

Computer-Aided Design, Synthesis, and Antiviral Evaluation of Novel Acrylamides as Potential Inhibitors of E3-E2-E1 Glycoproteins Complex from Chikungunya Virus

Gabriel Felipe Silva Passos ¹, Matheus Gabriel Moura Gomes ¹, Thiago Mendonça de Aquino ², João Xavier de Araújo-Júnior ¹, Stephannie Janaína Maia Souza ³, João Pedro Monteiro Cavalcante ³, Elane Conceição dos Santos ³, Ênio José Bassi ³, and Edeildo Ferreira da Silva-Júnior ^{1, 2 *}

¹ Laboratory of Medicinal Chemistry, Pharmaceutical Sciences Institute, Federal University of Alagoas, Maceió, Brazil; e-mails: gabrielfelipepassos@gmail.com (G.F.S.P.); matheus_gabriel199@hotmail.com (M.G.M.G.); jotaaraujo2004@gmail.com (J.X.A.J.)

² Center of Analysis and Research in Nuclear Magnetic Resonance, Chemistry and Biotechnology Institute, Federal University of Alagoas, Maceió, Brazil; e-mail: thiago.aquino@iqb.ufal.br (T.M.A.)

³ Immunoregulation Research Group, Laboratory of Research in Virology and Immunology, Institute of Biological and Health Sciences, Federal University of Alagoas, Maceió, Brazil; e-mails: stephanniemaia92@gmail.com (S.J.M.S.); j.p.monteirocavalcante@gmail.com (J.P.M.C.); elane.santos@icbs.ufal.br (E.C.S.); enio.bassi@icbs.ufal.br (Ê.J.B.)

* Correspondence: edeildo.junior@iqb.ufal.br; Tel.: +55-87-9-9610-8311 (E.F.S.J.)

* SUPPLEMENTARY MATERIAL *

Figure S1. ¹H NMR spectrum of (E)-3-(3,4-Dichlorophenyl)acrylic acid (**3a**)

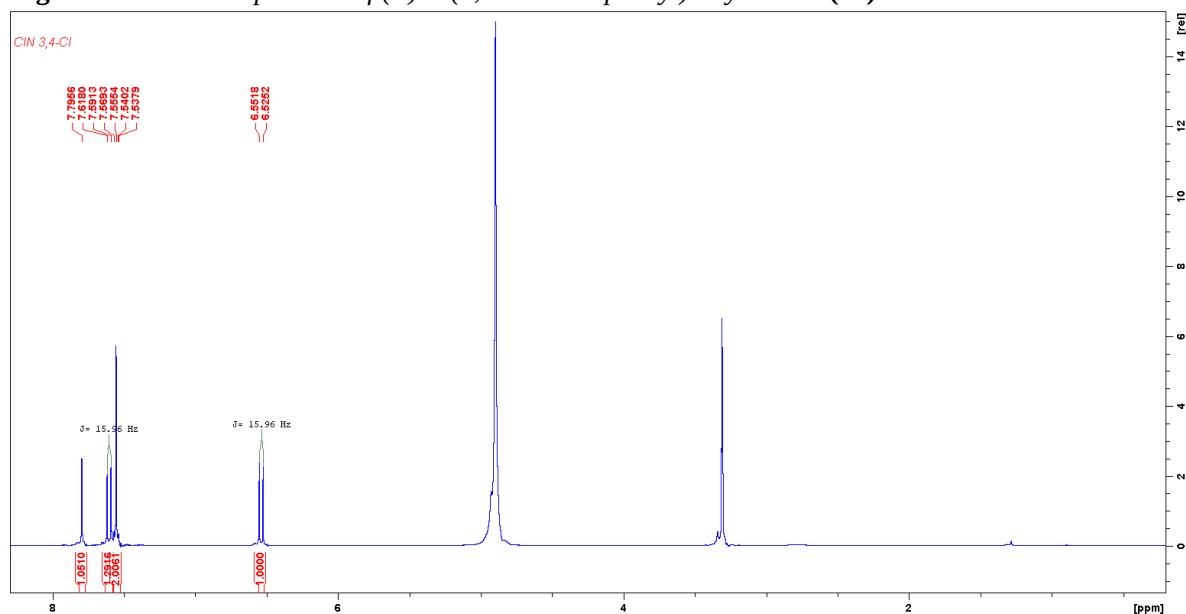


Figure S2. ^1H NMR spectrum of (*E*)-3-([1,1'-Biphenyl]-4-yl)acrylic acid (**3b**)

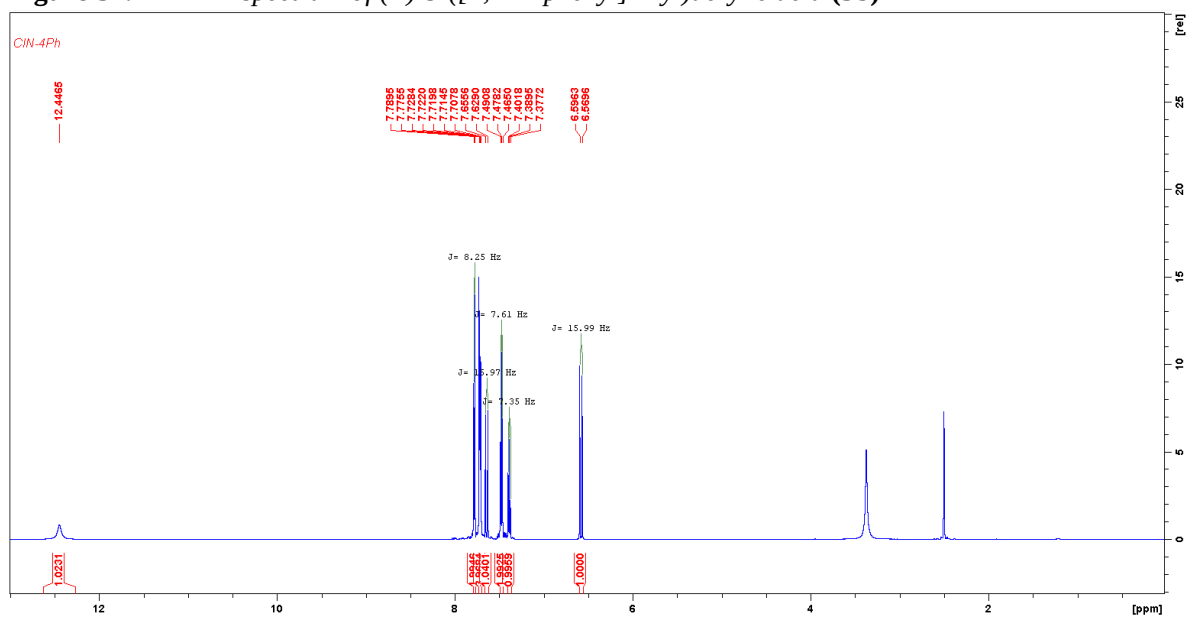


Figure S3. ^1H NMR spectrum of (*E*)-3-(4-(Trifluoromethyl)phenyl)acrylic acid (**3c**)

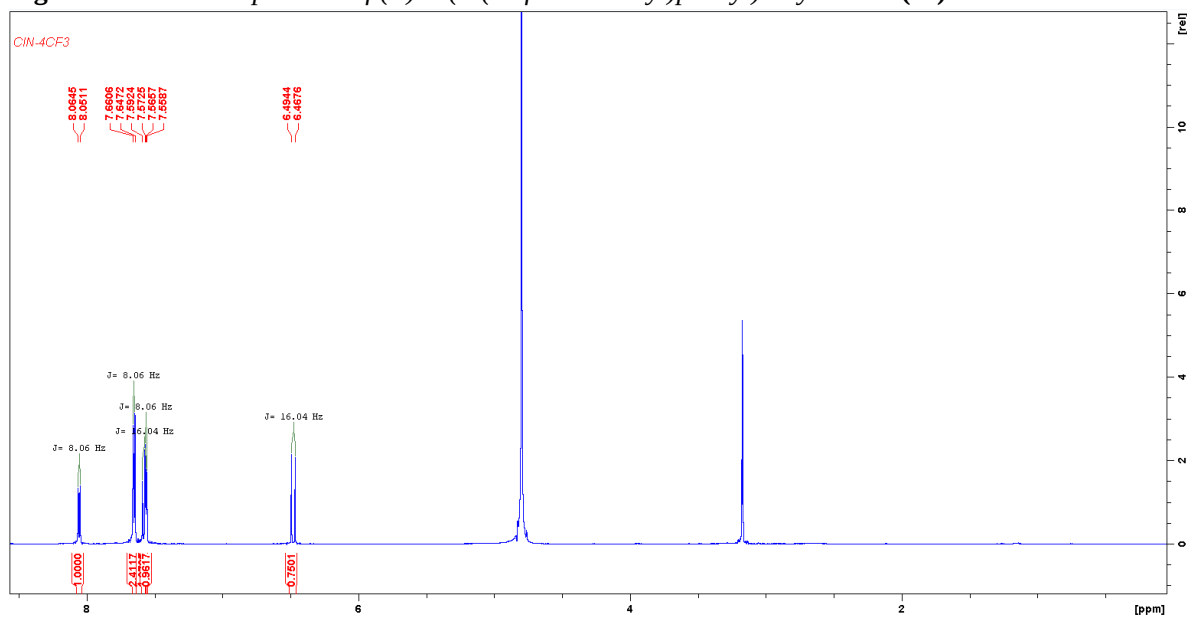


Figure S4. ^1H NMR spectrum of (*E*)-3-(2,3-Dichlorophenyl)acrylic acid (**3d**)

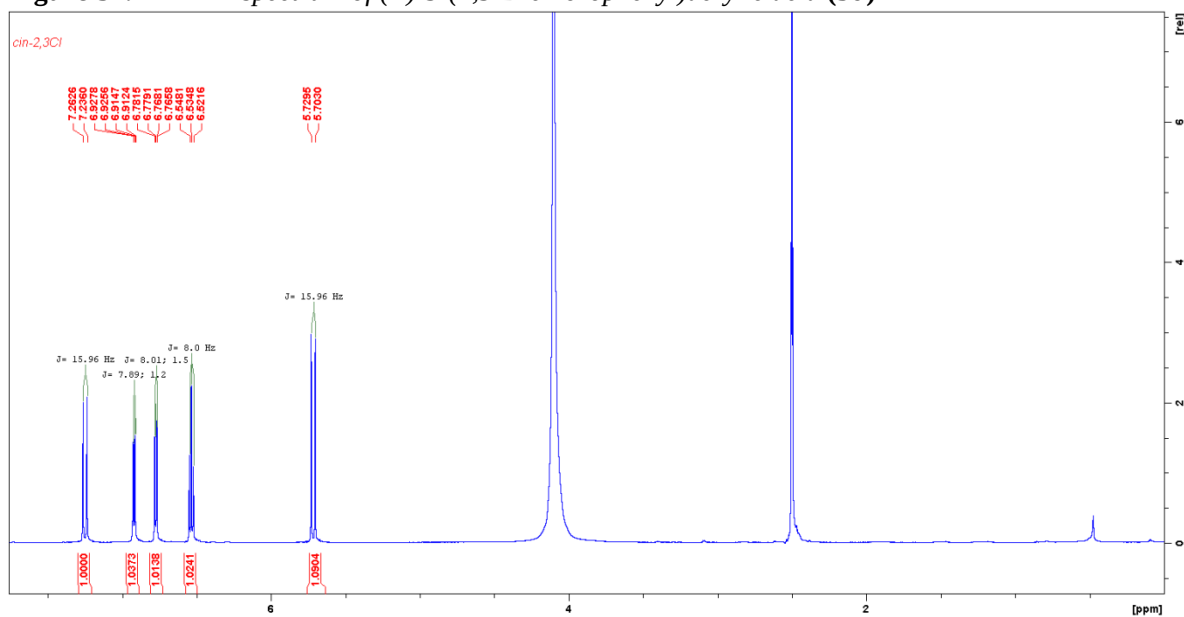


Figure S5. ^1H NMR spectrum of (*E*)-3-(4-Fluorophenyl)acrylic acid (**3e**)

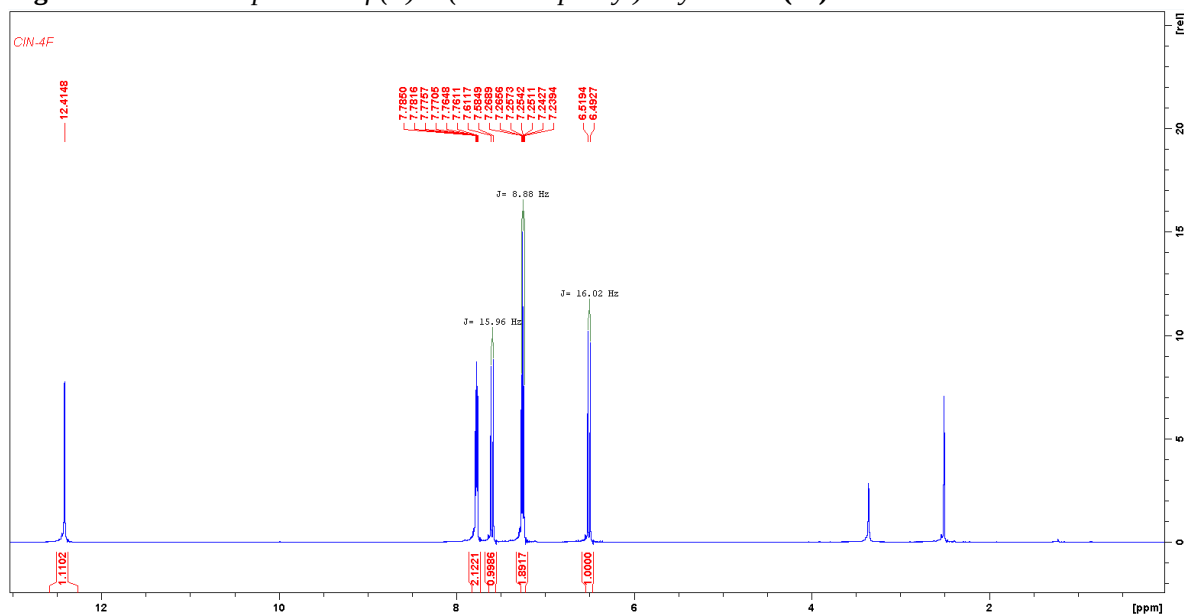


Figure S6. ^1H NMR spectrum of (*E*)-3-(2,4-Dichlorophenyl)acrylic acid (**3f**)

