

Supporting Information

Cu-Al mixed oxides catalysts for the azide-alkyne 1,3-cycloaddition in ethanol-water

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1. General methods

Commercially available reagents and solvents were used as received. Column chromatography was performed on Kiesel gel silica gel 60 (230-400 mesh). Melting points were determined using a Fisher-Johns apparatus and are uncorrected. The NMR spectra were obtained using Bruker Ascend-400 (400 MHz) and Bruker Avance DMX-500 (500 MHz) spectrometers. Chemical shifts (δ) are given in ppm and coupling constants J are given in hertz (Hz). Mass spectra (MS) were recorded on a GC-MS, Agilent Technologies 6890N, Detector 5973, column HP5-MS 30m x 0.25 mm x 0.25 μ m, in the chemical ionization mode using methane UAP grade as ionization gas. High-resolution mass spectra (HRMS) were recorded on a JEOL JMS-SX 102a and Agilent-MSD-TOF-1069A spectrometers. Microwave irradiation experiments were performed on a Discover System (CEM Corporation) single-mode microwave using standard sealed microwave glass vials. Simultaneous air jet cooling (3-4 bar) during microwave irradiation was performed by using a compressor. The nitrogen adsorption-desorption isotherm of HDL was obtained at -196 °C on Micromeritics ASAP 2020 equipment. Powder X-ray diffraction (XRD) was performed using a Philips X'Pert Instrument with Cu-K α radiation (45kV, 40 mA). SEM-EDS images and emission spectra were obtained using a Zeiss SUPRA 55 VP microscope with secondary electron and Oxford detector.

2. Experimental procedures

Synthesis of Cu-Al layered double hydroxide (LDH)

LDHs were prepared by dissolving 11.6 g of $\text{Cu}(\text{NO}_3)_2 \cdot 2.5\text{H}_2\text{O}$ and 9.37 g of $\text{Al}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ in 90 mL of deionized H_2O at room temperature. Then, 100 mL of 0.5M Na_2CO_3 was added at room temperature. The green gel formed, was heated to 40 °C in a microwave (90W, 250 psi) for 5 minutes. The obtained gel was washed five times with deionized H_2O to pH 7. The material was dried at 120° C for 18 hours.

Preparation of Cu(Al)O mixed oxides

The calcined material was obtained by heating of as-synthesized LDH at 540°C in a tubular furnace under N_2 flow for 6 hours. 7 g of a black solid is stable in air, which was characterized by XRD, IR, nitrogen physisorption and scanning electron microscopy was obtained.

Characterization of Cu-Al layered double hydroxide (LDH) and Cu(Al)O mixed oxides

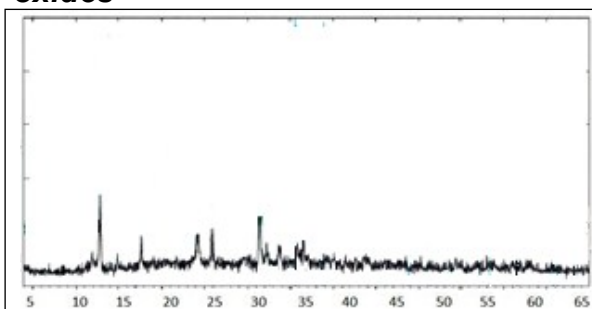


Figure S1. X-ray diffraction patterns of as-synthesized LDH

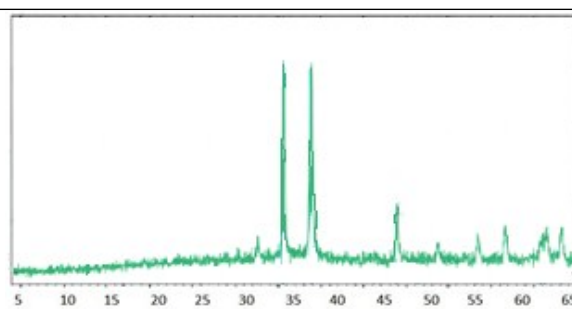


Figure S2. X-ray diffraction patterns of Cu(Al)O mixed oxide

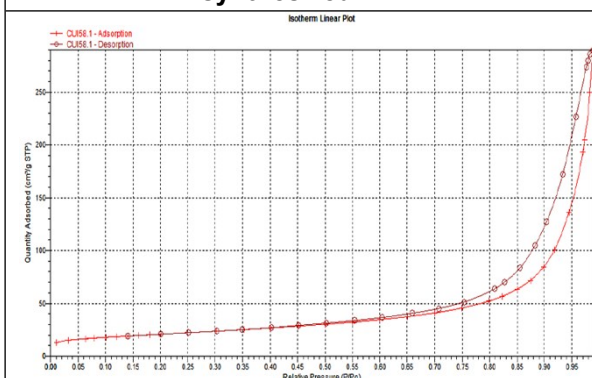


Figure S3. Nitrogen adsorption-desorption isotherms of as-synthesized LDH

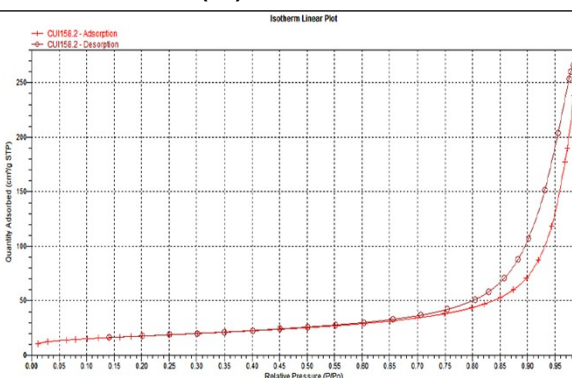


Figure S4. Nitrogen adsorption-desorption isotherms of Cu(Al)O mixed oxide

Table S1. The nitrogen adsorption-desorption analysis parameters of materials

Parameters	LDH	Mixed oxide
S_{BET} ($m^2 \cdot g^{-1}$)	74	63
Pore volume ($cm^3 \cdot g^{-1}$)	0.44	0.42
Pore size (Å)	161	174

Table S2. Composition of materials

Element	Weight% LDH	Weight% Mixed oxide
O	50.28	49.32
Al	11.79	12.39
Si	0.45	0.35
Cu	37.48	37.94
Total	100.00	100.00

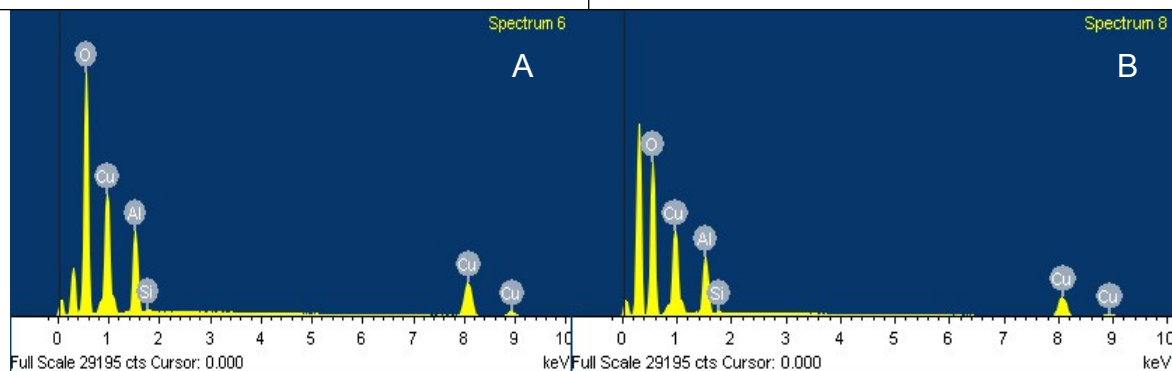


Figure S5. SEM-EDX spectra of (A) as-synthesized LDH and (B) Cu(Al)O mixed oxide

The as-synthesized LDH exhibited Cu–Al reflections associated with the layered double hydroxide crystal structure. The maxima correspond to typical diffraction by planes (1 1 0), (0 0 2), (1 1 1), (1 1 2), (0 2 0), (1 0 1) and (1 1 3) (Figure S1). These planes are similar to those shown by malachite [Cu₂CO₃(OH)₂] because of the presence of Cu in the material. Calcining the material yields a Cu(Al)O mixed oxide with a periclase-like structure with (110), (111), (202), (022), (113), (311) and (220) plane reflections, which are typical of CuO (Figure S2). The nitrogen adsorption-desorption isotherm of as-synthesized LDH (Figure S3) and the Cu(Al)O mixed oxide (Figure S4) showed a profile corresponding to type II of the IUPAC classification, typical for mesoporous materials. The as-synthesized LDH and the Cu(Al)O mixed oxide surface area, pore volume, and pore size are shown in the Table S1. SEM-EDS analysis revealed the presence of Cu in the as-synthesized LDH and the mixed oxide structure, as shown in the emission spectra of Figure S5 and elemental composition (Table S2). The thermal decomposition behaviour of the as-synthesized and calcinated hydrotalcite was observed by TGA analysis in nitrogen atmosphere Figure S6.

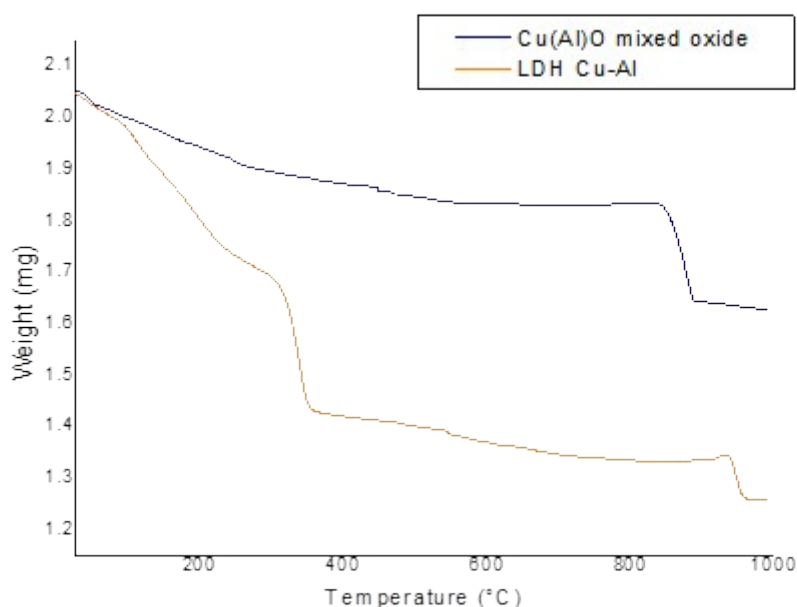


Figure S6

Characterization of Cu(Al)O mixed oxides after ten catalytic cycles

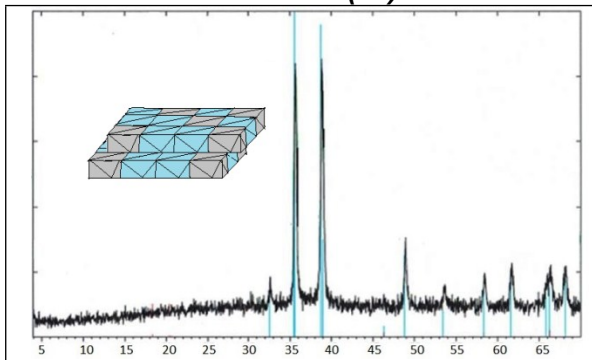


Figure S7. X-ray diffraction patterns Cu(Al)O mixed oxide

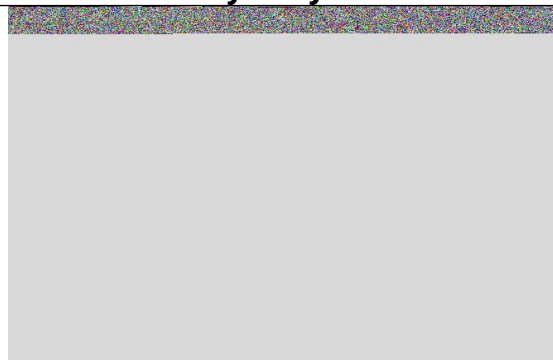


Figure S8. Nitrogen adsorption-desorption isotherms of Cu(Al)O mixed oxide

Table S3. The nitrogen adsorption-desorption analysis parameters of Cu(Al)O mixed oxide

Parameters	
S_{BET} ($m^2 \cdot g^{-1}$)	63
Pore volume ($cm^3 \cdot g^{-1}$)	0.42
Pore size (Å)	174

Table S4. Composition of materials Cu(Al)O mixed oxide

Element	Weight%
O	49.82
Al	12.08
Si	0.34
Cu	37.76
Total	100.00

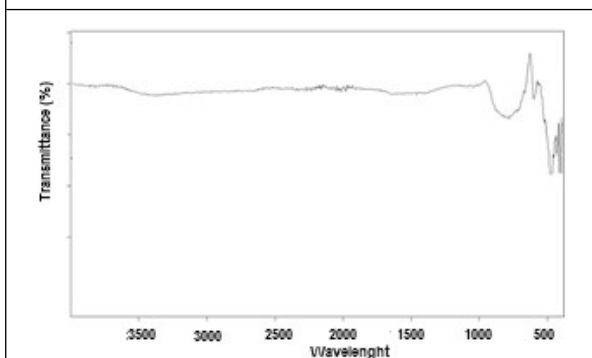


Figure S9. IR spectra of Cu(Al)O mixed oxide



Figure S10. SEM-EDX spectra of Cu(Al)O mixed oxide

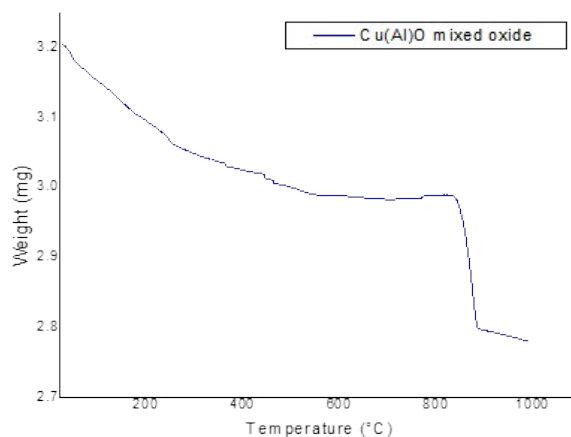


Figure S11. Thermograms of of Cu(Al)O mixed oxide

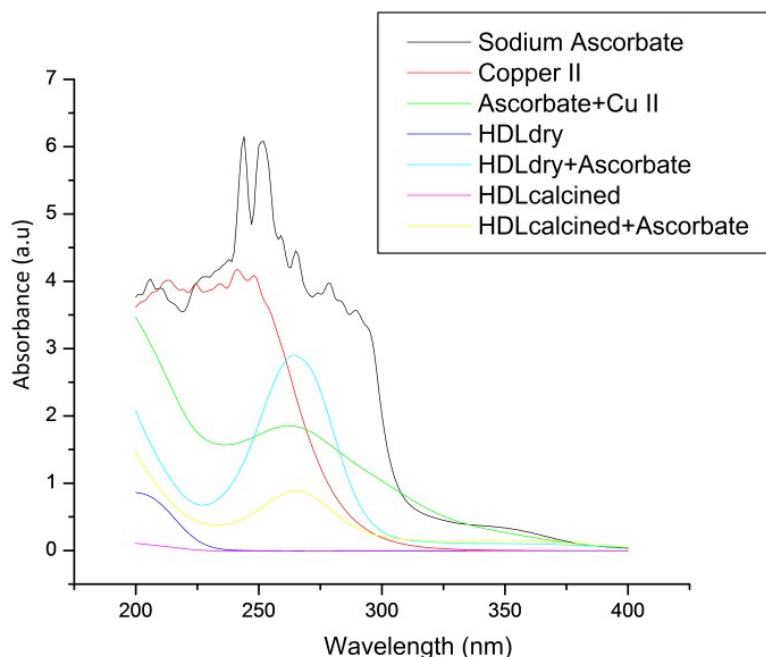
Determination of Cu II in the recovered EtOH-H₂O mixture

Figure S5. Quantification of Cu²⁺ by UV in the mixture EtOH-H₂O

General procedure for the synthesis of 1,2,3-triazoles 3a-3g

A mixture of catalyst (10 mg) and EtOH-H₂O (2 mL, 3:1 v/v) was placed in a microwave tube having a magnetic stirrer. Subsequently, alkyne **1a-1e** (1 mmol), benzyl halide **2a-2e** (1.2 mmol), NaN₃ (1.2 mmol), and sodium ascorbate (10 mg), were added to the mixture, which was heated under microwave irradiation (30 W, 80 °C) during 10 minutes. Then, the material was removed by centrifugation and washed with CH₂Cl₂ (5x5mL). The combined organic extracts were evaporated, giving the corresponding 1,2,3-triazole, which was purified by column chromatography (CH₂Cl₂ or hexanes-EtOAc 1:1) and/or recrystallization (CH₂Cl₂-hexanes, 1:2).

