SUPPORTING INFORMATION

Design, synthesis, antifungal activity, and QM/MM docking study of two azole derivatives with indole ring

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Contents:

1. Chemistry

1.1. Synthesis of the starting materials

*2-Bromo-1-(2-naphthyl)ethanone (**1b**)*: To a solution of **1** (50 mmol) in acetic acid three drops of bromic acid was added, then 50 mmol bromine solution in 2.5 ml acetic acid was added dropwise by vigorously stirring at 0-5 °C. The reaction mixture was warmed to room temperature and allowed to stir for 2 h then poured into ice water. The precipitate was filtered, washed with sodium bicarbonate solution, dried in dark, and crystallized from methanol/water (Yellow powder, 87% yield, mp: 81-2 °C (methanol/water)).

*1-(4-Chlorophenyl)-2-(1H-imidazol-1-yl)ethanone (**2a**) and 2-(1H-imidazol-1-yl)-1-(2-naphthyl)ethanone (**2b**)*: To a solution of imidazole (30 mmol) in 12.5 ml *N*,*N*-dimethylformamide (DMF) was slowly added a solution of 2,4-dichloroacetophenone (**1a**) or 2-bromo-1-(2-naphthyl)ethanone (**1b**) (10 mmol) in 2.5 ml DMF by vigorously stirring at 0-5 °C. The reaction mixture was allowed to stir for an additional 2 h at 0-5 °C then at room temperature overnight and poured into ice water. The resulting precipitate was filtered, dried, purified via crystallization from methanol/ethyl acetate (**2a**: yellow powder, 77% yield, mp: 157-9 °C (methanol/ethyl acetate); **2b**: yellow powder, 66% yield, mp: 220-3 °C (methanol/ethyl acetate)).

*1-(4-Chlorophenyl)-2-(1H-imidazol-1-yl)ethanol (**3a**) and 2-(1H-imidazol-1-yl)-1-(2-naphthyl)ethanol (**3b**)*: To a solution of **2a** or **2b** (1.8 mmol) in 18 ml methanol in ice bath sodium borohydride ($NaBH_4$) was added slowly. The reaction mixture was stirred for 1 h at 0-5 °C then dried under vacuum. The remaining residue was washed with ice water to give a yellow-brown powder, which was crystallized from ethyl acetate (**3a**: pale-yellow powder, 85% yield, mp: 180-2 °C (ethyl acetate); **3b**: yellow powder, 96% yield, mp: 156-8 °C (ethyl acetate)).

