

## Supplementary Information

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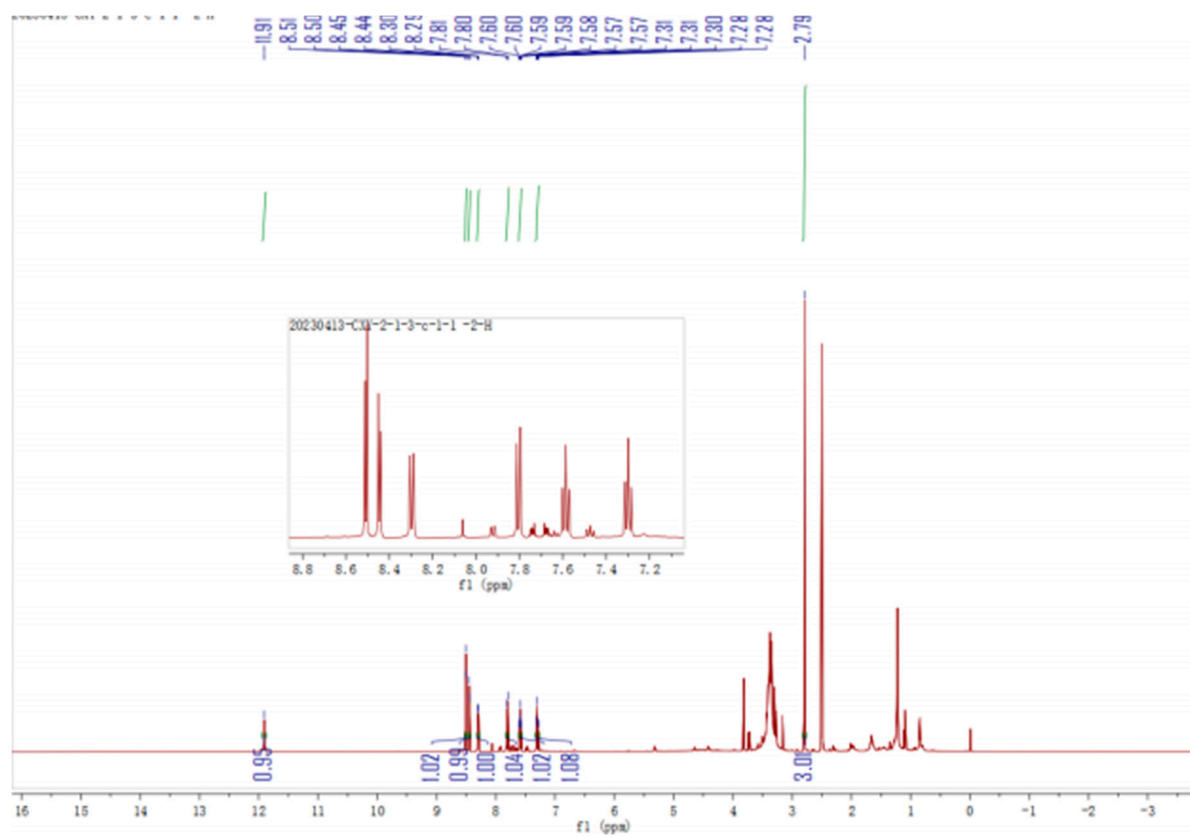


