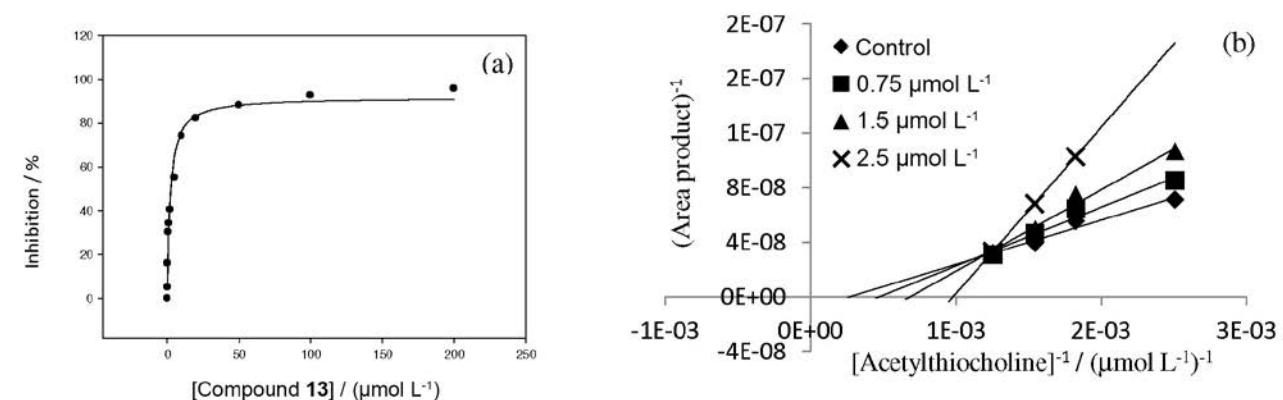
Cu(3-[*N*-(*n*-Octyl)aminobenzyl]-2-hydroxy-1,4-naphthoquinone)₂ (16**)****Figure S16.** IR (KBr) (a); mass spectrum (b); UV-Vis (c) of compound **16**.

Cu(3-[*N*(*n*-Butyl)4-trifluoromethoxy-aminobenzyl]-2-hydroxy-1,4-naphthoquinone)₂ (17)**Figure S17.** IR (KBr) (a); mass spectrum (b); UV-Vis (c) of compound 17.

Cu(3-[*N*-(*n*-Octyl)4-trifluoromethoxy-aminobenzyl]-2-hydroxy-1,4-naphthoquinone)₂ (18**)****Figure S18.** IR (KBr) (a); mass spectrum (b); UV-Vis (c) of compound **18**.

Cu(3-[*N*-(*n*-Butyl)4-chloro-aminobenzyl]-2-hydroxy-1,4-naphthoquinone)₂ (19**)****Figure S19.** IR (KBr) (a); mass spectrum (b); UV-Vis (c) of compound **19**.

Cu(3-[*N*-(*n*-Octyl)4-chloro-aminobenzyl]-2-hydroxy-1,4-naphthoquinone)₂ (20**)****Figure S20.** IR (KBr) (a); mass spectrum (b); UV-Vis (c) of compound **20**.

Figures of the inhibitory potency (IC_{50}) and mechanism of the action the most active compounds**Figure S21.** Dose-response curves plots of inhibition percentage (a) and inhibition mechanism studies; line Lineweaver-Burk graph (b) of compound 11 eeAChE-ICER.**Figure S22.** Dose-response curves plots of inhibition percentage (a) and inhibition mechanism studies; line Lineweaver-Burk graph (b) of compound 11 huAChE-ICER.**Figure S23.** Dose-response curves plots of inhibition percentage (a) and inhibition mechanism studies; line Lineweaver-Burk graph (b) of compound 13 eeAChE-ICER.

