

# Supplementary Information

## Conformational Variability in Sulfonamide Chalcone Hybrids: Crystal Structure and Cytotoxicity

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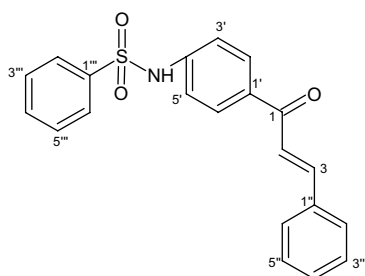
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### General information

Full characterization of the compounds was performed at Instituto de Química from Universidade Federal de Goiás as follows. Melting points were measured in a Microquímica MQAPF-301 apparatus. The infrared spectra were obtained in Bomem M102 Fourier Transform spectrometer. Samples were analyzed by the Fourier Transform Infrared (FTIR) transmission technique as KBr pellets (mixtures comprising 200 mg of KBr and 1 mg of sample). Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Avance III, operating at 500.13 MHz for <sup>1</sup>H and 125.77 MHz for <sup>13</sup>C, equipped with a 5 mm TBI probe (<sup>1</sup>H, <sup>13</sup>C and XBB). The NMR assignments of all the chalcone derivatives are described below. The NMR data of compounds **1**, **2**, **3** and **6** were compared to the literature and all of them could be confirmed. NMR data of compounds **4** and **5** are published for the first time here.

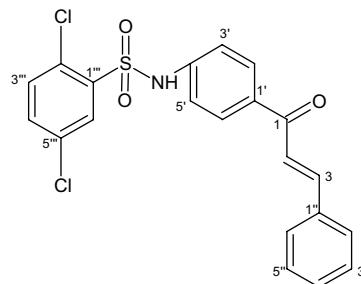
*N*-{4-[(2*E*)-3-Phenylprop-2-enoyl]phenyl}benzenesulfonamide (**1**)<sup>1</sup> (Figures S1 and S2)



Yield: 78%; m.p.: 143-145 °C; IR (KBr)  $\nu$  / cm<sup>-1</sup> 3215 (N-H), 1647 (C=O), 1606 (Ar-CO-C=C-Ar), 1573 (N-H), 1349 (S=O), 1220 (C-N), 1165 (S=O); <sup>1</sup>H NMR

(500 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  8.04 [d (AA'BB'), 2H, *J* 8.8 Hz, H-2' and H-6'], 7.84-7.89 (m, 2H, H-2''' and H-6'''), 7.84 [d, 1H, *J* 15.8 Hz, H-3 ( $\beta$ )], 7.81-7.87 (m, 2H, H-2'' and H-6''), 7.68 [d, 1H, *J* 15.8 Hz, H-2 ( $\alpha$ )], 7.62-7.67 (m, 1H, H-4'''), 7.56-7.62 (m, 2H, H-3''' and H-5'''), 7.43-7.47 (m, 3H, H-3'', H-4'', H-5''), 7.26 [d, 2H, (AA'BB'), *J* 8.8 Hz, H-3' and H-5'].

2,5-Dichloro-*N*-{4-[(2*E*)-3-phenylprop-2-enoyl]phenyl}benzenesulfonamide (**2**)<sup>2</sup> (Figures S3 and S4)

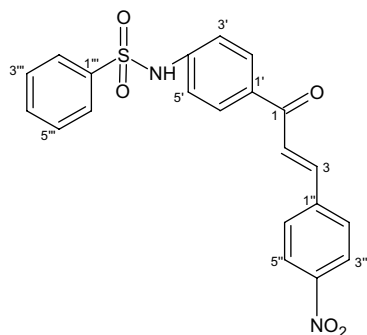


Yield: 82%; m.p. 204-207 °C; IR (KBr)  $\nu$  / cm<sup>-1</sup> 3148 (N-H), 1648 (C=O), 1602 (Ar-CO-C=C-Ar), 1562 (N-H), 1340 (S=O), 1287, 1222 (C-N), 1167 (S=O); <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  8.14 (d, 1H, *J* 2.6 Hz, H-6'''), 8.08 [d (AA'BB'), 2H, *J* 8.7 Hz, H-2' and H-6'], 7.84 [d, 1H, *J* 15.0 Hz, H-3 ( $\beta$ )], 7.83-7.89 (m, 2H, H-2'' and H-6''), 7.75 (dd, 1H, *J* 8.6, 2.6 Hz, H-4'''), 7.69 (d, 1H, *J* 8.6 Hz, H-3'''), 7.66 [d, 1H, *J* 15.0 Hz, H-2 ( $\alpha$ )], 7.45-7.47 (m, 1H, H-4''), 7.43-7.45 (m, 2H, H-3'' and H-5'''), 7.26 [d (AA'BB'), 2H, *J* 8.7 Hz, H-3' and H-5'].

