

Supplementary data

Differential Proliferation Effect of the Newly Synthesized Valine, Tyrosine and Tryptophan–Naphthoquinones in Immortal and Tumorigenic Cervical Cell Lines

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1. Infrared Characterization

Amino acids-1,4-naphthoquinone derivatives:

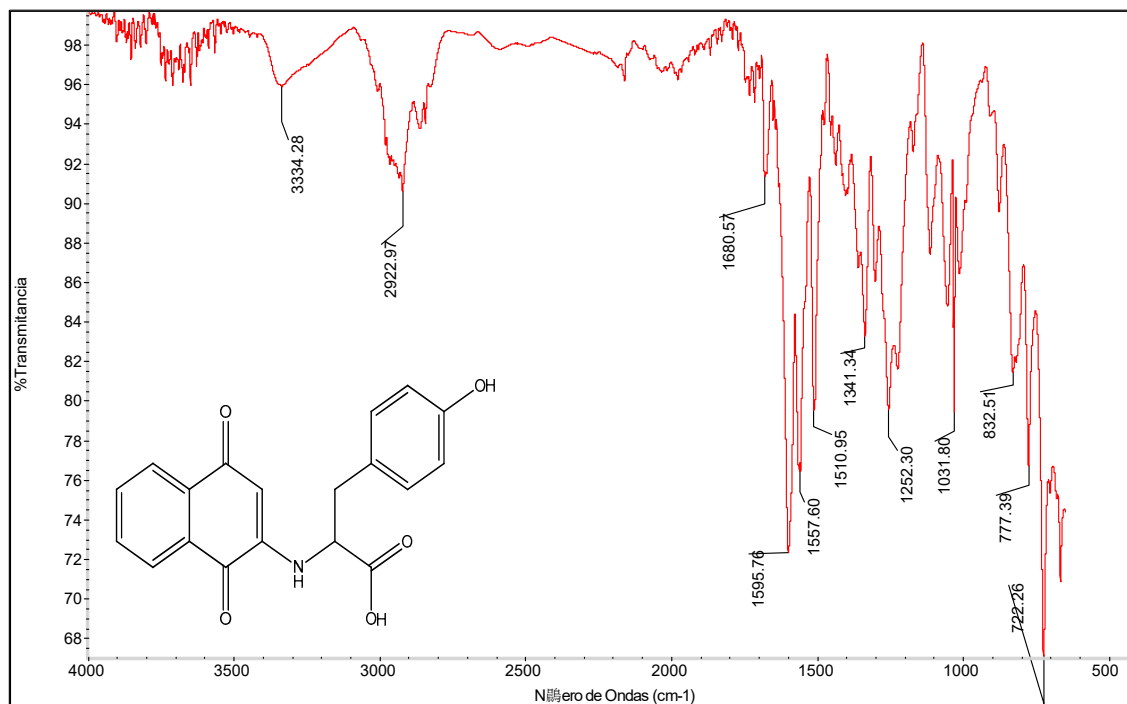


Figure S1. IR spectrum of 2-((1,4-dioxo-1,4-dihydro-naphthalen-2-yl)amino)-3-(4-hydroxyphenyl)propanoic acid (3a).

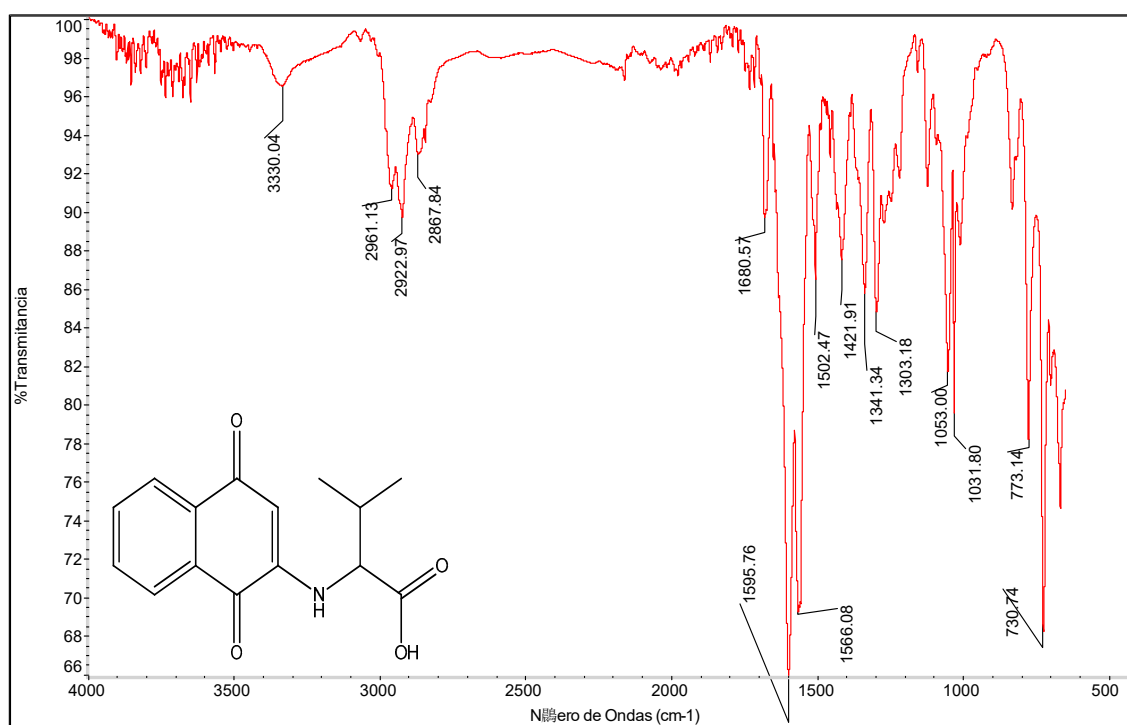


Figure S2. IR spectrum of 2-((1,4-dioxo-1,4-dihydro-naphthalen-2-yl)amino)-3-methylbutanoic acid (3b).

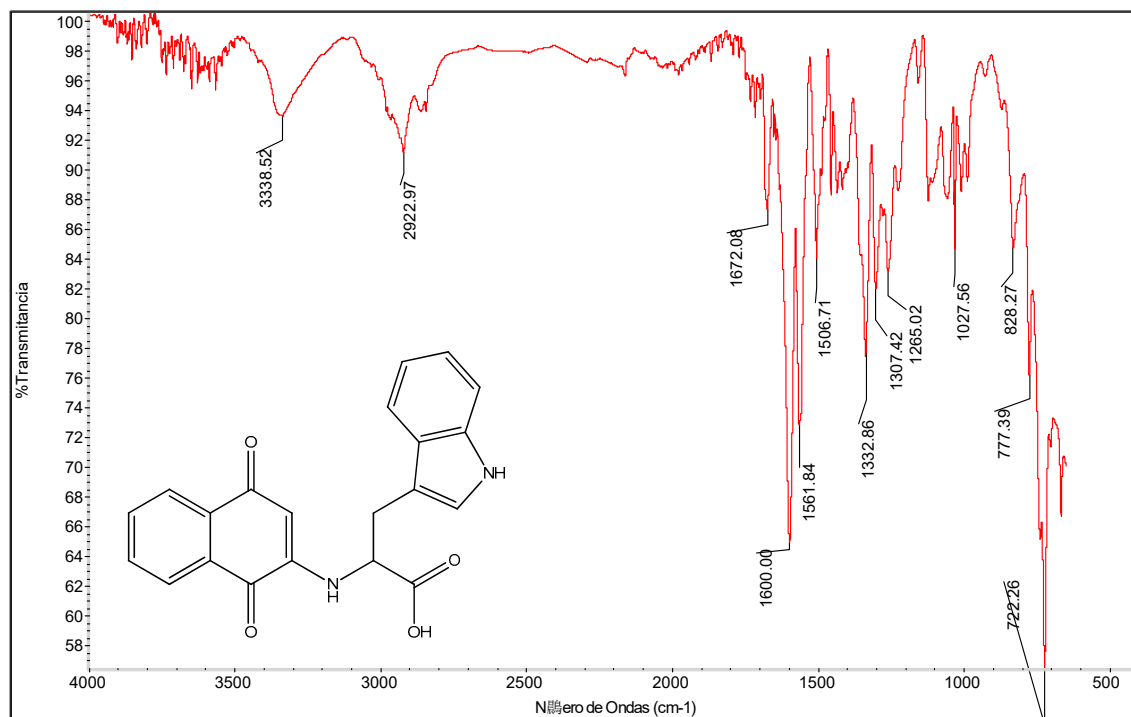


Figure S3. IR spectrum of 2-((1,4-dioxo-1,4-dihronaphthalen-2-yl)amino)-3-(1H-indol-3-yl)propanoic acid (3c).

