

## Supporting Information for

# Computational Design and Synthesis of Phthalimide Derivatives as TGF- $\beta$ Pathway Inhibitors for Cancer Therapeutics

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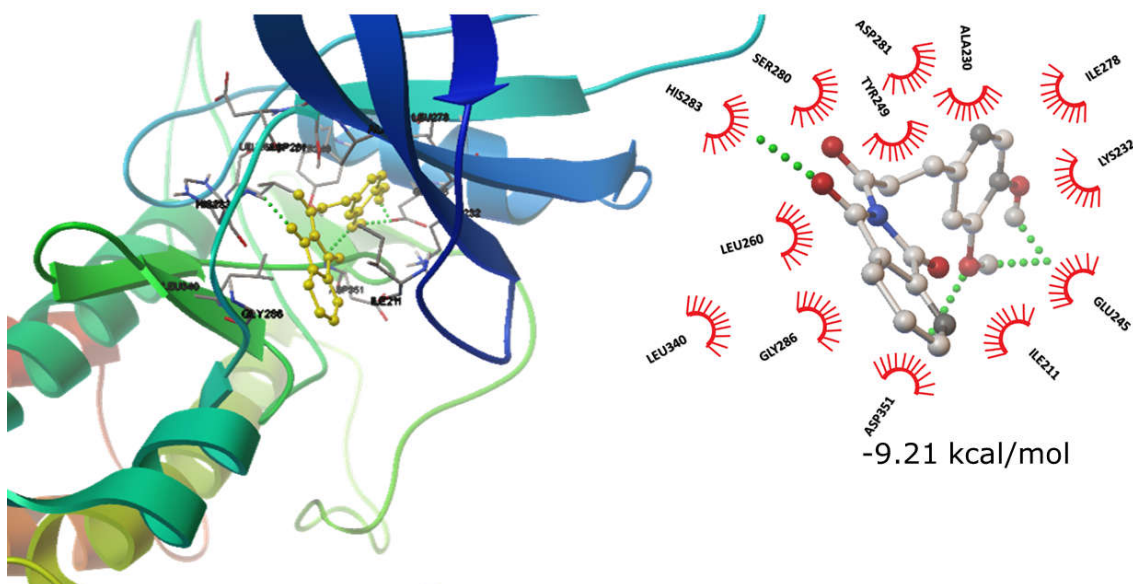


Figure S1. Interaction of the ligand **P1** 1-(E)-2-(3-(3,4-dihydroxyphenyl)acryloyl)isoindolin-1,3-dione with the TGF- $\beta$  receptor kinase I.

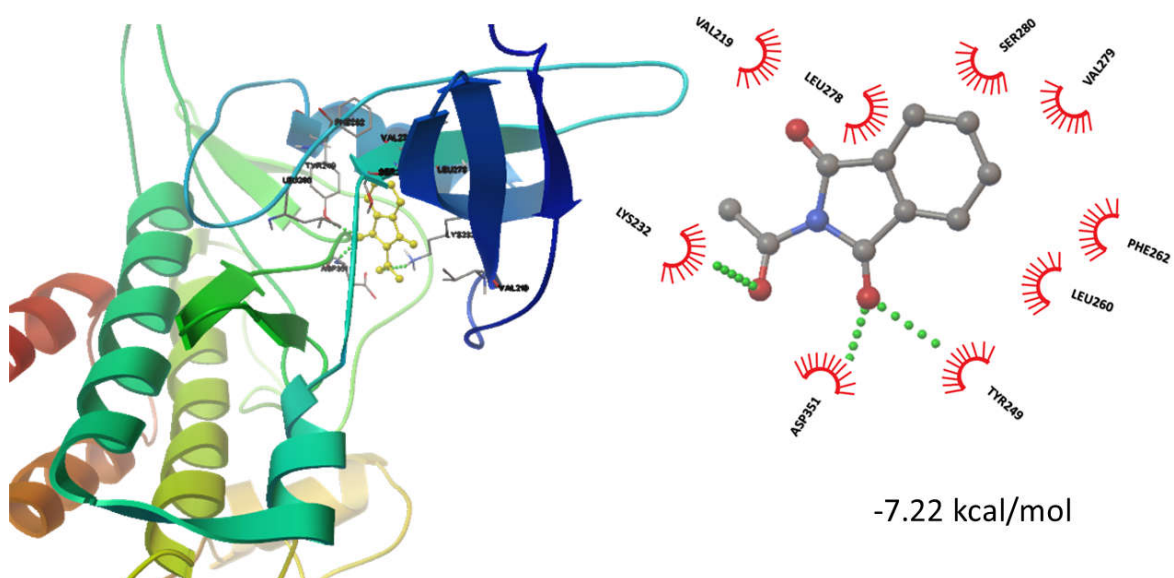


Figure S2. Interaction of the ligand **P2** 2-acetyl isoindolin-1,3-dione with the protein TGF- $\beta$  kinase I.

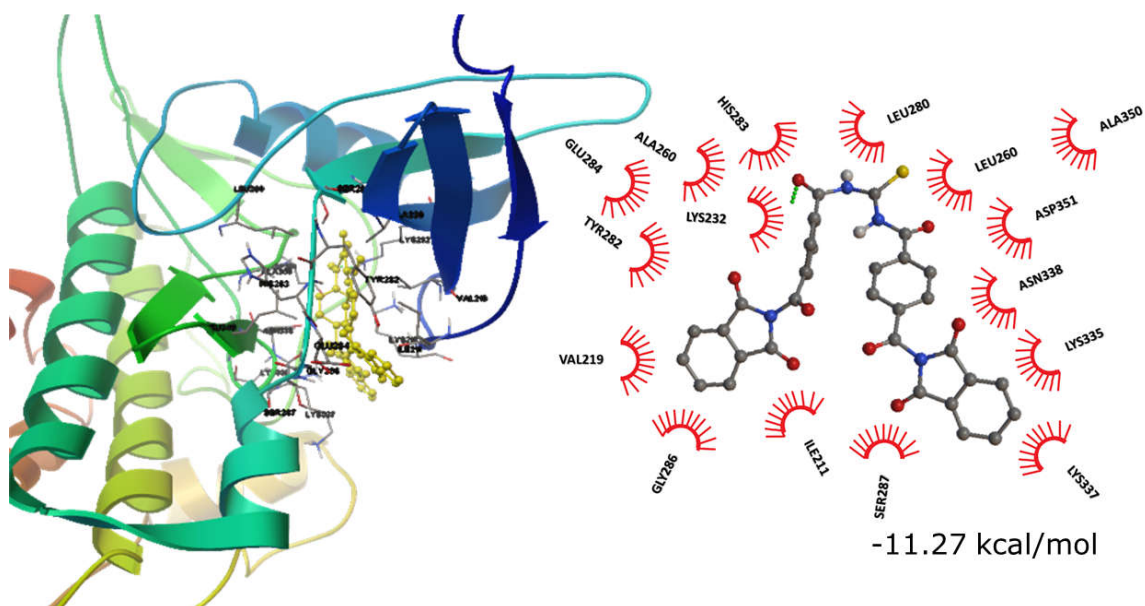


Figure S3. Interaction of ligand **P3** N,N'-thiocarbonylbis(4-(1,3-dioxoisoindolin-2-carbonyl)benzamide) with the protein TGF- $\beta$  kinase I.

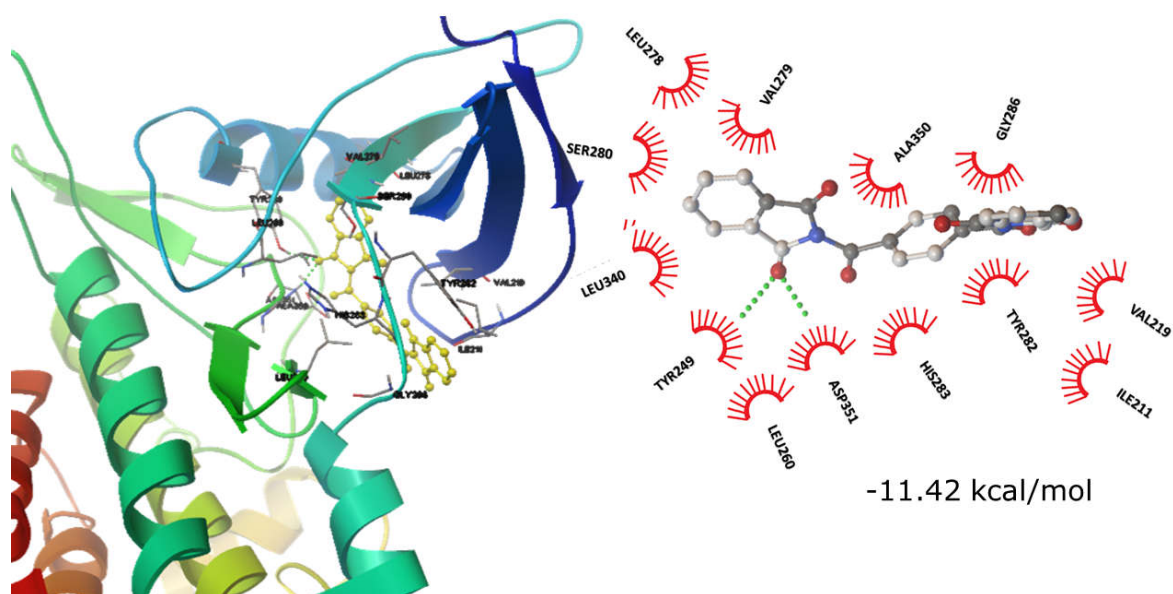


Figure S4. Interaction of the ligand **P4** 2,2'-terephthaloyl bis(isoindolin-1,3-dione) with the protein TGF- $\beta$  kinase I.