**Figure S1.** The  $^1\text{H}$ -NMR spectrum of compound 1

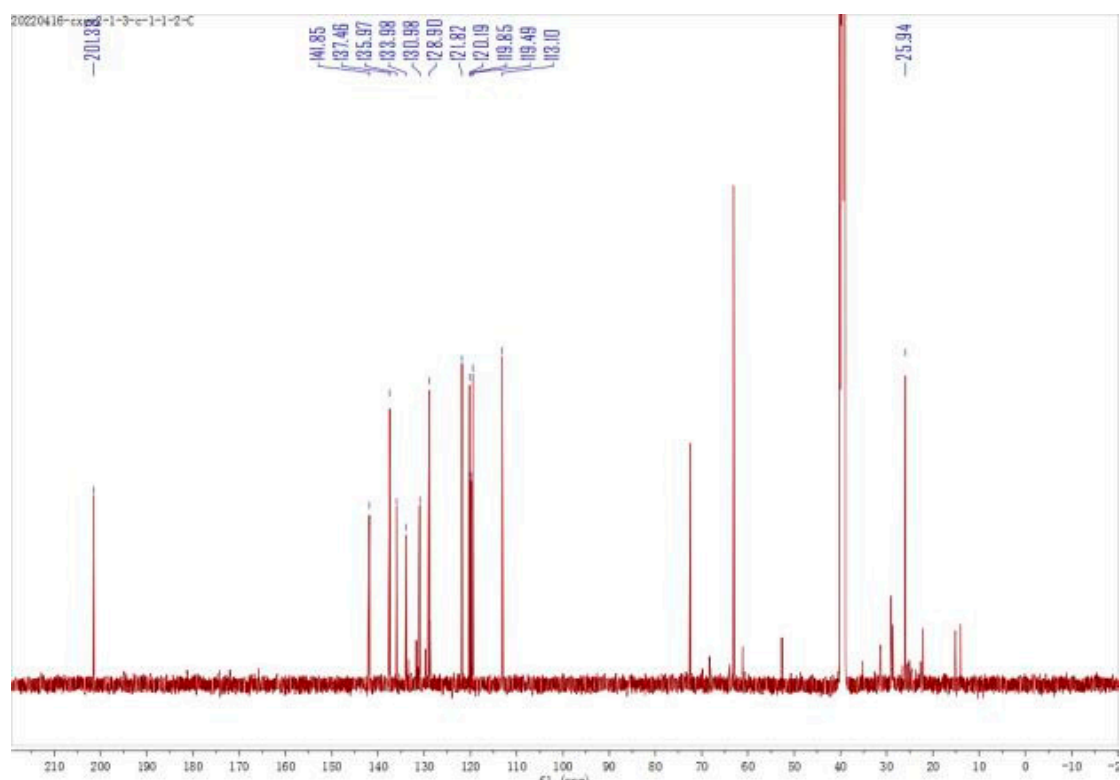


**Figure S2.** The  $^{13}\text{C}$ -NMR spectrum of compound 1

### ESI-MS Spectrum of compound 1

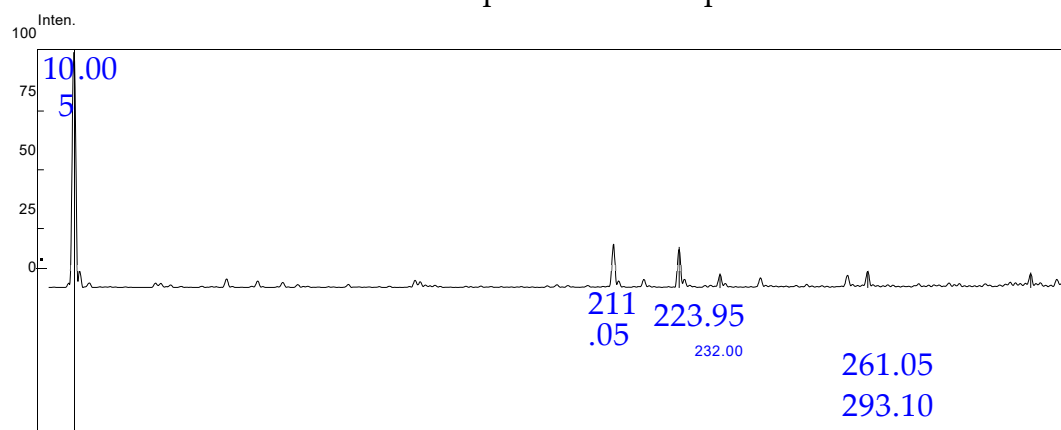