General procedure for the synthesis of alkynes 1b-1e

Alkynes **1b-1c** were synthesized according to our previously reported method.¹

Alkynes **1d-1e** were synthesized according to our previously reported method.²

General procedure for the synthesis of steroidal mesylate derivatives

Mesylates **4a**, **4c**, **4e** and **4g** were synthesized by literature procedures.³

General procedure for the synthesis of steroidal azide derivative-s

Azides **4b**, **4d**, **4f** and **4h** were synthesized by literature procedures.⁴

General procedure for the synthesis of 1,2,3-triazoles 5a-5f from steroidal azide

A mixture of catalyst (10 mg) and EtOH-H₂O (2 mL, 3:1 v/v) was placed in a microwave tube having a magnetic stirrer. Subsequently, alkyne **1d-1e** (1 mmol), steroidal azide derivatives **4b**, **4d**, **4f** or **4h** (1.2 mmol), and sodium ascorbate (10 mg), were added to the mixture, which was heated under microwave irradiation (30 W, 80 °C) during 10 minutes. Then, the material was removed by centrifugation and washed with CH₂Cl₂ (5x5mL). The combined organic extracts were evaporated, giving the corresponding 1,2,3-triazole, which was purified by column chromatography (CH₂Cl₂ or hexanes-EtOAc 1:1) and recrystallization (CH₂Cl₂-hexanes, 1:2).

General procedure for the synthesis of 1,2,3-triazoles 5a-5f from mesylate derivatives

A mixture of catalyst (10 mg) and EtOH-H₂O (2 mL,3:1) was placed in a microwave tube having a magnetic stirrer. Subsequently, alkyne **1d-1e** (1 mmol), mesilate derivatives **4a**, **4c**, **4e** or **4g** (1.2 mmol), NaN₃ (1.2 mmol), and sodium ascorbate (10 mg), were added to the mixture, which was heated under microwave irradiation (30 W, 80 °C) during 10 minutes. Then, the material was removed by centrifugation and washed with CH₂Cl₂ (5x5mL). The combined organic extracts were evaporated, giving the corresponding 1,2,3-triazole, which was purified by column chromatography (CH₂Cl₂ or hexanes-EtOAc 1:1) and recrystallization (CH₂Cl₂-hexanes, 1:2).

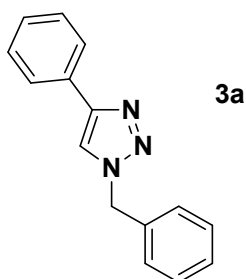
General procedure to screen the recyclability

A mixture of catalyst (10 mg) and EtOH-H₂O (2 mL, 3:1 v/v) was placed in a microwave tube having a magnetic stirrer. Subsequently, alkyne **1a** (1 mmol), benzyl halide **2a** (1.2 mmol), NaN₃ (1.2 mmol), and sodium ascorbate (10 mg), were added to the mixture, which was heated under microwave irradiation (30 W, 80 °C) during 10 minutes. Then, the material was removed by centrifugation and washed with

CH₂Cl₂ (5x5mL). The combined organic extracts were evaporated, giving the corresponding 1,2,3-triazole, which was purified by column chromatography (CH₂Cl₂ or hexanes-EtOAc 1:1) and/or recrystallization (CH₂Cl₂-hexanes, 1:2).

3. Characterization data

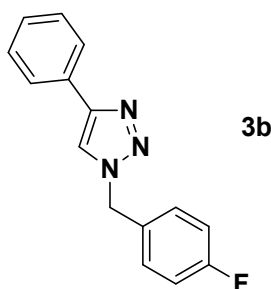
1-Benzyl-4-phenyl-1*H*-1,2,3-triazole (3a).



White solid, yield 98%, mp = 129-131 °C [Lit.⁵ mp = 127-130 °C].

FT-IR/ATR ν_{\max} cm⁻¹: 3108, 3081, 1686, 1482, 1403. NMR ¹H (CDCl₃, 500 MHz): δ = 5.56 (s, 2H, NCH₂), 7.28-7.32 (m, 3H, ArH), 7.35-7.41 (m, 5H, ArH), 7.65 (s, 1H, ArH, triazole), 7.77-7.80 (m, 2H, ArH). NMR ¹³C (CDCl₃, 125.7 MHz): δ = 54.2 (NCH₂), 119.5 (ArCH, triazole), 125.7 (2xArCH), 128.1 (2xArCH), 128.2 (ArCH), 128.78 (ArCH), 128.8 (2xArCH), 129.1 (2xArCH), 130.6 (C_{ipso}), 134.7 (C_{ipso}), 148.2 (C_{ipso}, triazole). EM (CI) for C₁₅H₁₃N₃ m/z : 236 [M+1]⁺, 264 [M+29]⁺, 276 [M+41]⁺, 91 (PhCH₂).

1-(4-Fluorobenzyl)-4-phenyl-1*H*-1,2,3-triazole (3b).

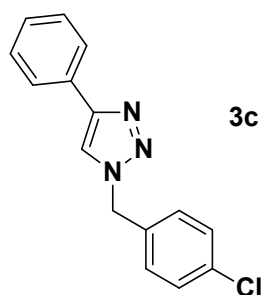


White solid, yield 90%, mp = 132-134 °C [Lit.⁵ mp = 128-130 °C].

FT-IR/ATR ν_{\max} cm⁻¹: 3119, 3083, 1601, 1480, 1350. NMR ¹H (CDCl₃, 500 MHz): δ = 5.55 (s, 2H, NCH₂), 7.06-7.11 (m, 2H, ArH), 7.30-7.36 (m, 3H, ArH), 7.40-7.44 (m, 2H, ArH), 7.68 (s, 1H, ArH, triazole), 7.80-7.83 (m, 2H, ArH). NMR ¹³C (CDCl₃, 125.7 MHz): δ = 53.5 (NCH₂), 116.1 (d, J = 22.6 Hz, 2xArCH), 119.4 (ArCH, triazole), 125.7 (2xArCH), 128.2 (ArCH), 128.8 (2xArCH), 129.9 (d, J = 8.8 Hz, 2xArCH), 130.4

(C_{ipso}), 130.6 (d, $J = 3.8$ Hz, C_{ipso}), 148.3 (C_{ipso}, triazole), 162.9 (d, $J = 247.6$ Hz, F-C_{ipso}).

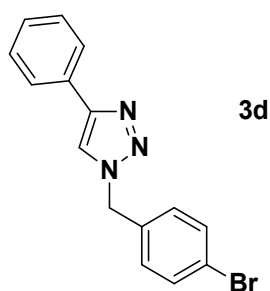
1-(4-Chlorobenzyl)-4-phenyl-1*H*-1,2,3-triazole (3c).



White solid, yield 95%, mp = 140-142 °C [Lit.⁵ mp = 142-145 °C].

FT-IR/ATR ν_{\max} cm⁻¹: 3108, 3082, 3065, 1595, 1578, 1481, 1411. NMR ¹H (CDCl₃, 500 MHz): δ = 5.52 (s, 2H, NCH₂), 7.21-7.24 (m, 2H, ArH), 7.29-7.36 (m, 3H, ArH), 7.37-7.41 (m, 2H, ArH), 7.66 (s, 1H, ArH, triazole), 7.77-7.80 (m, 2H, ArH). NMR ¹³C (CDCl₃, 125.7 MHz): δ = 53.5 (NCH₂), 119.5 (ArCH, triazole), 125.7 (2xArCH), 128.3 (ArCH), 128.8 (2xArCH), 129.35 (2xArCH), 129.36 (2xArCH), 130.4 (C_{ipso}), 133.2 (C_{ipso}), 134.8 (C_{ipso}), 148.4 (C_{ipso}, triazole). EM (CI) for C₁₅H₁₂ClN₃ m/z : 270 [M+1]⁺, 298 [M+29]⁺, 312 [M+41]⁺, 125 (Cl-PhCH₂).

1-(4-Bromobenzyl)-4-phenyl-1*H*-1,2,3-triazole (3d).

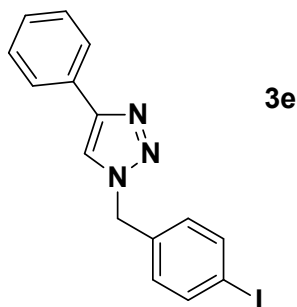


White solid, yield 85%, mp = 138-140 °C [Lit.⁶ mp = 151-152 °C].

FT-IR/ATR ν_{\max} cm⁻¹: 3106, 3082, 3055, 1686, 1577, 1481, 1407. NMR ¹H (CDCl₃, 500 MHz): δ = 5.54 (s, 2H, NCH₂), 7.19 (d, $J = 8.7$ Hz, 2H, ArH), 7.32-7.36 (m, 1H, ArH), 7.40-7.44 (m, 2H, ArH), 7.53 (d, $J = 8.7$ Hz, 2H, ArH), 7.69 (s, 1H, ArH, triazole), 7.80-7.83 (m, 2H, ArH). NMR ¹³C (CDCl₃, 125.7 MHz): δ = 53.5 (NCH₂), 119.5 (ArCH, triazole), 122.9 (Br-C_{ipso}), 125.7 (2xArCH), 128.3 (ArCH), 128.8

(2xArCH), 129.6 (2xArCH), 130.4 (C_{ipso}), 132.3 (2xArCH), 133.7 (C_{ipso}), 148.4 (C_{ipso}, triazole). EM (CI) for C₁₅H₁₂Br₁N₃ *m/z*: 314 [M+1]⁺, 342 [M+29]⁺, 356 [M+41]⁺, 91 (PhCH₂), 171 (Br-PhCH₂), 236 (C₁₅H₁₃N₃).

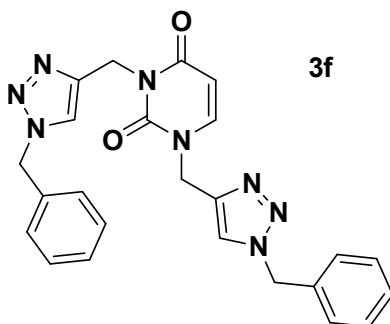
1-(4-Iodobenzyl)-4-phenyl-1*H*-1,2,3-triazole (3e).



White solid, yield 90%, mp = 167-169 °C. [Lit.⁶ mp = 154-156 °C].

FT-IR/ATR ν_{\max} cm⁻¹: 3108, 3081, 1686, 1581, 1482, 1403. NMR ¹H (CDCl₃, 500 MHz): δ = 5.49 (s, 2H, NCH₂), 7.03 (d, *J* = 8.1 Hz, 2H, ArH), 7.25-7.33 (m, 1H, ArH), 7.37-7.41 (m, 2H, ArH), 7.66 (s, 1H, ArH, triazol), 7.70 (d, *J* = 8.3 Hz, 2H, ArH), 7.77-7.80 (m, 2H, ArH). NMR ¹³C (CDCl₃, 125.7 MHz): δ = 53.7 (NCH₂), 94.7 (I-C_{ipso}), 119.6 (ArCH, triazole), 125.8 (2xArCH), 128.4 (ArCH), 128.9 (2xArCH), 129.9 (2xArCH), 130.4 (C_{ipso}), 134.4 (C_{ipso}), 138.4 (2xArCH), 148.5 (C_{ipso}, triazole). EM (CI) para C₁₅H₁₂I₁N₃ *m/z*: 362 [M+1]⁺, 390 [M+29]⁺, 402 [M+41]⁺, 217 (I-PhCH₂), 236 (C₁₅H₁₃N₃), 91 (PhCH₂).

1,3-Bis((1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl)pyrimidine-2,4-(1*H*,3*H*)-dione (3f).

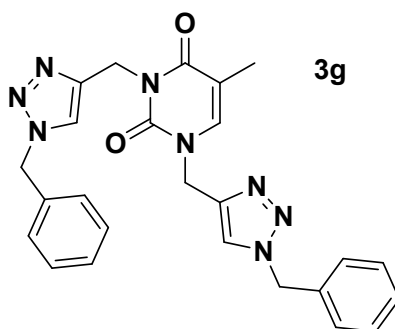


White solid, yield 90%, mp =175–176 °C [Lit.¹ mp = 171-172 °C].

FT-IR/ATR ν_{\max} cm⁻¹: 3133, 3067, 3012, 2954, 1700, 1650, 1555, 1496, 1452, 1434.

NMR ¹H (CDCl₃, 500 MHz): δ = 4.93 (s, 2H, CH₂NC=O), 5.15 (s, 2H, CH₂NC=O), 5.43 (s, 2H, NCH₂Ph), 5.47 (s, 2H, NCH₂Ph), 5.69 (d, J = 7.9 Hz, 1H, CH), 7.20–7.28 (m, 4H, ArH), 7.32–7.42 (m, 6H, ArH), 7.44 (d, J = 8.0 Hz, 1H, NCH), 7.49 (s, 1H, ArH, triazole), 7.62 (s, 1H, ArH, triazole). NMR ¹³C (CDCl₃, 125.7 MHz): δ = 36.2 (CH₂NC=O), 44.2 (CH₂NC=O), 54.2 (NCH₂Ph), 54.4 (NCH₂Ph), 102.0 (CH), 123.4 (ArCH, triazole), 123.7 (ArCH, triazole), 128.2 (2×ArCH), 128.4 (2×ArCH), 128.8 (ArCH), 129.0 (ArCH), 129.1 (2×ArCH), 129.3 (2×ArCH), 134.2 (C_{ipso}), 134.6 (C_{ipso}), 142.3 (C_{ipso}, triazole), 142.6 (NCH), 143.4 (C_{ipso}, triazole), 151.2 (N₂C=O), 162.6 (NC=O).

1,3-bis((1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (3g).

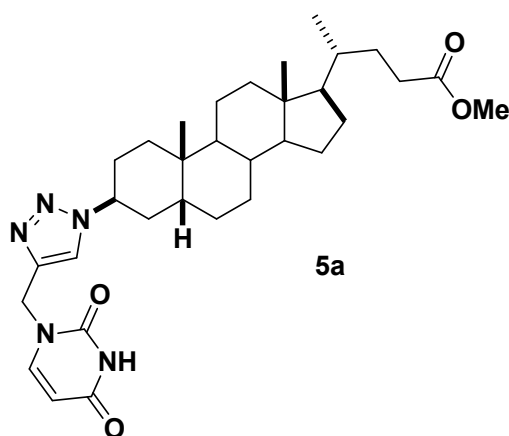


White solid, yield 90%, mp =187–189 °C [Lit.¹ mp = 187-189 °C].

FT-IR/ATR ν_{\max} cm⁻¹: 3133, 3115, 3068, 2956, 1697, 1672, 1646, 1550, 1496, 1453,

1432. NMR ¹H (CDCl₃, 500 MHz): δ = 1.86 (d, J = 1.0 Hz, 3H, CH₃), 4.91 (s, 2H, CH₂NC=O), 5.16 (s, 2H, CH₂NC=O), 5.43 (s, 2H, NCH₂Ph), 5.46 (s, 2H, NCH₂Ph), 7.21–7.28 (m, 4H, ArH), 7.29 (d, J = 1.1 Hz, 1H, NCH), 7.30–7.37 (m, 6H, ArH), 7.49 (s, 1H, ArH, triazole), 7.62 (s, 1H, ArH, triazole). NMR ¹³C (CDCl₃, 125.7 MHz): δ = 13.0 (CH₃), 36.4 (CH₂NC=O), 43.9 (CH₂NC=O), 54.2 (NCH₂Ph), 54.4 (NCH₂Ph), 110.3 (CCH₃), 123.5 (ArCH, triazole), 123.7 (ArCH, triazole), 128.2 (2×ArCH), 128.4 (2×ArCH), 128.8 (ArCH), 129.0 (ArCH), 129.1 (2×ArCH), 129.3 (2×ArCH), 134.3 (C_{ipso}), 134.7 (C_{ipso}), 138.7 (NCH), 142.6 (C_{ipso}, triazole), 143.5 (C_{ipso}, triazole), 151.2 (N₂C=O), 163.5 (NC=O).