Amino acids-2,3-dichloronaphthoquinone derivatives:

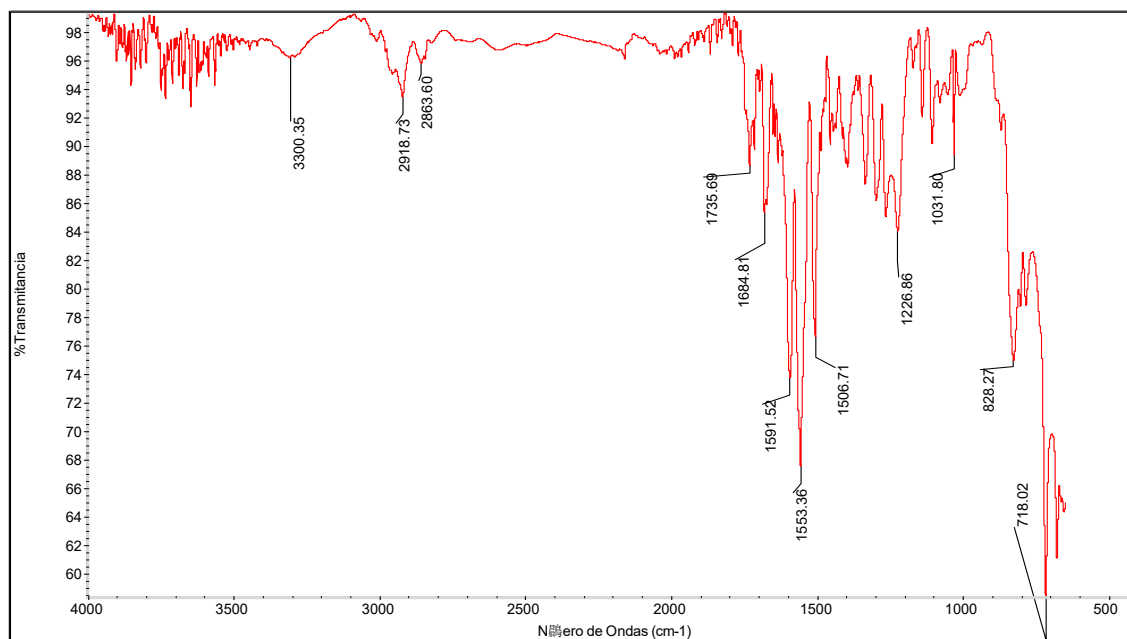


Figure S4. IR spectrum of 2-((3-chloro-1,4-dioxo-1,4-dihydronaphthalen-2-yl)amino)-3-(4-hydroxyphenyl)propanoic acid (4a).

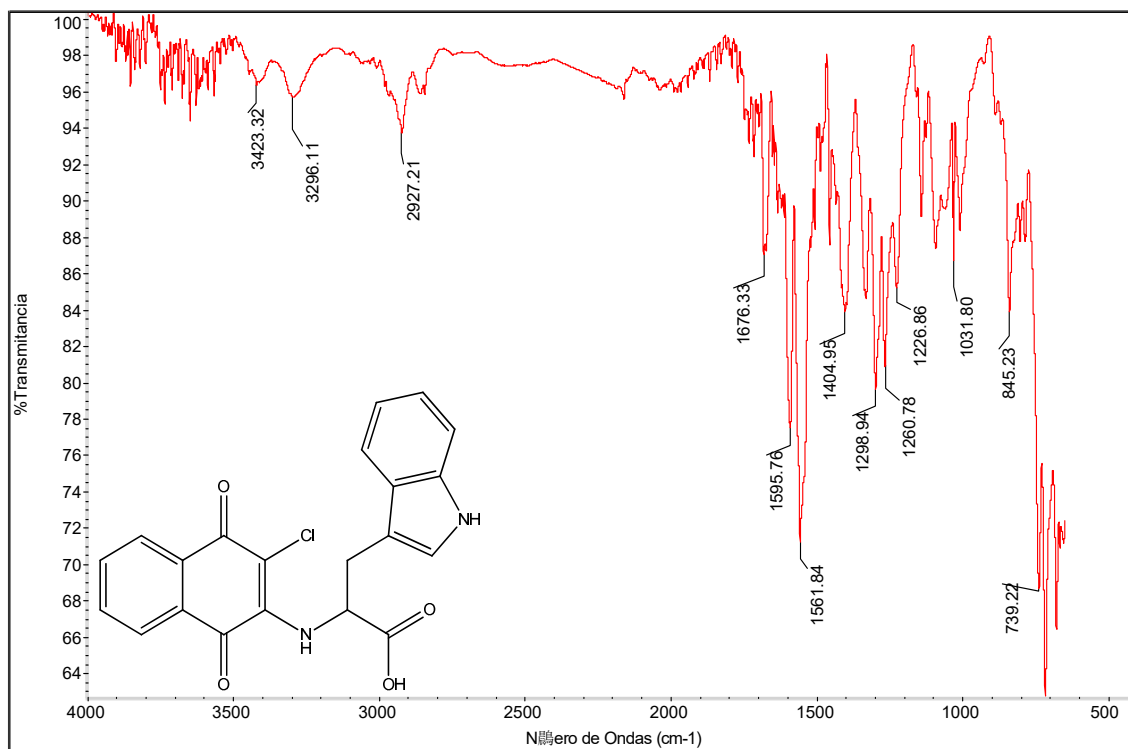


Figure S5. IR spectrum of 2-((3-chloro-1,4-dioxo-1,4-dihydronaphthalen-2-yl)amino)-3-methylbutanoic acid (4b).

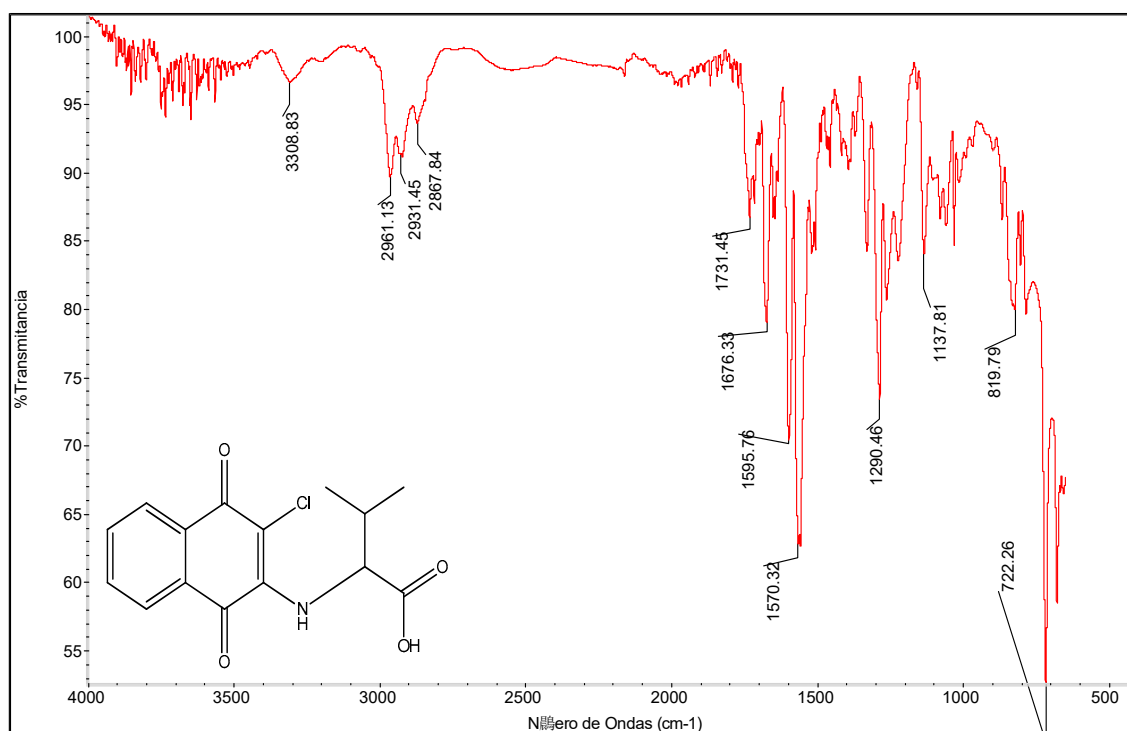
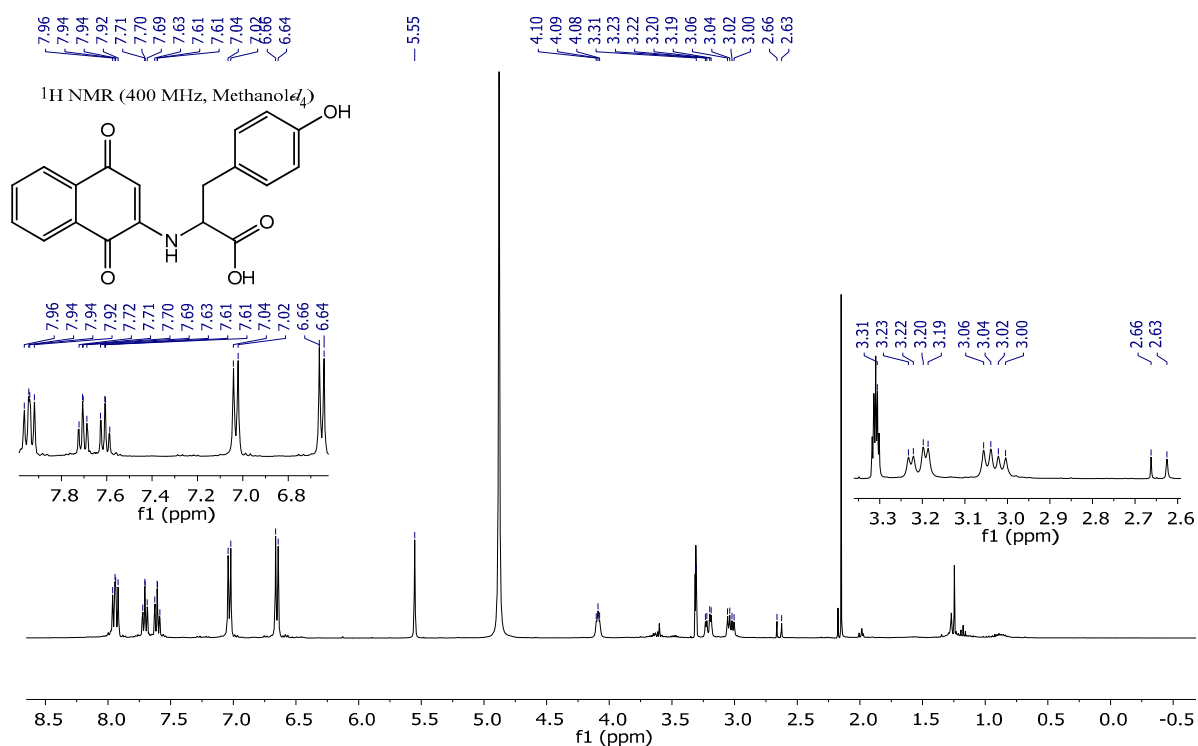


Figure S6. IR spectrum of 2-((3-chloro-1,4-dioxo-1,4-dihydronaphthalen-2-yl)amino)-3-(1H-indol-3-yl)propanoic acid (4c).