1.2. ^{1}H NMR spectra of the compounds

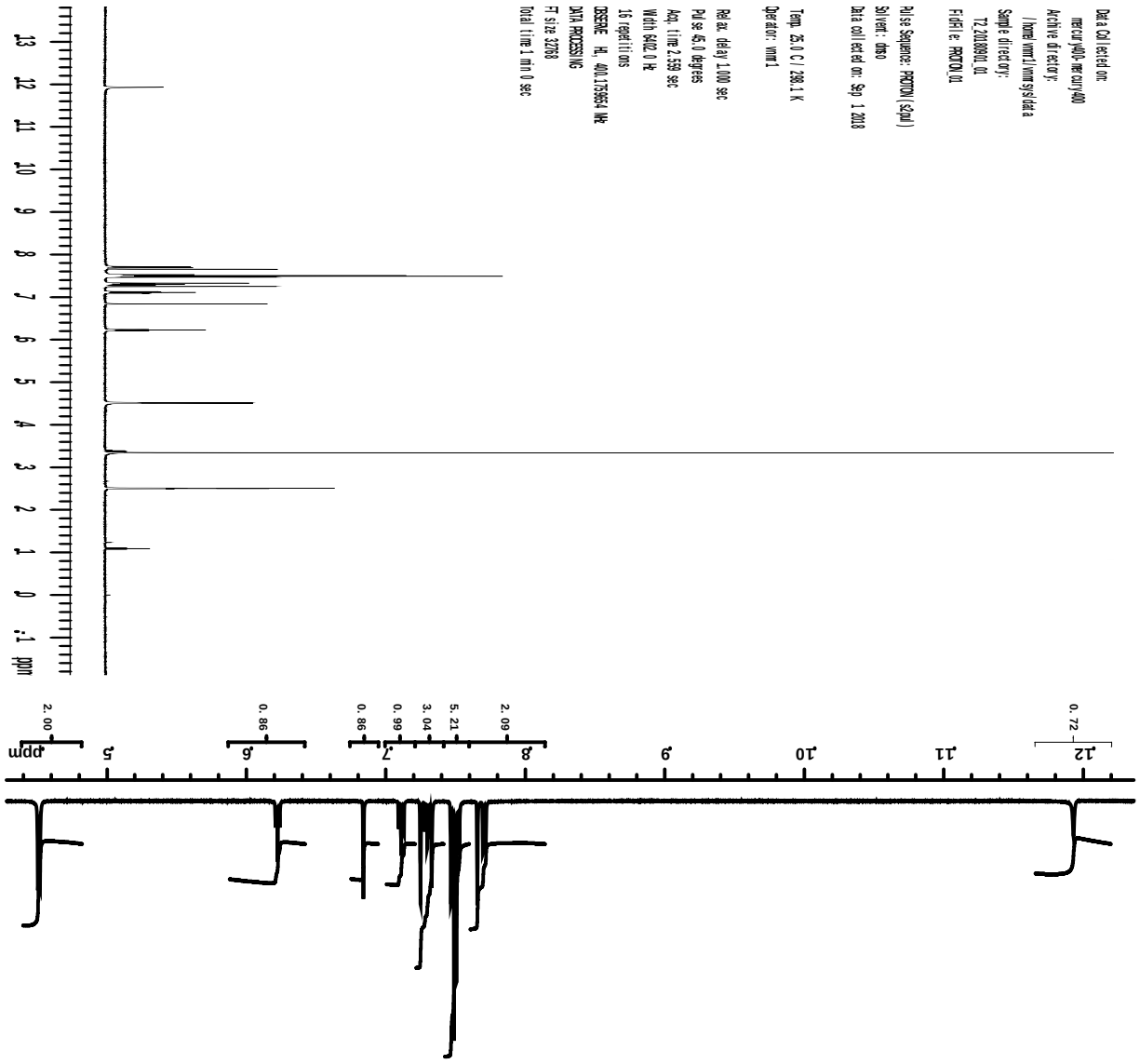


Figure S1. ^{1}H NMR spectrum of **4a**.