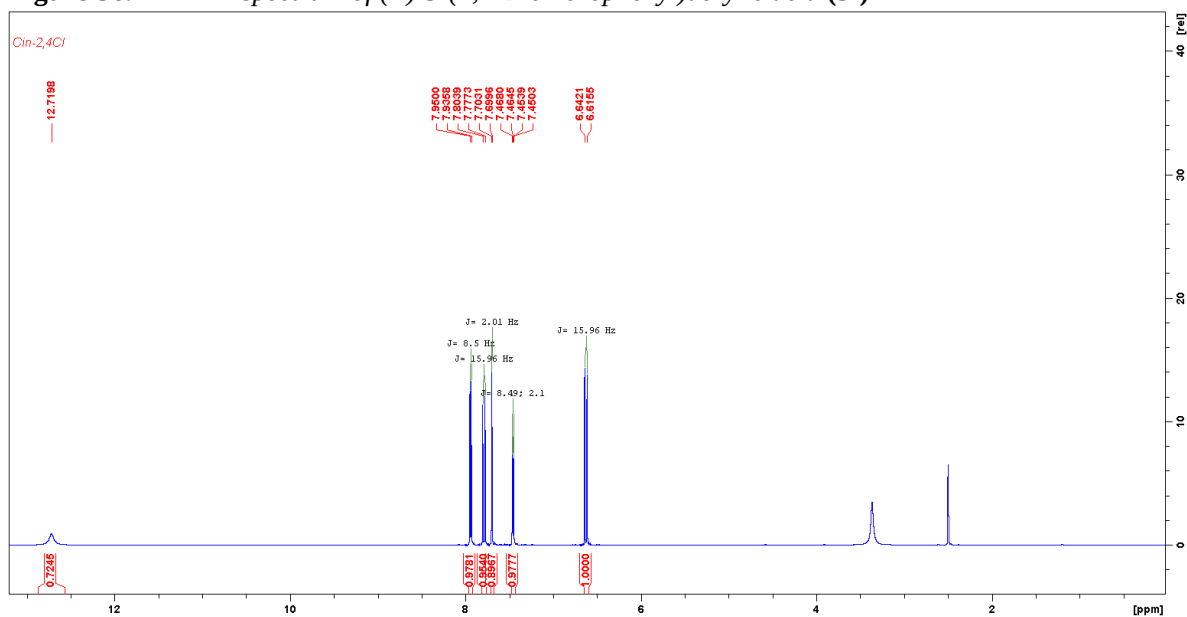


Figure S7. ^1H NMR spectrum of (*E*)-3-(3-Chlorophenyl)acrylic acid (**3g**)

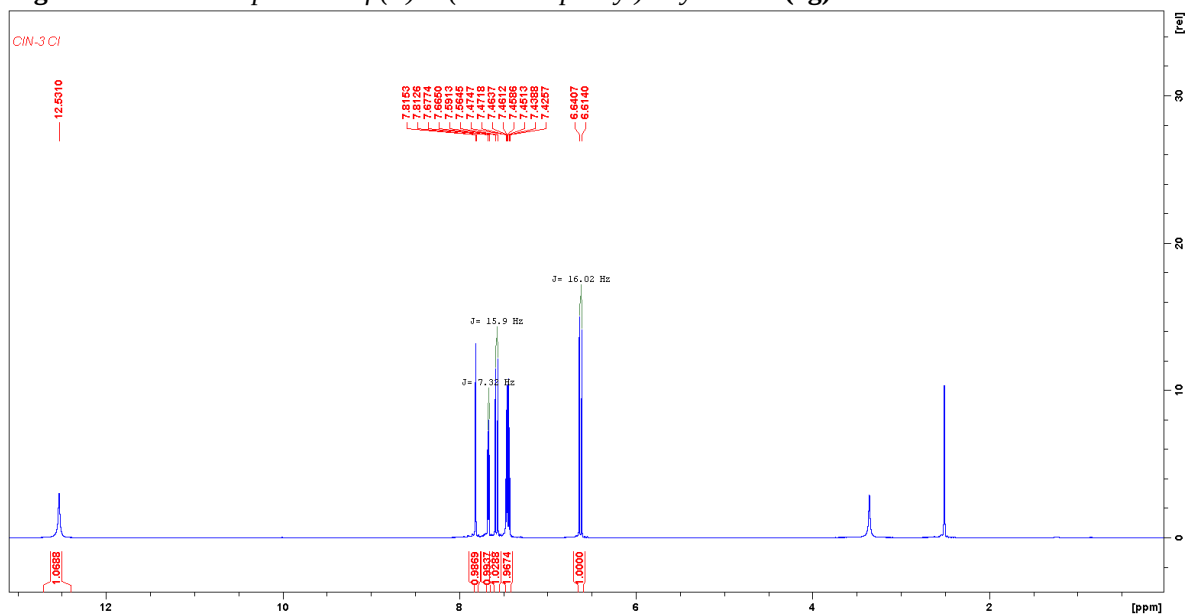


Figure S8. ^1H NMR spectrum of (*E*)-3-(3,4-Dimethoxyphenyl)acrylic acid (**3h**)

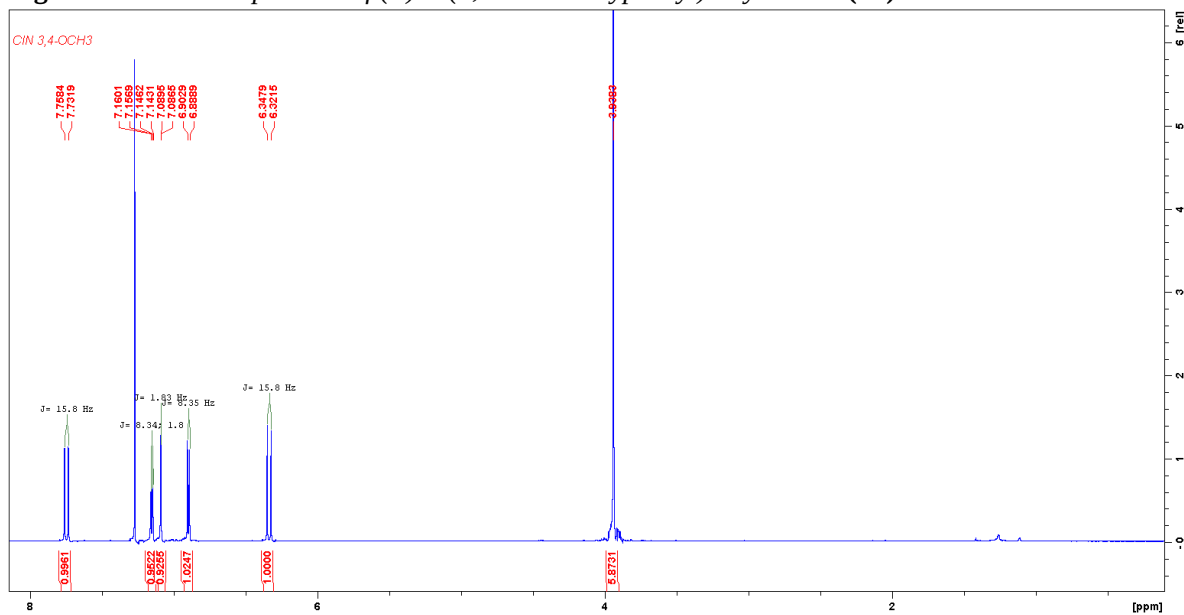


Figure S9. ^1H NMR spectrum of (*E*)-3-(2-Methoxyphenyl)acrylic acid (**3i**)

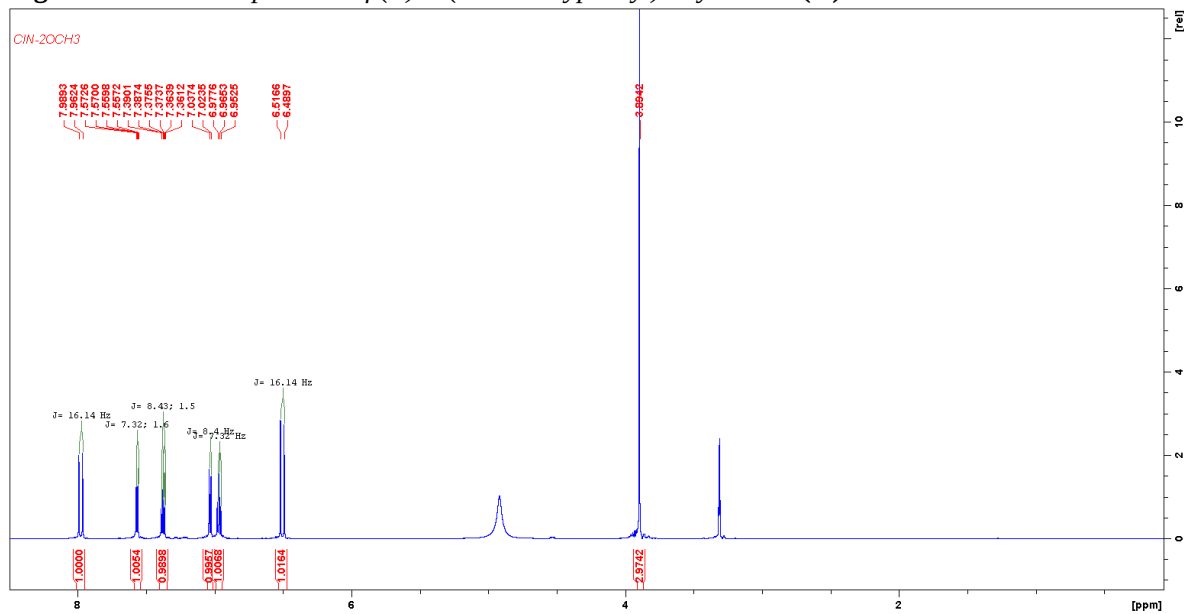


Figure S10. ^1H NMR spectrum of (*E*)-3-([1,1'-Biphenyl]-2-yl)acrylic acid (**3j**)

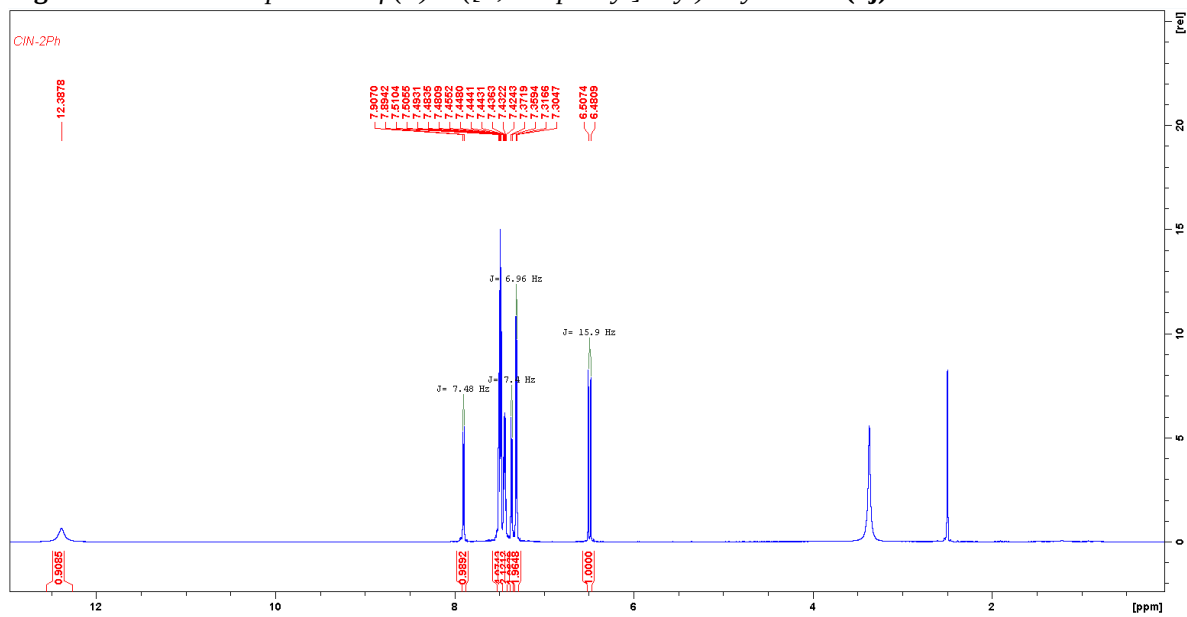


Figure S11. HPLC chromatogram of (*E*)-3-(3,4-Dichlorophenyl)-*N*-phenylacrylamide (**LQM328**)