2. NMR Characterization

Amino acids-1,4-naphthoquinone derivatives:

A



B

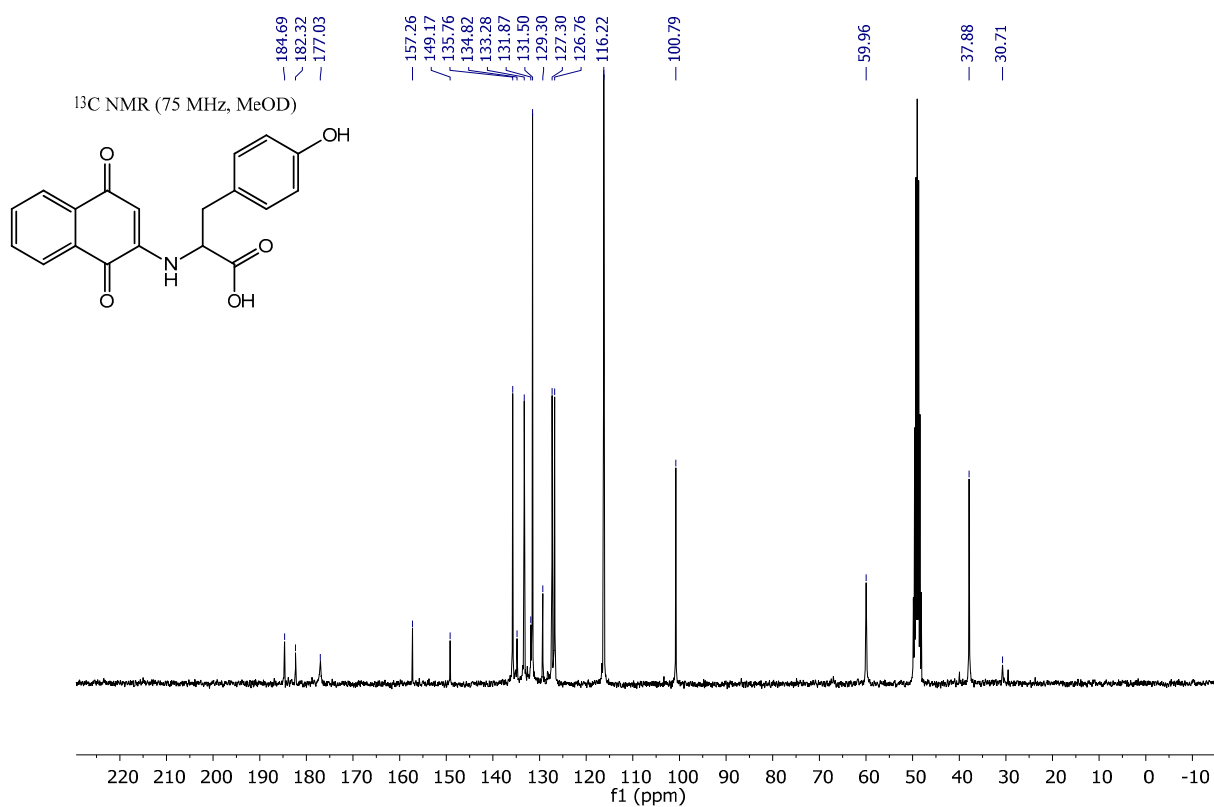
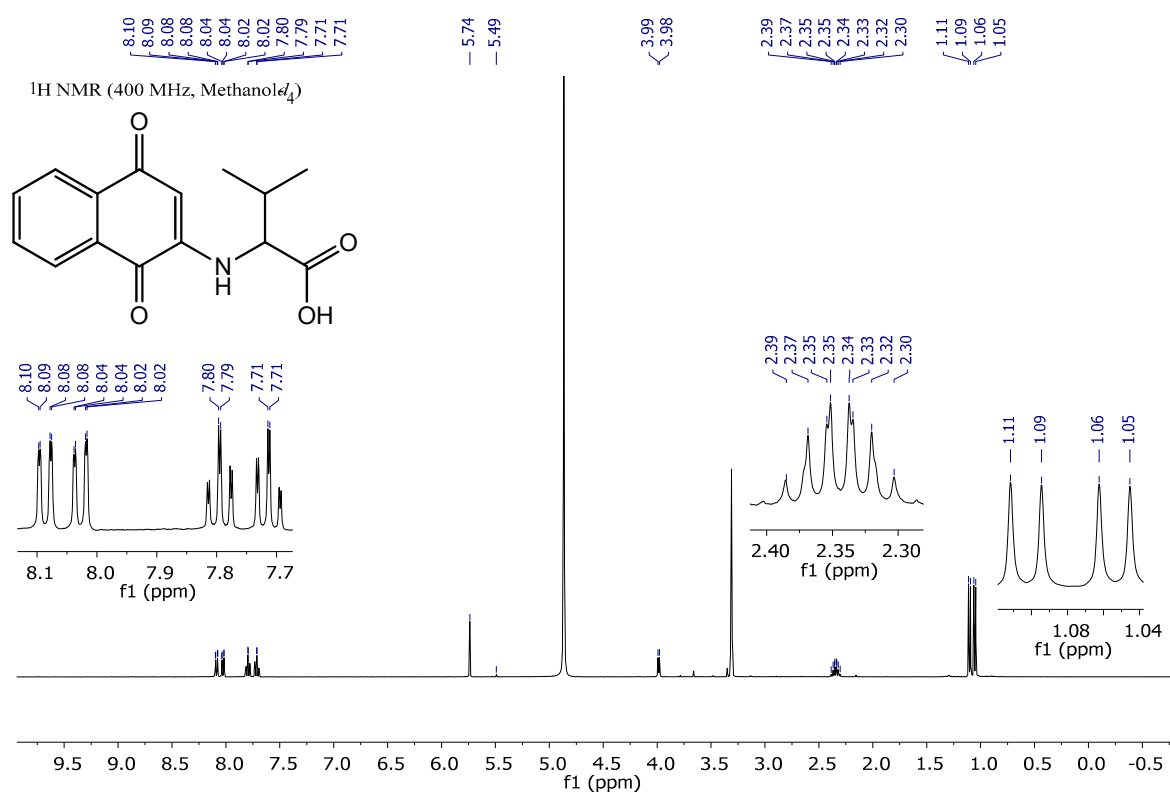


Figure S7. NMR spectrum of 2-((1,4-dioxo-1,4-dihydrophthalen-2-yl)amino)-3-(4-hydroxyphenyl)propanoic acid (3a), ¹H (A) and ¹³C (B).