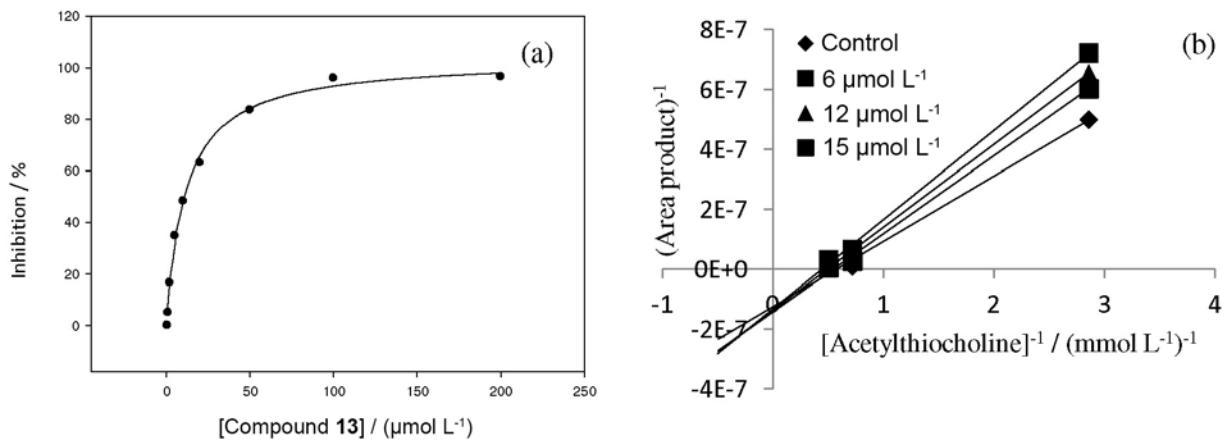


Figure S24. Dose-response curves plots of inhibition percentage (a) and inhibition mechanism studies; line Lineweaver-Burk graph (b) of compound **13** huAChE-ICER.

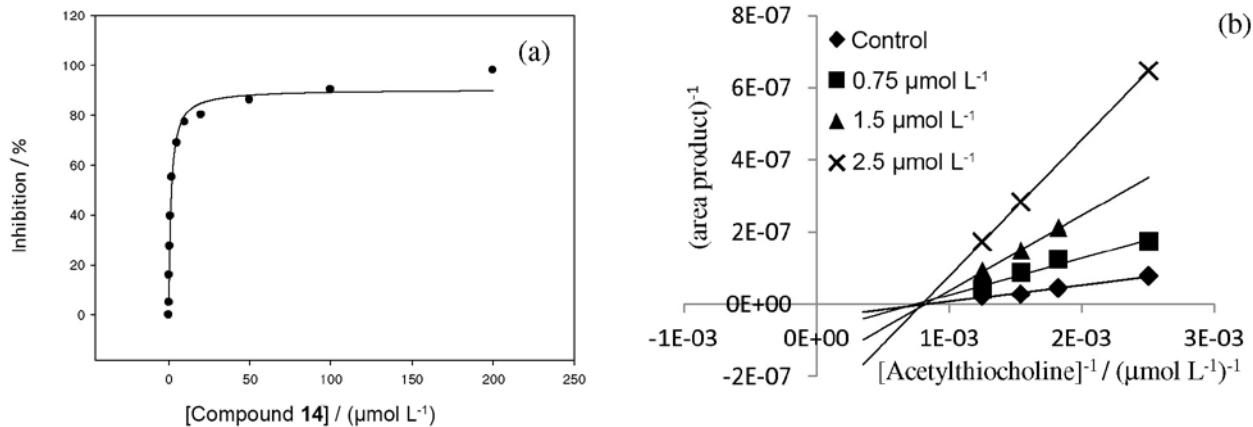


Figure S25. Dose-response curves plots of inhibition percentage (a) and inhibition mechanism studies; line Lineweaver-Burk graph (b) of compound **14** eeAChE-ICER.

