**Support information**

# Rational design and synthesis of new acetamide–indole–benzo[d]imidazole–carboxylic acid hybrids as dual PTP1B/α-glucosidase inhibitors

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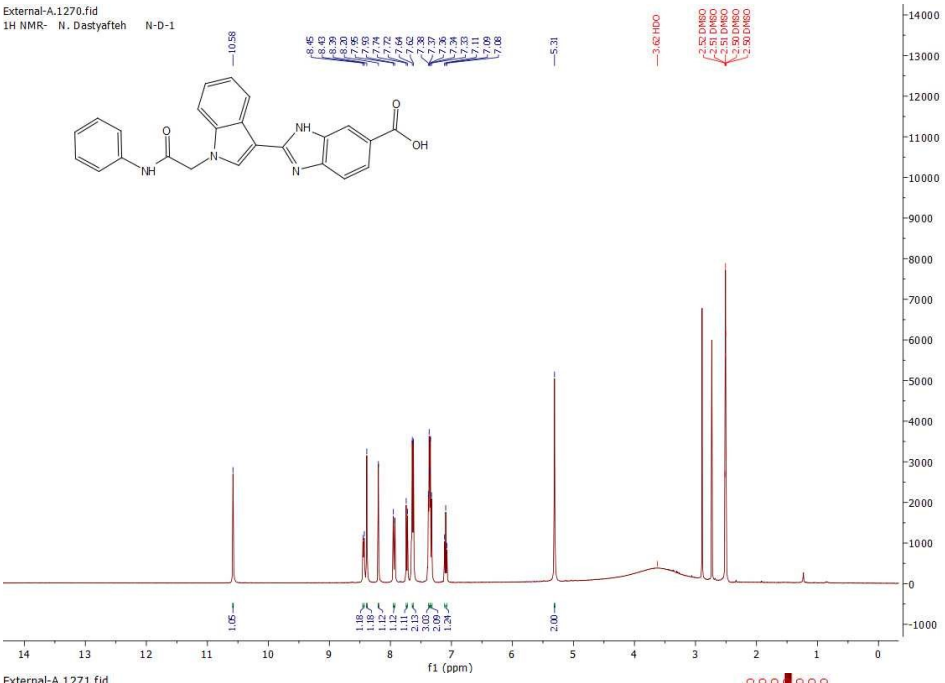
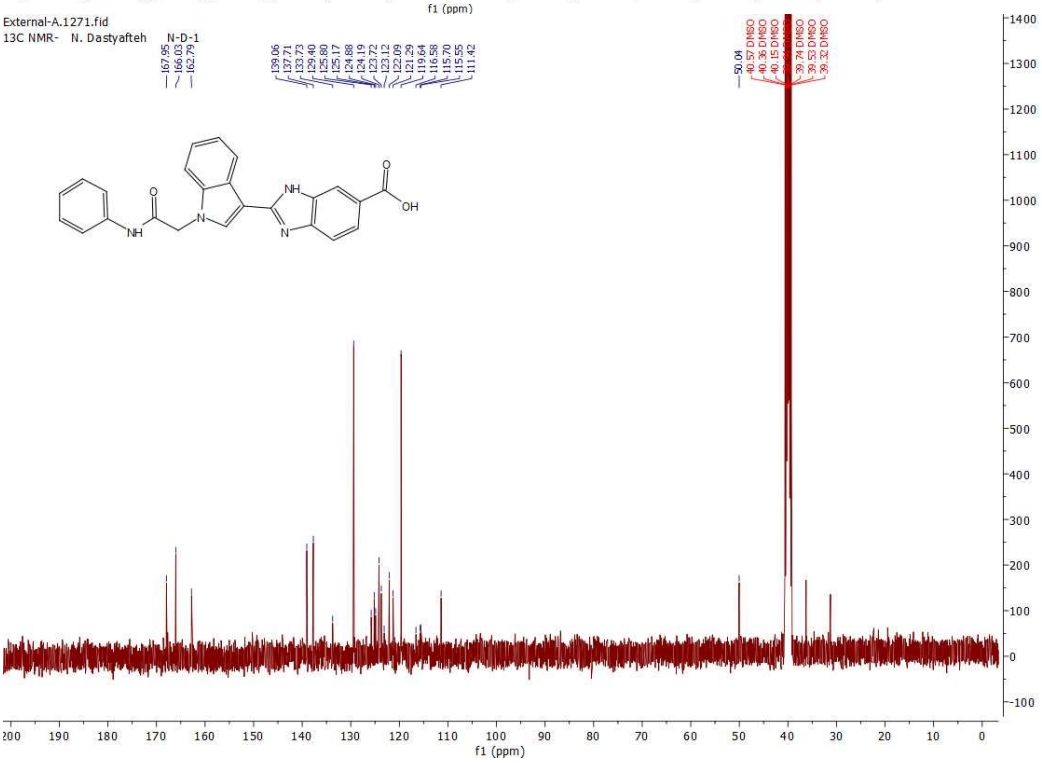
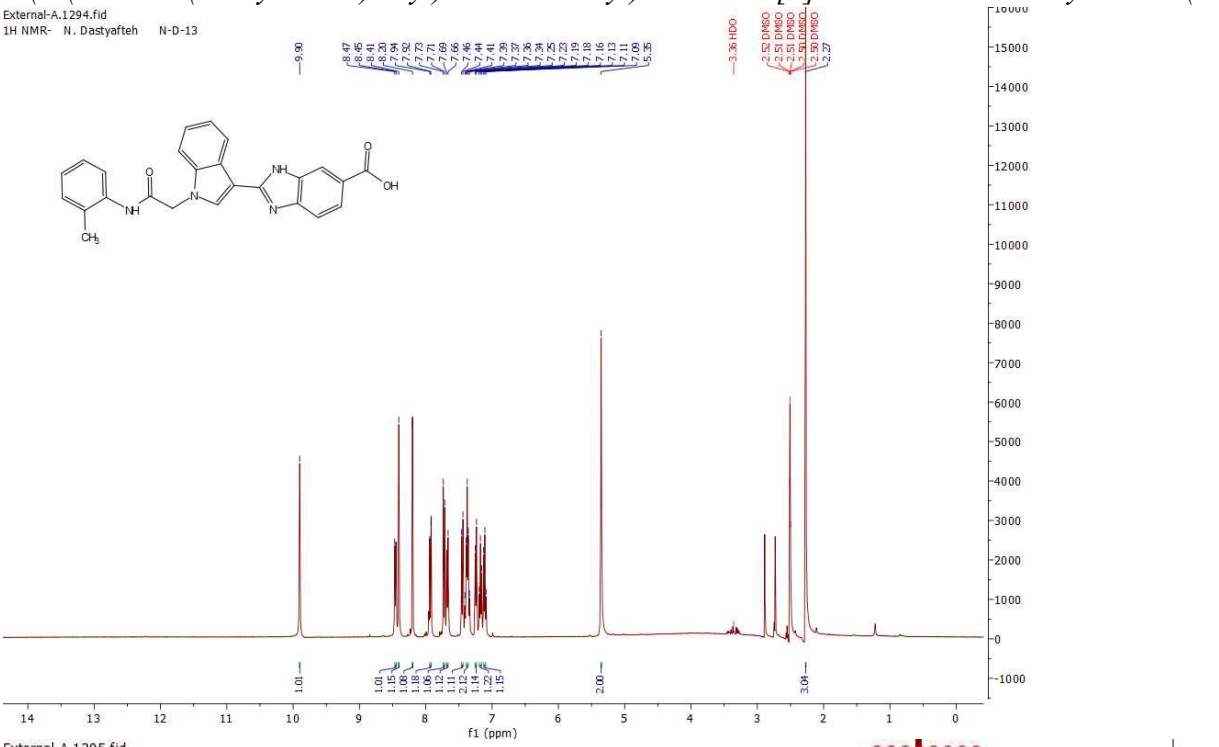
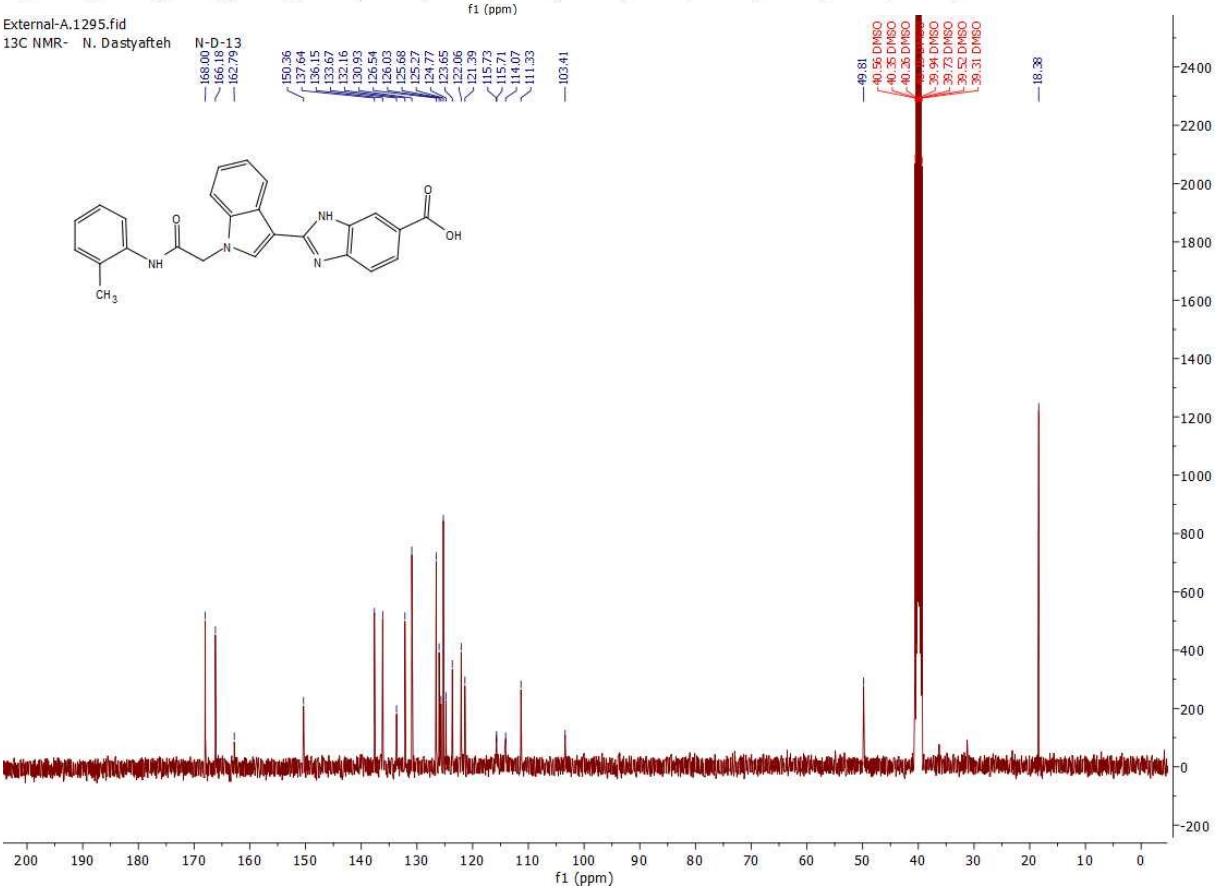
*2-(1-(2-oxo-2-(phenylamino)ethyl)-1H-indol-3-yl)-1H-benzo[d]imidazole-6-carboxylic acid (**8a**)*