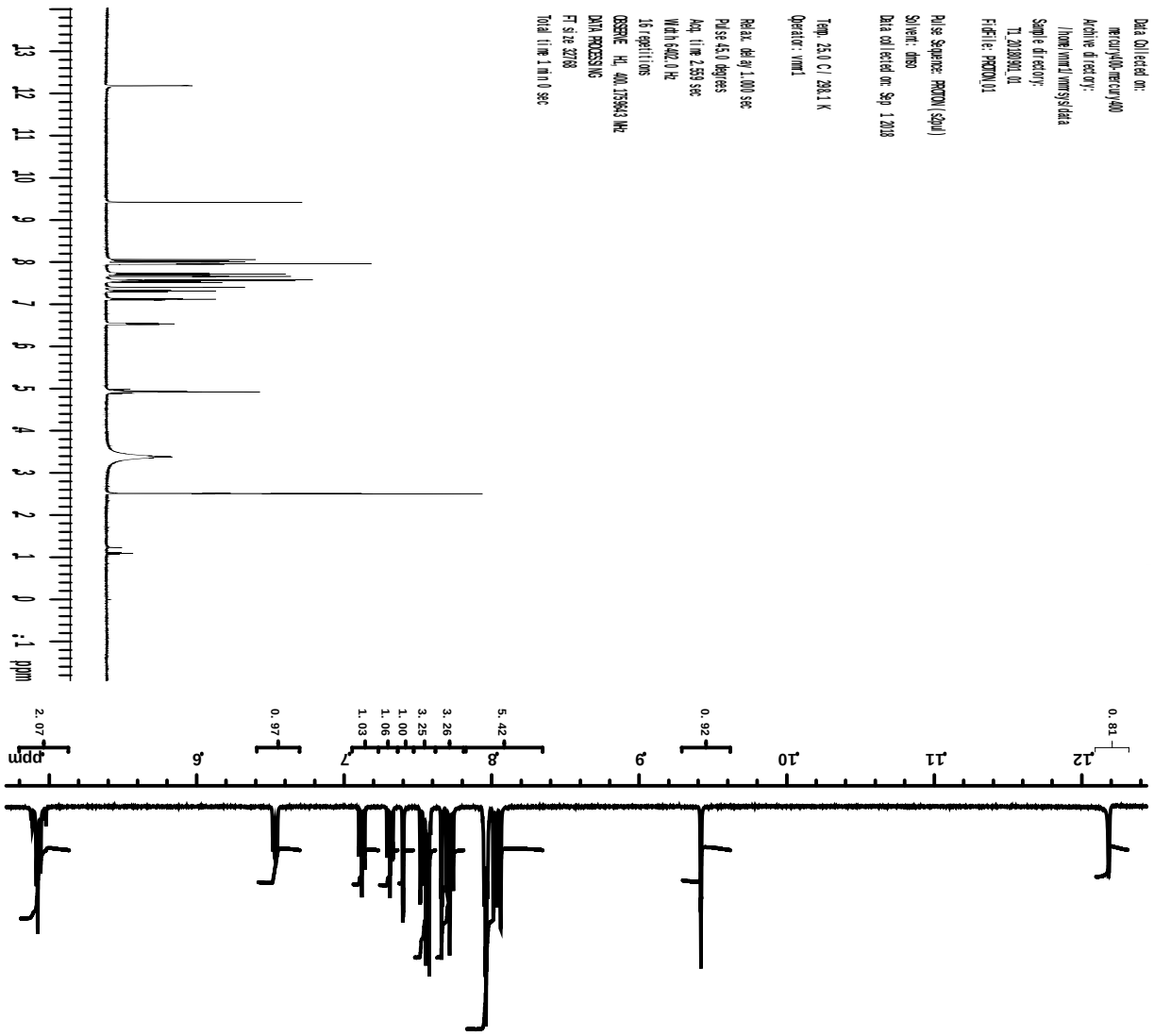


Figure S2. ^{1}H NMR spectrum of **4b**.