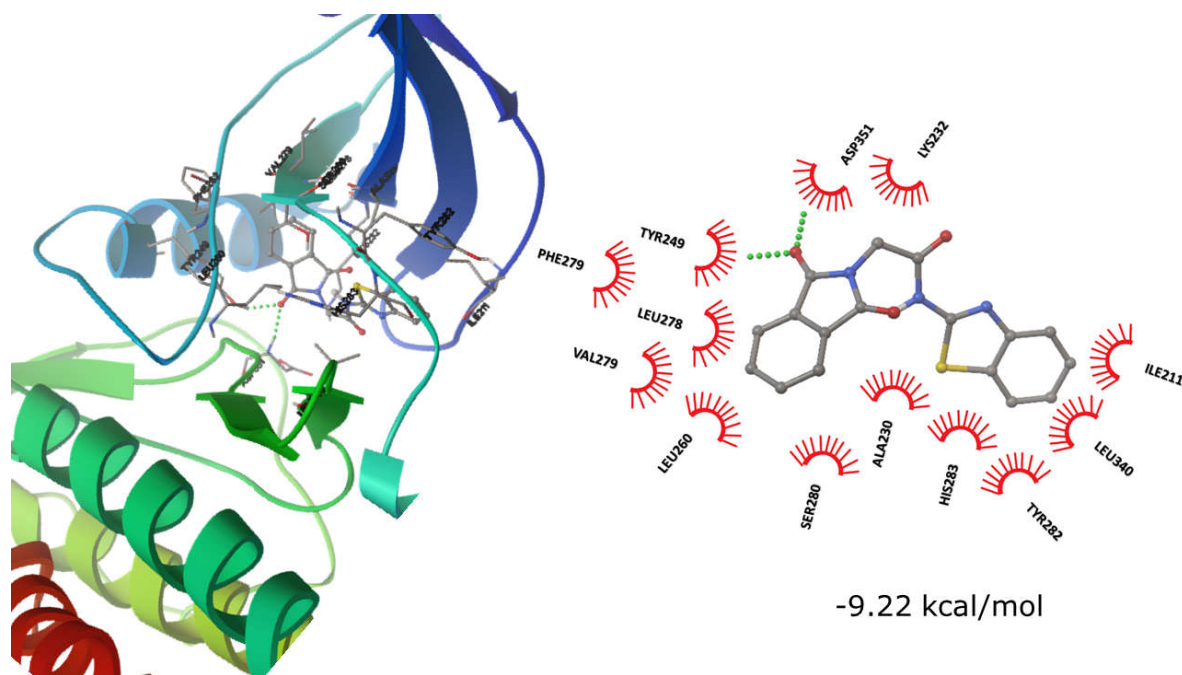


Figure S5. Interaction of the ligand **P5** 5-N-(benzo[d]thiazol-2-yl)-2-(1,3-dioxoisoindolin-2-yl)acetamide with the TGF- $\beta$  receptor kinase I.

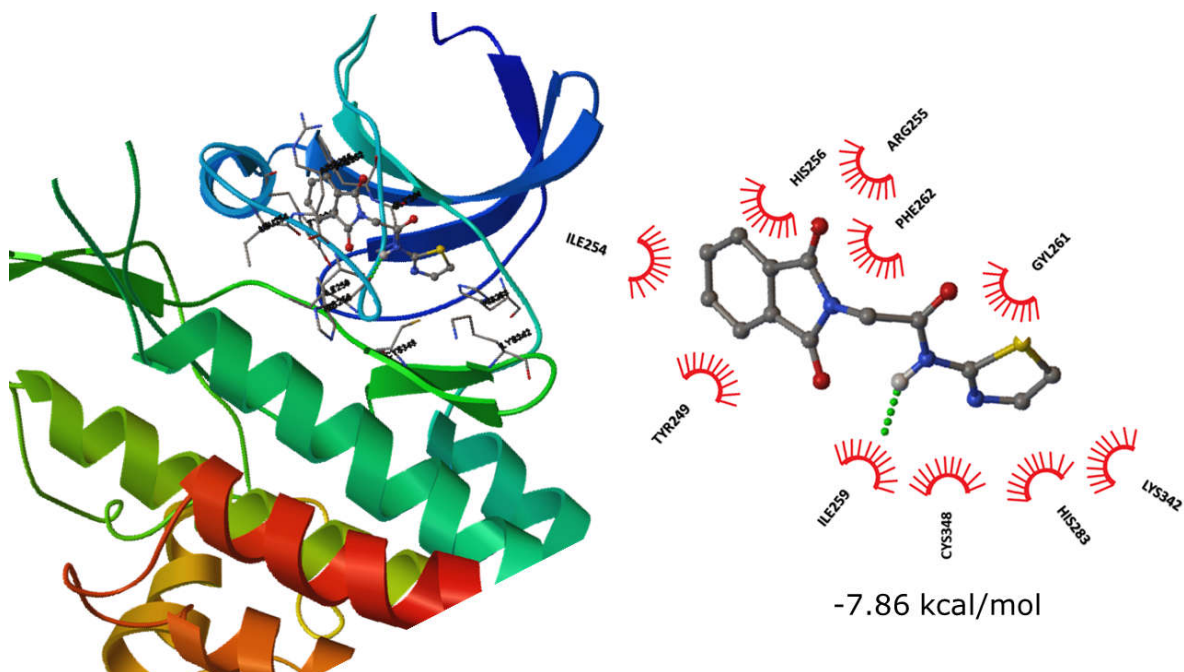


Figure S6. Interaction of the ligand **P6** 2-(1,3-dioxoisindolin-2-yl)-N-(thiazol-2-yl)acetamide with the TGF- $\beta$  receptor kinase I.

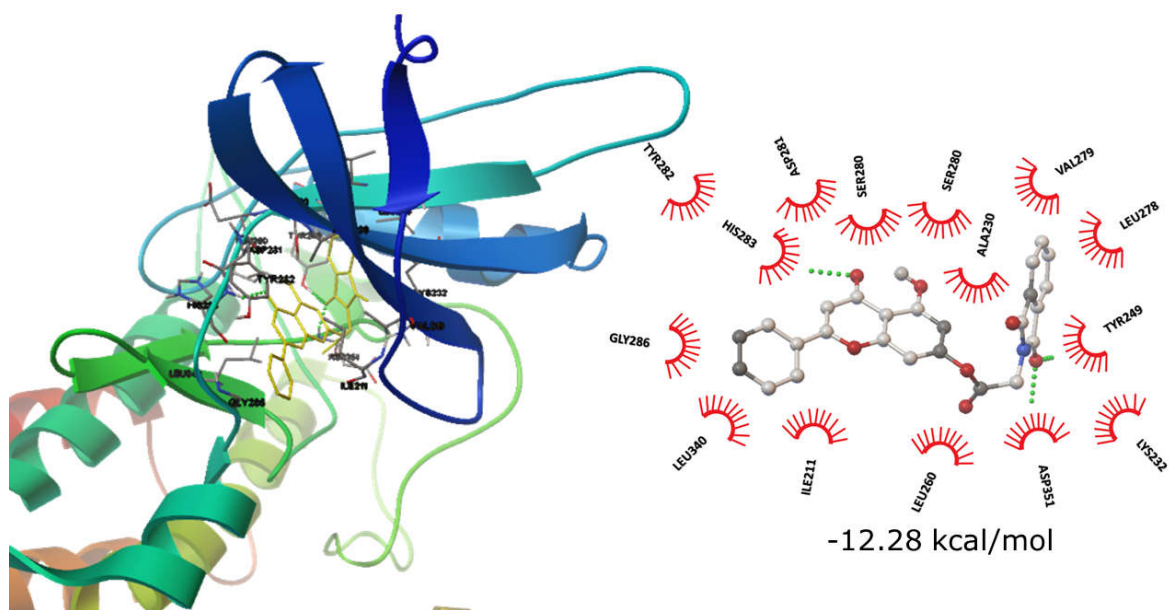


Figure S7. Interaction of ligand **P7** 5-hydroxy-4-oxo-2-phenyl-4H-chromen-7-yl 2-(1,3-dioxoisindolin-2-yl)acetate with TGF- $\beta$  kinase I protein.

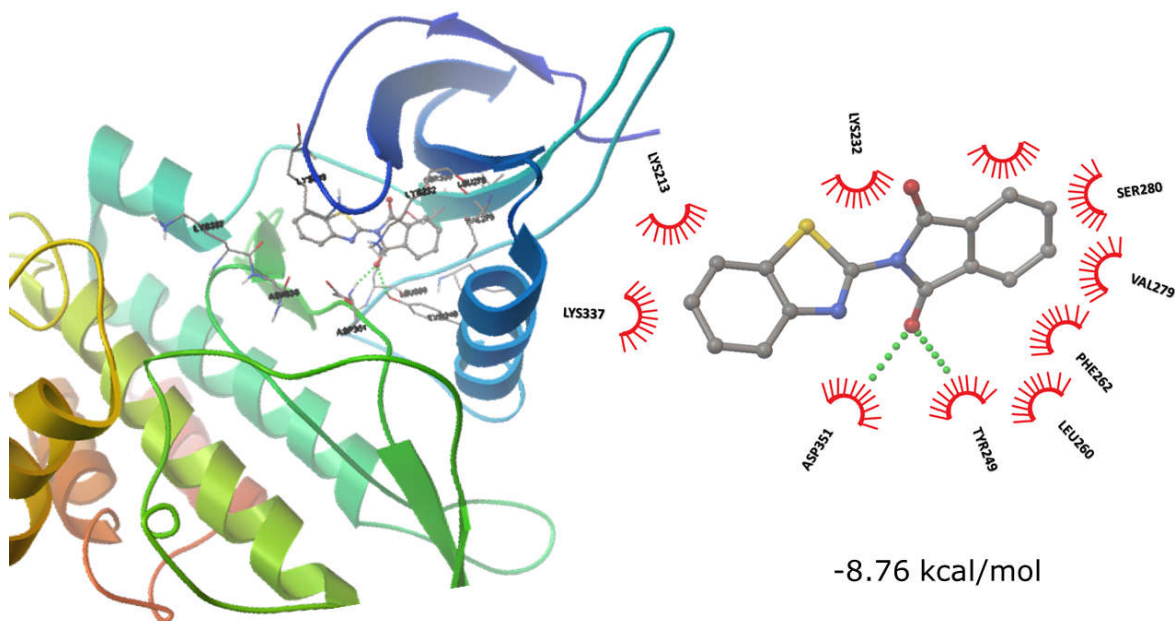


Figure S8. Interaction of the ligand **P8** 2-(benzo[d]thiazol-2-yl)isoindolin-1,3-dione with the protein TGF- $\beta$  kinase I.