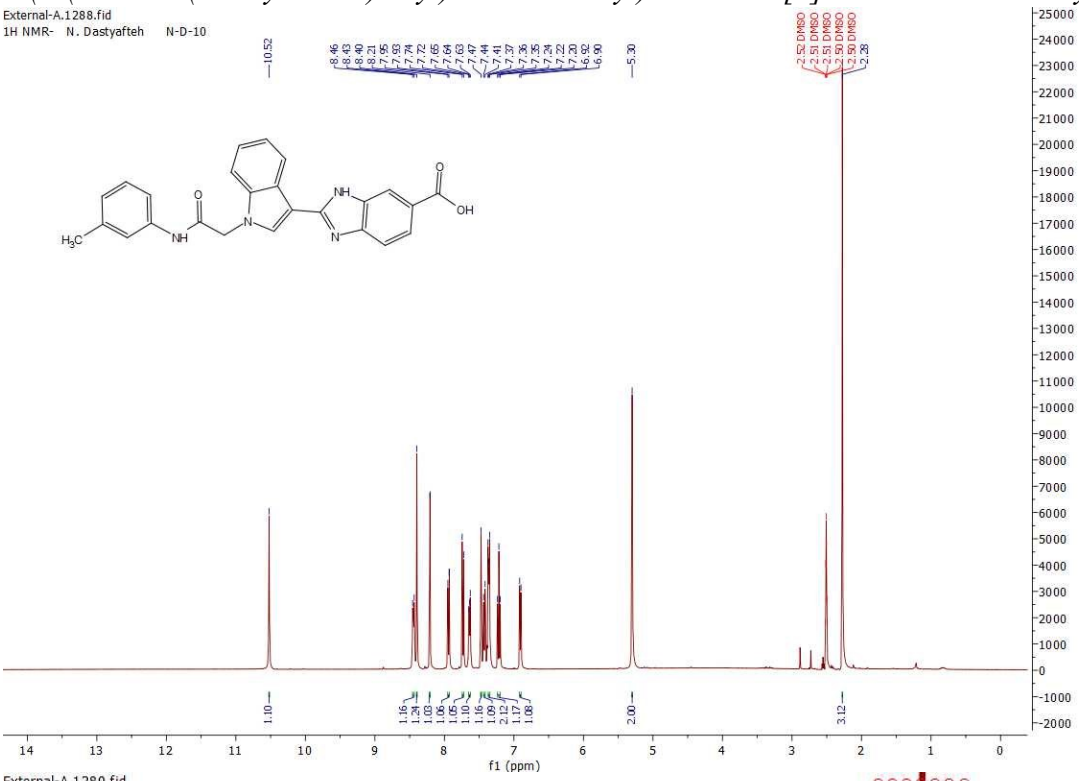



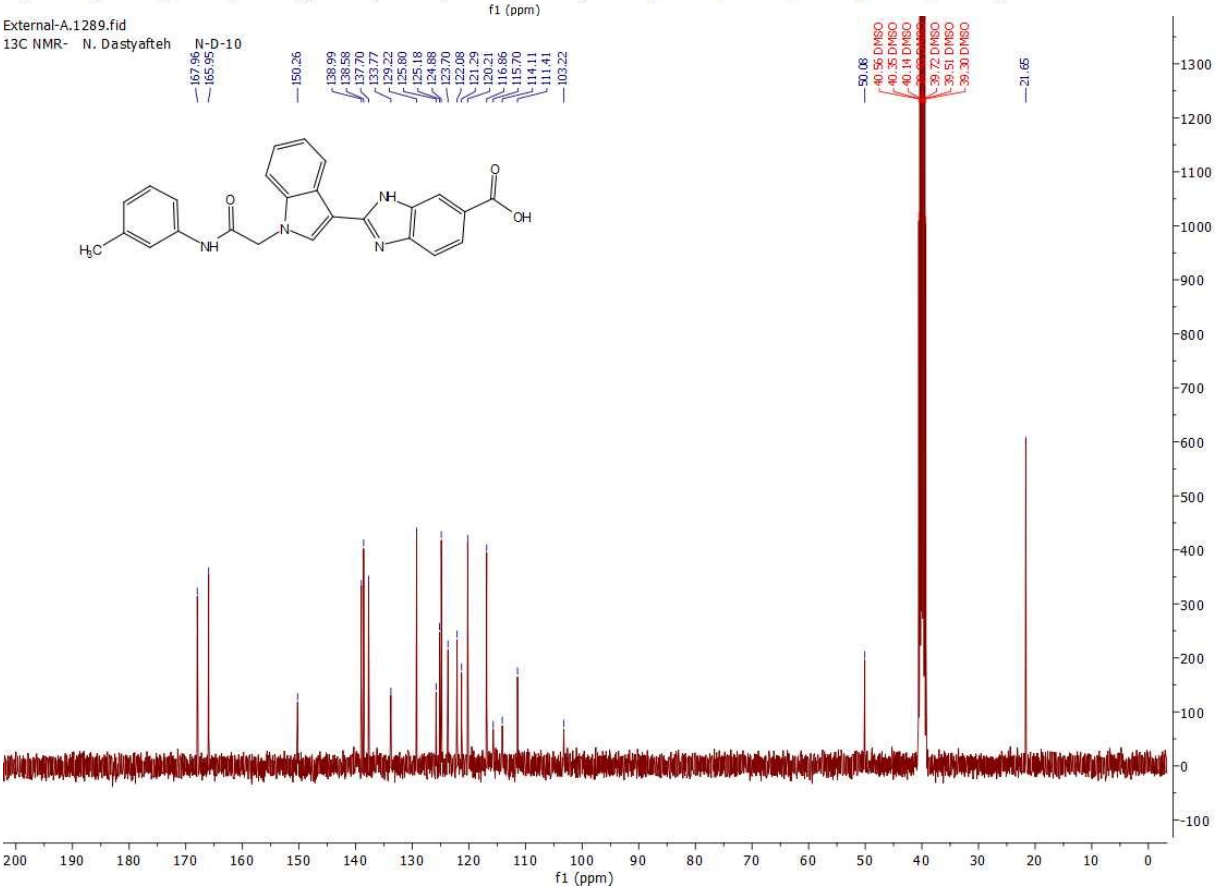
*2-(1-(2-oxo-2-(o-tolylamino)ethyl)-1H-indol-3-yl)-1H-benzo[d]imidazole-6-carboxylic acid (**8b**)*