1.3. ^{13}C NMR spectra of the compounds

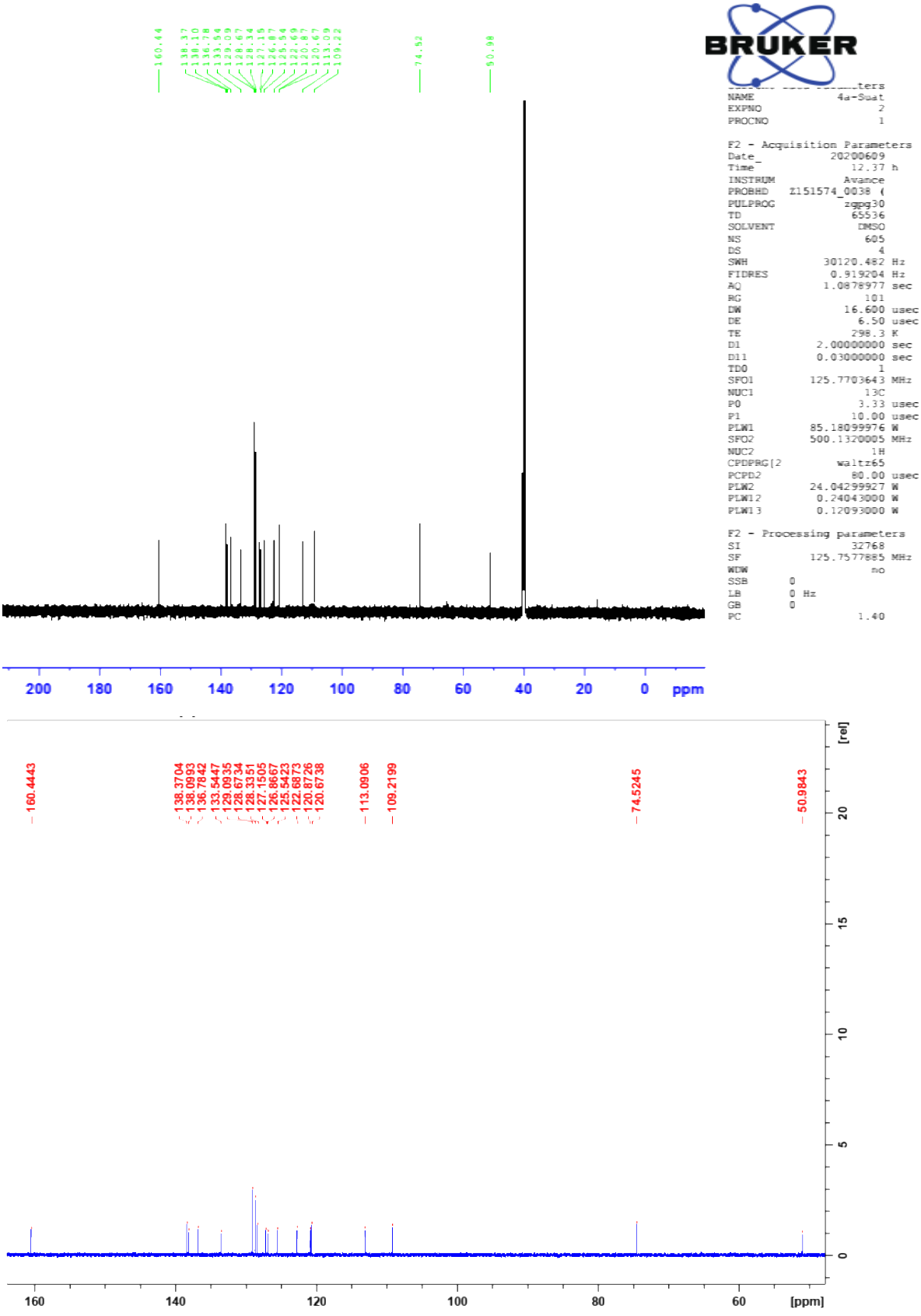
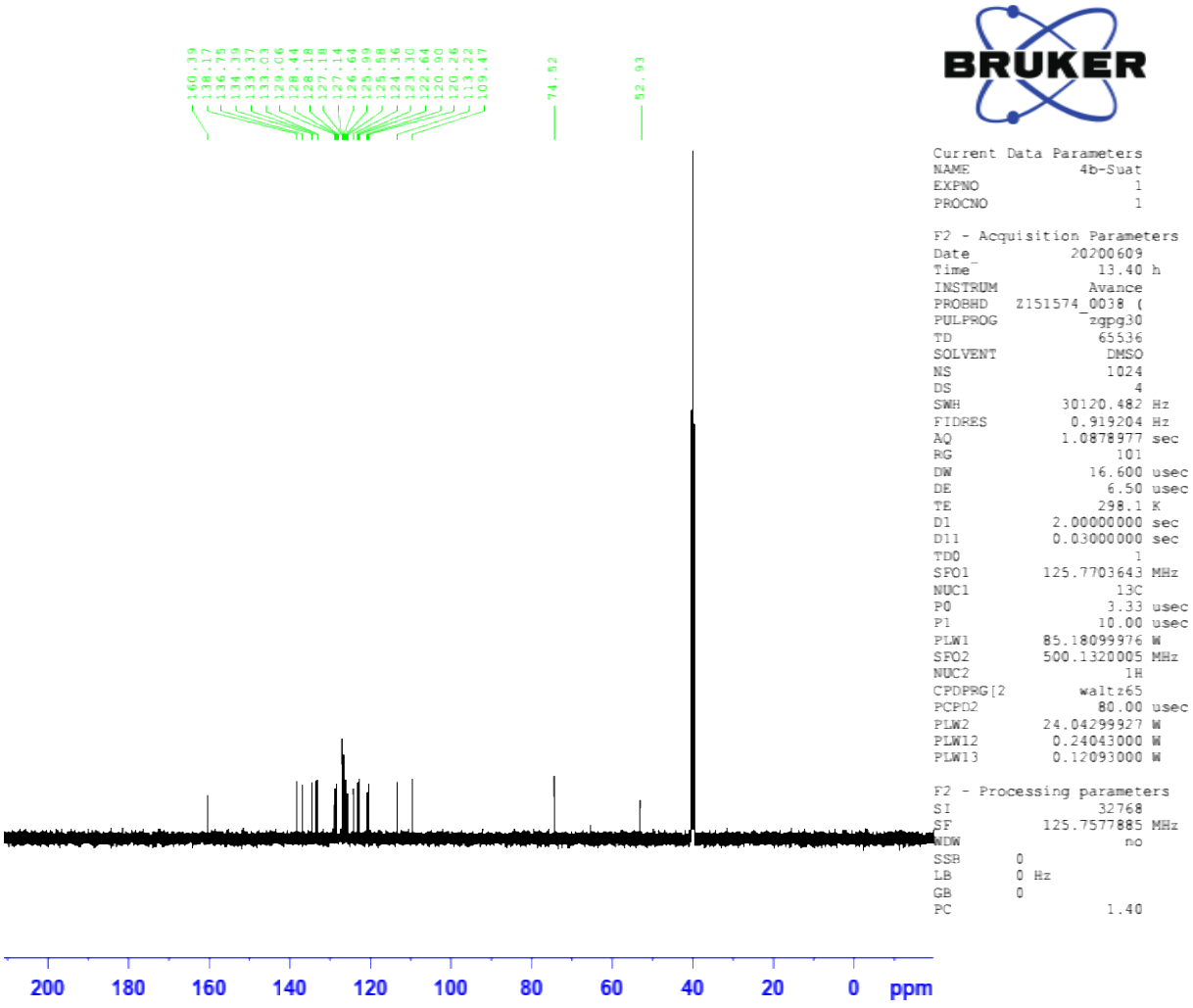