A



B

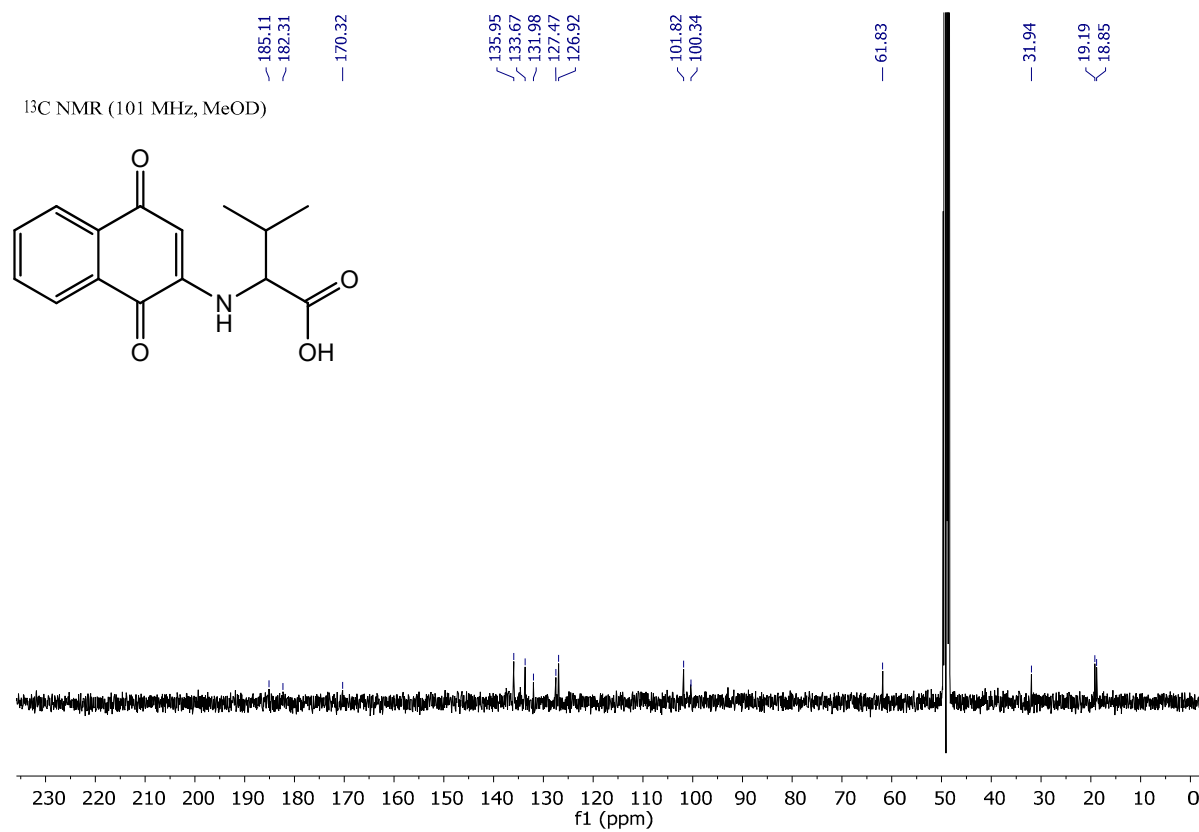
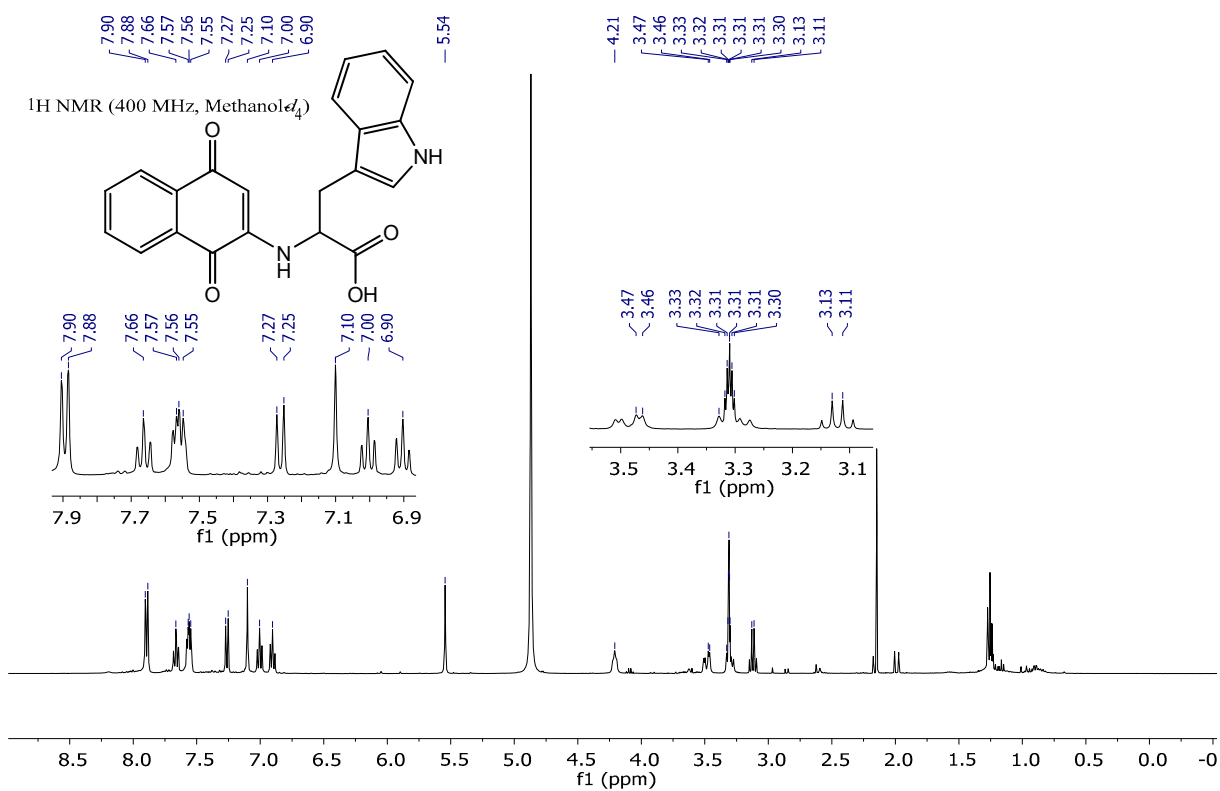


Figure S8. NMR spectrum of 2-((1,4-dioxo-1,4-dihydronaphthalen-2-yl)amino)-3-methylbutanoic acid (3b), ¹H (A) and ¹³C (B).

A



B

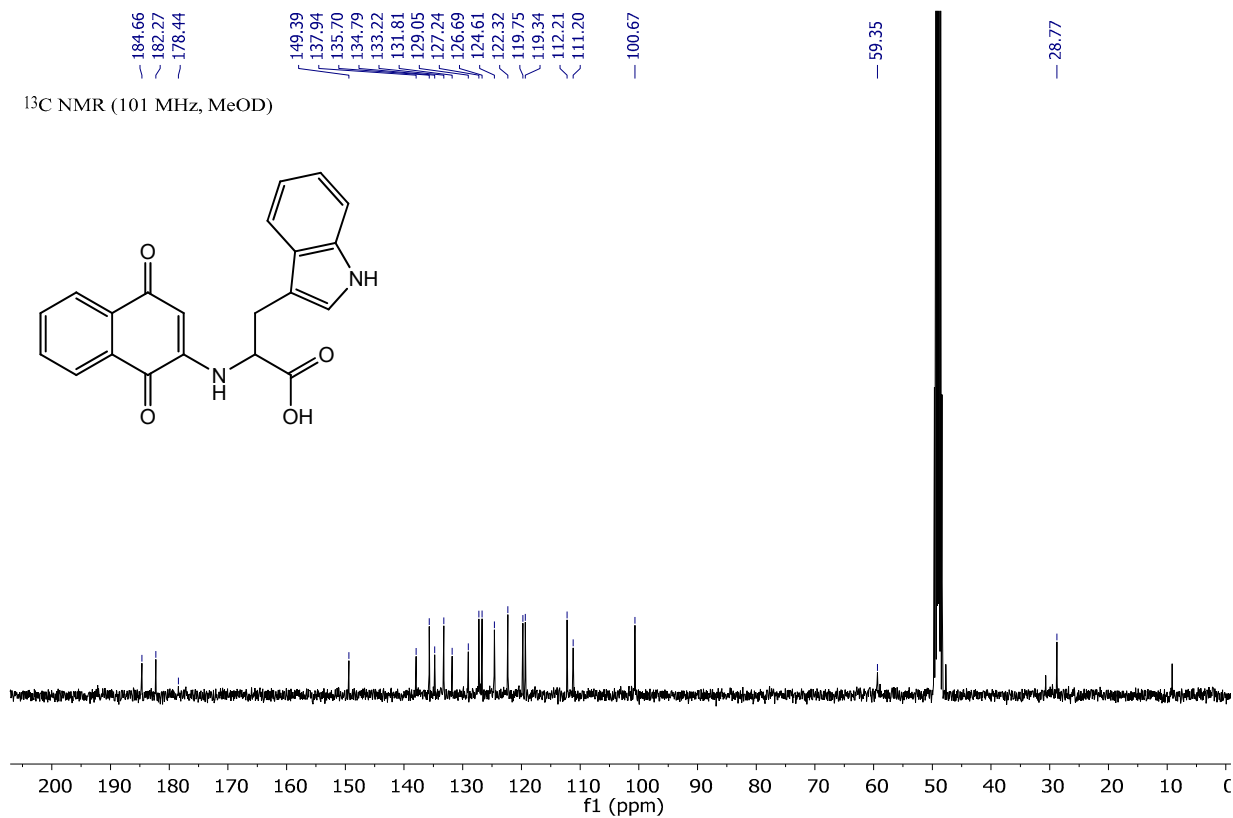
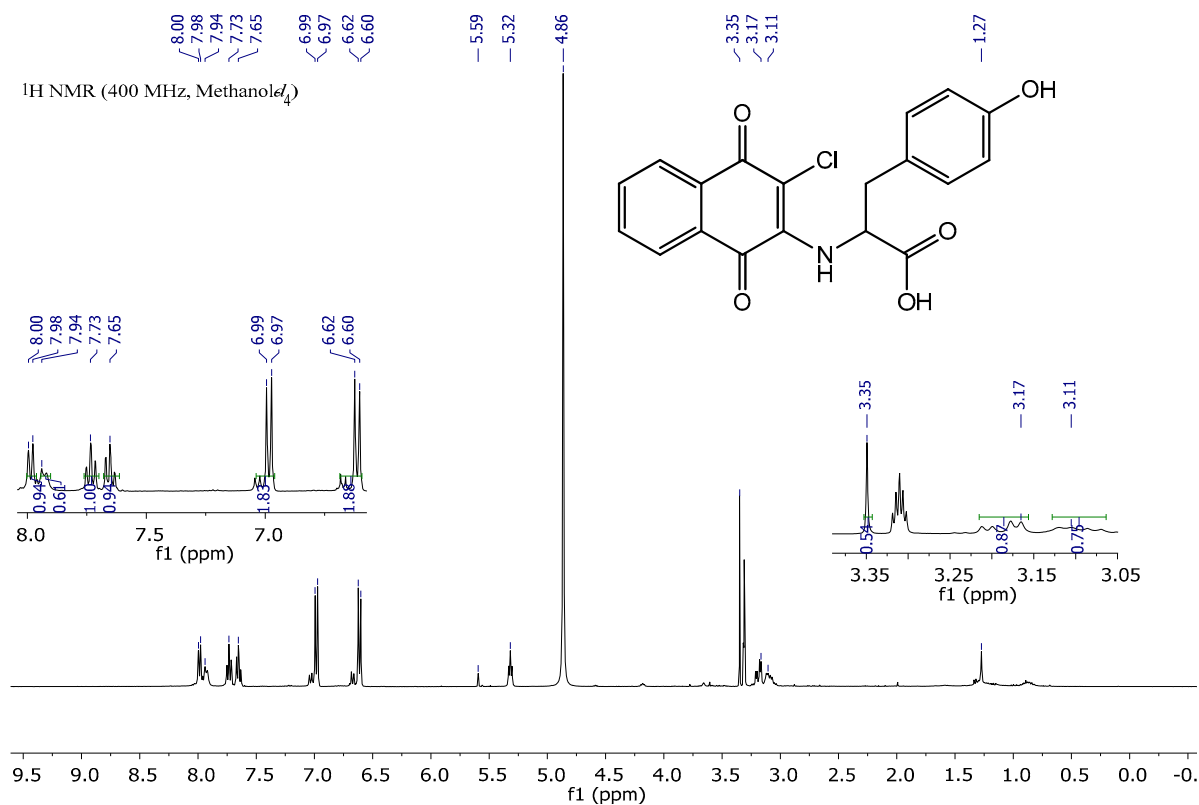