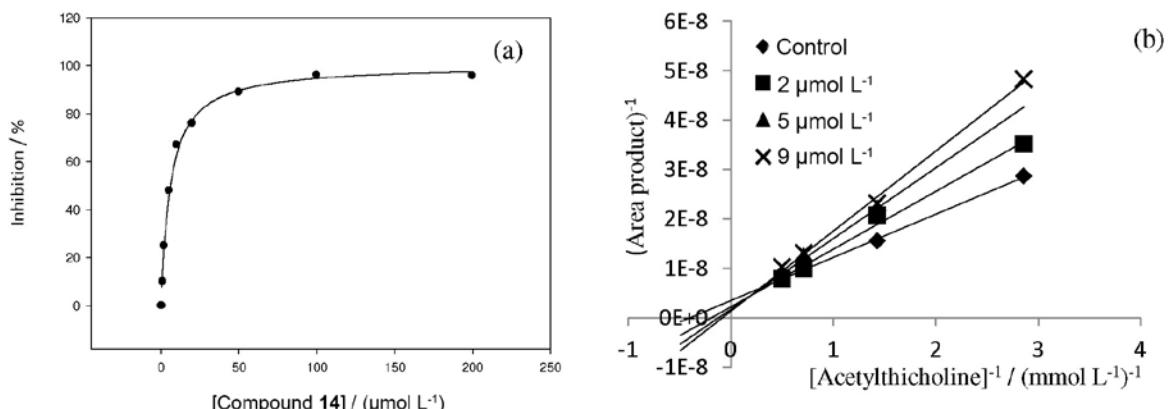


Figure S26. Dose-response curves plots of inhibition percentage (a) and inhibition mechanism studies; line Lineweaver-Burk graph (b) of compound **14** huAChE-ICER.

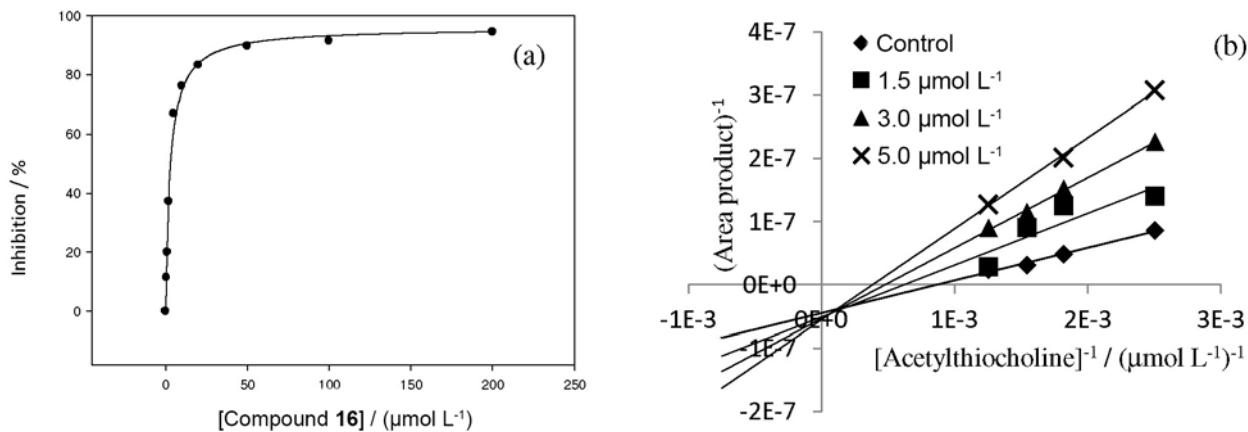


Figure S27. Dose-response curves plots of inhibition percentage (a) and inhibition mechanism studies; line Lineweaver-Burk graph (b) of compound 16 eeAChE-ICER.