(4*R*)-methyl 4-((3*S*,5*R*,10*S*,13*R*,17*R*)-3-(4-((2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)methyl)-1*H*-1,2,3-triazol-1-yl)-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)pentanoate (5a).



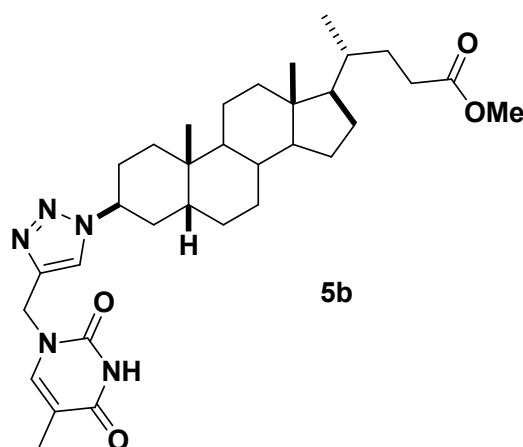
White solid, yield 90%, mp = 105-107°C, $[\alpha]^{25}_D = +23.75$ (c 0.1, CHCl₃).

NMR ¹H (500 MHz, CDCl₃): δ = 0.65 (s, 3H, CH₃), 0.91 (s, 3H, CH₃), 0.92 (d, 3H, *J* = 6.5 Hz, CH₃), 1.05-1.20 (m, 6H, CH₂, CH), 1.24-1.48 (m, 9H, CH₂, CH), 1.57-1.64 (m, 3H, CH₂, CH), 1.76-1.92 (m, 3H, CH₂), 1.96-2.04 (m, 3H, CH₂), 2.14-2.18 (m, 1H, CH₂), 2.19-2.26 (m, 1H, CH₂), 2.35 (m, 2H, CH₂), 3.66 (s, 3H, OCH₃), 4.67 (m, 1H, CH), 5.01 (d, *J* = 15.0 Hz, 1H, CH), 5.02 (d, *J* = 15.0 Hz, 1H, CH), 5.72 (d, *J* = 7.0 Hz, 1H, CH), 7.58 (d, 1H, *J* = 7.0 Hz, CH), 7.76 (s, 1H, ArH, triazole), 9.25 (brs, 1H, NH). NMR ¹³C (125.7 MHz, CDCl₃): δ = 12.0 (CH₃), 18.3 (CH₃), 21.0 (CH₂), 23.8 (CH₃), 24.2 (CH₂), 24.9 (CH₂), 26.1 (CH₂), 26.4 (CH₂), 28.2 (CH₂), 29.8 (CH₂), 30.7 (CH₂), 31.0 (CH₂), 31.1 (CH₂), 34.8 (C), 35.4 (CH), 35.6 (CH), 37.3 (CH), 40.1 (CH₂), 40.5 (CH), 42.8 (C), 43.0 (CH₂), 51.5 (OCH₃), 56.0 (CH), 56.6 (CH), 57.1 (CH), 102.6 (=CH), 122.8 (ArCH, triazole), 141.2 (C_{ipso}, triazole), 144.4 (=CH), 150.9 (NC=O), 163.6 (NC=O), 174.8 (OC=O). FT-IR/ATR ν_{\max} cm⁻¹: 3487, 2934, 2862, 1732, 1712,

Supporting Information

1675, 1462, 1436, 1241, 1208. HRMS (ESI-TOF) calculated for $C_{32}H_{47}N_5O_4 + H^+$: 566.3701; Found: 566.3702.

(4*R*)-methyl 4-((3*S*,5*R*,10*S*,13*R*,17*R*)-10,13-dimethyl-3-(4-((5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)methyl)-1*H*-1,2,3-triazol-1-yl)hexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)pentanoate (5b).



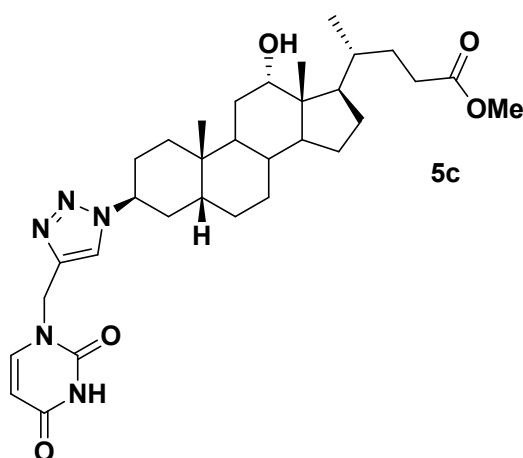
White solid, yield 98%, mp = 163-165°C, $[\alpha]^{25}_D = +21.52$ (c 0.1, $CHCl_3$).

NMR 1H (500 MHz, $CDCl_3$): δ = 0.64 (s, 3H, CH_3), 0.90 (s, 3H, CH_3), 0.91 (d, 3H, J = 6.4 Hz, CH_3), 1.04-1.20 (m, 6H, CH_2 , CH), 1.24-1.37 (m, 4H, CH_2), 1.38-1.48 (m, 5H, CH_2 , CH), 1.57-1.64 (m, 3H, CH_2 , CH), 1.76-1.89 (m, 3H, CH_2), 1.90 (d, J = 1.1 Hz, 3H, CH_3), 1.92-2.04 (m, 3H, CH_2), 2.14-2.18 (m, 1H, CH_2), 2.19-2.25 (m, 1H, CH_2), 2.35 (m, 2H, CH_2), 3.66 (s, 3H, OCH_3), 4.66 (m, 1H, CH), 4.94 (d, J = 15.0 Hz, 1H, CH), 4.98 (d, J = 15.0 Hz, 1H, CH), 7.37 (q, J = 1.2 Hz, 1H, CH), 7.73 (s, 1H, ArH, triazole), 9.04 (s, 1H, NH). NMR ^{13}C (125.7 MHz, $CDCl_3$): δ = 12.1 (CH_3), 12.3 (CH_3 , thymine), 18.3 (CH_3), 21.0 (CH_2), 23.8 (CH_3), 24.2 (CH_2), 24.9 (CH_2), 26.1 (CH_2), 26.4 (CH_2), 28.2 (CH_2), 29.8 (CH_2), 30.7 (C), 31.0 (CH_2), 31.1 (CH_2), 34.8 (C), 35.4 (CH), 35.6 (CH), 37.3 (CH), 40.2 (CH_2), 40.5 (CH), 42.76 (C), 42.8 (CH_2), 51.5 (OCH_3), 56.0 (CH), 56.6 (CH), 57.1 (CH), 111.2 (=C), 122.7 (ArCH, triazole), 140.3 (=CH), 141.5 (C_{ipso} , triazole), 150.9 (NC=ON), 164.1 (NC=O), 174.7 (OC=O). FT-

Supporting Information

IR/ATR ν_{\max} cm^{-1} : 2925, 2860, 1733, 1674, 1655, 1450, 1434, 1215, 1101, 1048, 777. HRMS (ESI-TOF) calculated for $\text{C}_{33}\text{H}_{49}\text{N}_5\text{O}_4 + \text{H}^+$: 580.3857; Found: 580.3860.

(4R)-methyl4-((5R,10S,12S,13R,17R)-3-(4-((2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)methyl)-1H-1,2,3-triazol-1-yl)-12-hydroxy-10,13-dimethylhexadecahydro-1H-cyclopenta[a]phenanthren-17-yl)pentanoate (5c).

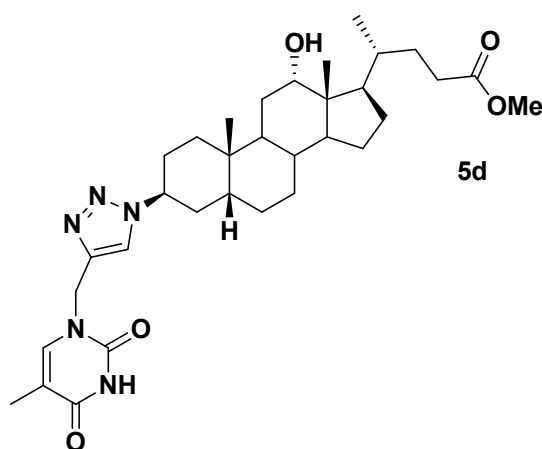


White solid, yield 65%, mp = 99-101°C, $[\alpha]_{\text{D}}^{25} = +42.80$ (c 0.1, CHCl_3).

NMR ^1H (500 MHz, CDCl_3): δ = 0.68 (s, 3H, CH_3), 0.89 (s, 3H, CH_3), 0.96 (d, 3H, J = 6.5 Hz, CH_3), 1.05-1.20 (m, 5H, CH_2 , CH), 1.24-1.48 (m, 9H, CH_2 , CH), 1.57-1.64 (m, 3H, CH_2 , CH), 1.76-1.92 (m, 3H, CH_2), 1.96-2.04 (m, 2H, CH_2), 2.14-2.18 (m, 1H, CH_2), 2.19-2.26 (m, 1H, CH_2), 2.35 (m, 2H, CH_2), 3.65 (s, 3H, OCH_3), 4.00 (dd, J = 3.8, 3.8 Hz, 1H, CH), 4.64 (m, 1H, CH), 4.96 (d, J = 15.1 Hz, 1H, CH), 5.0 (d, J = 15.1 Hz, 1H, CH), 5.69 (d, J = 7.9 Hz, 1H, CH), 7.55 (d, 1H, J = 7.9 Hz, CH), 7.74 (s, 1H, ArH, triazole), 9.47 (brs, 1H, NH). NMR ^{13}C (125.7 MHz, CDCl_3): δ = 12.8 (CH_3), 17.4 (CH_3), 23.6 (CH_2), 23.7 (CH_3), 24.9 (CH_2), 25.9 (CH_2), 26.4 (CH_2), 27.5 (CH_2), 28.8 (CH_2), 29.8 (CH_2), 30.6 (CH_2), 31.0 (CH_2), 31.1 (CH_2), 33.7 (CH), 34.4 (C), 35.1 (CH), 35.9 (CH), 37.3 (CH), 43.0 (CH_2), 46.6 (C), 47.5 (C), 48.4 (CH_2), 51.6 (OCH_3), 57.2 (CH), 73.2 (CH), 102.7 (=CH), 122.9 (ArCH, triazole), 141.3 (C_{ipso} , triazole), 144.5 (=CH), 151.1 (NC=ON), 163.8 (NC=O), 174.7 (OC=O). IR/ATR ν_{\max} cm^{-1} :

4828, 3071, 2931, 1678, 1448, 1376, 1348, 1243, 1093. HRMS (ESI-TOF) calculated for $C_{32}H_{47}N_5O_5 + H^+$: 582.3650; Found: 582.3653.

(4*R*)-methyl4-((5*R*,10*S*,12*S*,13*R*,17*R*)-12-hydroxy-10,13-dimethyl-3-(4-((5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)methyl)-1*H*-1,2,3-triazol-1-yl)hexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)pentanoate (5d).



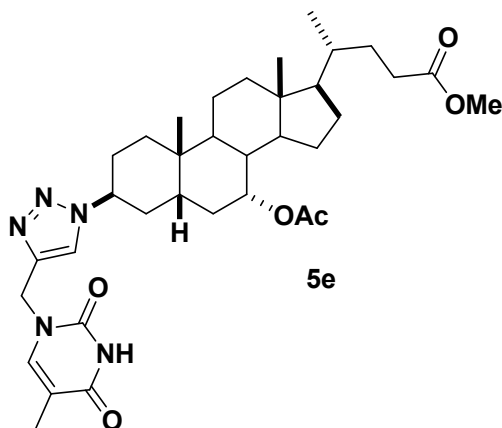
White solid, yield 70%, mp = 106-108°C [α]_D²⁵ = +46.97 (c 0.1, CHCl₃).

NMR ¹H (500 MHz, CDCl₃): δ = 0.67 (s, 3H, CH₃), 0.68 (s, 3H, CH₃), 0.89 (d, 3H, *J* = 6.4 Hz, CH₃), 1.04-1.20 (m, 5H, CH₂, CH), 1.24-1.37 (m, 4H, CH₂), 1.38-1.48 (m, 5H, CH₂, CH), 1.57-1.64 (m, 3H, CH₂, CH), 1.76-1.89 (m, 3H, CH₂), 1.90 (d, *J* = 1.1 Hz, 3H, CH₃), 1.92-2.04 (m, 2H, CH₂), 2.14-2.18 (m, 1H, CH₂), 2.19-2.25 (m, 1H, CH₂), 2.35 (m, 2H, CH₂), 3.66 (s, 3H, OCH₃), 4.01 (dd, *J* = 2.6, 2.6 Hz, 1H, CH), 4.64 (m, 1H, CH), 4.96 (d, *J* = 14.8 Hz, 1H, CH), 4.97 (d, *J* = 14.8 Hz, 1H, CH), 7.37 (q, *J* = 1.2 Hz, 1H, CH), 7.73 (s, 1H, ArH, triazole), 8.89 (s, 1H, NH). NMR ¹³C (125.7 MHz, CDCl₃): δ = 12.2 (CH₃), 12.7 (CH₃, thymine), 17.3 (CH₃), 23.5 (CH₃), 23.5 (CH₂), 24.7 (CH₂), 25.8 (CH₂), 26.2 (CH₂), 27.4 (CH₂), 28.7 (CH₂), 29.7 (CH₂), 30.5 (CH₂), 30.8 (CH₂), 31.0 (CH₂), 33.6 (CH), 35.0 (C), 35.7 (CH), 35.8 (CH), 37.2 (CH), 42.7 (CH₂), 46.6 (C), 47.4 (CH), 48.3 (CH), 51.5 (OCH₃), 57.2 (CH), 73.1 (CH), 111.1 (=C), 122.7 (ArCH, triazole), 140.3 (=CH), 150.7 (C_{ipso}, triazole), 164.0 (NC=ON), 174.6 (NC=O), 174.6 (OC=O). IR /ATR ν_{max} cm⁻¹: 4828, 3071, 2931, 1678, 1448,

Supporting Information

1376,1348,1243,1093. HRMS (ESI-TOF) calculated for $C_{33}H_{49}N_5O_5 + H^+$: 596.3767;
Found: 596.3760.

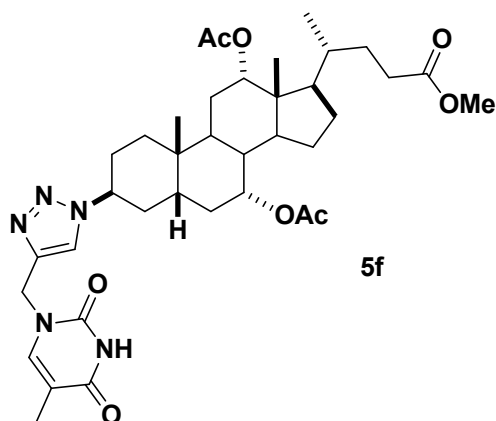
(4R)-methyl 4-((3S,5S,7R,10S,13R,17R)-7-acetoxy-10,13-dimethyl-3-(4-((5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)methyl)-1H-1,2,3-triazol-1-yl)hexadecahydro-1H-cyclopenta[a]phenanthren-17-yl)pentanoate (5e).



White solid, yield 95%, mp = 99-102°C, $[\alpha]^{25}_{\text{D}} = +25.29$ (c 0.1, CHCl₃).