*N*-{4-[(2*E*)-3-(4-Nitrophenyl)prop-2-enoyl]phenyl}benzenesulfonamide (**3**)<sup>3</sup> (Figures S5 and S6)

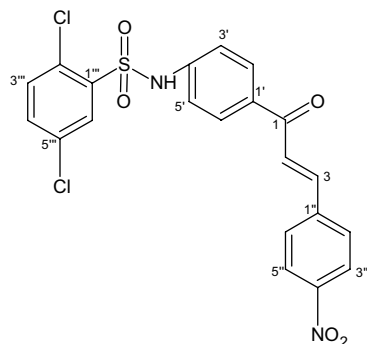
Yield: 55%; m.p. 178-181 °C; IR (KBr)  $\nu$  / cm<sup>-1</sup> 3311 (N-H), 1658 (C=O), 1607 (Ar-CO-C=C-Ar), 1516 (N-H), 1342 (S=O), 1281, 1223 (C-N), 1155 (S=O); <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  8.14 [d (AA'BB'), 2H, *J* 8.7 Hz,

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H-3'' and H-5''), 8.04 [d (AA'BB'), 2H,  $J$  8.7 Hz, H-2'' and H-6''), 8.03 [d, 1H,  $J$  16.0 Hz, H-3 ( $\beta$ )], 7.70 [d, 1H,  $J$  16.0 Hz, H-2 ( $\alpha$ )], 7.68 (m, 2H, H-2''' and H-6'''), 7.51 [d (AA'BB'), 2H,  $J$  8.8 Hz, H-2' and H-6'], 7.34-7.39 (m, 3H, H-3''', H-4''' and H-5'''), 6.76 [d (AA'BB'), 2H,  $J$  8.8 Hz, H-3' and H-5'].

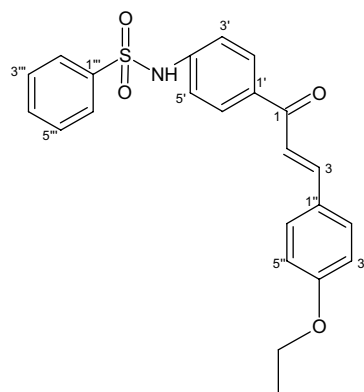
2,5-Dichloro-*N*-{4-[(2*E*)-3-(4-nitrophenyl)prop-2-enoyl]phenyl}benzenesulfonamide (**4**) (Figures S7 and S8)



Yield: 66%; m.p. 210-214 °C; IR (KBr)  $\nu$  /  $\text{cm}^{-1}$  3191 (N-H), 1656 (C=O), 1607 (Ar-CO-C=C-Ar), 1513 (N-H), 1343 (S=O), 1282, 1222 (C-N), 1164 (S=O);  $^1\text{H}$  NMR (500 MHz, DMSO- $d_6$ )  $\delta$  8.27 [d (AA'BB'), 2H,  $J$  8.8 Hz, H-3'' and H-5''), 8.14 (d, 1H,  $J$  2.5 Hz, H-6'''), 8.12 [d (AA'BB'), 2H,  $J$  8.8 Hz, H-2' and H-6'], 8.11 [d (AA'BB'), 2H,  $J$  8.8 Hz, H-2'' and H-6''], 8.04 [d, 1H,  $J$  15.6 Hz, H-3 ( $\beta$ )], 7.76 (dd, 1H,  $J$  8.5, 2.5, H-4'''), 7.72 [d, 1H,  $J$  15.6 Hz, H-2 ( $\alpha$ )], 7.70 (d, 1H,  $J$  8.5 Hz, H-3'''), 7.28 [d (AA'BB'), 2H,  $J$  8.8 Hz, H-3' and H-5'].

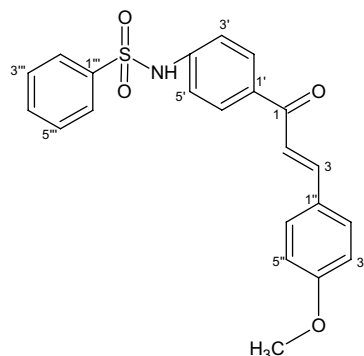
*N*-{4-[(2*E*)-3-(4-Ethoxyphenyl)prop-2-enoyl]phenyl}benzenesulfonamide (**5**) (Figures S9 and S10)

Yield: 65%; m.p. 152-154 °C; IR (KBr)  $\nu$  /  $\text{cm}^{-1}$  3201 (N-H), 1649 (C=O), 1600 (Ar-CO-C=C-Ar), 1567 (N-H), 1345 (S=O), 1291, 1247 (C-N), 1163 (S=O);  $^1\text{H}$  NMR (500 MHz, DMSO- $d_6$ )  $\delta$  8.04 [d (AA'BB'), 2H,  $J$  8.6 Hz, H-2' and H-6'], 7.84-7.89 (m, 2H, H-2''' and H-6'''), 7.78 [d (AA'BB'), 2H,  $J$  8.9 Hz, H-2'' and H-6''], 7.70 [d, 1H,  $J$  15.5 Hz, H-3 ( $\beta$ )], 7.65 [d, 1H,  $J$  15.6 Hz, H-2 ( $\alpha$ )],



7.61-7.66 (m, 2H, H-3''' and H-5'''), 7.56- 7.61 (m, 1H, H-4'''), 7.26 [d (AA'BB'), 2H,  $J$  8.6 Hz, H-3' and H-5'], 6.98 [d (AA'BB'), 2H,  $J$  8.9 Hz, H-3'' and H-5'']; 4.09 (q, 2H,  $J$  7.0 Hz, CH<sub>2</sub>), 1.34 (t, 3H,  $J$  7.0 Hz, CH<sub>3</sub>).