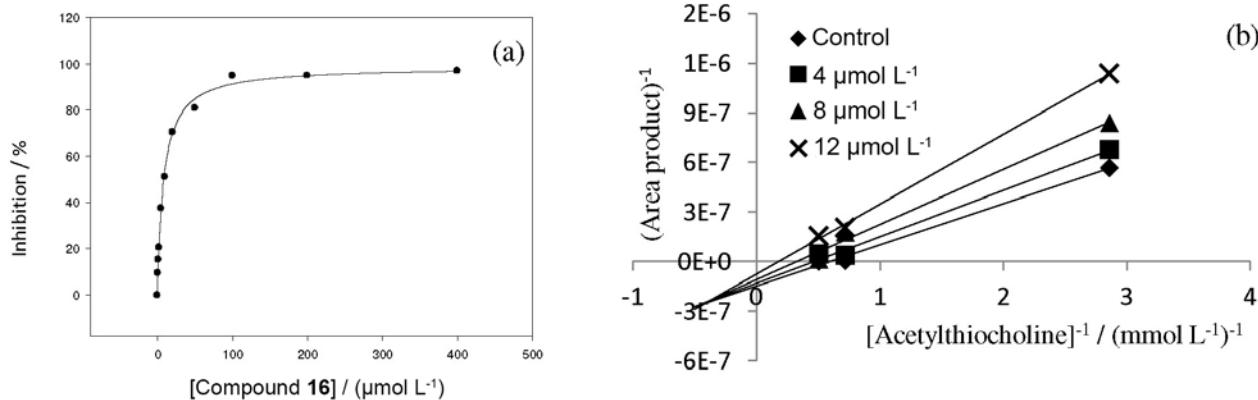


Figure S28. Dose-response curves plots of inhibition percentage (a) and inhibition mechanism studies; line Lineweaver-Burk graph (b) of compound 16 huAChE-ICER.

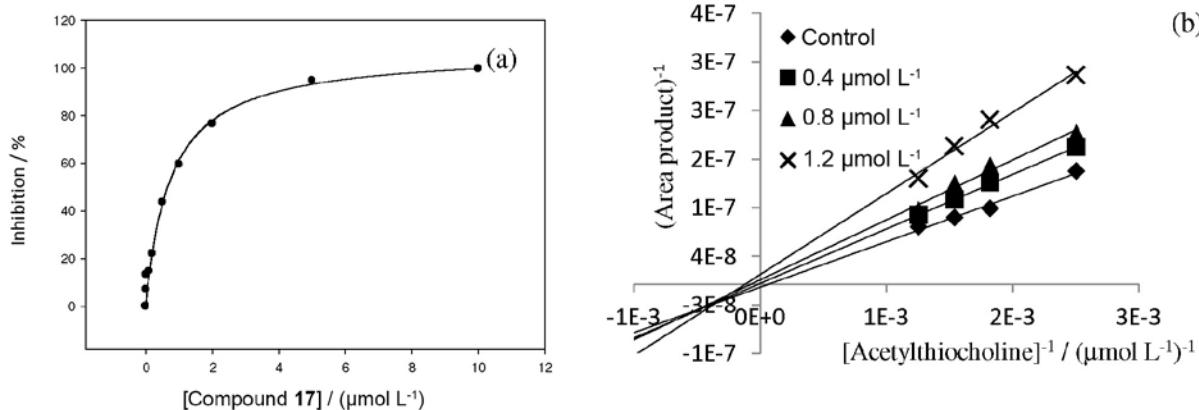


Figure S29. Dose-response curves plots of inhibition percentage (a) and inhibition mechanism studies; line Lineweaver-Burk graph (b) of compound 17 eeAChE-ICER.