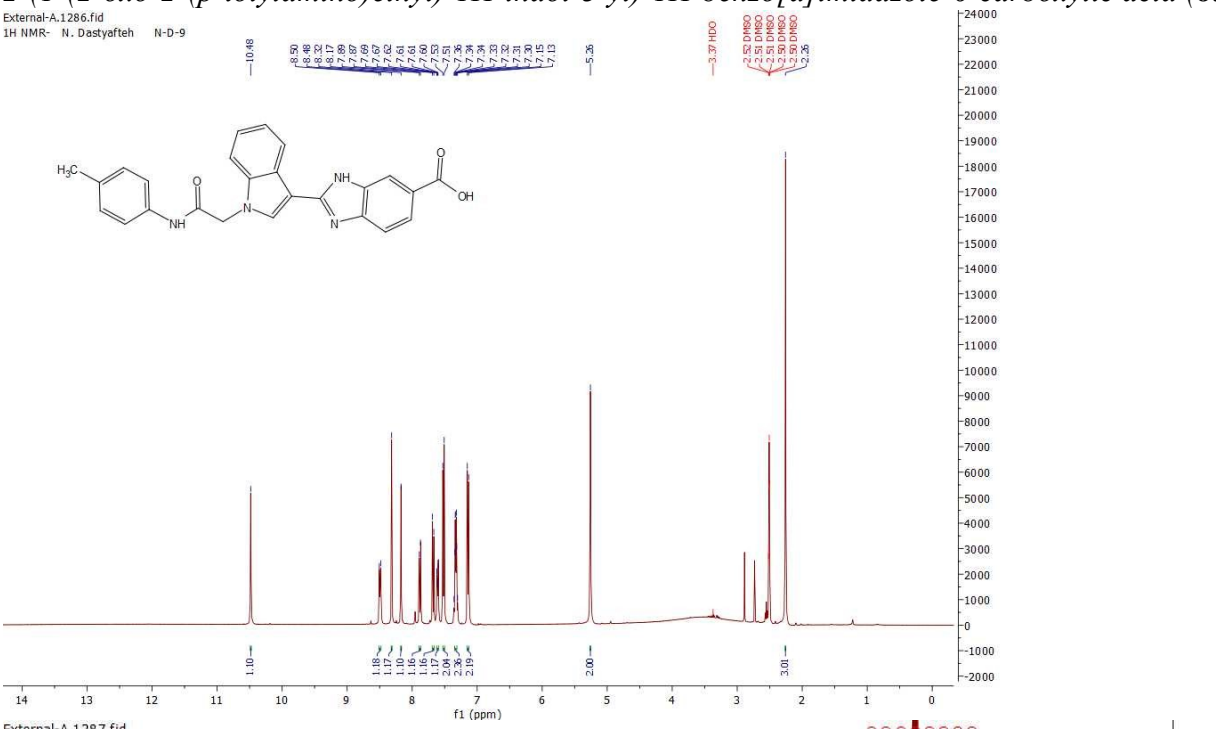



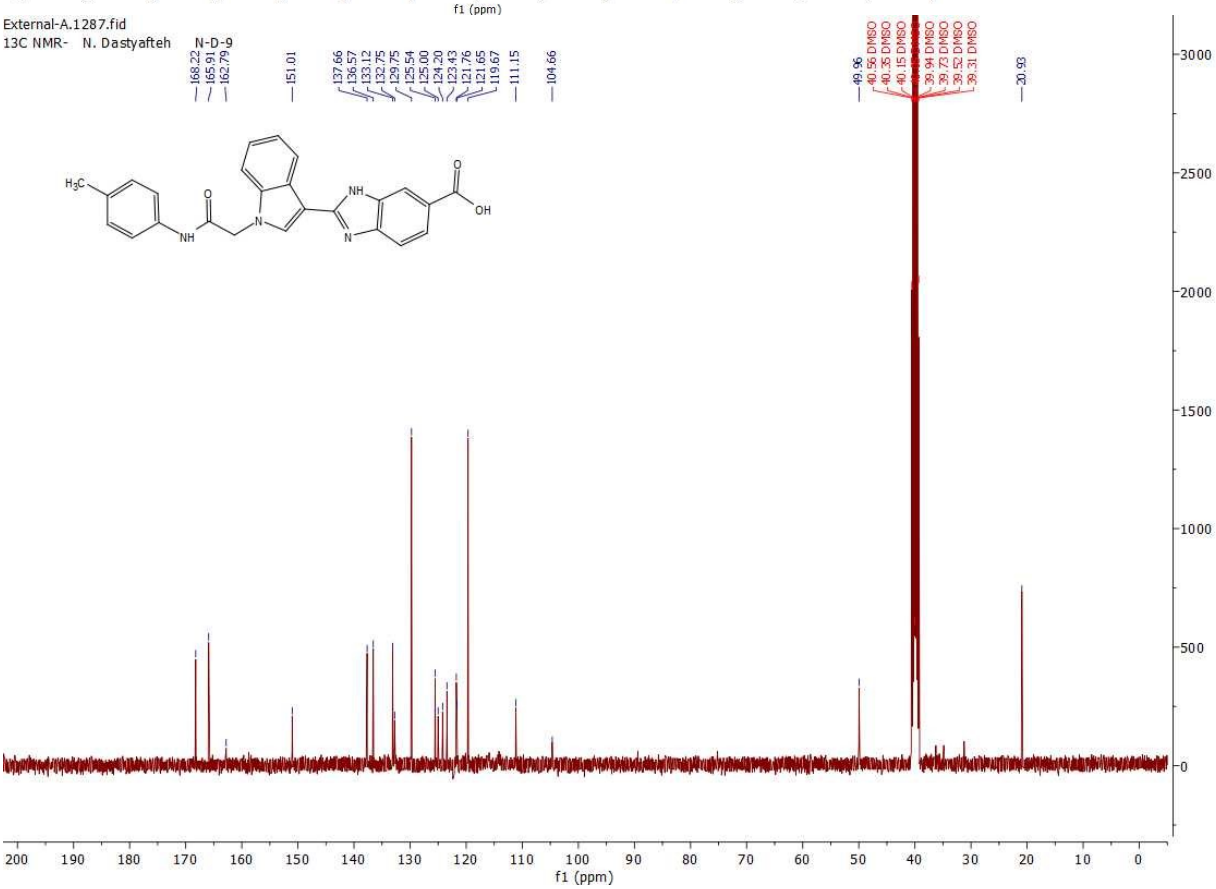
*2-(1-(2-oxo-2-(m-tolylamino)ethyl)-1H-indol-3-yl)-1H-benzo[d]imidazole-6-carboxylic acid (**8c**)*



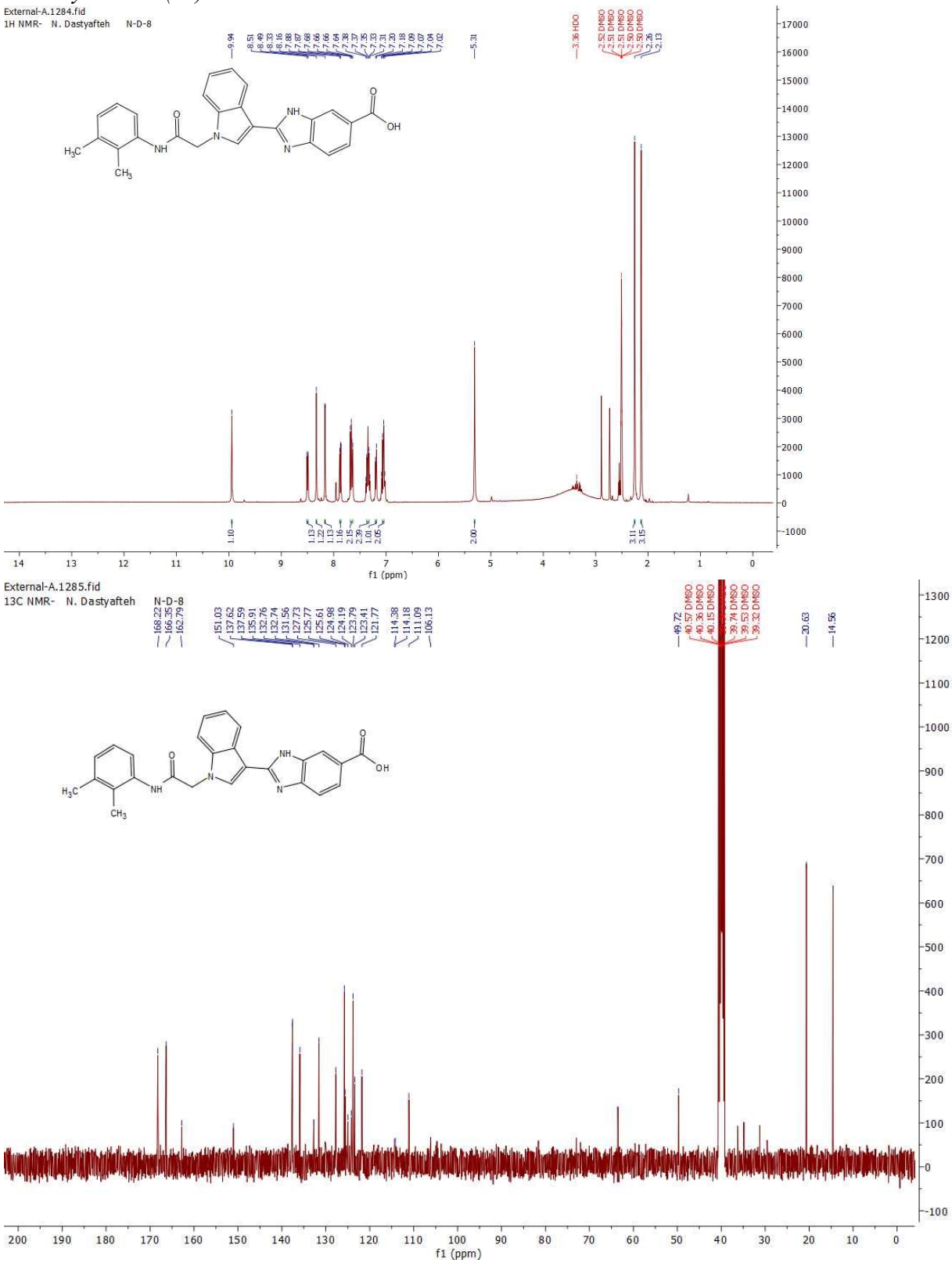



*2-(1-(2-oxo-2-(p-tolylamino)ethyl)-1H-indol-3-yl)-1H-benzo[d]imidazole-6-carboxylic acid (**8d**)*