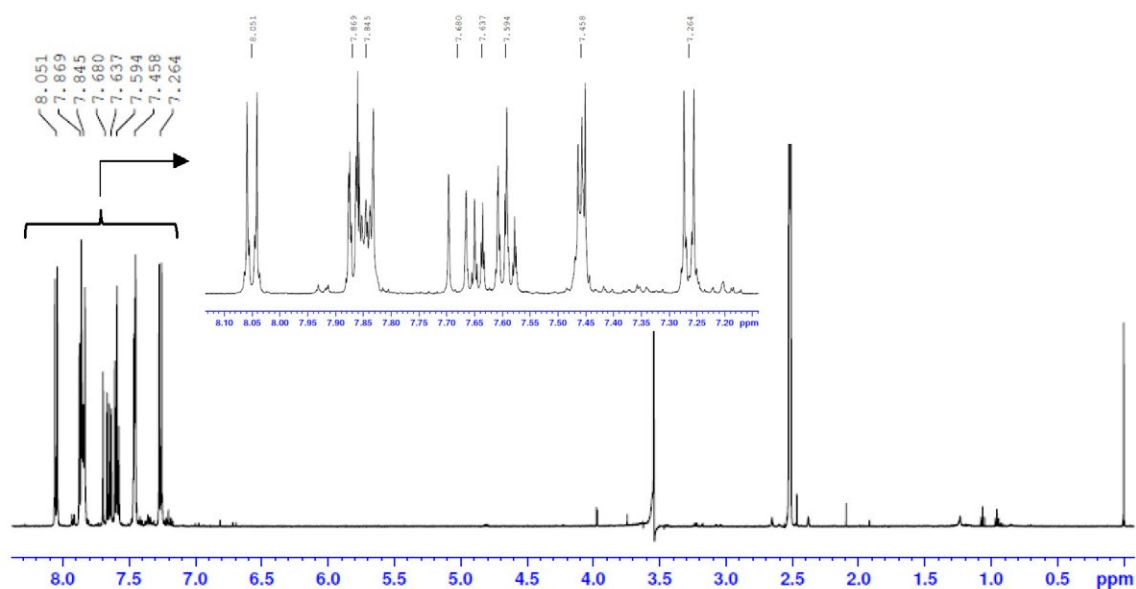
*N*-{4-[(2*E*)-3-(4-Methoxyphenyl)prop-2-enoyl]phenyl}benzenesulfonamide (**6**)<sup>3</sup> (Figures S11 and S12)



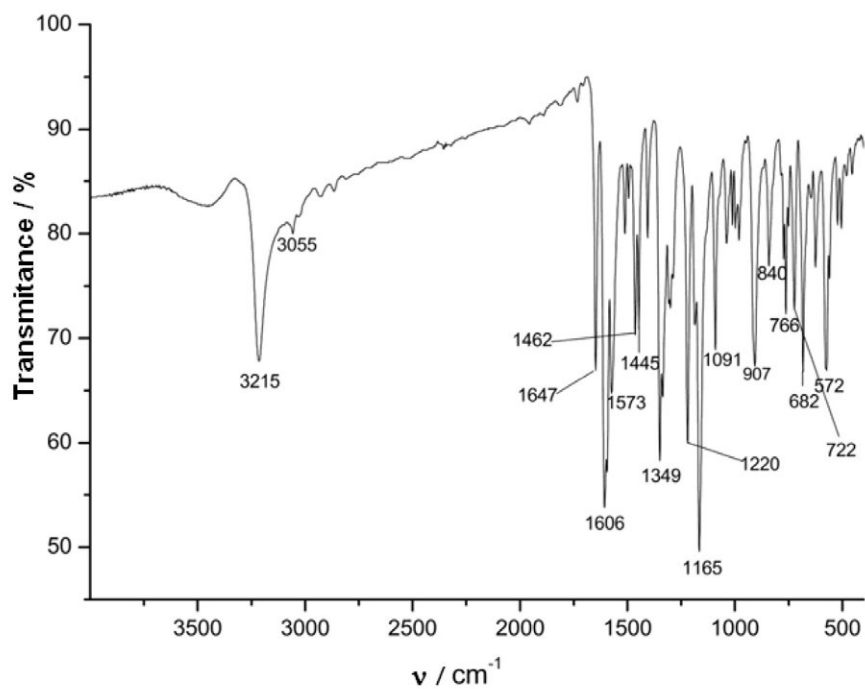
Yield: 57%; m.p. 173-175 °C; IR (KBr)  $\nu$  /  $\text{cm}^{-1}$  3210 (N-H), 1644 (C=O), 1597 (Ar-CO-C=C-Ar), 1560 (N-H), 1348 (S=O), 1298, 1257 (C-N), 1163 (S=O);  $^1\text{H}$  NMR (500 MHz, DMSO- $d_6$ )  $\delta$  8.05 [d (AA'BB'), 2H,  $J$  8.7 Hz, H-2' and H-6'], 7.84-7.89 (m, 2H, H-2''' and H-6'''), 7.81 [d (AA'BB'), 2H,  $J$  8.7 Hz, H-2'' and H-6''], 7.72 [d, 1H,  $J$  15.4 Hz, H-3 ( $\beta$ )], 7.66 [d, 1H,  $J$  15.4 Hz, H-2 ( $\alpha$ )], 7.61-7.66 (m, 2H, H-3''' and H-5'''), 7.56-7.61 (m, 1H, H-4'''), 7.26 [d (AA'BB'), 2H,  $J$  8.7 Hz, H-3' and H-5'], 7.01 [d (AA'BB'), 2H,  $J$  8.7 Hz, H-3'' and H-5''], 3.81 (s, 3H, OCH<sub>3</sub>).