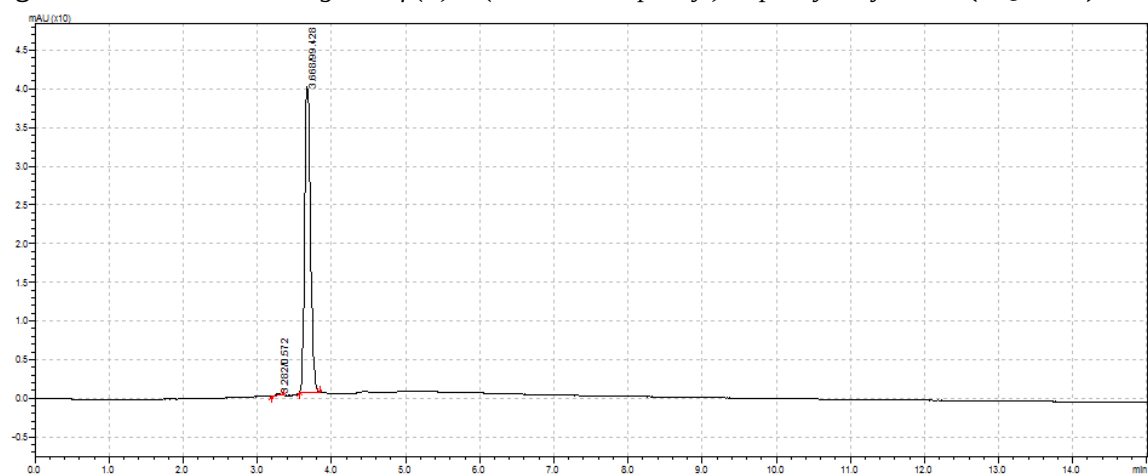


Figure S12. FT-IR spectrum of (*E*)-3-(3,4-Dichlorophenyl)-*N*-phenylacrylamide (**LQM328**)

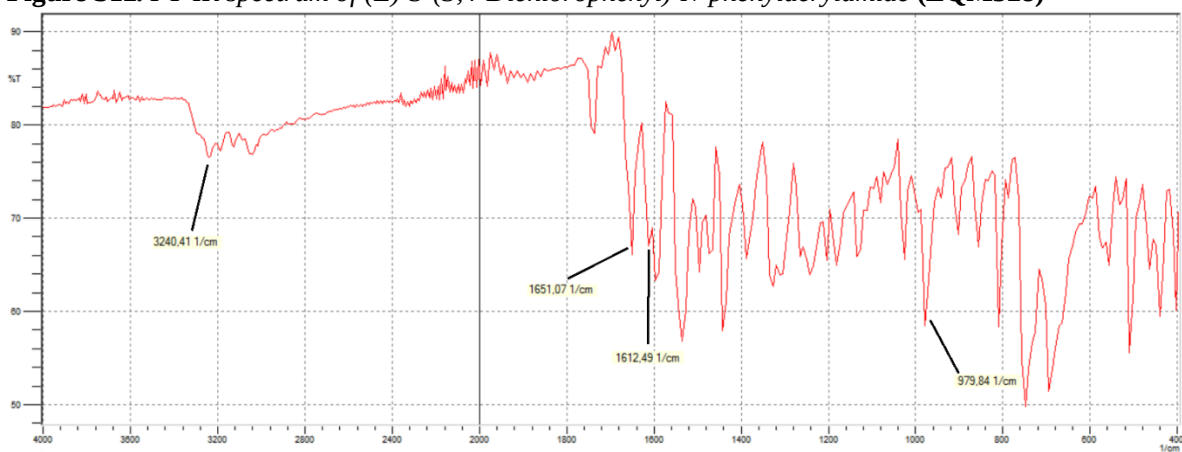


Figure S13. ^1H NMR spectrum of (*E*)-3-(3,4-Dichlorophenyl)-*N*-phenylacrylamide (**LQM328**)

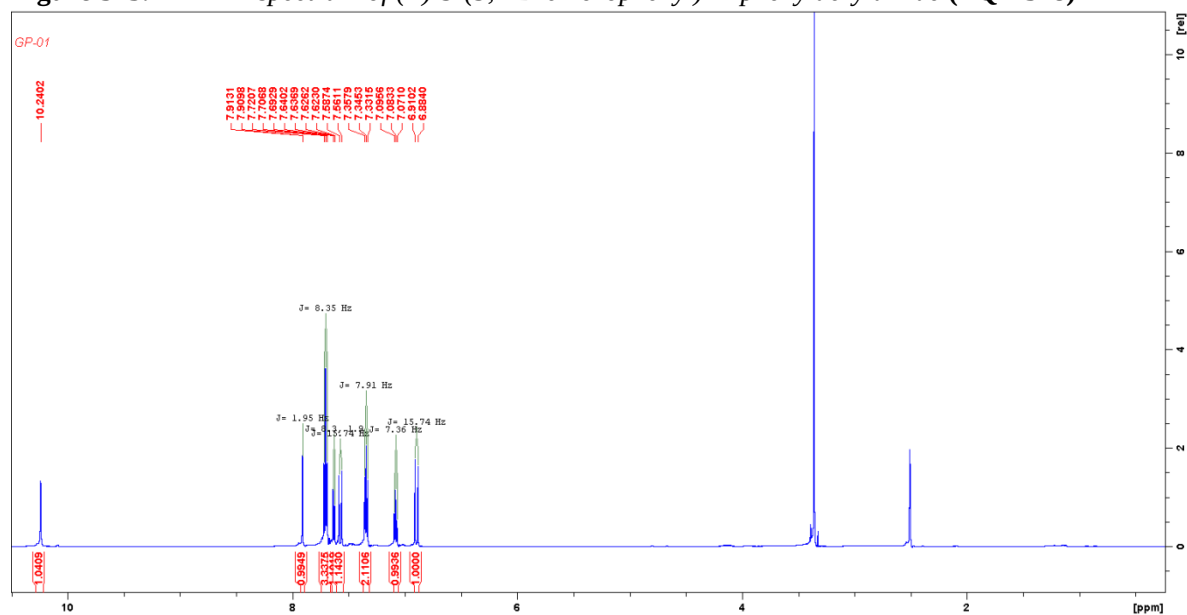


Figure S14. ^{13}C NMR spectrum of (*E*)-3-(3,4-Dichlorophenyl)-*N*-phenylacrylamide (**LQM328**)

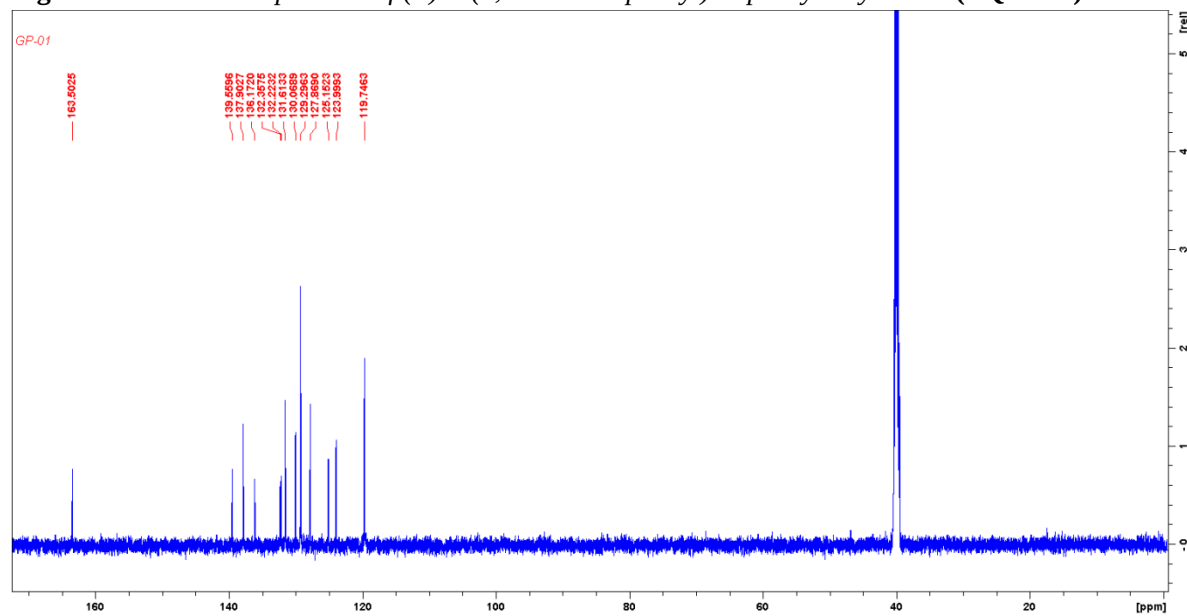


Figure S15. HPLC chromatogram of (*E*)-3-([1,1'-Biphenyl]-4-yl)-*N*-phenylacrylamide (**LQM329**)

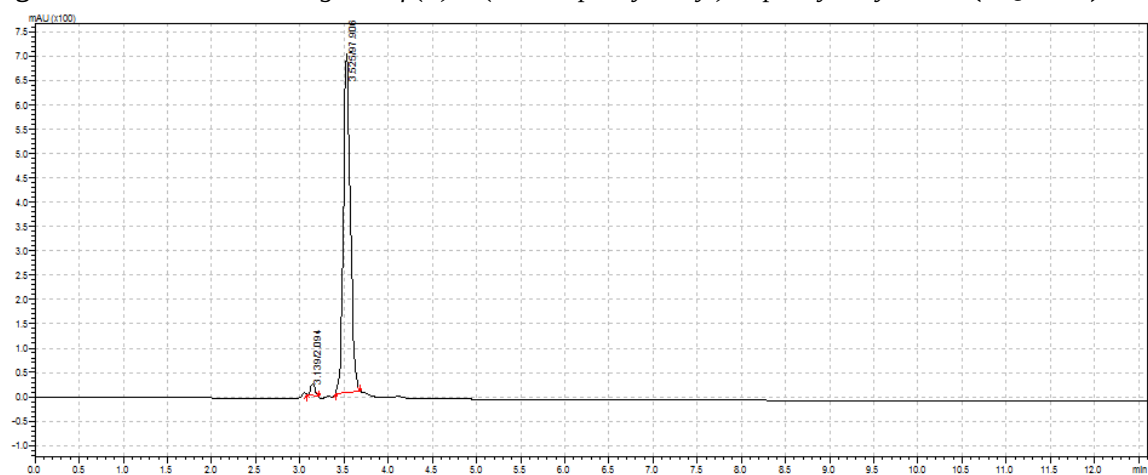


Figure S16. FT-IR spectrum of (*E*)-3-([1,1'-Biphenyl]-4-yl)-*N*-phenylacrylamide (**LQM329**)

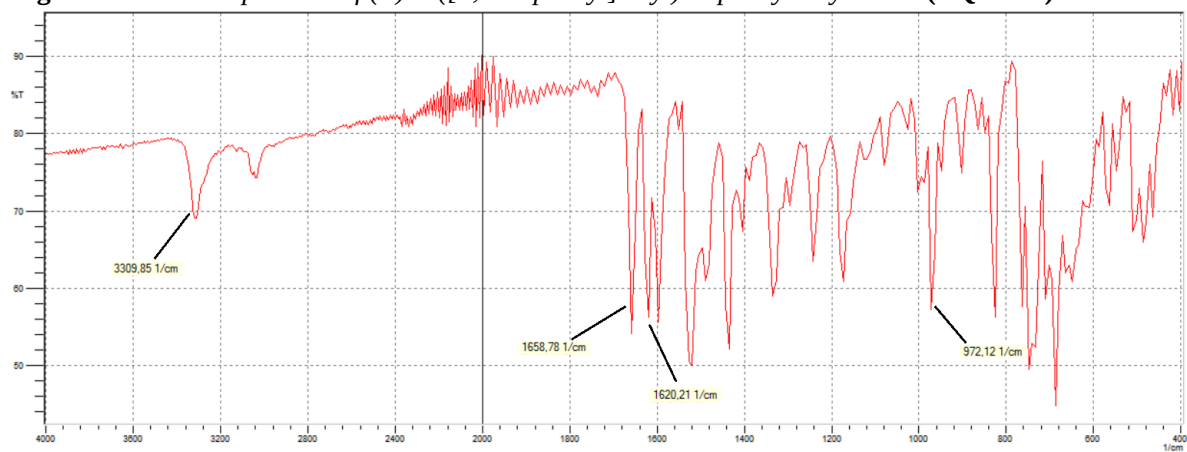


Figure S17. ^1H NMR spectrum of (*E*)-3-([1,1'-Biphenyl]-4-yl)-*N*-phenylacrylamide (**LQM329**)

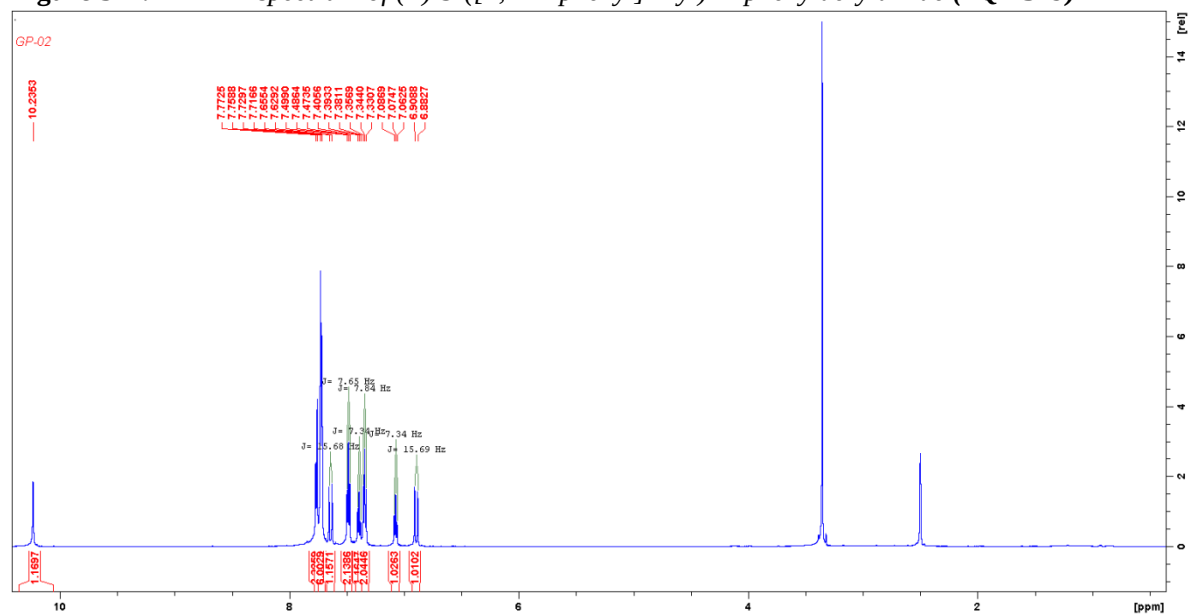


Figure S18. ^{13}C NMR spectrum of (*E*)-3-([1,1'-Biphenyl]-4-yl)-*N*-phenylacrylamide (**LQM329**)

