

# **Clean Grinding Technique: A Facile Synthesis and In silico Antiviral Activity of Hydrazones, Pyrazoles, and Pyrazines Bearing Thiazole Moiety Against SARS-CoV-2 main protease (M<sup>pro</sup>)**

**Sraa Abu-Melha<sup>1</sup>, Mastoura M. Edrees<sup>1,2\*</sup>, Sayed M. Riyadh<sup>3,4</sup>, Mohamad R. Abdelaziz<sup>5</sup>, Abdo A. Elfiky<sup>6</sup>, Sobhi M. Gomha<sup>3,7\*</sup>**

<sup>1</sup> Department of Chemistry, Faculty of Science, King Khalid University, Abha 61413, SA

<sup>2</sup> Department of Organic Chemistry, National Organization for Drug Control and Research (NODCAR), Giza 12311, Egypt

<sup>3</sup> Department of Chemistry, Faculty of Science, Cairo University, Giza, 12613, Egypt

<sup>4</sup> Department of Chemistry, Faculty of Science, Taibah University, Al-Madinah Al-Munawarah, 30002, Saudi Arabia

<sup>5</sup> Department of Pharmaceutical Chemistry, Faculty of Pharmacy, MIU University, Egypt

<sup>6</sup> Biophysics Department, Faculty of Science, Cairo University, Giza, Egypt

<sup>7</sup> Department of Chemistry, Faculty of Science, Islamic University in Al-Madinah Al-Munawarah, 42351, Saudi Arabia

\* Corresponding authors: s.m.gomha@gmail.com, mstorh@kku.edu.sa, Tel.: +20-237-400-304, +966545888764; Fax: +20-025-685-799