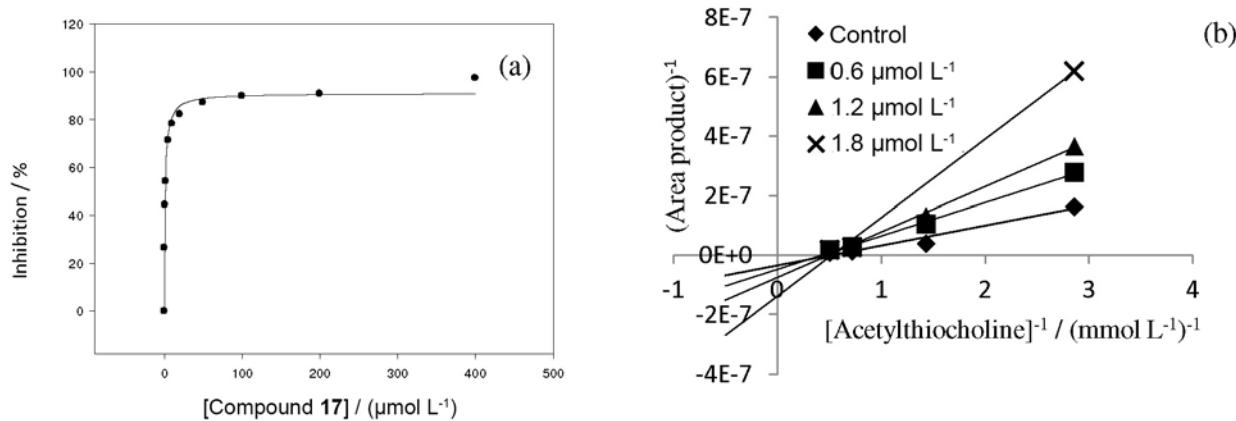


Figure S30. Dose-response curves plots of inhibition percentage (a) and inhibition mechanism studies; line Lineweaver-Burk graph (b) of compound **17** huAChE-ICER.

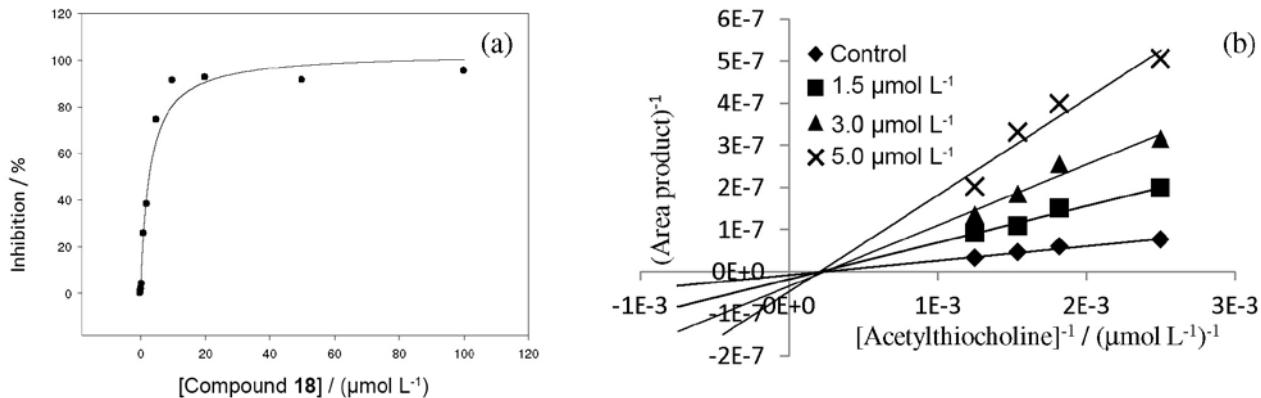


Figure S31. Dose-response curves plots of inhibition percentage (a) and inhibition mechanism studies; line Lineweaver-Burk graph (b) of compound **18** eeAChE-ICER.

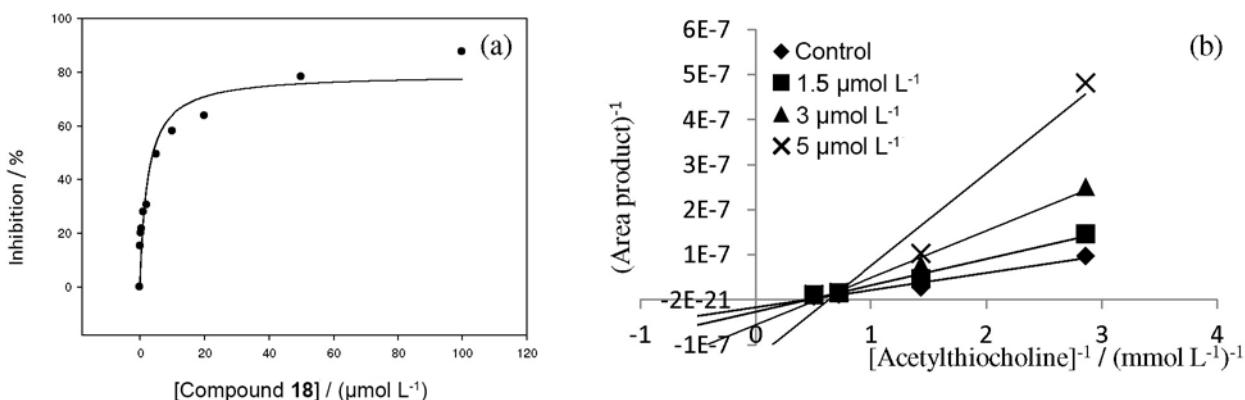


Figure S32. Dose-response curves plots of inhibition percentage (a) and inhibition mechanism studies; line Lineweaver-Burk graph (b) of compound **18** huAChE-ICER.