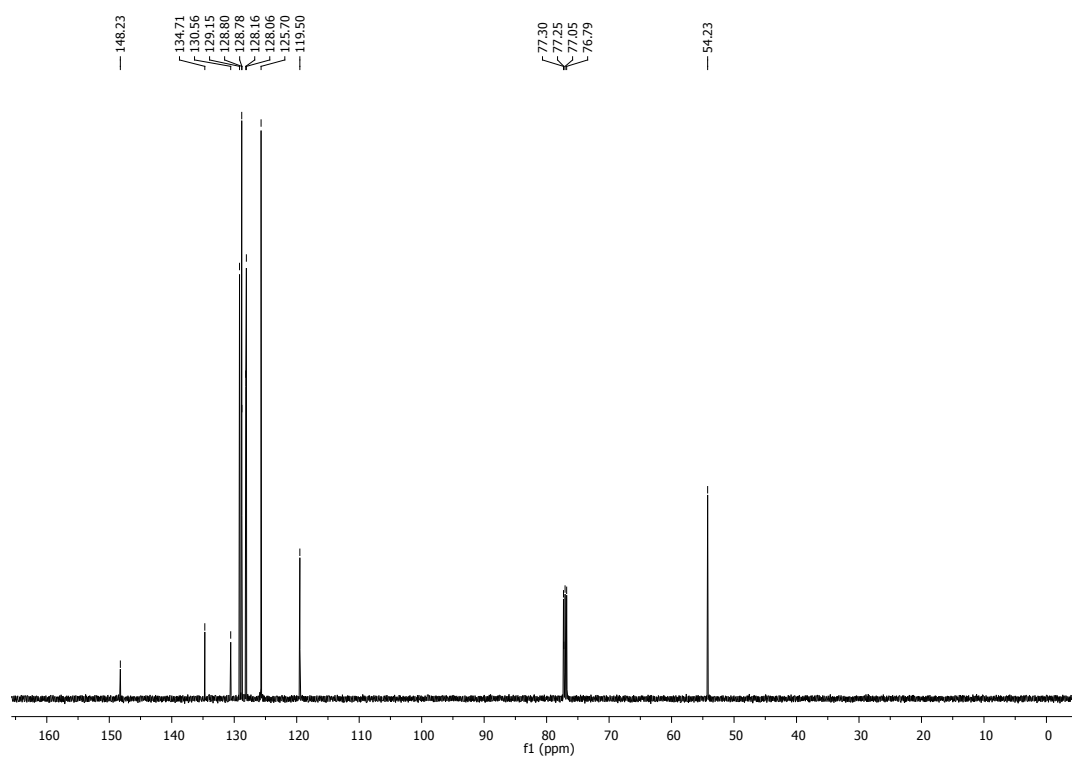
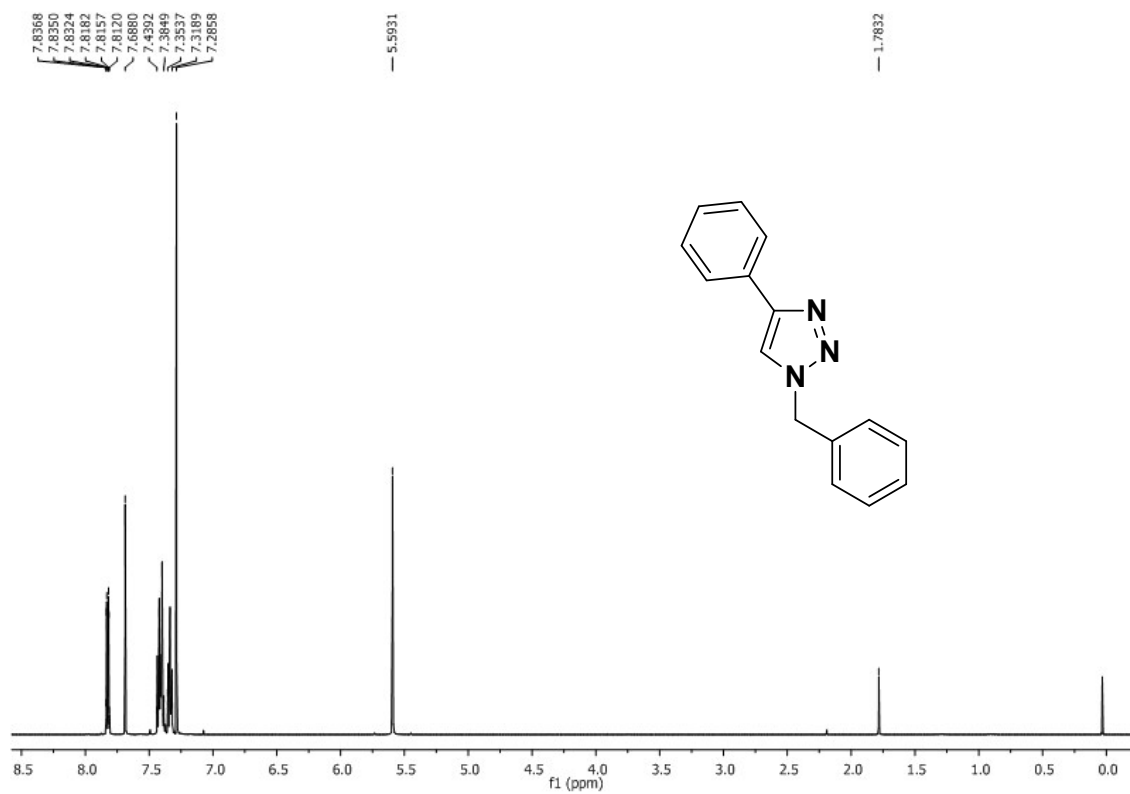
NMR ¹H (500 MHz, CDCl₃): δ = 0.66 (s, 3H, CH₃), 0.92 (s, 3H, CH₃), 0.93 (d, J = 6.6 Hz, 3H, CH₃), 1.05-1.52 (m, 11H, CH₂, CH), 1.58-1.70 (m, 4H, CH₂, CH), 1.76-1.88 (m, 3H, CH₂, CH), 1.90 (d, J = 0.8 Hz, 3H, CH₃, thymine), 1.95-2.03 (m, 3H, CH₂), 2.06 (s, 3H, CH₃, acetyl), 2.08-2.26 (m, 2H, CH₂), 2.34 (ddd, J = 14.0, 10.0, 5.0 Hz, 1H, CH₂), 2.61 (td, J = 14.0, 4.7, Hz, 1H, CH₂), 3.66 (s, 3H, OCH₃), 4.75 (m, 1H, CH), 4.91 (ddd, J = 14.0, 8.5, 3.0 Hz, 1H, CH), 4.93 (d, J = 15.1 Hz, 1H, CH), 4.96 (d, J = 15.1 Hz, 1H, CH), 7.35 (q, J = 0.8 Hz, 1H, =CH), 7.72 (s, 1H, ArH, triazole), 8.77 (brs, 1H, NH). NMR ¹³C (CDCl₃, 125.7 MHz): δ = 11.7 (CH₃), 12.3 (CH₃, thymine), 18.3 (CH₃), 20.8 (CH₂), 21.5 (CH₃, acetyl), 23.0 (CH₃), 23.5 (CH₂), 24.8 (CH₂), 28.0 (CH₂), 30.7 (CH₂), 30.88 (CH₂), 30.93 (CH₂), 31.0 (CH₂), 32.0 (CH₂), 34.2 (CH), 35.0 (C), 35.3 (CH), 36.4 (CH), 37.8 (CH), 39.5 (CH₂), 42.7 (C), 42.9 (CH₂), 50.4 (CH), 51.5 (OCH₃), 55.7 (CH), 56.9 (CH), 71.3 (CH), 111.1 (=C), 122.7 (ArCH, triazole), 140.2 (=CH), 141.6 (C_{ipso}, triazole), 150.8 (NC=ON), 163.9 (NC=O), 170.1 (OC=O, acetyl), 174.6 (OC=O). FT-IR/ATR ν_{max} cm⁻¹: 4848, 2930, 1679, 1436, 1373, 1244, 1018. HRMS (ESI-TOF) calculated for C₃₅H₅₁N₅O₆ + H⁺: 638.3912; Found: 638.3910.

(3*S*,5*S*,7*R*,10*S*,12*S*,13*R*,17*R*)-17-((*R*)-5-methoxy-5-oxopentan-2-yl)-10,13-dimethyl-3-(4-((5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)methyl)-1*H*-1,2,3-triazol-1-yl)hexadecahydro-1*H*-cyclopenta[*a*]phenanthrene-7,12-diyl diacetate (5f**).**



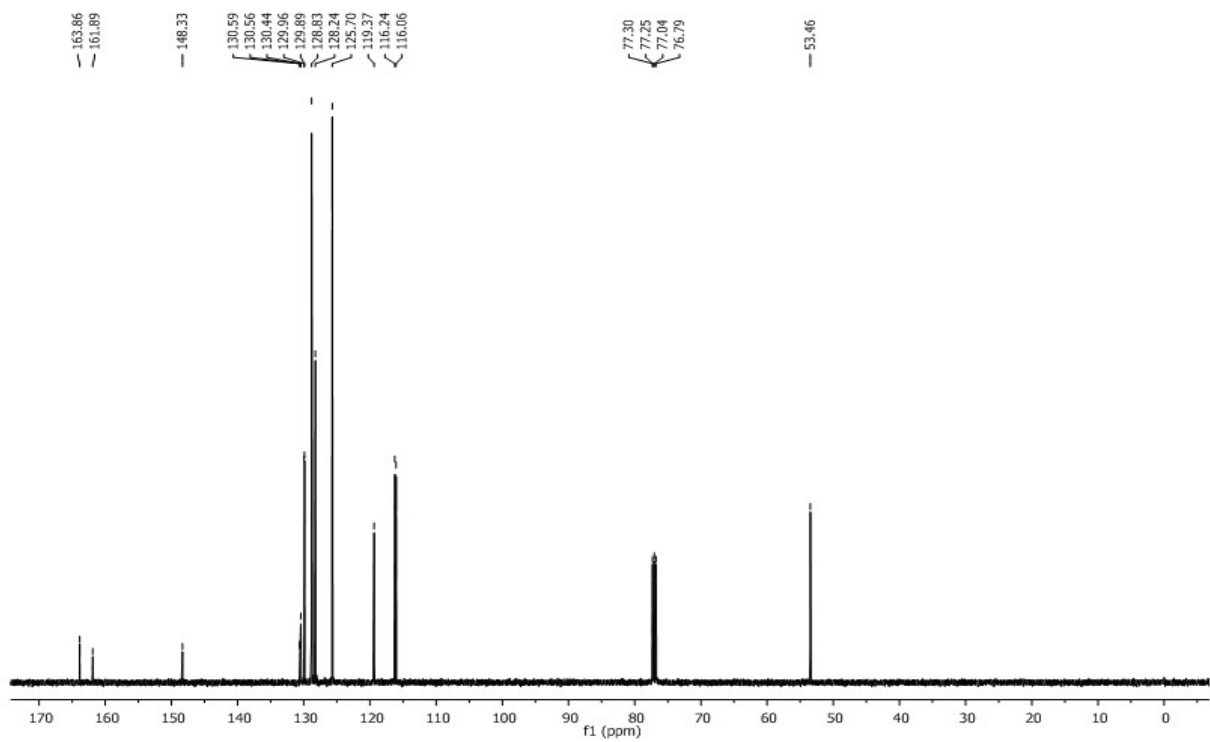
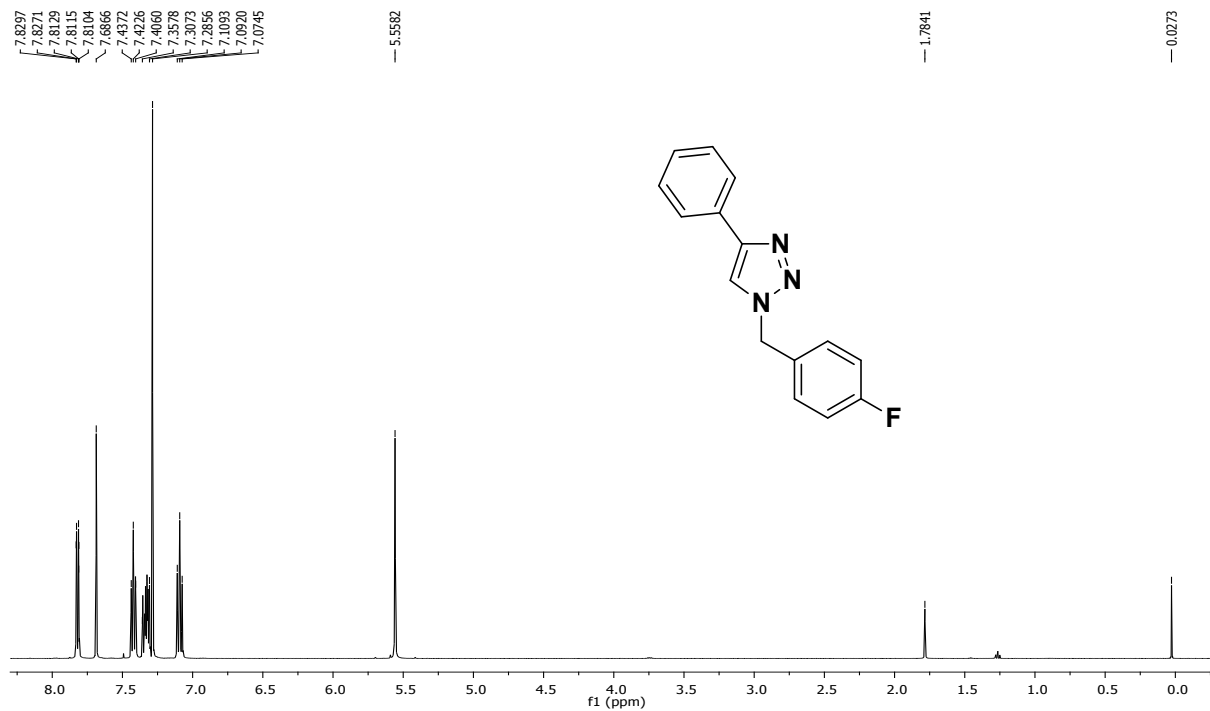
White solid, yield 90%, mp = 96-99°C, $[\alpha]_D^{25} = +35.42$ (c 0.1, CHCl₃).

NMR ¹H (500 MHz, CDCl₃): δ = 0.73 (s, 3H, CH₃), 0.81 (d, *J* = 6.5 Hz, 3H, CH₃), 0.90 (s, 3H, CH₃), 1.09-1.21 (m, 2H, CH₂), 1.24-1.47 (m, 4H, CH₂, CH), 1.53-1.70 (m, 6H, CH₂, CH), 1.72-1.87 (m, 5H, CH₂, CH), 1.90 (d, 3H, *J* = 1.2 Hz, CH₃), 1.95-2.08 (m, 2H, CH₂, CH), 2.10 (s, 3H, CH₃, acetyl), 2.11-2.13 (m, 2H, CH₂), 2.14 (s, 3H, CH₃, acetyl), 2.18-2.24 (m, 1H, CH₂), 2.32-2.38 (m, 1H, CH₂), 2.34 (ddd, *J* = 14.0, 10.0, 5.0 Hz, 1H, CH₂), 2.59 (td, *J* = 14.0, 4.0 Hz, 1H, CH₂), 3.66 (s, 3H, OCH₃), 4.60 (m, 1H, CH), 4.94 (s, 2H, CH), 4.95 (m, 1H, CH), 5.10 (dd, *J* = 2.3, 2.3 Hz, 1H, CH), 7.35 (q, *J* = 1.2 Hz, 1H, =CH), 7.69 (s, 1H, ArH, triazole), 8.58 (brs, 1H, NH). NMR ¹³C (CDCl₃, 125.7 MHz): δ = 12.2 (CH₃), 12.3 (CH₃, thymine), 17.5 (CH₃), 21.4 (CH₃, acetyl), 21.6 (CH₃, acetyl), 22.8 (CH₃, CH₂), 24.7 (CH₂), 25.7 (CH₂), 27.2 (CH₂), 29.0 (CH), 30.3 (CH₂), 30.77 (CH₂), 30.81 (CH₂), 30.9 (CH₂), 31.9 (CH₂), 34.5 (C), 34.6 (CH), 36.2 (CH), 37.7 (CH), 42.8 (C), 43.3 (CH), 45.1 (C), 47.4 (CH), 51.5 (OCH₃), 56.7 (CH), 70.8 (CH), 75.4 (CH), 111.1 (=C), 122.6 (ArCH, triazole), 140.2 (=CH), 141.6 (C_{ipso}, triazole), 150.7 (NC=ON), 163.8 (NC=O), 170.1 (OC=O, acetyl), 170.4 (OC=O, acetyl), 174.5 (OC=O). FT-IR/ATR ν_{max} cm⁻¹: 4920, 2926, 1682, 1446, 1375, 1242, 1025. HRMS (ESI-TOF) calculated for C₃₇H₅₃N₅O₈ + H⁺: 696.3967; Found: 696.3964.