---

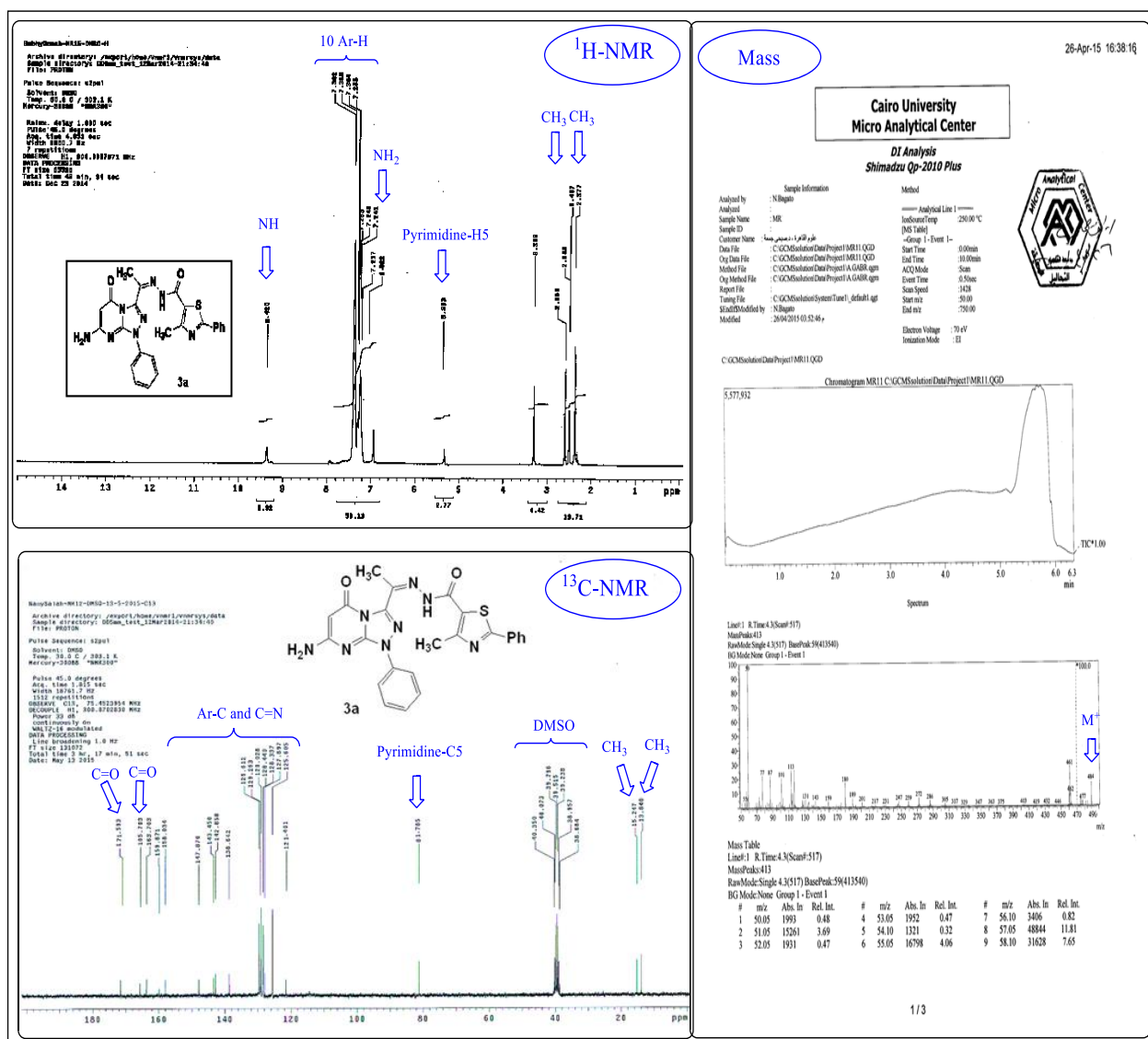


Figure S1. <sup>1</sup>H-NMR, <sup>13</sup>C-NMR and Mass spectra of compound 3a.