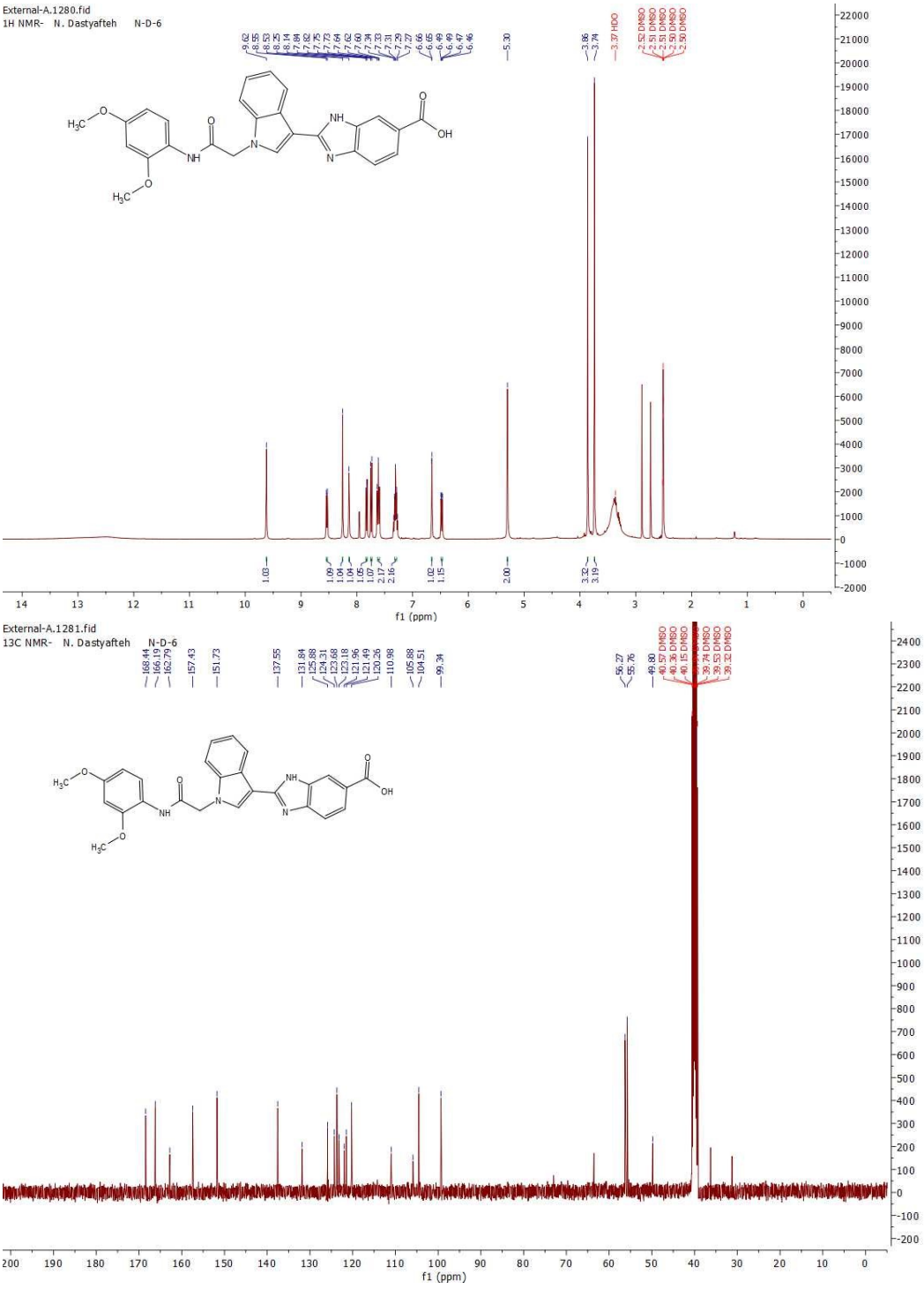


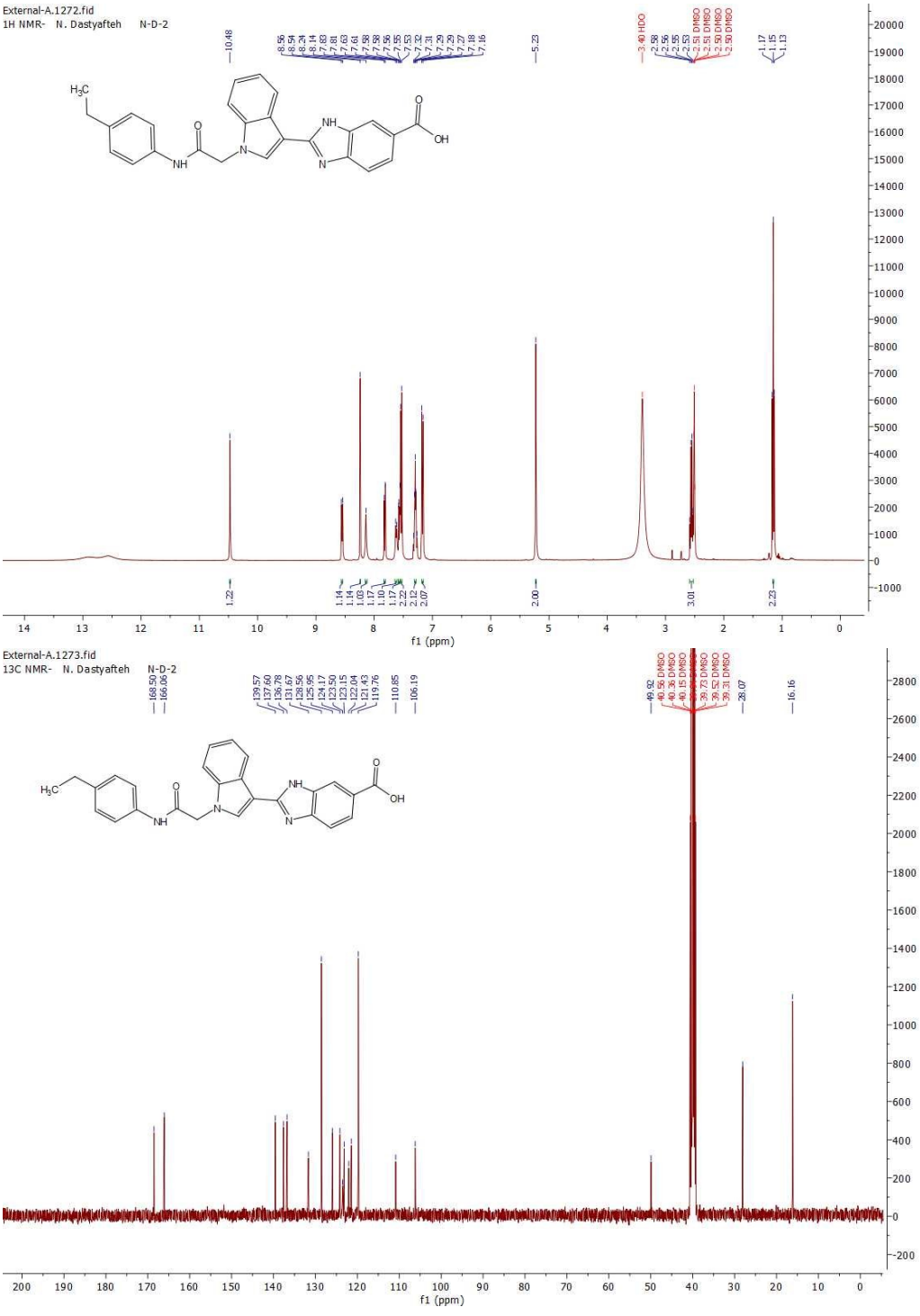
*2-(1-(2-((2,3-dimethylphenyl)amino)-2-oxoethyl)-1H-indol-3-yl)-1H-benzo[d]imidazole-6-carboxylic acid (**8e**)*



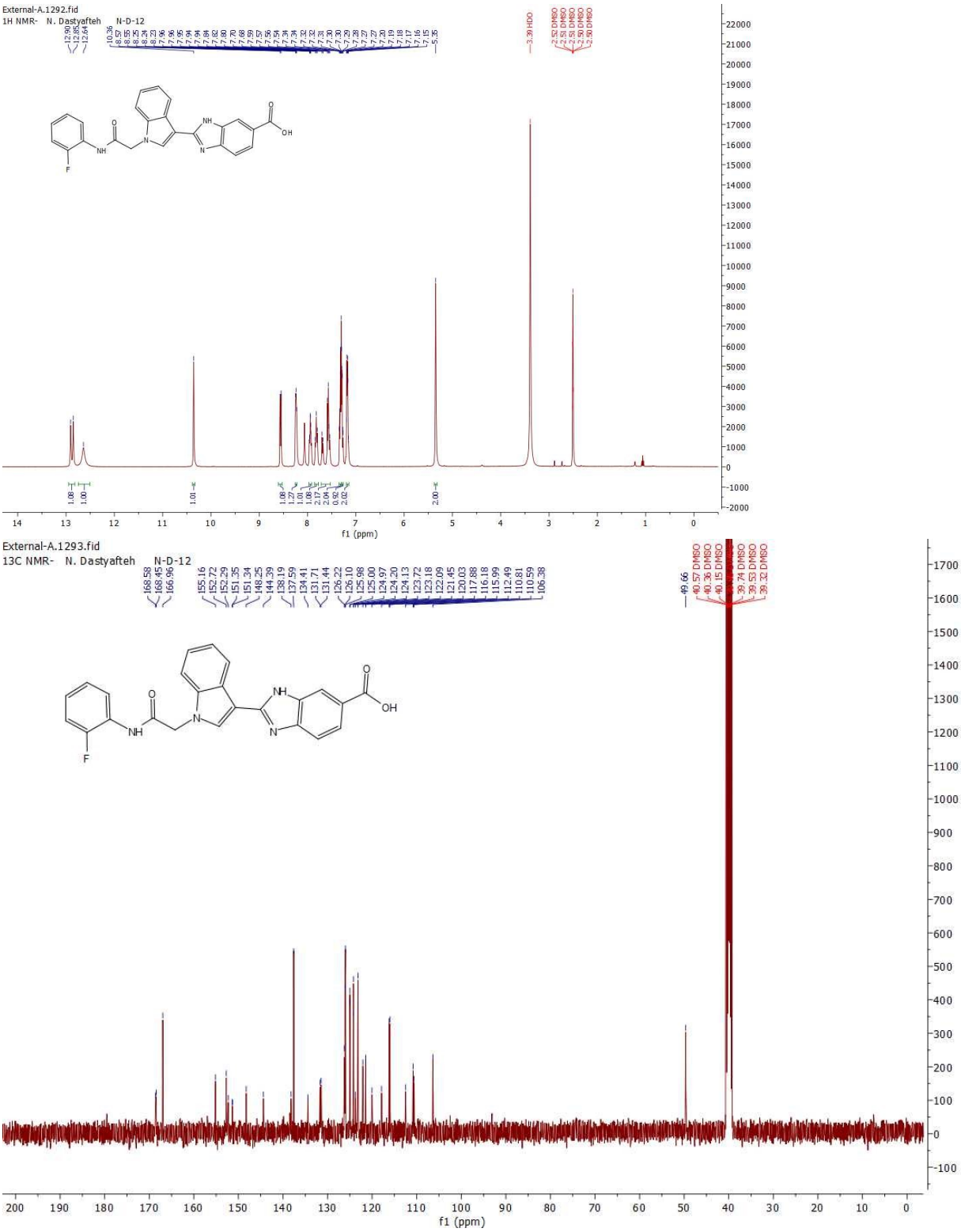
*2-(1-(2-((2,4-dimethoxyphenyl)amino)-2-oxoethyl)-1H-indol-3-yl)-1H-benzo[d]imidazole-6-carboxylic acid (**8f**)*