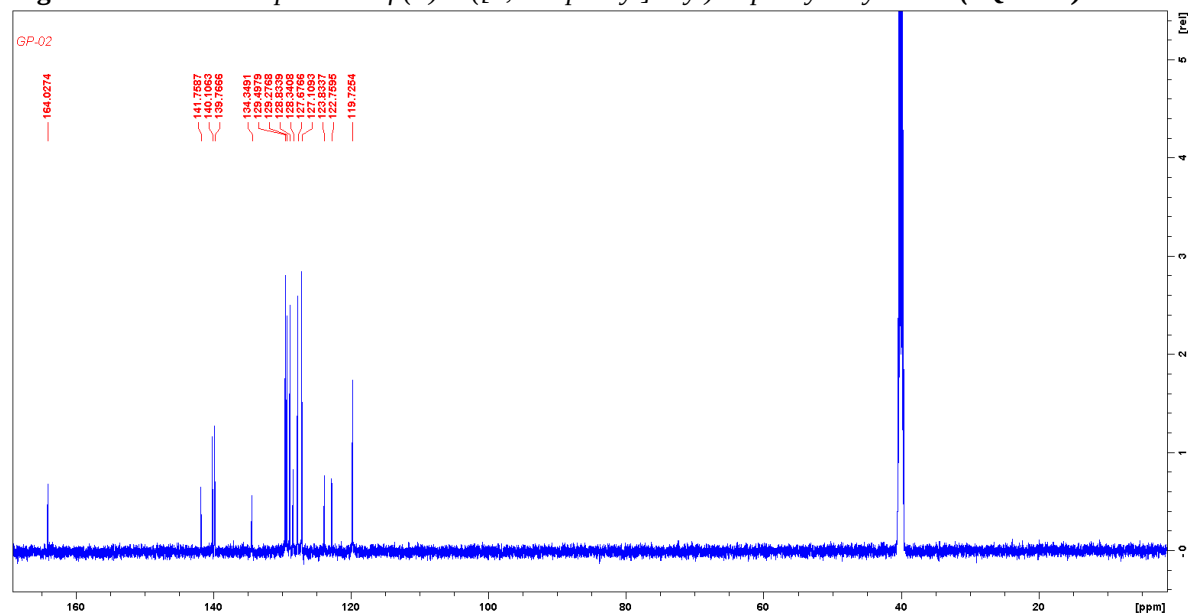


Figure S19. HPLC chromatogram of (E)-N-Phenyl-3-(4-(trifluoromethyl)phenyl)acrylamide (**LQM330**)

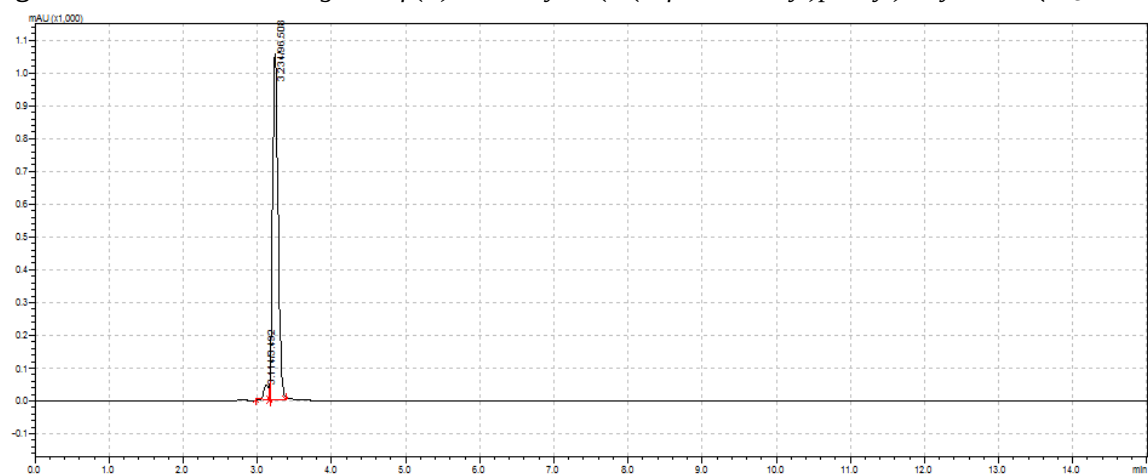


Figure S20. FT-IR spectrum of (E)-N-Phenyl-3-(4-(trifluoromethyl)phenyl)acrylamide (**LQM330**)

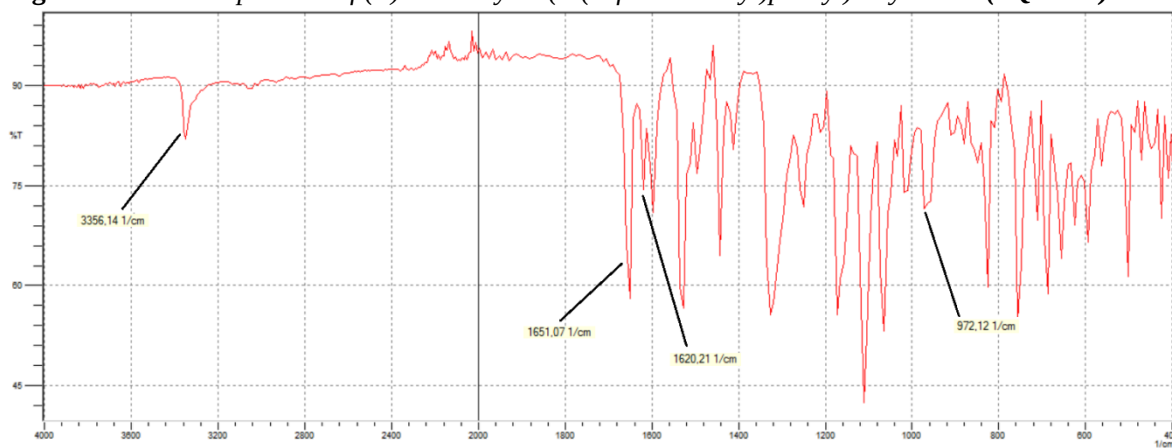


Figure S21. ^1H NMR spectrum of (*E*)-*N*-Phenyl-3-(4-(trifluoromethyl)phenyl)acrylamide (**LQM330**)

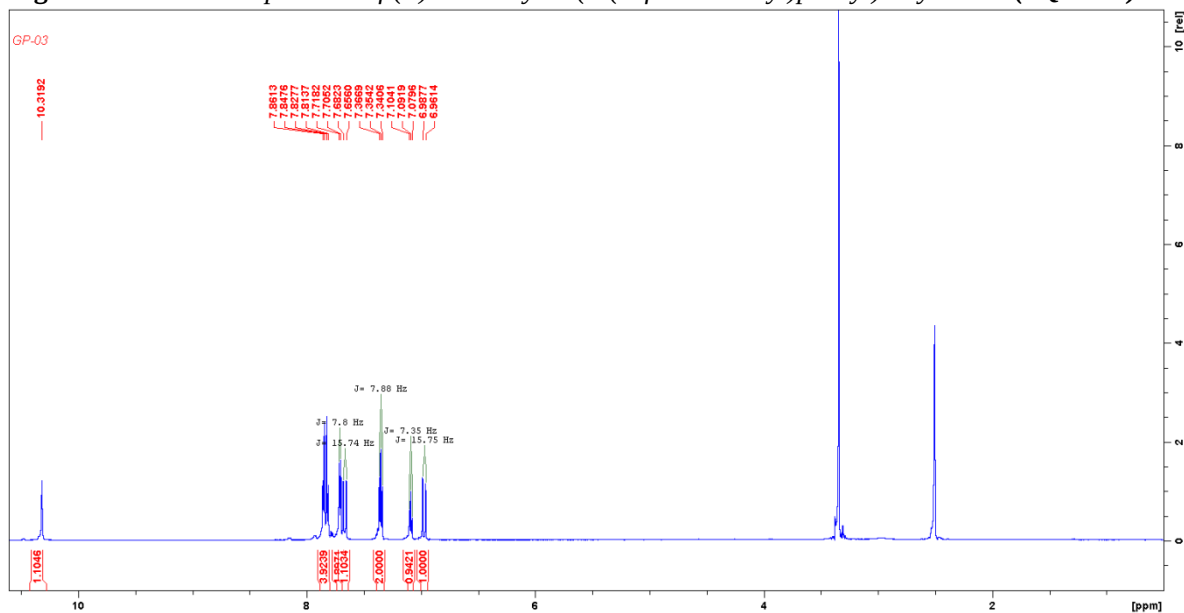


Figure S22. ^{13}C NMR spectrum of (*E*)-*N*-Phenyl-3-(4-(trifluoromethyl)phenyl)acrylamide (**LQM330**)

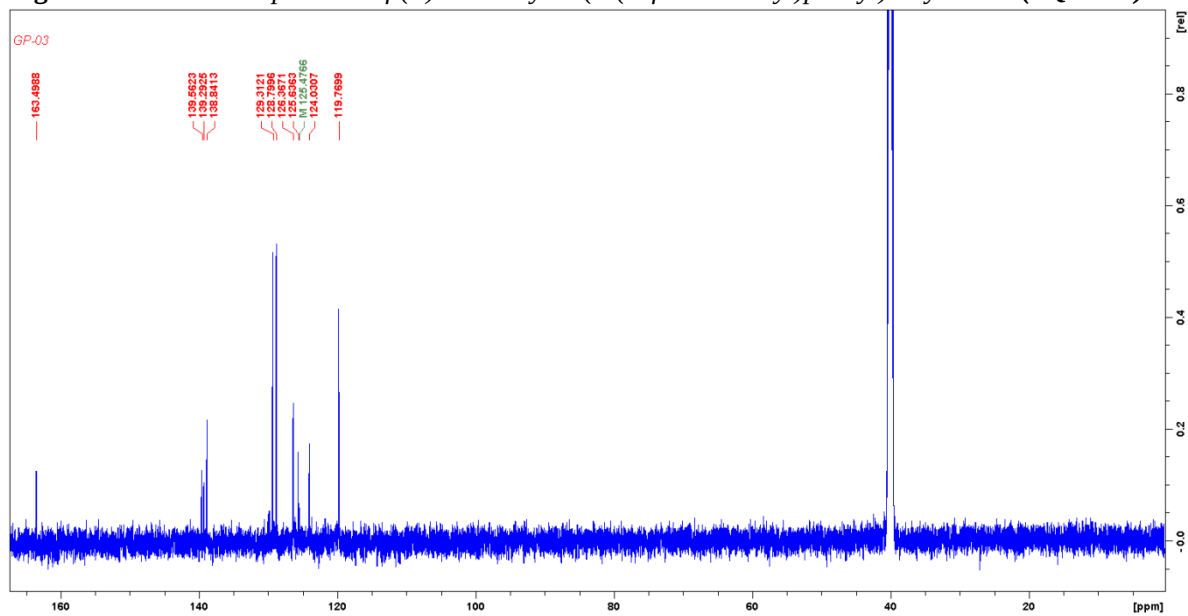


Figure S23. HPLC chromatogram of (*E*)-3-(2,3-Dichlorophenyl)-*N*-phenylacrylamide (**LQM331**)

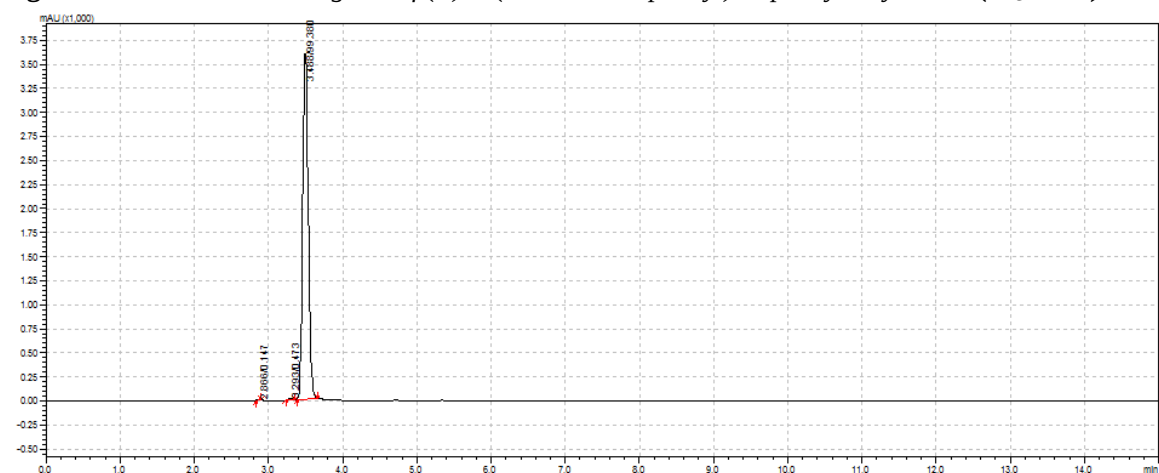


Figure S24. FT-IR spectrum of (*E*)-3-(2,3-Dichlorophenyl)-*N*-phenylacrylamide (**LQM331**)