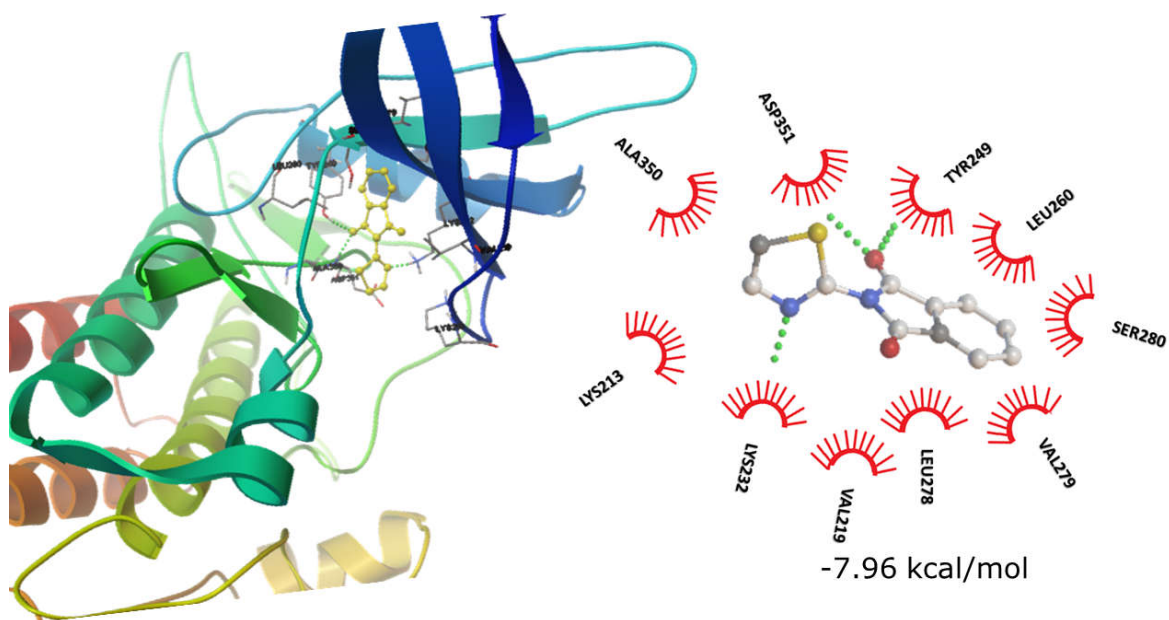


Figure S9. Interaction of the ligand **P9** 2-(thiazol-2-yl)isoindolin-1,3-dione with the protein TGF- $\beta$  kinase I.

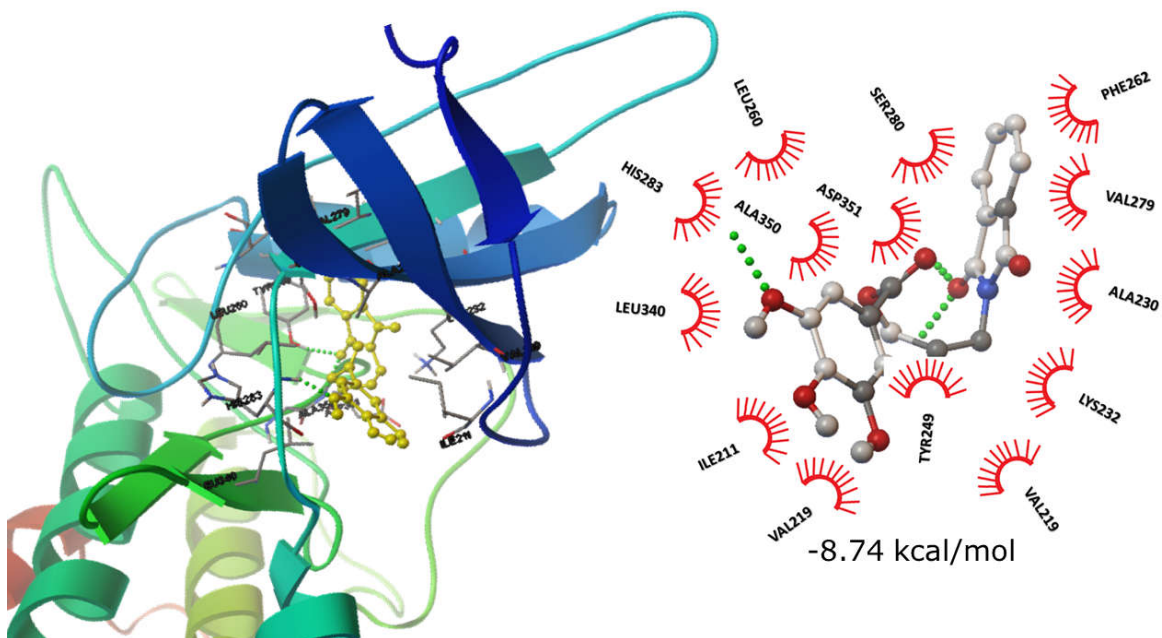


Figure S10. Interaction of the ligand **P10** 2-(3,4,5-trimethoxybenzoyl)isoindolin-1,3-dione with the protein TGF- $\beta$  kinase I.

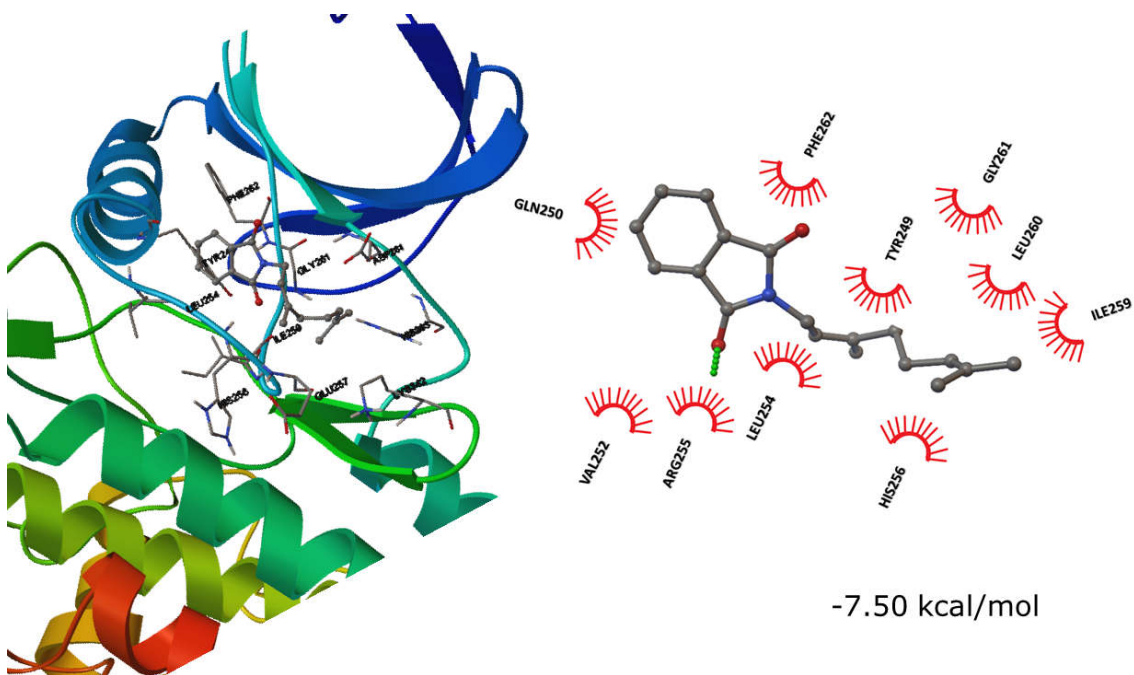


Figure S11. Interaction of the ligand **P11** (E)-2-(3,7-dimethylocta-2,6-dien-1-yl)isoindolin-1,3-dione with the protein TGF- $\beta$  kinase I.

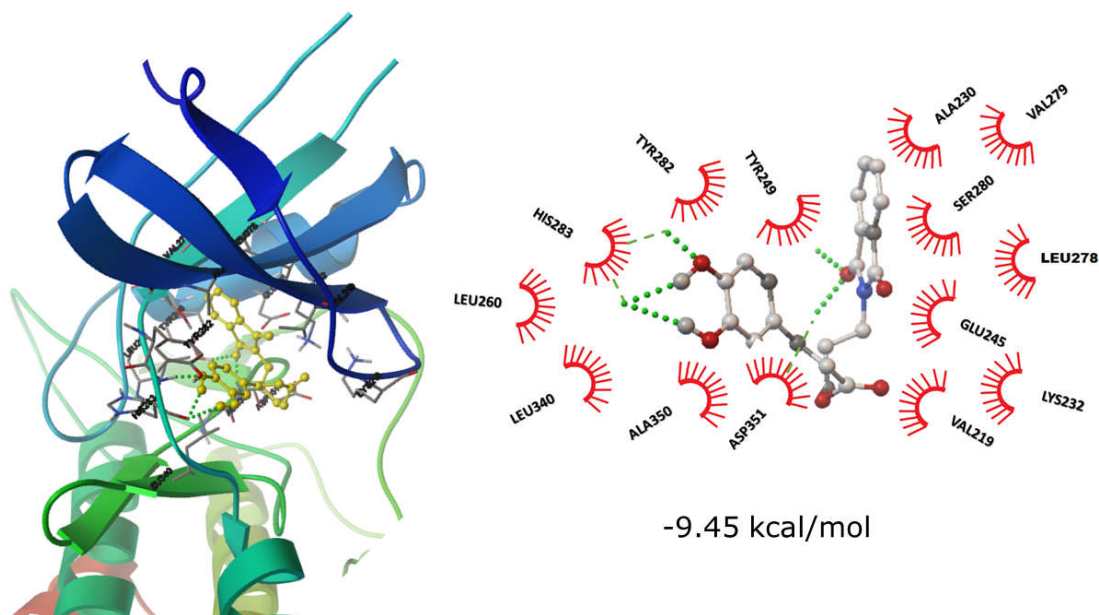


Figure S12. Interaction of the ligand **P12** (*E*)-2-(3-(3,4-dimethoxyphenyl)acryloyl)isoindolin-1,3-dione with the protein TGF- $\beta$  kinase I.

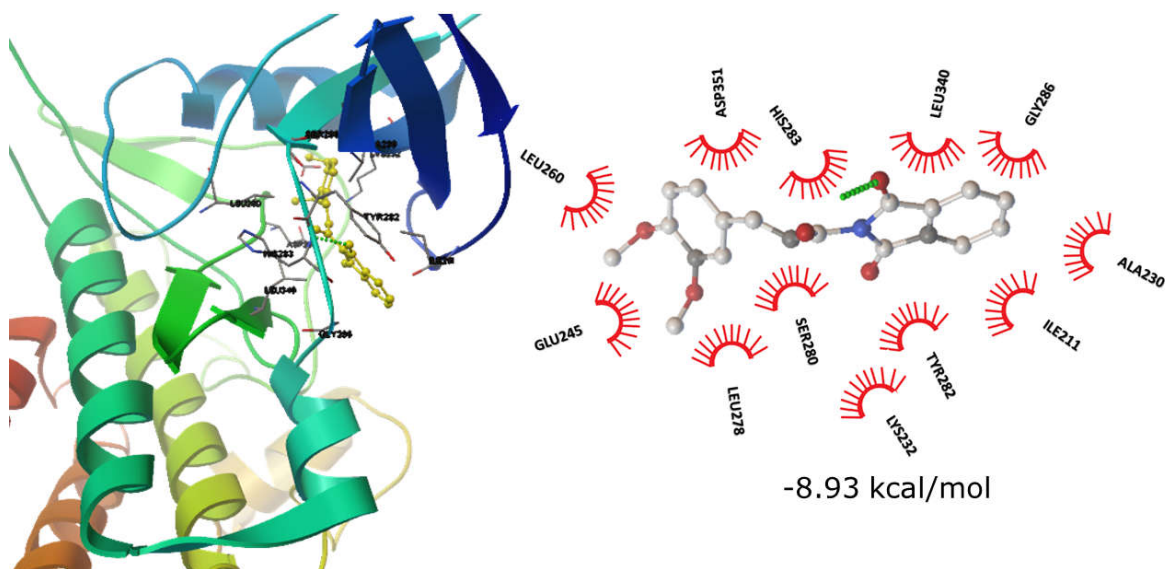


Figure S13. Interaction of the ligand **P13** 3-(1,3-dioxo isoindolin-3-yl)propyl (*E*)-3-(3,4-dihydroxyphenyl)acrylate with the protein TGF- $\beta$  kinase I.