**Figure S3.** ESI-MS Spectrum of compound 1

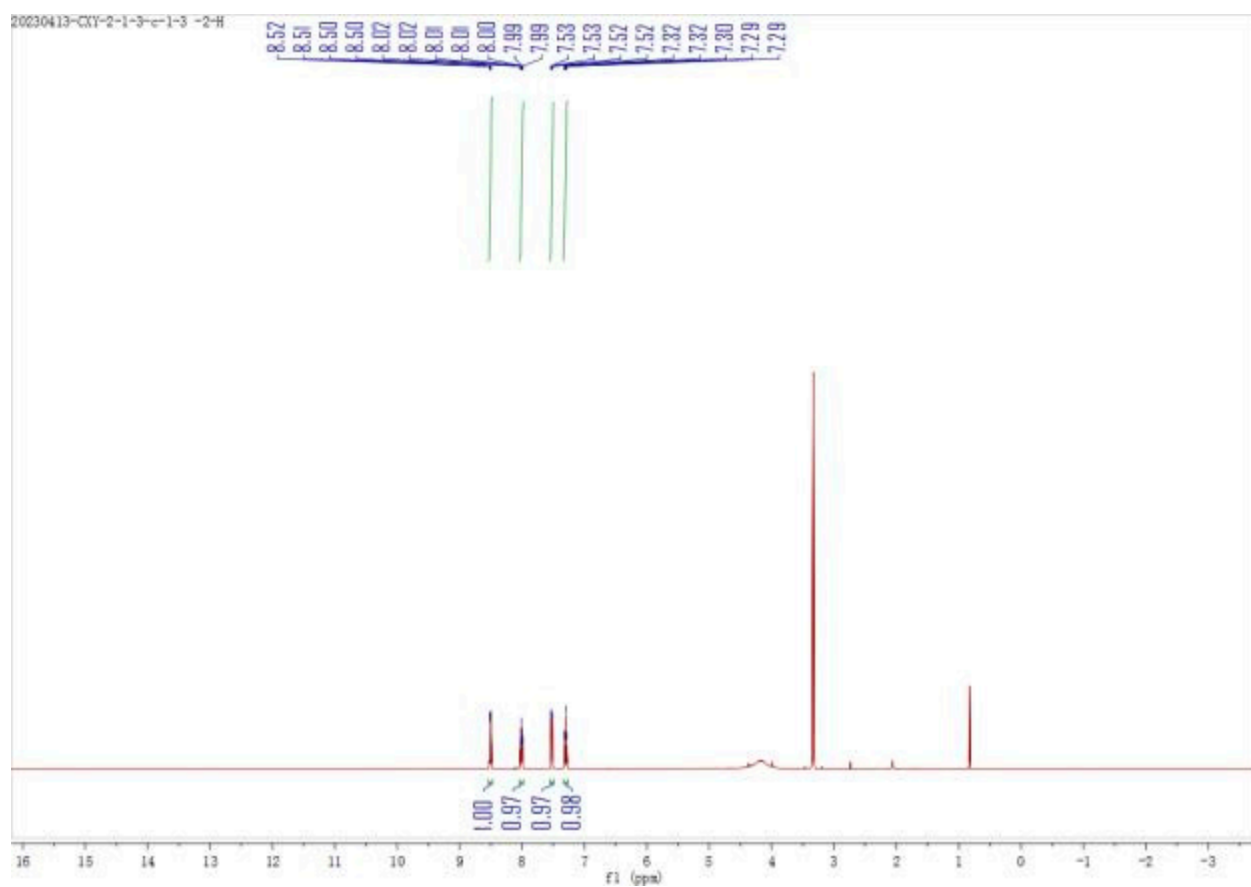


**Figure S4.** The  $^1\text{H}$ -NMR spectrum of compound 2

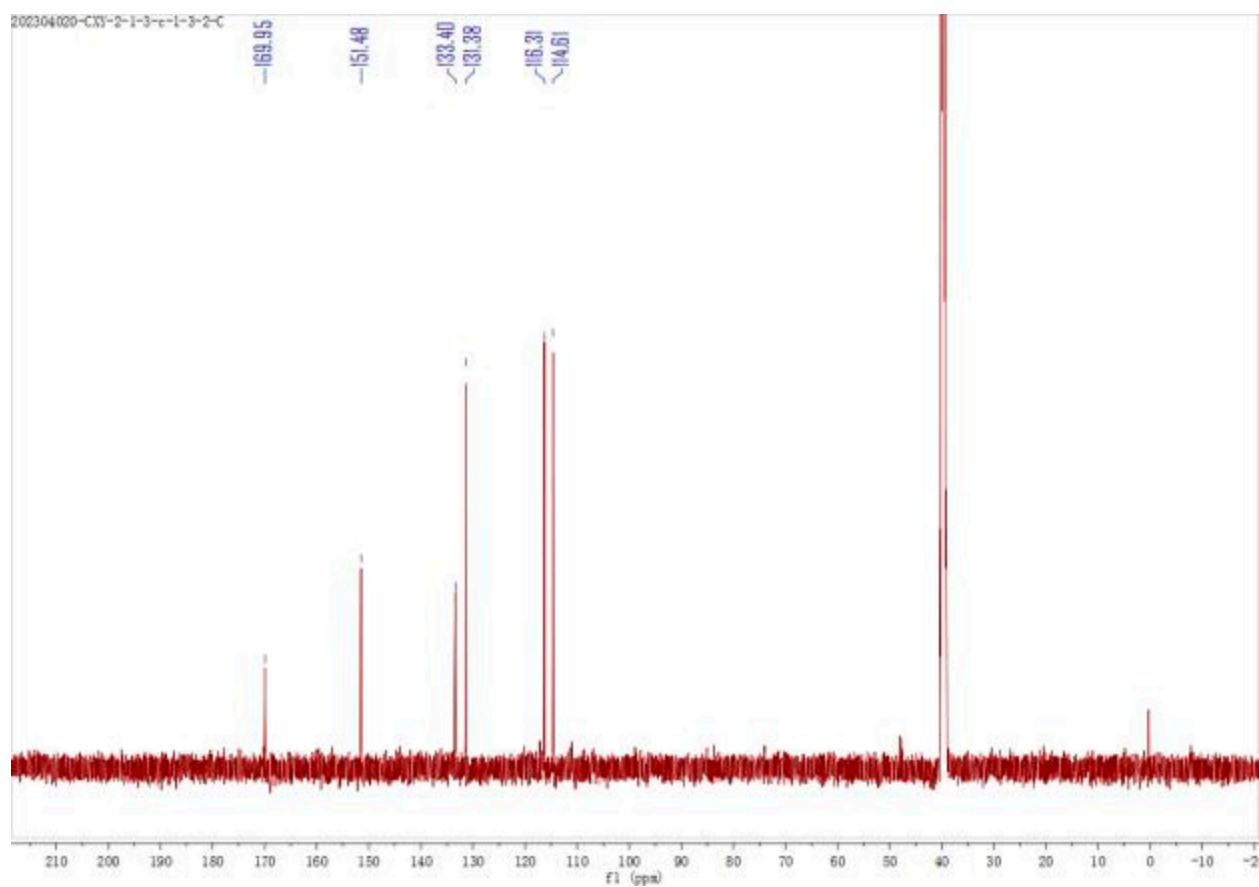


**Figure S5.** The  $^{13}\text{C}$ -NMR spectrum of compound 2

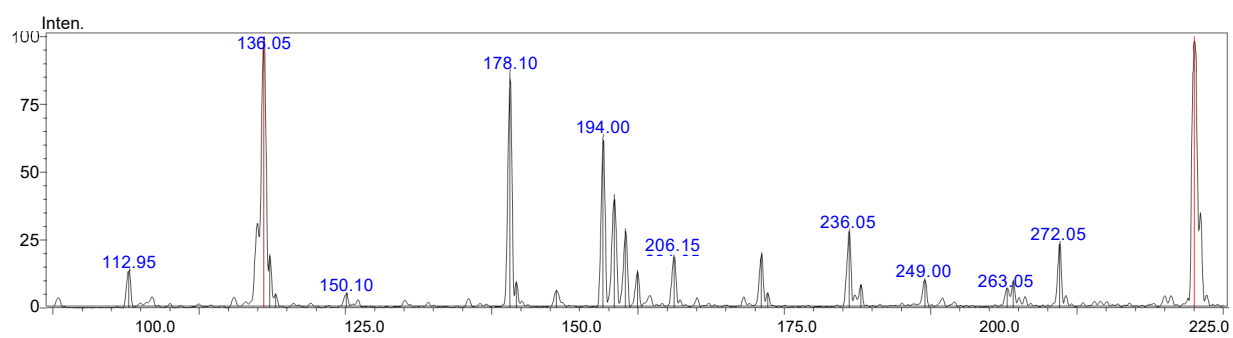