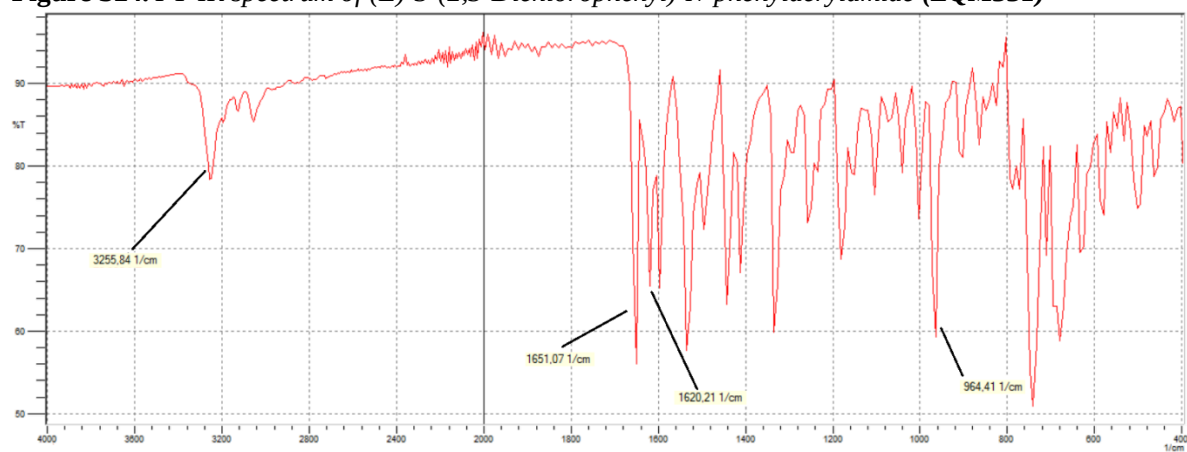


Figure S25. ^1H NMR spectrum of (*E*)-3-(2,3-Dichlorophenyl)-*N*-phenylacrylamide (**LQM331**)

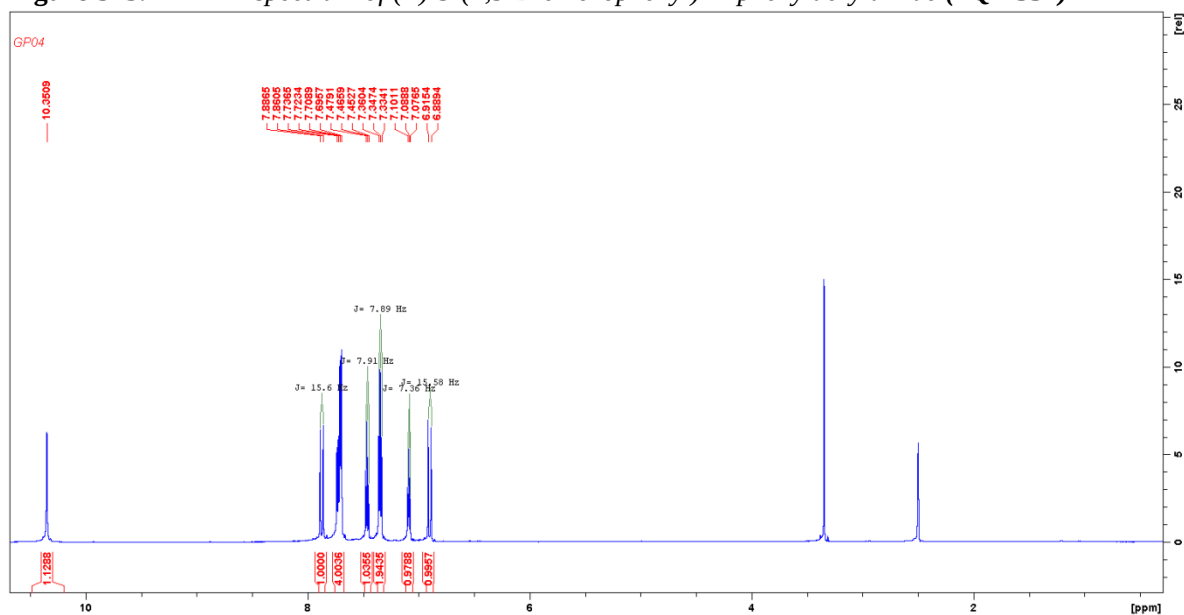


Figure S26. ^{13}C NMR spectrum of (*E*)-3-(2,3-Dichlorophenyl)-*N*-phenylacrylamide (**LQM331**)

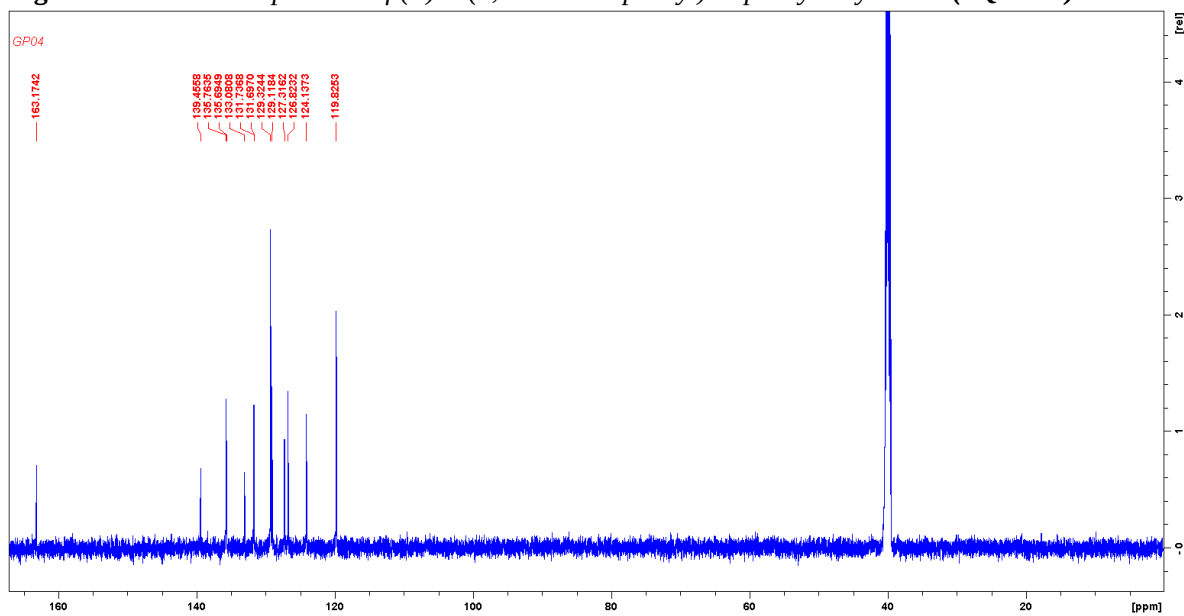


Figure S27. HPLC chromatogram of (*E*)-3-(4-Fluorophenyl)-*N*-phenylacrylamide (**LQM332**)

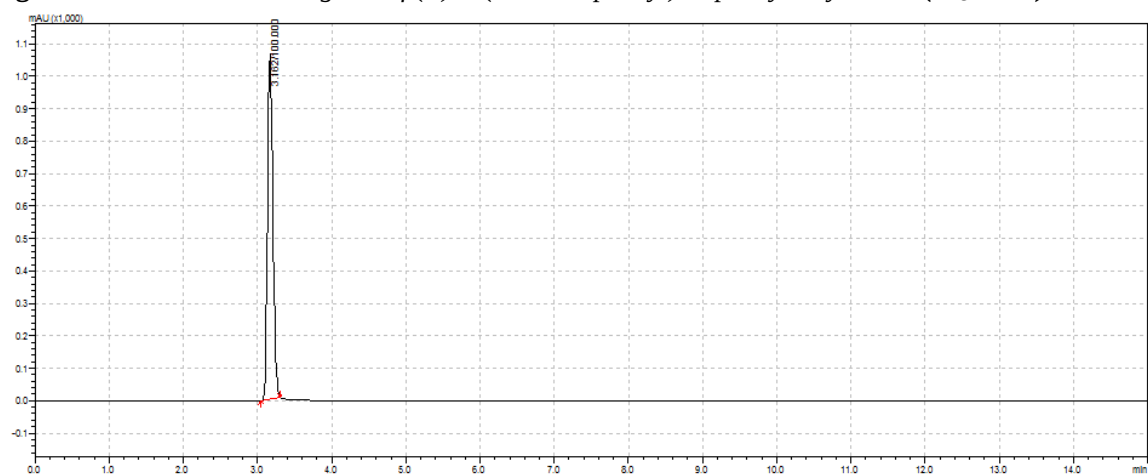


Figure S28. FT-IR spectrum of (*E*)-3-(4-Fluorophenyl)-*N*-phenylacrylamide (**LQM332**)

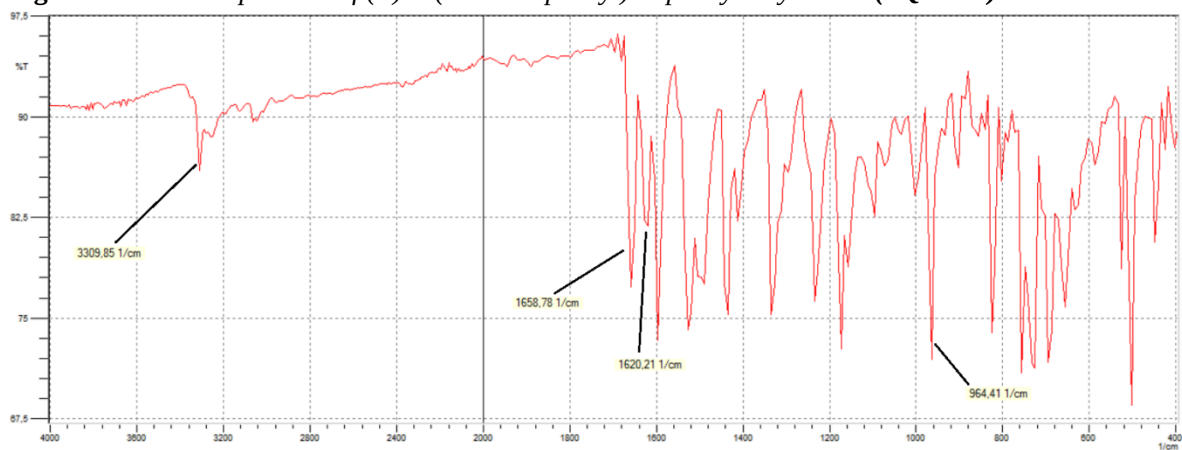


Figure S29. ^1H NMR spectrum of (*E*)-3-(4-Fluorophenyl)-*N*-phenylacrylamide (**LQM332**)

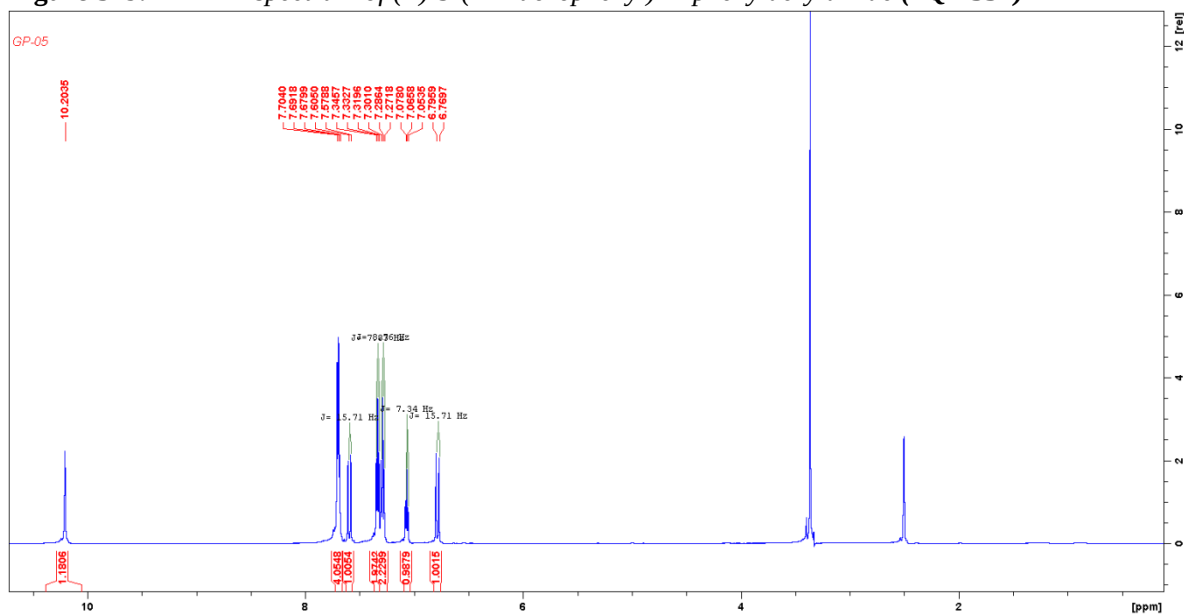


Figure S30. ^{13}C NMR spectrum of (*E*)-3-(4-Fluorophenyl)-*N*-phenylacrylamide (**LQM332**)