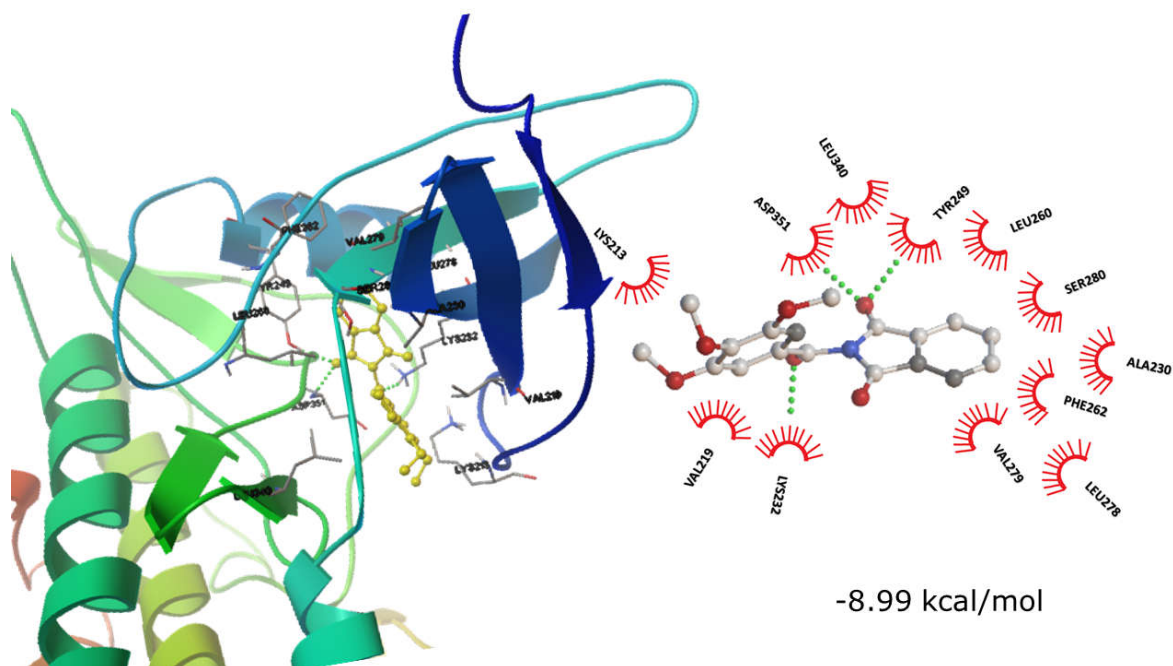


Figure S14. Interaction of the ligand **P14** 3-(1,3-dioxo isoindolin-2-yl)propyl 3,4,5-trihydroxybenzoate with the protein TGF- $\beta$  kinase I.

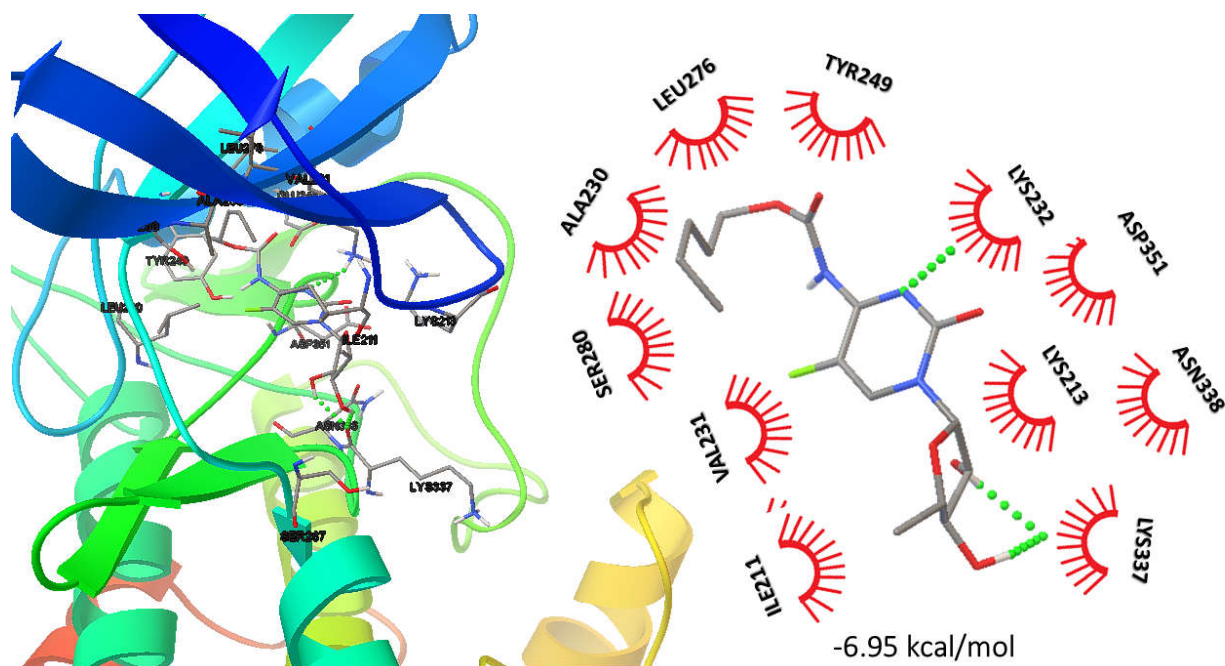


Figure S15. Interaction of the control **Capecitabine** with the protein TGF- $\beta$  kinase I.

Elucidation analysis

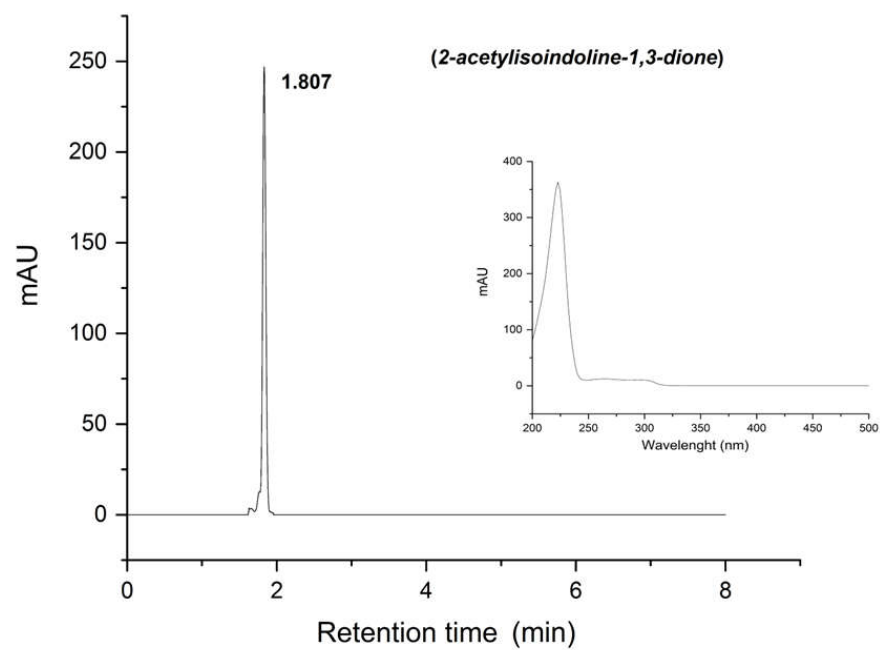


Figure S16. Chromatogram and UV-Vis spectrum of **P2** 2-acetyl isoindoline-1,3-dione.

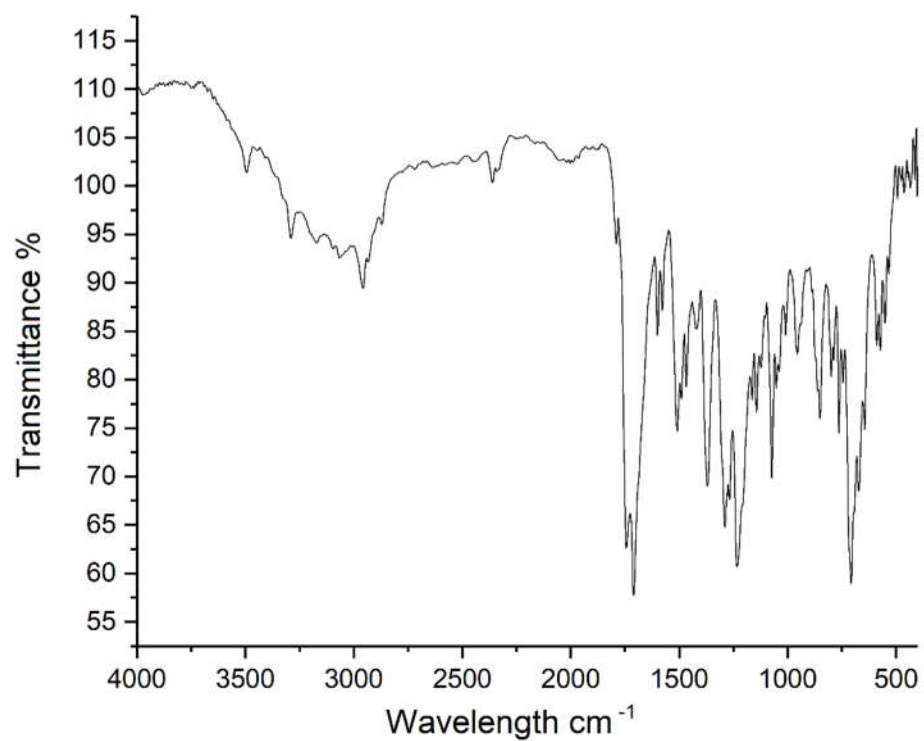


Figure S17. FT-IR spectrum of **P2** 2-acetyl isoindoline-1,3-dione.