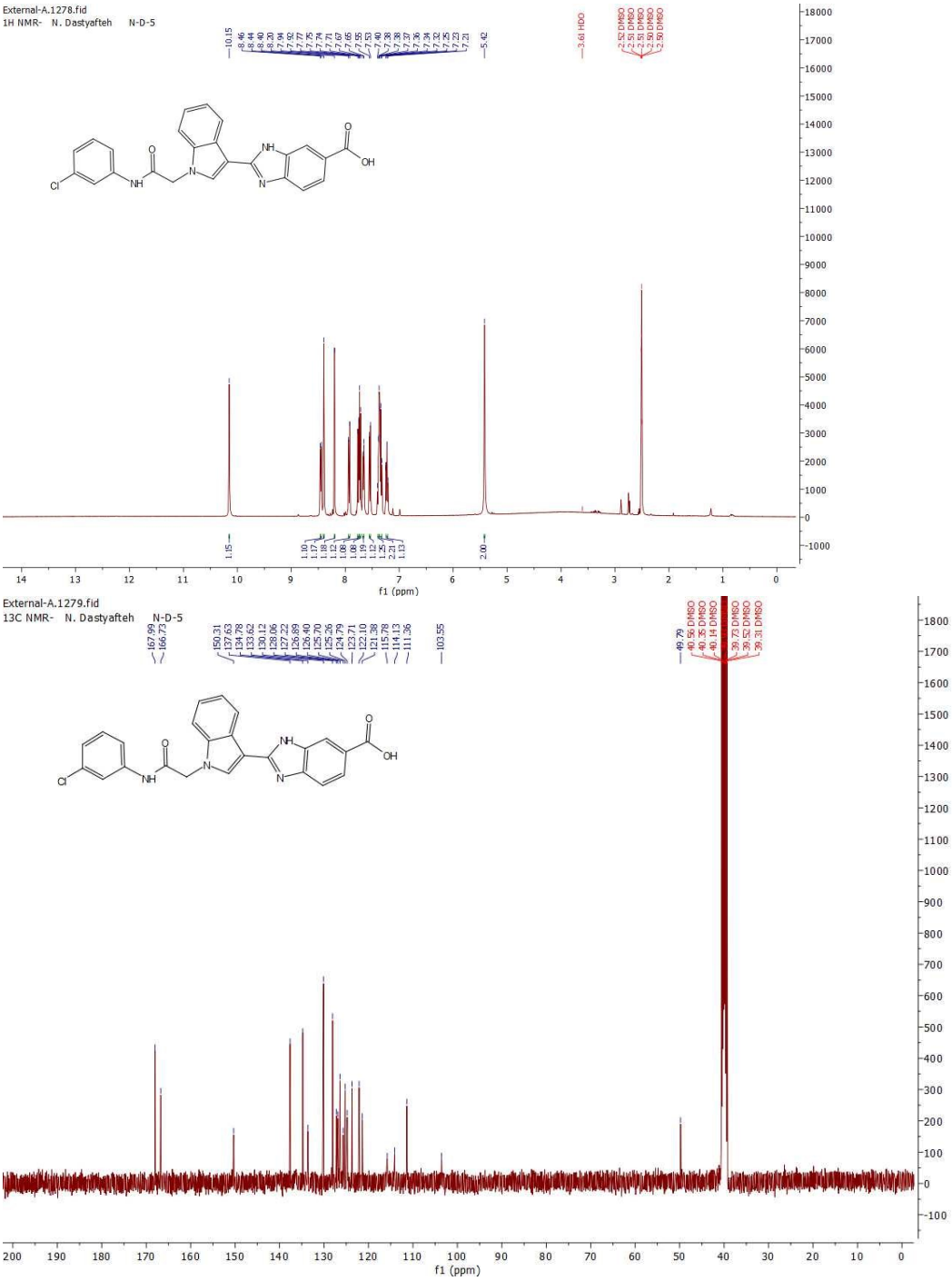
*2-(1-(2-((4-ethylphenyl)amino)-2-oxoethyl)-1H-indol-3-yl)-1H-benzo[d]imidazole-6-carboxylic acid (**8g**)*



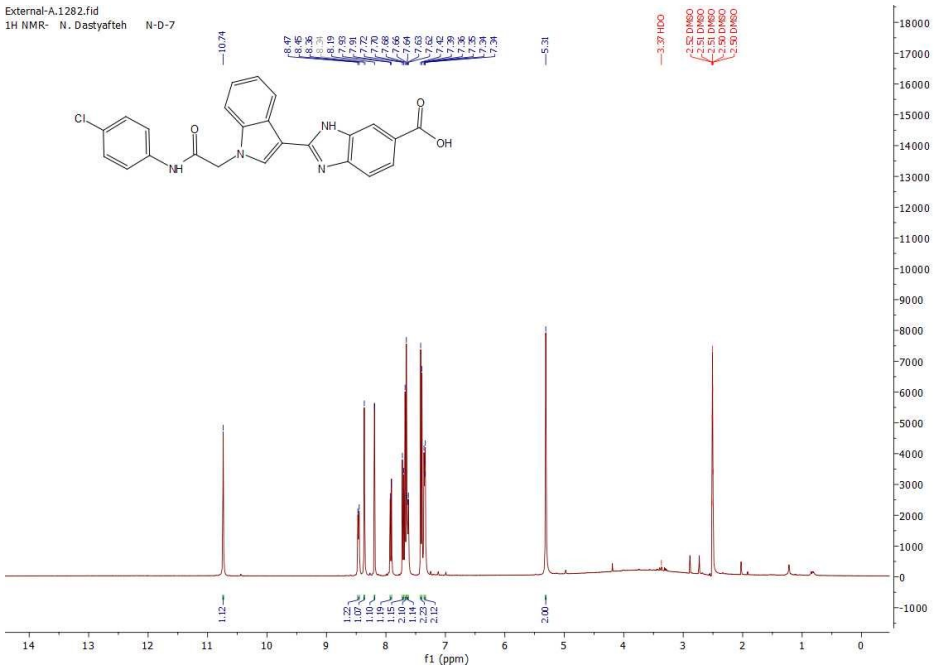
*2-(1-(2-((2-fluorophenyl)amino)-2-oxoethyl)-1H-indol-3-yl)-1H-benzo[d]imidazole-6-carboxylic acid (**8h**)*

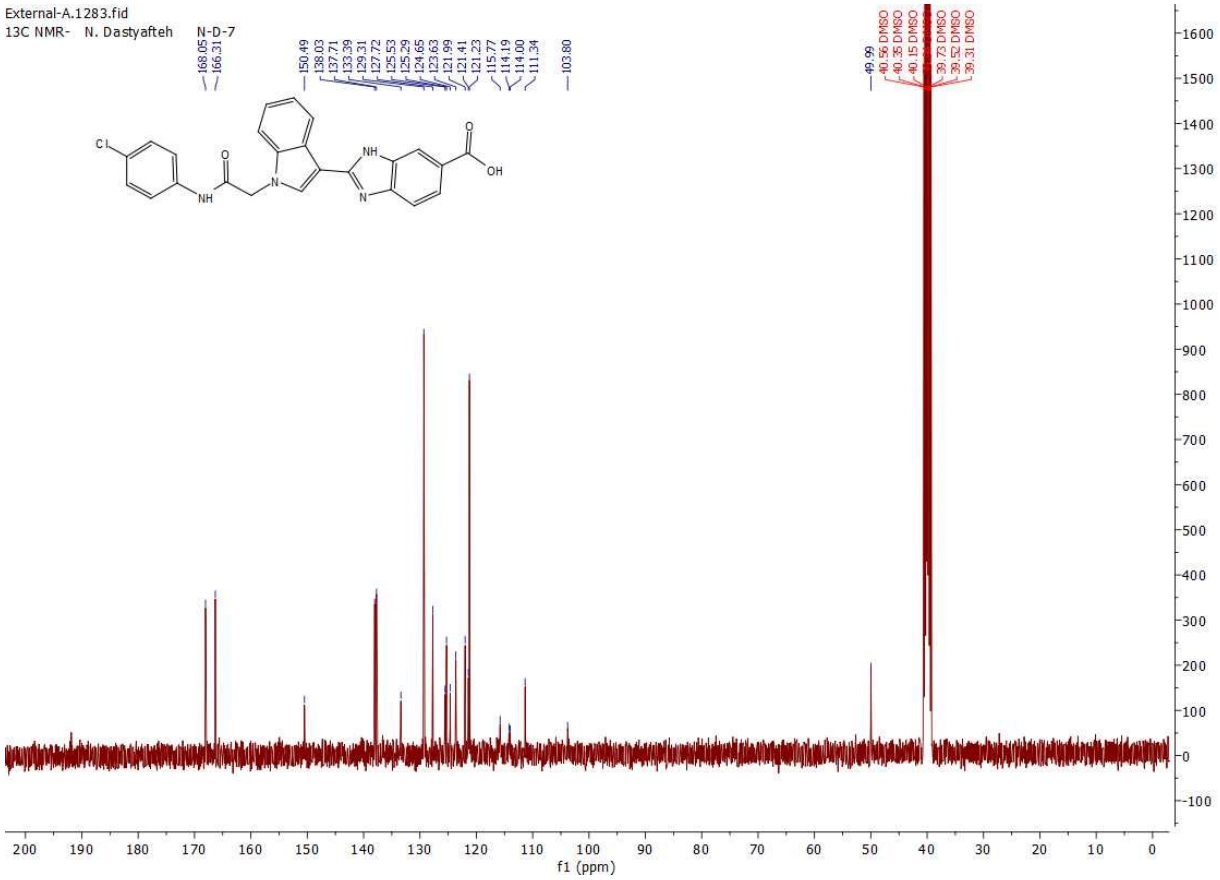


*2-(1-(2-((3-chlorophenyl)amino)-2-oxoethyl)-1H-indol-3-yl)-1H-benzo[d]imidazole-6-carboxylic acid (**8i**)*