Figure S3. ^{13}C NMR spectrum of **4a**.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123.30
122.64
120.90
120.26
113.22
109.47
74.52
52.93
Current Data Parameters
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EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
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Time 13.40 h
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PULPROG zgpg30
TD 65536
SOLVENT DMSO
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SWH 30120.482 Hz
FIDRES 0.919204 Hz
AQ 1.0878977 sec
RG 101
DW 16.600 usec
DE 6.50 usec
TE 298.1 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
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NUC1 13C
P0 3.33 usec
P1 10.00 usec
PLW1 85.18099976 W
SFO2 500.1320005 MHz
NUC2 1H
CPDPRG[2 waltz65
PCPD2 80.00 usec
PLW2 24.04299927 W
PLW12 0.24043000 W
PLW13 0.12093000 W
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40
20
0
ppm

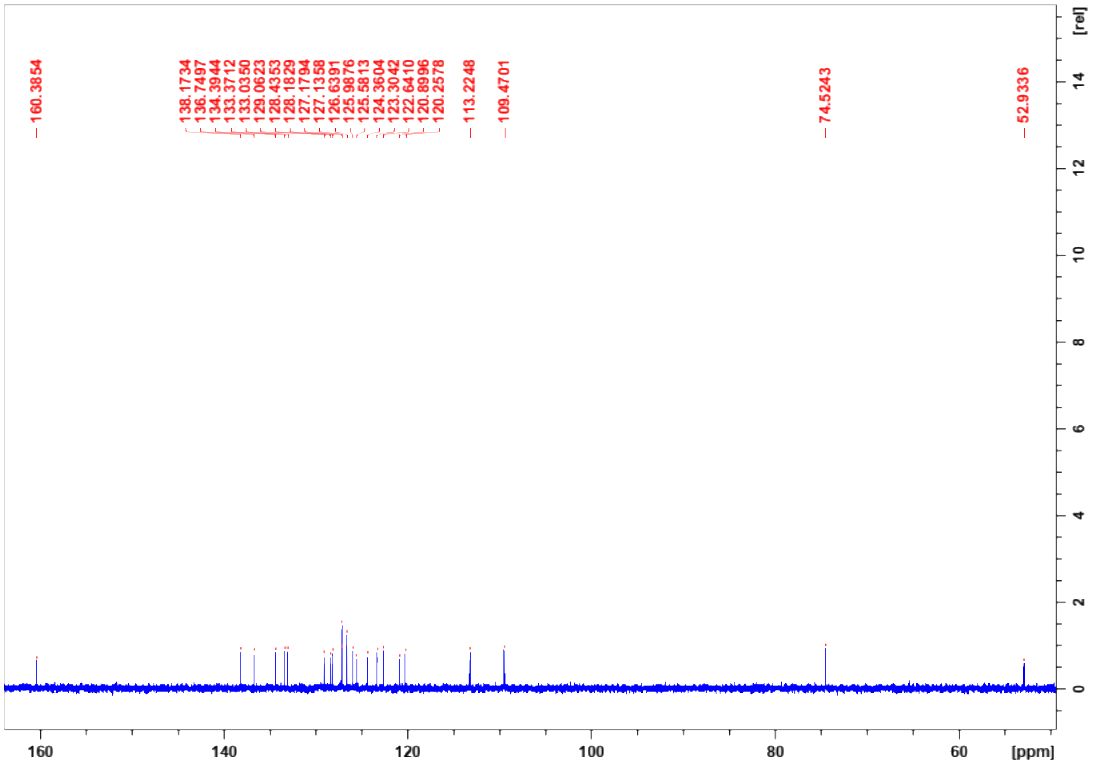
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Figure S4. ^{13}C NMR spectrum of **4b**.