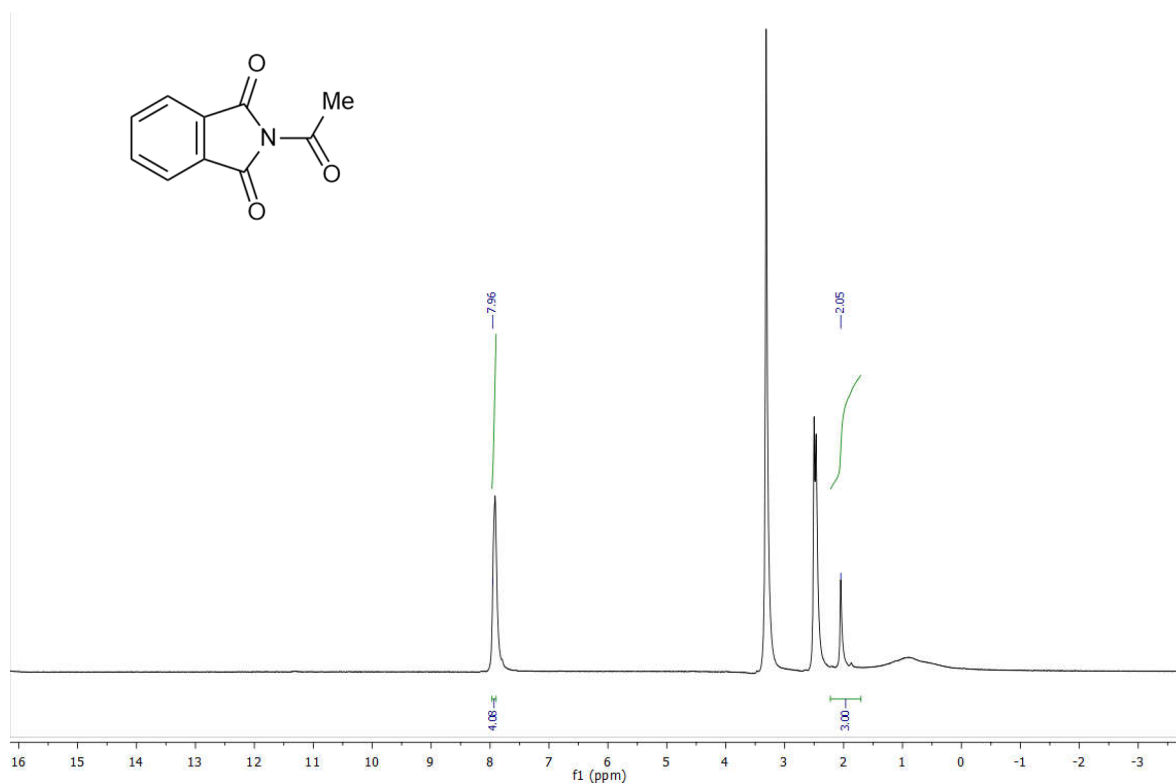


Figure S18. <sup>1</sup>H NMR spectrum of **P2** 2-acetyl isoindoline-1,3-dione.

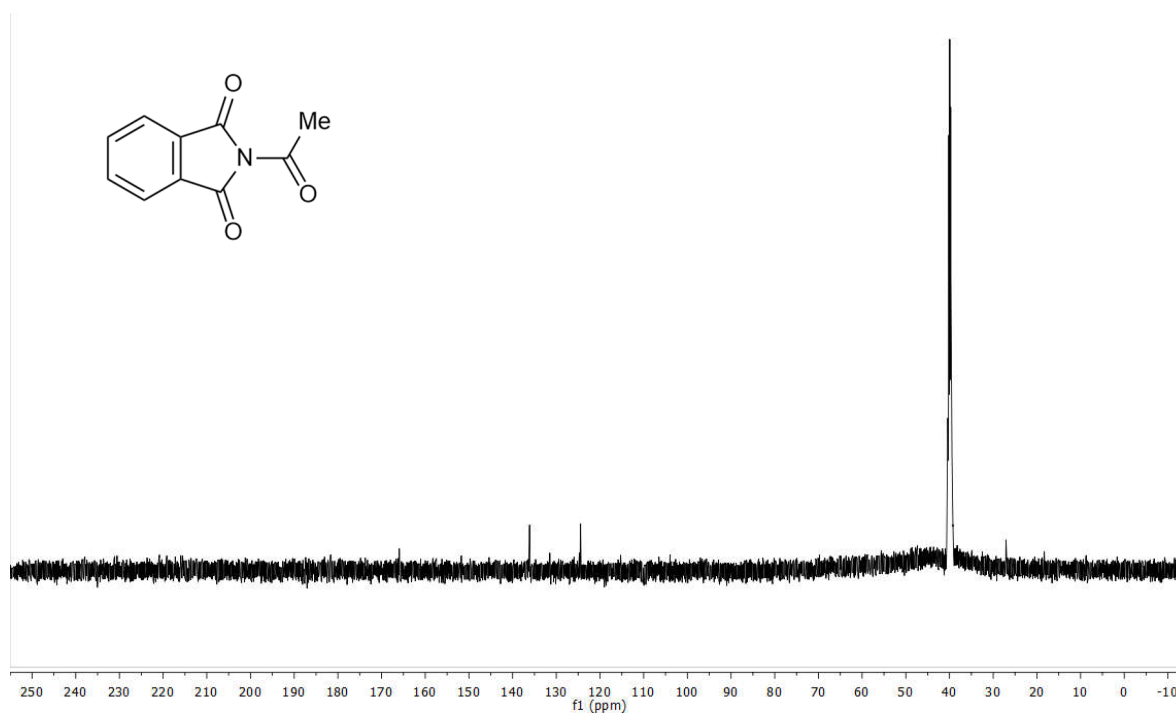


Figure S19. <sup>13</sup>C NMR spectrum of **P2** 2-acetyl isoindoline-1,3-dione.

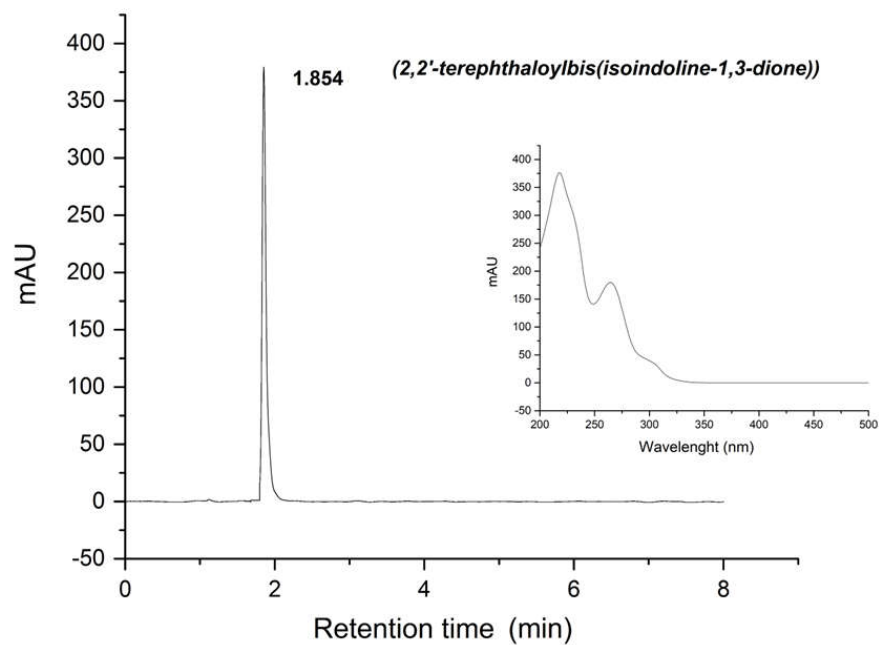


Figure S20. Chromatogram and UV-Vis spectrum of **P4** 2,2'-terephthaloyl bis(isoindolin-1,3-dione).

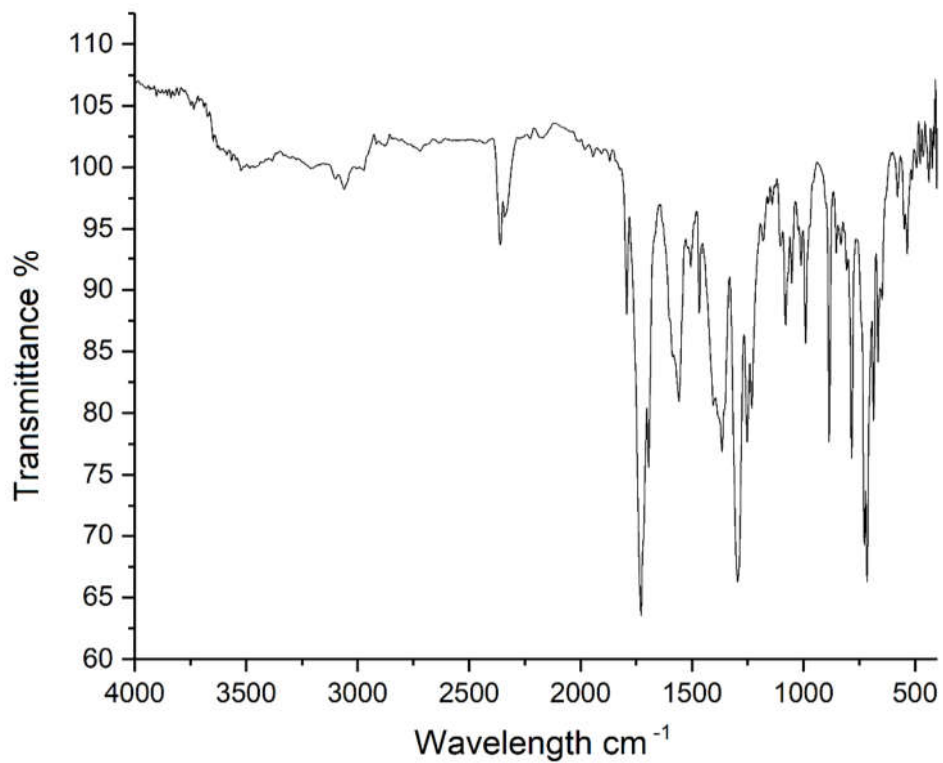


Figure S21. FT-IR spectrum of **P4** 2,2'-terephthaloyl bis(isoindolin-1,3-dione).