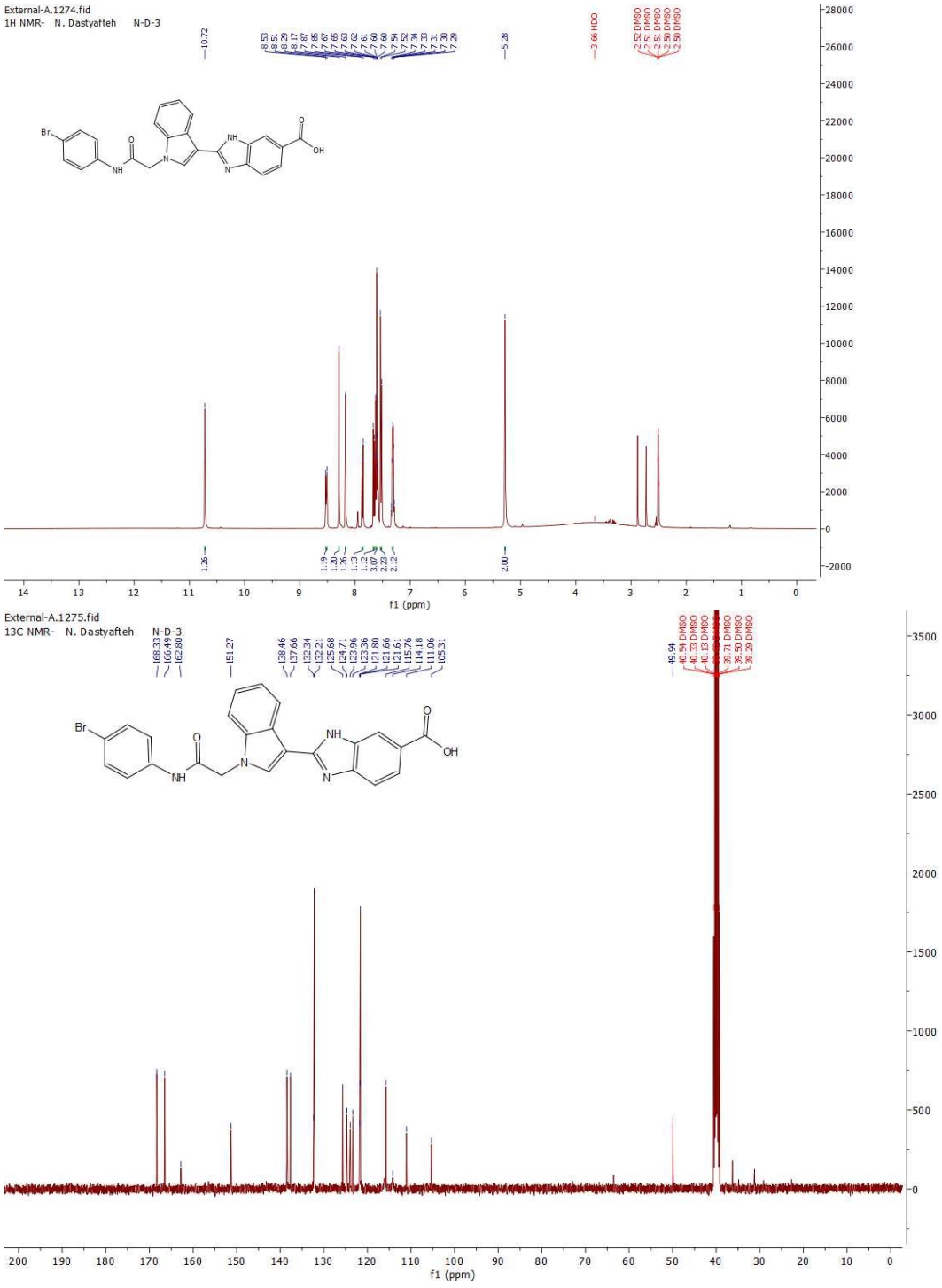



*2-(1-(2-((4-chlorophenyl)amino)-2-oxoethyl)-1H-indol-3-yl)-1H-benzo[d]imidazole-6-carboxylic acid (**8j**)*

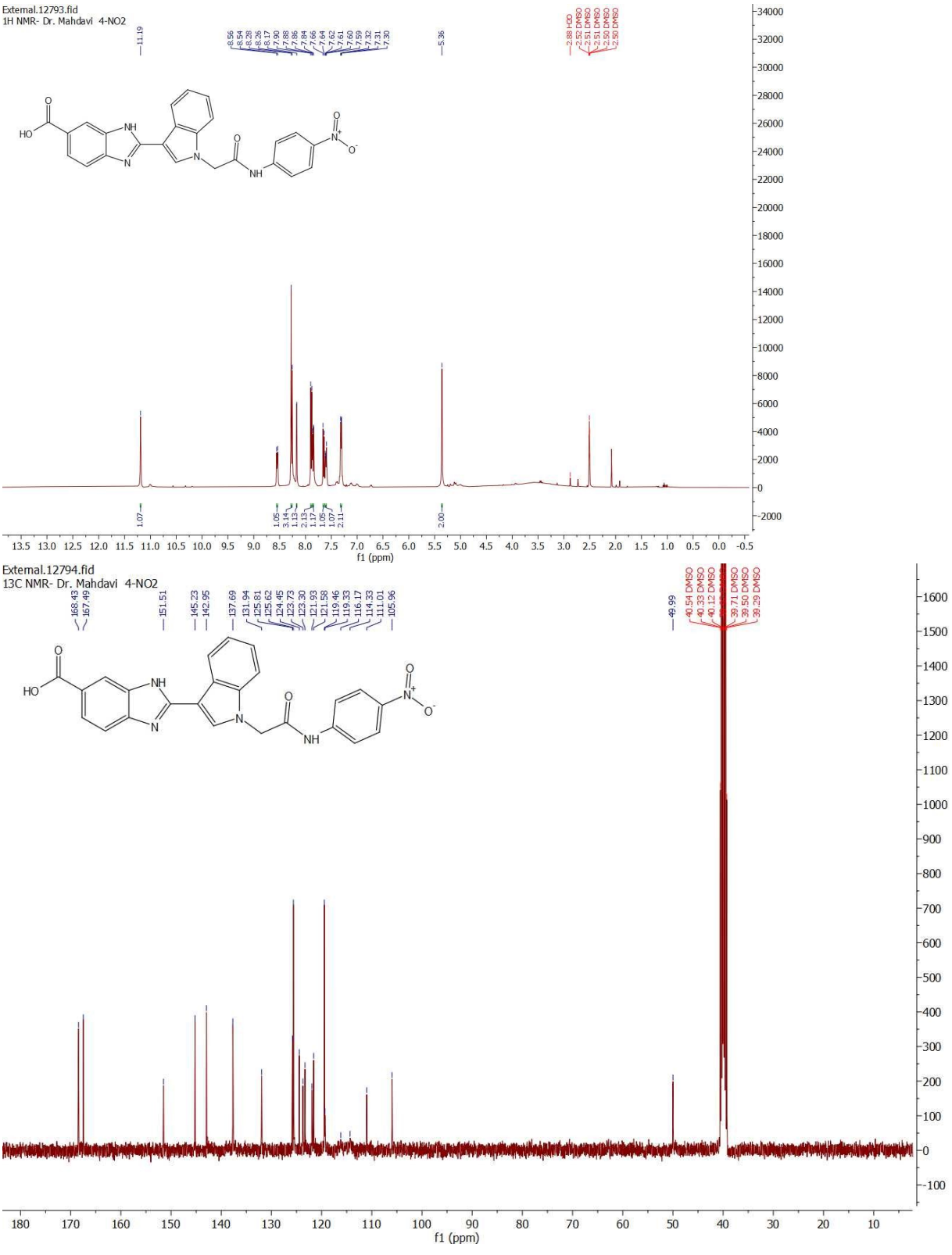


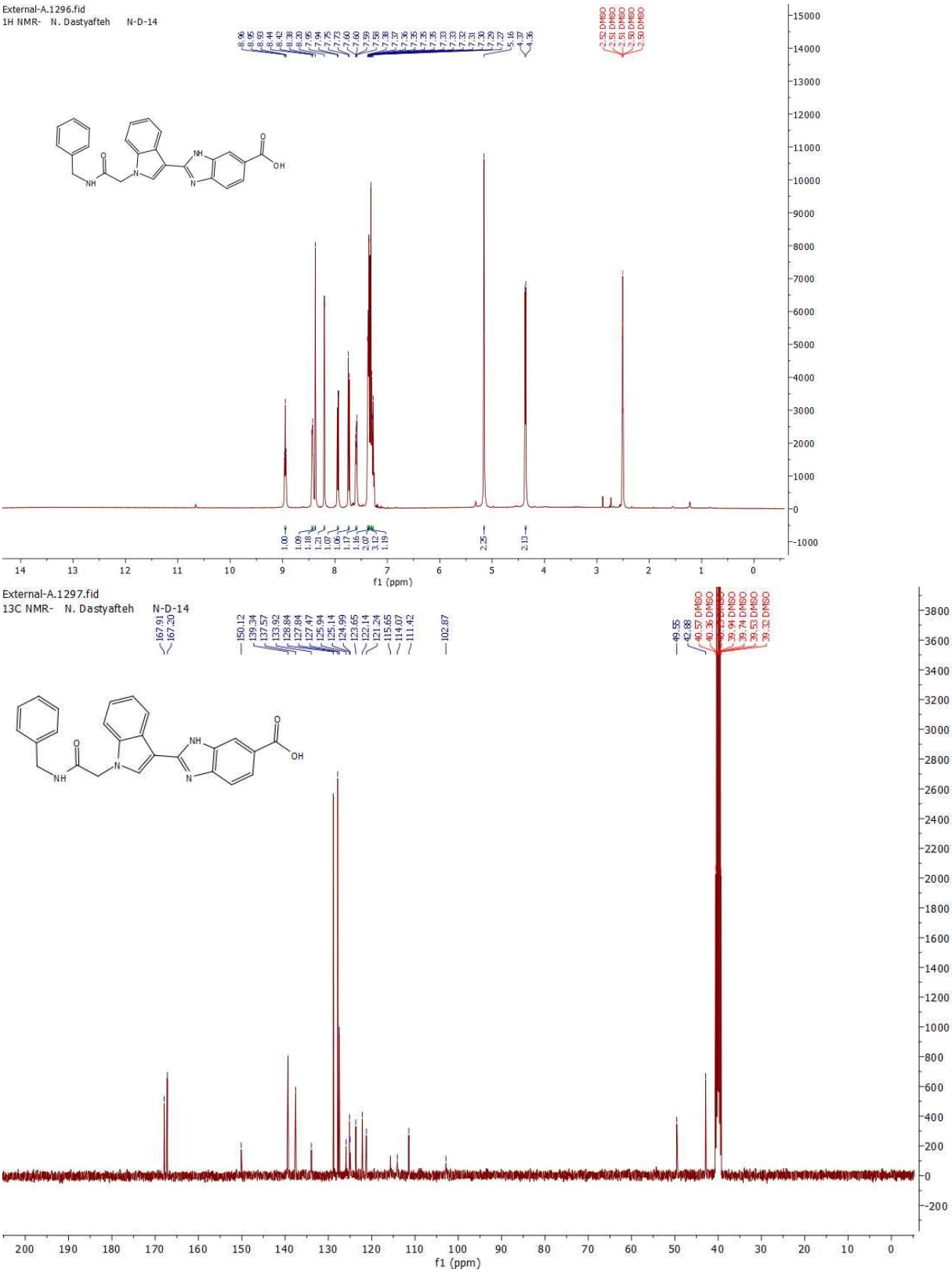

*2-(1-(2-((4-bromophenyl)amino)-2-oxoethyl)-1H-indol-3-yl)-1H-benzo[d]imidazole-6-carboxylic acid (**8k**)*