## References

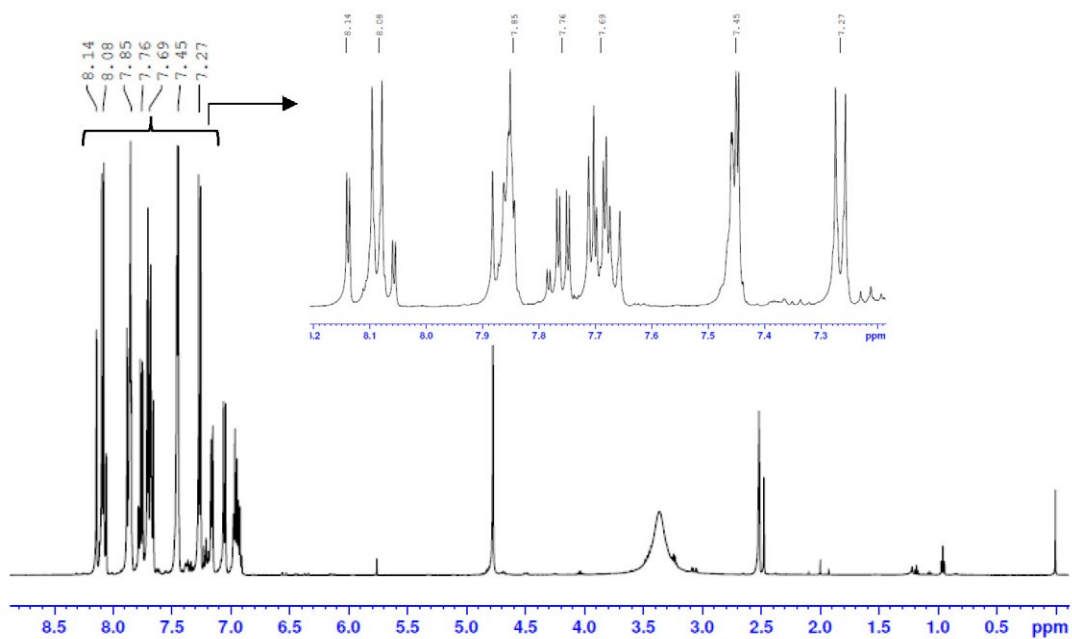
- Iqbal, H.; Prabhakar, V.; Sangith, A.; Chandrika, B.; Balasubramanian, R.; *Med. Chem. Res.* **2014**, *23*, 4383.
- Domínguez, J. N.; Leon, C.; Rodrigues, J.; Domingues, N. G.; Gut, J.; Rosenthal, P.; *Il Farmaco* **2005**, *60*, 307.
- Moustafa, O. S.; Ahmad, R. A.; *Phosphorus, Sulfur Silicon Relat. Elem.* **2003**, *178*, 475.



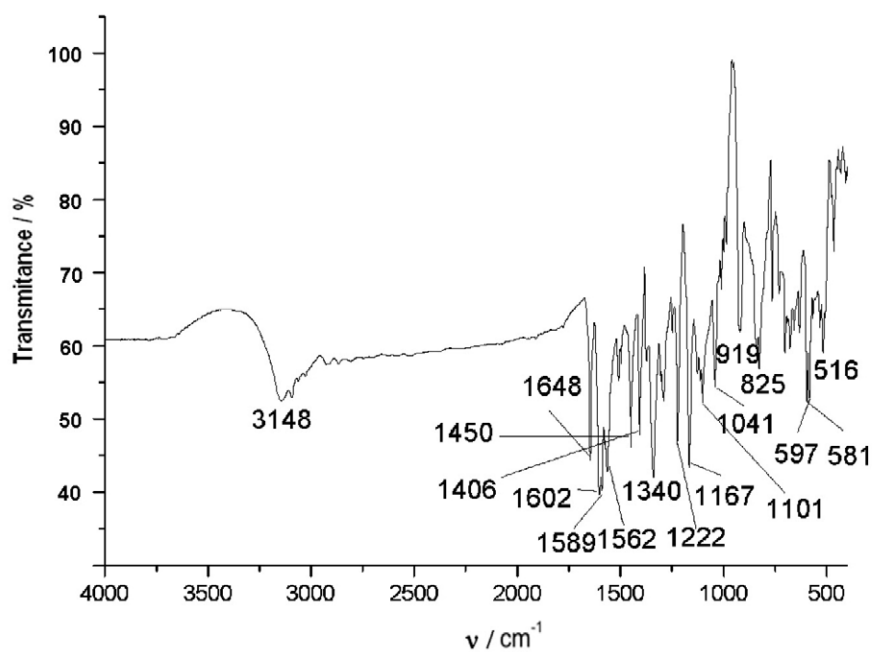
**Figure S1.**  $^1\text{H}$  NMR spectrum (500 MHz,  $\text{DMSO}-d_6$ ) of *N*-{4-[(2*E*)-3-phenylprop-2-enoyl]phenyl}benzenesulfonamide (**1**).