**Figure S6.** ESI-MS Spectrum of compound 2

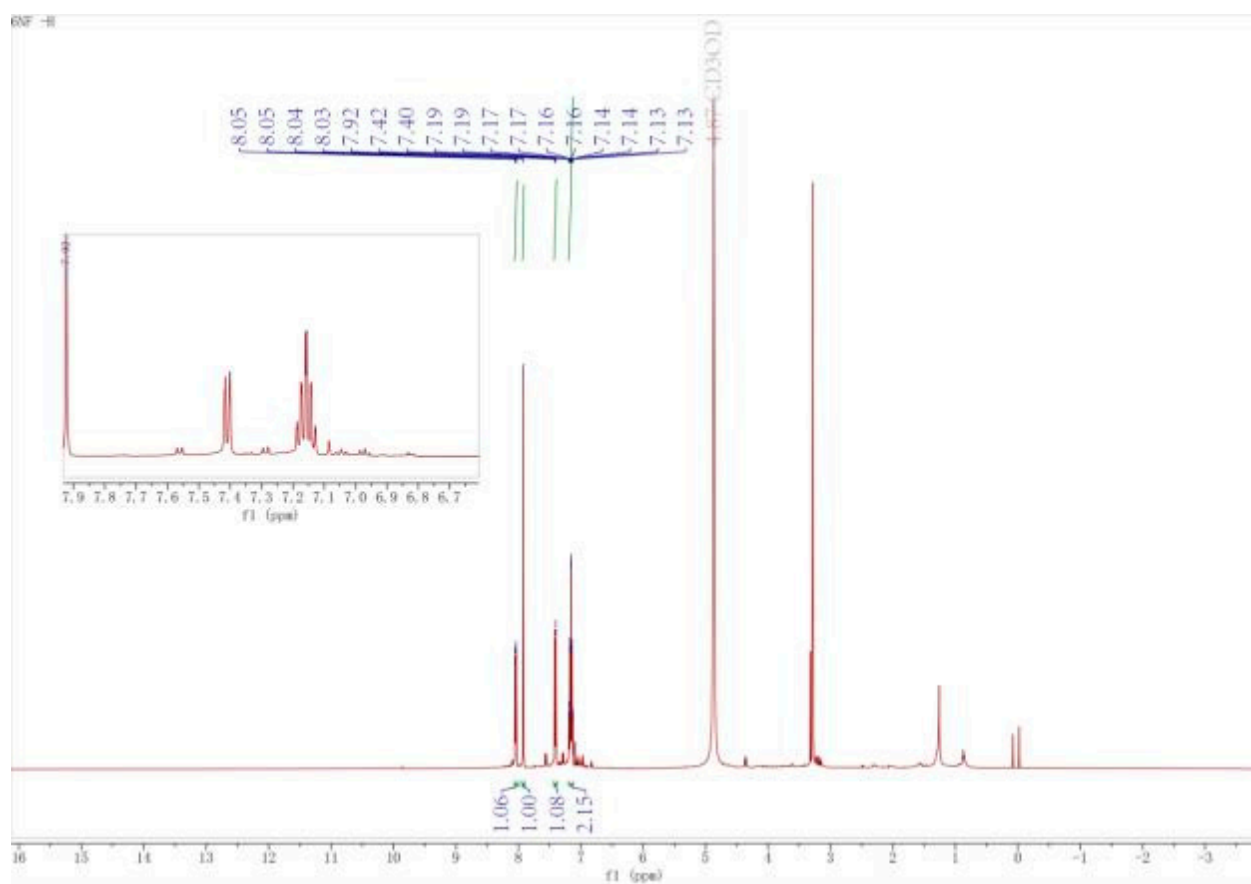


**Figure S7.** The  $^1\text{H}$ -NMR spectrum of compound 3

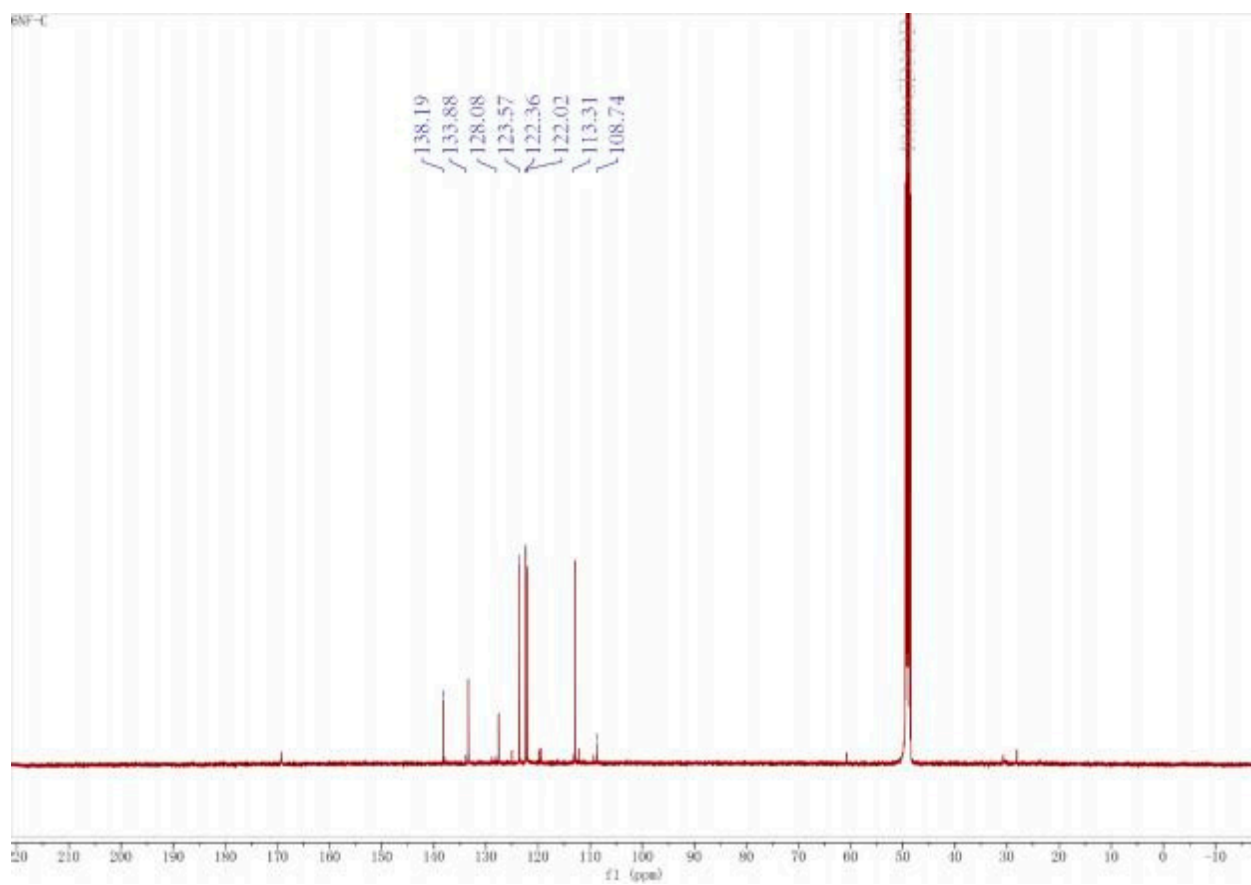


**Figure S8.** The <sup>13</sup>C-NMR spectrum of compound 3

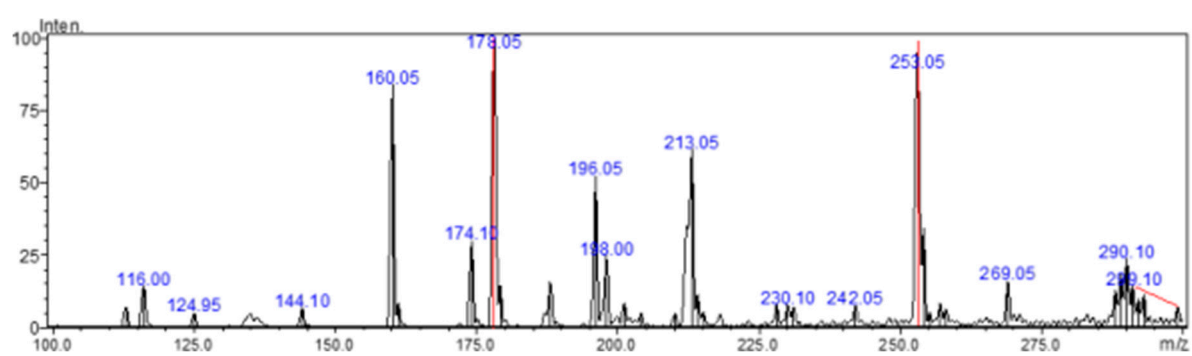