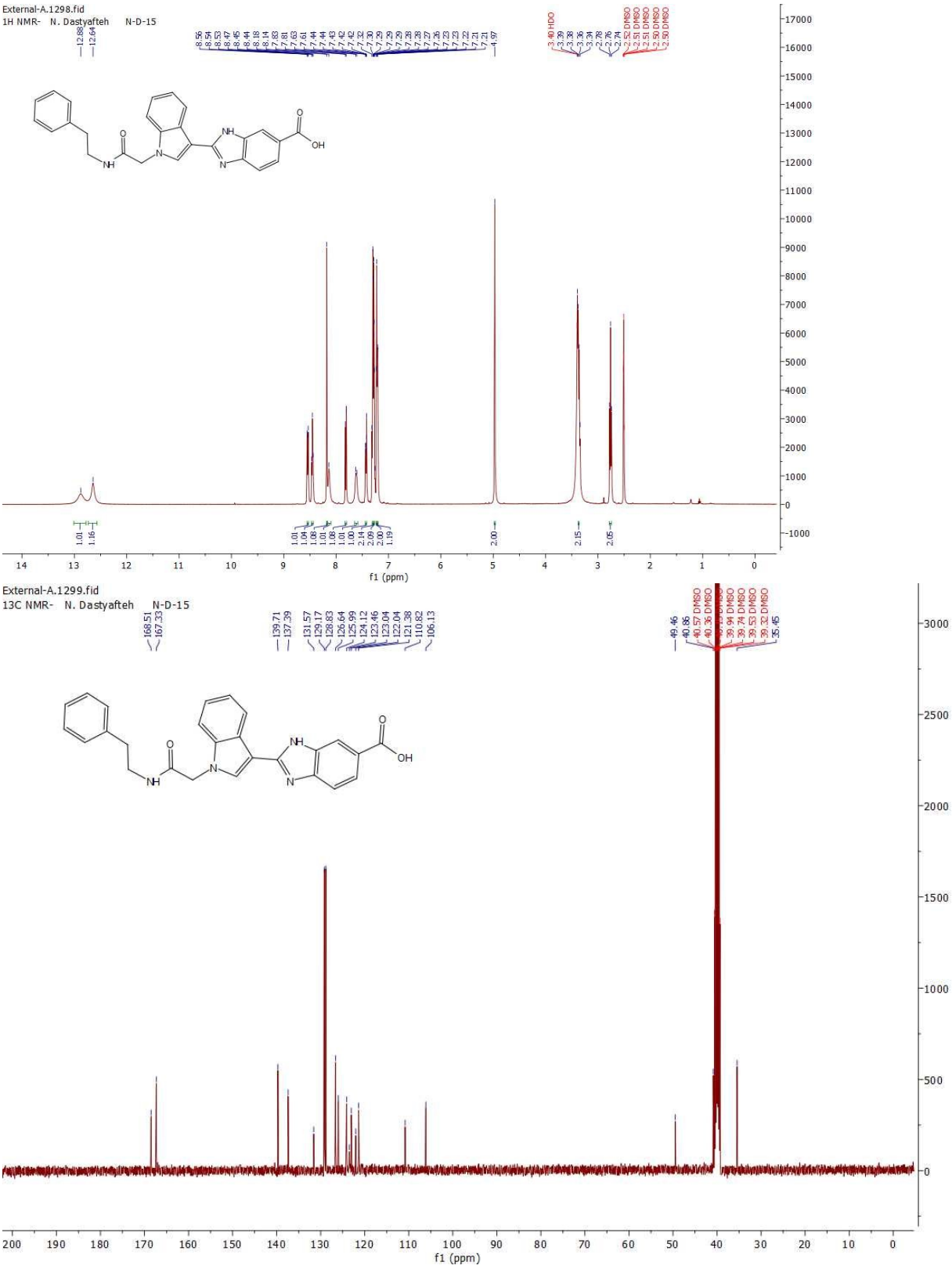

*2-(1-(2-((4-nitrophenyl)amino)-2-oxoethyl)-1H-indol-3-yl)-1H-benzo[d]imidazole-6-carboxylic acid (**8l**)*




*2-(1-(2-(benzylamino)-2-oxoethyl)-1H-indol-3-yl)-1H-benzo[d]imidazole-6-carboxylic acid (**8m**)*

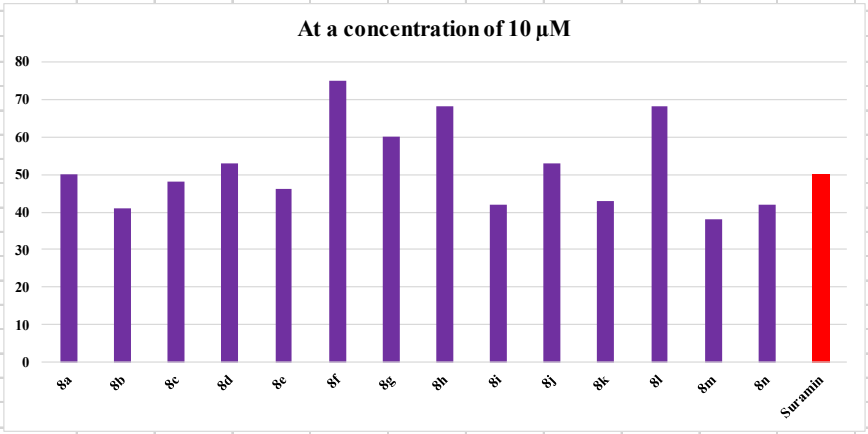



*2-(1-(2-oxo-2-(phenethylamino)ethyl)-1H-indol-3-yl)-1H-benzo[d]imidazole-6-carboxylic acid* ***(8n)***




*%inhibition in anti-PTP1B assay*

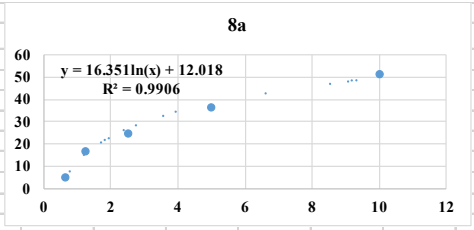
| Compund | In (%) |
|---|---|
| 8a | 50 |
| 8b | 41 |
| 8c | 48 |
| 8d | 53 |
| 8e | 46 |
| 8f | 75 |
| 8g | 60 |
| 8h | 68 |
| 8i | 42 |
| 8j | 53 |
| 8k | 43 |
| 8l | 68 |
| 8m | 38 |
| 8n | 42 |
| Suramin | 50 |




*Determination of $IC_{50}$ values in anti-PTP1B assay*

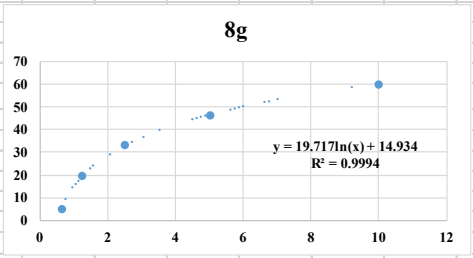
**8a**

| Conc. | OD Blank | OD Total | OD Final | In (%) |
|---|---|---|---|---|
| 10 | 0.02 | 0.31 | 0.29 | 51.66667 |
| 5 | 0.01 | 0.39 | 0.38 | 36.66667 |
| 2.5 | 0.03 | 0.48 | 0.45 | 25 |
| 1.25 | 0.01 | 0.51 | 0.5 | 16.66667 |
| 0.625 | 0.01 | 0.58 | 0.57 | 5 |
| | | | IC50 | 10.20684 |



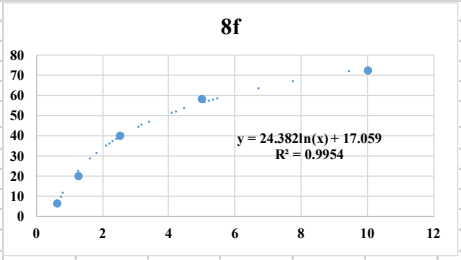

**8g**

| Conc. | OD Blank | OD Total | OD Final | In (%) |
|---|---|---|---|---|
| 10 | 0.03 | 0.27 | 0.24 | 60 |
| 5 | 0.02 | 0.34 | 0.32 | 46.66667 |
| 2.5 | 0.01 | 0.41 | 0.4 | 33.33333 |
| 1.25 | 0.02 | 0.5 | 0.48 | 20 |
| 0.625 | 0.03 | 0.6 | 0.57 | 5 |
| | | | IC50 | 5.921964 |



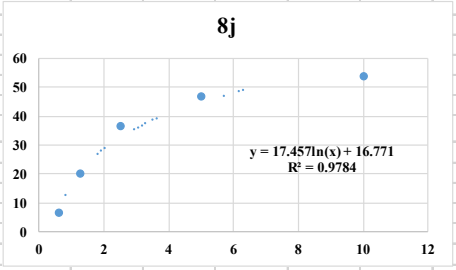

**8f**

| Conc. | OD Blank | OD Total | OD Final | In (%) |
|---|---|---|---|---|
| 10 | 0.04 | 0.208 | 0.168 | 72 |
| 5 | 0.03 | 0.28 | 0.25 | 58.33333 |
| 2.5 | 0.02 | 0.38 | 0.36 | 40 |
| 1.25 | 0.01 | 0.49 | 0.48 | 20 |
| 0.625 | 0.01 | 0.57 | 0.56 | 6.666667 |
| | | | IC50 | 3.86143 |