1.4. LC-MS spectra of the compounds

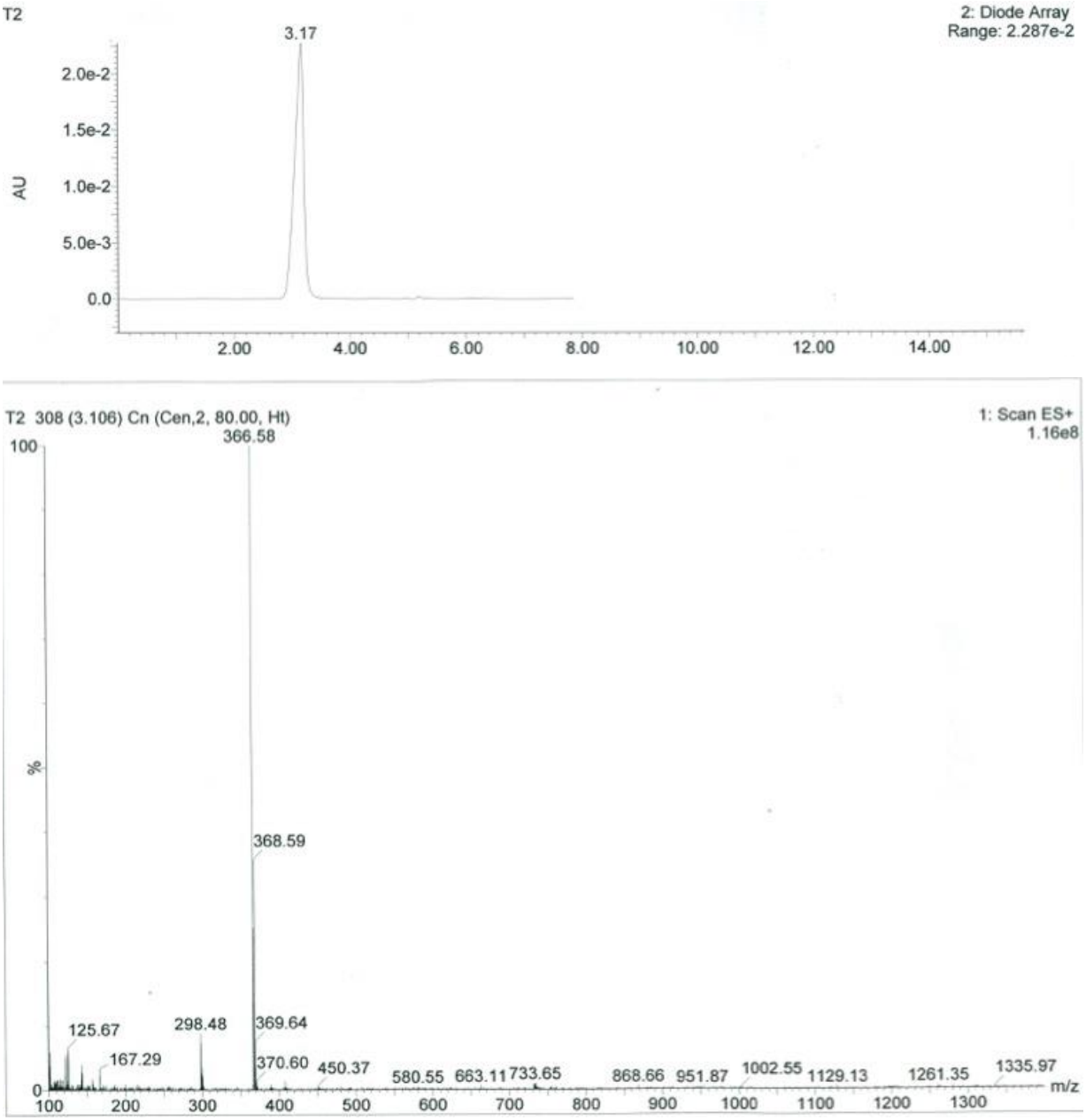

Figure S5. LC-MS spectrum of **4a**.