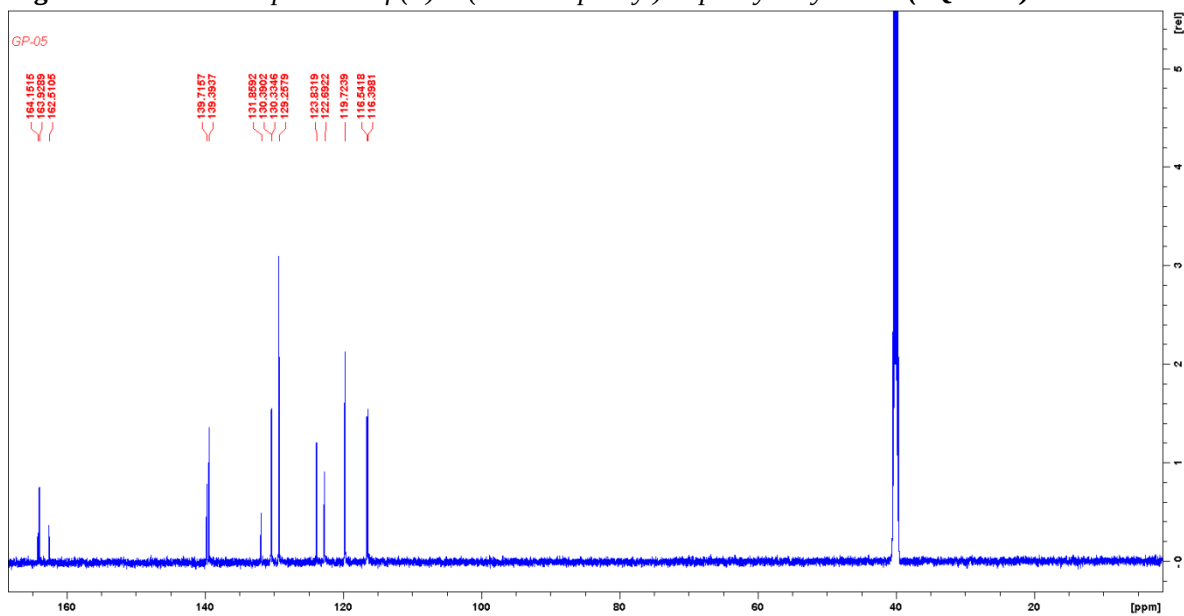


Figure S31. HPLC chromatogram of (E)-3-(2,4-Dichlorophenyl)-N-phenylacrylamide (**LQM333**)

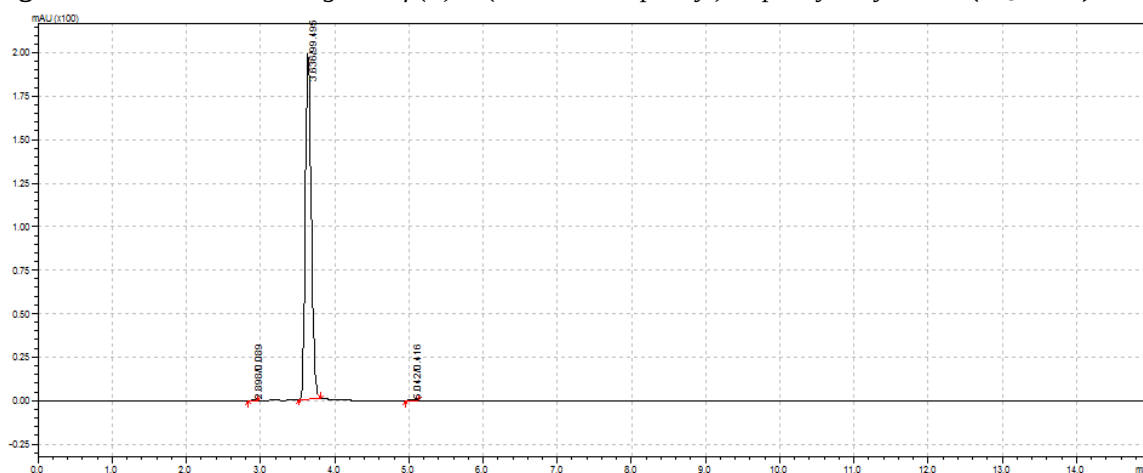


Figure S32. FT-IR spectrum of (E)-3-(2,4-Dichlorophenyl)-N-phenylacrylamide (**LQM333**)

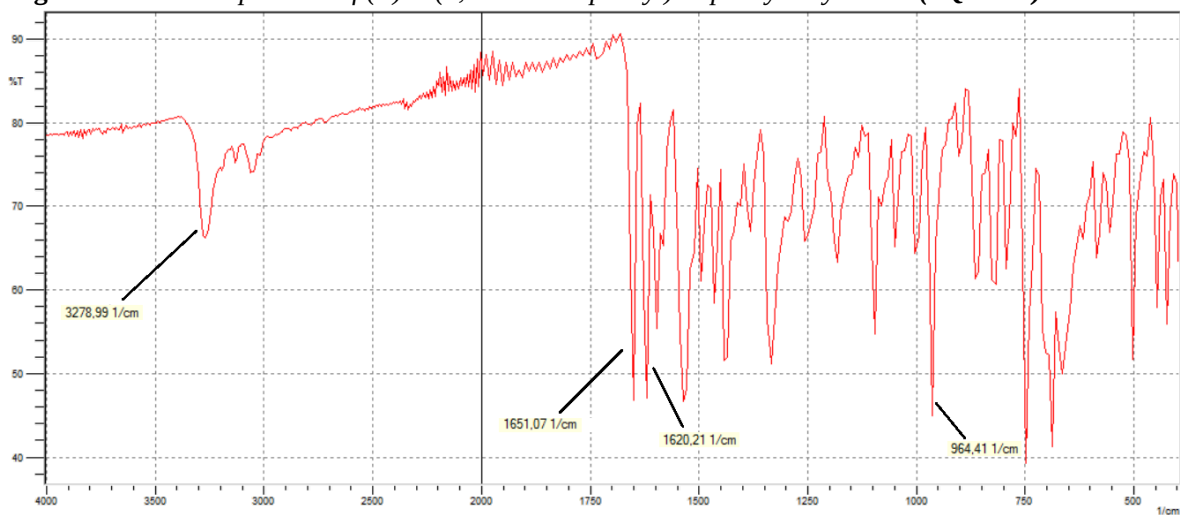


Figure S33. ^1H NMR spectrum of (*E*)-3-(2,4-Dichlorophenyl)-*N*-phenylacrylamide (**LQM333**)

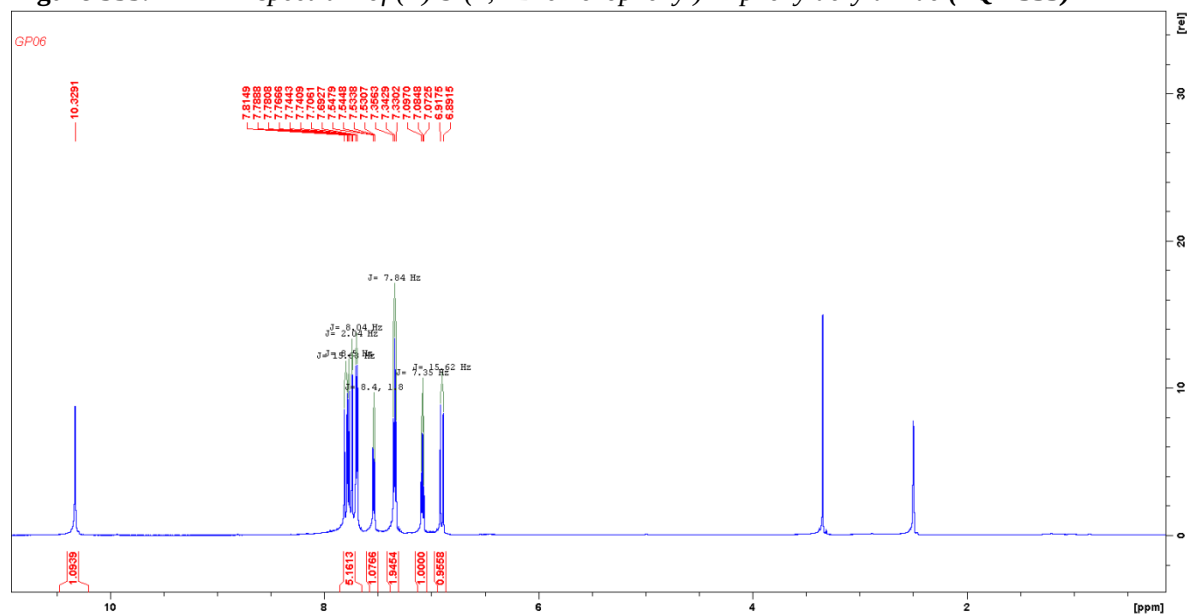


Figure S34. ^{13}C NMR spectrum of (*E*)-3-(2,4-Dichlorophenyl)-*N*-phenylacrylamide (**LQM333**)

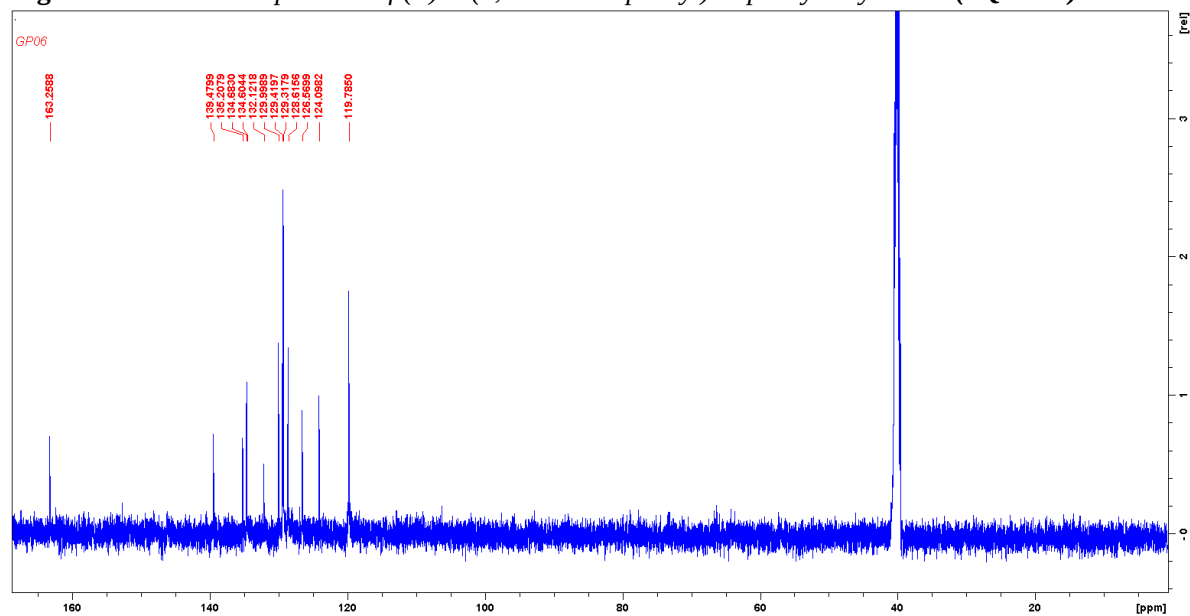


Figure S35. HPLC chromatogram of (*E*)-3-(3-Chlorophenyl)-*N*-phenylacrylamide (**LQM334**)

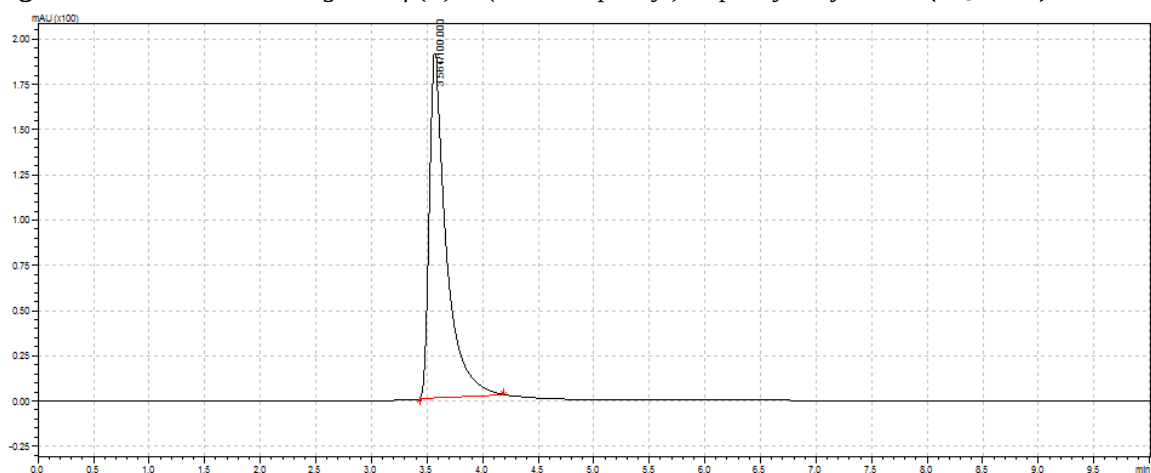
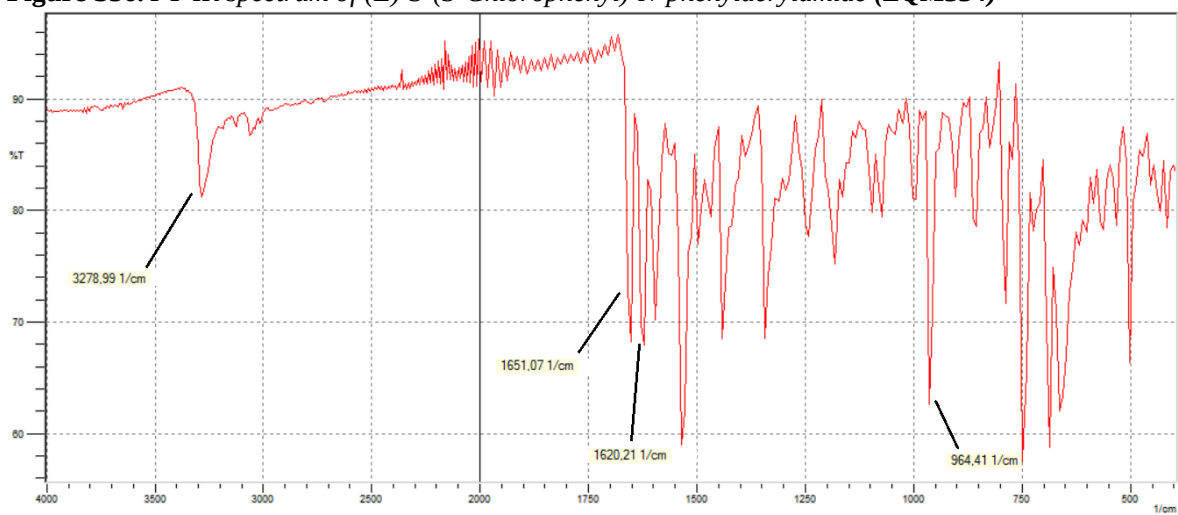


Figure S36. FT-IR spectrum of (*E*)-3-(3-Chlorophenyl)-*N*-phenylacrylamide (**LQM334**)



1H NMR spectrum of compound 10b in CDCl₃.