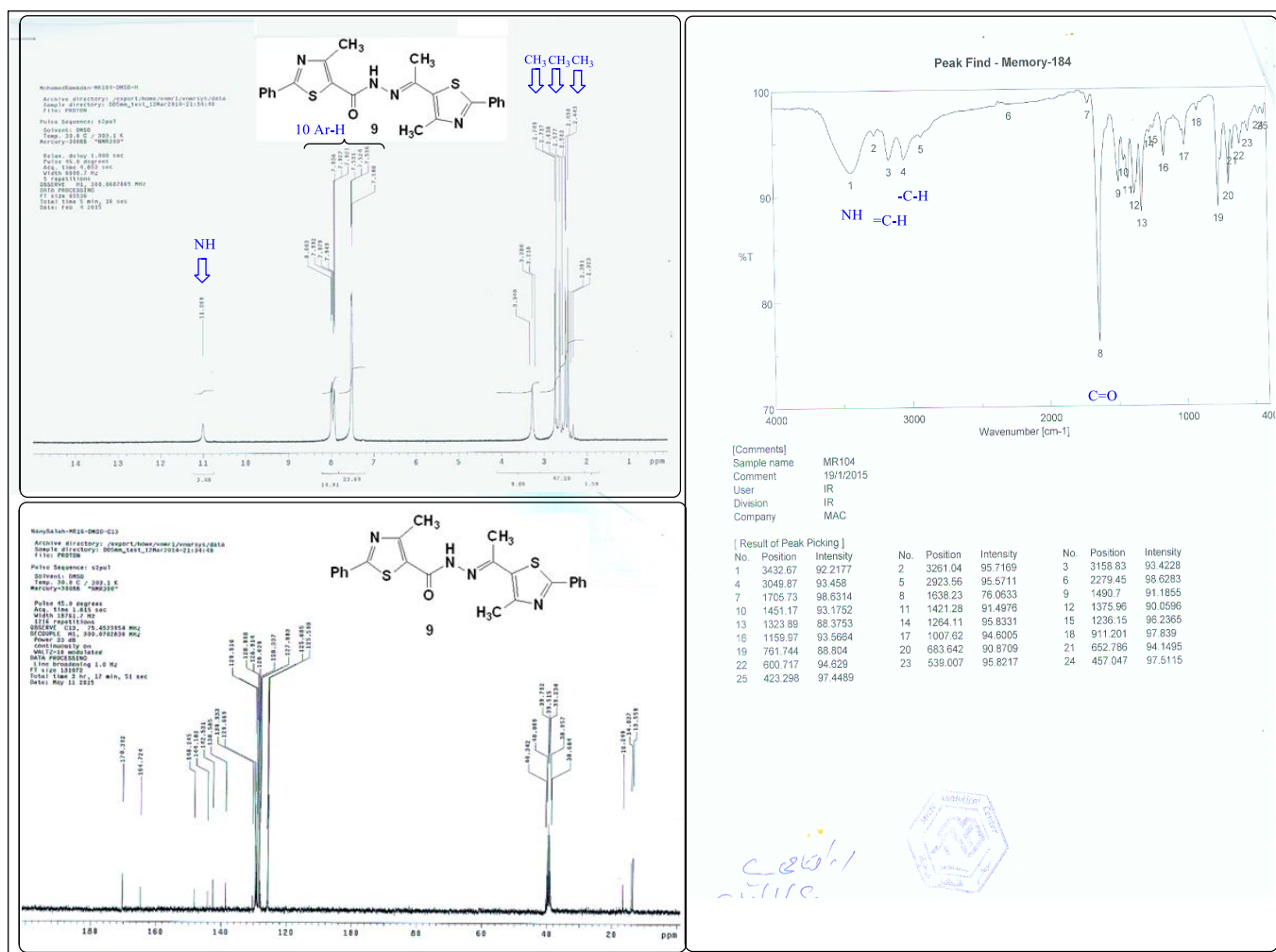


Figure S2. <sup>1</sup>H-NMR, <sup>13</sup>C-NMR and IR spectra of compound 9.

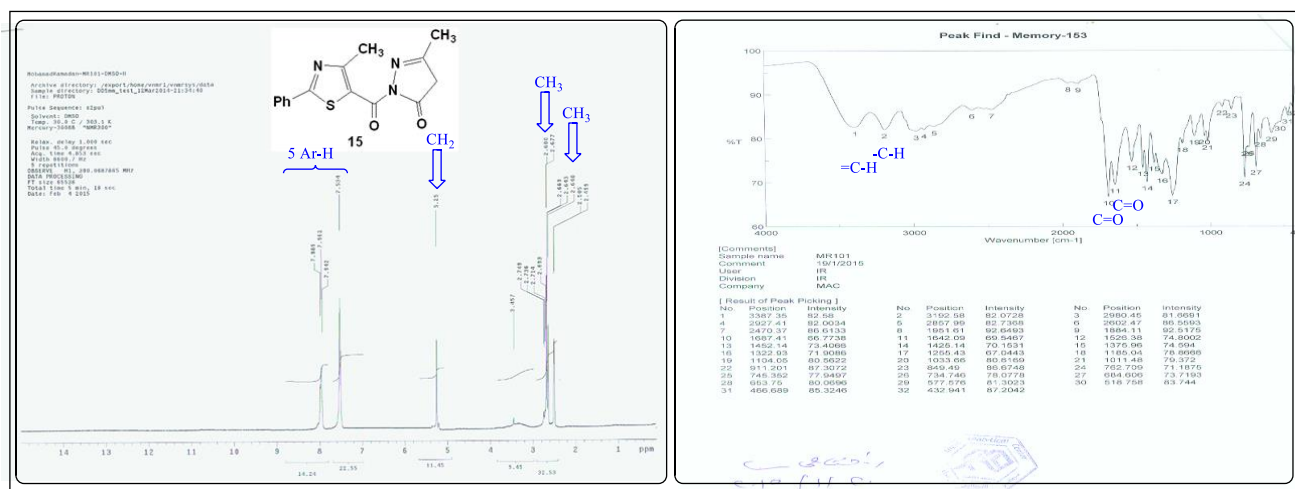


Figure S3. <sup>1</sup>H NMR and IR spectra of compound 15.