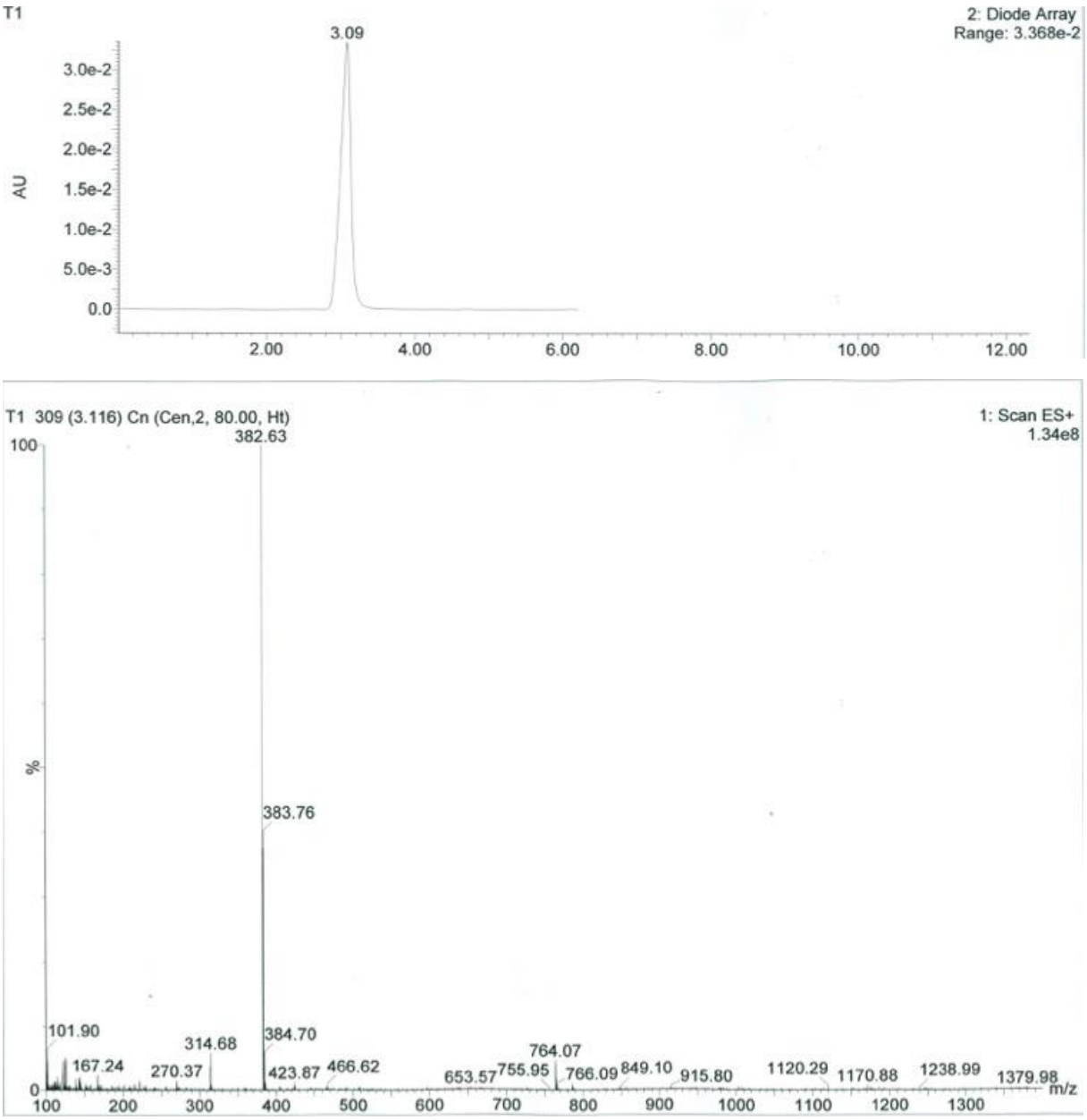

Figure S6. LC-MS spectrum of **4b**.