**Figure S9.** LCMS Spectrum of compound 3

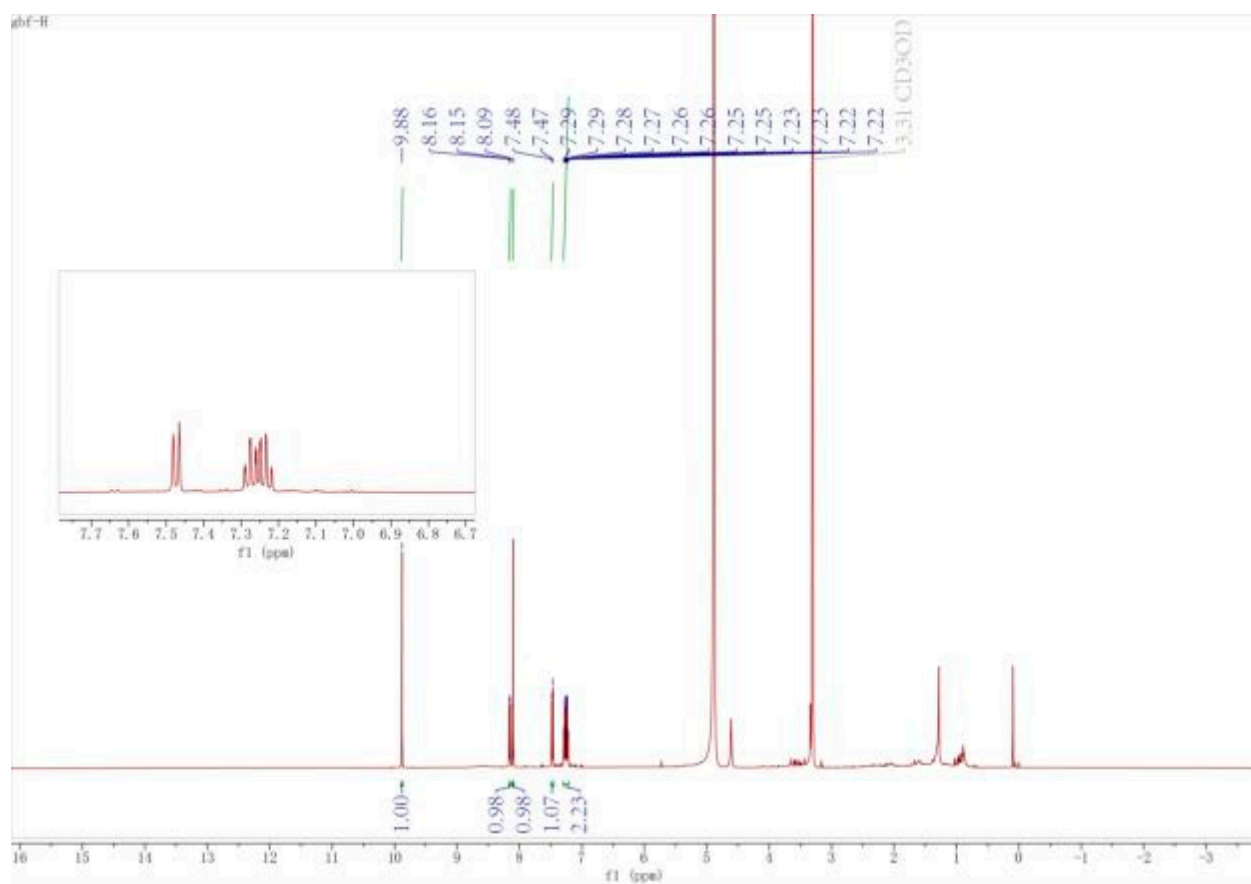


**Figure S10.** The <sup>1</sup>H -NMR spectrum of compound 4

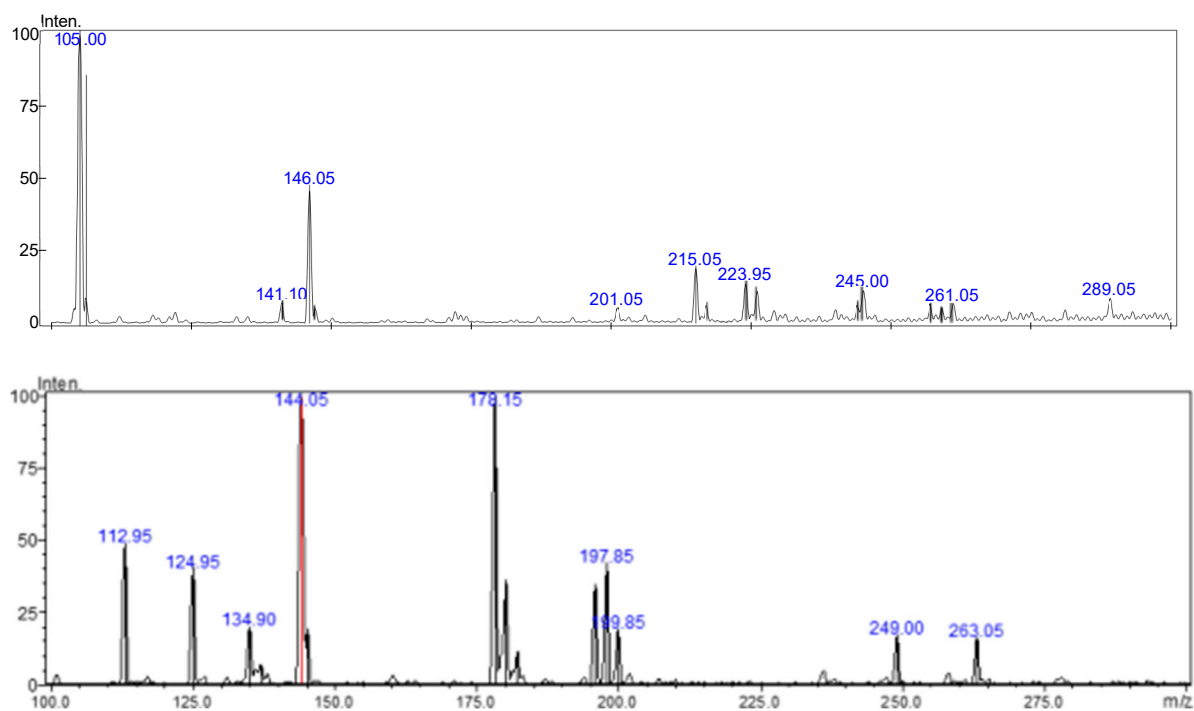
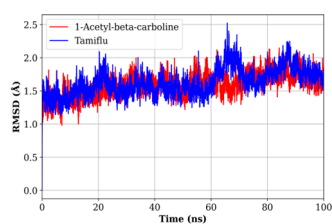
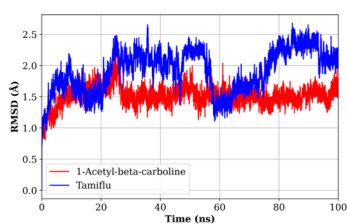


**Figure S11.** LCMS Spectrum of compound 4

A



B



C

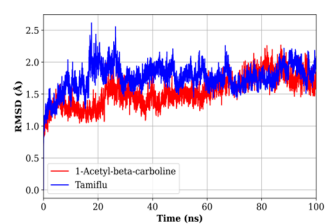


**Figure S12.** RMSD values for PARP1 (A), CDC25B (B), and PTGS2 (C) complex with 1-acetyl-beta-carboline and Tamiflu as the test and reference ligands respectively.