Figure S9. NMR spectrum of 2-((1,4-dioxo-1,4-dihydronaphthalen-2-yl)amino)-3-(1H-indol-3-yl)propanoic acid (3c), ¹H (A) and ¹³C (B).

Amino acids-2,3-dichloronaphthoquinone derivatives:

A



B

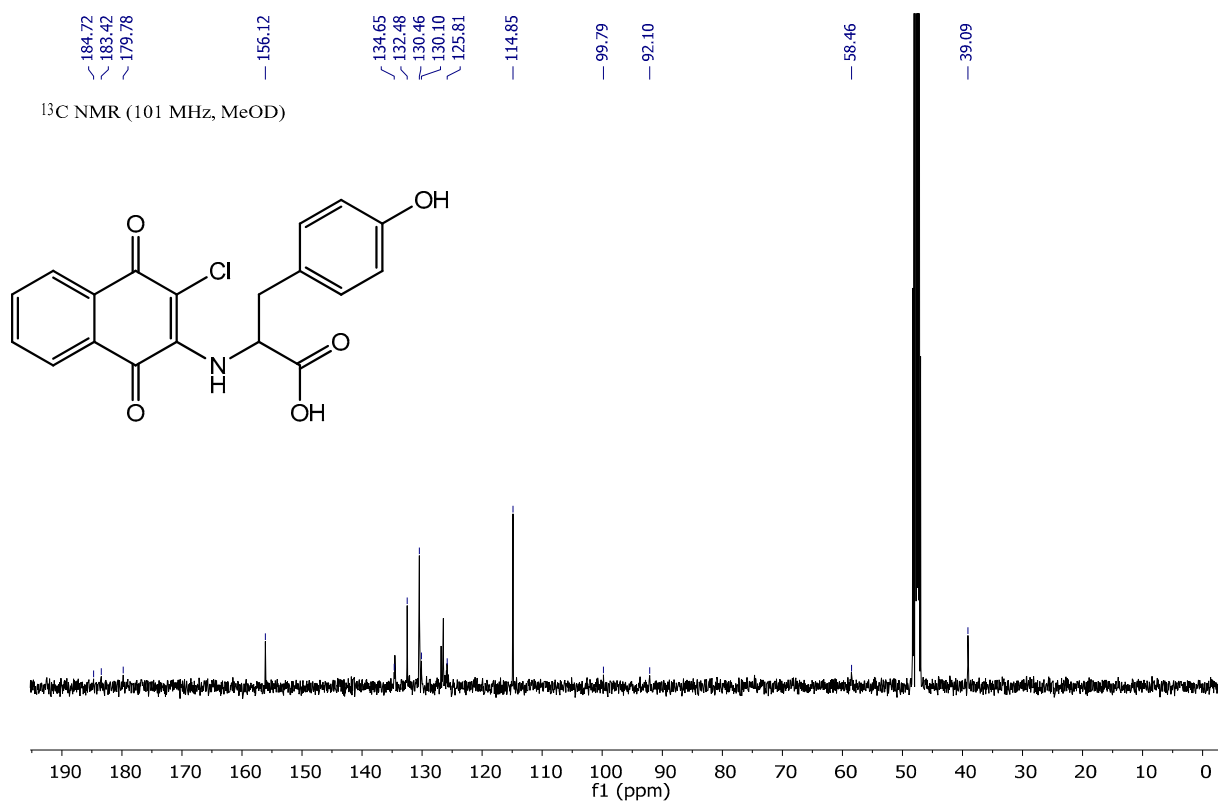
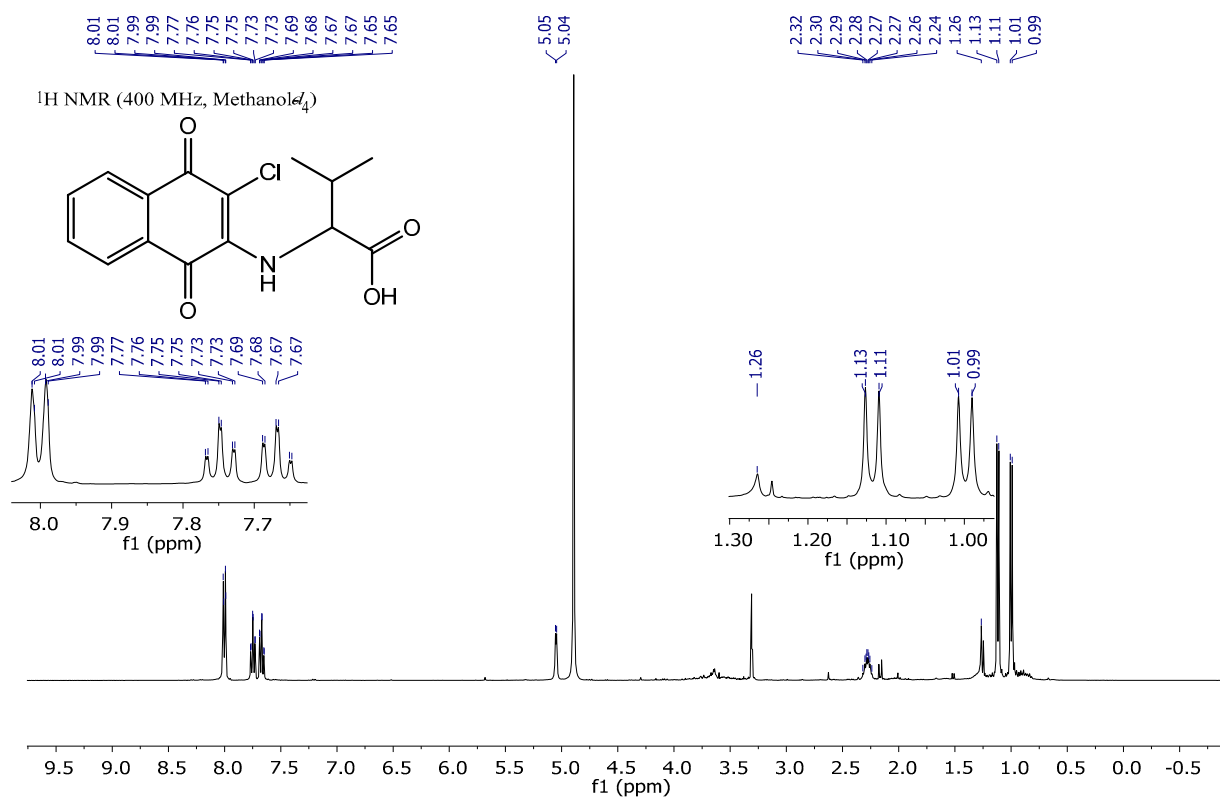


Figure S10. NMR spectrum of 2-((3-chloro-1,4-dioxo-1,4-dihydronaphthalen-2-yl)amino)-3-(4-hydroxyphenyl)propanoic acid (4a), ¹H (A) and ¹³C (B).