4. ^1H and ^{13}C NMR spectra for 1,2,3 triazoles ^1H NMR and ^{13}C NMR for compound 3a

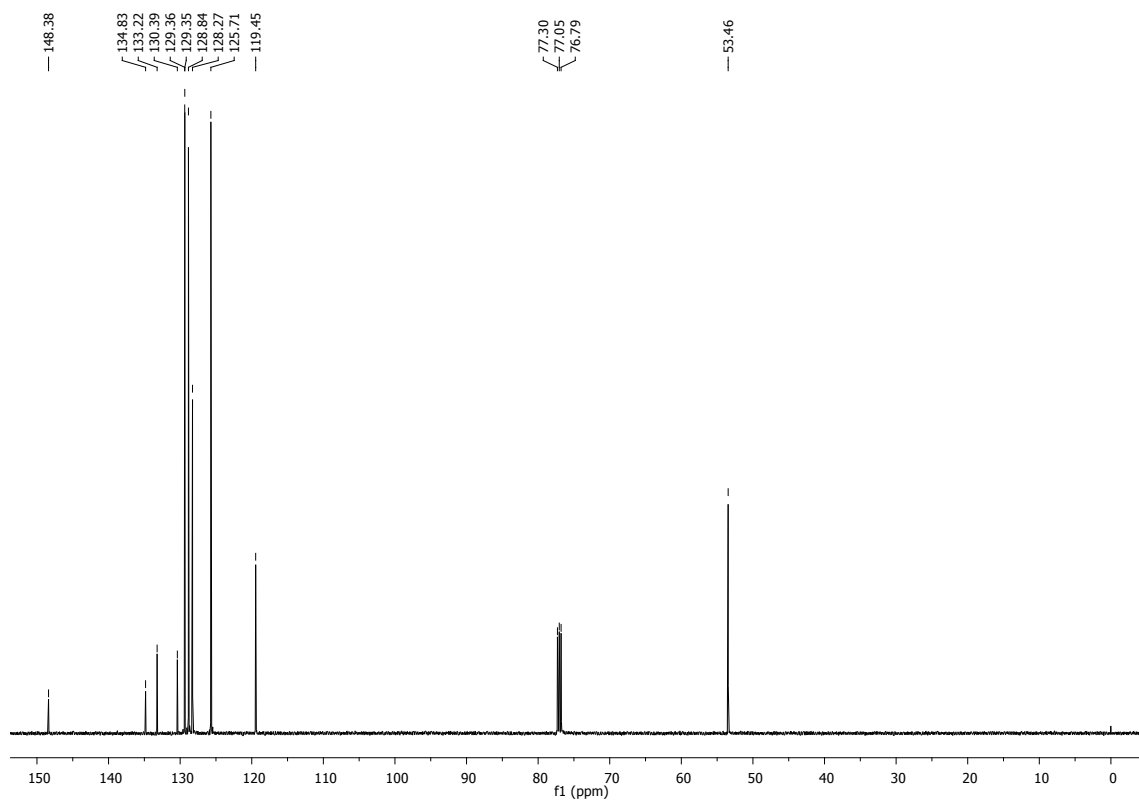
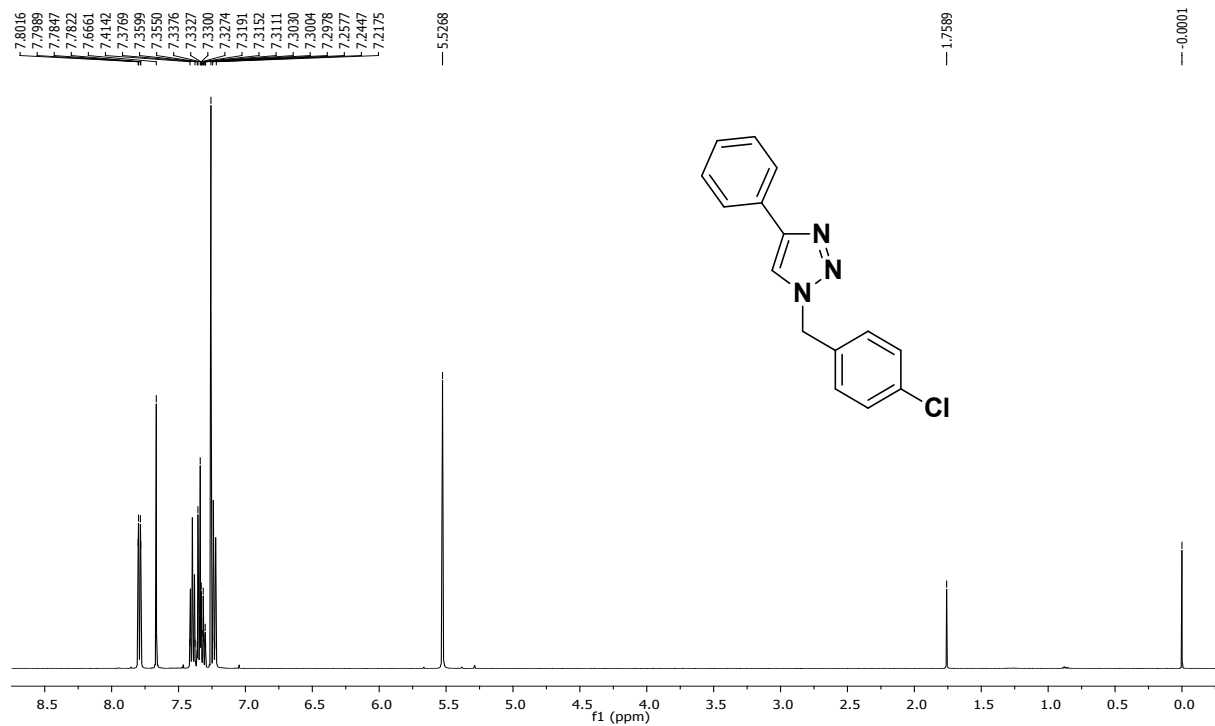
Supporting Information

^1H NMR and ^{13}C NMR for compound 3b



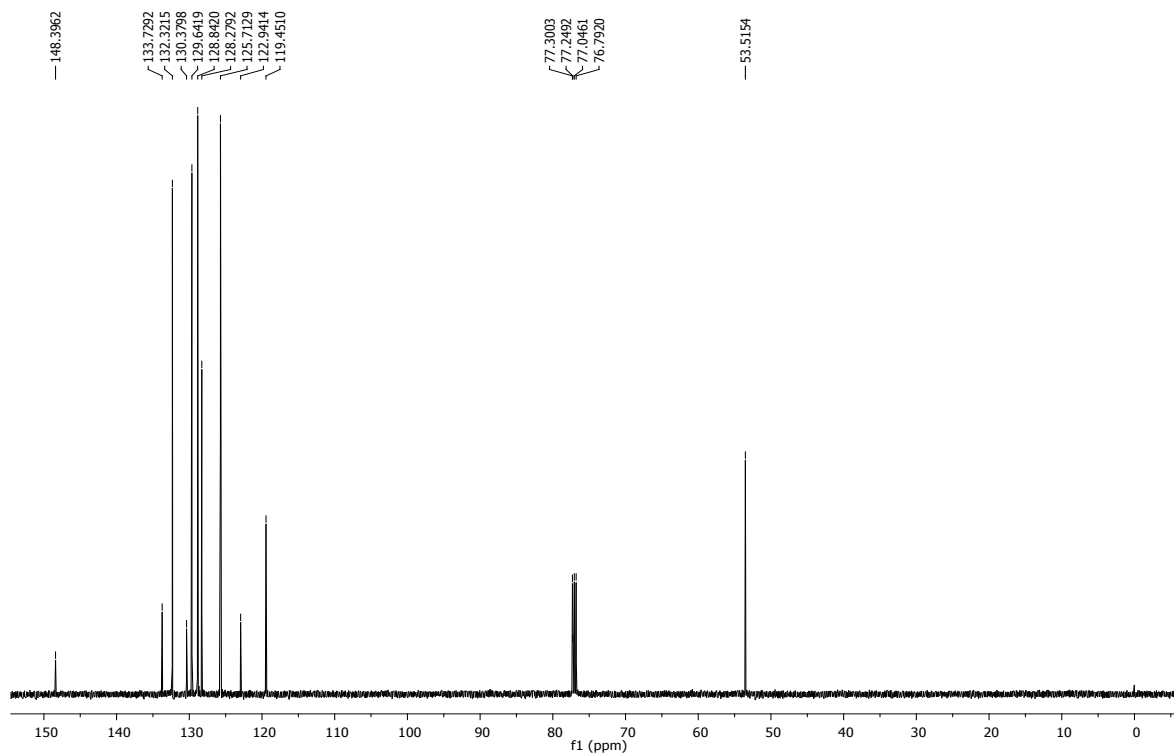
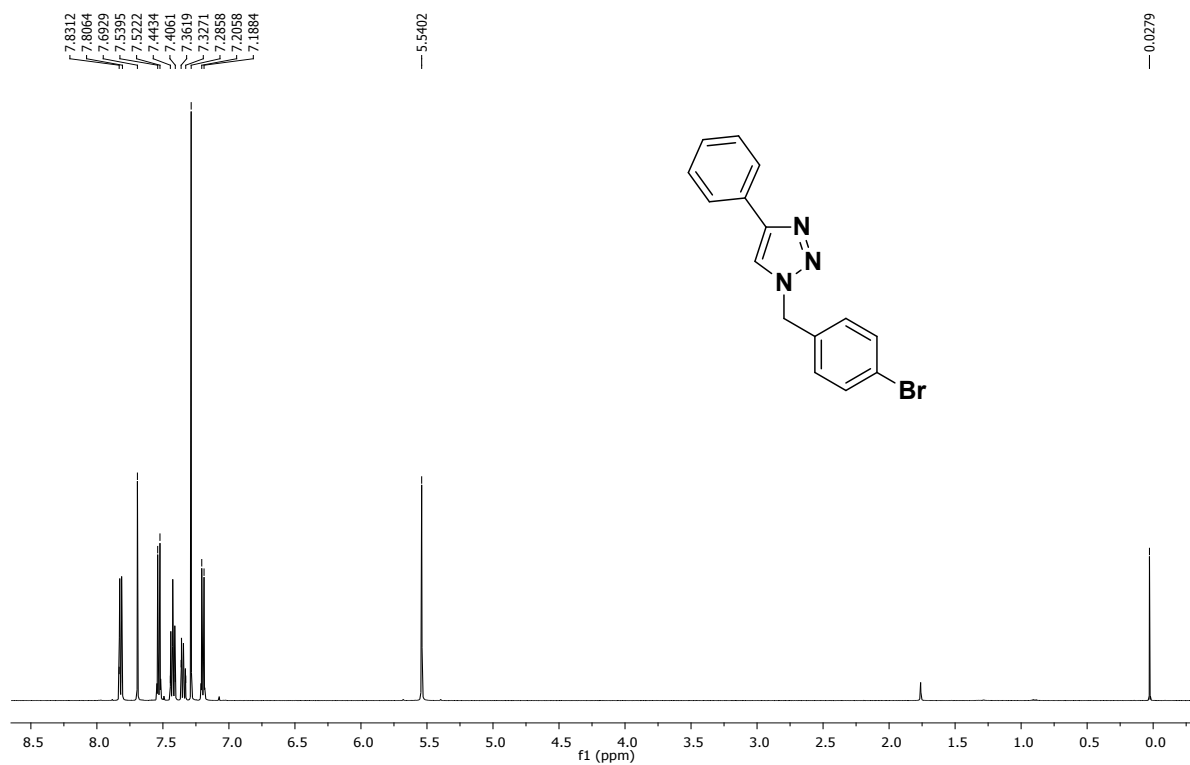
Supporting Information

^1H NMR and ^{13}C NMR for compound 3c



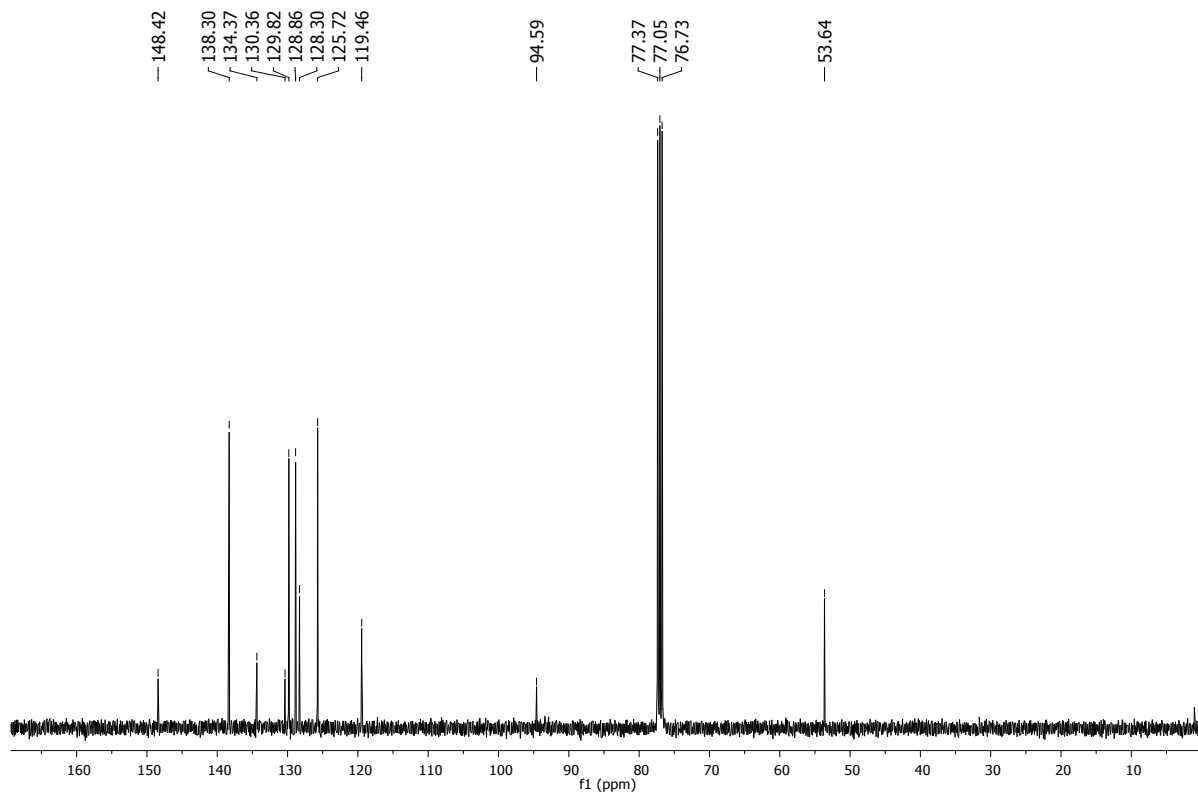
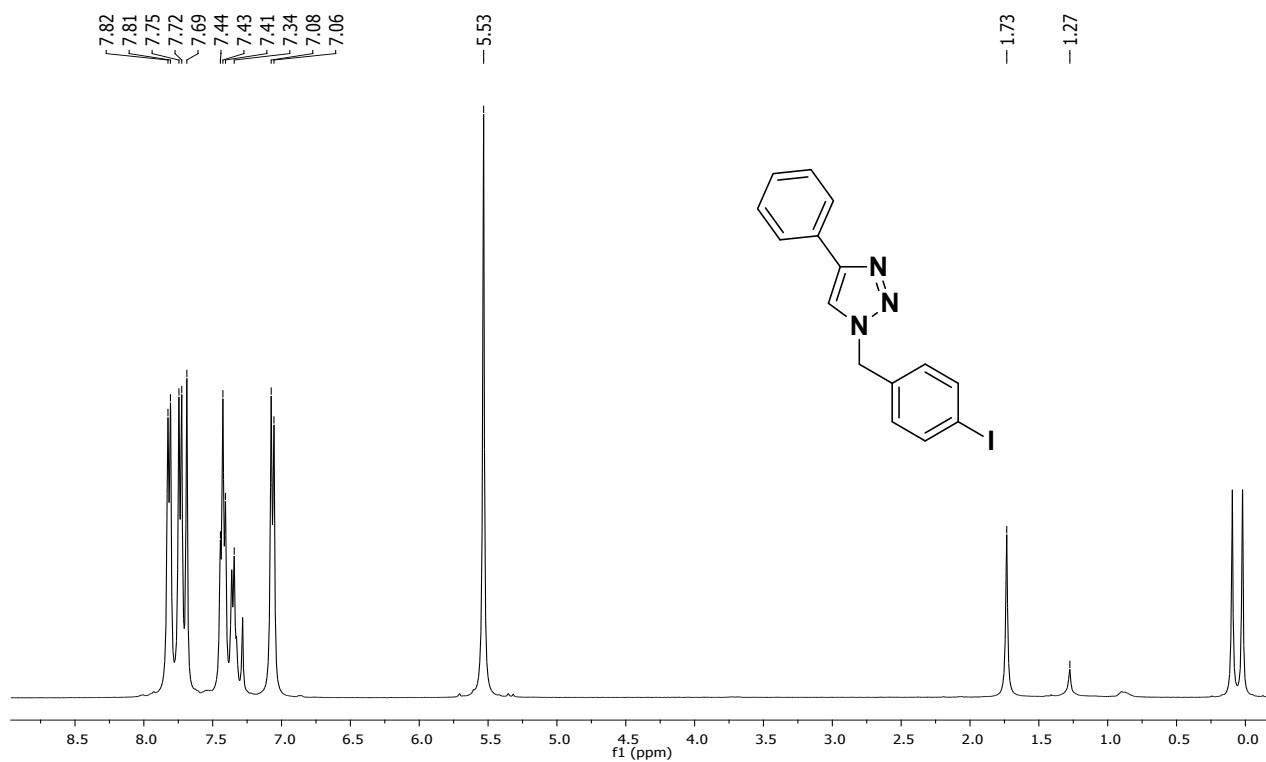
Supporting Information