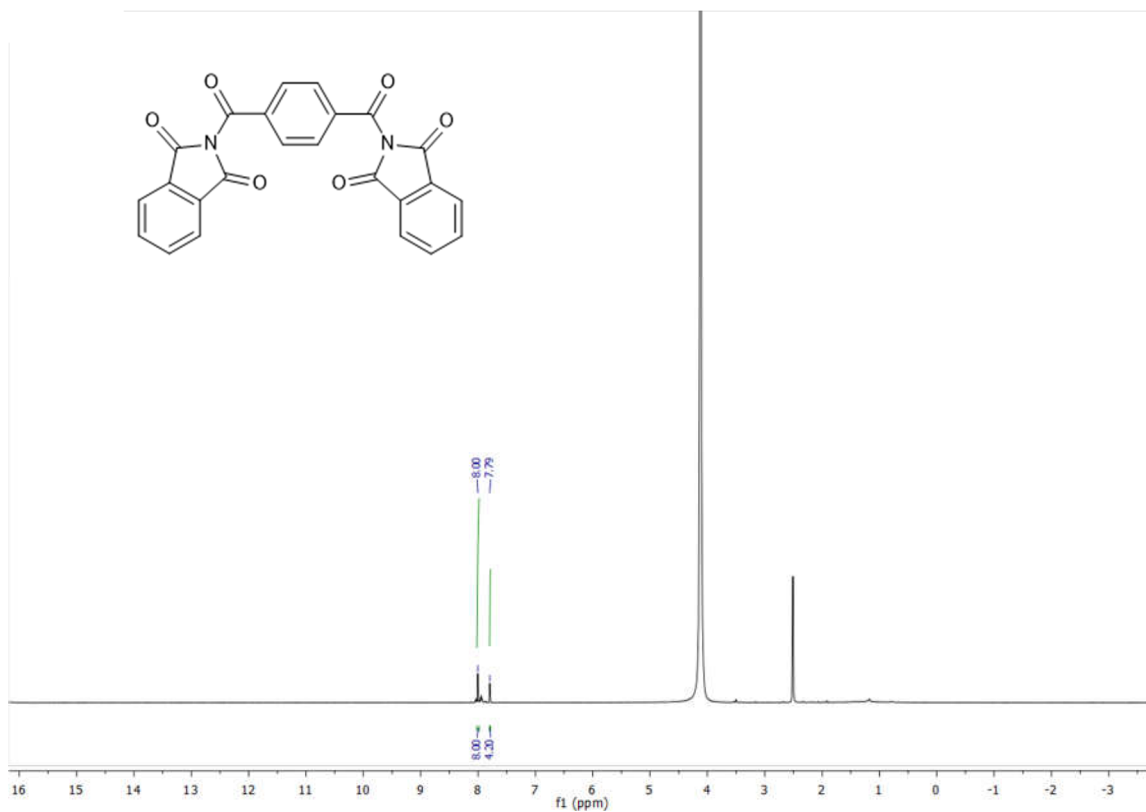


Figure S22. <sup>1</sup>H NMR spectrum of **P4** 2,2'-terephthaloyl bis(isoindolin-1,3-dione).

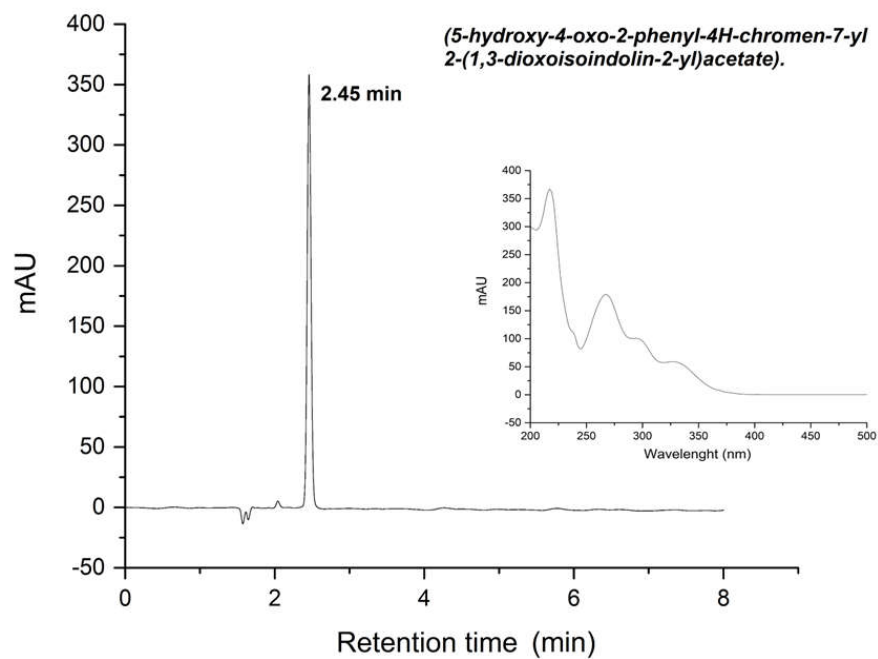


Figure S23. Chromatogram and UV-Vis spectrum of **P7** 5-hydroxy-4-oxo-2-phenyl-4H-chromen-7-yl 2-(1,3-dioxoisoindolin-2-yl)acetate.

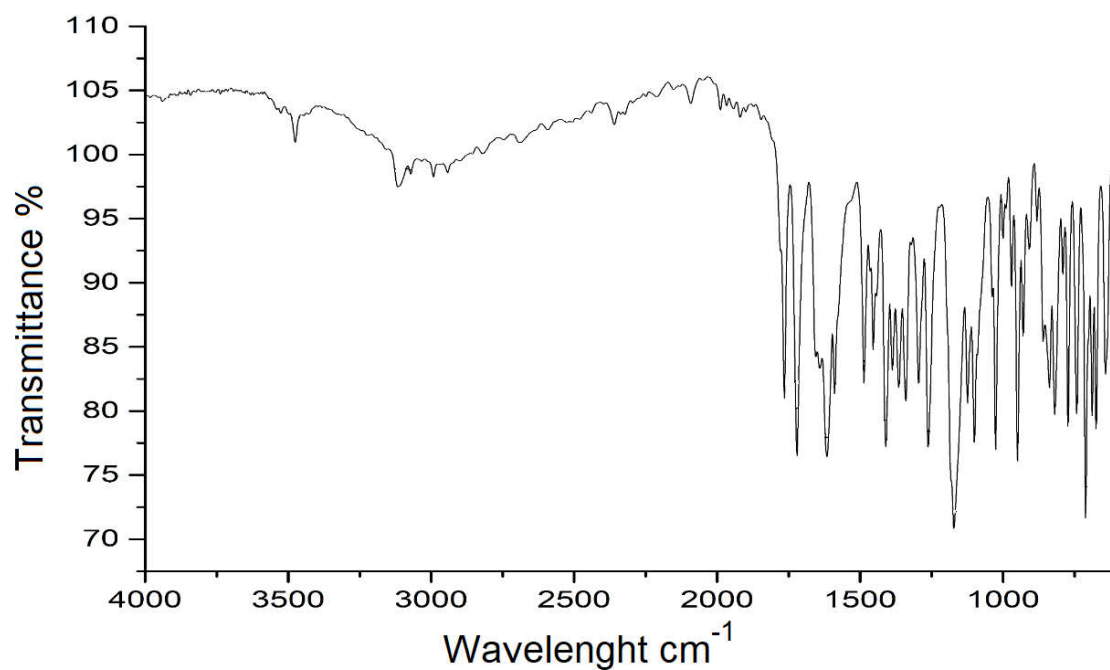


Figure S24. FT-IR spectrum of **P7** 5-hydroxy-4-oxo-2-phenyl-4H-chromen-7-yl 2-(1,3-dioxoisindolin-2-yl)acetate.



Figure S25.  $^1\text{H}$  NMR spectrum of **P7** 5-hydroxy-4-oxo-2-phenyl-4H-chromen-7-yl 2-(1,3-dioxoisindolin-2-yl)acetate.

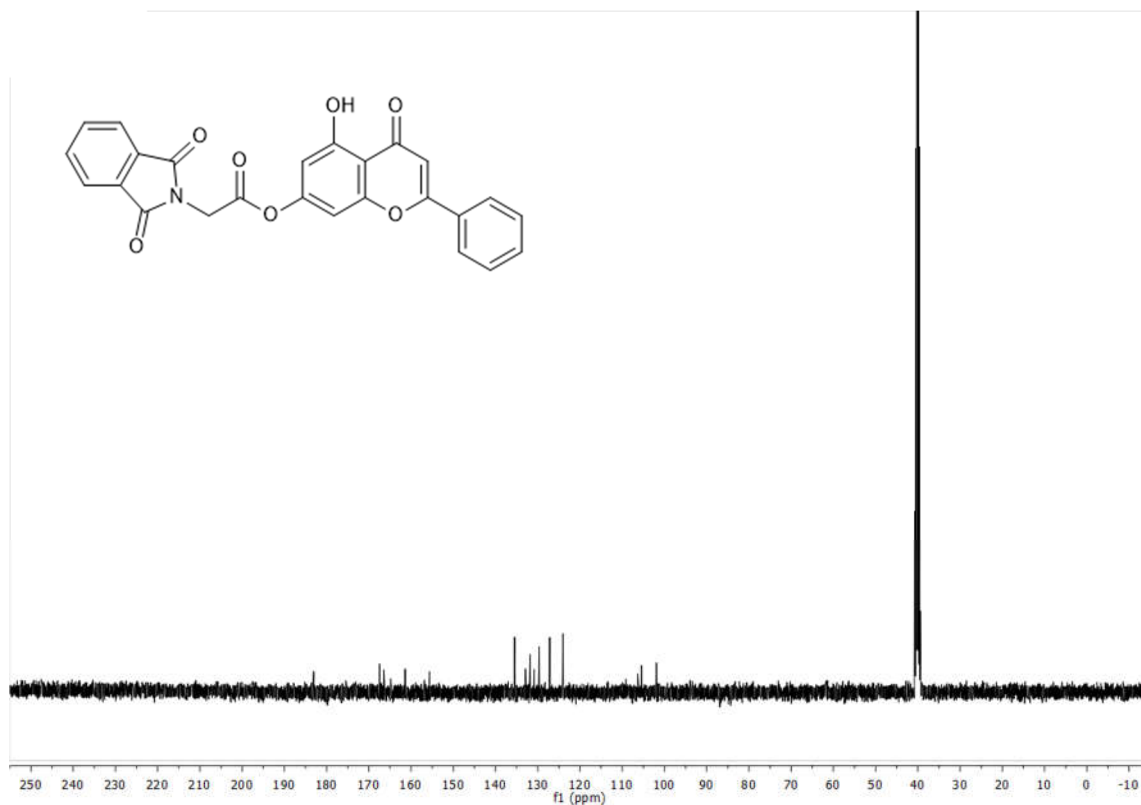


Figure S26.  $^{13}\text{C}$  NMR spectrum of **P7** 5-hydroxy-4-oxo-2-phenyl-4H-chromen-7-yl 2-(1,3-dioxoisindolin-2-yl)acetate.