A



B

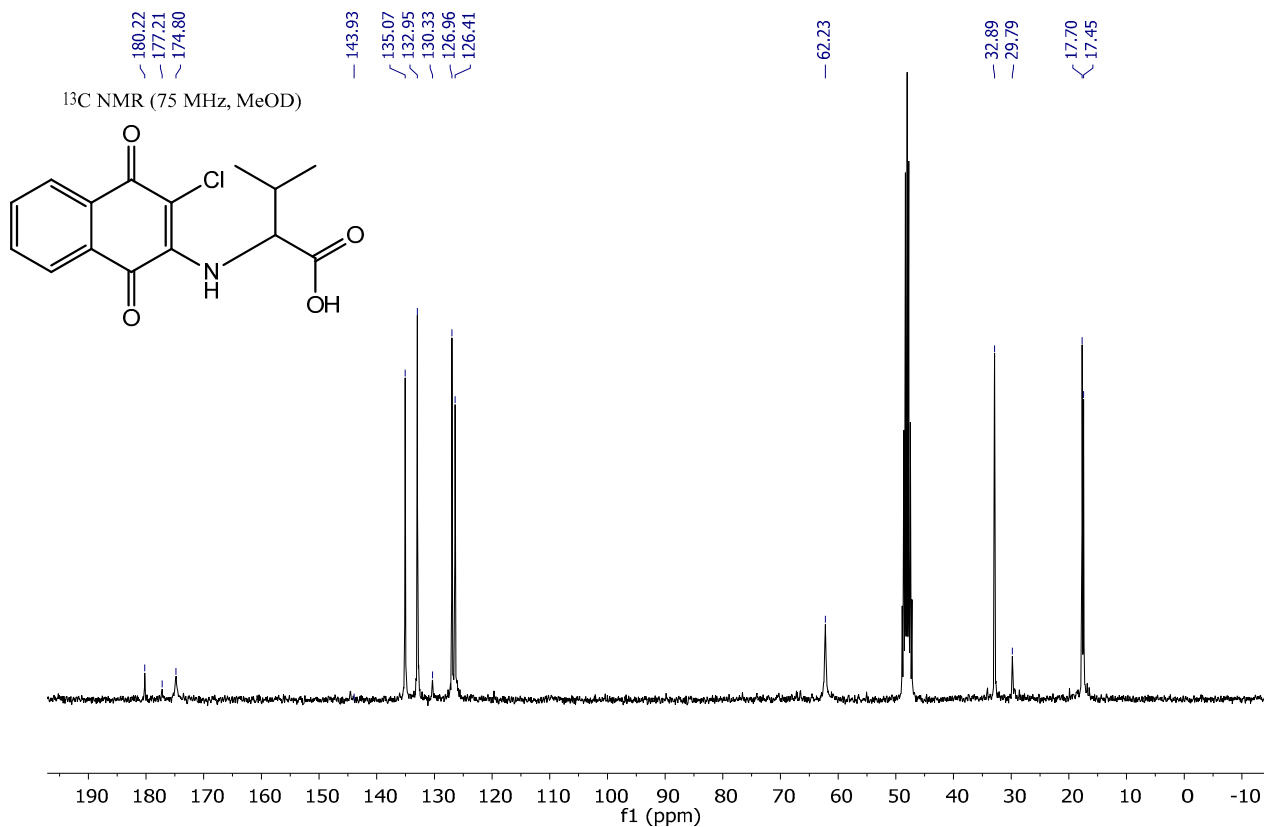
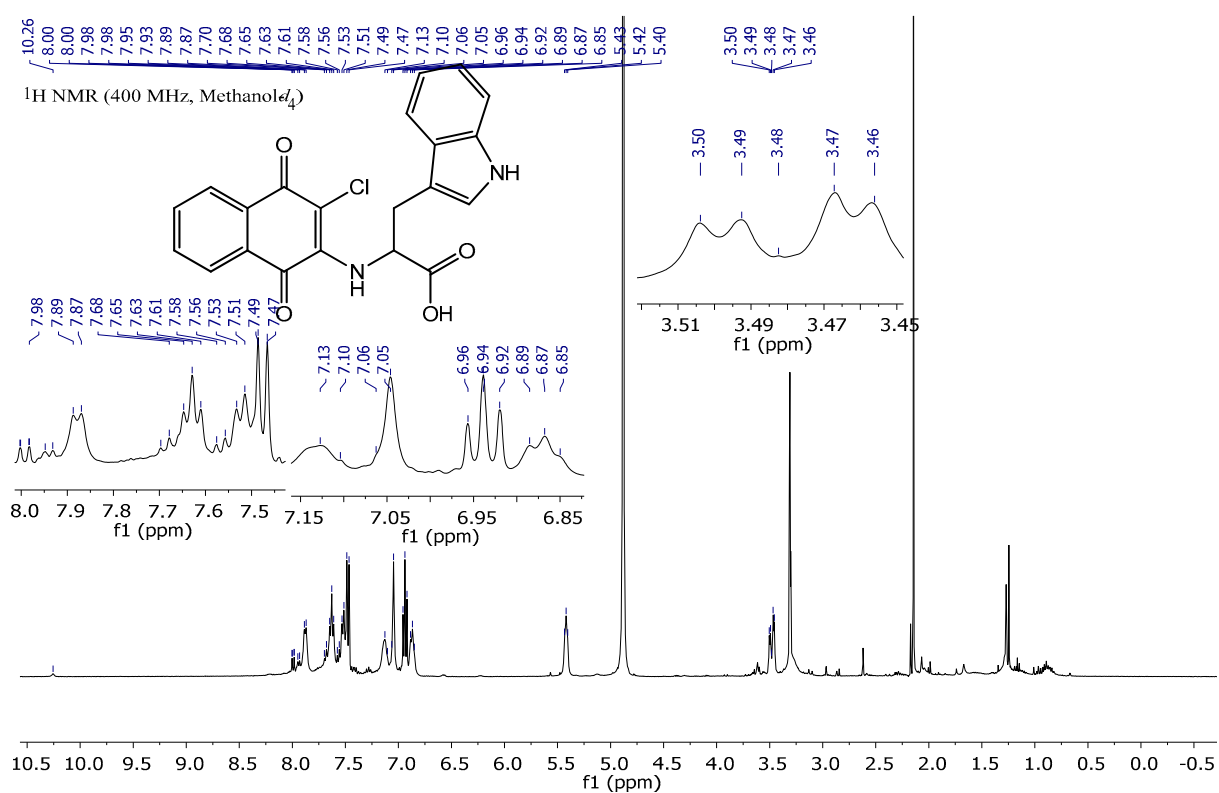


Figure S11. NMR spectrum of 2-((3-chloro-1,4-dioxo-1,4-dihydronaphthalen-2-yl)amino)-3-methylbutanoic acid (4b), ¹H (A) and ¹³C (B).

A



B

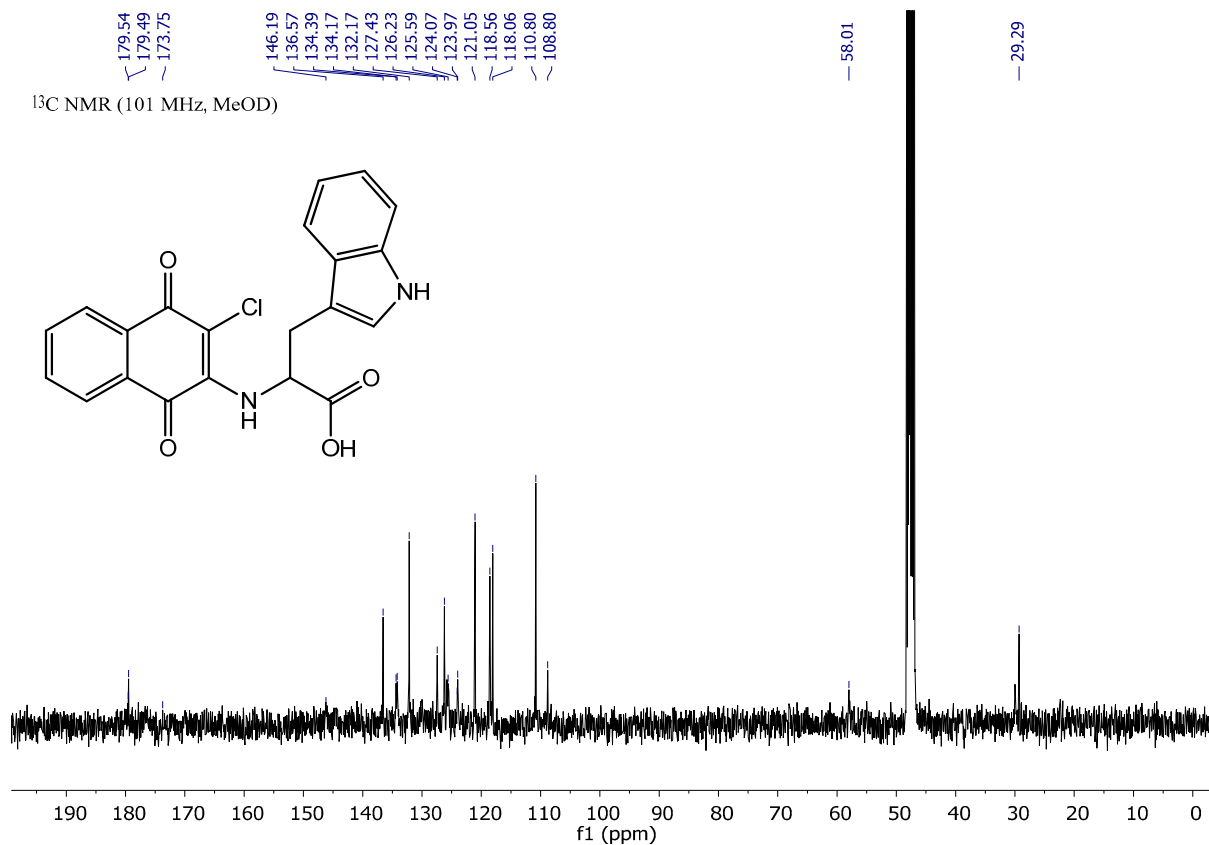


Figure S12. NMR spectrum of 2-((3-chloro-1,4-dioxo-1,4-dihydronaphthalen-2-yl)amino)-3-(1H-indol-3-yl)propanoic acid (4c), ¹H (A) and ¹³C (B).