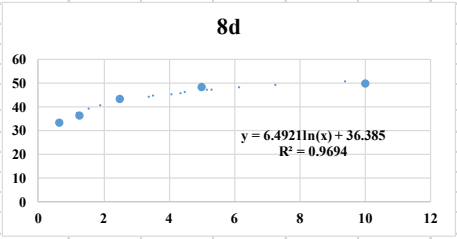

**8j**

| Conc. | OD Blank | OD Total | OD Final | In (%) |
|---|---|---|---|---|
| 10 | 0.1 | 0.377 | 0.277 | 53.83333 |
| 5 | 0.08 | 0.4 | 0.32 | 46.66667 |
| 2.5 | 0.07 | 0.45 | 0.38 | 36.66667 |
| 1.25 | 0.06 | 0.54 | 0.48 | 20 |
| 0.625 | 0.05 | 0.61 | 0.56 | 6.666667 |
| | | | IC50 | 6.709183 |



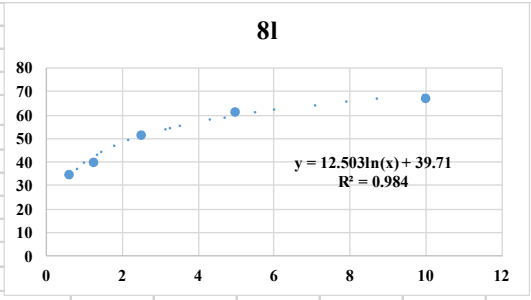

**8d**

| Conc. | OD Blank | OD Total | OD Final | In (%) |
|---|---|---|---|---|
| 10 | 0.09 | 0.39 | 0.3 | 50 |
| 5 | 0.06 | 0.37 | 0.31 | 48.33333 |
| 2.5 | 0.03 | 0.37 | 0.34 | 43.33333 |
| 1.25 | 0.01 | 0.39 | 0.38 | 36.66667 |
| 0.625 | 0.01 | 0.41 | 0.4 | 33.33333 |
| | | | IC50 | 8.148573 |



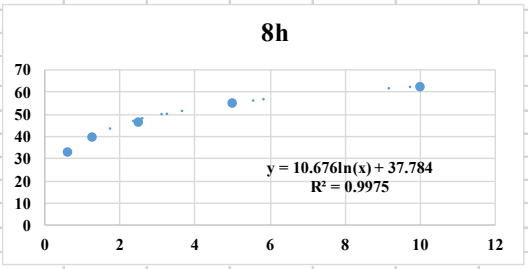
**8l**

| Conc. | OD Blank | OD Total | OD Final | In (%) |
|---|---|---|---|---|
| 10 | 0.05 | 0.245 | 0.195 | 67.5 |
| 5 | 0.03 | 0.26 | 0.23 | 61.66667 |
| 2.5 | 0.02 | 0.31 | 0.29 | 51.66667 |
| 1.25 | 0.02 | 0.38 | 0.36 | 40 |
| 0.625 | 0.01 | 0.4 | 0.39 | 35 |
| | | | IC50 | 2.277327 |



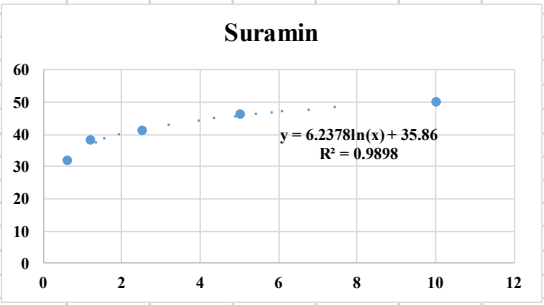

**8h**

| Conc. | OD Blank | OD Total | OD Final | In (%) |
|---|---|---|---|---|
| 10 | 0.08 | 0.303 | 0.223 | 62.83333 |
| 5 | 0.07 | 0.34 | 0.27 | 55 |
| 2.5 | 0.06 | 0.38 | 0.32 | 46.66667 |
| 1.25 | 0.06 | 0.42 | 0.36 | 40 |
| 0.625 | 0.05 | 0.45 | 0.4 | 33.33333 |
| | | | IC50 | 3.140082 |



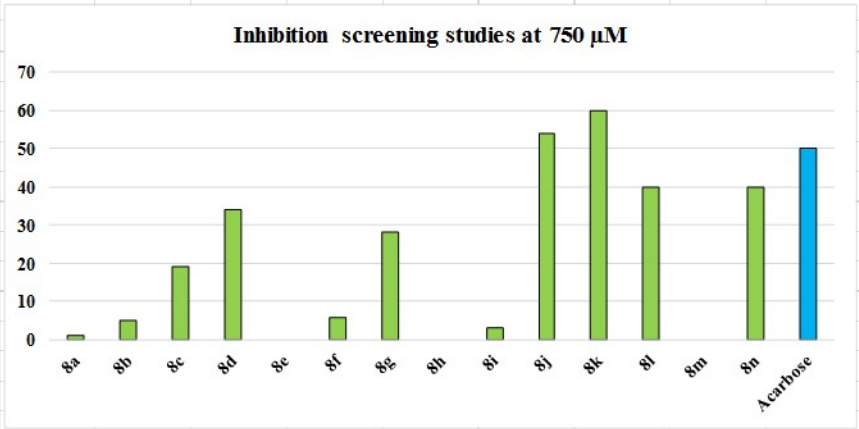

**Suramin**

| Conc. | OD Blank | OD total | OD Final | In (%) |
|---|---|---|---|---|
| 10 | 0.094 | 0.384 | 0.29 | 49.82699 |
| 5 | 0.063 | 0.373 | 0.31 | 46.36678 |
| 2.5 | 0.091 | 0.431 | 0.34 | 41.17647 |
| 1.2 | 0.066 | 0.516 | 0.45 | 38 |
| 0.6 | 0.057 | 0.657 | 0.6 | 32 |
| | | | IC50 | 10.0074 |



*%inhibition in anti-α-glucosidase assay*

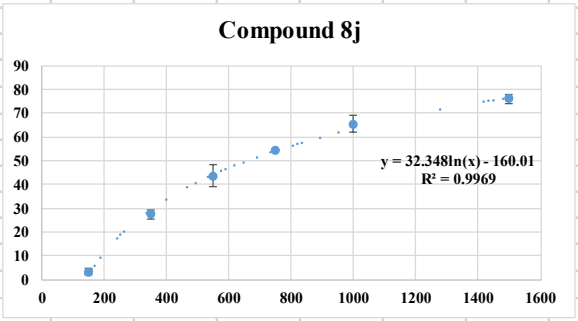
| Compound | Inhibition (%) |
|---|---|
| 8a | 1 |
| 8b | 5 |
| 8c | 19 |
| 8d | 34 |
| 8e | 0 |
| 8f | 6 |
| 8g | 28 |
| 8h | 0 |
| 8i | 3 |
| 8j | 54 |
| 8k | 60 |
| 8l | 40 |
| 8m | 0 |
| 8n | 40 |
| Acarbose | 50 |



*Determination of $IC_{50}$ values in anti-α-glucosidase assay*

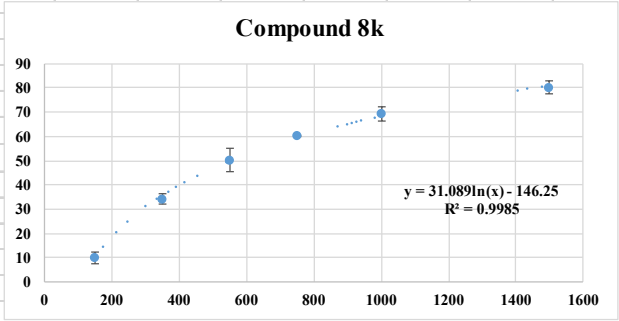
Inhibition activity (%)

| [Compound 8j] ( | Repetition I | Repetition I | Repetition I | Mean | SE |
|---|---|---|---|---|---|
| 1500 | 76 | 74 | 78 | 76 | 2 |
| 1000 | 65 | 69 | 62 | 65.33333 | 3.511885 |
| 750 | 54.4 | 54.6 | 54.3 | 54.43333 | 0.152753 |
| 550 | 39 | 43.4 | 48.7 | 43.7 | 4.856954 |
| 350 | 25.5 | 27.7 | 29.3 | 27.5 | 1.907878 |
| 150 | 2.1 | 3.4 | 4.6 | 3.366667 | 1.250333 |
| | | | IC50 | 659.9801 | 1.269635 |




Inhibition activity (%)

| [Compound 8k] ( | Repetition I | Repetition I | Repetition I | Mean | SE |
|---|---|---|---|---|---|
| 1500 | 78.2 | 79.2 | 83.4 | 80.26667 | 2.759227 |
| 1000 | 72.5 | 69.3 | 66.2 | 69.33333 | 3.150132 |
| 750 | 60.6 | 60.3 | 60 | 60.3 | 0.3 |
| 550 | 54 | 52 | 45 | 50.33333 | 4.725816 |
| 350 | 36.1 | 31.9 | 34.7 | 34.23333 | 2.138535 |
| 150 | 10 | 7.5 | 12.5 | 10 | 2.5 |
| | | | IC50 | 551.434 | 0.94944 |




Inhibition activity (%)

| [Acarbose] (μ | Repetition I | Repetition I | Repetition I | Mean | SE |
|---|---|---|---|---|---|
| 1000 | 54 | 55.1 | 56 | 55.03333 | 1.001665 |
| 750 | 50.2 | 49.78 | 50 | 49.99333 | 0.210079 |
| 550 | 46.1 | 44.3 | 43.2 | 44.53333 | 1.464013 |
| 350 | 32.5 | 38 | 39.1 | 36.53333 | 3.536005 |
| 150 | 23.1 | 20.3 | 21.6 | 21.66667 | 1.40119 |
| 75 | 9.6 | 10.9 | 8 | 9.5 | 1.452584 |
| | | | IC50 | 750.2861 | 0.675028 |