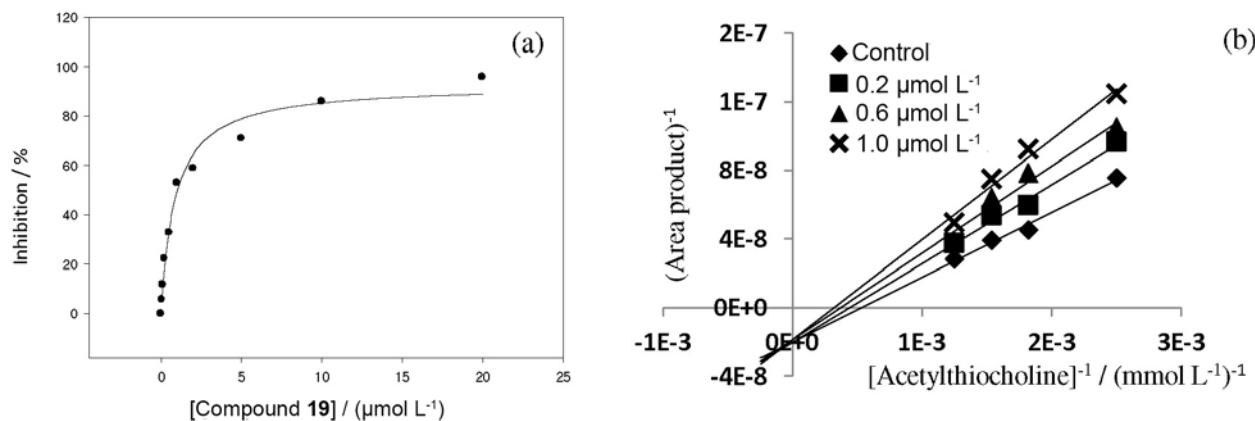


Figure S33. Dose-response curves plots of inhibition percentage (a) and inhibition mechanism studies; line Lineweaver-Burk graph (b) of compound 19 eeAChE-ICER.

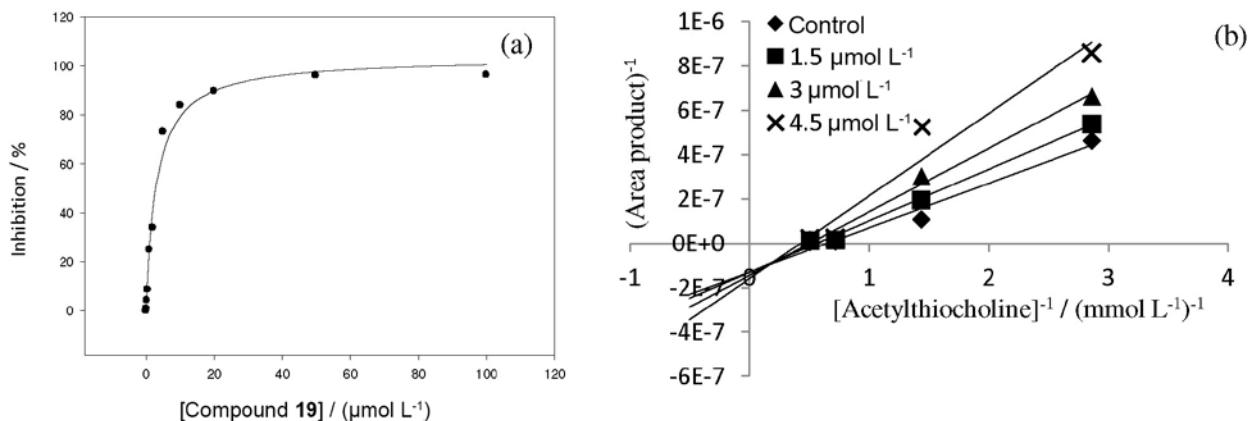


Figure S34. Dose-response curves plots of inhibition percentage (a) and inhibition mechanism studies; line Lineweaver-Burk graph (b) of compound 19 huAChE-ICER.