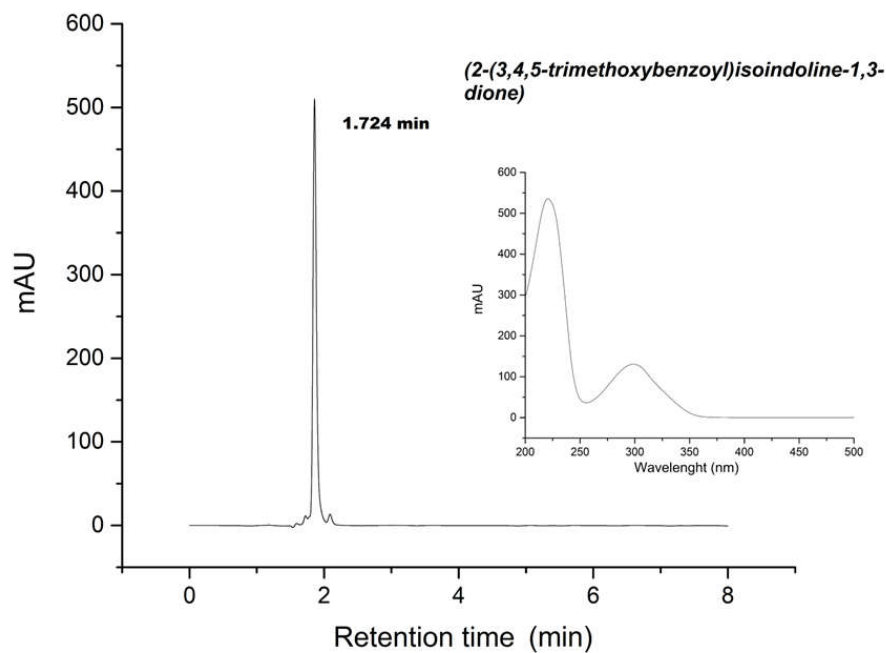


Figure S27. Chromatogram and UV-Vis spectrum of **P10** 2-(3,4,5-trimethoxybenzoyl)isoindolin-1,3-dione.

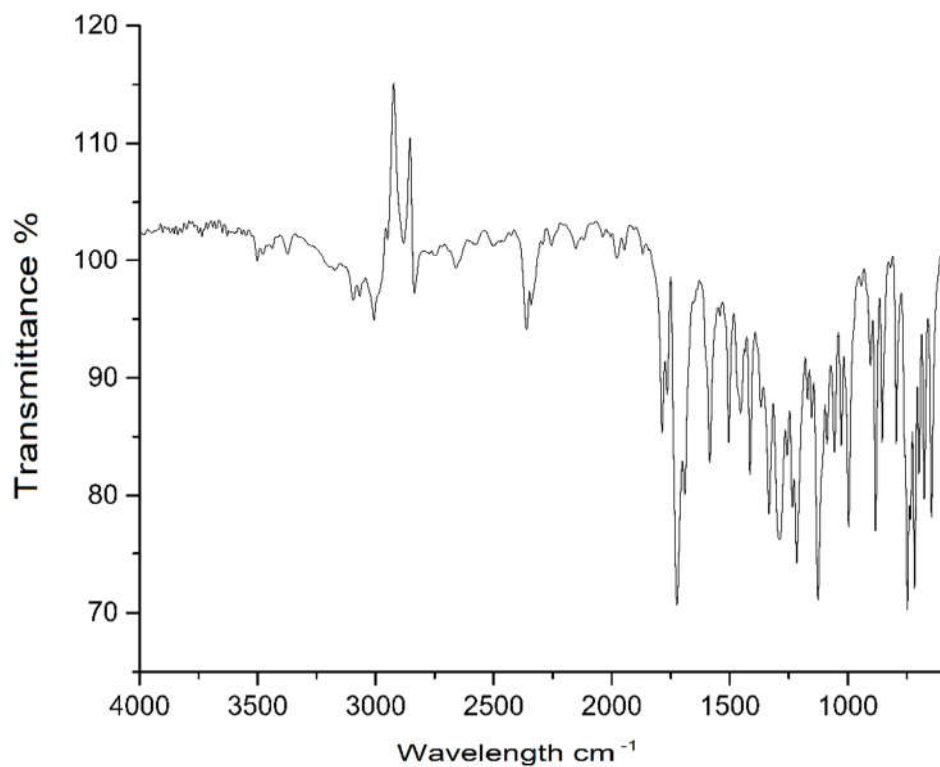


Figure S28. FT-IR spectrum of **P10** 2-(3,4,5-trimethoxybenzoyl)isoindolin-1,3-dione.

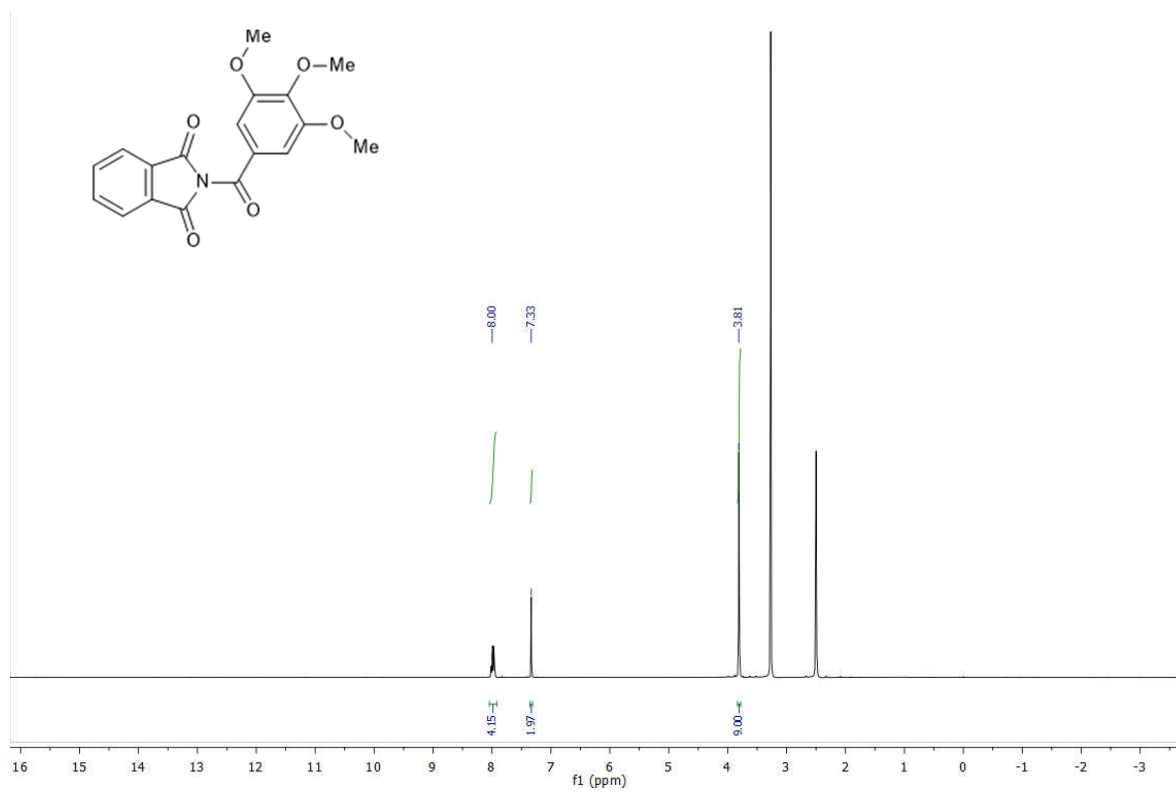


Figure S29.  $^1\text{H}$  NMR spectrum of **P10** 2-(3,4,5-trimethoxybenzoyl)isoindolin-1,3-dione.

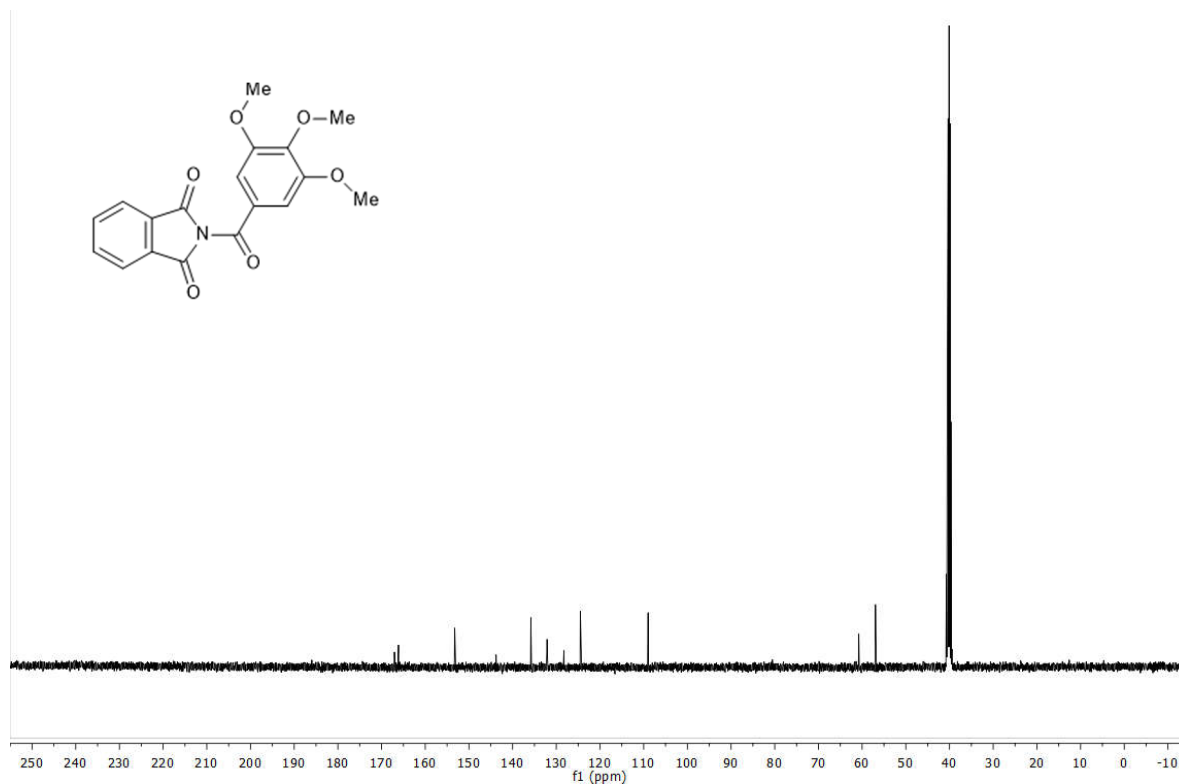


Figure S30.  $^{13}\text{C}$  NMR spectrum of **P10** 2-(3,4,5-trimethoxybenzoyl)isoindolin-1,3-dione.