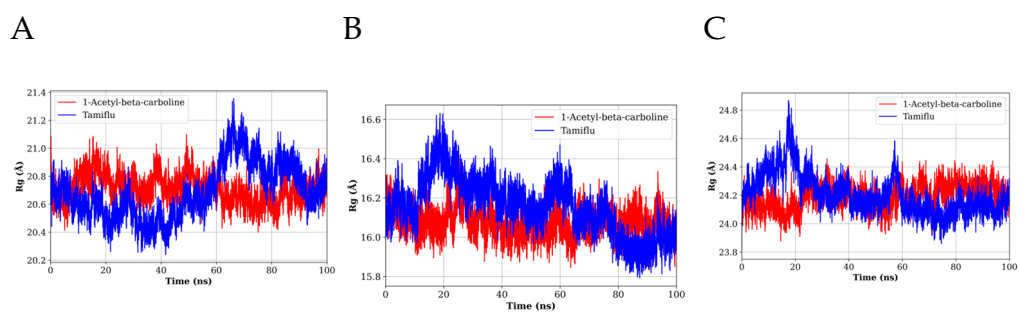
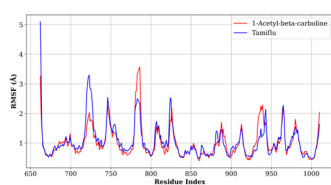
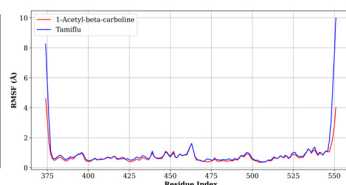


**Figure S13.** Radius of gyration for PARP1 (A), CDC25B (B), and PTGS2 (C) complex with 1-acetyl-beta-carboline and Tamiflu as the test and reference ligands respectively.

A



B



C

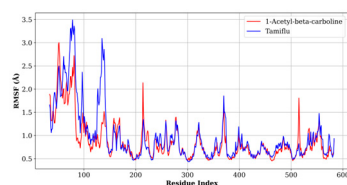


**Figure S14.** Backbone RMSF for PARP1 (A), CDC25B (B), and PTGS2 (C) complex with 1-acetyl-beta-carboline and Tamiflu as the test and reference ligands respectively.

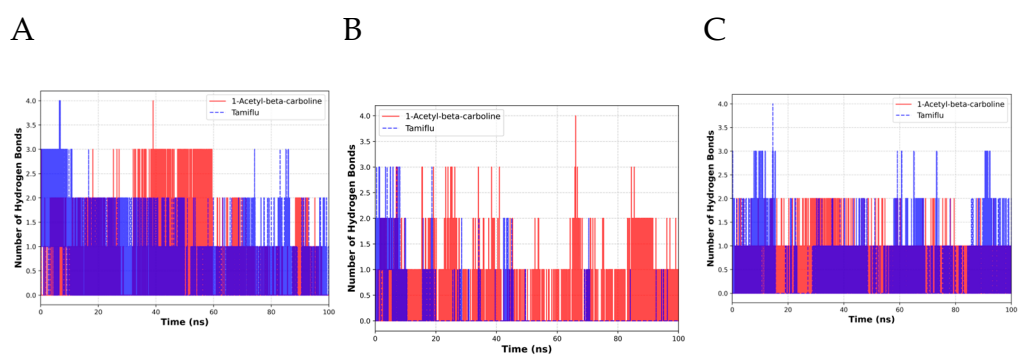


**Figure S15.** Total number of hydrogen bonds for PARP1 (A), CDC25B (B), and PTGS2 (C) complex with 1-acetyl-beta-carboline and Tamiflu as the test and reference ligands respectively.

**Table S1.** Summary statistics of the drug and reference molecular dynamics.

| RMSD                          |                             |                         |                             |                         |            |           |            |           |              |
|-------------------------------|-----------------------------|-------------------------|-----------------------------|-------------------------|------------|-----------|------------|-----------|--------------|
|                               |                             |                         |                             |                         | Reference  |           | Drug       |           |              |
| Cliff's<br>Delta <sup>5</sup> | MW p-<br>value <sup>4</sup> | MW<br>Stat <sup>3</sup> | KS p-<br>value <sup>2</sup> | KS<br>Stat <sup>1</sup> | Medi<br>an | Me<br>an  | Med<br>ian | Me<br>an  | Rece<br>ptor |
| -0.09                         | 0                           | 4572809<br>6.5          | 0                           | 0.09                    | 1.61       | 1.63      | 1.59       | 1.59      | PARP<br>1    |
| -0.68                         | 0                           | 1597184<br>5.5          | 0                           | 0.62                    | 1.98       | 1.92      | 1.52       | 1.52      | CDC2<br>5B   |
| -0.55                         | 0                           | 2262238<br>9            | 0                           | 0.45                    | 1.77       | 1.76      | 1.53       | 1.54      | PTGS<br>2    |
| Radius of gyration            |                             |                         |                             |                         |            |           |            |           |              |
|                               |                             |                         |                             |                         | Reference  |           | Drug       |           |              |
| Cliff's<br>Delta <sup>5</sup> | MW p-<br>value <sup>4</sup> | MW<br>Stat <sup>3</sup> | KS p-<br>value <sup>2</sup> | KS<br>Stat <sup>1</sup> | Medi<br>an | Me<br>an  | Med<br>ian | Me<br>an  | Rece<br>ptor |
| 0.14                          | 0                           | 5706549<br>7.5          | 0                           | 0.23                    | 20.66      | 20.6<br>9 | 20.71      | 20.7<br>1 | PARP<br>1    |
| -0.36                         | 0                           | 3181529<br>1            | 0                           | 0.36                    | 16.16      | 16.1<br>5 | 16.07      | 16.0<br>8 | CDC2<br>5B   |

|   |     |         |   |      |       |      |      |      |      |
|---|-----|---------|---|------|-------|------|------|------|------|
| 0 | 0.6 | 5022497 | 0 | 0.14 | 24.18 | 24.2 | 24.2 | 24.1 | PTGS |
|   |     | 1.5     |   |      |       | 1    |      | 9    | 2    |