**Figure S2.** IR spectrum (KBr) of *N*-{4-[(2*E*)-3-phenylprop-2-enoyl]phenyl}benzenesulfonamide (**1**).



**Figure S3.** <sup>1</sup>H NMR spectrum (500 MHz, DMSO-*d*<sub>6</sub>) of 2,5-dichloro-*N*-{4-[(*2E*)-3-phenylprop-2-enoyl]phenyl}benzenesulfonamide (**2**).



**Figure S4.** IR spectrum (KBr) of 2,5-dichloro-*N*-{4-[(*2E*)-3-phenylprop-2-enoyl]phenyl}benzenesulfonamide (**2**).

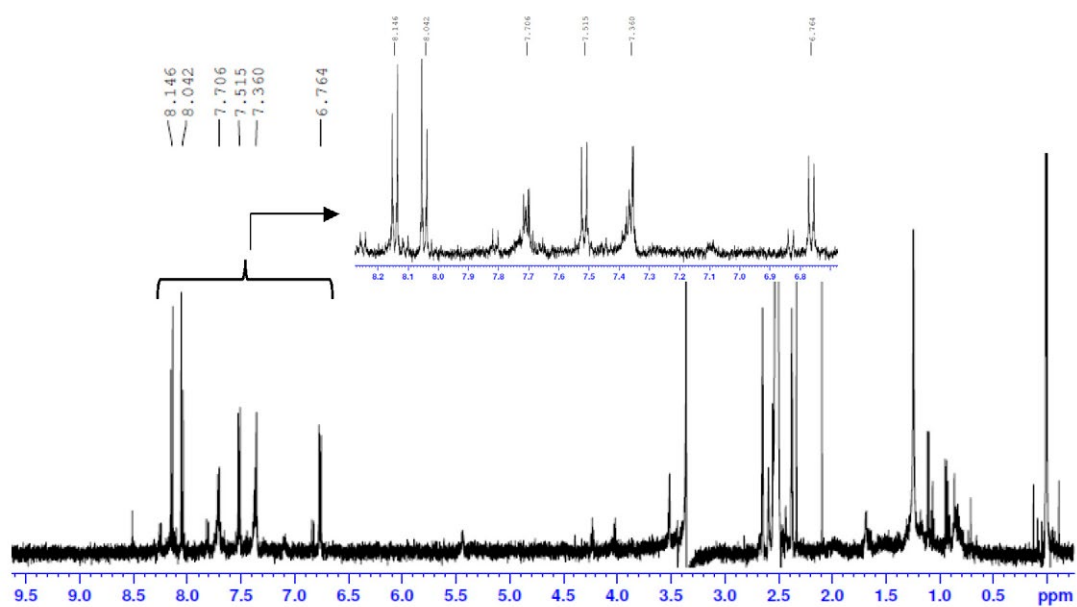


Figure S5.  $^1\text{H}$  NMR spectrum (500 MHz,  $\text{DMSO-}d_6$ ) of *N*-{4-[(2*E*)-3-(4-nitrophenyl)prop-2-enoyl]phenyl}benzenesulfonamide (**3**).

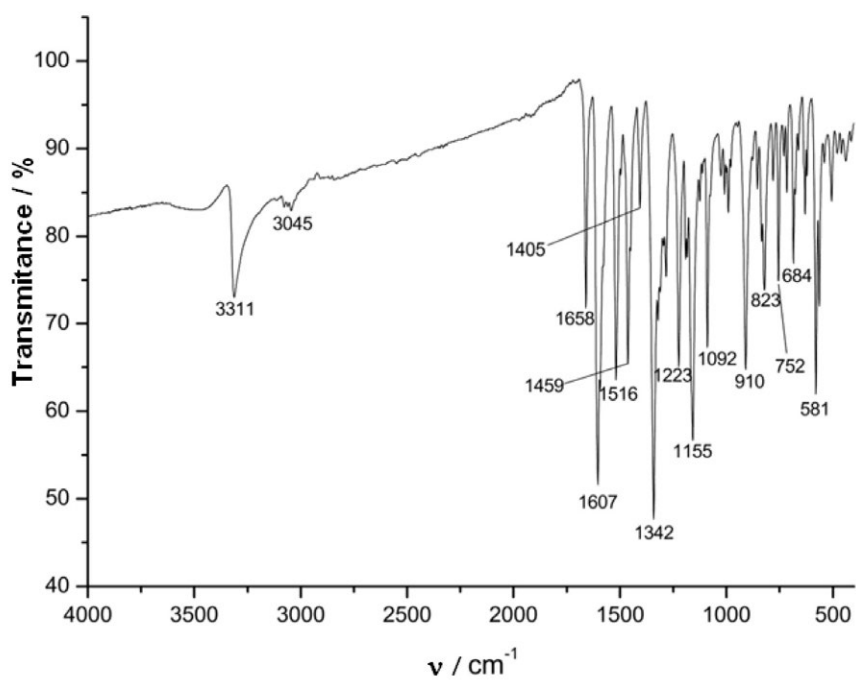


Figure S6. IR spectrum (KBr) of *N*-{4-[(2*E*)-3-(4-nitrophenyl)prop-2-enoyl]phenyl}benzenesulfonamide (**3**).