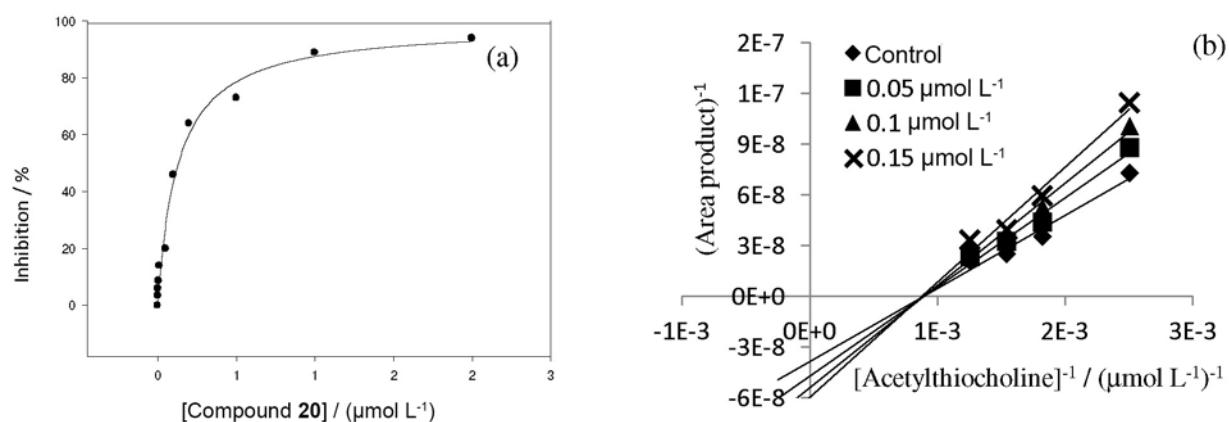


Figure S35. Dose-response curves plots of inhibition percentage (a) and inhibition mechanism studies; line Lineweaver-Burk graph (b) of compound 20 eeAChE-ICER.

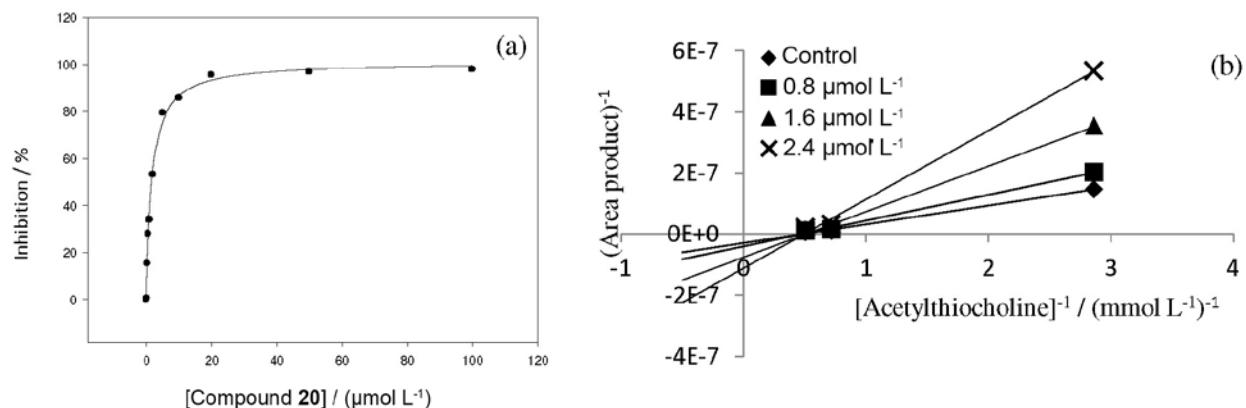


Figure S36. Dose-response curves plots of inhibition percentage (a) and inhibition mechanism studies; line Lineweaver-Burk graph (b) of compound **20** huAChE-ICER.