3. Mass Spectrometry Characterization

Amino acids-1,4-naphthoquinone derivatives:

| | | | |
|------------------------|-------------------|----------------|-----------------------------|
| Data Filename | Nfa Tyr.d | Sample Name | Nfa Tyr |
| Sample Type | Sample | Position | P1-B4 |
| Instrument Name | LC QTOF-LANCIC | User Name | |
| Acq Method | Ine directa pos.m | Acquired Time | 3/15/2019 1:12:48 PM |
| IRM Calibration Status | Success | DA Method | Everardo ESI MS.m |
| Comment | | | |
| Sample Group | | Info. | |
| Stream Name | LC 1 | Acquisition SW | 6200 series TOF/6500 series |
| | | Version | Q-TOF B.06.01 (B6172 SP1) |

User Spectra

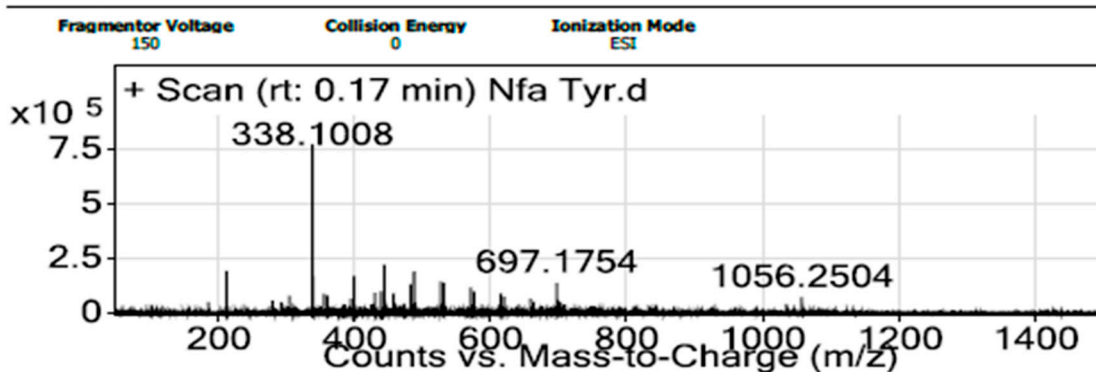


Figure S13. MS spectrum of 2-((1,4-dioxo-1,4-dihydronphthalen-2-yl)amino)-3-(4-hydroxyphenyl)propanoic acid (3a).

| | | | |
|------------------------|-------------------|----------------|-----------------------------|
| Data Filename | Nfa Va.d | Sample Name | Nfa Va |
| Sample Type | Sample | Position | P1-B5 |
| Instrument Name | LC QTOF-LANCIC | User Name | |
| Acq Method | Ine directa pos.m | Acquired Time | 3/15/2019 1:17:54 PM |
| IRM Calibration Status | Success | DA Method | Everardo ESI MS.m |
| Comment | | | |
| Sample Group | | Info. | |
| Stream Name | LC 1 | Acquisition SW | 6200 series TOF/6500 series |
| | | Version | Q-TOF B.06.01 (B6172 SP1) |

User Spectra

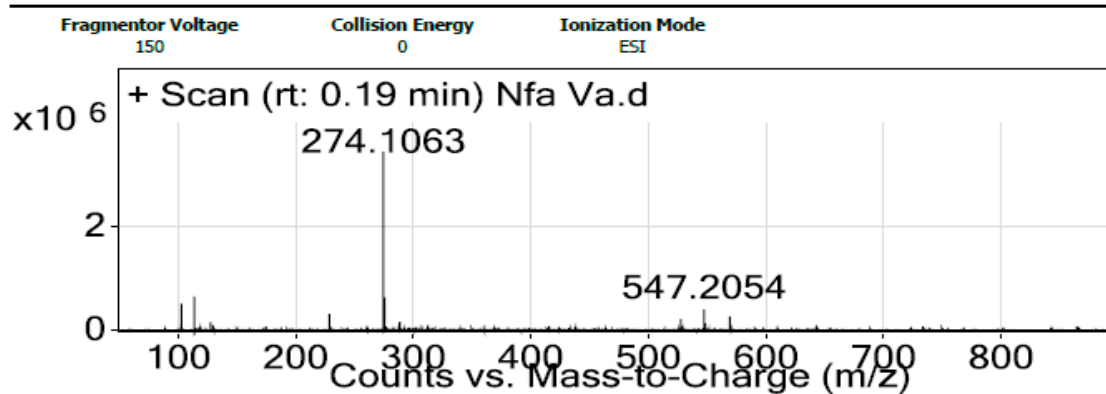


Figure S14. MS spectrum of 2-((1,4-dioxo-1,4-dihydronaphthalen-2-yl)amino)-3-methylbutanoic acid (3b).

| | | | |
|------------------------|-------------------|---------------|----------------------|
| Data Filename | Nfa Trp.d | Sample Name | Nfa Trp |
| Sample Type | Sample | Position | P1-B6 |
| Instrument Name | LC QTOF-LANCIC | User Name | |
| Acq Method | Ine directa pos.m | Acquired Time | 3/15/2019 1:22:59 PM |
| IRM Calibration Status | Success | DA Method | Everardo ESI MS.m |
| Comment | | | |

| | | | |
|--------------|------|----------------|-----------------------------|
| Sample Group | | Info. | |
| Stream Name | LC 1 | Acquisition SW | 6200 series TOF/6500 series |
| | | Version | Q-TOF B.06.01 (B6172 SP1) |

User Spectra

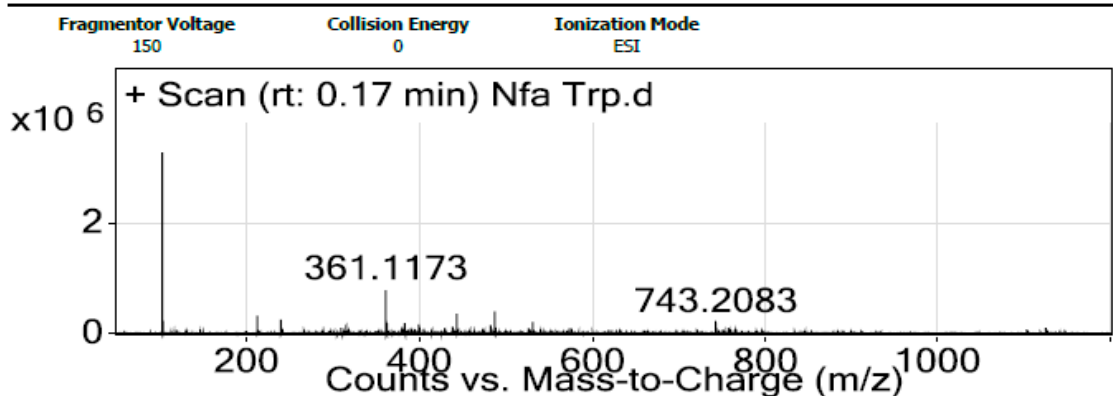
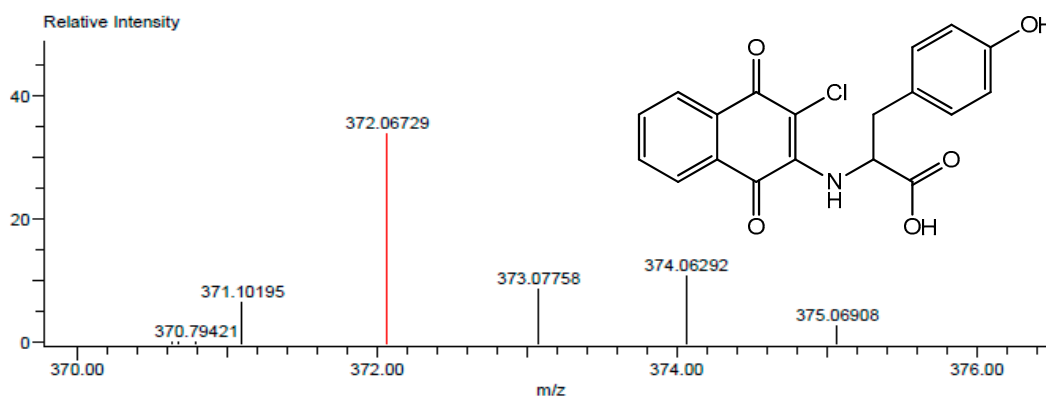


Figure S15. MS spectrum of 2-((1,4-dioxo-1,4-dihydronaphthalen-2-yl)amino)-3-(1H-indol-3-yl)propanoic acid (3c).