^1H NMR and ^{13}C NMR for compound 3d



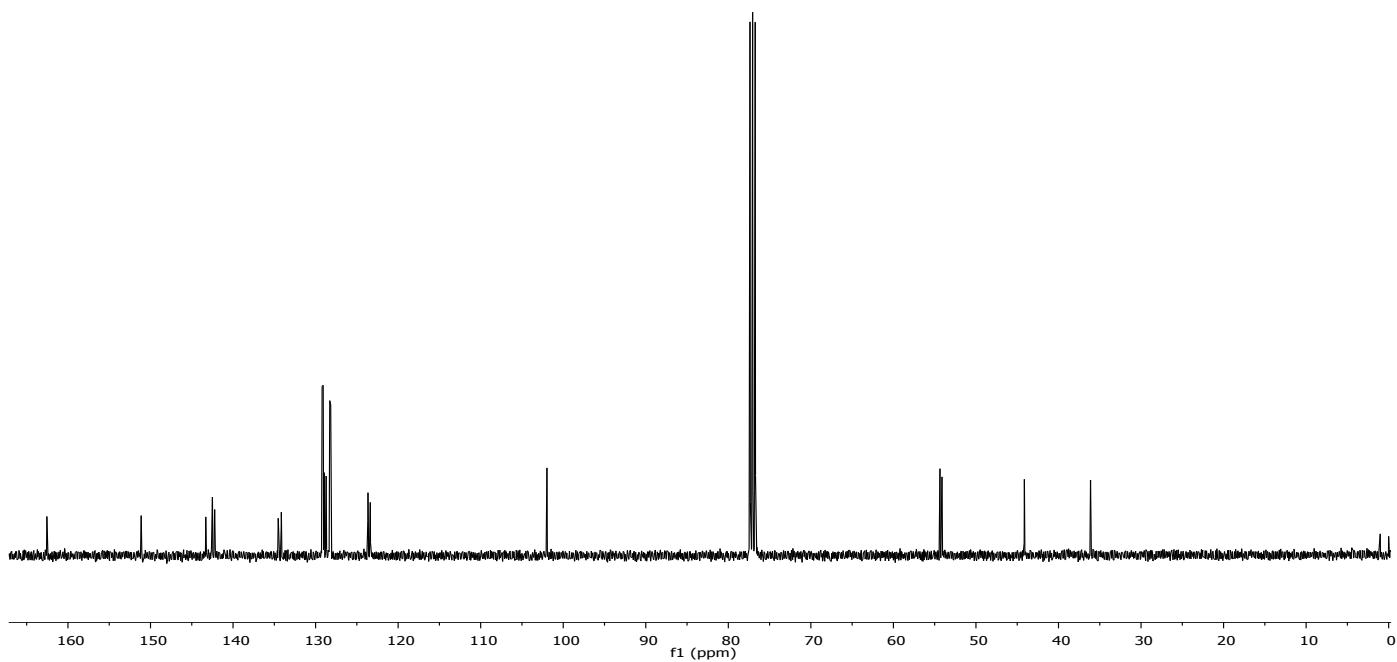
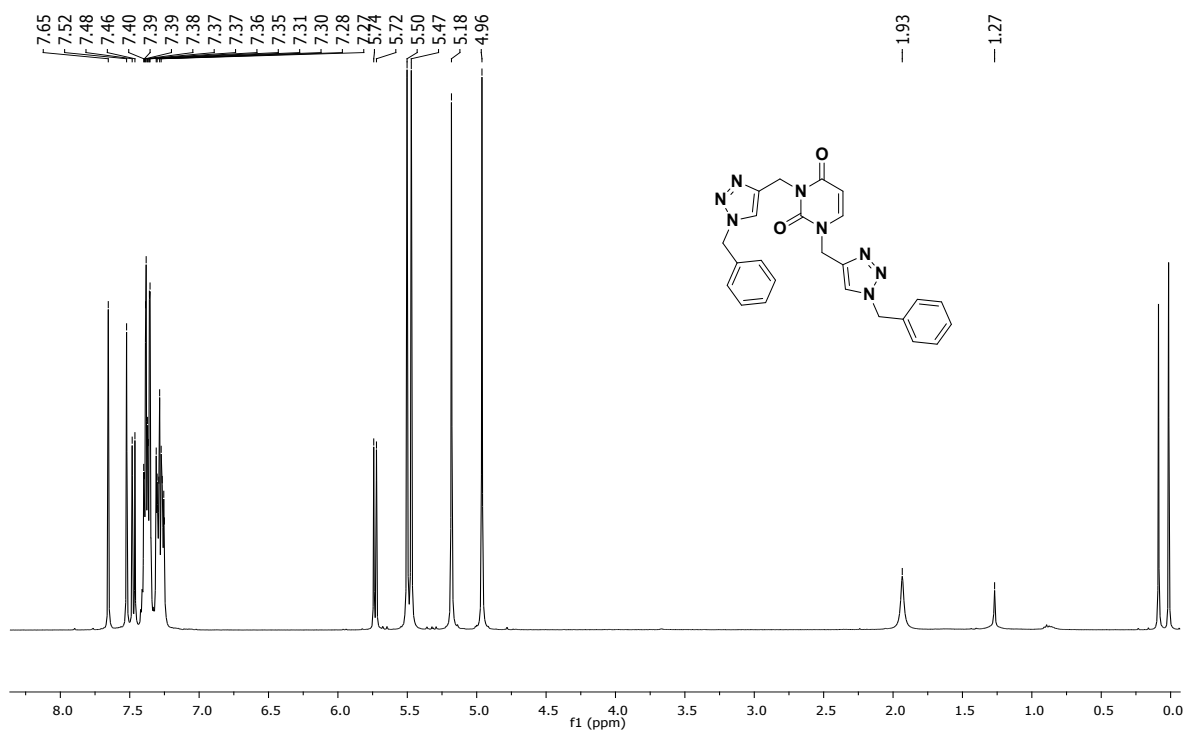
Supporting Information

^1H NMR and ^{13}C NMR for compound 3e



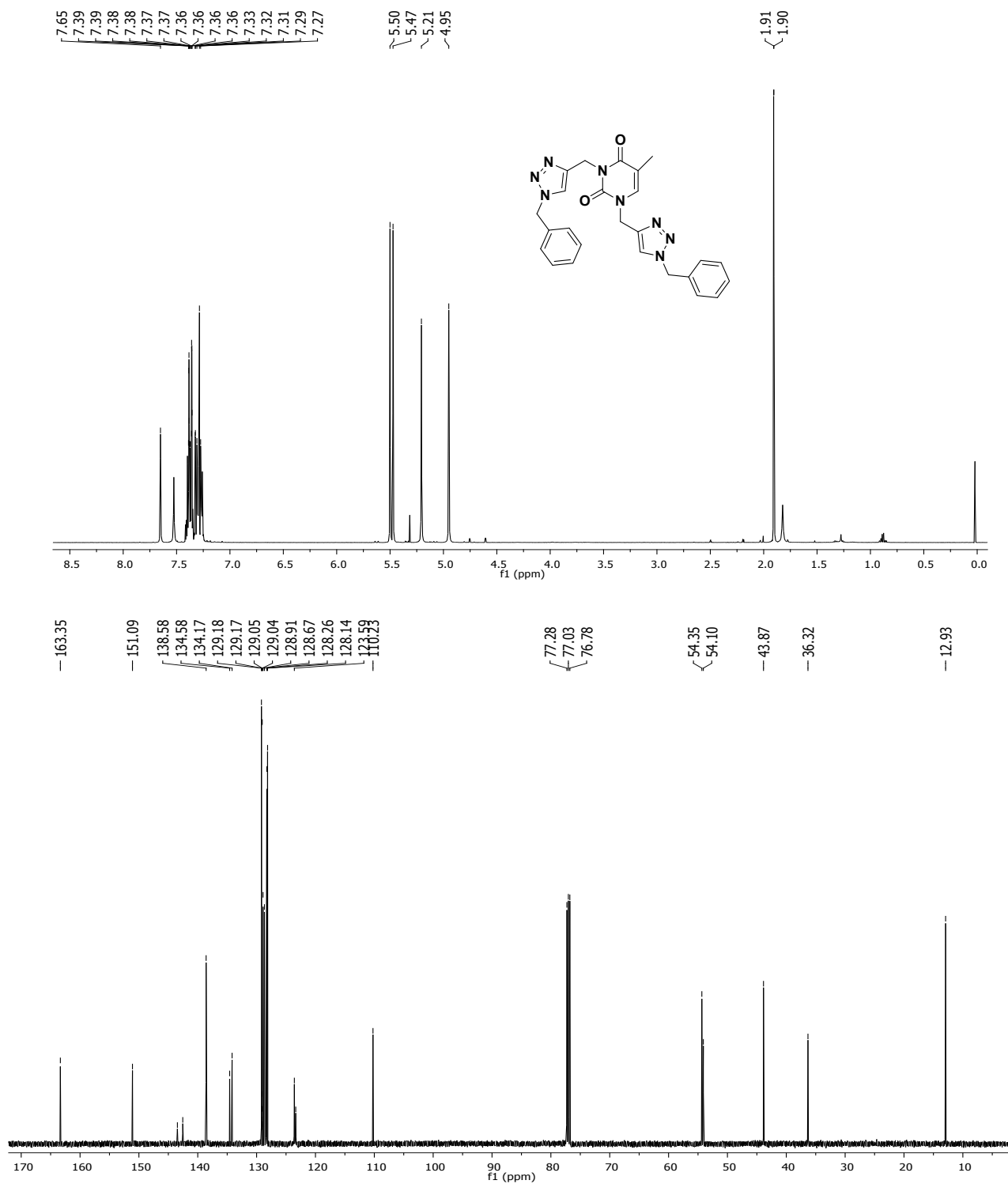
Supporting Information

^1H NMR and ^{13}C NMR for compound 3f



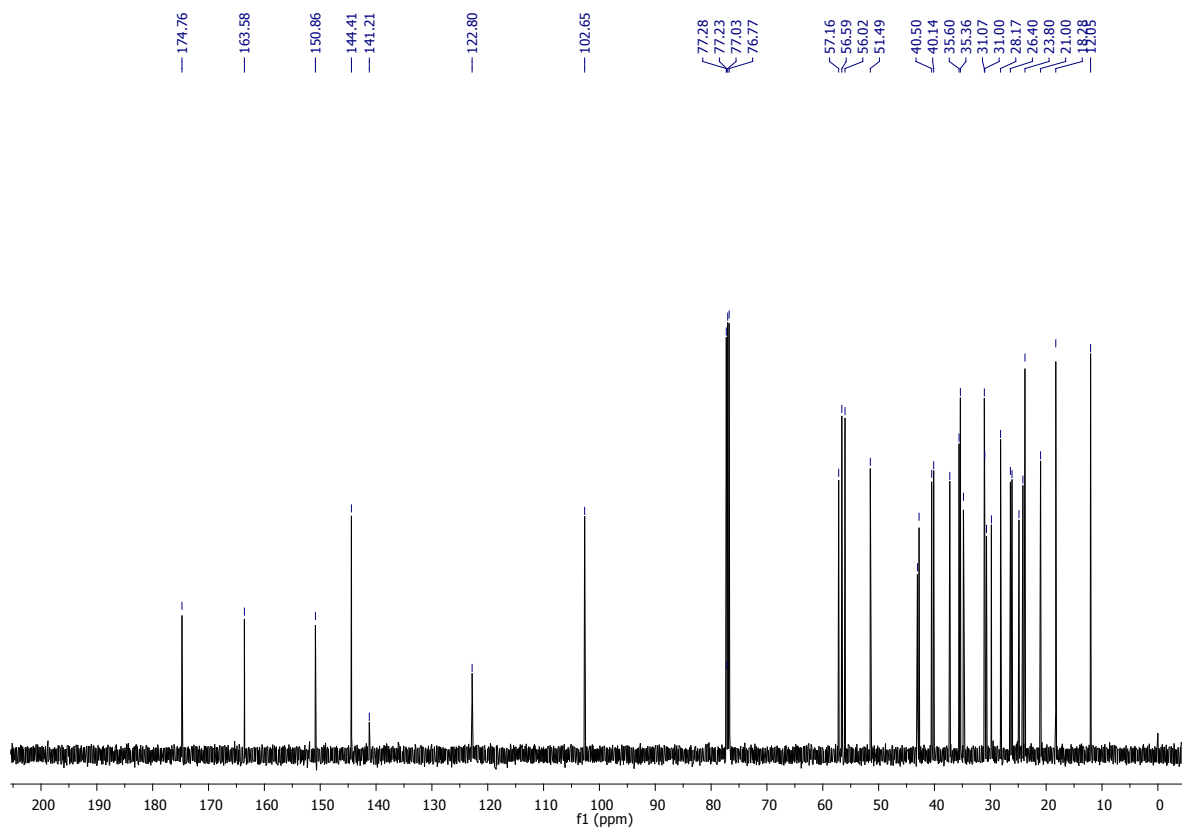
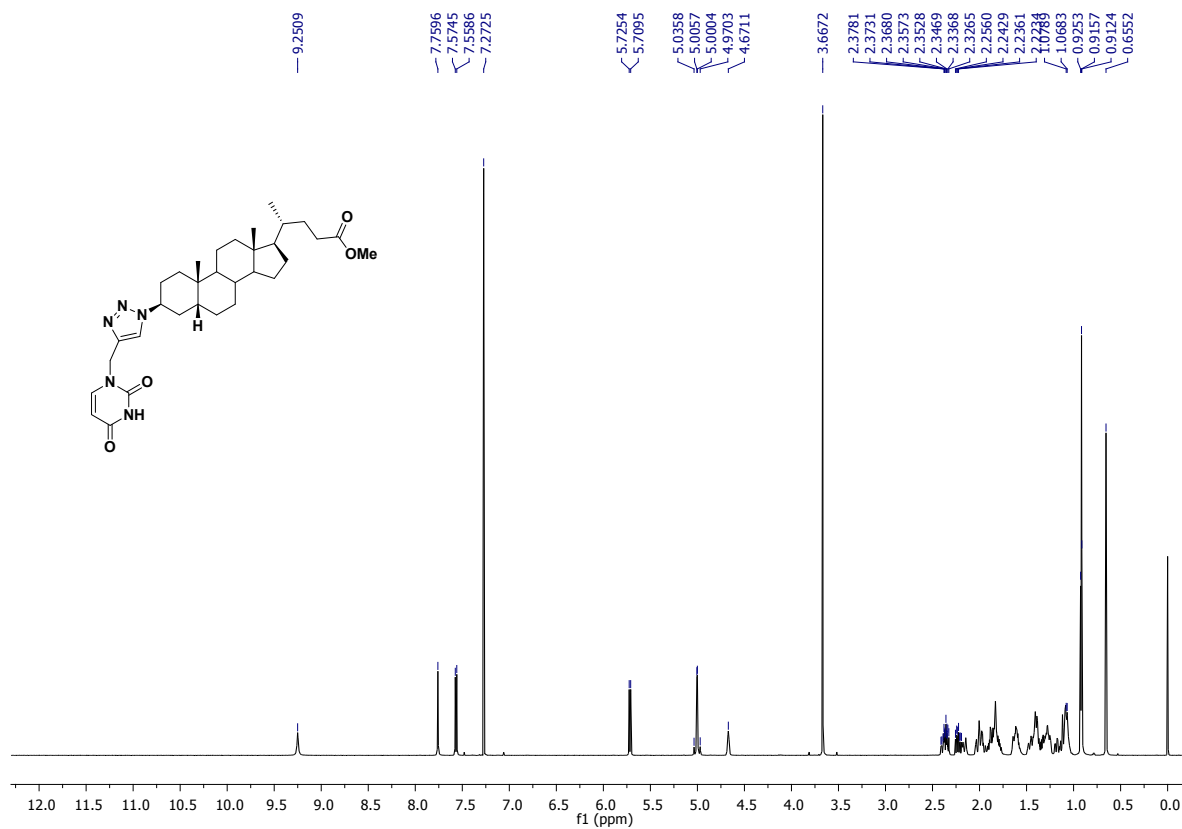
Supporting Information