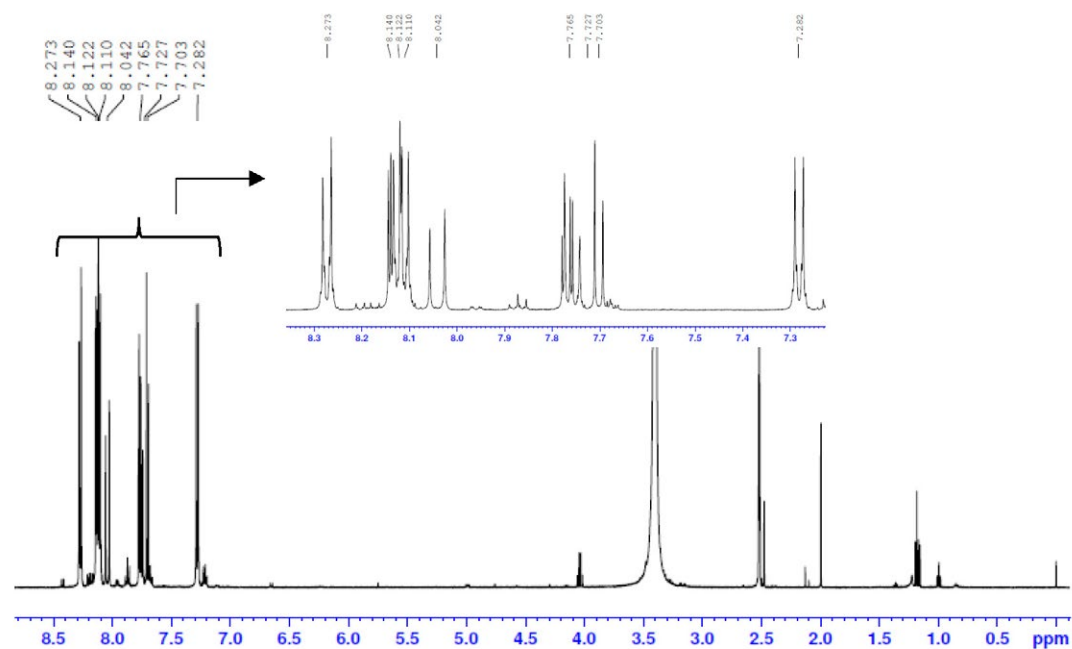


Figure S7. <sup>1</sup>H NMR spectrum (500 MHz, DMSO-*d*<sub>6</sub>) of 2,5-dichloro-*N*-{4-[(*E*)-3-(4-nitrophenyl)prop-2-enoyl]phenyl}benzenesulfonamide (4).

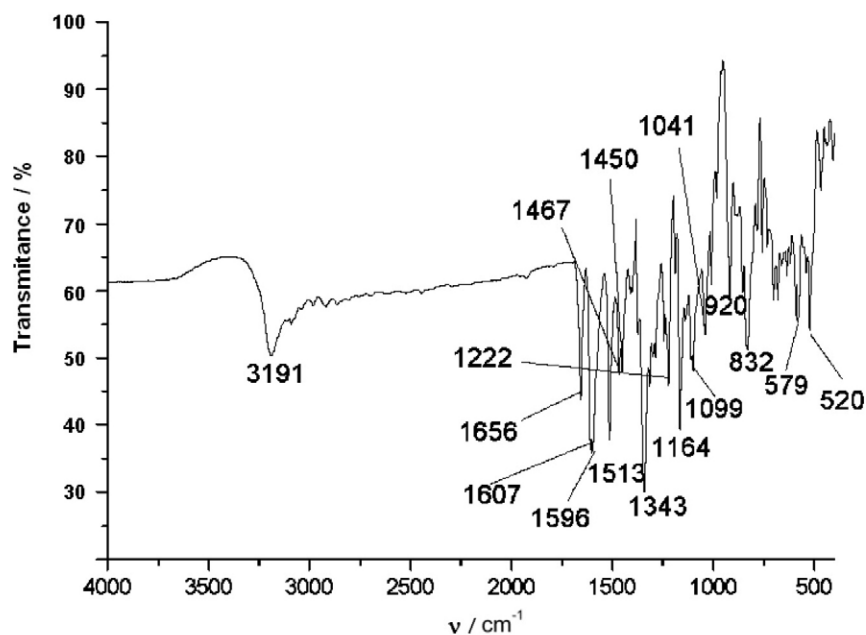


Figure S8. IR spectrum (KBr) of 2,5-dichloro-*N*-{4-[(*E*)-3-(4-nitrophenyl)prop-2-enoyl]phenyl}benzenesulfonamide (4).