Amino acids-2,3-dichloronaphthoquinone derivatives:

| | |
|---|--|
| Data:U-1240 NCI Tyr | Acquired:3/12/2019 3:12:11 PM |
| Sample Name:Dr. Braulio Rodriguez / Ernesto Rivera | Operator:AccuTOF |
| Description: | Mass Calibration data:Cal Peg 600 |
| Ionization Mode:ESI+ | Created:3/12/2019 3:43:36 PM |
| History:Determine m/z[Peak Detect[Centroid,30,Area];Correct Base[1.0%];Smooth.. | Created by:AccuTOF |
| Charge number:1 | Tolerance:50.00(mmu) |
| Element: ¹² C:1 .. 19, ¹ H:1 .. 15, ³⁵ Cl:1 .. 1, ¹⁴ N:1 .. 1, ¹⁶ O:1 .. 5 | Unsaturation Number:1.0 .. 100.0 (Fra... |



| Mass | Intensity | Calc. Mass | Mass Difference (mmu) | Mass Difference (ppm) | Possible Formula |
|-----------|-----------|------------|-----------------------|-----------------------|--|
| 372.06729 | 35830.25 | 372.06387 | 3.42 | 9.19 | ¹² C ₁₉ ¹ H ₁₅ ³⁵ Cl ₁ ¹⁴ N ₁ ¹⁶ O ₅ |

Figure S16. MS spectrum of 2-((3-chloro-1,4-dioxo-1,4-dihydronaphthalen-2-yl)amino)-3-(4-hydroxyphenyl)propanoic acid (4a).

| | | | |
|-------------------------------|-------------------|----------------------|----------------------|
| Data Filename | NCI Va.d | Sample Name | NCI Va |
| Sample Type | Sample | Position | P1-B2 |
| Instrument Name | LC QTOF-LANCIC | User Name | |
| Acq Method | Ine directa pos.m | Acquired Time | 3/15/2019 1:02:38 PM |
| IRM Calibration Status | Success | DA Method | Everardo ESI MS.m |
| Comment | | | |

| | | | |
|---------------------|------|-----------------------|-----------------------------|
| Sample Group | | Info. | |
| Stream Name | LC 1 | Acquisition SW | 6200 series TOF/6500 series |
| | | Version | Q-TOF B.06.01 (B6172 SP1) |

User Spectra

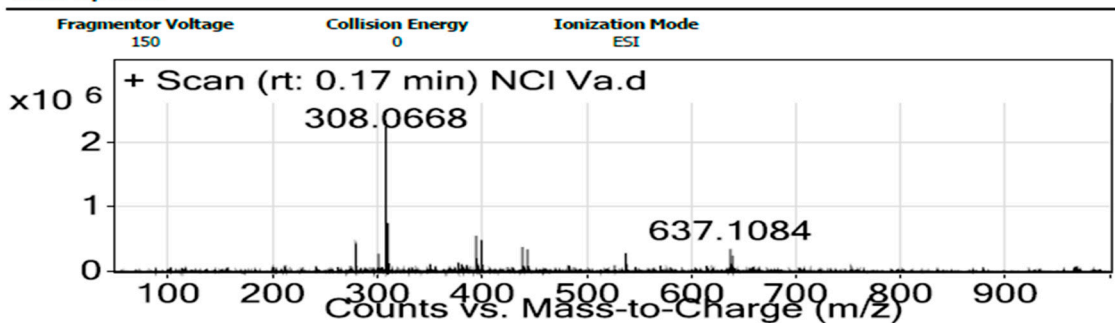


Figure S17. MS spectrum of 2-((3-chloro-1,4-dioxo-1,4-dihydronaphthalen-2-yl)amino)-3-methylbutanoic acid (4b).

| | | | |
|-------------------------------|-------------------|----------------------|----------------------|
| Data Filename | NCI Trp.d | Sample Name | NCI Trp |
| Sample Type | Sample | Position | P1-B3 |
| Instrument Name | LC QTOF-LANCIC | User Name | |
| Acq Method | Ine directa pos.m | Acquired Time | 3/15/2019 1:07:43 PM |
| IRM Calibration Status | Success | DA Method | Everardo ESI MS.m |
| Comment | | | |

| | | | |
|---------------------|------|-----------------------|-----------------------------|
| Sample Group | | Info. | |
| Stream Name | LC 1 | Acquisition SW | 6200 series TOF/6500 series |
| | | Version | Q-TOF B.06.01 (B6172 SP1) |

User Spectra

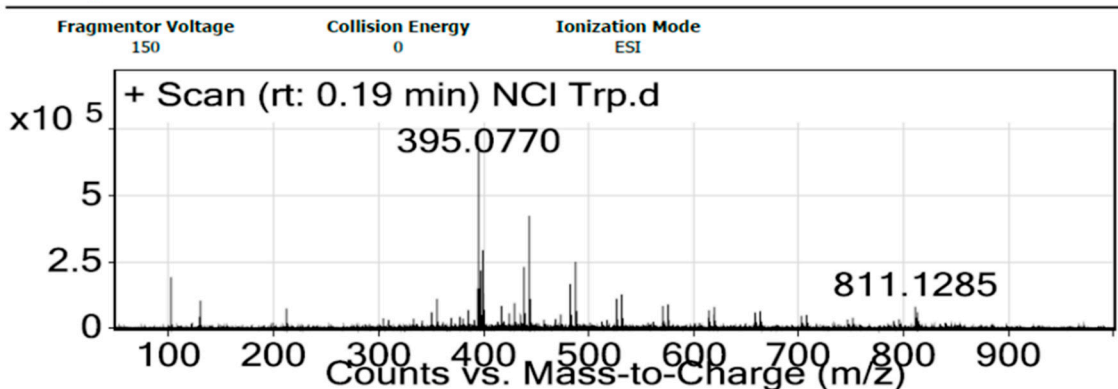


Figure S18. MS spectrum of 2-((3-chloro-1,4-dioxo-1,4-dihydronaphthalen-2-yl)amino)-3-(1H-indol-3-yl)propanoic acid (4c).

4. EPR Characterization

Compound 2-((1,4-dioxo-1,4-dihydronaphthalen-2-yl)amino)-4-(methylthio)butanoic acid

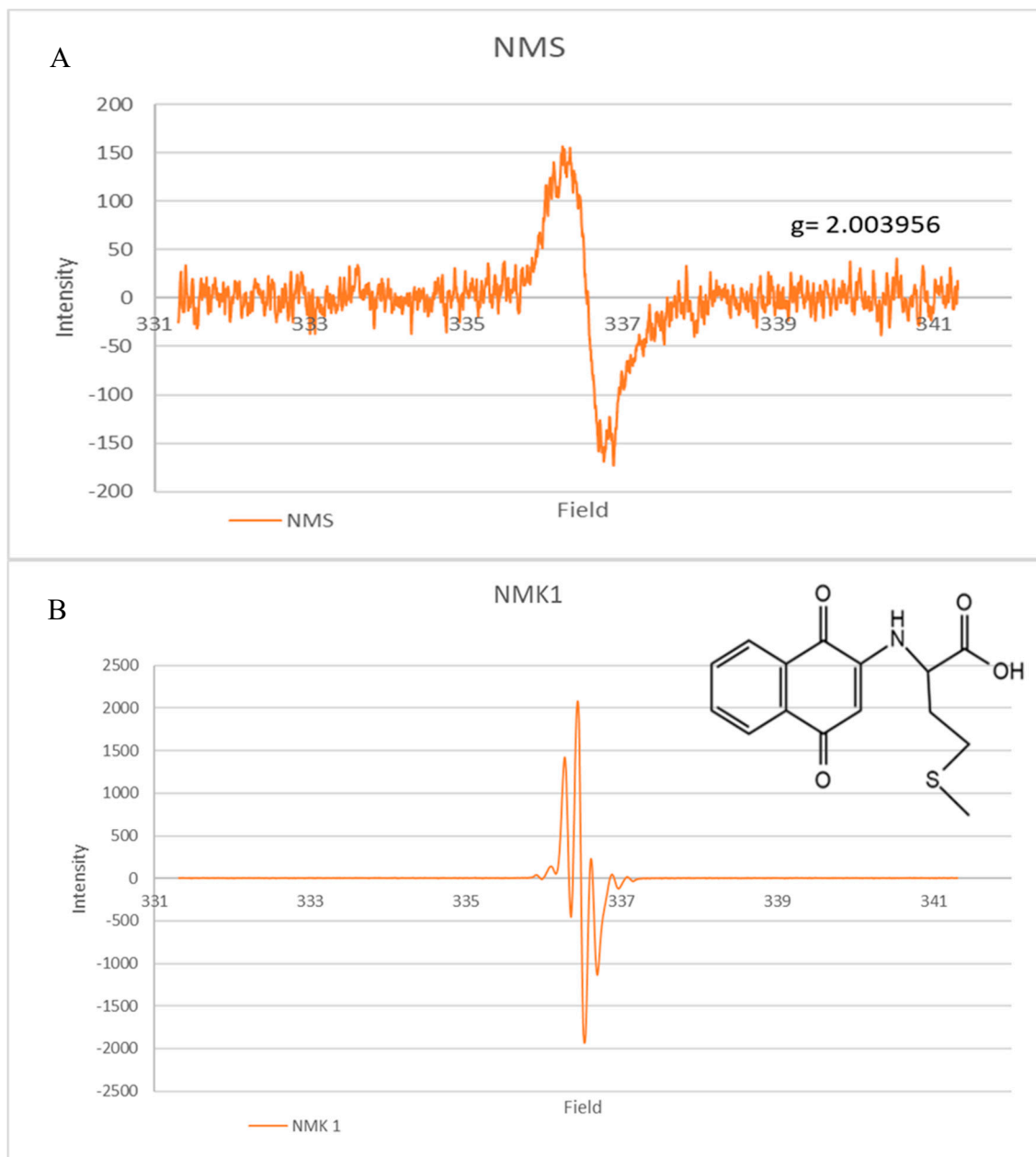


Figure S19. EPR spectrum of 2-((1,4-dioxo-1,4-dihydronaphthalen-2-yl)amino)-4-(methylthio)butanoic acid, in solid state (A) and KOH 1N solution (B).