¹H NMR and ¹³C NMR for compound 3g



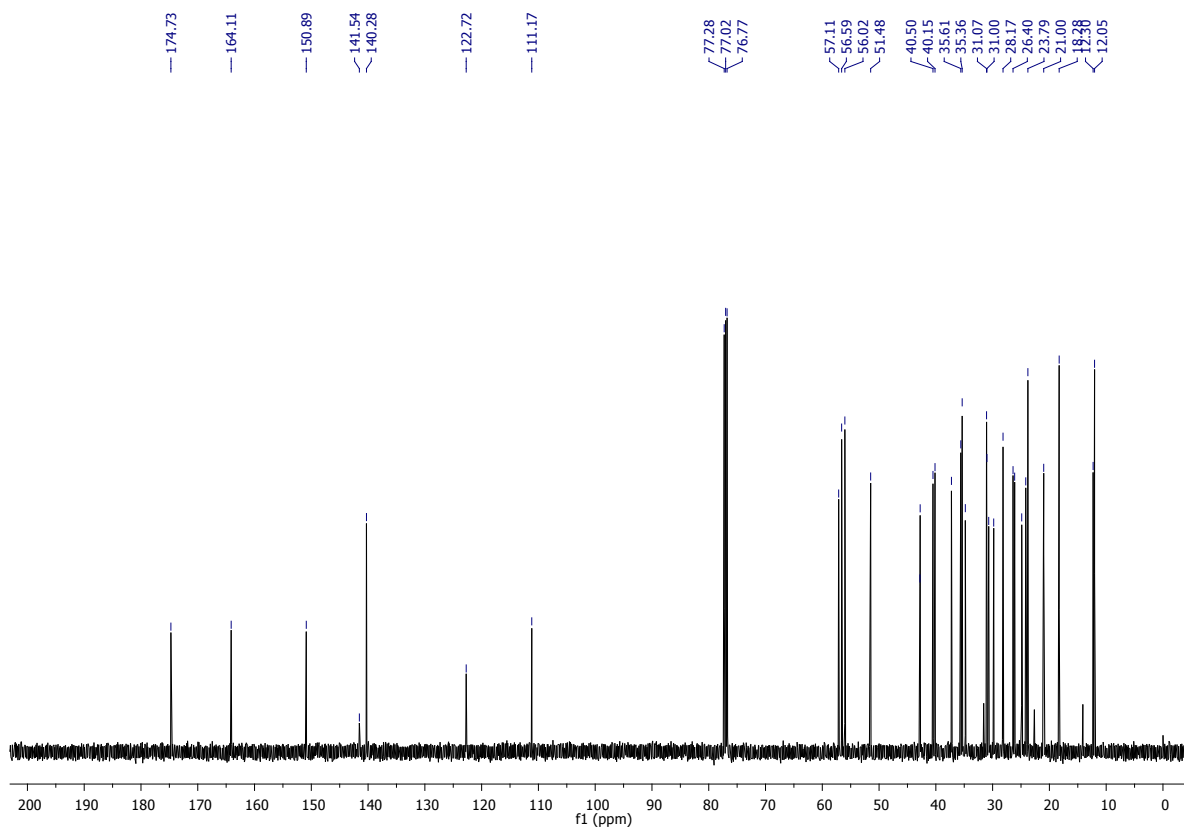
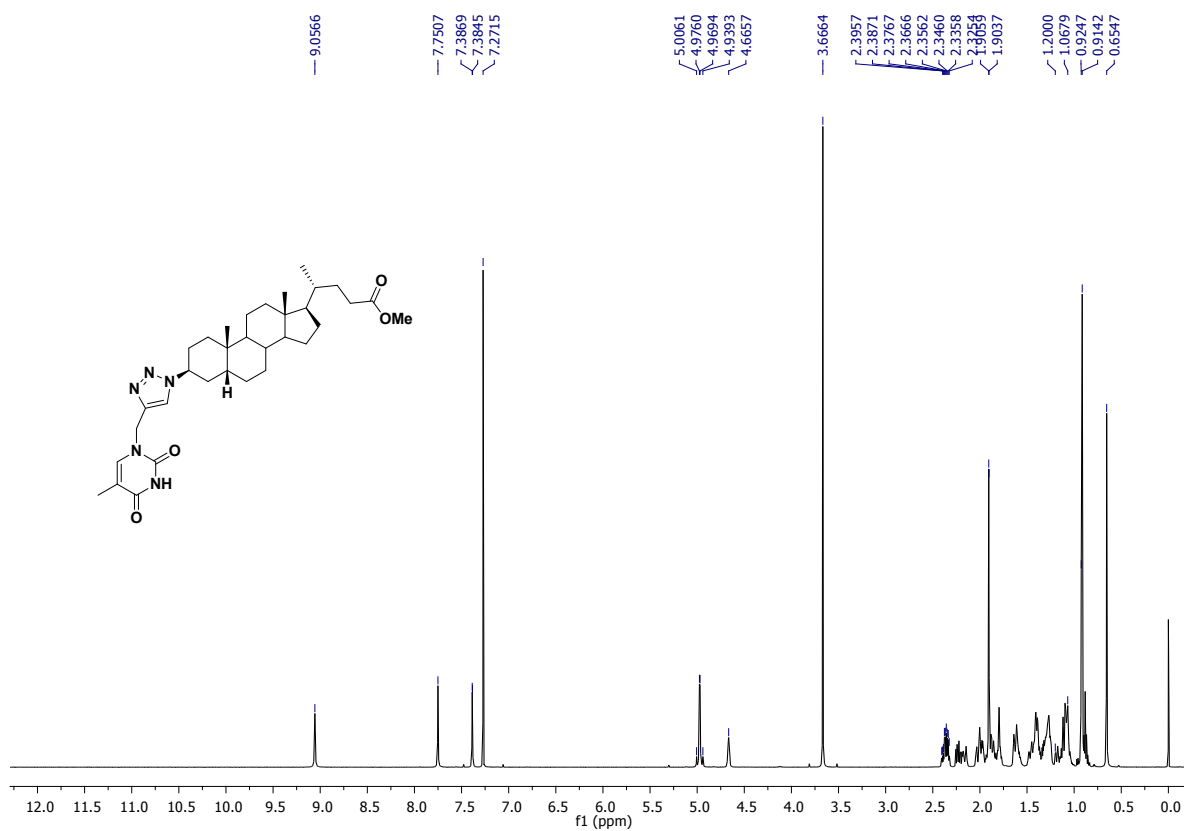
Supporting Information

¹H NMR and ¹³C NMR for compound 5a



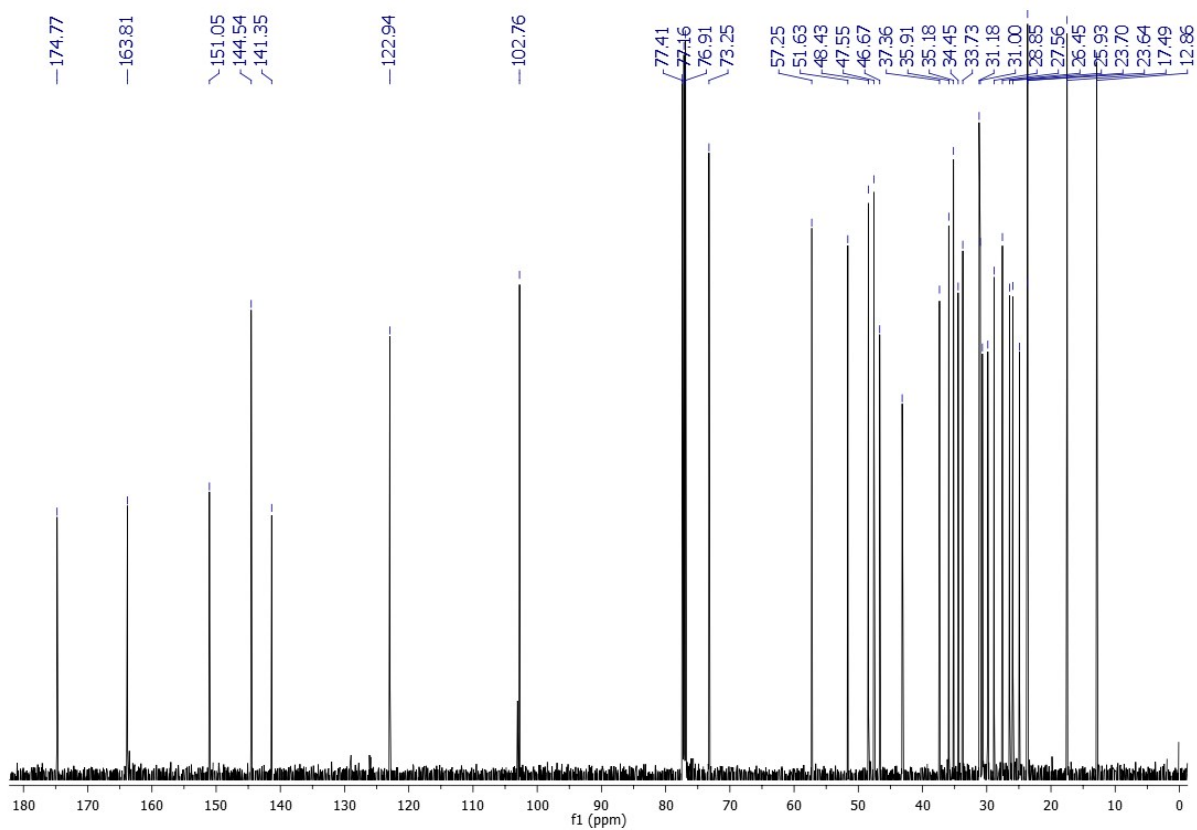
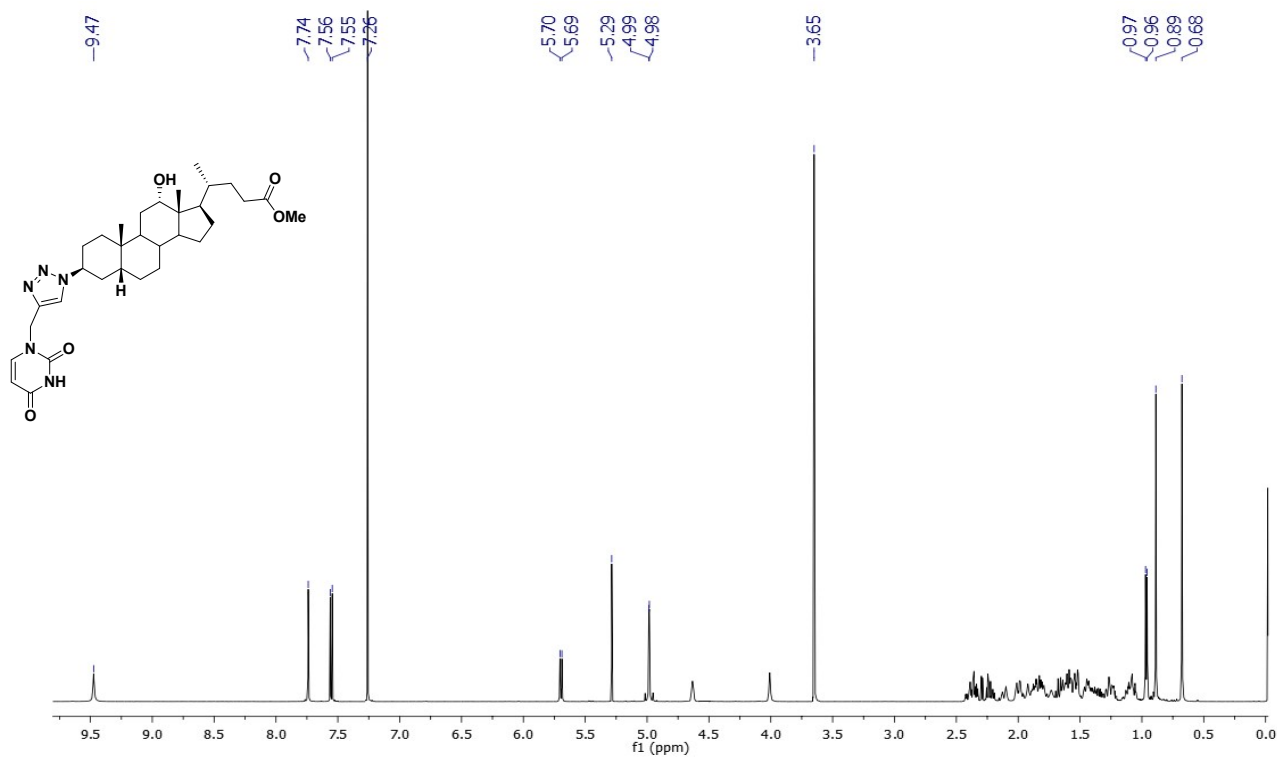
Supporting Information

¹H NMR and ¹³C NMR for compound 5b



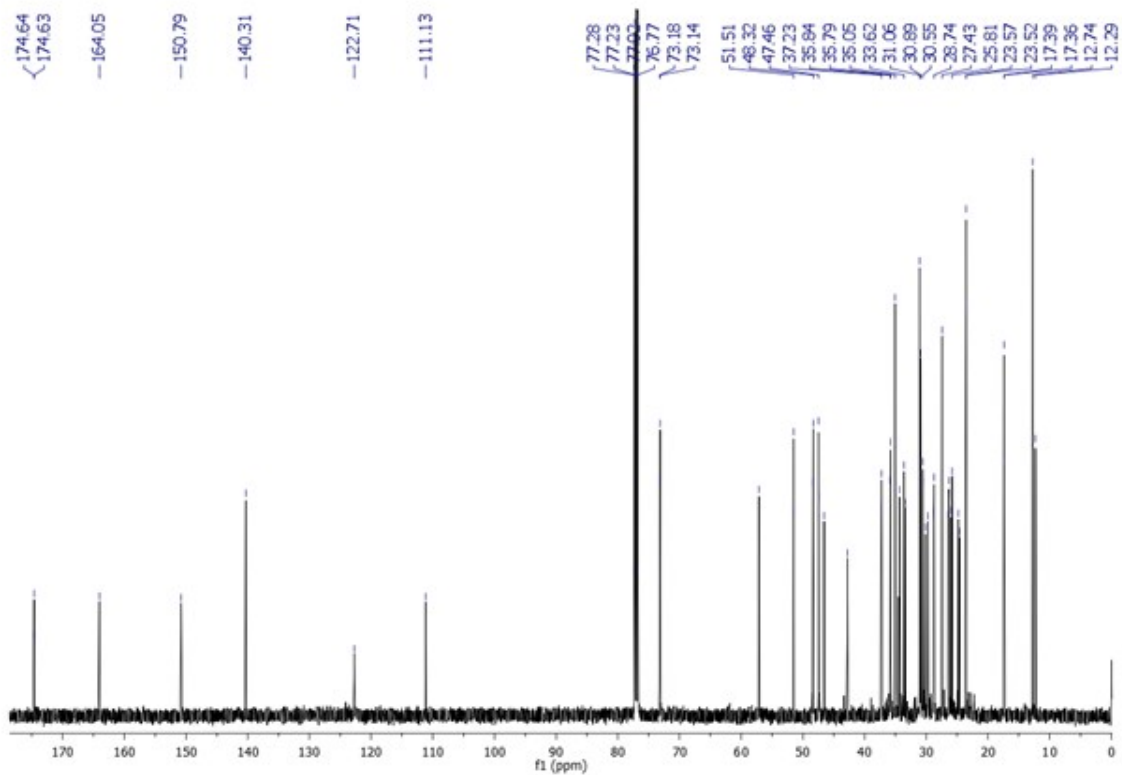
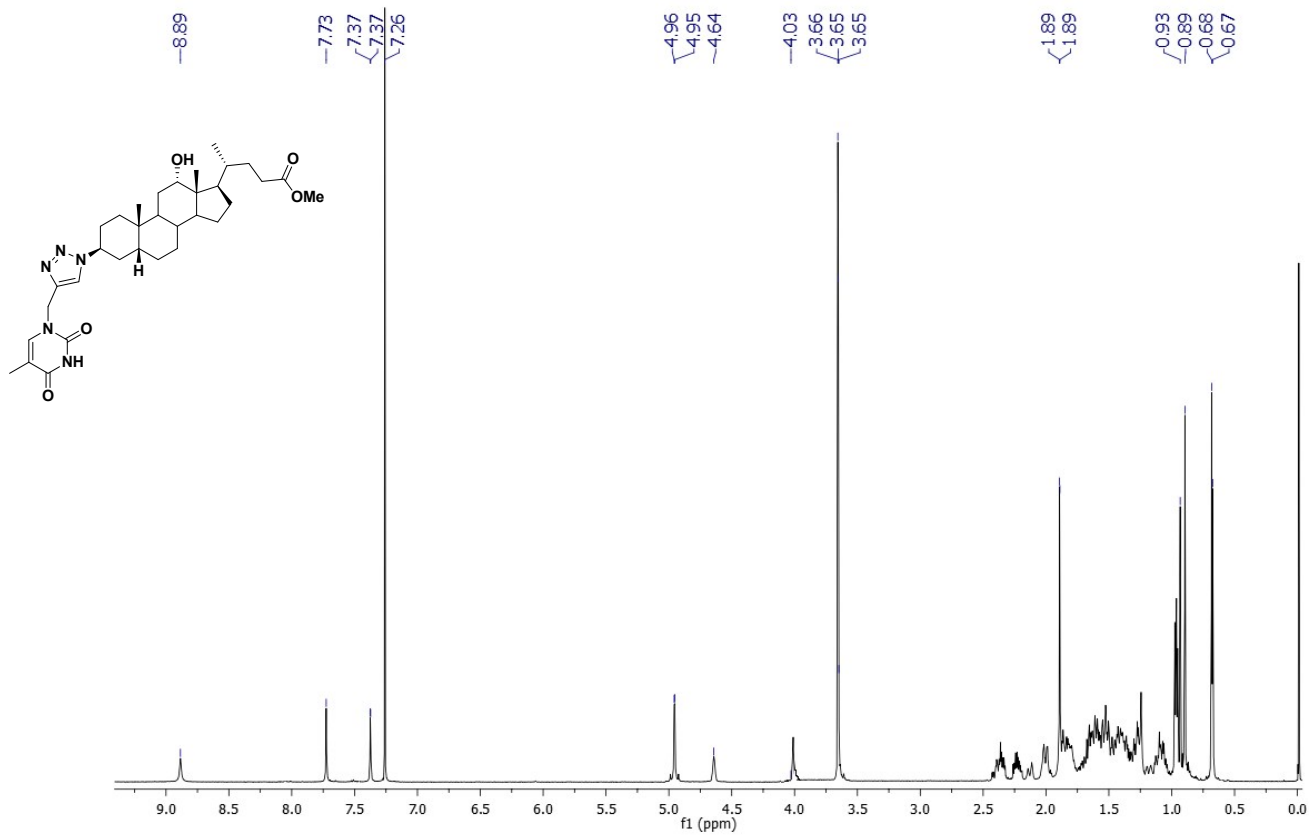
Supporting Information