Chemical Shifts (ppm): 7.7168, 7.7081, 7.6984, 7.1115, 7.6117, 7.6063, 7.5932, 7.5964, 7.5846, 7.5802, 7.4882, 7.4860, 7.4751, 7.4768, 7.3992, 7.3985, 7.3329, 7.0948, 7.0725, 7.0703, 6.9688, 6.8825.

Integration values: 0.5605, 7.556, 7.682, 8.418, 9.120, 9.5136, 1.0000.

Peak assignments and coupling constants:

- 7.7168, 7.7081, 7.6984, 7.1115, 7.6117, 7.6063, 7.5932, 7.5964, 7.5846, 7.5802, 7.4882, 7.4860, 7.4751, 7.4768, 7.3992, 7.3985, 7.3329, 7.0948, 7.0725, 7.0703, 6.9688, 6.8825: Multiplet, $J = 7.89$ Hz.
- 7.556, 7.682, 8.418, 9.120: Multiplet, $J = 15.73$ Hz.
- 9.5136: Multiplet, $J = 7.36$ Hz.
- 1.0000: Multiplet, $J = 15.72$ Hz.
- 3.9 ppm: Singlet.
- 2.5 ppm: Doublet.

GP-07

163.6421

139.6070

138.9432

137.5443

134.2095

129.8108

129.3387

128.7172

126.6174

124.5615

123.5558

119.7397

39.6070

[ppm]

Figure S39. HPLC chromatogram of (*E*)-3-(3,4-Dimethoxyphenyl)-*N*-phenylacrylamide (**LQM335**)

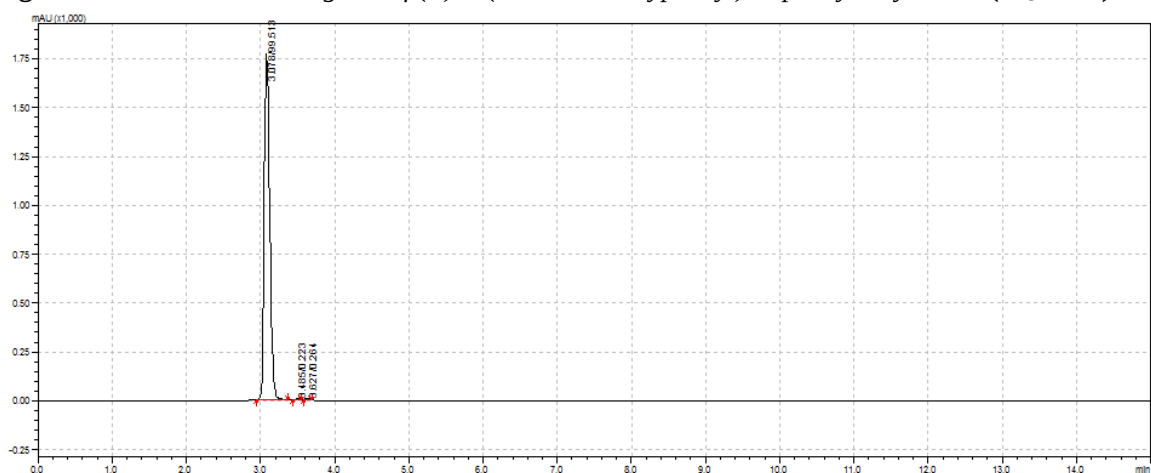


Figure S40. FT-IR spectrum of (*E*)-3-(3,4-Dimethoxyphenyl)-*N*-phenylacrylamide (**LQM335**)

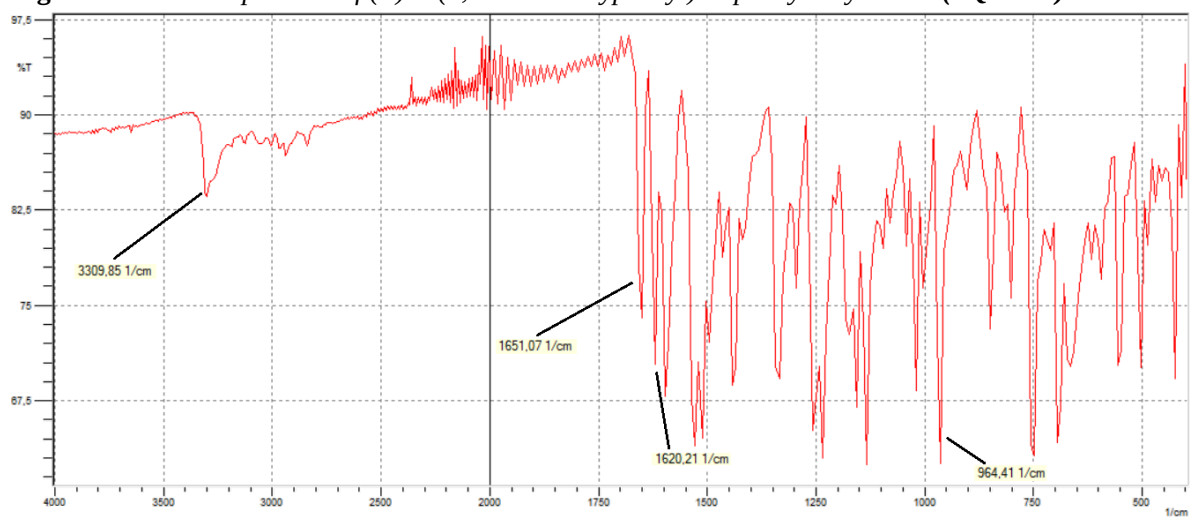


Figure S41. ^1H NMR spectrum of (*E*)-3-(3,4-Dimethoxyphenyl)-*N*-phenylacrylamide (**LQM335**)

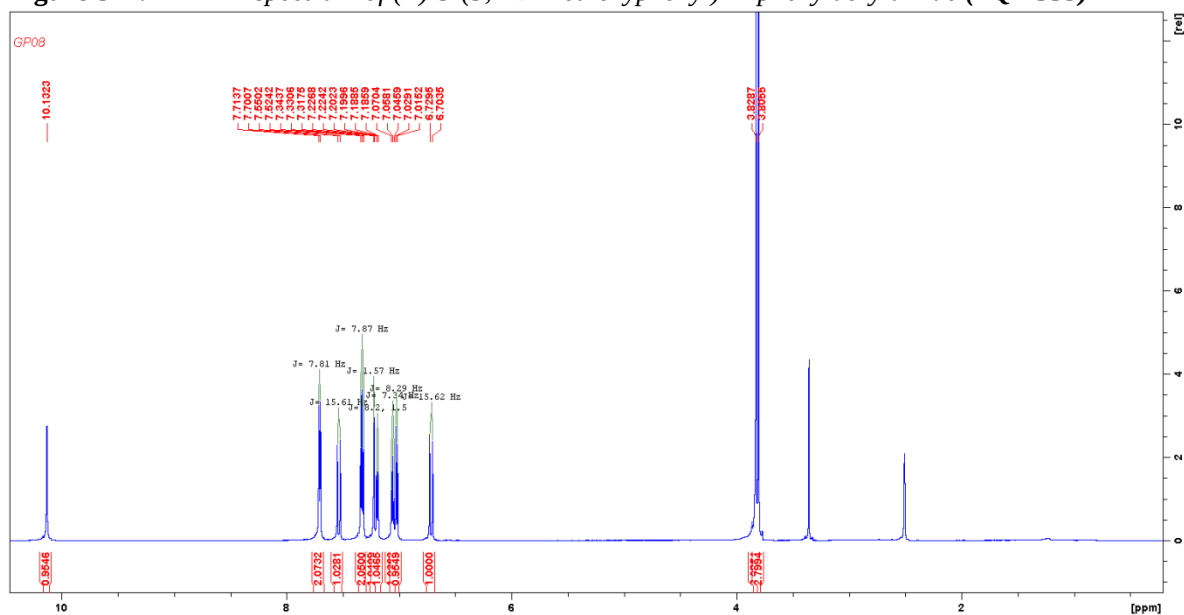


Figure S42. ^{13}C NMR spectrum of (*E*)-3-(3,4-Dimethoxyphenyl)-*N*-phenylacrylamide (**LQM335**)

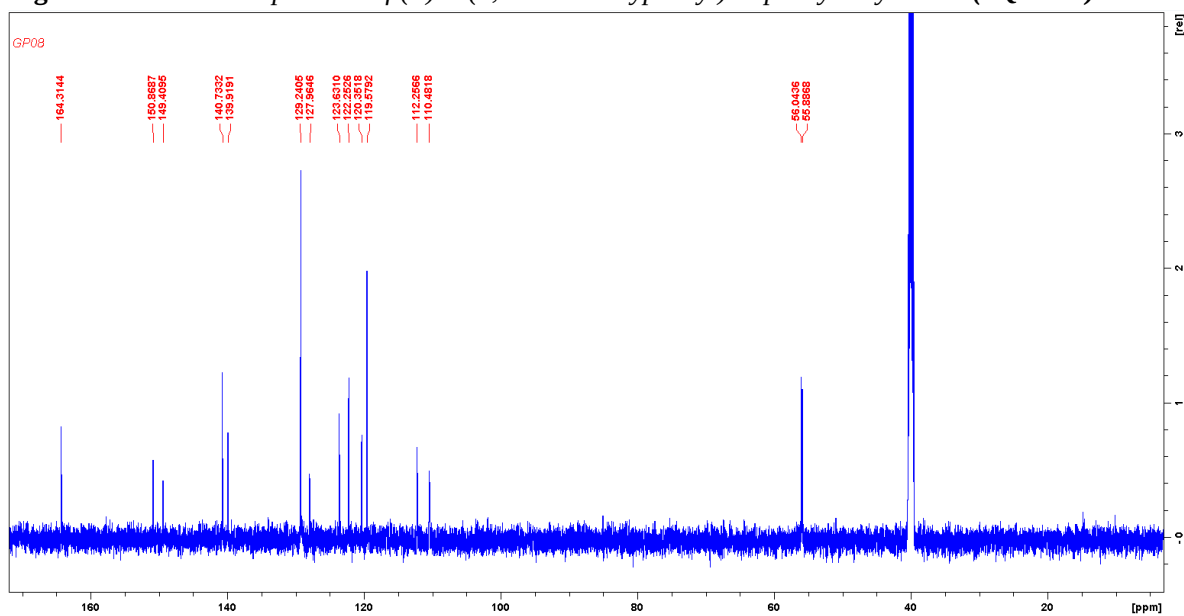


Figure S43. HPLC chromatogram of (*E*)-3-(2-Methoxyphenyl)-*N*-phenylacrylamide (**LQM336**)

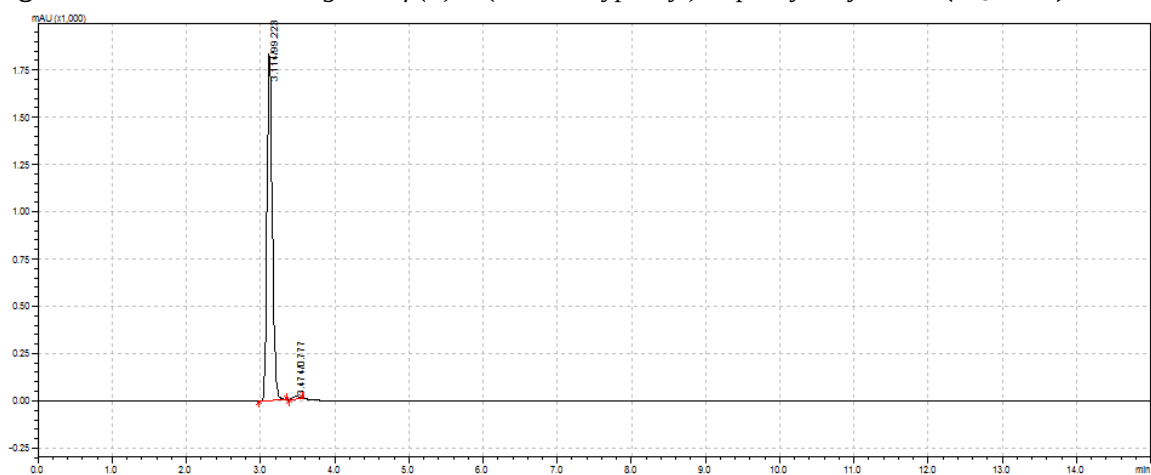


Figure S44. FT-IR spectrum of (*E*)-3-(2-Methoxyphenyl)-*N*-phenylacrylamide (**LQM336**)