RMSF

|                    |                    |                   |                    |                   | Reference |      | Drug |      |      |
|--------------------|--------------------|-------------------|--------------------|-------------------|-----------|------|------|------|------|
| Cliff's            | MW p-              | MW                | KS p-              | KS                | Medi      | Me   | Med  | Me   | Rece |
| Delta <sup>5</sup> | value <sup>4</sup> | Stat <sup>3</sup> | value <sup>2</sup> | Stat <sup>1</sup> | an        | an   | ian  | an   | ptor |
| -0.06              | 0.21               | 56874             | 0.24               | 0.08              | 0.9       | 1.05 | 0.87 | 1.01 | PARP |
|                    |                    |                   |                    |                   |           |      |      |      | 1    |
| -0.14              | 0.02               | 13628             | 0.02               | 0.16              | 0.68      | 0.94 | 0.64 | 0.76 | CDC2 |
|                    |                    |                   |                    |                   |           |      |      |      | 5B   |
| -0.09              | 0.01               | 138562.           | 0.06               | 0.08              | 0.77      | 0.98 | 0.73 | 0.88 | PTGS |
|                    |                    | 5                 |                    |                   |           |      |      |      | 2    |

Total number of hydrogen bonds

|                    |                    |                   |                    |                   | Reference |      | Drug |      |      |
|--------------------|--------------------|-------------------|--------------------|-------------------|-----------|------|------|------|------|
| Cliff's            | MW p-              | MW                | KS p-              | KS                | Medi      | Me   | Med  | Me   | Rece |
| Delta <sup>5</sup> | value <sup>4</sup> | Stat <sup>3</sup> | value <sup>2</sup> | Stat <sup>1</sup> | an        | an   | ian  | an   | ptor |
| 0                  | 0.31               | 1245849           | 0                  | 0.03              | 0         | 0.63 | 0    | 0.6  | PARP |
|                    |                    | 588               |                    |                   |           |      |      |      | 1    |
| 0.16               | 0                  | 1455447           | 0                  | 0.18              | 0         | 0.2  | 0    | 0.34 | CDC2 |
|                    |                    | 500               |                    |                   |           |      |      |      | 5B   |

|      |   |         |   |      |   |     |   |      |      |
|------|---|---------|---|------|---|-----|---|------|------|
|      |   | 1426471 |   |      |   |     |   |      | PTGS |
| 0.14 | 0 |         | 0 | 0.17 | 0 | 0.5 | 1 | 0.62 |      |
|      |   | 059     |   |      |   |     |   |      | 2    |

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<sup>1</sup>Kolmogorov-Smirnov statistic, <sup>2</sup>Kolmogorov-Smirnov p-value,  $p < 0.05$  indicates significant difference in the distributions, <sup>3</sup>Mann-Whitney U test statistic, <sup>4</sup>Mann-Whitney U test p-value,  $p < 0.05$  indicates significant difference in the medians, <sup>5</sup>Cliff's delta, positive values indicate reference values are higher than the drug values.

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**Table S2.** SwissADME results relevant to absorption.

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| <b>log Kp</b> | <b>Pgp</b>       | <b>BBB</b>      | <b>GI</b>         | <b>Molecule</b>                           |
|---------------|------------------|-----------------|-------------------|-------------------------------------------|
| <b>(cm/s)</b> | <b>substrate</b> | <b>permeant</b> | <b>absorption</b> |                                           |
| -5.93         | No               | Yes             | High              | 1-acetyl- $\beta$ -carboline<br>(1)       |
| -5.82         | No               | Yes             | High              | 1 <i>H</i> -indole-3-<br>carbaldehyde (2) |
| -6.28         | No               | Yes             | High              | Anthranilic acid (3)                      |
| -5.87         | No               | Yes             | High              | Indole-3-carboxylic<br>acid (4)           |
| -11.13        | Yes              | No              | Low               | Tamiflu                                   |

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**Table S3.** Inhibitory potential to important metabolic enzymes.

| CYP3A4 | CYP2D6 | CYP2C9 | CYP2C1<br>9 | CYP1A2 | Molecule                                  |
|--------|--------|--------|-------------|--------|-------------------------------------------|
| Yes    | No     | No     | No          | Yes    | 1-acetyl- $\beta$ -carboline<br>(1)       |
| No     | No     | No     | No          | Yes    | 1 <i>H</i> -indole-3-<br>carbaldehyde (2) |
| No     | No     | No     | No          | No     | Anthranilic acid (3)                      |
| No     | No     | No     | No          | Yes    | Indole-3-carboxylic<br>acid (4)           |
| No     | No     | No     | No          | No     | Tamiflu                                   |

**Table S4.** Druglikeness evaluation of potential drug compounds and Tamiflu.

| Alerts        |       |        |                  | Violations |        |         |         |             | Molecule                              |
|---------------|-------|--------|------------------|------------|--------|---------|---------|-------------|---------------------------------------|
| Leadlikene ss | Brenk | PAIN S | BAS <sup>1</sup> | Muegge e   | Egan n | Veber r | Ghose e | Lipinski ki |                                       |
| 1             | 0     | 0      | 0.55             | 0          | 0      | 0       | 0       | 0           | 1-acetyl-β-carboline (1)              |
| 1             | 1     | 0      | 0.55             | 1          | 0      | 0       | 2       | 0           | 1 <i>H</i> -indole-3-carbaldehyde (2) |
| 1             | 1     | 0      | 0.85             | 1          | 0      | 0       | 3       | 0           | Anthranilic acid (3)                  |
| 1             | 0     | 0      | 0.85             | 1          | 0      | 0       | 1       | 0           | Indole-3-carboxylic acid (4)          |
| 2             | 1     | 0      | 0.55             | 2          | 1      | 1       | 0       | 0           | Tamiflu                               |

<sup>1</sup>Bioavailability score