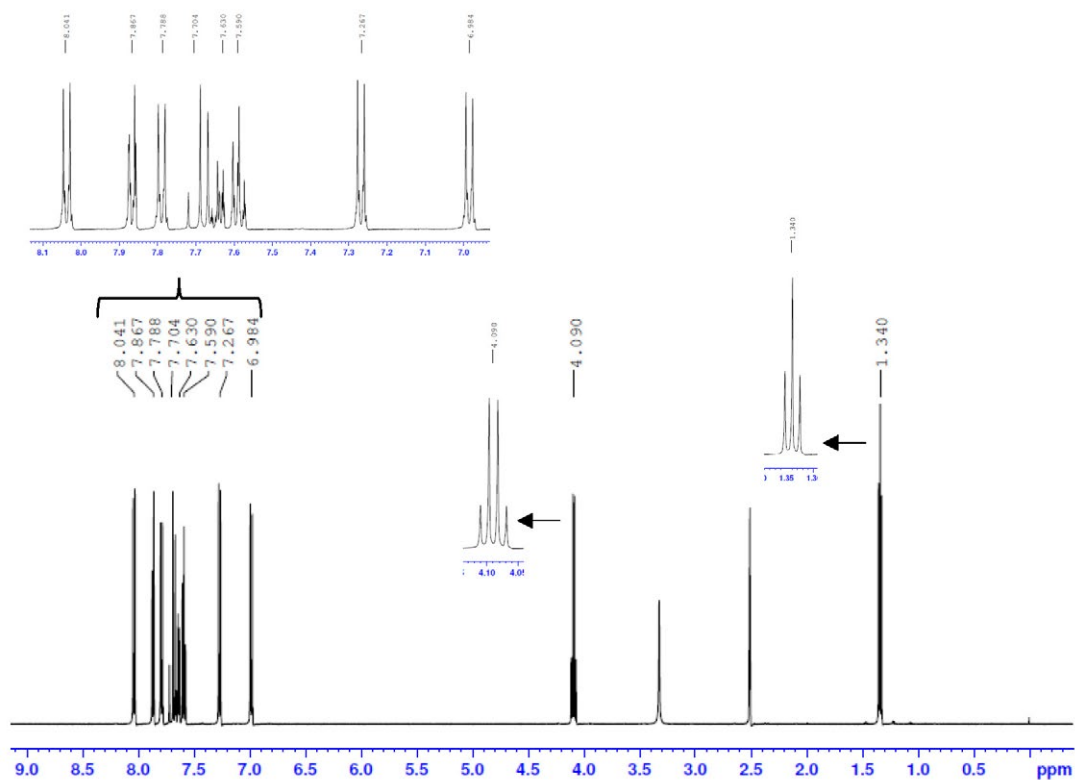


Figure S9. <sup>1</sup>H NMR spectrum (500 MHz, DMSO-*d*<sub>6</sub>) of *N*-{4-[(2*E*)-3-(4-ethoxyphenyl)prop-2-enyl]phenyl}benzenesulfonamide (5).

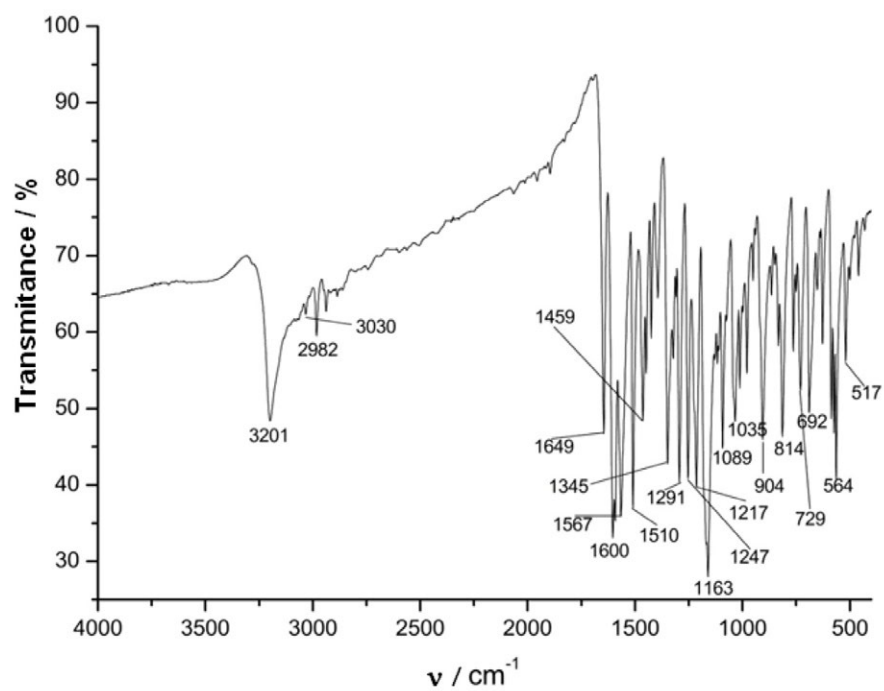


Figure S10. IR spectrum (KBr) of *N*-{4-[(2*E*)-3-(4-ethoxyphenyl)prop-2-enyl]phenyl}benzenesulfonamide (5).