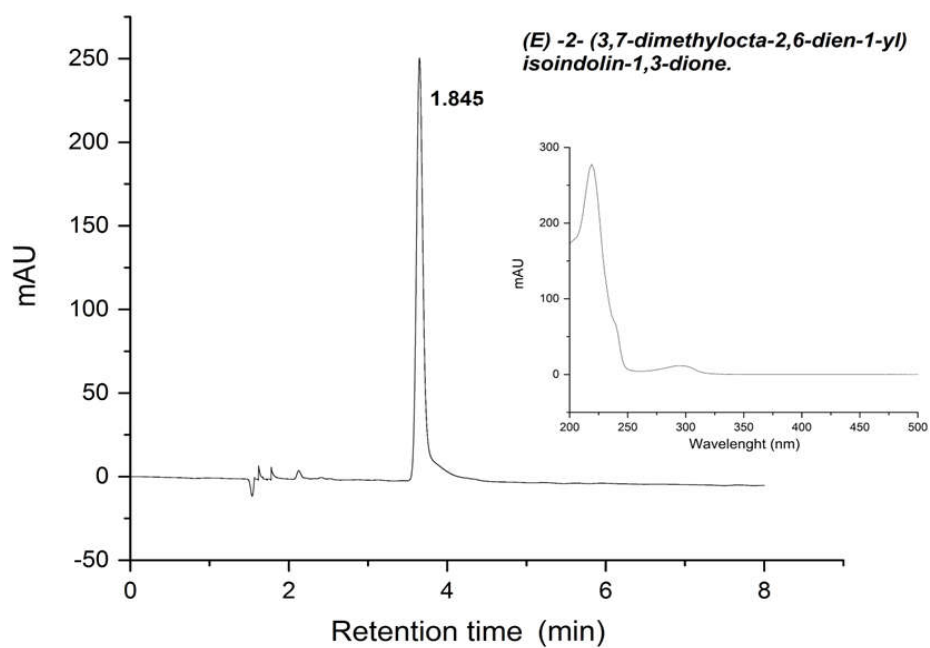


Figure S31. Chromatogram and UV-Vis spectrum of **P11** (E)-2-(3,7-dimethylocta-2,6-dien-1-yl)isoindolin-1,3-dione.

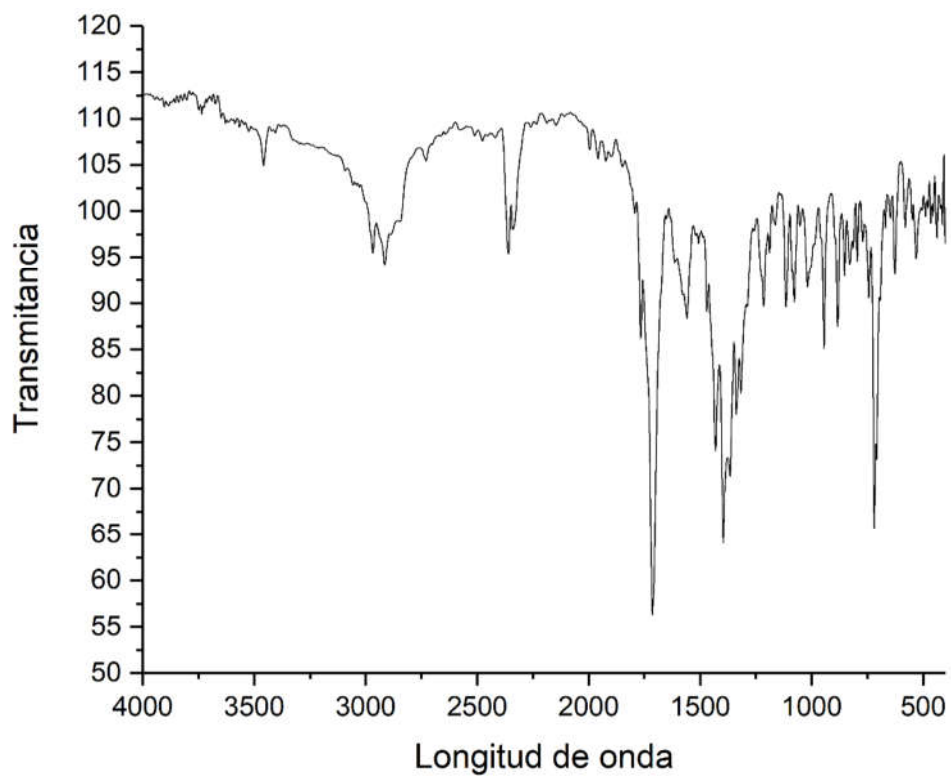


Figure S32. FT-IR spectrum of **P11** (E)-2-(3,7-dimethylocta-2,6-dien-1-yl)isoindolin-1,3-dione.

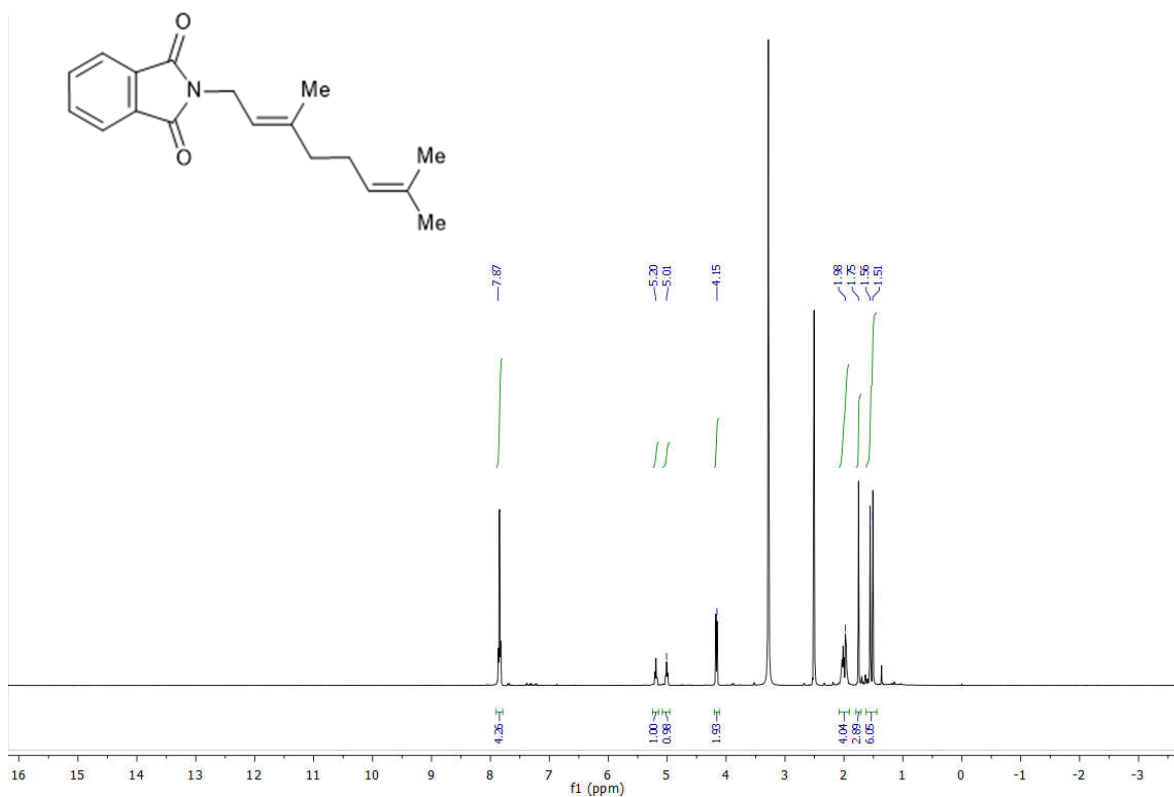


Figure S33.  $^1\text{H}$  NMR spectrum of **P11** (E)-2-(3,7-dimethylocta-2,6-dien-1-yl)isoindolin-1,3-dione.

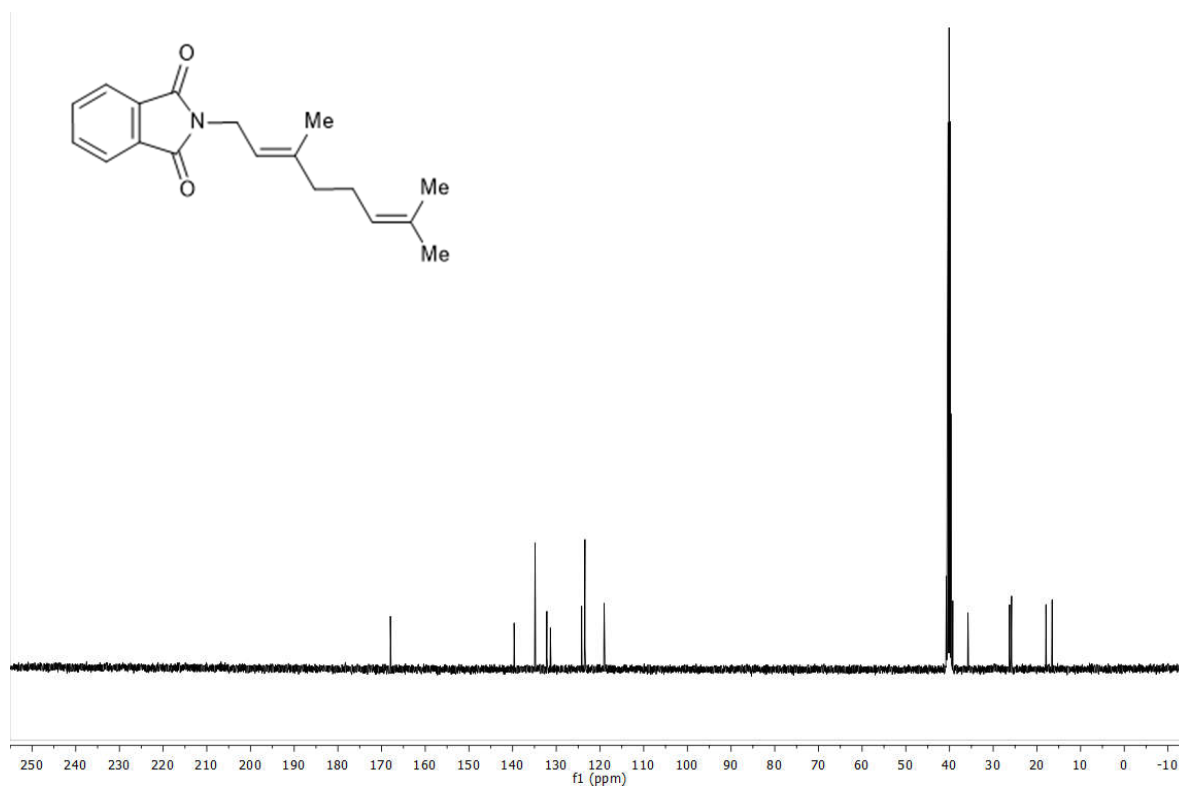


Figure S34.  $^{13}\text{C}$  NMR spectrum of **P11** (E)-2-(3,7-dimethylocta-2,6-dien-1-yl)isoindolin-1,3-dione.