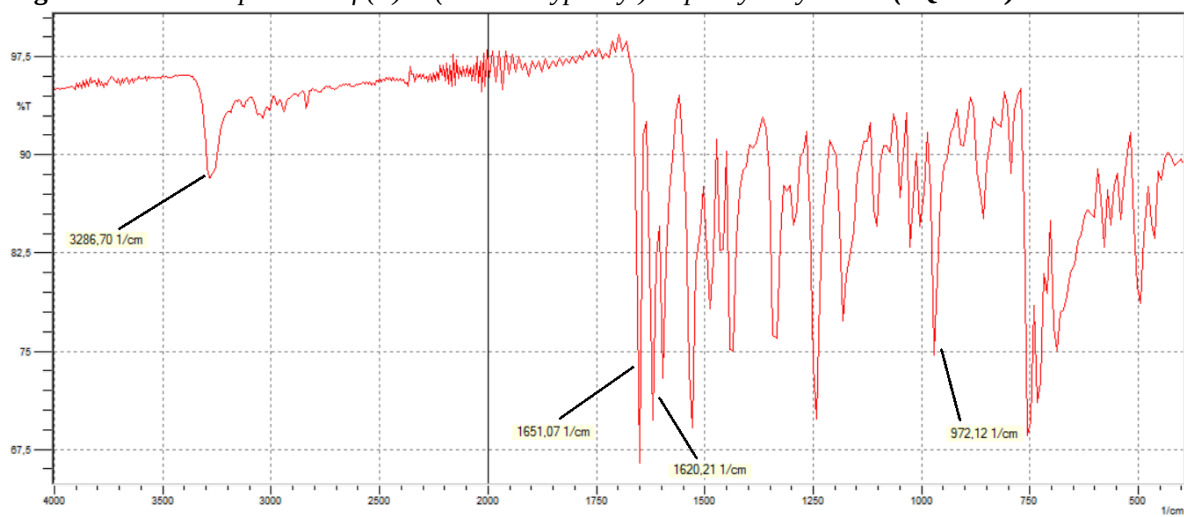


Figure S45. ^1H NMR spectrum of (*E*)-3-(2-Methoxyphenyl)-*N*-phenylacrylamide (**LQM336**)

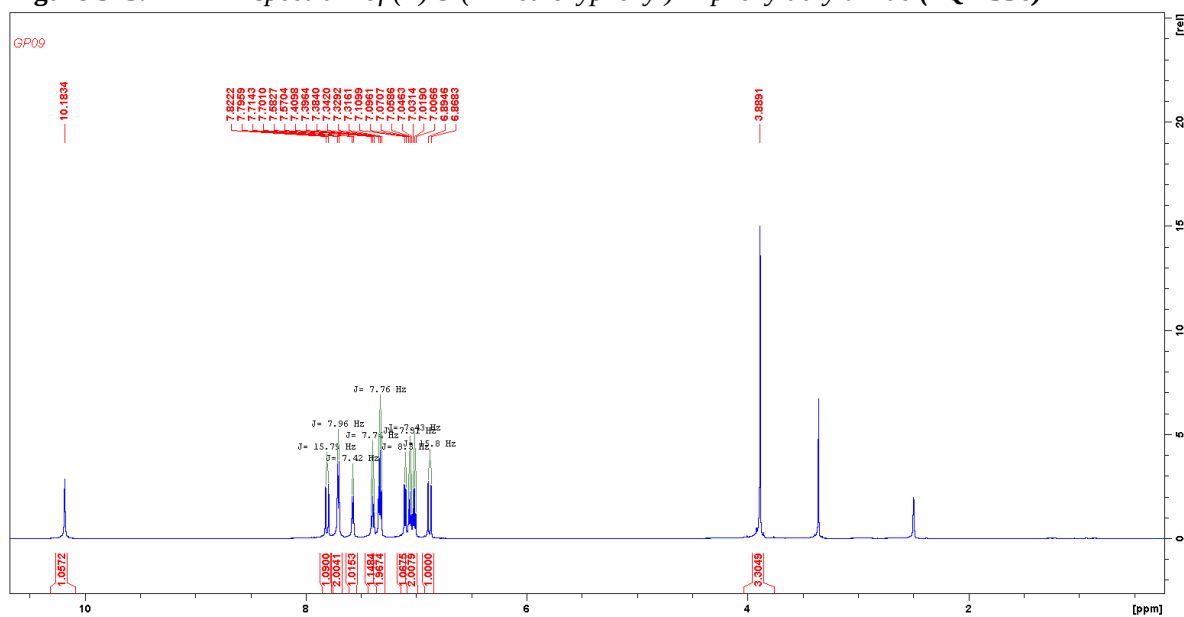


Figure S46. ^{13}C NMR spectrum of (*E*)-3-(2-Methoxyphenyl)-*N*-phenylacrylamide (**LQM336**)

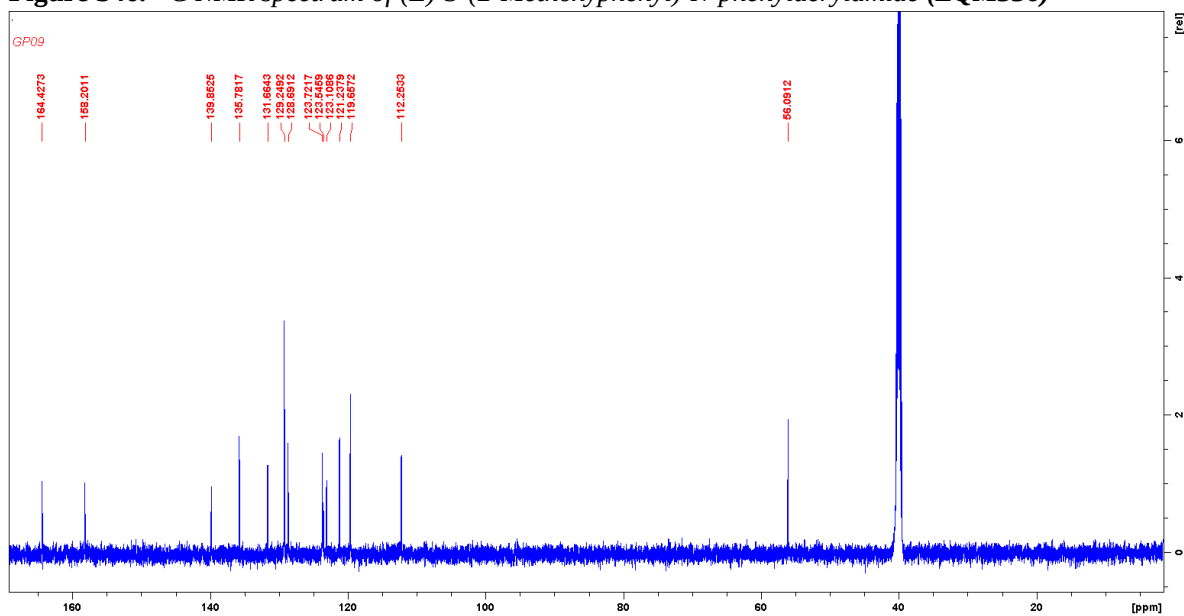


Figure S47. HPLC chromatogram of (*E*)-3-([1,1'-Biphenyl]-2-yl)-*N*-phenylacrylamide (**LQM337**)

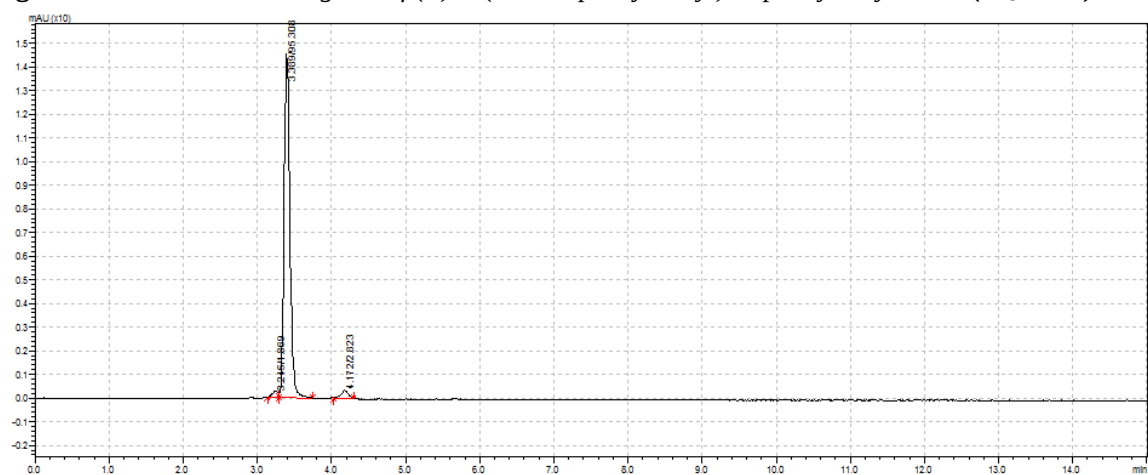


Figure S48. FT-IR spectrum of (*E*)-3-([1,1'-Biphenyl]-2-yl)-*N*-phenylacrylamide (**LQM337**)

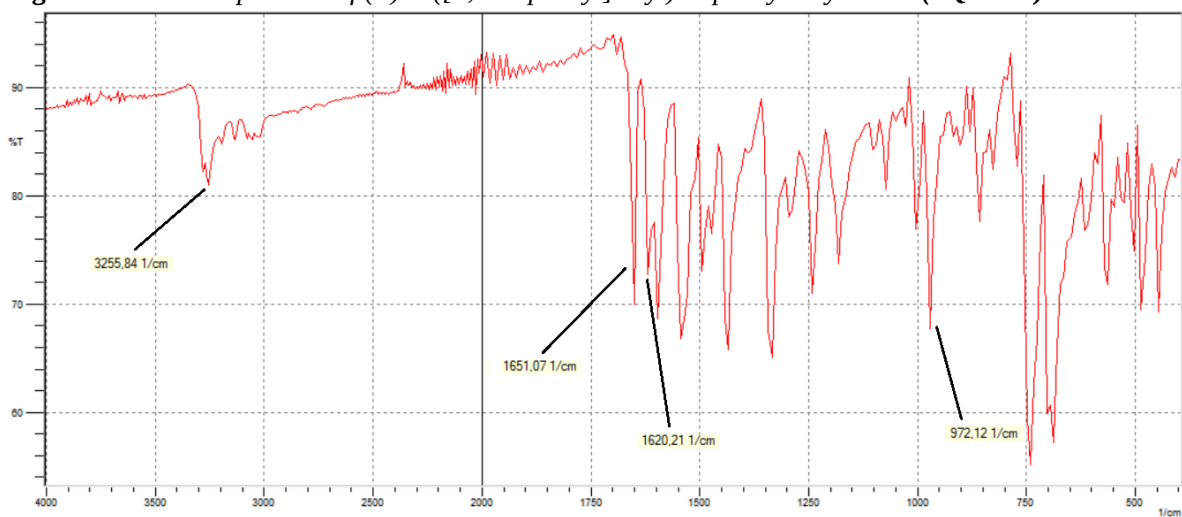


Figure S49. ^1H NMR spectrum of (*E*)-3-([1,1'-Biphenyl]-2-yl)-*N*-phenylacrylamide (**LQM337**)

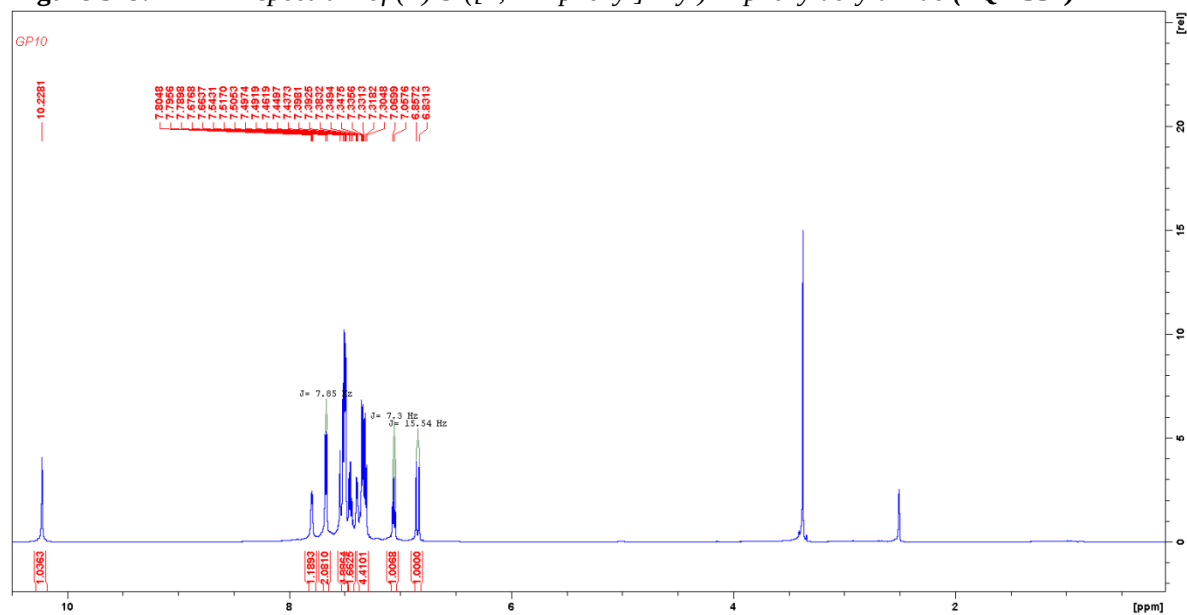


Figure S50. ^{13}C NMR spectrum of (*E*)-3-([1,1'-Biphenyl]-2-yl)-*N*-phenylacrylamide (**LQM337**)