2. Molecular docking

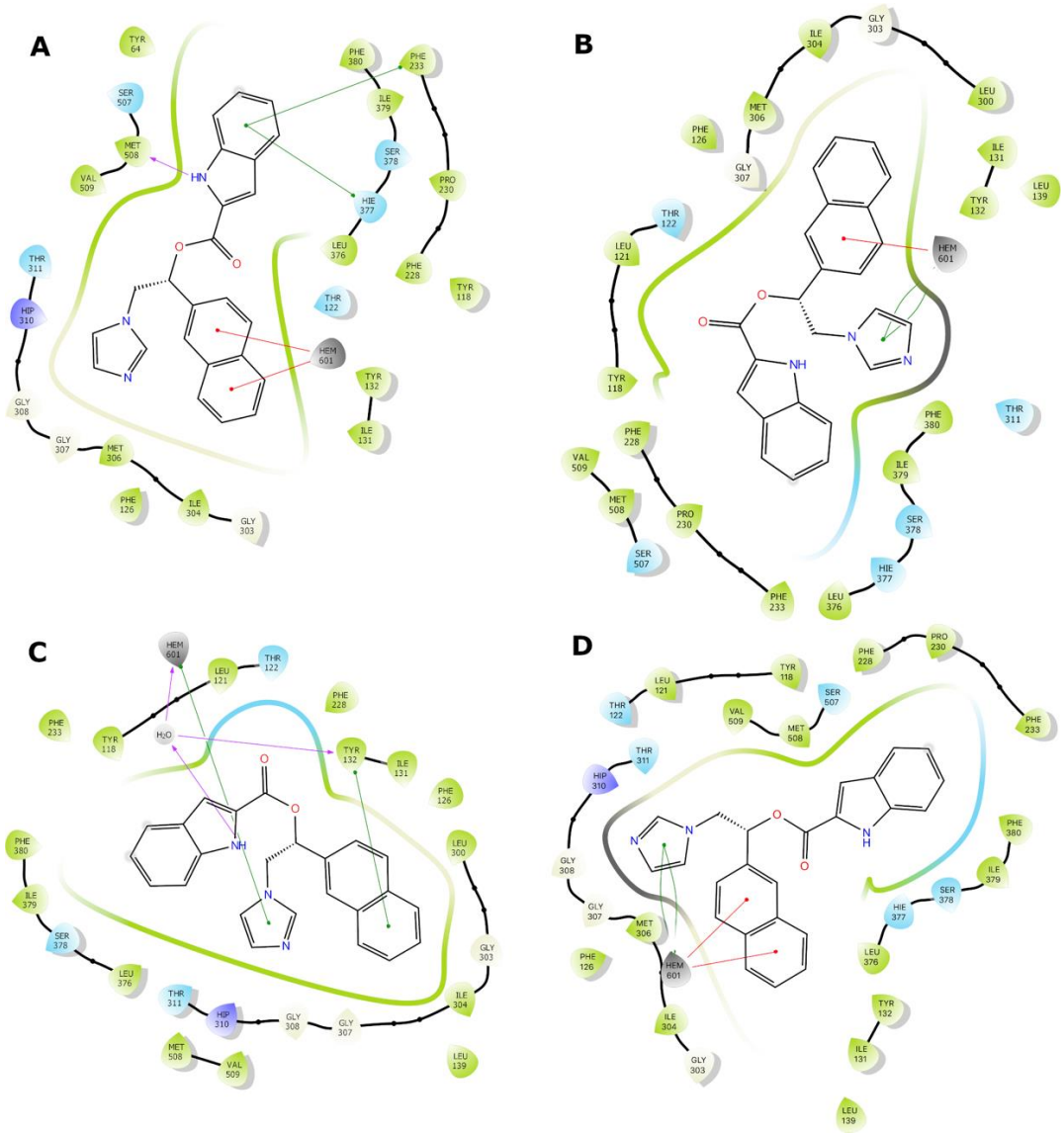

Figure S7. Binding interactions of **4b** predicted by SP (A), XP (B), Induced Fit (C), and QPLD (D) protocols of Glide.