¹H NMR and ¹³C NMR for compound 5c



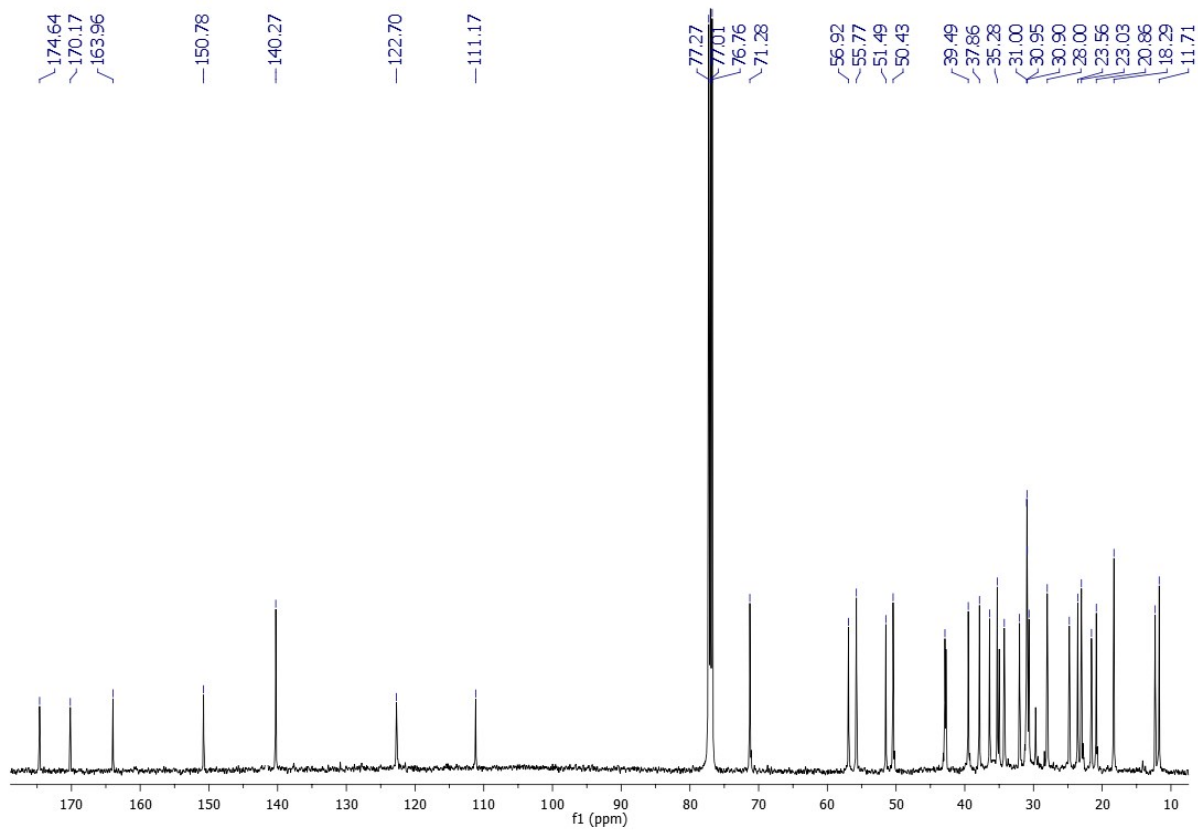
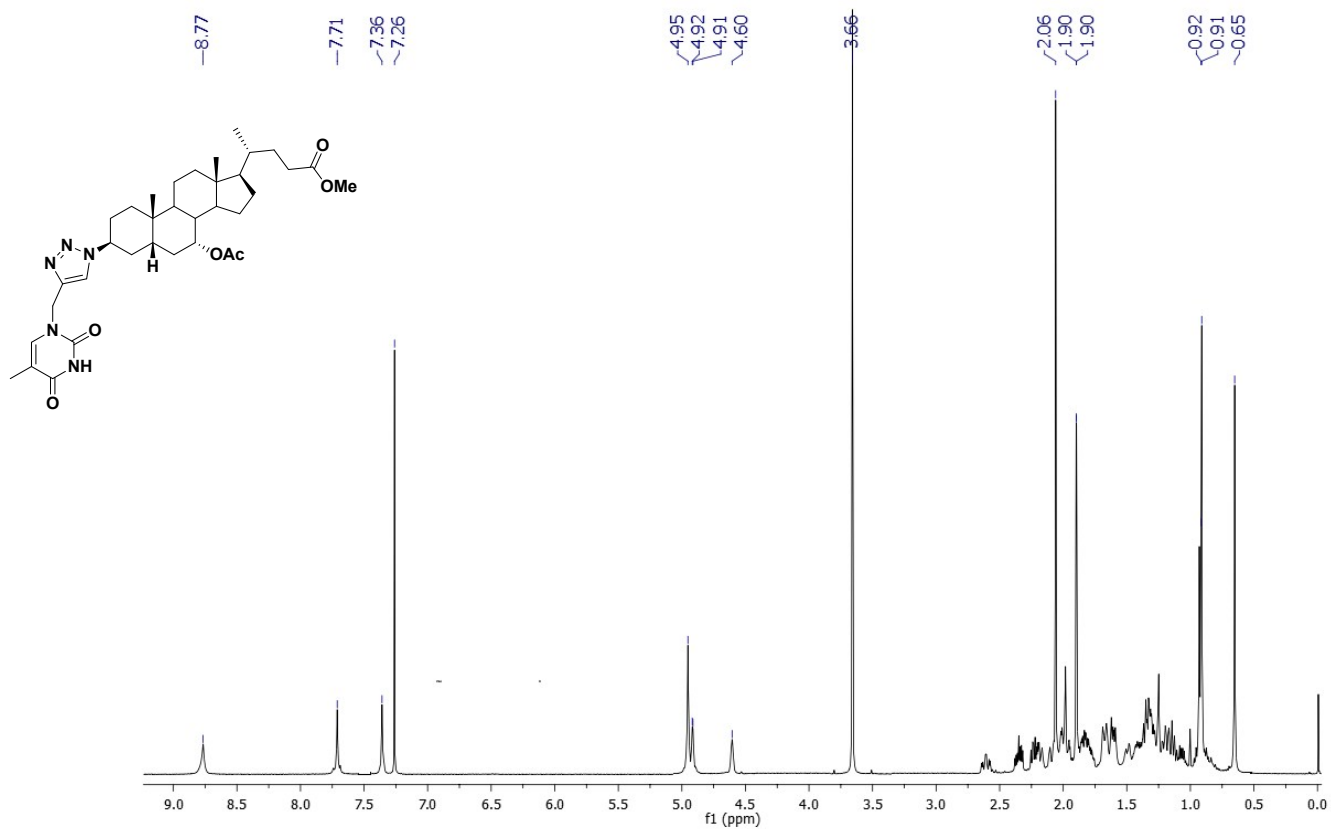
Supporting Information

¹H NMR and ¹³C NMR for compound 5d



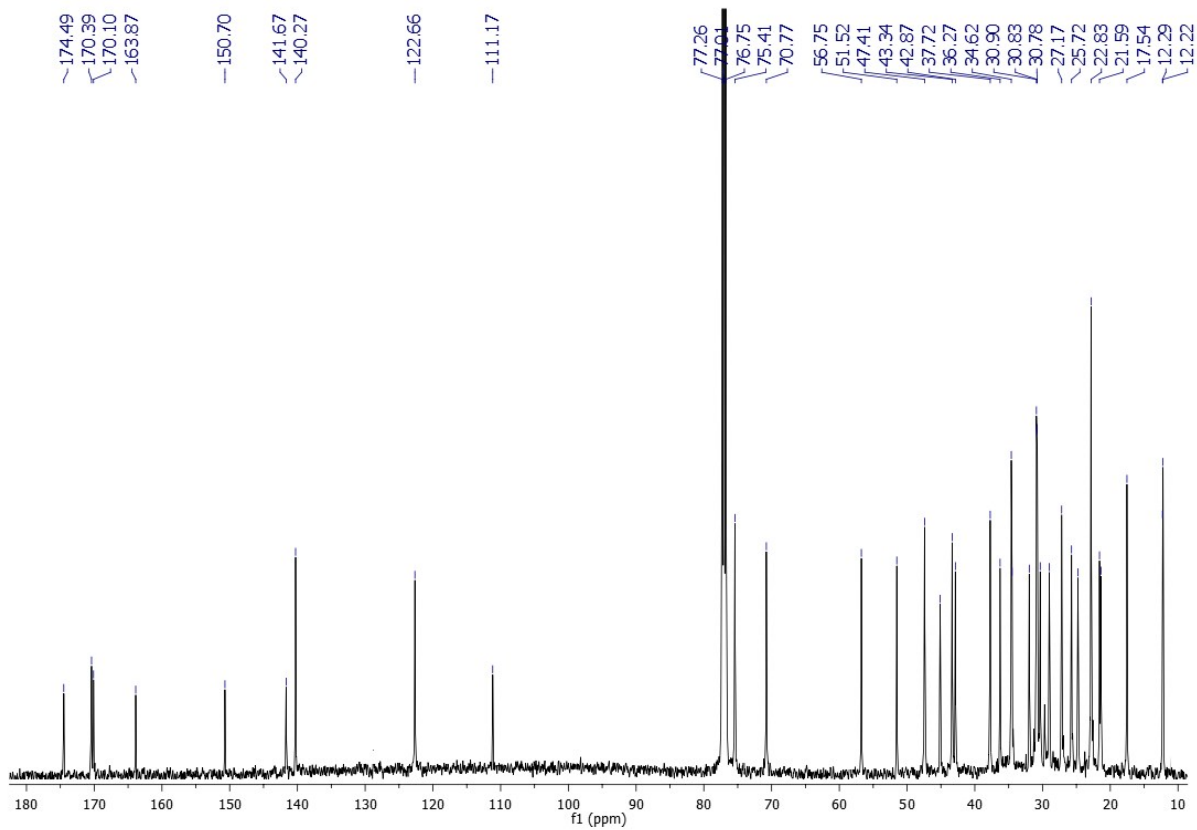
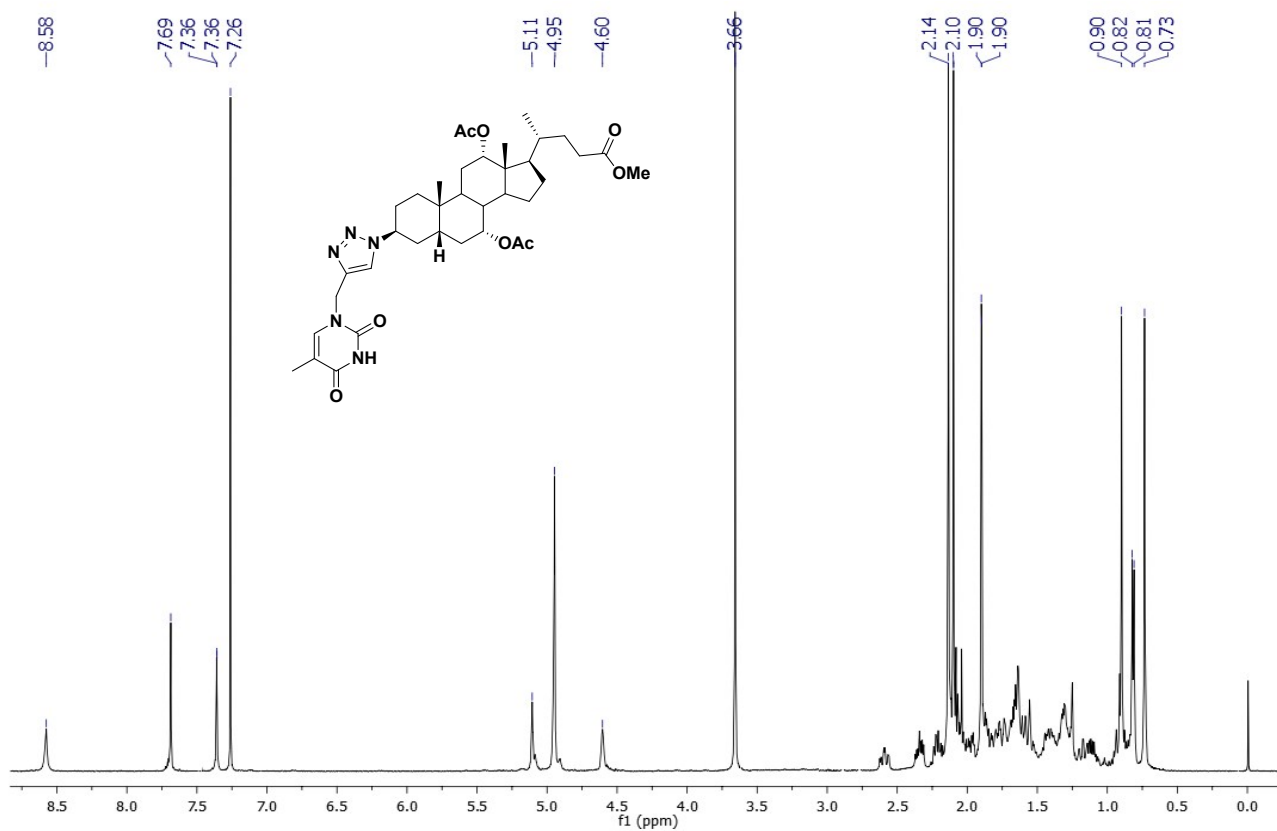
Supporting Information

¹H NMR and ¹³C NMR for compound 5e



Supporting Information

¹H NMR and ¹³C NMR for compound 5f



5. References

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