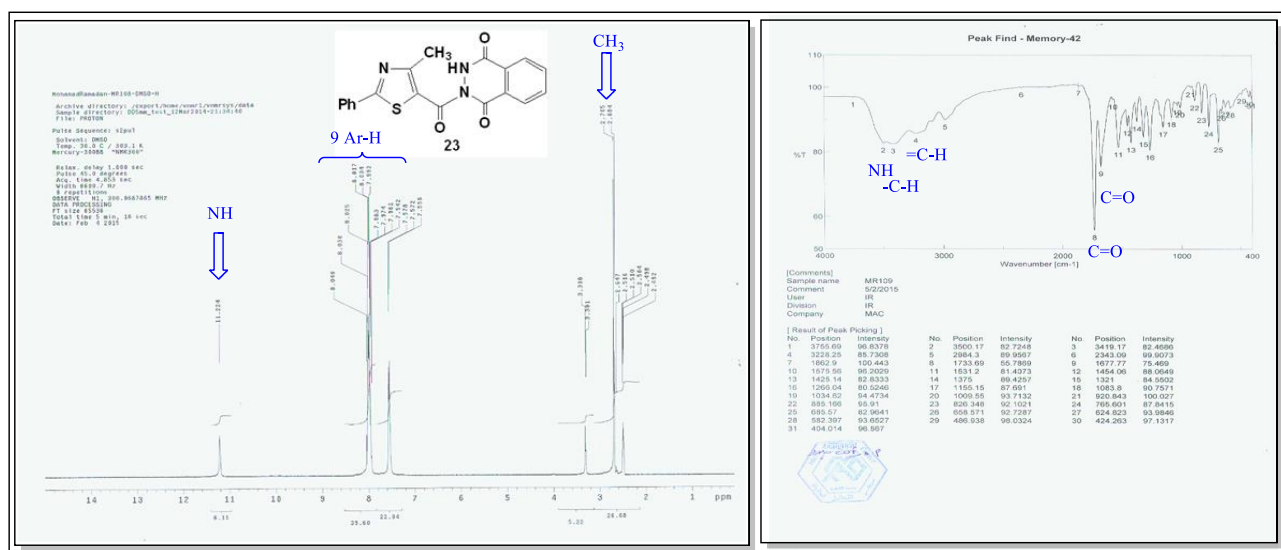
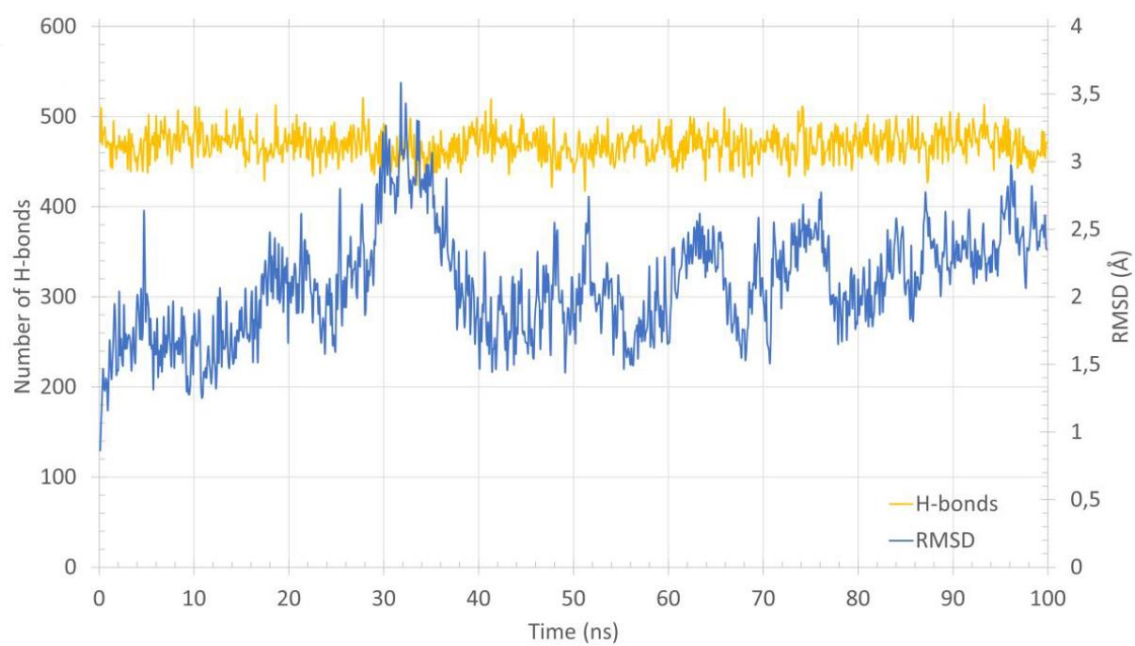
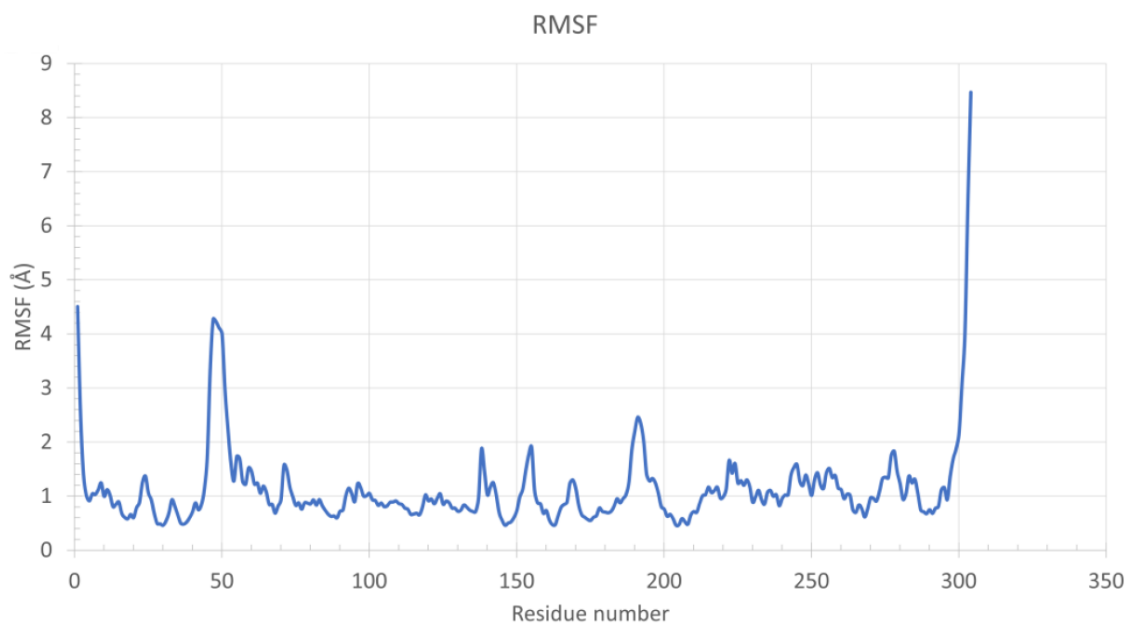


Figure S4. <sup>1</sup>H NMR and IR spectra of compound 23.



**Figure S5.** Molecular Simulations.



**Figure S6.** Molecular Simulations (RMSF).