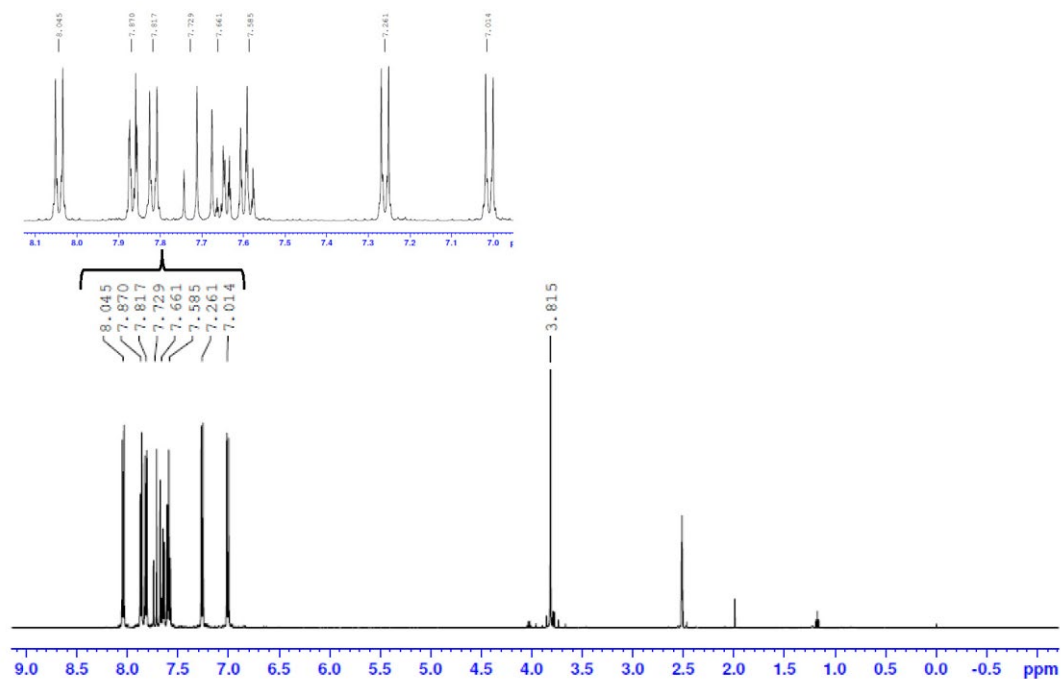


Figure S11.  $^1\text{H}$  NMR spectrum (500 MHz,  $\text{DMSO-}d_6$ ) of *N*-{4-[(2*E*)-3-(4-methoxyphenyl)prop-2-enoyl]phenyl}benzenesulfonamide (**6**).

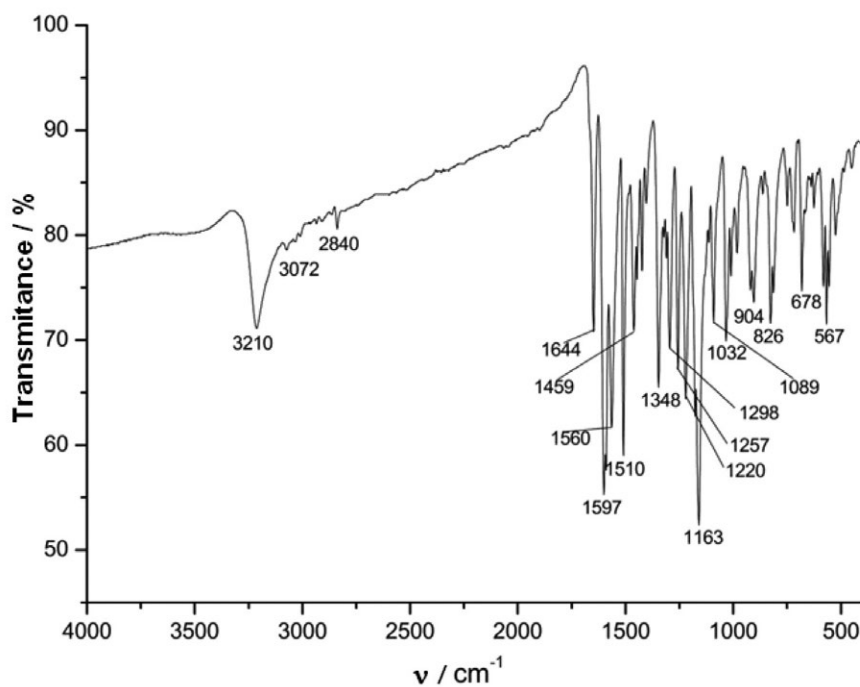


Figure S12. IR spectrum (KBr) of *N*-{4-[(2*E*)-3-(4-methoxyphenyl)prop-2-enoyl]phenyl}benzenesulfonamide (**6**).

## References

- Iqbal, H.; Prabhakar, V.; Sangith, A.; Chandrika, B.; Balasubramanian, R.; *Med. Chem. Res.* **2014**, *23*, 4383.
- Domínguez, J. N.; Leon, C.; Rodrigues, J.; Domingues, N. G.; Gut, J.; Rosenthal, P.; *Il Farmaco* **2005**, *60*, 307.
- Moustafa, O. S.; Ahmad, R. A.; *Phosphorus, Sulfur Silicon Relat. Elem.* **2003**, *178*, 475.